

T.K. Lim

Edible Medicinal and Non-Medicinal Plants

Volume 12,
Modified Stems, Roots, Bulbs

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Introduction

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This book continues as volume twelve of a multi-compendium on *Edible Medicinal and Non-Medicinal Plants*. It covers such plants with edible modified storage subterranean stems (corms, rhizomes, stem tubers) and unmodified subterranean stem stolons, above-ground swollen stems and hypocotyls, storage roots (tap root, lateral roots, root tubers) and bulbs that are eaten as conventional or functional food as vegetables and spices, as herbal teas, and may provide a source of food additive or nutraceuticals. A list of such edible plant species from families Acanthaceae to Zygophyllaceae are presented in a tabular form and 32 such edible species from the families Alismataceae, Amaryllidaceae, Apiaceae, Araceae, Araliaceae, Asparagaceae, Asteraceae, Basellaceae, Brassicaceae and Campanulaceae had been covered in detail in preceding volume nine. Nineteen edible species from the families Amaranthaceae, Cannaceae, Ciboitiaceae, Convolvulaceae, Cyperaceae, Dioscoreaceae, Euphorbiaceae and Fabaceae had been covered in detail in volume ten and eighteen edible species in the families Iridaceae, Lamiaceae, Marantaceae, Nelumbonaceae, Nyctaginaceae, Nymphaeaceae, Orchidaceae, Oxalidaceae, Piperaceae, Poaceae, Rubiaceae and Simaroubaceae in volume eleven. This present volume twelve covers in detail 21 edible species from the families Solanaceae (1), Tropaeolaceae (1), Typhaceae (2) and Zingiberaceae (17). Other species from these families with edible modified stems, roots and bulbs are listed in Table 1. Many plants with such

edible plant parts that are better known for their edible fruits or flowers have been covered in earlier volumes and for those better known for other non-reproductive plant parts will be covered in latter volumes.

Table 1 Plants with edible modified stems, roots and bulbs in the families: Solanaceae, Tropaeolaceae, Typhaceae and Zingiberaceae

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Solanaceae	<i>Hyoscyamus vulgaris</i> Neck	NF	In France, starch of root recommended as famine food for extending bread flour, after removal of bitter element	Parmentier (1781) (Cited by Freedman (2009))
Solanaceae	<i>Jaltomata procumbens</i> (Cav.) J.L.Gentry	Creeping False Holly, Jaltomate	Roots eaten raw or boiled	Altschul (1973), Facciola (1990)
Solanaceae	<i>Solanum ajanhuiri</i> Juz. & Bukasov	Ajanhuri	Root tuber edible	Codex (2014)
Solanaceae	<i>Solanum berthaultii</i> Hawkes	Wild Potato	Tubers used like the cultivated potato	Gupta and Kanodia (1968)
Solanaceae	<i>Solanum candolleanum</i> Berthault	Gentil Achochil Chocke	Tubers used like the cultivated potato	Gupta and Kanodia (1968)
Solanaceae	<i>Solanum curtilobum</i> Juz. & Bukasov	Ckaisallabitter Potatoes	Root tuber edible	Arbizu and Tapia (1994)
Solanaceae	<i>Solanum demissum</i> Lindl.	Papa Cimarrona, Papa Del Monte	Tubers cooked and eaten	Facciola (1990)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Solanaceae	<i>Solanum fendleri</i> A.Gray	Fendler Potato, Wild Potato	In southwestern United States, root tuber eaten raw or boiled with clay, by Native American Keresan Pueblo groups	Yanovsky (1936), White (1944), Hedrick (1972), Gibbons and Tucker (1979), and Facciola (1990)
Solanaceae	<i>Solanum jamesii</i> Torr.	Colorado Wild Potato	In southwestern United States, tuber eaten raw or boiled with clay, by Native American Keresan Pueblo group and also eaten by Navajo Indians. Tubers also baked or ground into flour	Saunders (1920), Yanovsky (1936), White (1944), Harrington (1974), and Facciola (1990)
Solanaceae	<i>Solanum paucijugum</i> Bitter	Sacha Pappa	Root tuber edible	Facciola (1990)
Solanaceae	<i>Solanum tuberosum boreale</i> Gray	Wild Potato	Root tubers are quite edible when cooked and eaten by Navajo and other Indians	Saunders (1920)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Solanaceae	<i>Solanum tuberosum</i> L.	Potato, Irish Potato	Russet or baking potato best for roasting, frying or baking; all-purpose potatoes used for soups, stews and mashing, red and newer cultivars best for boiling, creaming and in cold salads	Facciola (1990), Phillips and Rix (1993), Wagih and Wiersema (1996), Hu (2005), van Wyk (2006), and Santich et al. (2008)
Solanaceae	<i>Solanum tuberosum</i> L. subsp. <i>andigenum</i> (Juz. & Bukasov) Hawkes	Andigena	Root tuber edible	Codex (2014)
Solanaceae	<i>Solanum verrucosum</i> Schltdl.	Papa Morda	Root tuber edible	Facciola (1990)
Solanaceae	<i>Solanum juzepczukii</i> Bukasov	Bitter Potatoes	Root tuber edible	Arbizu and Tapia (1994)
Tropaeolaceae	<i>Tropaeolum tuberosum</i> Ruiz & Pavon	Mashua, Tuberous Nasutium, Anu, Anyu	An ancient food crop from the Andes Tubers eaten boiled, eaten as vegetable or added to stews	Popenoe et al. (1989), Facciola (1990), Johns (1981), Groen et al. (1996), Flores et al. (2003), and Codex (2014)
Typhaceae	<i>Typha angustata</i> Bory & Chaub. = <i>Typha domingensis</i> Pers.	Narrow-Leaved Cumbungi, Bulrush; Googol Bon, Hati Ghah (Assamese)	Rhizome, young shoots and inflorescence are eaten	Patiri and Borah (2007)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Typhaceae	<i>Typha angustifolia</i> L.	Narrow-Leaf Cattail	Rootstock boiled eaten like potatoes	Facciola (1990)
Typhaceae	<i>Typha australis</i> K. Schum. & Thonn.	Bullrush, Cat's Tail	French Guinea: rhizomes eaten in times of famine.	Irvine (1952)
Typhaceae	<i>Typha capensis</i> (Rohrb.) N.E.Br	Cattail	Rhizome eaten	Fox et al. (1982), Kunkel (1984), and Facciola (1990)
Typhaceae	<i>Typha domingensis</i> Pers	Narrow-Leaved Cumbungi, Bulrush	Rhizomes used to extract flour	Tanaka (1976), Low (1989), Facciola (1990), and Harden (1993)
Typhaceae	<i>Typha latifolia</i> L.	Common Cat-Tail	In China, the root is peeled, sun-dried, ground into flour and made into cakes which are then steamed. It may make a useful mixture with ordinary flours, and be substituted for corn-starch in puddings	Read (1946), Saunders (1920), Schofield (2003), and Codex (2014)
Typhaceae	<i>Typha laxamannii</i> Lepech.	Scented Flag	Rhizome source of meal made into cakes	Hedrick (1972) and Facciola (1990)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Typhaceae	<i>Typha muelleri</i> Rohrb. = <i>Typha orientalis</i> C.Presl	Bullrush, Reed Mace, Yinbun	In Australia, roots eaten raw by the Brisbane tribe. Roots also roasted in a hollow in the ground and eaten hot	Irvine (1957)
Typhaceae	<i>Typha orientalis</i> C.Presl	Broad-Leaved Cumbungi, Bulrush	Roots edible	Low (1989) and Harden (1993)
Zingiberaceae	<i>Achasma loroglossum</i> (Gagnep) K. Larsen	Karphul, Gandh Tora (<u>Assamese</u>)	Aromatic rhizomes eaten fresh or with betelnut or as masticatory. Small bits are added in curries for flavour	Patiri and Borah (2007)
Zingiberaceae	<i>Alpinia calcarata</i> (Haw.) Roscoe	Indian Ginger, Snap Ginger	Rhizome used as galangal substitute	Seidemann (2005)
Zingiberaceae	<i>Alpinia caerulea</i> (R.Br.) Benth.	Australian Blue Ginger; Native Ginger	Young Rhizome eaten raw or cooked	Cribb and Cribb (1987), Facciola (1990), and Seidemann (2005)
Zingiberaceae	<i>Alpinia conchigera</i> Griff.	Lesser Alpinia, Mussel Galanagl; Lengkuas Ranting (<u>Malay</u>); Riềng Rừng (<u>Vietnamese</u>)	Rhizome used as food flavouring and flavouring of alcoholic drinks	Perry (1980), Wong et al. (2005), Seidemann (2005), and Faridah et al. (2010)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Zingiberaceae	<i>Alpinia galanga</i> (Linn.) Willd.	Galangal, Greater Galangal; Languas, Lenguas (<u>Indonesia</u> , <u>Malaysia</u>), Phrikgnak (<u>Assamese</u>); Riềng Nếp (<u>Vietnamese</u>)	Rhizomes used as spice fresh or cooked in everyday cooking, in curries and meat dishes. Essential oil extract from rhizome used to flavour liquers, ice cream, pasrt, etc. Rhizome eaten in Karbi, Assam India. In Indonesia, young rhizomes are sliced and used in side dishes as sayur or sambal and the juice is used in the preparation of <i>dengdeng</i>	Watt (1908), Ochse and van den Brink (1980), Scheffer and Jansen (1999), Seidemann (2005), van Wyk (2006), and Kar and Borthakur (2008)
Zingiberaceae	<i>Alpinia latilabris</i> Ridl.	Ry (<u>Vietnamese</u>)	Rhizome used as food flavouring. In Vietnam, bitter rhizome used as spice	Wong et al. (2005) and Tanaka and Nguyen (2007)
Zingiberaceae	<i>Alpinia malaccensis</i> (Burm.f.) Roscoe	Malacca Galangal; Riềng Malacca (<u>Vietnamese</u>)	Rhizome used as spice	Burkill (1966), Kashio and Johnson (2001), Seidemann (2005), and Sirat et al. (2011)
Zingiberaceae	<i>Alpinia nigra</i> (Gaertn) Burt.	Tora (<u>Assamese</u>); Tareng (<u>Mishing</u>), Tharai (<u>Bodo</u>)	Young shoots and rhizomes are eaten either raw or cooked	Patiri and Borah (2007)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Zingiberaceae	<i>Alpinia officinarum</i> Hance	Lesser Galangal, Smaller Galangal, Chinese Ginger; Riềng Thuoc (Vietnamese)	Rhizome used as spice for flavouring	Ly et al. (2003) and Seidemann (2005)
Zingiberaceae	<i>Alpinia zerumbet</i> (Pers.) B.L. Burtt & R.M. Sm.	Bright Ginger, Pink Porcelain Lily, Light Ginger; Riềng Đẹp, Riềng âm (Vietnamese)	Rhizome edible, used as spice for flavouring	Seidemann (2005)
Zingiberaceae	<i>Boesenbergia pandurata</i> (Roxb.) = <i>Boesenbergia rotunda</i> (L.) Mansfield	See below	As for <i>Boesenbergia rotunda</i>	Facciola (1990)
Zingiberaceae	<i>Boesenbergia rotunda</i> (L.) Mansfield	Chinese Keys, Temu Kunchi (Indonesia, Malaysia), Krachai (Thai)	Widely used as a spice in cooking traditional Malay, Indonesian, Laotian and Thai cuisine – mixed vegetable dishes, fish curries, soups and pickles. Aromatic rhizome used in <i>ulam</i> (raw vegetable salad) in Malaysia and in salads in Thailand	Ibrahim and Nugroho (1999), Saidin (2000), and van Wyk (2006)
Zingiberaceae	<i>Curcuma aeruginosa</i> Roxb.	Pink and Blue Ginger, Dark Blue Temu	Rhizome used as spice	Burkill (1966)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Zingiberaceae	<i>Curcuma amada</i> Roxb.	Tharmit Tharve Am Haladhi, Am-Ada (<u>Assamese</u>)	Rhizome eaten in Karbi, Assam. Rhizome is used to prepare salad or chutney or eaten raw. It is also used as medicinal for its zedoary content	Patiri and Borah (2007) and Kar and Borthakur (2008)
Zingiberaceae	<i>Curcuma angustifolia</i> Roxb.	Indian Arrowroot	Rhizome has edible starch	Ibrahim and Jansen (1996a)
Zingiberaceae	<i>Curcuma aromatica</i> Salisb.	Wild Turmeric, Yellow Zedoary	Rhizome used as spice, source of starch	Ibrahim and Jansen (1996a) and Hu (2005)
Zingiberaceae	<i>Curcuma australasica</i> Hook.f.	Native Ginger	Tuberous roots roasted and eaten by aborigines	Cribb and Cribb (1987)
Zingiberaceae	<i>Curcuma caulina</i> J. Graham = <i>Hitchenia caulina</i> (J. Graham) Baker.	Chavar	In India (Deccan), tuberous root eaten	Watt (1908)
Zingiberaceae	<i>Curcuma domestica</i> Valetton = <i>Curcuma longa</i> L.	Turmeric	Rhizome used as spice	Phillips and Rix (1993) and Hu (2005)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Zingiberaceae	<i>Curcuma longa</i> L	Turmeric, Kunyit, Temu Kunyit (<u>Malaysia</u>), Khamin (<u>Thai</u>)	Rhizome used as culinary spice in Asian dishes, curries. Ground turmeric used in food industry as colouring agent in processed sauces, curry pastes and sauces, turmeric oil and oleoresins similarly used. Roots eaten in Meghalaya	Burkill (1966), Morton (1976), Ochse and van den Brink (1980); Facciola (1990), Dahal and Idris (1999), Saidin (2000), Hu (2005), Sawian et al. (2007), and Walter and Lebot (2007)
Zingiberaceae	<i>Curcuma mangga</i> Valeton & Zijp	Mango Ginger; Temu Pauh, Temu Mangga (<u>Malaysia</u>); Khamin Khao (<u>Thai</u>)	Rhizome used as spice	Burkill (1966), Morton (1976), Ochse and van den Brink (1980), and Facciola (1990), Saidin (2000), and van den Burgh (1994)
Zingiberaceae	<i>Curcuma phaeocaulis</i> Valeton	E Zhu (<u>Chinese</u>)	Rhizome used as spice	Lu et al. (2013)
Zingiberaceae	<i>Curcuma pierreana</i> Gagnep.	NF	Rhizome highly aromatic, source of starch	Ibrahim and Jansen (1996a)
Zingiberaceae	<i>Curcuma pseudomontana</i> R. Grah.	Hill Turmeric	In India (Deccan), rhizomes eaten	Watt (1908)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Zingiberaceae	<i>Curcuma purpurascens</i> Blume	Temu Tis, Koneng Pinggang, Kunir Tinggang (<u>Indonesia</u>)	Rhizome edible	Ochse and van den Brink (1980)
Zingiberaceae	<i>Curcuma zanthorrhiza</i> Roxb.	Temu Lawak (<u>Malaysia</u>)	Rhizome used as spice or eaten raw	Burkill (1966), Ochse and van den Brink (1980), Facciola (1990), Jansen (1996), and Saidin (2000)
Zingiberaceae	<i>Curcuma zedoaria</i> (Christm.) Roscoe	Zedoary, Temu Kuning (<u>Malaysia</u>)	Rhizome used as spice, young rhizome added to salads	Burkill (1966) Morton (1976), Ochse and van den Brink (1980), Facciola (1990), Ibrahim and Jansen (1996 b), and Saidin (2000)
Zingiberaceae	<i>Hedychium coronarium</i> J.König	White Ginger Lily	Tubers eaten in India (Deccan)	Watt (1908) and Lim (2014)
Zingiberaceae	<i>Hornstedtia scottiana</i> (F.Muell.) K.Schum.	Jiddo, Scotts Ginger	Tuberous root eaten edible	Wikipedia (2014)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Zingiberaceae	<i>Kaempferia galanga</i> L.	Cekur, Kencur	Rhizome eaten as spice to flavour food	Burkill (1966), Ochse and van den Brink (1980), and Facciola (1990)
Zingiberaceae	<i>Kaempferia pandurata</i> Roxb. = <i>Boesenbergia rotunda</i> (L.) Mansf.	Kencur, Temu Putri, Kunir Putih, Ardong, Kunci Pepet	Rhizome eaten as spice to flavour food in Java	Ochse and van den Brink (1980)
Zingiberaceae	<i>Kaempferia rotunda</i> L.	Round-Rooted Galangal Kencur, Temu Putri, Kunir Putih, Ardong, Kunci Pepet	Rhizome eaten as spice to flavour food in Java	Burkill (1966), Ochse and van den Brink (1980), and Facciola (1990)
Zingiberaceae	<i>Languas galanga</i> (L.) Stuntz	Greater Galangal, False Galangal Langkuas, Lenguas	Rhizome used as a spice	Burkill (1966), Morton (1976), and Phillips and Rix (1993)
Zingiberaceae	<i>Languas javanica</i> (Blume) Burkill = <i>Alpinia javanica</i> Blume	Puar Putih, Tepus Putih, Kantan Hutan	Rhizome used as food, scentless and bitter	Burkill (1966)
Zingiberaceae	<i>Zingiber amaricans</i> Blume = <i>Zingiber zerumbet</i> subsp. <i>zerumbet</i>	Lampuyang Pahit (Malay)	Young rhizome tip eaten raw with rice edible	Ochse and van den Brink (1980) and Facciola (1990)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Zingiberaceae	<i>Zingiber aromaticum</i> Valeton = <i>Zingiber zerumbet</i> subsp. <i>zerumbet</i>	Lampuyang Pahit	Rhizome edible fragrant, bitter and pungent	Ochse and van den Brink (1980)
Zingiberaceae	<i>Zingiber cassumunar</i> Roxb. = <i>Zingiber montanum</i> (J.König) Link ex A.Dietr.	Cassumunar Ginger; Bengal Gingermoran Ada (<u>Assamese</u>); Bonglai (<u>Malaysia</u>)	In Assam, India and Malaysia, rhizomes used as condiments; rhizome juice with honey is used for cough problems	Saidin (2000), Seidmann (2005), and Barua et al. (2007)
Zingiberaceae	<i>Zingiber chrysostachys</i> Ridley	Lempui (<u>Malaysia</u>)	Pungent rhizomes used as spice, substitute for <i>Z.</i> <i>zerumbet</i>	Jansen (1999) and Seidmann (2005)
Zingiberaceae	<i>Zingiber montanum</i> (J.König) Link ex A.Dietr.	Cassumunar Ginger, Bengal Root, Banglai (<u>Indonesia</u>), Bunglai, Bolai (<u>Malaysia</u>)	Rhizomes used for food flavouring	Wolf et al. (1999)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Zingiberaceae	<i>Zingiber officinale</i> Roscoe	Ginger, Halia (<u>Malaysia</u>),	Underground rhizome widely used as culinary spice, fresh, whole, slices, diced, crushed or powdered, preserved or pickled. Used to flavour beverages, drinks ale, etc.; used in bakery product and processed food, desserts and cakes, jams, marmalades and confectionaries	Burkill (1966), Ochse and van den Brink (1980), Cribb and Cribb (1987), Facciola (1990), Sutarno et al. (1999), Saidin (2000), Walter and Lebot (2007), van Wyk (2006), Phillips and Rix (1993)
Zingiberaceae	<i>Zingiber ottensii</i> Valetton	Bunglai Hantu, Panglai Hideung (<u>Indoneisa</u>), Lampoyang Hitam, Kunyit Hitam, Berseh Hitam	Pungent rhizome used as flavouring in traditional Malay cuisine	Jansen (1999), Saidin (2000)
Zingiberaceae	<i>Zingiber spectabile</i> Griff.	Black Gingerwort, Tepus Tanah, Tepus Halia(<u>Malaysia</u>)	Rhizome used as flavouring in traditional Malay cuisine	Burkill (1966), Wolf et al. (1999), Saidin (2000), and Seidemann (2005)

Family	Scientific Name	Common /Vernacular Names	Edible Part Use	Reference
Zingiberaceae	<i>Zingiber zerumbet</i> (L.) Roscoe ex Sm.	Wild Ginger, Zerumbert Ginger, Shampoo Ginger; Lampoyang (<u>Malaysia</u>), Phrilang Dung (<u>Assamese</u>)	Rhizome used as flavouring in traditional Malay cuisine; Rhizome eaten in Karbi, Assam	Ochse and van den Brink (1980), Cribb and Cribb (1987), Facciola (1990), Wolf et al. (1999), Saidin (2000), Seidemann (2005), and Kar and Borthakur (2008)
Zingiberaceae	<i>Zingiber zerumbet</i> (L.) Smith var. <i>zerumbet</i>	Lempuyang Gajah, Lempuyan Kapur, Lampunyang Badak (<u>Indonesia</u>)	Rhizome used as flavouring in traditional Malay cuisine	Wolf et al. (1999)
Zingiberaceae	<i>Zingiber zerumbet</i> (L.) Smith var. <i>amaricans</i> Blume	Lampuyan Pahit, Lempuyang Pait, Lempuyan Emprit (<u>Indonesia</u>), Hui Dam (<u>Thai</u>)	As above	Wolf et al. (1999)
Zingiberaceae	<i>Zingiber zerumbet</i> (L.) Smith var. <i>aromaticum</i> (Valeton) Theilade	Lampuyang Wangi, Lempuyang Wangi (<u>Indonesia</u>), Lampoyang, Lempoyang, Tepus (<u>Malaysia</u>)	As above	Wolf et al. (1999)
Zygophyllaceae	<i>Tribulus solanderi</i> F. Muell.	Nf	Roots eaten roasted	Cribb and Cribb (1987)

NF not found

As in the preceding eleven volumes, topics covered include: taxonomy (botanical name and synonyms); common English and vernacular names; origin and distribution; agro-ecological requirements; edible plant part and uses; plant botany; nutritive and medicinal/ pharmacological properties with up-to-date research findings, traditional medicinal uses; other non-edible uses; and selected/cited references for further reading.

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Solanum tuberosum

T. K. Lim¹ 

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Scientific Name

***Solanum tuberosum* L.**

Synonyms

Solanum andigenum Juz. & Bukasov, *Solanum andigenum* subsp. *aya-papa* Bukasov & Lechn., *Solanum andigenum* subsp. *bolivianum* Lechn., *Solanum andigenum* subsp. *ecuatorianum* Lechn., *Solanum aquinas* Bukasov, *Solanum chilense* Berthault, *Solanum chilotanum* Hawkes, *Solanum cultum* Berthault, *Solanum diemii* Brücher, *Solanum fonckii* Phil., *Solanum kesselbrenneri* Juz. & Bukasov, *Solanum leptostigma* Juz. & Buk., *Solanum molinae* Juz., *Solanum oceanicum* Brücher, *Solanum ochoanum* Lechn., *Solanum sanmartiniense* Brucher, *Solanum subandigena* Hawkes, *Solanum tascalense* Brucher, *Solanum tuberosum* var. *guaytecarum* Hawkes, *Solanum tuberosum* var. *tuberosum*, *Solanum tuberosum* subsp. *tuberosum*, *Solanum zykini* Lechn.

Family

Solanaceae

Common/English Names

Common Potato, Irish Potato, European Potato, Potato, Spud, White Potato

Vernacular Names

Afrikaans: Aartappel

Albanian: Patate

Arabic: Batates

Austria: Aardapfel, Ärdäppel, Bramburi, Erdapfel
(German)

Bulgarian: Kartof

Burmese: Ah Lou, Ar Loo

Chinese: Ma Ling Shu, Tǔdòu, Yángyù

Croatian: Krumpir

Czech: Brambor

Danish: Kartoffel, Kartoffler

Dutch: Aardappel, Aardappelen

Estonian: Kartul

Ethiopia: Dinittch

Finnish: Peruna, Potaati

French: Pomme De Terre, Patata

Gabon: Émongo-a-mutangani (Baduma), Amongo-mbé-ntanga (Bakèlè), Mongu-Bibamba (Balumbu), Mbala-bibamba (Bapunu), Mbala-yi-mutangeni (Bavarama, Bavungu, Eshira), Lifita-la-gibamba (Bavili), mbongo-y'utangani (Benga), imongo-i-ntangani (Béséki), Amonghe-ntangha (Fang), futa-wu-otangani (Mindumu), égwéta-a gébamba (Mitsogo), mongo-y'atanga (Mpongwè, Galoa, Nkomi, Orungu), mongo-a-gebamba (Ngowé)

German: Herdapfel, Inkatrüffel, Kartoffel, Kartoffeln, Kautüffel, Ketüffel, Krumbirn, Krumbiir, Tartuffli

Greek: Patáta

Hungarian: Burgonya

Icelandic: Kartafla

India: Aalu (Bengali), Bataka, Batata (Gujerati), Alu, Salooalu (Hindi), Urulaikkilangnku (Tamil)

Indonesia: Kentang

Italian: Pomi Di Terra, Patata, Tartufo

Japanese: Jagaimo

Korean: Gamsa

Khmer: Damlong Barang

Laotian: Man Falangx

Latvian: Kartupelis

Malaysia: Ubi Kentang

Morocco: Batâtâ, Btâtâ (Moroco), Pomme De Terre (French)

Nepali: Alu, Aloo

Papua New Guinea: Poteto

Peru: Papa Común

Philippines: Papas, Patatas (Cebu Bisaya, Bikol, Tagalog)

Polish: Ziemniaki

Portuguese: Batata, Batata-Da-Terra-Semelha, Batateira

Romanian: Cartof

Russian: Kartoffel, Kartoška

Serbian: Krompir

Slovakian: Zemiak, Bramboru

Slovenian: Krompir

Spanish: Papa, Patata

Swedish: Jordpäron, Kartoffel, Potatis, Potät, Tartuffe

Switzerland: Ardoffel, Mailinterra, Tartuffel, Tiffel, Truffel (French, Romansh Switzerland), Erdbirne, Erpele, Frundbirne, Gummel (German, Schwyz Canton), Grundbirn, Happere, Hardopfel, Harpfel (German, Upper Valais)

Welsh: Cloron, Tatws

Thai: Man-Farang, Man-Alu

Turkish: Patates

Ukrainian: Kartóplja

Vietnamese: Cây Khoai Tây, Khoai Tay

Origin/Distribution

The potato originated in the Andean regions of Peru and Bolivia. The potato was introduced into Spain from South America in the latter half of the sixteenth century. From Spain, the potato was introduced to adjacent countries and within 100 years was being grown fairly extensively in many regions of Europe. Distribution beyond Europe soon occurred with the introduction into India in the seventeenth century and China and Japan in the eighteenth century.

Agroecology

Potato is a cool climate crop. It prefers day temperatures of 20–25°C and night temperatures below 20 °C. Such temperature conditions are conducive to growth and tuberisation. Night temperatures above 22 °C retard tuberisation. In the tropics it is usually grown in the highlands above 800 m where the temperatures are cooler. In PNG they are grown in altitude between 1500 m and 2200 m. High light intensities are required for optimum dry matter production. It is susceptible to frost and freezing. Potato requires a well distributed rainfall of 500–750 mm in a growing period of 3–4.5 months.

Potato grows on a wide range of soils but not waterlogged soils. It grows best in loose, friable soil and well-drained

mineral or organic soils with medium loam or light or medium silty textures. Deep soils with good aeration and permeability give good growth and high tuber yields. Potato tolerates a wide range of pH from 4.8–7.

Edible Plant Parts and Uses

Potato is a very versatile food crop that can be used in multivariate ways. It is eaten cooked and occasionally raw. Potato can be boiled, steamed, microwaved, baked, fried, grilled, mashed and added to soups, stews, curries, pies, vegetable salads, dumplings, pancakes ('rosti') and goes well with all sorts of meat and seafood. One common dish is mashed potato where boiled, peeled potato is mashed with butter, margarine, milk or yoghurt. Potato is also consumed as fresh fries, pomes fries, wedges, potato bread (such as boxty) and hash browns. Potato is also thinly sliced and made into chips and crisps by baking or deep-frying for snack appetiser or as a side dish. Potatoes have been used to prepare a product known as chuño, which has played an important role in the diet of the population of the highland and lowland Andes of South America. Potato can be processed into many dehydrated, frozen or canned tubers. Potatoes can also be processed into alcohol and alcoholic beverages including vodka and schnapps.

Potato tuber storage protein, patatin, was found to have potential as food ingredients, in cheese making (Spellbrink et al. 2015). When patatin was added to milk during cheese making, the lipase preferentially released short-chain fatty acids that contributed to cheese flavour in a dose-dependent manner. Fortuitously, the lipase activity was found mainly in the curd.

Potato flour/potato starch is an important processed product from potato and has highly versatile uses in manufacturing convenience foods—ready to cook instant curries, dhals and snacks. Potato flour/starch can be used to prepare potato mash, snack foods, extruded foods, sweets and other bakery products (cakes, bread, pancakes, etc.), weaning foods and baby foods. Its protein content is superior to that of

cassava and yam flour, slightly inferior to that of refined maize meal and wheat flour and similar to that of rice. Potato flour has higher levels of fibre than refined wheat flour, maize meal and rice but lower levels of fibre than cassava and yam flour. Its carbohydrate and energy contents are comparable to those of similar foods. The high starch content in potato flour can improve the functional properties of several food products. It has a higher heat point than cornstarch, so it may be superior for certain foods that require high temperatures. Another health benefit is that potato flour or potato starch is gluten-free and is used as a substitute for wheat to make gluten-free food products for people with gluten intolerance. It can be also blended with wheat flour to make instant noodles, the Indian 'paratha' bread and the Indian sweet preparation 'gulab jamun' (potato flour, wheat flour and milk). It is commonly used as thickeners in soups, sauces and gravies. Potato starch is much used for determining the diastatic value of malt extract (Grieve 1971). A volatile oil—chemically termed amylic alcohol, in Germany known as *Fuselöl*—is distilled by fermentation from potato spirit. Boiled with weak sulphuric acid, potato starch is changed into glucose or grape sugar, which by fermentation yields alcohol, this spirit being often sold under the name of British Brandy.

Potato starch/flour is widely used for making commercial extruded and blended potato chips/crisp snack food, viz. Pringles and Lay's Stax brands.

The carbohydrate (starch and sugar) composition of tubers plays an important role in determining variety usage. Processing varieties, for example, must have relatively high starch and low reducing sugar (glucose/fructose) levels. Starch content is directly related to specific gravity (SG) or dry matter (DM) in tubers. Typically, 60–80 % of the dry matter is present as starch. Therefore, high specific gravity or high dry matter (solids) tubers contain high levels of starch. Generally, table varieties have low SG below 1.069 and low DM below 18.1 %. Some examples are Desiree, Red Pontiac, Sequoia, Sebago, Bintje, Patrones, Denali, Granola, Tess, Pontiac, Bison, Red Bison and Nadine. Varieties with high SG above 1.079 and high DM above 20.3 % are used for processing, e.g.

Atlantic, Snowden, Shepody, Niska, Chipeta, Norvalley, Ivory Crisp, Dakota Pearl, Gemchip, Russet Burbank, Ranger Russet and Kennebec.

Botany

An erect or sprawling herb, 30–100 cm tall, with robust angular, branched and winged stem glabrous or sparsely pubescent with simple and glandular hairs (Plates 1 and 2). Stolons bearing underground tubers; tubers white, brown, yellowish brown, pink, red, purple or purplish blue; globose, oblate or elliptic; 3–10 cm in diameter; fleshy; and with axillary buds (eyes) and numerous lenticels (Plates 3, 4, 5, 6, 7, 8, and 9). Leaves alternate, interruptedly odd-pinnate, with 6–8 pairs of leaflets and smaller, unequal interstitial leaflets; petiole 2.5–5 cm long, leaflet blade ovate or oblong, 2–10 cm by 1–6 cm, dark green, pinnatinerved, mostly sparingly pilose. Inflorescences appearing terminal, leaf opposed, or axillary, many-flowered, sparingly branched panicles. Pedicel articulate near middle, 1–2 cm. Calyx campanulate with 5-lanceolate lobes sparsely pubescent; Corolla white, pink, or blue purple (Plate 2), sometimes all on one plant, rotate to rotate–stellate, 2.5–3 cm in diameter, with 5 deltate lobes, 5 mm; filaments thick with five free, erect yellow anthers, 5–6 mm. Ovary glabrous. Style 8 mm with capitate stigma, berry green or yellowish green, often striped, globose, smooth, 1.5–2 cm in diameter. Seeds numerous (300), flat, suborbicular to ovate, small, yellowish brown embedded in mucilaginous pulp.



Plate 1 Potato plant habit



Plate 2 Leaves and flower



Plate 3 Potatoes with different skin colours



Plate 4 Desiree potatoes



Plate 5 Bintje potatoes



Plate 6 Kipfler potatoes



Plate 7 Purple Congo potatoes



Plate 8 Royal blue potatoes



Nutritive/Medicinal Properties

The proximate nutrient value per 100 g edible portion of raw, skin potato was reported as: water 83.29 g, energy 58 kcal (243 kJ), protein 2.57 g, total lipid 0.10 g, ash 1.61 g, carbohydrate 12.44 g, total dietary fibre 2.5 g, minerals (Ca 30 mg, Fe 3.24 mg, Mg 23 mg, P 38 mg, K 413 mg, Na 10 g, Zn 0.35 mg, Cu 0.423 mg, Mn 0.602 mg, Se 0.3 µg), vitamins (vitamin C 11.4 mg, thiamine 0.021 mg, riboflavin 0.038 mg, niacin 1.033 mg, pantothenic acid 0.302 mg, vitamin B6 0.239 mg), total folate 17 µg, total saturated fatty acids 0.026 g (10:0 0.001 g, 12:0 0.003 g, 14:0 0.001 g, 16:0 0.016 g, 18:0 0.004 g), total monounsaturated fatty acids 0.002 g (16:1 undifferentiated 0.001 g and 18:1 undifferentiated 0.001 g) and total polyunsaturated fatty acids 0.043 g (18:2 undifferentiated 0.032 g and 18:3 undifferentiated 0.010 g) (USDA-ARS 2014). The variety × location interaction and location effects of soluble and insoluble dietary fibre contents of six Canadian potato varieties were significant on a dry weight basis (Mullin et al. 1993). The same effects for total dietary fibre were significant after storage except for soluble fibre in the skins, insoluble fibre in the flesh and whole potatoes. On a fresh weight basis, the range of soluble fibre was 0.9–1.30 % for both fresh and stored potatoes; for insoluble fibre the range was 0.6–0.8 % and 0.6–0.7 % for fresh and stored samples, respectively.

The following sugars were found in cold-stored Kennebec potato tubers with stearic acid as internal standard: β-D-fructose; α-glucose, β-D-glucose, myo-inositol and sucrose (Varns and Shaw 1973). Potato tubers were found to contain citric and malic acids in the ratio of nearly 20:1 together with a small amount of isocitric acid (Curl and Nelson 1940).

A total of 17 fatty acids were detected in quantifiable amounts in all genotypes of *Solanum phureja* and *S. tuberosum* (Dobson et al. 2004). The predominant fatty acid was linoleic followed by α-linolenic and palmitic acids. 15-Methyl hexadecanoate was present as a minor acid in both

species. For both species, the contents (both as absolute levels and as percent compositions) of linoleic acid decreased and α -linolenic acid increased in tubers over the whole storage period. Niacin degradation in potato followed first-order kinetics, where the rate constant increased with an increase in the temperature of 50–120 °C (isothermal process) (Nish et al. 2009). The results obtained indicate a niacin degradation of a similar magnitude in all three modes of cooking, namely, normal open pan cooking, pressure cooking and a newly developed and patented fuel-efficient ‘EcoCooker’. Potatoes had been found to contain a number of health-promoting phytonutrients such as phenolics, flavonoids, folates, kukoamines and carotenoids (Ezekiel et al. 2013). Pigmented potatoes contained high concentration of phenolic acids as compared to white-fleshed potatoes and richer in natural colourants and antioxidants.

Proteins

Potato had been reported to have several types of protein. Osborne and Campbell (1896) isolated a globulin from potato tubers by salt extraction which they designated ‘tuberin’. Kon (1928) reported on the nutritional value of tuberin, the globulin of potato. Groot et al. (1947) separated tuberin into two fractions by electrophoresis. Slack (1948) concluded that the only true protein present in potato was a globulin. Lindner et al. (1960) fractionated potato tuber proteins into tuberin, globulin II, albumin, prolamine and glutelin. Stegmann and Loeschcke (1961), Desborough and Peloquin (1966) and Nakasone et al. (1972) separated tuber proteins into additional fractions by electrophoresis and chromatography. Kapoor et al. (1975) fractionated protein in Red Pontiac tuber into tuberin, the main proteins (71 %), and found that 40 % of tuberin was albumin. All the protein fractions except prolamine were well balanced in essential amino acids and comparable to FAO reference protein. Methionine was the limiting amino acid of the potato fractions. The chemical score, essential amino acid indices and biological value of albumin, globulin, glutelin and residual protein did not vary significantly. Since all the fractions except prolamine, which is a negligible portion of

total protein, are of high nutritional quality, Red Pontiac has high-quality protein. Potato tubers had 1.67 % N/dry matter (Gorinstein et al. 1988). Of the total N content, 43 % was dialyzable N and 32.9 % true protein N. The protein, by solubility fractionation, provided 67 % albumin, 23 % globulin, 1.4 % prolamine and 9 % glutelins. Albumin had two major protein species, one of 45×10^3 and the other of $12\text{--}25 \times 10^3$ daltons. Prolamine and glutelins contained protein bands coinciding in molecular weight with those of albumin and globulin. Some minor losses in protein composition of potatoes occurred during processing. Ultrafiltration gave the best yield recovery of protein from potato juice compared to polyelectrolyte coagulation and cryoconcentration (Wojnowska et al. 1981). Depending on the method of potato juice concentration, differences were observed in: foaming and emulsifying properties, wettability, swelling and buffer capacity of preparations. The dried preparations contained a high level of proteolytic enzyme inhibitors and glycoalkaloids. Thermal inactivation of preparations before drying led to 43–48 % destruction of protease inhibitors and 81–89 % glycoalkaloids. At the same time, it was observed that thermal treatment led to distinct changes in the amino acid composition of the proteins and had an adverse effect on the properties of the dried preparations.

Racusen and Foote (1980) reported that a glycoprotein of molecular mass about 45,000 accounted for about 20 % of the total soluble protein in potato and proposed the alternative name ‘patatin’, based on ‘patata’, the original American Indian-derived Spanish word for potato. Park et al. (1983) estimated the molecular mass of patatin to be about 40,000 and showed extensive heterogeneity with forms differing in electrophoretic mobility at pH 8.6 and in mobility on SDS–PAGE. Paiva et al. (1983) demonstrated that there was a linear relationship between the amount of patatin, expressed as a percentage of total soluble protein, and the logarithm of tuber weight from 0.3 to 300 g, with patatin forming about 40 % of the total soluble protein in tubers above about 200 g. Under normal conditions, patatin was found in only trace amounts, if at all, in leaves, stems or roots of plants which were either

actively forming tubers or which had been grown under long days to prevent tuberisation. However, if tubers and axillary buds were removed, patatin could accumulate in stems and petioles. Patatin was reported to account for 30–40 % of the total soluble protein in potato tubers (Andrews et al. 1988). Besides being a storage protein, it also exhibited lipid acyl hydrolase and acyltransferase activities. It was active with phospholipids, monoacylglycerols and p-nitrophenyl esters and moderately active with galactolipids but is apparently inactive with di- and triacylglycerols. Isolated patatin at room temperature was found to be a highly structured molecule at both secondary and tertiary levels (Pots et al. 1998). About 33 % of the residues adopted an α -helical and 46 % a β -stranded structure. Patatin was thermally destabilised at temperatures exceeding 28 °C. It was shown that parts of the α -helical contributions unfold in the 45–55 °C region, whereas the β -stranded parts unfold more gradually at temperatures of 50–90 °C. Patatin from potato tuber was found to have a molecular mass of 45 kDa (Liu et al. 2003). van Koningsveld et al. (2001) reported the soluble potato proteins to mainly compose of patatin and protease inhibitors. Potato proteins were soluble at neutral and strongly acidic pH values. The tertiary structure of patatin was irreversibly altered by precipitation at pH 5. At mildly acidic pH, the overall potato protein solubility was dependent on ionic strength and the presence of unfolded patatin. Thermal unfolding of the protease inhibitors was correlated with a decrease in protease inhibitor activities and resulted in an ionic strength-dependent loss of protein solubility.

Three protein inhibitors of proteolytic enzymes with molecular weights 21, 22 and 23 kD were isolated from potato tubers (Valueva et al. 1997). The 21- and 22-kD proteins were shown to be serine proteinase inhibitors with different specificities. The 21-kD protein inhibited human leucocyte elastase and trypsin effectively but was less effective towards chymotrypsin. The 22-kD protein was an inhibitor of cysteine proteinases and suppressed the activities of papain, ficin and bromelain with the same affinities. None of the isolated proteins inhibited subtilisin, pepsin or cathepsin D. The 21-kD protein consisted of two disulphide-linked polypeptide chains

with molecular weights of 16.5 kD and 4.5 kD. The 22-kD and 23-kD proteins possessed a single polypeptide chain. The N-terminal 22–25 amino acid sequences of these three proteins exhibited significant homology to other plant inhibitors from the Kunitz soybean inhibitor superfamily. Three protein proteolytic enzyme inhibitors with molecular masses 21, 22 and 23 kDa were isolated from intact potato tubers (Valueva et al. 1998). The 21 and 22 kDa proteins denoted as PSPI-21 and PSPI-22, respectively, were serine proteinase inhibitors with different specificity. The 23 kDa protein denoted as PCPI-23 was an inhibitor of plant cysteine proteinases. The PSPI-21 molecule consisted of two disulphide-linked polypeptide chains with molecular masses of 16.5 kDa and 4.5 kDa. The PSPI-22 and PCPI-23 had one polypeptide chain. They exhibited significant homology to other plant inhibitors which were members of the soybean Kunitz inhibitor family. It was found that at least PSPI-21 and PSPI-22 could predominantly accumulate in potato tubers infected with *Phytophthora infestans*. A 21-kD protein isolated earlier from potato tubers was found to have two isoforms, with pI 6.3 and 5.2 (Valueva et al. 1999). The primary structures of the two forms consisted of 187 and 186 amino acid residues. Both isoforms were composed of two polypeptide chains, designated A and B, linked by a single disulphide bond between Cys-146 of the A chain and Cys-7 of the B chain. The amino acid sequences of the A chains of the two forms, consisting of 150 residues each, differed in a single amino acid residue at position 52 (Val → Ile), while the B chains, containing 37 and 36 residues, respectively, had substitutions at nine positions (Leu-8 → Ser-8, Lys-25 → Asp-26 → Asn-25, Glu-26, Ile-31 → Ser-32 → Val-31-Leu-32, Lys-34-Gln-35-Val-36 → Gln-37 → Gln-34-Glu-35-Val-36). Both isoforms formed stable inhibiting complexes with human leukocyte elastase and were less effective against chymotrypsin and trypsin.

Protein concentrates isolated from potato fruit juice by precipitation with ethanol or ferric chloride afforded exhibited yield of 69 % and 86.5 % of total protein, respectively, and high nutritional value; values of essential amino acid index (EAAI) were 81.7 % and 82.7 %, respectively (Bártová and Bárta 2009). Fraction of patatin proteins (39–43 kDa)

represented with EAAI value of 86.1 % the nutritionally improved protein component. Lipid acyl hydrolase activity of patatin family was not negatively affected by cooled ethanol precipitation. Sun et al. (2013) reported that patatin purified from potato fruit juice possessed a monosaccharide composition of rhamnose, mannose, glucose and galactose with a molar ratio of 41:30:21:8, and patatin consisted of (1 → 3) linked α -mannose, (1 → 4) linked α -galactose, (1 → 4) linked β -glucose and (1 → 2) linked α -rhamnose. Potato fruit juice, prepared using Canadian variety of potatoes, was found to compose 22.9 % patatin, 53.3 % protease inhibitors and 23.7 % high MW proteins (Waglay et al. 2014). $(\text{NH}_4)_2\text{SO}_4$ precipitation led to the highest yield (98.6 %) and to the recovery of protein isolates enriched in patatin with high resolubility. FeCl_3 precipitation resulted in the highest purification factor (6.2) and isolates with the lowest relative proportion of high MW proteins (<4.6 %). FeCl_3 and MnCl_2 were identified as the best precipitating agents for the enrichment of isolates with >15 kDa protease inhibitors. Trypsin inhibiting activities of protease inhibitors were highly preserved upon protein isolation than the chymotrypsin ones. Acidic-based protein isolate showed the highest specific lipid acyl hydrolase activity of patatin towards o-nitrophenyl butyrate, whereas the FeCl_3 -based one exhibited the highest activity towards 4-nitrophenyl laurate. A protein with molecular weight of 21 kD denoted as PKSI was isolated from potato tubers (*Solanum tuberosum* cv. Istrinskii) (Revina et al. 2004). The N-terminal sequence of the protein consisted of 19 amino acid residues and was highly homologous to sequences of the known inhibitors from group C of the subfamily of potato Kunitz-type proteinase inhibitors. The protein effectively inhibited the activity of subtilisin but was inactive against trypsin, chymotrypsin and the cysteine proteinase papain. A protein of 22 kDa designated as PKTI-22 was isolated from potato tubers (*Solanum tuberosum* cv. Istrinskii) (Revina et al. 2010). The protein efficiently suppressed the activity of trypsin but affected chymotrypsin less and did not affect subtilisin Carlsberg. The N-terminal sequence of PKTI-22 (20 amino acid residues) was found to be highly

homologous with the amino acid sequences of the potato Kunitz-type proteinase inhibitors of group B (PKPI-B).

Peksa et al. (2013) found that the quality of protein depended on potato variety but not on its flesh colour or total protein content. Leucine limited the quality of protein of the majority of coloured potato varieties. Purple-fleshed varieties Vitelotte and Blaue Anneliese, yellow-fleshed Verdi as well as red-fleshed Herbie 26, Highland B. Red and Rosemarie were found to have the best amino acid profiles and essential amino acid index.

Two enzymes involved in the biosynthesis of starch in potato were extracted from potato juice; Q-enzyme in crystalline form was precipitated with ethanol at low temperature (Gilbert and Patrick 1952a) and phosphorylase (Gilbert and Patrick 1952b).

Phytosterols

Free sterols, β -sitosterol and stigmasterol were isolated from white-fleshed potato (Schwartz and Wall 1955). Raw potatoes were found to contain (mg/100 g) 0.98 mg total phytosterols comprising 0.04 mg campesterol, 0.10 mg stigmasterol, 0.54 mg β -sitosterol, 0.30 mg Δ^5 -avensterol and also 0.05 mg squalene (Chiou et al. 2009). In the Katahdin variety of *Solanum tuberosum*, incorporation of mevalonic acid-2- C^{14} into the major sterols, stigmasterol and β -sitosterol, occurred in 1 week (Johnson et al. 1964). Incorporation into β -sitosterol started sooner and occurred to a greater degree than in the case of stigmasterol.

The following phytosterols had been reported to occur in unsaponifiable lipids from potato leaves: β -sitosterol and a methylsterol assumed to be lophenol or citrostadienol (Schreiber et al. 1961); cycloartenol, 24-methyl-cycloartenol and α -sitosterol (Schreiber and Osske 1962, 1963, 1964); lophenol, 24-methylene-lophenol and 4 α -methyl-5 α -stigmaster-7,24(28)-diene-3 β -ol (24-ethylidene-lophenol) (Osske and Schreiber 1965; Schreiber and Osske 1962, 1963, 1964); Δ^5 -campesterol, stigmasterol and cholesterol (Ardenne et al. 1963, 1965; Johnson et al. 1963; Osske and Schreiber 1965)

and cyclolaudenol (Schreiber and Osske 1964). From haulm and tuber sprouts of potato cv. Desiree fractions, Δ^5 -sterols and Δ^7 -sterols, 4-methyl-sterols, triterpenic alcohols, tocopherols and hydrocarbons were isolated (Stanković et al. 1990). Sterol and triterpenic alcohol fractions of unsaponifiable lipids of the haulm and tuber sprouts were found to contain twelve sterols and four triterpenic alcohols, respectively. The lipid components identified were cholesterol, campesterol, stigmasterol β -sitosterol, 24*R*-4-stigmasten-3-on, cycloeucalenol, obtusifoliol, lophenol, 24-methylene-lophenol, 24-ethylidene-lophenol, 24-methylene-cycloartenol, cycloartenol, lanosterol, β -amyrin, phytol, C_{23} -to C_{33-n} -parafins, C_{19} -and C_{31} -cyclohexyl hydrocarbons, C_{22} -to C_{38} -olefins and squalene. 24*R*-4-stigmasten-3-on, Δ^7 -campesterol, Δ^7 -stigmasterol, lanosterol, cycloeucalenol and obtusifoliol had not been identified previously in unsaponifiable lipids from haulm and sprouts.

The level of glycoalkaloids present in freshly cut potato tuber discs started to increase after 24 h of incubation (Bergenstråhle et al. 1992). This accumulation was inhibited by the sterol synthesis inhibitor, tridemorph, and was thus due to synthesis de novo. Concomitant to the accumulation of glycoalkaloids, there was an increase in the specific activity of a glycoalkaloid-specific enzyme, UDP-glucose:solanidine glucosyltransferase (solanidine-GT). Other sterol-metabolizing enzymes S-adenosyl-L-methionine:cycloartenol methyltransferase (cycloartenol-MT) exhibited different time-course curves. Addition of ethephon or tridemorph inhibited the accumulation of sterols and sterol precursors in potato tuber discs (Bergenstråhle et al. 1996). In the 4,4-dimethylsterol fraction and the 4 α -methylsterol fraction, only compounds with a nonalkylated side chain were found. The 4-desmethylsterols synthesised de novo were, in tridemorph-treated discs, pollinastanol and 5 α -cholest-8-en-3 β -ol; in ethephon-treated discs, isofucosterol; and, in control discs, isofucosterol and cholesterol. The cholesterol concentration decreased concurrently with the accumulation of glycoalkaloids. The results showed that cholesterol synthesis

was stimulated in potato discs and indicated cholesterol to be a precursor of glycoalkaloids in potato.

Potato Starch

The amylose content of starches ranged between 15.0 % and 23.1 % and differed significantly among different potato cultivars (Kaur et al. 2007). Pasting temperatures of different potato starches ranged from 64.5 to 69.5 °C, the highest for Kufri Sindhuri (Patna) and the lowest for Kufri Bahar (Jalandhar). The transmittance value decreased progressively during refrigerated storage of pastes from different potato starches. The transition temperatures (onset temperature (To); peak temperature (Tp); conclusion temperature (Tc)), gelatinisation temperature range (R) and enthalpies of gelatinization (DHgel) of the starches from different potato cultivars differed significantly. Potato starch showed the presence of exceptionally large size granules. The granules showed the size between 32.37 and 42.05 µm. Kufri Lauvkar (Gwalior) starch showed the presence of smaller size granules, and Kufri Chipsona-2 (Modipuram) showed larger granules. Ash content ranged from 0.06 to 0.45 %. Swelling power (SP) ranged from 29.27 to 48.61 % and solubility ranged from 4.17 to 36.98 %. Peak viscosity ranged from 4145 to 6803 cP, hot paste viscosity (HPV) 1950–3204 cP, cold paste viscosity (CPV) 2351–3606 cP, setback viscosity 282–436 cP, breakdown (BD) 1850–4490 cP, pasting temperature (Ptemp) 64.50–69.40 °C and pasting time (PT) 3.60–5.70 min. Ash content which mainly represented the phosphorus content in potato starch was positively correlated to hot paste viscosity, To and Tp, and negatively correlated with SP. Amylose content was positively correlated to HPV and cold paste viscosity. Amylose content was negatively correlated to transmittance measured after storage of 0, 24 and 72 h. Solubility was positively correlated with To and Tp. Solubility was positively correlated with To and Tp. PV showed significant positive correlation with BD and negative correlation with PT. HPV showed significant positive correlation with CPV and negative correlation with transmittance. CPV showed positive correlation to PT, Ptemp,

Tp and Tc and negative correlation to transmittance. BD showed highly negative correlation with PT and positive correlation with transmittance. Ptemp showed highly positive correlation with transition temperatures To, Tp and Tc and negative correlation with transmittance. To showed significant positive correlation with Tp and Tc and Tp also showed significant positive correlation with Tc. Mean granule size did not correlate significantly with PV, BD and Ptemp.

Scanning electron microscopy showed potato starch granules to be oval and irregular shaped with average diameter of 15 μm , and the granule diameter increased after storage (Ezekiel et al. 2010). Pasting temperature of starch separated from potato varied from 64.6 to 67.7 $^{\circ}\text{C}$ before storage, and it varied from 66.9 to 69.4 $^{\circ}\text{C}$ after 90-day storage at different temperatures. Peak viscosity was lower after storage at 8 $^{\circ}\text{C}$ and higher at 16 $^{\circ}\text{C}$. Hot paste viscosity decreased, while breakdown viscosity and set back viscosity increased after storage, and there was no significant change in cold paste viscosity. A significant decrease in pasting time and increase in pasting temperature was observed after storage. Phosphorus content showed significant positive correlation with peak viscosity ($R^2 = 0.452$) and breakdown viscosity ($R^2 = 0.685$) and a negative correlation with amylose content ($R^2 = -0.674$). X-ray diffraction analysis of potato starch samples revealed B-type pattern. Scanning electron microscopy (SEM) showed the presence of oval and irregular-shaped potato starch granules with a diameter range of 15–16 μm (Ezekiel et al. 2007). Mean granule size of starch separated from potatoes stored at 12 $^{\circ}\text{C}$ ranged from 18 to 25 μm and irradiation treatment resulted in an increase in the proportion of small size granules. The irradiation of potatoes with 0.5 kGy caused a significant increase in setback and pasting temperature. Pasting temperature of starch was observed to vary with the storage temperature. Starch separated from potatoes stored at higher temperature showed lower pasting temperature and vice versa. The starch from potatoes stored at 8 $^{\circ}\text{C}$ showed higher peak, trough and breakdown viscosity and lower setback. Peak viscosity increased and swelling volume decreased with increase in storage temperature.

Miča (1976) found that during storage of potatoes, changes occurred in starch content, starch granule size, phosphorus, potassium and calcium content in the starch. The potassium content decreased during storage as a function of temperature. The phosphorus content decreased at +2 °C and increased at +10 °C. The calcium content increased in the final stage of storage. The phosphorus content in the starch decreased during storage. Onset and peak transition temperatures and gelatinisation enthalpy of potato starch from 42 potato genotypes intercorrelated (Kim et al. 1995). Transition temperatures intercorrelated with pasting temperature. Gelatinisation enthalpy correlated with Brabender pasting temperature and peak paste viscosity, and onset temperature correlated with phosphorus content. Potato starch differential scanning calorimetry (DSC) characteristics did not correlate with amylose, intrinsic viscosity or water binding.

The physico-chemical properties of Irish potato starch were reported by Nwokocha et al. (2014) as follows: 14.64 % moisture, 0.11 % ash, 0.23 % fat, 0.07 % nitrogen, 0.07 % phosphorus and 25.08 % amylose; particle characteristics (particle number 97, maximum diameter 47 mm, minimum diameter 13.39 mm, mean diameter 28.58 mm, length/diameter 1.37, roundness 0.68); gelatinisation properties (onset temperature 61.3 °C, peak temperature 64.2 °C, completion temperature 67 °C, gelatinisation range 5.7 °C, endothermic enthalpy 14.35 J/g); and pasting properties (pasting temperature 69 °C, temperature at peak viscosity 95 °C, peak viscosity during heating (PV) 750 BU, viscosity at 95 °C 750 BU, viscosity after 30 min holding at 95 °C (HPV) 475 BU, viscosity on cooling to 50 °C (CPV) 800 BU, stability ratio (HPV/PV) 0.63, setback ratio (CPV/HPV) 1.89). Irish potato had a paste clarity of 6.5 and syneresis of 3.55 % based on 1 % and syneresis on 5 % aqueous starch pastes. Irish potato had larger starch granules, higher phosphorus and lower amylose contents than sweet potato starch. It also exhibited a lower gelatinisation temperature, higher swelling power and amylose leaching compared to sweet potato starch. Sweet potato starch exhibited a higher pasting temperature, higher paste stability and setback ratio and greater stability to shear thinning than Irish potato starch. The rheological properties

indicated non-Newtonian behaviour for the two starch pastes. The storage and loss moduli of the two starch pastes were frequency dependent with values higher for sweet potato at all points within the angular frequency range employed. Irish potato starch paste exhibited higher paste clarity and lower syneresis than sweet potato starch paste. Irish potato has superior properties for application as thickener, while sweet potato is better in withstanding severe processing conditions. The extent of the annealing effect of potato starch depended on the difference between onset and annealing temperatures, and prolonged treatment time increased the effect (Karlsson and Eliasson 2003). Treating samples at 50 °C for 24 h caused a shift in gelatinisation onset temperature of 11–12 °C for isolated starch and 7–11 °C for in situ samples. Starch/water systems and tissue samples behaved similarly when exposed to time/temperature treatments. The starches separated from mealier potato cultivars (Kufri Jyoti and Kufri Badshah) showed lower transition temperatures (T_o ; T_p and T_c) and peak height indices (PHI) and higher gelatinisation temperature range (R) and enthalpies of gelatinisation (ΔH_{gel}) than the starch from least mealy cultivar (Pukhraj) (Kaur et al. 2002). Swelling power, solubility, amylose content and transmittance values were observed to be higher for Kufri Jyoti and Kufri Badshah potato starches, while turbidity values were lower for these starches. The rheological properties of starches showed significant variation in the peak G' , G'' and peak $\tan \delta$ values. Kufri Badshah and Kufri Jyoti starches showed higher peak G' , G'' and lower peak $\tan \delta$ values than Pukhraj starch during heating and cooling cycles. Kufri Jyoti and Kufri Badshah starches showed higher breakdown in G' than starch from the Pukhraj potato cultivar. The large-sized granules of the starches from Kufri Badshah and Kufri Jyoti appeared to be associated with higher values of peak G' and G'' and consistency coefficient. Starch from the least mealy cultivar (Pukhraj) showed higher retrogradation, which increased progressively during storage at 4 °C for 120 h.

In all potato starches examined, the phosphorus content ranged from 308 to 1244 ppm (Noda et al. 2007). Furthermore, samples differing manifestly in their phosphorus content

indicated that enhancing the starch phosphate resulted in significant increases in the swelling power, peak viscosity and breakdown and significant but small increases in the onset and peak temperatures of gelatinisation. Other starch quality parameters, such as the amylose content, median granule size and the gelatinisation enthalpy, did not change significantly due to the degree of phosphate substitution of starch. The amylose of potato starches had a negative correlation with the peak viscosity (PV) and breakdown (BD) and a positive correlation with the setback viscosity (SV) and peak viscosity temperature (PVT) (Zaidul et al. 2007). By contrast, phosphorus had a positive correlation with PV, BD and SV and a negative correlation with PVT. In addition, the median granule size had a positive correlation with PV and BD. By contrast, a negative correlation of the median granule size was observed with SV and PVT. The correlation coefficients of amylose–phosphorus, amylose–granule size and phosphorus–granule size interactions indicated that amylose had more influence than had phosphorus or had the median granule size on PV and BD.

Starch and K content of potato tubers increased with progressing age, whereas a decrease was observed in growth rate, starch synthesis per day and K uptake per day (Lindhauer and De Fekete 1990). Positive correlations between the rates of K uptake, starch production and growth indicate that the dynamic phase of K supply to the tubers was of greater importance for starch synthesizing processes than the influence of total K content. The activity of starch synthesis enzymes (sucrose synthase, UDP-D-glucose pyrophosphatase, starch phosphorylase, amylases) related to tuber K content did not differ significantly. Of the purified potato starch branching enzyme (SBE) I and SBE II, the former was more active than SBE II on an amylose substrate, whereas SBE II was more active than SBE I on an amylopectin substrate (Rydber et al. 2001). Both enzymes were stimulated by the presence of phosphate. After debranching of the products, the majority of dextrans with a degree of polymerisation (dp) greater than 60 were absent for SBE I and those with a dp greater than 70 for SBE II. Full-length cDNAs encoding a second starch branching enzyme (SBE A) isoform was isolated from potato

tubers (Jobling et al. 1999). The predicted protein has a molecular mass of 101 kDa including a transit peptide of 48 amino acids. Multiple forms of the SBE A gene exist which differ mainly in the length of a polyglutamic acid repeat at the C-terminus of the protein. High-amylose starch is in great demand by the starch industry for food and industrial applications for its unique functional properties. A very high-amylose potato starch was produced by genetic modification through simultaneously inhibiting two isoforms of starch branching enzyme to below 1 % of the wild-type activities (Schwall et al. 2000). The amylose content was increased to levels comparable to the highest commercially available maize starches. Additionally, the phosphorus content of the starch was increased more than fivefold. The granular interior of octenylsuccinic maize starch had higher fluorescent intensity than that of octenylsuccinic potato starch (Wang et al. 2013). The degree of substitution of octenylsuccinic maize starch degraded less than that of octenylsuccinic potato starch under the same degree of gelatinisation. The results implied that maize starch displayed much more homogeneous octenylsuccinic anhydride reaction pattern when compared to potato starch.

Carotenoids

The carotenoid pattern in four yellow- and four white-fleshed potato cultivars (*S. tuberosum*) was dominated by violaxanthin, antheraxanthin, lutein and zeaxanthin, which were present in different ratios, whereas neoxanthin, β -cryptoxanthin and β,β -carotene generally were only minor constituents (Breithaupt and Bamedi 2002). Antheraxanthin was found to be the only carotenoid epoxide present in native extracts. The total concentration of the four main carotenoids reached 175 $\mu\text{g}/100\text{ g}$, whereas the sum of carotenoid esters accounted for 41–131 $\mu\text{g}/100\text{ g}$. Therefore, carotenoid esters were regarded as quantitatively significant compounds in potatoes. Carotenoid contents reported in potatoes ranged from 50 to 100 μg per 100 g fresh weight (FW) in white-fleshed varieties to 2000 μg per 100 g FW in deeply yellow to orange-fleshed cultivars (Brown 2005). The carotenoids in potato

were mainly xanthophylls: lutein, zeaxanthin and violaxanthin with traces of either α -carotene or β -carotene, indicating potato to be not a source of provitamin A carotenoids. White- and yellow-fleshed potato contained xanthophyllous carotenoids (Brown 2006). The total carotenoid content of white cultivars and breeding lines ranged from 50 to 100 μg per 100 g FW. Yellow-fleshed cultivars may have carotenoid contents up to 270 μg , while more intensely yellow breeding clones will range up to 800 μg . Although the concentration of anthocyanin in skin tissue was quite high, it constituted such a small volume of the whole tuber that generally a red-skinned white-fleshed potato had no more than 1.5 mg per 100 g FW when skin and flesh were extracted together. However, potatoes with anthocyanin in the flesh ranged from 15 to nearly 40 mg per 100 g FW. Carotenoids are found in all potatoes in the flesh (Brown et al. 2008). White-fleshed varieties were reported to contain 50 to 100 μg per 100 g fresh weight (FW) and moderately yellow-fleshed varieties 100 to 350 μg per 100 g FW. The more intensely yellow-fleshed genotypes, which may look orange, at the higher extremes contained levels above 1000 μg per 100 g FW. The highest level published is 2600 μg per 100 g FW in diploid germplasm derived from South American *Papa Amarilla* cultivars. Potato generally possessed predominantly lutein, a xanthophyll, also found in the human retina, and must be obtained in the diet. The genotypes with extremely high levels of total carotenoids had zeaxanthin, an isomer of lutein, also present in the human retina. Total anthocyanins ranged from 1.5 mg to 48 mg per 100 g FW in a solidly pigmented purple-skinned, purple-fleshed breeding line.

Based on the carotenoid profile, sixty potato cultivars (commercial, bred, old and native cultivars) were segregated into three groups according to the major pigment in the carotenoid profile: violaxanthin (37 cultivars, especially those with higher carotenoid content), lutein (16 cultivars) and neoxanthin (7 cultivars) (Fernandez-Orozco et al. 2013). Other minor carotenoids were antheraxanthin, β -cryptoxanthin and β -carotene, while zeaxanthin was absent in all sample. The total carotenoid content ranged from 50.0 to 1552.0 $\mu\text{g}/100$ g dry wt, with an average value of about 435.3 $\mu\text{g}/100$ g dry wt.

Sipancachi, Poluya and Chaucha native cultivars showed the highest carotenoid content (1020.0, 1478.2 and 1551.2 µg/100 g dry wt, respectively). Xanthophyll esters were present in most cultivars, mainly as diesterified forms, being observed a direct correlation between the carotenoid content and the esterified fraction, suggesting that the esterification process facilitated the accumulation of these lipophilic compounds within the plastids. Yellow-fleshed potatoes were found to contain significant amounts of lutein and zeaxanthin (Burgos et al. 2013). The gastric and duodenal digestive stability of lutein and zeaxanthin in boiled tubers of the different accessions ranged from 70 to 95 %, while the efficiency of micellarisation ranged from 33 to 71 % for lutein and from 51 to 71 % for zeaxanthin. For all accessions, amounts of lutein and zeaxanthin after micellarisation were significantly lower than the original amount found in the boiled samples. The accession 701862 showed the highest bioaccessible lutein concentration (280 µg/100 g, FW), and the accessions 703566 and 704218 showed the highest bioaccessible zeaxanthin concentration (above 600 µg/100 g, FW). Considering the mean potato intake in the Andes (500 g per day), the accession 701862 provides 14 % of the lutein intake suggested for health benefits, and the accessions 703566 and 704218 provide 50 % more than the suggested zeaxanthin intake.

Phenolic Compounds (Phenolic Acids, Flavonoids and Anthocyanins)

Phenolic compounds could be broadly classified into phenolic acids (C6-C1 and C6-C3 structures) and flavonoids (C6-C3-C6 backbone) (Schieber and Saldaña 2009). They reported the following phenolic compounds in potatoes: (a) hydroxycinnamic acids, 5-*O*-caffeoylquinic acid (chlorogenic acid), 4-*O*-caffeoylquinic acid (cryptochlorogenic acid), 3-*O*-caffeoylquinic acid (neochlorogenic acid) and *p*-coumaric acid and ferulic acid; (b) hydroxybenzoic acids, gallic acid, protocatechuic acid, vanillic acid and salicylic acid; (c) non-anthocyanin flavonoids, catechin, epicatechin, eriodictiol, naringenin, kaempferol glycosides and quercetin glycosides; (d) anthocyanins, petunidin glycosides, malvidin glycosides,

pelargonidin glycosides and peonidin glycosides; and (e) dihydrocaffeoyl polyamines, N^1, N^{12} -bis(dihydrocaffeoyl)spermine (kukoamine A); N^1, N^8 -bis(dihydrocaffeoyl)spermidine; N^1, N^4, N^{12} -tris(dihydrocaffeoyl)spermine and N^1, N^4, N^8 -tris(dihydrocaffeoyl)spermidine. Besides chlorogenic acid and its isomers, caffeic, *p*-coumaric and ferulic acids as well as various benzoic acid derivatives such as gallic, protocatechuic, vanillic and salicylic acids were found in potato peels, however, usually in lower amounts (Onyeneko and Hettiarachchy 1993; De Sotillo et al. 1994a; Lewis et al. 1998a; Mattila and Hellström 2007). About 50 % of the phenolic compounds were found to be located in the potato peel and adjoining tissues, while the rest decreased in concentration from the outside towards the centre of potato tubers (Hasegawa et al. 1966). Freeze-dried aqueous extracts of potato peel waste were found to contain chlorogenic (50.31 %), gallic (41.67 %), protocatechuic (7.81 %) and caffeic (0.21 %) acids as major phenolics (De Sotillo et al. 1994b). The greatest amounts of phenolic acids resulted when potato peel waste homogenate was refluxed with water for 30 min yielding a total concentration of 48 mg/100 g (De Sotillo et al. 1994a). Four phenolic acids (chlorogenic, gallic, protocatechuic and caffeic) were characterised as major components. Aqueous extracts were stored 20 days and after 7 days at 25 °C exposed to light; chlorogenic acid had degraded to caffeic acid. Nara et al. (2006) found that in potato peels phenolic acids were not only present in their free form but occurred also in bound form, as shown for ferulic acid. The total polyphenolic content in potato peel was found to be 3.93 mg/g powder, and the major phenolic acids present were predominantly gallic acid, caffeic acid, chlorogenic acid and protocatechuic acid (Singh and Rajini 2008). The total phenolic acid content of potato flowers (626 mg/100 g fresh wt) was 21 and 59 times greater than that of leaves and stems, respectively (Im et al. 2008). For all samples, chlorogenic acid and its isomer contributed 96–98 % to the total. Total phenolic acid levels (in g/100 g fresh wt) of peels of five potato varieties grown in Korea ranged from 6.5 to 42.1 and of the flesh (pulp) from 0.5 to 16.5, with peel/pulp ratios ranging

from 2.6 to 21.1. The total phenolic acid content for 25 American potatoes ranged from 1.0 to 172. The highest amounts were present in red and purple potatoes. Home processing of pulp with various forms of heat induced reductions in the phenolic content. Eleven compounds were isolated from potato peels and included chlorogenic acid, other phenolic compounds, 2 glycoalkaloids, 3 low molecular weight amide compounds and 2 unsaturated fatty acids, including an ω -3 fatty acid (Wu et al. 2012). The potato peels contained a higher amount of phenolic compounds than the flesh. Among the different solvents tested, methanol exhibited the highest extraction ability for phenolic compounds from potato peels, with total phenolics amounting to 2.91 mg gallic acid equivalent/g dry weight (Mohdaly et al. 2010, 2013). The phenolic acid compounds found in the potato peels included: chlorogenic, caffeic, gallic, ferulic, *p*-hydroxybenzoic, *p*-coumaric and *trans*-*O*-hydroxycinnamic acids. Deusser et al. (2012) reported that chlorogenic acid and its isomers, neochlorogenic and cryptochlorogenic acids, were the major phenolic compounds in potato peel. Glycoalkaloid contents were highest in the peel and lowest in the inner flesh. Potato peel as a source of dietary fibre in bread was found to be superior to wheat bran in the contents of certain minerals, in total dietary fibre, in water-holding capacity, in its lower quantity of starchy components and in its lack of phytate (Toma et al. 1979). These dietary advantages were not lost in baking quality trials.

Four related phenolic amides were detected during metabolic profiling of potato (*Solanum tuberosum*) tubers (Parr et al. 2005). They were identified as N^1, N^{12} -bis(dihydrocaffeoyl)spermine (kukoamine A); N^1, N^8 -bis(dihydrocaffeoyl)spermidine; N^1, N^4, N^{12} -tris(dihydrocaffeoyl)spermine; and N^1, N^4, N^8 -tris(dihydrocaffeoyl)spermidine. Solid phase extraction (SPE) of N^1, N^{12} -bis(dihydrocaffeoyl)spermine (kukoamine A) from potato peels was optimised using a molecularly imprinted polymer (MIP) (Piletska et al. 2012). The kukoamine A purified from potato extract using MIP was exceptionally pure ($\approx 90\%$). Kukoamines (kukoamin A) had been associated with

reduced blood pressure (Funayama et al. 1980), and they had also been used to treat trypanosomiasis, a type of sleeping sickness caused by parasitic trypanosomatids like *Crithidia fasciculata* (Ponasik et al. 1995). Kukoamine A inhibited trypanothione reductase as a mixed inhibitor ($K_i = 1.8 \mu\text{M}$, $K_{ii} = 13 \mu\text{M}$). Kukoamine shows no significant inhibition of human glutathione reductase ($K_i > 10 \text{ mM}$) and thus provided a novel selective drug lead.

The free phenolic compounds found in four potato cultivars in Tenerife (Canary Islands) were (+)-catechin, chlorogenic acid, caffeic acid, *p*-coumaric acid and ferulic acid (Verde Méndez et al. 2004). A significant and negative correlation was established between (+)-catechin and *p*-coumaric acid. A considerable contribution to the daily intake of flavonoids was observed with the actual consumption of potatoes. Range of phenolic compounds (mg/100 g dm) in tubers of varying flesh colour was reported by Navarre et al. (2011) as follows: yellow type, 1.1–20.1 mg neochlorogenic acid, 0.7–4.5 mg caffeoyl putrescine, 22.9–211 mg chlorogenic acid, 3.8–32.7 mg cryptochlorogenic acid, 0.5–9.6 mg caffeic acid, 1.36–14.1 mg rutinose and 0.31–4.49 mg kaempferol-3-rutinose; white type, 0.7–10.7 mg neochlorogenic acid, 0.6–12 mg caffeoyl putrescine, 31–170 mg chlorogenic acid, 3.8–22.8 mg cryptochlorogenic acid, 4.7–14.4 mg caffeic acid, 0.37–6.91 mg rutinose and 0.13–1.37 mg kaempferol-3-rutinose; white/purple type, 0.1–18.8 mg neochlorogenic acid, 0.2–16 mg caffeoyl putrescine, 21.9–231 mg chlorogenic acid, 1.0–22.47 mg cryptochlorogenic acid, 2.0–47.6 mg caffeic acid, 0.29–1.72 mg rutinose and 0.15–2.5 mg kaempferol-3-rutinose; red/purple type, 2.9–43.7 mg neochlorogenic acid, 1.3–8.7 mg caffeoyl putrescine, 80.4–473 mg chlorogenic acid, 12.6–63.9 mg cryptochlorogenic acid, 5.2–15.9 mg caffeic acid, 0.48–3.54 mg rutinose, and 0.46–0.3 mg kaempferol-3-rutinose. Chlorogenic acids (CGA) concentrations in potato skins were 37–636 mg/100 g dry weight (DW) and were three to four times greater than those in the flesh (Weidel et al. 2014). Storage reduced the CGA levels in potatoes by up to 81 %. The studied potato purees contained 4–11 mg CGA/100 g DW. In addition, the quinic acid contents of potato flesh (11–95

mg/100 g DW) and puree (11–22 mg/100 g DW) were determined. None of the tested samples contained caffeic acid.

Coloured-fleshed potato varieties were characterised by about three times higher amount of total phenolic content than traditional yellow-fleshed ones (Rytel et al. 2014). The predominating phenolic acids in potato were chlorogenic acid and its isomers, which account about 90 % of total phenolic content in tubers. The phenolic acid content decreased by 80 % after peeling the blue-fleshed potatoes and by 60 % after peeling the yellow variety. The dried potato dice obtained from yellow-fleshed potatoes had no content of phenolic acids, but those produced from coloured-fleshed potatoes contained about 4 % of the original phenolic content of the raw material. Chlorogenic acid amounted about 97 % of total phenolic acid content, and the rest was neochlorogenic acid. Concentrations of total phenolics in yellow (3.2 g/kg) and purple (3.1 g/kg) potato cultivars were twofold greater than in the white potato cultivar (1.5 g/kg) (Kaspar et al. 2013). Anthocyanins were low to non-detectable in white (0 g/kg) and yellow potatoes (0.3 g/kg). Purple potatoes anthocyanin concentration (6.2 g/kg) was 20-fold greater than in yellow potatoes (0.3 g/kg) and white potatoes (0 g/kg). Carotenoid concentrations in white and purple potatoes were similar (1.3 mg/kg), while yellow potatoes had a 45-fold greater carotenoid concentration (58.1 mg/kg) compared to white and purple potatoes. Consumers ranked the aroma and appearance of white and yellow potatoes higher than purple potatoes. However, no significant differences were observed in overall acceptance between the potato cultivars. Four individual anthocyanins were detected as the major components of a purple potato cultivar, and the total anthocyanin content was 273.5 mg of cyanidin-3-glucoside equiv/100 g of dry seeds (Zhao et al. 2011). Purple potato anthocyanins delayed the quenching of bovine serum albumin (BSA) caused by chromium. It was found that the anthocyanin could protect the secondary and tertiary structures of BSA by probably interacting with chromium in advance.

Over 30 compounds were identified in potato tubers: ascorbic acid, tyrosine, phenylalanine and tryptophan; quinic

acid derivative; caffeic acid; 1-*O*-caffeoyl quinic acid; 5-*O*-feruloyl quinic acid; 4,5-di-*O*-caffeoyl quinic acid; caffeoyl-D-glucose; caffeic acid derivative; chlorogenic acid; neochlorogenic acid; cryptochlorogenic acid; 3-*O*-caffeoyl,5-*O*-feruloylquinic acid; quercetin-3-*O*-glu-rut; caffeoyl methyl quinate; gentisic acid glucoside; salicylic acid glucoside; ferulic acid amide; rutin; quercetin; quercetin dimethyl ether; kaempferol-3-*O*-glucoside; caffeoyl putrescine; caffeoyl spermine derivative; bis(dihydrocaffeoyl)spermine; bis(dihydrocaffeoyl)spermidine; tri(dihydrocaffeoyl)spermine; N¹,N⁴, N⁸, N¹²-tetra(dihydrocaffeoyl)spermine; N¹,N⁴,N⁸-tris(dihydrocaffeoyl)spermidine; solanine; and chaconine (Shakya and Navarre 2006). Some of these were deemed to possess either nutritional value in functional foods or were involved in plant disease resistance

Pigmented potato (*Solanum tuberosum*) varieties were found to be a rich source of anthocyanins, a subgroup of flavonoids, in particular acylated derivatives (Eichhorn and Winterhalter 2005). Petunidin derivatives were detected in all varieties except Highland Burgundy Red, where pelargonidin was found to be the only anthocyanidin. Malvidin was the predominant aglycone of the variety Vitelotte. Of the four selected cultivars, Shetland Black was the only one containing minor amounts of peonidin derivatives. Coumaric acid derivatives (i.e. 3-*p*-coumaroylrutinoside-5-glucosides of petunidin, pelargonidin, peonidin and malvidin) were separated from non-acylated anthocyanins as well as chlorogenic acids by means of solid phase extraction, countercurrent chromatography and preparative HPLC.

The flavonoids, in order of abundance, were reported to be catechin, epicatechin, eriodictyol, kaempferol and naringenin (Brown 2005). Potatoes were reported to contain phenolic compounds, with chlorogenic acid predominating and constituting about 80 % of the total phenolic acids. Up to 30 µg per 100 g FW of flavonoids was present in the flesh of white-fleshed potatoes with roughly twice the amount present in red- and purple-fleshed potatoes. The predominant flavonoids were catechin and epicatechin. Red and purple potatoes derived their colour from anthocyanins. The skin

alone may be pigmented, or the flesh may be partially or entirely pigmented. Whole unpeeled with complete pigmentation in the flesh may have up to 40 mg per 100 g FW of total anthocyanins. Red-fleshed potatoes possessed acylated glucosides of pelargonidin, while purple potatoes had, in addition, acylated glucosides of malvidin, petunidin, peonidin and delphinidin.

Verma et al. (1972) found that light-grown and dark-grown potato sprouts of cv. Kufri Sindhuri and Kufri Sheetman contained anthocyanins, pelargonidin 3-rhamnoglucoside 5-glucoside and acylated pelargonidin, while light-grown sprouts of Kufri Chamatkar and Kufri Sheetman contained pelargonidin glucoside. Dark-grown sprouts of Kufri Chamatkar contained leucocyanidin(s), while pigmentation was visually observed in the light-grown sprouts of the same variety. Lewis et al. (1998a) identified and quantified the major anthocyanins, flavonoids and phenolic acids in the tubers (skin and flesh), flowers and leaves of 26 cultivars of *Solanum tuberosum* with coloured skins and/or flesh. Red tubers contained mostly pelargonidin-3-(*p*-coumaroyl-rutinoside)-5-glucoside (200–2000 µg/g FW) plus lesser amounts of peonidin-3-(*p*-coumaroyl-rutinoside)-5-glucoside (20–400 µg/g FW). Light to medium purple tubers contained petunidin-3-(*p*-coumaroyl-rutinoside)-5-glucoside (1000–2000 µg/g FW) plus small amounts of malvidin-3-(*p*-coumaroyl-rutinoside)-5-glucoside (20–200 µg/g FW), while dark purple to black tubers contained similar levels of petunidin-3-(*p*-coumaroyl-rutinoside)-5-glucoside together with much higher concentrations of malvidin-3-(*p*-coumaroyl-rutinoside)-5-glucoside (2000–5000 µg/g FW). Tuber flesh also contained chlorogenic acid (30–900 µg/g FW) and lower amounts of vanillic, caffeic, sinapic, gallic, syringic, *p*-coumaric and cinnamic acids plus low concentrations of flavonoids (0–30 µg/g FW). Tuber skins showed much higher levels (1000–4000 µg/g FW) of chlorogenic acid. The major anthocyanins in flowers were present as the rutinosides or other glycosides of pelargonidin, petunidin and malvidin, while glycosides of cyanidin and delphinidin were found in some flowers, together with many of the same phenolic acids as found in tubers. The commonest flavonoids included rutin, kaempferol-3-rutinoside

and two quercetin–rhamnose glucosides. Flowers and leaves contained higher concentrations of flavonoids which fell into two patterns, with some cultivars containing high concentrations of quercetin-3-glycosides, while others had much lower concentrations. Principal component analysis (PCA) revealed a strong association between the various coloured *S. tuberosum* cultivars with distinct differences from the other wild *Solanum* species (Lewis et al. 1998b). Similarly, PCA showed that there were close correlations between the tuber skin and flesh components. The major flavonoids in the skin and flesh were catechin, epicatechin, eriodictyol and naringin. Two acylated pelargonidin glycosides were isolated from red tubers of an anthocyanin-rich tetraploid potato (hybrid seedlings between cultivars of *Solanum tuberosum* and *S. andigena*) (Naito et al. 1998). In cultivars with less coloured potato tubers, the developing tubers remained white for a longer time, with anthocyanin concentrations increasing gradually up to a maximum at a certain tuber weight depending on the cultivar (Lewis et al. 1999). The concentration of flavonoids was lower than that of anthocyanins but followed a similar pattern. Phenolic acid levels were about twice those of the anthocyanins and reached their maximum at a slightly lower tuber weight than anthocyanins and flavonoids. During cold storage (4 °C), the anthocyanin concentration in coloured tubers increased, whereas tubers stored at higher temperatures did not show this increase. The distribution of anthocyanins altered during tuber development and also during cold storage. The major pigment was identified as pelargonidin 3-*O*-[(4"-*O*-(*trans*-*p*-coumaroyl)- α -L-6"-rhamnopyranosyl- β -D-glucopyranoside)]-5-*O*-[β -D-glucopyranoside) and the minor pigment as pelargonidin 3-*O*-[4"-*O*-(*trans*-ferruloyl)- α -L-6"-rhamnopyranosyl- β -D-glucopyranoside]-*O*-[β -D-glucopyranoside]. Also detected were pelargonidin-3-acylrutinoside-5-glucoside, *p*-coumaric and ferulic acids. The main anthocyanins (acylated with caffeic acid) of purple sprouts of a Norwegian potato cultivar, *Solanum tuberosum* isolated from a purified methanolic extract, were determined to be the novel anthocyanins, petunidin 3-*O*-[6-*O*-(4-*O*-*E*-caffeoyl-*O*- α -rhamnopyranosyl)- β -glucopyranoside]-5-*O*- β -

glucopyranoside (10 %) and peonidin 3-*O*-[6-*O*-(4-*O*-*E*-caffeoyl-*O*- α -rhamnopyranosyl)- β -glucopyranoside]-5-*O*- β -glucopyranoside (6 %) in addition to petunidin, 3-*O*-[6-*O*-(4-*O*-*E*-*p*-coumaroyl-*O*- α -rhamnopyranosyl)- β -glucopyranoside]-5-*O*- β -glucopyranoside, petanin (37 %), and peonidin 3-*O*-[6-*O*-(4-*O*-*E*-*p*-coumaroyl-*O*- α -rhamnopyranosyl)- β -glucopyranoside]-5-*O*- β -glucopyranoside, peonanin (25 %) (Fossen et al. 2003). The same major anthocyanins, however, in other proportions (4, 54, and 32 %, for 1, 3 and 4, respectively), were also found in the thin violet zone located in the flesh 0.5–1 cm from the surface of the tubers. On average the highest amounts of anthocyanins were found in the skin (0.65 g/kg FW) of 27 potato cultivars and four breeding clones (Jansen and Flamme 2006). The corresponding values of samples taken from whole tubers (0.31 g/kg FW) and flesh (0.22 g/kg FW) were significantly lower. Among them Peru Purple revealed the highest anthocyanin content in the skin with 2.96 g/kg FW. A similar high value was reached by Violettfleischige and clone 1.81.202–92 N. There were considerable differences in the amounts of anthocyanins between the 31 cultivars/breeding clones. There were also no significant changes in the anthocyanin contents of tubers during storage for 135 days. In dry matter, starch and protein contents, the coloured potato cultivars/breeding clones were comparable with traditional cultivars. Glycoalkaloids were mainly localised in the skin of coloured potatoes. The major anthocyanin glycosides found in purple and coloured potato tubers were pelargonidin 3-[6-*O*-(4-*O*-*E*-*p*-coumaroyl-*O*- α -rhamnopyransoyl)- β -D-glucopyranoside]-5-*O*- β -D-glucopyranoside; peonidin 3-[6-*O*-(4-*O*-*E*-*p*-coumaroyl-*O*- α -rhamnopyransoyl)- β -D-glucopyranoside]-5-*O*- β -D-glucopyranoside; petunidin 3-[6-*O*-(4-*O*-*E*-*p*-coumaroyl-*O*- α -rhamnopyransoyl)- β -D-glucopyranoside]-5-*O*- β -D-glucopyranoside; peonidin 3-[6-*O*-(4-*O*-*E*-caffeoyl-*O*- α -rhamnopyransoyl)- β -D-glucopyranoside]-5-*O*- β -D-glucopyranoside; petunidin 3-[6-*O*-(4-*O*-*E*-caffeoyl-*O*- α -rhamnopyransoyl)- β -D-glucopyranoside]-5-*O*- β -D-glucopyranoside; petunidin 3-[6-*O*-(4-*O*-*E*-feruoyl-*O*- α -rhamnopyransoyl)- β -D-glucopyranoside]-5-*O*- β -D-glucopyranoside; malvidin 3-[6-*O*-

(4-*O-E*-feruoyl-*O-α*-rhamnopyransoyl)- β -D-glucopyranoside]-5-*O-β*-D-glucopyranoside; and malvidin 3-[6-*O*-(4-*O-E-p*-coumaroyl-*O-α*-rhamnopyransoyl)- β -D-glucopyranoside]-5-*O-β*-D-glucopyranoside (Lachman and Hamouz 2005).

In an antioxidant profiling study of 23 Andean potato cultivars, concentrations of the health-promoting carotenoids, lutein and zeaxanthin, ranged from 1.12 to 17.69 $\mu\text{g/g}$ of dry weight (DW) and from 0 to 17.7 $\mu\text{g/g}$ of DW, with cultivars 704353 and 702472 showing the highest levels in lutein and zeaxanthin, respectively (Andre et al. 2007b). In contrast, β -carotene was rarely reported in potato tubers; remarkable levels of this dietary provitamin A carotenoid were detected in 16 native varieties, ranging from 0.42 to 2.19 $\mu\text{g/g}$ of DW. The amount of α -tocopherol found ranged from 2.73 to 20.80 $\mu\text{g/g}$ of DW and was clearly above the quantities generally reported for commercial varieties. Chlorogenic acid and its isomers dominated the polyphenolic profile of each cultivar. Dark purple-fleshed tubers from the cultivar 704429 contained exceptionally high levels of total anthocyanins (16.33 mg/g of DW). The main anthocyanin was identified as petanin (petunidin-3-*p*-coumaroyl-rutinoside-5-glucoside). Pigmented potato varieties are a rich source of anthocyanins, in particular acylated derivatives. The major anthocyanins found in pigmented potatoes (e.g. purple-fleshed varieties) include coumaric acid derivatives (i.e. 3-*p*-coumaroylrutinoside-5-glucosides of petunidin, pelargonidin, peonidin and malvidin) from non-acylated anthocyanins as well as chlorogenic acids. Dark purple-fleshed potato contained exceptionally high levels of total anthocyanins, and the main anthocyanin was identified as petanin.

The free phenolic compounds found in Tenerife (Canary Islands) potato samples were (+)-catechin, chlorogenic acid, caffeic acid, *p*-coumaric acid and ferulic acid (Del Mar Verde Méndez et al. 2004). Potato samples belonging to Colorado cultivar, ssp. *andigena*, had mean concentrations of total phenolic compounds and chlorogenic acid higher than those found for Kerr's Pink and Cara cultivars, ssp. *tuberosum*, and for Negra cultivar, *S. x chaucha*. In contrast, *p*-coumaric acid

was not detected in any potato samples of the Colorado cultivar. Traditional potatoes presented a higher mean concentration of ferulic acid than recently imported potatoes. Polyphenol (phenolic acids, flavanols and flavonols) contents decreased from the tuber peel (2 mm) via the outer (1 cm) to the inner flesh and differed among potato cultivars grown in Luxembourg (Deusser et al. 2012). The cultivars Vitelotte and Luminella had the highest polyphenol contents (5202 and 572 $\mu\text{g/g}$ dry weight (DW) in the outer flesh), whereas Charlotte and Bintje had the lowest contents (19.5 and 48.0 $\mu\text{g/g}$ DW). Chlorogenic acid and its isomers (neo- and cryptochlorogenic acid) were the major polyphenols. Glycoalkaloid (α -chaconine and α -solanine) contents were highest in the peel and lowest in the inner flesh; values in the flesh were below guideline limits in all cultivars. Phenylpropanoids, including chlorogenic acid (CGA), were higher in potato samples from the northern latitudes, as was the expression of phenylpropanoid genes including phenylalanine ammonia lyase (PAL), which had over a tenfold difference in relative abundance (Payyavula et al. 2012). Phenylpropanoid gene expression appeared coordinately regulated and was well correlated with metabolite pools, except for hydroxycinnamoyl-CoA:quinatehydroxycinnamoyl transferase. Anthocyanins were more abundant in Alaskan samples and correlated with flavonoid genes including dihydroflavonol-4-reductase (DFR) ($R^2 = 0.91$), UDP-glucose:flavonoid 3-*O*-glucosyltransferase (UGT) ($R^2 = 0.94$) and flavanone 3-hydroxylase (F3H) ($R^2 = 0.77$). The most abundant anthocyanin was petunidin-3-coum-rutinoside-5-glucoside, which ranged from 4.7 mg/g in Alaska to 2.3 mg/g in Texas. Positive correlations between tuber sucrose and anthocyanins ($R^2 = 0.85$) suggested a stimulatory effect of sucrose. Smaller variation was observed in total carotenoids, but marked differences occurred in individual carotenoids, which had over a tenfold range. Violaxanthin, lutein and zeaxanthin were the predominant carotenoids in tubers from Alaska, Texas and Florida, respectively. Unlike in the phenylpropanoid pathway, poor correlations occurred between carotenoid transcripts and metabolites. Among purple, white and yellow potatoes, purple potatoes contained the most total phenolics, which decreased

during development (from 14 to 10 mg/g), as did the activity of phenylalanine ammonia lyase (Payyavula et al. 2013). The major phenolic, 5-chlorogenic acid (5CGA), decreased during development in all cultivars. Products of later branches of the phenylpropanoid pathway also decreased, including quercetin 3-*O*-rutinoside, kaempferol 3-*O*-rutinoside and petunidin 3-*O*-(*p*-coumaroyl)rutinoside-3-glucoside (from 6.4 to 4.0 mg/g). Violaxanthin and lutein were the two most abundant carotenoids and decreased 30–70 % in the yellow and white potatoes. Sucrose, which could regulate phenylpropanoid metabolism, decreased with development in all cultivars and was highest in purple potatoes. Total protein decreased by 15–30 % in two cultivars. Expression of most phenylpropanoid and carotenoid structural genes decreased during development. Navarre et al. (2013) found that the nutritional value of potatoes varied in accordance with changes in phenylpropanoid metabolism during tuber development. Phenylpropanoid concentrations were highest in immature tubers, as were some transcript levels and enzyme activities including phenylalanine ammonia lyase (PAL). Phenylpropanoid concentration differences between mature and immature tubers varied by genotype but in some cases were approximately threefold. The most abundant phenylpropanoid was chlorogenic acid (5CGA), which decreased during tuber maturation. Hydroxycinnamoyl-CoA:quinate hydroxycinnamoyl transferase (HQT) transcripts were highly expressed relative to other phenylpropanoid genes, but were not well correlated with 5CGA concentrations ($R^2 = -0.16$), whereas HQT enzyme activity was. In contrast to 5CGA, less abundant chlorogenic isomers increased during development. Concentrations of hydroxycinnamic acid amides were higher in immature tubers, as was expression of arginine and ornithine decarboxylases. Expression of several genes involved in carbohydrate or shikimate metabolism, including sucrose synthase and 3-deoxy-D-arabino-heptulosonate 7-phosphate (DAHP), showed similar developmental patterns to phenylpropanoid pools, as did shikimate dehydrogenase enzyme activity. Sucrose, glucose and fructose concentrations were highest in immature tubers. Exogenous treatment of potatoes with sugars stimulated phenylpropanoid biosynthesis,

suggesting sugars contributed to the higher phenylpropanoid concentrations in immature tubers.

A total of 62 HCAs (hydroxycinnamic acids)/its conjugates HCAs (chlorogenic acid, cryptochlorogenic acid and neochlorogenic acid)/DHCAs (dihydrohydroxycinnamic acid conjugates) were found in extracts from peel and flesh of 15 Colombian potato cultivars (Narváez-Cuenca et al. 2013). Among them, only twelve compounds were common to all cultivars in both peel and flesh. The less commonly described compounds accounted for 7.1–20.1 % w/w of the total amount of HCAs/HCAcs/DHCAcs in whole tubers, highlighting their contribution to the total phenolic profile of potato tubers. Among the 15 Colombian cultivars, the abundance (mg/100 g DW whole tuber) of neochlorogenic acid (0.8–7.4 mg) ranged in similar quantities as the less commonly reported feruloyl octopamine (1.2–5.2 mg), 5-*O*-feruloyl quinic acid (0.1–7.5 mg), *cis*- chlorogenic acid (1.1–2.2 mg), caffeoyl putrescine (0.6–2.5 mg), sinapoyl hexose (0.1–1.8 mg), N^1, N^{14} -*bis*-(dihydrocaffeoyl)spermine (0.2–1.7 mg), N^1, N^{10} -*bis*-(dihydrocaffeoyl)spermidine (1.1–2.6 mg) and N^1, N^5, N^{14} -*tris*-(dihydrocaffeoyl)spermine (trace, 11.1 mg). A total of 31 compounds were identified and quantified in a white potato cultivar and a purple potato cultivar, Urenika, extracts (Chong et al. 2013). The compounds included several types of anthocyanins, hydroxycinnamic acid (HCA) derivatives and hydroxycinnamic amides (HCAA). Six classes of compounds, namely, organic acids, amino acids, HCA, HCAA, flavonols and glycoalkaloids, were present in both extracts, but quantities varied between the two extracts.

Monomeric anthocyanin content in red-fleshed potatoes (*Solanum tuberosum* and *S. stenotomum*) ranged from 2 to 40 mg/100 g tuber fresh weight (Rodriguez-Saona et al. 1998). Two breeding clones, NDOP5847–1 and NDC4069–4, showed anthocyanin content >35 mg/100 g. All red potato samples showed similar pigment profiles, with pelargonidin-3-rutinoside-5-glucoside acylated with *p*-coumaric acid being the major anthocyanin (ca 70 %). The presence of glycoalkaloids in colour extracts was also detected. Some red-

fleshed potatoes may be good potential sources of food colourants.

Anthocyanin content was as high as 150 mg cyanidin-3-glucoside equivalent/100 g (*Solanum stenotomum* subsp. *stenotomum*), and total phenolic content ranged from 110 mg (*S. stenotomum* subsp. *goniocalyx*) to 5120 mg (*S. tuberosum* subsp. *andigenum*) of GAE/100 g DW in 20 varieties of native Andean potatoes from 4 different *Solanum* species of different colours (Guisti et al. 2014). The presence of chlorogenic, caffeic, coumaric, ferulic, sinapic, gallic and protocatechuic acids had been reported in potatoes (Rodriguez-Saona et al. 1998; Lewis et al. 1998a; Reddivari et al. 2007a, b). Recently, Guisti et al. (2014) identified that the following phenolic compounds were tyrosine, 3-*O*-caffeoylquinnic acid, chlorogenic acid, 4-*O*-caffeoylquinnic acid, caffeic acid and quercetin–rutinoside derivative. Three anthocyanidins were identified in red potato extracts (cyanidin, pelargonidin and peonidin) and four anthocyanidins identified in the saponified samples of red potato extracts (cyanidin-3-rutinoside-glucoside, pelargonidin-3-rutinoside-5-glucoside (predominant), peonidin-3-rutinoside-5-glucoside and pelargonidin-3-rutinoside) (Guisti et al. 2014). Major anthocyanins identified in the red potato extracts were pelargonidin-3-rutinoside-5-glucoside, pelargonidin-3-caffeoyl-rutinoside-5-glucoside, petunidin-3-caffeoyl-rutinoside-5-glucoside, petunidin-3-*p*-coumaroyl-rutinoside-5-glucoside, pelargonidin-3-*p*-coumaroyl-rutinoside-5-glucoside, peonidin-3-*p*-coumaroyl-rutinoside-5-glucoside, pelargonidin-3-ferruloyl-rutinoside-5-glucoside and petunidin-3-ferruloyl-rutinoside-5-glucoside. Five major anthocyanidins were identified in purple potato extracts: cyanidin, petunidin, pelargonidin, peonidin and malvidin. Petunidin and peonidin were the most predominant anthocyanidins in purple potato extract. Anthocyanidins identified in saponified purple potato extracts were cyanidin 3-rutinoside-5-glucoside, petunidin-3-rutinoside-5-glucoside, pelargonidin-3-rutinoside-5-glucoside, petunidin-3-rutinoside-5-glucoside and malvidin-3-rutinoside-5-glucoside. Eight major anthocyanins were identified in purple potato extracts: petunidin-3-caffeoyl-rutinoside-5-glucoside, cyanidin-3-*p*-coumaroyl-rutinoside-5-glucoside,

petunidin-3-*p*-coumaroyl-rutinoside-5-glucoside, petunidin-3-ferruloyl-rutinoside-5-glucoside, pelargonidin-3-*p*-coumaroyl-rutinoside-5-glucoside, peonidin-3-*p*-coumaroyl-rutinoside-5-glucoside, malvidin-3-*p*-coumaroyl-rutinoside-5-glucoside and peonidin-3-ferruloyl-rutinoside-5-glucoside.

Anthocyanin composition of coloured sections of potato tubers of genotypes CO97216-3P/PW comprised ten detectable anthocyanins, pelargonidin-3-*p*-coumaroylrutinoside-5-glucoside, cyanidin-3-*p*-coumaroylrutinoside-5-glucoside, peonidin-3-*p*-coumaroylrutinoside-5-glucoside, petunidin-3-*p*-coumaroylrutinoside-5-glucoside, malvidin-3-*p*-coumaroylrutinoside-5-glucoside, malvidin-3-*o*-caffeoyl-rutinoside-5-glucoside, delphinidin-3-*p*-coumaroylrutinoside-5-glucoside, petunidin-3-*o*-caffeoyl-rutinoside-5-glucoside, malvidin-3-rutinoside-5-glucoside and petunidin-3-rutinoside-5-glucoside, but two components, malvidin-3-*p*-coumaroylrutinoside-5-glucoside (trivial name negretetin) and petunidin-3-*p*-coumaroylrutinoside-5-glucoside (trivial name petanin), predominated (Stushnoff et al. 2010). The non-pigmented section also accumulated anthocyanins, but to a much lesser degree. The ratio of accumulation of individual anthocyanins varied between 2.5-fold higher for the minor components to 20-fold higher for the dominant anthocyanins. The anthocyanin content was, on average, 6.7-fold higher in the pigmented tissues. The pigmented tissues also had approximately 2.5-fold higher levels of chlorogenic acid than the non-pigmented sections suggesting a general increase in phenolic components. However, the levels of two other major phenolic components, feruloyl and caffeoyl putrescine, were not significantly different. There were also no significant differences in ascorbate or glutathione levels or indeed in their oxidation state. However, the major glycoalkaloids, solanine and chaconine, were elevated in the purple tissue over the non-pigmented tissues. The pigmented genotypes Purple Majesty (PM), Mountain Rose (MRR), CO97216-1P/P (216) and CO97226-2R/R (226) had higher anthocyanin and total phenol contents than the non-pigmented genotypes. The red genotypes, MR and 226, contained mainly pelargonidin-3-*p*-coumaroylrutinoside-5-glucoside, whereas the purple

genotypes, PM and 216, contained a wider range of anthocyanins, but petunidin- and malvidin-3-*p*-coumaroylrutinoside-5-glucoside derivatives predominated. It was notable that only 216 contained appreciable amounts of peonidin-3-*p*-coumaroylrutinoside-5-glucoside. The higher total phenol content was reflected in the levels of the major polyphenolic component of potato tubers, chlorogenic acid, which was substantially higher in the pigmented genotypes (216, 226, PM and MRR) than the non-pigmented genotypes. However, this trend did not apply to all polyphenolic components as illustrated by the levels of detectable hydroxycinnamic amine derivatives. Two pigmented genotypes (216 and 226) had considerably elevated levels of glycoalkaloids compared with other genotypes.

The biosynthetic pathway for anthocyanins, caffeoylquinates and other major phenolic derivatives (tyrosine, caffeoylputrescine, feruloyl putrescine) in potato tuber were schematically described by Stushnoff et al. (2010). The enzymes involved in the biosynthesis of anthocyanins pelargonidin from dihydrokaempferol were dihydroflavonol reductase (DFR), anthocyanin synthase (AS) and UDP-glucose:3-*O*-flavonoid glucosyltransferase (GFG); from dihydroquercetin to cyanidin were DFR, AS and GFG and from cyanidin to peonidin anthocyanidin-glycoside-3'-*O*-methyl transferase (AGMT); from dihydromyricetin to delphinidin were DFR, AS and GFG and from delphinidin to petunidin AGMT; and from petunidin to malvidin AGMT. The enzymes involved in anthocyanin glycosylation were anthocyanidin-3-*O*-glycosyl transferase (A3GT), anthocyanidin-5-*O*-glycosyl transferase (A5GT) and UDP-glucose:3-*O*-flavonoid glucosyltransferase (GFG). AGA (anthocyanidin-3'-*O*-glycoside-6'-*O*-acyl transferase) incorporated anthocyanin glycosides with hydroxycinnamoyl groups. Other enzymes involved in the biosynthesis of caffeoylquinates and other major enzymes were arogonate dehydratase (ADT), chalcone isomerase (CHI), chalcone synthase (CHS), cinnamate-4-hydroxylase (C4H), 4-coumarate ligase (4CL), chorismate mutase (CM), flavonone-3-hydroxylase (F3H), ferulate 5-hydroxylase (F5H), flavonoid-3'-hydroxylase (F3'H), flavonoid-3',5'-hydroxylase

(F3'5'H), flavonol synthase (FLS), hydroxycinnamoyl-CoA:shikimate hydroxycinnamoyl transferase (HCT), hydroxycinnamoyl-CoA:quinate hydroxycinnamoyl transferase (HQT), phenylalanine ammonia lyase (PAL), prephenate dehydratase (PDH) and putrescine N-hydroxycinnamoyl transferase (PHT). Also, common genes that were differentially expressed both in the purple versus white sector included caffeoyl-CoA *O*-methyltransferase, leucoanthocyanidin dioxygenase, glutathione *S*-transferase, dihydroflavonol 4-reductase, cytochrome *b5*, cytochrome *b5* DIF-F, MYB transcription factor MYB73, salicylic acid-binding protein 2, specific tissue protein 2, organ-specific protein S2, flavanone 3 β -hydroxylase, lipase class 3, anthocyanin 1, putative orcinol *O*-methyltransferase, cytochrome P450, phosphoprotein phosphatase, putative disease resistance protein and epoxide hydrolase I (Stushnoff et al. 2010).

Studies showed that concentrated culture filtrate (CCF) of *Phytophthora infestans* but not lipopolysaccharides (LPS) from *Pectobacterium atrosepticum* induced differential accumulation of major phenolics chlorogenic acid, phenolamides and flavonols including rutin (quercetin-3-*O*-rutinoside) and nicotiflorin (kaempferol-3-*O*-rutinoside) among 5 potato cultivars (Kröner et al. 2012). Total phenolics were related with resistance to *P. atrosepticum* but not to *P. infestans*. However, nicotiflorin was inversely related with resistance to both pathogens. Rutin, but not nicotiflorin, inhibited pathogen growth in-vitro at physiological concentrations.

Fresh cutting of five long-term-stored potato cultivars (Agria, Cara, Liseta, Monalisa and Spunta) induced the biosynthesis of three flavonols, quercetin 3-rutinoside, quercetin 3-diglucoside and quercetin 3-glucosylrutinoside (Tudela et al. 2002). The flavonols were detected after a lag period of 3 days of cold storage. The content ranged from 6 to 14 mg/100 g of fresh weight depending on the cultivar after 6 days of storage. Chlorogenic acid as the main caffeic acid derivative and the amino acids, tyrosine and tryptophan were also quantified. The flavonol induction was higher in fresh-cut

potatoes stored under light than in the dark. Domestic cooking such as boiling, microwaving and frying provoked a partial loss of the flavonols, which were retained in the range of 4–16 mg per serving (213 g). Steam cooking resulted in the highest retention of caffeic acid derivatives and aromatic amino acids compared with the other cooking methods studied. The results implied that due to the large amount of potatoes consumed in the Western diet, fresh-cut potatoes could be a significant source of health-promoting phenolics. For the pigmented potatoes, cooking heating treatment did not cause any changes in the phenolic acids content, while anthocyanins showed only a small decrement (16–29 %) (Mulinacci et al. 2008). The cv. Highland Burgundy Red showed anthocyanins and phenolic acid concentrations close to 1 g/kg and more than 1.1 g/kg, respectively. Vitellotte Noire showed the highest amounts of resistant starch. Potato starch digestibility and % of resistant starch, considered as a component of dietary fibre, were affected both by cultivar and by heating/cooling treatments.

Potato Suberin and Waxes

Suberin a cell-wall biopolymer with aliphatic and aromatic domains had been reported to consist a fatty acid polyester with esterified ferulic acid (Serra et al. 2010). In potato, ferulic acid esters were also the main components of periderm wax. Suberin and waxes embedded in the suberin polymer were reported to be key compounds in the control of transpiration in the tuber periderm of potato. They reported a potato gene encoding a fatty ω -hydroxy acid/fatty alcohol hydroxycinnamoyl transferase (FHT), which was involved in the biosynthesis of suberin and suberin-associated wax in the biosynthesis of suberin and suberin-associated wax. Suberin in potato wound periderm was known to be a polyester containing long-chain fatty acids and phenolics embedded within the cell wall (Yan and Stark 2000). Carboxyl-labelled phenylalanine precursors provide evidence for the concurrent development of phenolic esters and of monolignols typical of lignin. Experiments with ring-labelled phenylalanine precursors demonstrate a predominance of sinapyl and guaiacyl structures among suberin's phenolic moieties. It was

found that the insoluble intermediates of suberin biosynthesis indicated probable covalent linkages between moieties of its polyester and polysaccharide domains. Bernards and Razem (2001) described a hydrogen peroxide-generating system with NAD(P)H-dependent oxidase-like properties associated with the oxidation of hydroxycinnamic acids (and their derivatives) in the formation of potato suberin poly(phenolics) during suberisation. Native and wound periderm of potato tuber contained up to 20 % extractable lipids (waxes) (Schreiber et al. 2005). Besides linear long-chain aliphatic wax compounds, alkyl ferulates were detected as significant constituents. In wound periderm they amounted to more than 60 % of the total extracts. Within 1 month of storage, suberin amounts in the polymer increased twofold in native periderm ($180 \mu\text{g}/\text{cm}^2$), whereas in wound periderm about $75.0 \mu\text{g}/\text{cm}^2$ suberin polymer was newly synthesised. Among the isolated fragments from controlled hydrolysis of the suberin aliphatic or aromatic domains were two hydroxyphenyl derivatives reported previously in lignins and a novel aliphatic–aromatic ester trimer (Arrieta-Baez and Stark 2006). Together these protocols helped to characterise the carbohydrate types that were bound covalently to the suberin polyester and to identify the interunit covalent linkages among the aliphatic ester, phenolic and carbohydrate moieties in suberised potato tissue. Depolymerisations of potato suberin by cutinase-catalysed hydrolysis produced higher proportions of aliphatic monomers than hydrolysis with the NaOMe procedure (Järvinen et al. 2009). Monomers released by the two methods were mainly α , ω -dioic acids and ω -hydroxy acids, but the ratios of the detected monomers were different, at 40.0 and 32.7 % for methanolysis and 64.6 and 8.2 % for cutinase, respectively. The most abundant monomeric compounds were octadec-9-ene-1,18-dioic acid and 18-hydroxyoctadec-9-enoic acid, which accounted for ca. 37 and 28 % of all monomers, respectively. A suberin-enriched fraction, molecular weight (MW) = ca. $44 \times 10^3 \text{ g/mol}$, silated from potato, was found to be a mixture of carbohydrates and polyesters of aliphatic long-chain hydroxy fatty acids and diacids linked via ester bonds to the phenolics, MW = ca. $27 \times 10^3 \text{ g/mol}$, formed by guaiacyl and *p*-hydroxyphenyl structures (Mattinen et al. 2009).

Phenolics in potato peels may be important sources of antioxidants for various applications.

Composition of periderm wax of potato tuber was reported as hydrocarbon 31 %, wax ester 7 %, fatty alcohol 24 %, fatty acid 11 % and unknown 27 % (Espelie et al. 1980). Chain-length distribution of the fatty alcohols, fatty acids, ω -hydroxy acids and dicarboxylic acids in the polar fraction of the chloroform extract of potato tuber were fatty alcohols C₁₆ (0.03 %), C₁₈ (0.03 %), C₂₀ (0.02 %), C₂₂ (0.01 %), C₂₄ (0.02 %), C₂₆ (0.05 %) and C₂₈ (0.05 %); fatty acids C₁₆ (0.04 %), C₁₈ (0.03 %), C₂₀ (0.02 %), C₂₂ (0.03 %), C₂₄ (0.04 %), C₂₆ (0.05 %) and C₂₈ (0.05 %); ω -hydroxy acids C₂₂ (0.01 %) and C₂₄ (<0.01 %); and dicarboxylic acids C₂₂ (<0.01 %) and C₂₄ (<0.01 %). Substance classes detected in chloroform/methanol extracts of native and wound periderm of potato tuber were linear long-chain aliphatic compounds (alkanes, alcohols and carboxylic acids) and aromatic compounds (mainly esters between primary alcohols and ferulic acid and, in traces, caffeic acid and feroyltyramine) Schreiber et al. 2005). In native periderm the aromatic fraction amounted to about two-thirds of the aliphatic fraction after 28 days. In wound periderm aliphatic and aromatic fractions were present in equal amounts up to 21 days. Carboxylic acids in ferulic acid esters had chain lengths ranging from C₁₆ to C₃₂ with the chain lengths C₁₆, C₁₈, C₂₁, C₂₃, C₂₈ and C₃₀ dominating. The suberin content of native periderm increased with storage time (0–28 days) from 100 to 180 $\mu\text{g}/\text{cm}^2$. The amount of newly forming wound periderm reached 75 $\mu\text{g}/\text{cm}^2$ after 30 days. Substance classes detected consisted of linear long-chain aliphatic compounds (alcohols, carboxylic acids, α,ω -dicarboxylic acids, ω -hydroxy acids and 2-hydroxy acids) and of aromatic compounds (coumaric, ferulic and anisinic acids). In both native and wound periderm, chain lengths of 2-hydroxy fatty acids slightly decreased during storage time.

The principal components of potato leaf cuticular waxes were very long-chain n-alkanes, 2-methylalkanes and 3-methylalkanes (3.1–4.6 $\mu\text{g}/\text{cm}^2$), primary alcohols (0.3–0.7

$\mu\text{g}/\text{cm}^2$), fatty acids (0.3–0.6 $\mu\text{g}/\text{cm}^2$) and wax esters (0.1–0.4 $\mu\text{g}/\text{cm}^2$) (Szafranek and Synak 2006). The most abundant hydrocarbons were n-hentriacontane, 2-methyltriacontane, n-nonacosane and n-heptacosane. The relative composition of the alkanes was very similar in the four cultivars. The major primary alcohols were 1-tetracosanol (12–18 % of the total 1-alkanols), 1-hexacosanol (39–42 %) and 1-octacosanol (24–29 %). The distribution pattern was very similar in all four potato varieties. The most abundant fatty acids were tetracosanoic acid (32–46 % of the total fatty acids) and hexacosanoic acid (19–25 %). Three of the potato varieties displayed similar distributions of fatty acid homologues, but the Perkoz contained a relatively higher percentage of triacontanoic acid (20 %). A homologous series of very long-chain secondary alcohols was identified in the potato leaf waxes. The fragmentation patterns of the mass spectra of native 2-alkanols derived from potato waxes were similar to those of the 2-hexadecanol and 2-tricosanol standards. The sterol fraction consisted of two constituents only, cholesterol (1–60 ng/cm^2) and β -sitosterol; the terpenoid β -amyirin was also found. A homologous series of methyl ketones (2-ketones, alkan-2-ones) with chain lengths from C_{25} to C_{33} was present in the potato waxes. Potato methyl ketones were accompanied by ketones with the carbonyl group in positions 8, 10, 12, 14 and 16 as follows: nonacosanone, nonacosane-8-one, nonacosane-10-one, nonacosane-12-one and nonacosane-14-one; hentriacontanone, hentriacontan-8-one, hentriacontan-10-one, hentriacontan-12-one, hentriacontan-14-one and hentriacontan-16-one; tritriacontanone, tritriacontan-8-one, tritriacontan-10-one, tritriacontan-12-one, tritriacontan-14-one and tritriacontan-16-one. Potato waxes also contained detectable levels of very long-chain C_{22} to C_{32} aldehydes (13–17 ng/cm^2). The most abundant of these were tetracosanal, hexacosanal, octacosanal and triacontanal. The distribution patterns of individual aldehydes were all quite similar in three of the four potato varieties studied; the exception was the Perkoz variety, which contained larger amounts of triacontanal and less hexacosanal. Homologous esters of very long-chain fatty acids with long primary

alcohols (wax esters) were present in the cuticular waxes of the four potato varieties, but at different levels. The wax ester constituents were saturated straight-chain fatty acids and primary alcohols from C₁₄ to C₂₈ and from C₂₀ to C₂₈, respectively. The main esters were those of hexadecanoic (ca. 20 %), octadecanoic (10 %), eicosanoic (30 %), docosanoic (15 %) and tetracosanoic (8 %) acids. The distribution patterns of the fatty acids in the wax esters differed from those of the free fatty acids in potato waxes. The alcohols liberated from the wax esters consisted predominantly of docosanol (ca. 17 %), tetracosanol (20 %), hexacosanol (30 %) and octacosanol (15 %). Also present were benzoic acid esters and methyl, ethyl, isopropyl and 2-phenylethyl esters of fatty acids. Benzoic acid hexacosanyl, tetracosanyl and pentacosanyl esters predominated in the potato waxes. Potato waxes from all four varieties contained methyl esters of the even-carbon-numbered acids from C₁₆ to C₂₆ with yields from 2 to 8 ng/cm². Besides the methyl esters of saturated fatty acids, methyl linoleate and methyl linolenate were also present. The most prominent methyl esters were those of low molecular weight fatty acids (C16:0, C18:2, C18:3, C18:0). In addition, ethyl esters of saturated fatty acids (C16–C26)—mainly the ethyl esters of hexadecanoic, octadecanoic, eicosanoic and tetracosanoic acids—were found as minor components.

Phytohormones and Endogenous Tuber-Inducing Compounds

Potato plant had been reported to contain phytohormones like jasmonic acid, auxins (IAA), gibberellins (GA), cytokinins, abscisic acid (ABA), ethylene and strigolactones. The involvement of all major classes of endogenous hormones in potato tuber dormancy was reviewed by Suttle [2004b](#)). Based on available evidence, it was concluded that both ABA and ethylene were required for dormancy induction, but only ABA was needed to maintain bud dormancy. An increase in cytokinin sensitivity and content appeared to be the principal factors leading to the loss of dormancy. Changes in

endogenous IAA and GA content appeared to be more closely related to the regulation of subsequent sprout growth.

Cytokinin-like substances were found in potato tubers near the end of their innate dormant period (Engelbrecht and Bielinska-Czarnecka 1972). Alcoholic extracts of potato tubers were found to contain cytokinins which could be separated from endogenous growth inhibitors (Antis and Northcote 1975). Three cell division inducing cytokinin compounds were extracted from sprouting potato tubers (Van Staden 1976). They were identified as zeatin riboside, isopentenyladenosine and isopentenyladenine. The main cytokinin detected in the water-soluble fraction of potato tuber was identified as zeatin ribotide (Koda 1982). The level of butanol-soluble cytokinin in elongating stolon tips was low, while that of water-soluble cytokinin was extremely high. Upon swelling of the stolon tips, the former increased greatly as the latter decreased. Following fractionation by HPLC, a total of eight endogenous cytokinins were detected in potato cv. Russet Burbank tuber apical bud tissue, and these were zeatin riboside-5'-monophosphate (ZRMP), zeatin-*O*-glucoside (ZOG), zeatin (Z), zeatin riboside (ZR), isopentenyl adenosine-5'-monophosphate (IPMP), isopentenyl adenine-9-glucoside (IP-9-G), isopentenyl adenine (IP) and isopentenyl adenosine (IPA) (Suttle 1998b). Regardless of postharvest storage temperature or endodormancy status, IP-9-G was the most abundant cytokinin detected, while ZRMP and ZOG were the least abundant ones. In tubers preincubated at a growth-permissive temperature (20 °C) prior to extraction, the loss of endodormancy was preceded by significant increases in the endogenous levels of Z, ZR, IPMP and IP-9-G. When stored continuously at a growth-inhibiting temperature (3 °C), significant increases in ZR, IP-9-G and IP + IPA were observed. The total content of cytokinins increased by over sevenfold during postharvest storage, and this increase was a result of de novo biosynthesis.

Potato tubers stored in 80 % O₂ and 12 % CO₂ produced ethylene at much higher rates (Creech et al. 1973). In all cases where sprouting occurred, the rate of ethylene production increased. Endogenous ethylene was found to be essential for

the full expression of potato microtuber endodormancy, and its involvement may be restricted to the initial period of endodormancy development (Suttle 1998a).

Potato (cv. Russet Burbank) microtubers generated in-vitro from single-node explants contained substantial amounts (approximately 250 pmol/g fresh weight) of free abscisic acid (ABA) and were completely dormant for a minimum of 12 weeks (Suttle and Hultstrand 1994). Microtubers that developed in the presence of 10 tzm fluridone (FLD) contained considerably reduced amounts (approximately 5–25 pmol (g fresh weight) of free ABA and exhibited a precocious loss of dormancy. Suttle (1995) demonstrated that ABA was readily metabolised by potato tubers and that the principal route of catabolism consisted of the oxidative metabolism of ABA to phaseic and dihydrophaseic acids with minimal esterification to conjugated ABA. The results also suggest that a decline in endogenous ABA below a threshold level was not a prerequisite for the loss of potato tuber dormancy and the onset of sprout growth.

Immediately after harvest, the endogenous contents of gibberellins GA₁₉, GA₂₀ and GA₁ were relatively high (0.48–0.62 ng/g fresh weight) in potato tubers (Suttle 2004a). The content of these GAs declined between 33 and 93 days of storage. Internal levels of GA₁₉, GA₂₀ and GA₁ rose slightly between 93 and 135 days of storage reaching levels comparable to those found in highly dormant tubers immediately after harvest. Levels of GA₁₉, GA₂₀ and GA₁ continued to increase as sprout growth became more vigorous. Neither GA₄ nor GA₈ was detected in any tuber sample regardless of dormancy status. Dormant tubers exhibited a time-dependent increase in apparent GA sensitivity. The results did not support a role for endogenous GA in potato tuber dormancy release but were consistent with a role for GAs in the regulation of subsequent sprout growth.

Tuberisation in potato plants had been considered to be controlled both by tuberonic acid TA and its glucoside formed in leaves under short-day conditions (Koda and Okazawa 1988; Koda et al. 1988). The tuber-inducing compound from

potato leaves was identified as 3-oxo-2-(5'- β -D-glucopyranosyloxy-2'-Z-pentenyl)-cyclopentane-1-acetic acid, and its aglycone was named as tuberonic acid (Yoshihara et al. 1989). The chemical structure of tuberonic acid (3-oxo-2-[5-hydroxy-2-cis-pentenyl]-cyclopentane-1-acetic acid), the aglycone of a potato tuber-inducing substance isolated from potato leaves, was closely related to that of jasmonic acid (Koda et al. 1991). Jasmonic acid and its methyl ester showed strong tuber-inducing activity (Koda et al. 1991, 1992a).

Jasmonic acid endogenous level in potato tubers with unsprouted buds was 325 ng/g dry weight, diminishing during sprouting to 164 ng (Castro et al. 1999). The high levels of jasmonic acid found in potato tuber buds in correlation with the capacity of this compound to induce radial expansion of the meristematic cells in the buds indicated the participation of jasmonic acid in the growth of these organs during the process of bud transformation into sprouts. Theobroxide a natural compound from the fungus *Lasiodiplodia theobromae* was found to have a significantly inductive effect on potato tuber formation in-vitro and in-vivo. The results suggested that the inductive effect of theobroxide on tuber formation is probably achieved by stimulating jasmonic acid (JA) and tuberonic acid (TA) synthesis as it increased endogenous levels of JA and TA and lipoxygenase (LOX) activity.

No significant changes were found in free auxin (indole-3-acetic acid, IAA) level during dormancy of potato tubers stored at 4 °C followed by a rapid decrease during sprouting (Sukhova et al. 1993). It was found that IAA did not appear to have a significant effect on tuber dormancy, while cytokinins were probably necessary for sprouting initiation. Under non-inductive long-day (LD) conditions, the free auxin IAA concentration increased from the apex to the lower parts of the potato plant (Roumeliotis et al. 2012). Average IAA concentrations of 560, 2510 and 3250 pmol of IAA/g fresh weight (FW) were measured for the shoot apex, middle and basal part of the stem, respectively. Under LD conditions, the free auxin concentration in the stolon apical meristem (STAM) was 270 pmol/g FW. After a small initial decrease after the switch to SD (inductive) conditions on day 5 (70 pmol/g FW),

IAA levels increased dramatically to a maximum of 1050 pmol/g FW on day 16, at which time the first tubers were observed. The tuber apex had the lowest concentrations of free IAA (110 pmol/g FW) but in similar concentration ranges to those in the perimedullary region (120 pmol/g FW) and the pith (170 pmol/g FW). The highest concentration of IAA was observed in the tuber heel (240 pmol). IAA levels of whole tuber samples were ~160 pmol/g FW, significantly less than at tuber swelling (1050 pmol/g FW). Strigolactones were detected in stolons of in-vivo growing potato plants, and the role these may play in tuberisation remained unclear. Strigolactones were measured for the first time in potato roots. Studies suggested that auxin and strigolactone had the capacity to modulate each other's levels and distribution in a dynamic feedback loop required for the coordinated control of axillary shoot branching (Gomez-Roldan et al. 2008; Hayward et al. 2009). The results of a recent study by Pasare et al. (2013) suggested that strigolactones could have an effect, solely or in combination with other phytohormones, in the morphology of potato plants and also in controlling stolon development and maintaining tuber dormancy.

Potato leaves were found to contain a high basal level of free and conjugated salicylic acid (Yu et al. 1997). HPLC of acidic compounds from potato leaves soluble in aqueous methanol showed the presence of salicylic acid, benzoic acid, ferulic acid, caffeic acid or cinnamic acid (Coquoz et al. 1998). Radiolabelling studies with untreated leaves showed that salicylic acid was synthesised from phenylalanine and that both cinnamic and benzoic acid were intermediates in the biosynthesis pathway. However, the natural occurrence of salicylic acid was not detected in the leaves of potato plants that had been grown under tuber-inducing conditions (short days) and had begun to form tubers (Koda et al. 1992b). The results appeared to exclude the possibility of the involvement of salicylic acid in the natural tuberisation of potato plants.

Alkaloids

Solanine was first reported in potato by Baup (1826) who found much higher levels in the sprouts than in the tuber. The

major glycoalkaloids in the cultivated potato were reported to be α -, β - and γ -solanine and α -, β - and γ -chaconine, all six compounds having the same steroidal base (solanidine) but differing in the attached sugar molecule linked glycosidically (Bretzlöff 1971). Potato tubers contained glycoalkaloids, α -solanine and α -chaconine, and the aglycones, demissidine and solasodine (Cahill et al. 2010). A means of distinguishing solanidine and demissidine by formation of their respective 3 β -trifluoroacetates with trifluoroacetic anhydride was demonstrated using gas–liquid chromatography (King 1980). Two major steroid glycoalkaloids, in addition to α -solanine and α -chaconine, were isolated from leaves and aged tuber slices of potato, *Solanum tuberosum* var. Kennebec, which possessed the germplasm of *Solanum demissum* (Shih and Kuć 1974). They were glycosides of tomatidenol and were identified as α - and β -solamarine. The compounds were not found in tuber peel or freshly sliced Kennebec tubers or in 20 other cultivars. The total glycoalkaloid content of the aged potato slices increased dramatically on ageing; α -solanine and α -chaconine both increased in these slices, but the greatest increase was in the former (Fitzpatrick et al. 1977). Appearing solely in the aged slices of potato Kennebec variety, α - and β -solamarine appeared early in the storage period and gradually decreased over the storage period. Analyses of the unaged slices indicated that the glycoalkaloid content and composition of the potato tubers was little affected by storage. Ageing of potato sprouts did not change their glycoalkaloid content.

The glycoalkaloids, aglycones and carbohydrate components found in *Solanum* species including *S. tuberosum* were reported by Woolfe and Poats (1987): glycoalkaloid α -solanine, its aglycone solanidine and carbohydrate components trisaccharide, solatriose (D-galactose, L-rhamnose, D-glucose); glycoalkaloid α -chaconine, its aglycone solanidine and carbohydrate component trisaccharide, chacotriose (D-glucose and 2 molecules of L-rhamnose); glycoalkaloid dehydrocommersonine, its aglycone solanidine and carbohydrate component tetrasaccharide, commertetrose (D-galactose and 3 molecules of D-glucose); glycoalkaloid demissine, its aglycone demissidine and carbohydrate component tetrasaccharide, lycotetraose (D-galactose, D-

glucose, D-glucose, D-xylose); glycoalkaloid α -solanine, its aglycone tomatidenol and carbohydrate component trisaccharide, solatriose (D-galactose, L-rhamnose, D-glucose); and glycoalkaloid β -solanine, its aglycone tomatidenol and carbohydrate component trisaccharide chacotriose (D-glucose, 2 molecules of L-rhamnose). Glycoalkaloids β - and γ -solanines and β - and γ -chaconines were products of partial hydrolysis of the respective α -glycosides.

Solanidin glycosides (mg/kg FW) had been reported in all parts of potato plant. Highest concentrations were found in flowers 2150–5000 mg (Lampitt et al. 1943; Wood and Young 1974; Kozukue et al. 1987); flower petals 3060–4970 mg and calyces 4770–5710 mg (Kozukue et al. 1987); unripe berries 420–1080 mg (Boemer and Mattis 1924; Lampitt et al. 1943); young leaves 230–1000 mg (Wood and Young 1974; Kozukue et al. 1987); and sprouts 1950–17,700 mg (extremely high due to illumination of sprouts) (Wood and Young 1974; Kozukue et al. 1987). Glycoalkaloid (TGA) content in the stolons ranged from 150–540 mg, roots 180–400 mg, stems 23–33 mg, growing tops 300–860 mg (Lampitt et al. 1943; Wood and Young 1974; Kozukue et al. 1987), and lateral stems 30–71 mg (Kozukue et al. 1987). There were normal levels of TGA (mg/100 g FW) in various tuber tissues: whole tuber 7.5 (4.3–9.7) mg, flesh 1.2–5 mg, skin 2–3 % of tuber 30–60 mg, peel 10–15 % of tuber 15–30 mg, bitter tuber 25–80 mg, and peel from bitter tuber 150–220 mg (Wood and Young 1974). TGA levels in small tubers of 10–40 g were high 96–448 mg (Verbist and Monnet 1979). Friedman and Dao (1992) reported TGA (α -chaconine and α -solanine) contents of different parts of the new NDA 1725 potato cultivar (mg/100 g of fresh weight) as follows: tubers, 14.7; main stems, 32.0; small stems, 45.6; roots, 86; leaves, 145; and sprouts, 997. The α -chaconine content of several other potato cultivars ranged from 1.17 to 13.5 mg/100 g of fresh weight and the corresponding α -solanine content from 0.58 to 5.9 mg/100 g of fresh weight. The corresponding values for potato berries were 22.1 and 15.9 mg/100 g of fresh weight, respectively. Friedman et al. (2003a, b) reported 12–543 mg/kg FW TGA content in potato peel. Potato peels, accounting for about one-seventh of the whole tuber weight, contained solanine and

solanidine, respectively, at concentrations 2.5 and 6.2 times higher than the remaining tuber tissue or approximately 30 % of the total glycoalkaloid amount (Zitnak 1961). The outer 3 mm of the tuber contained approximately half of the TGA; however, it represented only 14 % of total potato weight. Free alkaloid solanidine was detected in concentrations up to 200 ppm or 33 % of the total glycoalkaloid level in bitter Netted Gem potatoes. Continuous illumination with 15- and 25-W incandescent light for 10 days increased glycoalkaloid content of peelings (12–14 % of tuber weight) in uncured potatoes by a factor of 3.2 and 2.8, respectively, while the corresponding factor for cured tubers was only 1.8 for both lights (Zitnak 1981). The peeled tuber portion (86–88 % of tuber weight) had negligible amounts of glycoalkaloids, averaging about 1 mg per 100 g of fresh weight. The rise of glycoalkaloid levels in peels of uncured tubers was nearly linear to 164.7 mg/100 g (15 W light) with no indication of levelling off. Bushway et al. (1983) found raw peels to contain 1.30–56.67 mg/100 g peel (wet weight), α -chaconine and 0.5–50.16 mg/100 g peel (wet weight) α -solanine. Raw flesh from the same potatoes contained 0.02–2.32 mg/100 g flesh (wet weight) α -chaconine and 0.01–2.18 mg/100 g flesh (wet weight) of α -solanine.

The tubers of Polish potato cultivars were reported to contain between 12 and 159 mg/kg glycoalkaloids, German cultivars 20 and 220 mg/kg, American cultivars 20 to 130 mg/kg and British cultivars 36 to 142 mg/kg (Dale and Mackay 1994; Nowacki 2009). The average TGA content (α -solanine and α -chaconine combined) for the different Swedish domestic early potato varieties ranged from 51 to 221 mg/kg fresh weight (Hellenäs et al. 1995a). α -Solanine constituted on average between 35 and 41 % of the glycoalkaloids detected. The glycoalkaloid concentrations in individual samples were in the range 31–344 mg/kg. The variety Ulster Chieftain accounted for 88 % of the samples above 200 mg/kg. The established Swedish consumer potato variety Magnum Bonum was found to contain potentially toxic levels of the glycoalkaloids (α -solanine and α -chaconine) in the tubers, ranging from 61 to 665 mg/kg fresh weight with an average of 254 mg/kg (Hellenäs et al. 1995b). Sixty-six percent of the samples exceeded a temporary maximum residue limit of 200

mg/kg; 8 % were above 400 mg/kg. Peeling did not significantly remove the glycoalkaloids in tubers with a high content. Tömösközi-Farkas et al. (2006) reported that tested Hungarian potato varieties contained between 0.09 and 15 mg/100 g glycoalkaloids. The content of glycoalkaloids in the new varieties of potato was lower than the limit of the official food regulations. A cross-Canada survey of B5141-6³ potatoes grown at 12 locations showed a distinct bitter off-flavour found to be due to the presence of unusually high total glycoalkaloid content (TGA), mostly in excess of 20 mg per 100 g of fresh weight (Zitnak and Johnston 1970). Samples of check varieties commonly grown in the selected locations, Kennebec, Irish Cobbler and Netted Gem, showed comparably low, normal TGA levels. Significant differences in tuber glycoalkaloid (TGA) content were found among five commercial varieties and B5141-6 grown at 39 different locations in 28 states in America (Sinden and Webb 1972). Line B5141-6 had the highest average TGA content, 29.3 mg/100 g in 1970 and 28.1 mg/100 g in 1971. Average TGA contents in 1970 of Kennebec, Russet Burbank, Katahdin, Irish Cobbler and Red Pontiac were 9.7, 7.9, 7.9, 6.2 and 4.3 mg/100 g, respectively. There were also significant location effects. Storage of potatoes at 5 °C increased the proportions of the 4-*O*- α -D-galactoside of calystegine B₂ and the trihydroxylated calystegine A₃ (Watson et al. 2000). The following ranges of total glycoalkaloid (α -chaconine and α -solanine) and calystegine (A₃ and B₂) levels were observed for the eight USA potato varieties (Atlantic, Dark Red Norland, Ranger Russet, Red Lasoda, Russet Burbank, Russet Norkota, Shepody and Snowden): dry flesh, 5–592 and 6–316 mg/kg; dry peel, 84–2226 and 218–2581 mg/kg; dry whole potatoes, 40–883 and 34–326 mg/kg; wet flesh, 1–148 and 1–68 mg/kg; wet peel, 12–429 and 35–467 mg/kg; and wet whole potatoes, 7–187 and 5–68 mg/kg (Friedman et al. 2003b). The two water-soluble nortropane alkaloids, calystegines A₃ and B₂, were found to be potent glycosidase inhibitors. The α -solanine content of Pakistani potato varies from 45.98 to 2742.60 mg/100 g of dry weight (DW) in peel and from 4.01 to 2466.56 mg/100 g of DW in flesh (Aziz et al. 2012). Similarly,

α -chaconine content varied from 4.42 to 6818.40 mg/100 g of DW in potato peel and from 3.94 to 475.33 mg/100 g DW in flesh portion. The total glycoalkaloids (TGA) concentration varied from 177.20 to 5449.90 mg/100 g of DW in peel and from 3.08 to 14.69 mg/100 g of DW in flesh portion of all the potato cultivars tested. All the potato cultivars contained lower concentration of TGA than the limits recommended as safe, except two cultivars, namely, FD 8-3 (2539.18 mg/100 g of DW) and Cardinal (506.16 mg/kg). The dietary intake assessment of potato cultivars revealed that Cardinal, FD 35-36, FD 8-3 and FD 3-9 contained higher amount of TGA in whole potato, although FD 8-3 only possessed higher content of TGA (154.93) in its flesh portion rendering it unfit for human consumption. Potato tubers of all somatic hybrids (except one clone) between tetraploid *Solanum tuberosum* cv. Dejima and the dihaploid clone ATDH-1 induced by another culture from *Solanum acuale*-T (acl-T) were found to contain four glycoalkaloids, namely, α -chaconine, α -solanine, α -tomatine and demissine derived from the fusion parents. The lack of α -tomatine in the remaining clone may be due to somaclonal variation (Kozukue et al. 1999). *S. tuberosum* tubers contained α -chaconine and α -solanine, whereas acl-T and ATDH-1 tubers were found to contain α -tomatine and demissine.

The content of solanidine glycosides (mg/kg fresh weight) of individually analysed small tubers of four *S. tuberosum* cultivars grown in pots in a glasshouse were determined as follows: Bintje range 73–88 mg, average 126 mg; AM 78-3778 range 321–1484 mg, average 721 mg; Arabesque range 95–265 mg, average 1155 mg; and Pimpernel 132–1287 mg, average 522 mg. The average solanidine glycoside content of field-grown mature-harvested tubers were Bintje 40 mg, AM 78-3778 360 mg, Arabesque 58 mg and Pimpernel 146 mg (Van Gelder et al. 1988).

Three samples of commercial chips 3 contained 9.5–72 mg TGA/100 g chips (Sizer et al. 1980). Removal of peel lowered TGA content in finished chips. Two types of fried peels contained more α -chaconine (2.18–92.82 mg/100 g cooked peel) and α -solanine (1.09–72.09 mg/100 g cooked peel)

(Bushway et al. 1983). Four commercial potato peel products—wedges, slices, fried peels and baked-fried peels—contained 3.60–13.71 mg α -chaconine/100 g cooked product and 1.60–10.48 mg α -solanine/100 g cooked product. The major glycoalkaloids in fried, baked, microwaved and boiled potatoes were α -chacocine ranging from 0.04 to 97.9 mg/100 g product and α -solanine 0.04 to 48 mg/100 g product (Bushway and Ponnampalam 1981). A slight loss of TGA was observed with frying. TGA contents (mg/100 g product) in various potato products reported were in baked jacket potato 99–113 mg, fried skins 567–1450 mg, frozen mashed potato 2–5 mg, frozen baked potato 80–123 mg, frozen chips 2–29 mg, canned peeled potato 1–2 mg, dehydrated potato flour 65–76 mg, dehydrated potato flakes 15–23 mg (Bushway and Ponnampalam 1981), frozen skins 65–121 mg (Bushway et al. 1983), boiled peeled potato 24–42 mg (Mondy and Gosselin 1988), and frozen fried potato 4–31 mg (Bushway and Ponnampalam 1981; Saito et al. 1990). Commercial potato products, such as potato crisps, chips and tinned new potatoes, have been found to contain similar low levels <10 mg/100 g on equivalent fresh weight basis were within those accepted as safe by breeders of commercial potatoes. Friedman and Dao (1992) reported the following glycoalkaloid contents in freeze-dried French fries (0.08–0.84 mg/100 g of product), skins (3.1–20.3 mg/100 g of product), potato chips (2.4–10.9 mg/100 g of product) and potato pancake powders (4.5–6.5 mg/100 g product). In the UK, potato products, when calculated on an equivalent fresh weight basis, all contained <10 mg/100 g (Davies and Blincow 1984). They reported the following mean glycoalkaloid levels in potato: main crop 10.4 mg/100 g, UK earlies 11.3 mg/100 g and imported earlies 12.3 mg/100 g.

The most abundant glycoalkaloids in potato were reported as α -solanine and α -chaconine (Friedman and McDonald 1997). The cultivated potato (*Solanum tuberosum*) contained α -solanine and α -chaconine in the ratio of 0.3 to 0.8 (α -solanine to α -chaconine) (Friedman et al. 2003a). Glycoalkaloids (α -solanine and α -chaconine) had been reported to contribute flavour to potatoes but at higher concentrations (>200 mg/kg) caused bitterness (Friedman

2006). Potatoes containing over 0.02 % steroid glycoalkaloids are considered toxic to man, and at this concentration they would impart a distinctly bitter flavour (Kuc 1984).

Arachidonic acid and eicosapentaenoic acids, two polyunsaturated fatty acids isolated from *Phytophthora infestans*, were found to be potent inhibitors of steroid glycoalkaloid (α -chaconine and α -solanine) accumulation in potato. Both acids elicited the localised accumulation of sesquiterpenoids including rishitin, lubimin, phytuberin, phytuberol and solavetivone. Rishitin and lubimin generally comprised 85–90 % of the total sesquiterpenoids which accumulated. The steroid glycoalkaloids and sesquiterpenoids appeared to have a role in disease resistance to some fungal pathogens.

Potato tubers protected from light contained 0.05–0.65 mg/100 g α -solanine and 0.3–0.63 mg/100 g α -chaconine, and concentrations in leaf samples ranged from 0.64 to 22.6 mg α -solanine/100 g and 0.06 to 55.7 mg α -chaconine/100 g (Phillips et al. 1996). Shakya and Navarre (2008) reported more than 50 glycoalkaloids with solanidane or solanidane-like aglycones in wild and three cultivars of *S. tuberosum*. Basal glycoalkaloid (α -chaconine and α -solanine) levels in tubers varied between potato cultivars (Petersson et al. 2013). Wounding and light exposure, but not heat, increased tuber glycoalkaloid levels, and the relative response differed among the cultivars. Also, calystegine levels (A_3 , B_2 and B_4) in potato tubers varied between cultivars, with calystegine B_4 showing the most marked variation. However, the total calystegine level was not affected by wounding or light exposure. There was strong variation among potato cultivars with regard to postharvest glycoalkaloid increases, suggesting that the biosynthesis of glycoalkaloids and calystegines occurred independently of each other.

The tubers of 14 potato varieties were analysed for glycoalkaloids. The levels of glycoalkaloids in tubers of 14 potato varieties were all within the safe limits for human consumption (Uppal 1987). The peels of tuber contained about 60–70 % of the total glycoalkaloids present in the whole tuber. The levels of glycoalkaloids in leaves and tubers were

correlated ($R^2 = 0.865$). There was a significant increase in the content of glycoalkaloids in peels of tubers exposed to sunlight. Glycoalkaloid contents increased at the rate of 1.9 mg/100 g fresh weight per day in peels of Kufri Jyoti tubers exposed to diffused sunlight. The principal glycoalkaloids α -solanine and α -chaconine were present in higher concentration in the peel than in the flesh of 12 commercial varieties of Mexican potato varieties (Sotelo and Serrano 2000). The main alkaloid in the peel of the potatoes was α -chaconine comprising about 65–71 % of the total glycoalkaloids. The high concentration of α -chaconine in peel, which was more toxic than α -solanine, afforded more protection to the tuber against predators. Based on the results, the consumption of the 12 commercial varieties of Mexican potatoes did not represent any danger to human health. Of 27 Japanese potato varieties, May Queen and Sherry showed high contents of total glycoalkaloids (α -solanine, α -chaconine) (180 mg/kg and 320 mg/kg, respectively) among the raw potatoes of middle size (ca. 100 g) (Shimoi et al. 2007). In contrast, Inca Red showed the lowest content of 21 mg/kg. Higher contents of total glycoalkaloids were found in smaller potatoes. The content of total glycoalkaloids varied in the range of 48–350 mg/kg in the potatoes in commercial foods with peel.

The tubers of the early potato variety Aster, harvested in the first period, contained the highest amount of glycoalkaloids, while the tubers of the middle-late variety Bryza, harvested in the second and third periods, contained the lowest amount of glycoalkaloids (Peřsa et al. 2002). Peeling of tubers caused a decrease of α -solanine and α -chaconine contents in the investigated varieties. The highest amounts of glycoalkaloids and nitrates were removed during peeling, blanching and frying (Rytel et al. 2005). In the processed potatoes, the ratio of α -chaconine to α -solanine decreased. French fries ready for consumption contained only 3–8 % of the glycoalkaloids and 5–6 % of the nitrates found in the raw material. Significant decrease of glycoalkaloids, particularly α -solanine, and nitrate contents was observed during the process of potato chips production (Peřsa et al. 2006). The ratio of α -chaconine to α -solanine contents during potato processing was

maintained at a similar level during the whole process and was about 2.5:1. The highest amounts of glycoalkaloids were removed during peeling, slicing, washing and frying, and the highest amounts of nitrates during peeling and frying.

Percival et al. (1996) found that regardless of cultivar, glycoalkaloid concentrations were increased after light exposure compared with initial concentrations. Average daytime irradiance during this period was 232 $\mu\text{mol}/\text{m}^2/\text{s}$. Glycoalkaloid concentrations fluctuated with time and continuous accumulation of glycoalkaloids with time was not demonstrated. Glycoalkaloid synthesis was maximal in the sequence pink-skinned cv. Kerrs Pink < white-skinned cv. Pentland Hawk < red-skinned cv. Desiree. Exposure to daylight altered the ratio of α -chaconine/ α -solanine in tubers of cv. Desiree but not those in cv. Pentland Hawk and Kerrs Pink. Glycoalkaloid concentrations in all cultivars were higher than the recommended food safety level; this was reached after 8 days in cv. Kerrs Pink and Desiree and at 13 days in Pentland Hawk. Coloured-fleshed potato varieties contained lower than 300 mg/kg DW of glycoalkaloids (Tajner-Czopek et al. 2012). Red-fleshed varieties contained 8 % higher glycoalkaloid content than blue-fleshed varieties. The highest changes of proportion between α -solanine and α -chaconine were in crisps. The peeling process decreased the glycoalkaloid content in tubers regardless of variety. The highest decrease of glycoalkaloid was found in crisps and French fries. The glycoalkaloid content in the boiled peeled potatoes was less than 9 mg/100 g, but in A, Montsana and Puebla varieties, both glycoalkaloids were absent. Potatoes of coloured-fleshed varieties studied were characterised by a low glycoalkaloid content at 5.47 mg/100 g (Rytel et al. 2013). The production of dehydrated potato dice influenced the decrease in glycoalkaloids content in potato products. The majority of glycoalkaloid compounds were removed during the peeling (70 %) and blanching process (29 %). Potato dice blanched at the highest temperature (85 °C) and pre-dried at 120 °C was characterised by the lowest quantity of glycoalkaloids content, whereas the highest content of these compounds was found in dice blanched potato at the lowest temperature (65 °C) and

pre-dried at 120 °C. The blanching process had greater influence on the decrease in glycoalkaloids content than pre-drying process.

Nikolic and Stankovic (2003) reported an optimal solid–liquid–liquid system for hydrolytic extraction of solanidine, a steroidal aglycone, from potato vines. Solanidine hydrolytic extraction (DHE) of more than 98 % was achieved when 10 % (w/v) hydrochloric acid in 50 % (volume) methanol was the first liquid phase and chloroform was the second liquid phase. The yield of solanidine (q(S)) under these conditions was calculated to be 0.24 g/100 g of potato vines. A run yielded 98 mg of solanidine (86.7 % recovery from potato crude extract) in a one-step separation using centrifugal partition chromatography (CPC) (Attoumbré et al. 2013). The purity of the isolated solanidine was over 98 %. α -Chaconine (54 mg) and α -solanine (15 mg) were separated from crude potato extract in one step of purification using CPC (Attoumbré et al. 2012). A run yielded 98 mg of solanidine (86.7 % recovery from potato crude extract) in a one-step separation using centrifugal partition chromatography (CPC) (Attoumbré et al. 2013). The purity of the isolated solanidine was over 98 %. α -Chaconine (54 mg) and α -solanine (15 mg) were separated from crude potato extract in one step of purification using CPC (Attoumbré et al. 2012). Using response surface methodology, optimal ultrasound-assisted extraction (UAE) conditions resulted in the recovery of 1102 μ g steroidal alkaloids/g dried potato peel (DPP) (Hossain et al. 2014). In contrast, solid–liquid extraction (SLE) yielded 710.51 μ g/g glycoalkaloid DPP. Recoveries of individual glycoalkaloids using UAE yielded 273, 542.7, 231 and 55.3 μ g/g DPP for α -solanine, α -chaconine, solanidine and demissidine, respectively, whereas for SLE yields were 180.3, 337.6, 160.2 and 32.4 μ g/g DPP for α -solanine, α -chaconine, solanidine and demissidine, respectively.

The polyhydroxylated nortropane alkaloids called calystegines were found in the tubers and leaves of *Solanum tuberosum* (Nash et al. 1993). They were found to be potent inhibitors of glycosidases and may be responsible for neurological disorders in livestock. Calystegines A₃ and B₂

had been demonstrated to occur in the leaves, skins and sprouts of *S. tuberosum* (Asano et al. 1997). Calystegine B2 was a strong competitive inhibitor of the α -galactosidase activity in human and animal livers. Human β -xylosidase was inhibited by all four nortropanes calystegines A₃, B₁, B₂ and C₁. Calystegines A₃ and B₂ were found in various parts of the tubers (whole potato, peel, flesh and sprouts) (Kvasnicka et al. 2008; Griffiths et al. 2008). On average, calystegine concentrations in the peel were about 13 times that found in the flesh for the five *S. tuberosum* group Tuberosum cultivars (Griffiths et al. 2008). The calystegine content of sprouts of the four cultivars was found to include small amounts of four additional types, calystegine B₃, B₄, N₁ and X₂, in addition to the more abundant A₃ and B₂. Concentrations in the sprouts were on average 100 times higher than that in the tuber flesh and 8 times higher than in the peel. No correlation was found between sprout concentration and either flesh or peel calystegine concentration.

Volatiles and Miscellaneous Compounds

Potato flavour is a complex trait resulting from the presence of a combination of volatile and non-volatile compounds (sugars, glycoalkaloids, major umami amino acids and 5'-ribonucleotides) (Morris et al. 2011). Tuber-specific overexpression of a potato α -copaene synthase gene resulted in enhanced levels (up to 15-fold higher than controls) of the sesquiterpene α -copaene. A positive correlation ($R^2 = 0.8$) between transgene expression level and α -copaene abundance was observed. No significant changes in the levels of volatiles other than α -copaene were detected. Sensory analysis suggested that α -copaene was not a major component of potato flavour. There were strong correlations between umami compounds amino acids, glutamate and aspartate, and the 5'-nucleotides, guanosine monophosphate (GMP) and adenosine monophosphate (AMP) with flavour attributes and acceptability scores from a trained evaluation panel, suggesting umami to be important component of potato flavour (Morris et al. 2007). A range of non-volatile

metabolites including the major umami compounds, glycoalkaloids and sugars in cooked potato tuber were found to impact on potato flavour (Morris et al. 2010). Correlation and principal component analyses revealed differences between the potato cultivars and storage conditions and demonstrated associations of metabolites with the different sensory attributes.

Studies by Burton and Meigh (1971) suggested that sprout inhibiting volatile constituent(s) of potato may be olefinic, ethereal and/or sulphur containing. Ethylene may be produced in very small quantities, insufficient to be an active olefinic constituent. Of the identified aromatic compounds evolved by stored potato tubers, benzothiazole, 1,4-dimethylnaphthalene and 1,6-dimethylnaphthalene were found to be comparatively potent inhibitors of sprout growth in the potato tuber (Meigh et al. 1973). The growth-suppressing activity of the two dimethylnaphthalenes was comparable with that of isopropyl-(*N*-3-chlorophenyl)-carbamate, used commercially in potato storage. Filmer and Rhodes (1984) found 1,4,6-trimethylnaphthalene to be an effective sprout suppressants compared to 1,4-dimethylnaphthalene; 1,4,5-trimethylnaphthalene; 2,3,6-trimethylnaphthalene; and 1,6,7-trimethylnaphthalene in bioassays based on both excised cultured shoot tips and intact potato tubers. Two volatile compounds produced by potato tubers with sprout growth-inhibitory activity was identified as diphenylamine and dibenzothiophene; the former was found to be an effective sprout suppressant for whole tubers (Filmer and Rhodes 1985). Treatment of nondormant potato tubers with vapours of six 8–10-carbon α,β -unsaturated carbonyl compounds suppressed sprout growth at 16 °C (95 % relative humidity) over ca. 3 months in storage in a concentration-dependent manner (Knowles and Knowles 2012). The volatile metabolites produced by sprout and associated tuber tissues following treatment with 3-octen-2-one, 3-nonen-2-one and 3-decen-2-one were the corresponding alkyl ketones and alkyl secondary alcohols. In contrast, (*E*)-2-octenal, (*E*)-2-nonenal and (*E*)-2-decenal were metabolised by two pathways: (1) parent compound to the corresponding alkyl aldehyde and then to the alkyl primary alcohol and (2) parent compound to the alkenyl

primary alcohol. The concentrations of the parent ketone and aldehyde declined rapidly following application, and the most persistent metabolites were 2-nonanol and (E)-2-nonen-1-ol, respectively.

2-Methoxy-3-isopropylpyrazine was found to be a major contributor to the earthy aroma of potato (Buttery and Ling 1973). Other volatile compounds identified included heptanol, octanol, octan-3-ol, hexan-2-one and non-*cis*-3-enol. Twelve volatile aroma compounds were found in potato tubers from different varieties after harvesting: two unknowns, acetaldehyde, propanal, 2-butanone, pentanal, hexanal, heptanone, *n*-heptanal, 2-hexenal, octanal and nonanone (Khan et al. 1977). The major volatile aroma compounds in potato tubers were identified as: *n*-pentanol, *n*-hexanol, (*E*)-2-hexenal, *n*-heptanal, (*E,E*)-2,4-decadienal and (*E,Z*)-2,4-decadienal (Fischer 1991). There were clear quantitative differences in the aromatic spectrum over a wide range of nitrogen and potassium inputs. Individual components altered within the spectrum especially after high nitrogen inputs. It was postulated that changes in the aroma of potato after increased fertiliser inputs were due to saturated and unsaturated aldehydes with their low sensory. Ulrich et al. (2000) identified the following volatiles in raw potato extract: 2,3-butanedione; 2,3-pentanedione; hexanal; 1-penten-3-ol; pyridine; 2-methyl-1-butanol; 2-pentylfuran; (*E*)-2-(1-pentyl)furan; 1-hexanol; (*E*)-2-octenal; 2-furancarboxaldehyde; (*E*)-2-nonenal; (*E,Z*)-2-6-nonadienal; phenylacetaldehyde; (*Z*)-3-nonen-1-ol; β -damascenone; 2,4-decadienal; benzyl alcohol; phenylethyl alcohol; pyrazine; methylpyrazine; 2,5-dimethylpyrazine; 2,6-dimethylpyrazine; 2-ethyl-6-methylpyrazine; 2,6-diethylpyrazine; 3-ethyl-2,5-dimethylpyrazine; 2-ethyl-3,5-dimethylpyrazine; and antioxidant activity and total phenolics in different genotypes of potato (*Solanum tuberosum* L.).

The following volatiles were emitted by potato foliage: *trans*-2-hexenal, 1-hexanol, 2-hexanol, 3-hexanol, *trans*-2-hexen-L-ol, *trans*-3-hexen-L-ol, *cis*-3-hexen-L-ol, *cis*-2-hexen-1-ol and linalool (Visser and Avé 1978; Visser et al. 1979). Bolter et al. (1997) identified the following volatiles in the

head space of intact potato plants ((*Z*)-3-hexen-1-ol; nonanal; decanal; linalool; 4,8-dimethyl-1,3(*E*),7-nonatriene; β -caryophyllene; α -selinene; β -selinene; myrcene, limonene; ledol; δ -cadinene; γ -cadinene and α -pinene) and from Colorado beetle (*Leptinotarsa decemlineata*)-infested and damaged potato plants ((*Z*)-3-hexen-1-ol; (*Z*)-3-hexen-1-yl-butyrate, heptanal, octanal, nonanal, decanal, linalool, 4,8-dimethyl-1,3(*E*),7-nonatriene; 1,4,8-trimethyl-1,3(*E*),7-(*E*),11-decatraene; β -caryophyllene; α -selinene; β -selinene; selinene; 3-pentanone; sabinene; myrcene; limonene; methyl salicylate; ledol; α -cubebene; α -copaene; β -elemene; α -humulene; germacrene D; δ -cadinene; γ -cadinene; (*Z*)-3-hexen-1-yl acetate; β -sesquiphellandrene; (*E*)- α -bergamotene; indole; 1,8-cineole; furfural; γ -muurolene; α -curcumene; tricyclene; (*E*)- β -farnesene; and α -pinene). Two cyclic sesquiterpenes, caryophyllene and germacrene D, were identified in the volatile secretions of potato leaves; caryophyllene was found to be a food attractant for potato Colorado beetle (Khalilova et al. 1997). Fourteen volatile sesquiterpenoids were identified in headspace samples collected from potato plants mechanically damaged or fed upon by the Colorado beetle larvae: β -caryophyllene, *trans*- α -bergamotene, sesquisabinene, α -humulene, (*E*)- β -farnesene, (–)-germacrene D, *trans*- β -bergamotene, α -zingiberene, bicyclogermacrene, (+)-germacrene A, β -sesquiphellandrene, germacrene D-4-ol, caryophyllene oxide and ledol (Weissbecker et al. 2000). The antennae of the predaceous stinkbug *Perillus bioculatus* responded to β -caryophyllene, α -humulene, (*E*)- β -farnesene, (–)-germacrene D and germacrene D-4-ol. Two sesquiterpenes that coeluted, α -zingiberene and bicyclogermacrene, together also elicited olfactory responses of *P. bioculatus*, whereas the individual compounds did not. Karlsson et al. (2013) proposed that volatiles, such as sesquiterpenes and aldehydes, mediated oviposition behaviour of the Guatemalan potato moth *Tecia solanivora* and were correlated with biosynthetically related, non-volatile compounds of potato tubers, such as steroidal glycoalkaloids, which influenced larval survival. Survival of larvae was negatively correlated with the tuber content of the steroid glycoalkaloids α -solanine and α -chaconine: healthy potatoes contained lower amounts than stressed tubers,

ranging from 25 to 500 µg/g and from 30 to 600 µg/g, respectively. Analysis of volatile compounds emitted by potato tubers revealed that stressed tubers could clearly be distinguished from healthy tubers by the composition of their volatile profiles. Compounds that contributed to this difference were, e.g. decanal, nonanal, isopropyl myristate, phenylacetaldehyde, benzothiazole, heptadecane, octadecane, myristicin, *E,E*- α -farnesene and verbenone. Earlier they found that Guatemalan moth females showed a strong response to several sesquiterpenes and monoterpenes that were emitted from potato foliage only (Karlsoon et al. 2009). Potato foliage of three phenological stages, from sprouting to tuberisation and flowering, released more than 30 sesquiterpenes which appeared to mediate host finding and oviposition in the Guatemalan moth. The main compounds were β -caryophyllene, germacrene D-4-ol, germacrene D, kunzeaol and (*E,E*)- α -farnesene. In addition, antennae responded to methyl phenylacetate, a floral fragrance that was released in large amounts from flowering plants and that was also present in potato tuber headspace. Female and male moths were attracted to methyl phenylacetate; this compound may accordingly contribute to female attraction to tuber-bearing potato plants in the field as well as to potato tubers in storage. Mated females of the potato tuberworm moth *Phthorimaea operculella* were attracted to volatiles released from intact potato tuber but unmated females did not (Arab et al. 2007). The polyphagous predator *Orius insidiosus* were attracted to volatiles from tubers damaged by *P. operculella* larvae, but did not respond to intact or mechanically damaged tubers. Methyl jasmonate (MeJA) was the only compound identified from the headspace of potato tubers. Behavioural bioassays with synthetic MeJA confirmed that the response of the insects is dependent on MeJA concentration.

The following volatiles were detected from potato tubers infected with *Erwinia carotovora*: acetone, ethanol, 2-butanone, acetaldehyde, methyl acetate, ethyl acetate, propanethiol, hydrogen sulphide, methyl sulphide, n-propanol and isobutanol (Varns and Glynn 1979). The following volatiles were generated by potato tubers infected with *Erwinia carotovora*: acetone; 2-propenal; 2-methyl propanal;

2-butanone; acetic acid; 1 hexene; 1-butanol; 2-methylhexane; 2-pentanone; heptane; dimethyl sulphide; methylcyclohexane; toluene; hexanal; octane; octene; 2-methyl-octane; ethyl benzene; xylene; 3-methyl-octane; 1,2,3-trimethylcyclohexane; 1,2-dimethyl benzene; 1-methyl-2-propyl-cyclopentane; 1-heptene; 1-ethyl-4-methylcyclohexane; nonane; 2,4-dimethyl-hexane; propyl-cyclohexane; 1-ethyl-2-methyl-benzene; phenol; 2-methyl-nonane; 3-methyl-nonane; octanal; trimethyl benzene; 2,2,3,4-tetramethyl-pentane; 1,2-undecadiene; decane; 4-methyldecane; limonene; (2-methylpropyl)-cyclohexane; 3-methyl-bicyclo[3.2.1]-oct-2-ene; 3-methyldecane; 5,6-dimethyl-decane; 1-methyl-4-(1-methyl)-ethyl benzene); nonanol; 3-methyl-1-heptene; naphthalene; decanal; 2-phenoxyethanol; long-chain aliphatic (heptadecane); butanoic acid; 1(3*H*)isobenzofuranone; long-chain aliphatic; hexacosane; 3,4-dimethyl-1-decene; 3-methylnonane and 1-hexacosanol (de Lacy Costello et al. 1999). The following volatiles were generated by potato tubers infected with *Bacillus polymyxa*: acetone, 2-methyl-pentane, acetic acid, hexane, but-1-ene, cyclohexane, 2-methyl-1-pentene, 2-methylhexane, 3-methylhexane, heptane, methylcyclohexane, *N,N*-dimethyl-formamide, toluene, hexanal, xylene, 1-ethyl-3-methyl-benzene, decanal, 2-phenoxyethanol, 1-pentadecene, phytol and 1-chloro-tetradecane (de Lacy Costello et al. 1999). The following volatiles were generated by potato tubers infected with *Arthrobacter* sp.: acetone; 2-methyl-pentane; acetic acid; hexane; but-1-ene; cyclohexane; 2-methyl-1-pentene; 2-methylhexane; 3-methylhexane; 2,3-dihydrofuran; 1,2-dimethyl-*cis*-cyclopentane; heptane; methylcyclohexane; toluene; octane; xylene; 1-ethyl-3-methyl-benzene; nonanal; decanal; 2-phenoxyethanol and hexacosane (de Lacy Costello et al. 1999). The following volatiles were generated by potato tubers inoculated with sterile distilled water: acetone; 2-propenal; 2-methyl-pentane; 3-methyl-pentane; 2-butanone; acetic acid; hexane, 1-butanol; cyclohexane; 2-methyl-1-pentene; (*E*)-2-butene; 2-methylhexane; 2-pentanone; 2,3,-dimethyl-pentane; 3-methylhexane; 2,4-dimethylheptene; 1,2-dimethyl-*cis*-cyclopentane; (*E*)-2-butenal; heptane; methylcyclohexane; toluene; hexanal; octane; ethylbenzene;

xylene; 3,4-dihydro-2*H*-pyran; 1,2-dimethyl benzene; nonane; 2,4-dimethyl-hexane; propyl-cyclohexane; 1-ethyl-2-methyl-benzene; phenol; 2-methyl-nonane; trimethyl benzene; 1-ethyl-3-methyl-benzene; decane; 4-methyldecane; limonene; (2-methylpropyl)-cyclohexane; 1-methyl-3-propyl-benzene; 2-methyldecane; 3-methyldecane; 1-methyl-4-(1-methyl)-ethyl benzene); 2,9-methyldecane; decanal; 2-phenoxyethanol; dodecane; 1(3*H*)isobenzofuranone; phytol; 3,4-dimethyl-1-decene; 3-methylnonane; 1-hexacosanol; 1-eicosanol; ((dodecyloxy)methyl)-oxirane; 3,5,24-trimethyl-tetracontane; and 1-chloro-tetradecane (de Lacy Costello et al. 1999).

Schütz et al. (1999) found 2-ethyl-1-hexanol in significant amounts in the headspace of potato tubers infected by *Phytophthora infestans*. The following volatile compounds were collected from potato tuber inoculated with *Fusarium coeruleum* and *P. infestans* after incubation at 10°C for 42 days: acetone, 2-methyl propanal; butanal; acetic acid; 2-butenal; 3-methyl-butenal; 1-butanol; cyclohexane; 2-methylhexane; 2-methylhexane; heptane; acetamide; methylcyclohexane; 1-pentanol; *N,N*-dimethylformamide; toluene; hexanal; acetic acid butyl ester; 2-furancarboxaldehyde; *N,N*-dimethylacetamide; xylene; 2-heptanone; styrene; benzaldehyde; phenol; 2-pentylfuran; benzyl alcohol; 2-ethyl-1-hexanol; limonene; 2-octenal; acetophenone; 1-octanol; methyl benzoate; nonanal; undecane; naphthalene; *iso*-menthol; decanal; 2-phenoxyethanol; verbenone; dodecane; benzothiazole; tridecane; copaene; tetradecane; caryophyllene; *iso*-caryophyllene; *n*-dodecanol; pentadecane; hexadecane; butylated hydroxyl toluene; 2-methylpropanoic acid-2,2-dimethyl-1-(2-hydroxy-1-methylethyl)-propyl ester; and 2-methylpropanoic acid-3-hydroxy-2,4,4-trimethyl-pentyl ester (de Lacy Costello et al. 2001). The following volatile compounds were collected in the headspace of potato tuber inoculated with sterile distilled water after incubation at 10 °C for 42 days: acetone, acetic acid, 2-methyl propanal, 2-butenal, 1-butanol, cyclohexane, 2-methylhexane, methylcyclohexane, heptane, toluene, hexanal, xylene, phenol, limonene, decanal, 2-phenoxyethanol and dodecane (de Lacy Costello et al. 2001).

Volatiles generated from potatoes inoculated with *Ralstonia solanacearum*, pathogen of potato brown rot include 1-hepten-3-ol; 3,6-dimethyl-3-octanone; 3-ethyl-3-methyl-pentane; 1-chlorooctane; benzothiazole; 3-methylbutanoic acid; 2,2,3,4-tetramethyl-pentane; 2,3,4-trimethylhexane; 4 methyl-octane; and 4 methyl-2-propyl-1-pentanol (Blasiolo et al. 2014). Volatiles generated from potatoes inoculated with *Clavibacter michiganensis* subsp. *sepedonicus* pathogen of potato ring rot disease include: 2-propanol, 3-methyl-3-buten-2-one and toluene. Possible volatile compounds are detected in the head space of *R. solanacearum* diseased tubers include: methanol, 2-propanol; acetaldehyde; 2-propane; acetic acid; ethyl acetate; dimethyl sulphide; 2-butanone; cyclohexane; hexanal; 3-methyl-3-buten-1-ol; 2,3-butanedione; 2 pentanone and dimethyl disulphide. Possible volatile compounds detected in the head space of *Clavibacter michiganensis* subsp. *sepedonicus* diseased tubers include: methanol, 2-propanol; acetaldehyde; ethanol; acetic acid; ethyl acetate; 2-butanone; cyclohexane; hexanal; 3-methyl-3-buten-1-ol; 2,3-butanedione; 2 pentanone and toluene.

A wide range of C₁–C₄ alcohols and carbonyls were identified in the volatile profile of *Erwinia carotovora*-infected potato tubers compared to healthy tubers (Waterer and Prtichard 1984). A total of 81 volatile metabolites were detected from Russet Burbank potatoes inoculated with *Erwinia carotovora* ssp. *carotovora* (ECC), *Erwinia carotovora* ssp. *atroseptica* (ECA) and *Fusarium sambucinum* (FSA), of which 58 were specific to one or common to a few but not to all inoculations/diseases (Liu et al. 2005). Acetic acid ethenyl ester was unique to ECA, while 1-methyl-4-(1-methylethenyl)-cyclohexene; dimethyl; 1,4-cyclohexadiene; and methoxy-(1,1-dimethyl-2-dihydroxy-ethyl)-amine were unique to ECC, and 2,5-norbornadiene; 4-methylene-1-(1-methylethyl)-bicyclo[3.1.0]hexane; propylene oxide; trichloroethylene; and styrene were unique to FSA. Volatiles uniquely emitted by non-wounded non-inoculated tubers were dichloroacetonitrile, α -phenyl-benzeneacetaldehyde and fluoroethane, and volatile uniquely emitted by wounded non-inoculated tubers was 1,3-cyclopentadiene. The other volatile

compounds included: 1,2-dimethoxy-ethene; 1-butanol; 2-methyl-1-butanol; 1-butanol, 2-methyl-, acetate; 1-butanol, 3-methyl-, acetate; 1-pentanol; 1-propanol; 3-hydroxy-2-butanone; acetic acid, 2-methylpropyl ester; acetic acid, methyl ester; acetone; borane-methyl sulphide complex; 2-methyl butanoic acid; ethyl ester butanoic acid; 2,2,3-trimethyl-cyclobutane; dimethyl trisulphide; ethanol; ethyl acetate; methyl ethyl disulphide; methyl ester pentanoic acid; thiirane; DL-3,4-dimethyl-3,4-hexanediol; 2,2-dimethyl-butane; 4-methylene-L-(1-methylethyl)-cyclohexene; azetidine; 4-methyl-1-(1-methylethyl)-bicyclo[3.1.0]hex-2-ene; bicyclo[4.1.0]hept-4-en-3-ol; 1-methyl-5-(1-methylethenyl)-cyclohexene; methyl hydrazine; dimethyl disulphide; 1,2,4-benzenetricarboxylic acid; 1-undecene; 2-methyl-5-(1-methylethyl)-bicyclo[3.1.0]hexan-2-ol; methyl nitrate; 2-methyl-2-propanamine; 1,3-dimethyl benzene; dimethyl ether; 1,4-dichlorobenzene; α ,4-dimethyl-benzenemethanol; methylene chloride; 1,2-dimethyl benzene; 6,6-dimethyl-2-methylene-bicyclo[3.1.1]heptane; 1-methyl-4-(1-methylethylidene)-cyclohexene; methylpropyl disulphide; *N,N*-dimethyl-1-butanamine; 2-butanone; 2-cyclopenten-1-one; 3-carene; 2-methyl-4,6-octadiyn-3-one; α -myrcene; α -phellandrene; α -pinene; 1,2-dichlorobenzene; 1,3-dichlorobenzene; 1-methyl-3-(1-methylethyl)-benzene; 1-methyl-4-(1-methylethyl)-benzene; 2-methyl-5-(1-methylethyl)-bicyclo[3.1.0]hex-2-ene; 1-methoxy-3-methyl butane; chloroform; dipropyl disulphide; ethylbenzene; formic acid; methyl-hydrazine oxalate (1:1); 1,3-cycloheptadien-1-Imethyl ketone; limonene, *p*-xylene; and trichloromonofluoromethane.

Black spot-related pigments were partially purified from bruised tubers of two commercial potato cultivars (cv. Bildtstar and cv. Lady Rosetta) (Stevens and Davelaar 1996). Chemical characterisation showed that these pigments consisted of protein and a relatively small amount of covalently bound constituents. They did not contain eumelanin. Quinic acid was detectable in hydrolysates of the pigments from Bildtstar but not in those of Lady Rosetta, which indicated that chlorogenic acid may take part in black spot formation but was not essential for the discolouration.

The results supported the hypothesis that black spot pigments were products of non-regulated reactions between nucleophilic amino acid residues in proteins and quinones, which were derived from endogenous substrates of polyphenol oxidase, indicating that black spot formation most probably occurred in disintegrated cells. Quantification of polyphenol oxidase (PPO), soluble protein and endogenous PPO substrates demonstrated that the content of free tyrosine was the predominant determinant for the biochemical potential for black spot synthesis (Stevens and Davelaar 1997).

Phytochemicals in Boiled/Cooked/Processed Potatoes

Volatile compounds in identified boiled potatoes of various cultivars included: methanol, ethanol, acetaldehyde, propanal, 2-methylbutanal, 2-methylpropanal, 2-methylbutanal, 3-methylbutanal, acetone, 2,3-butanedione, hydrogen sulphide, dimethyl disulphide, methyl mercaptan, ethyl mercaptan, methanethiol, diacetyl and ethanethiol (Self and Swain 1963). Volatile compounds produced by boiling potatoes were identified as hydrogen sulphide, acetaldehyde, methanethiol, acrolein, acetone, ethanethiol, dimethyl sulphide, isobutyraldehyde, n-butyraldehyde, isovaleraldehyde, butanal, 3-methylbutanal, 3-methyl-2-butanone and methyl isopropyl ketone, along with some unidentified components (Self et al. 1963). Thirty-five components were identified in potato essences and 20 in a potato granule essence (Nursten and Sheen 1974). 2-Methoxy-3-ethylpyrazine was present in potato volatiles and in potato sprout essence. Butanal and 3-methylbutanal was found only in cooked or processed (granulated) but not raw potatoes. Volatile compounds identified in the headspace of boiled Russet Burbank potatoes included: 2-hexenal; heptanal; c4-heptenal; octanal; octenal, nonanal; 2-nonenal; decanal; 2,4-decadienal; 2,4-hetadienal; 2,4-nonadienal; 2,6-nonadienal; benzaldehyde; furfural; pentanol; hexanol; 2-octen-1-ol; 1-octen-3-ol; 1-octen-3-one; 2-undecanone; 3,5-octadien-2-one; 1,5-octadien-3-one; hexanoic acid; ethyl benzaldehyde; ethyl heptanoate; 2-methoxy-3-isopropylpyrazine; 2-methyl-3-isopropylpyrazine;

2-pentylfuran and pentyl oxirane (Josephson and Lindsay 1987). Dilute aqueous solutions of *c*4-heptenal exhibited boiled potato-like aromas, and at relatively high concentrations (greater than 0.7 ppb), the added *c*4-heptenal contributed to distinct staling-type flavour defects to both fresh and mashed potatoes. When added at levels between 0.1 and 0.4 ppb, *c*4-heptenal enhanced overall earthy, potato-like flavours in freshly boiled mashed potatoes, but these levels caused stale flavours in reconstituted dehydrated potatoes. Pentenal, 3-isopropyl-2-methoxypyrazine, hexanal, 2-heptanone, benzaldehyde, nonanal, naphthalene, decanal, copaene and pentadecane were identified in headspace concentrates of freshly boiled, earthy, musty-flavoured Russet Burbank potato tubers (Mazza and Pietrzak 1990).

The following compounds were identified in the steamed volatile oil of potatoes: 1-octen-3-ol; *trans*-2-octenal; *trans*-2-octenol; geraniol; 2-pentylfuran; phenylacetaldehyde; *trans*-2-nonenal; furfural; hexanal; acetaldehyde; isobutyraldehyde; heptanal; 2-heptenal; nonenal; 2,4-decadienal; benzaldehyde; methional; furfural; 2-methylbutanol; 3-methylbutanol; pentanol; 2-octen-1-ol; nerol, linalool and benzyl alcohol; terpineol; octenol; heptanone, 2-heptanone; 1-octen-3-one; 2-nonen-4-one; 2-decanone; methyl-2-hydroxybenzoate; methyl salicylate; biphenyl; naphthalene; 1-methylnaphthalene; pyridine; benzothiazole; and 3,5-dimethyl-1,2,4-trithiolane (Buttery et al. 1970). The difference thresholds of the six compounds in the reconstituted dehydrated mashed potato products varied from 0.05–3.1 ppm (Guadagni et al. 1971). Only 2-methoxy-3-ethylpyrazine (0.1–0.2 ppm) was effective in increasing the flavour level of all four brands of dehydrated potatoes; it also proved to be effective in increasing the potato flavour level of potato salad, dehydrated scalloped potatoes and potato soup. Potato salad stored at 3 °C for 1 week required at least 0.2 ppm of this compound to maintain its initial flavour difference from the control sample. Phenylacetaldehyde, oct-1-en-3-ol, methional and 2-methoxy-3-isopropylpyrazine were ineffective in increasing the flavour of reconstituted mashed potatoes. Volatile compounds that contribute to the flavour of steam-cooked mashed potatoes and reconstituted dehydrated potato granules were characterised

and identified as pentenal; hexanal; 2-heptenal; octanal; 2,4-octadienal; octanol; furfuryl alcohol; *cis*-farnesol; mentadienol; 2,3-butadione; 2-butanone; 1-penten-3-one; 2-nonen-4-one; 3,5-octanedione; 2-methyl-3-octanone; 1,2-cyclohexandione; farnesyl acetone; geranylacetone; pentadecane; 2-pyridine methanol; 2-ethylfuran; 5-methylfural; dimethyl trisulphide; and dimethyl tetradisulphide (Salinas et al. 1994). The following volatiles were detected in raw and boiled potatoes: pentanal; hexanal; heptanal; 2-heptenal; 4-heptenal; 2-octenal; 2-nonenal; 2, 4-decadienal; 2,4-heptadienal; 2,4-nonadienal; 2,6-nonadienal; phenylacetaldehyde; 2-methylbutanol; ethanol, pentanol; benzyl alcohol; 1-penten-3-one; 1-methyl-2-pyrrolidone; acetic acid; propanoic acid; hexanoic acid; (*E*)-9-octadecene; 2-isobutyl-3-methoxypyrazine; 3-isobutyl-2-methoxypyrazine; 2-ethylfuran; and 2-pentylfuran (Petersen et al. 1998).

Mutti and Grosch (1999) found 45 odorants of boiled potatoes, of which 42 were identified. *trans*-4,5-Epoxy-(*E*)-2-decenal; methional; 2-acetyl-1-pyrroline; dimethyltrisulphide; 2,3-diethyl-5-methylpyrazine; vanillin; sotolon; decanal; (*E,E*)-2,4-nonadienal; (*E,E*)-2,4-decadienal, (*E*)- β -damascenone, furaneol, methanethiol, 3-isopropyl-2-methoxypyrazine and dimethyl sulphide were reported with a higher flavour dilution factor. Ulrich et al. (2000) reported the following basic odorants (component and sensory attribute) of boiled potato aroma: diacetyl (buttery, sweet, caramel); hexanal (green); (*E*)-2-pentenal (roasty, rubber, unpleasant); 2-methylbutanol (unpleasant, sweat); 2-pentylfuran (unpleasant, green beans, cooked); methylpyrazine (nutty, strong); octan-2-one (mushroom, earthy); 2,6-dimethylpyrazine (nutty, warm); 2-methyl-5-isopropylpyrazine or 2-ethyl-6-methylpyrazine (nutty, warm, chemical); 3-ethyl-2,5-dimethylpyrazine (nutty, earthy, herbaceous); 2-ethyl-3,5-dimethylpyrazine (roasty, coffee-like); methional (cooked potato); pyrrole (nutty, roasty), 1-octanol; (*E,E*)-3,5-octadienone (nutty); (*E,E*)-2,6-nonadienal (fatty, cucumber); phenylacetaldehyde (flowery); 2,4-decadienal (fatty, unpleasant); unknown (unpleasant); and unknown (baked). Additional to these positive aroma compounds, an unknown substance, (*E*)-2-pentenal, 2-pentylfuran and at least four different dienals ((*E,E*)-2,4-

heptadienal, (*E,E*)-2,4-octadienal, (*E,Z*)-2,6-nonadienal, (*E,E*)-2,4-decadienal) were found to be off-flavour components. Eight compounds (pentanal, hexanal, nonanal, (*E*)-2-octenal, 2,4-heptadienal, (*E*)-2-nonenal, (*E,E*)-2,4-nonedienal and 2,4-decadienal) were deemed as potential contributors to boiled potato off-flavour, since these compounds could be detected during GC sniffing and increased in concentration during storage (Peterson et al. 1999). Off-flavours in boiled potatoes were found to be strongly correlated with the presence of 2-pentenal, 2-hexenal, 2-heptenal, 2-pentylfuran and 2-decenal (Blanda et al. 2010). In all, about 50 compounds were detected.

Mäder et al. (2009) found that processing potatoes to potato flakes markedly diminished the content of free phenolic compounds, total phenolics and glycoalkaloids, mainly due to peeling and leaching. The influence of thermal exposure was less significant. About 43 % of the initial phenolic acids (caffeic acid, gallic acid, ferulic acid, p-coumaric acid, p-hydroxybenzoic acid, protocatechuic acid, vanillic acid, catechin and three isomers of caffeoylquinic acid: chlorogenic, neochlorogenic and cryptochlorogenic acid) and 10 % of the glycoalkaloids (α -solanine and α -chaconine) remained after processing. Steam peeling had a higher influence on glycoalkaloid losses compared to that on phenolics. The highest amounts of phenolic compounds and glycoalkaloids were found in peeling by-product. During processing, the amount of chlorogenic acid decreased, whereas the concentration of neochlorogenic acid increased due to isomerisation.

Phytochemicals in Dehydrated Potatoes

2-Methylpropanal produced a characteristic wet fur flavour note, while 2- and 3-methylbutanal modified this flavour and contributed burnt flavour notes in explosion-puffed dehydrated potatoes (Sapers 1970). N-hexenal was also present. Acetone, which was also present in the headspace vapour of explosion-puffed dehydrated potatoes, was found as a major headspace component of fresh boiled potatoes. This compound and smaller amounts of 2- and 3-methylbutanal were produced in

overcooked fresh potatoes which lacked the puffing off-flavour. Heights of peaks corresponding to 2-methylpropanal plus acetone, 2-methylbutanal plus 3-methylbutanal, hexanal and ethyl butyrate of explosion-puffed dehydrated potatoes were determined (Sapers et al. 1970). The intensity of the off-flavour was found to be associated with the heights of the 2-methylpropanal plus acetone and 2-methylbutanal plus 3-methylbutanal peaks. Peak heights of ten potato volatile components were associated with the intensity of a toasted off-flavour produced by the explosion puffing process (Sapers et al. 1971). Four of these and two additional minor components were found to have pyrazine-like aromas; two components had aromas characteristic of the thermal degradation of dry proline-glucose mixtures and two components had burnt aromas. 2-Methylpyrazine, 2, 5-dimethylpyrazine, furfural, 5-methylfurfural, benzaldehyde and phenylacetaldehyde were identified, and an ethylmethylpyrazine, ethyldimethylpyrazine and trimethylpyrazine were tentatively identified. The results suggested that the toasted off-flavour was due to the presence of alkylpyrazines, compounds derived from proline, products of sugar pyrolysis and products of Strecker degradation reactions. Flavour volatiles associated with storage changes of potato flakes were benzaldehyde, hexanal, heptanal, 2-hexenal and 2-pentylfuran (Sapers et al. 1972). Comparisons of dehydrated potato flakes drum dried at different rates and to different moisture contents indicated that overdrying reduced flake stability due to thermal damage during dehydration and to the low water activity of the overdried product (Sapers et al. 1974).

During the production of dehydrated cooked potato, the concentration of glycoalkaloids (α -chaconine and α -solanine) (TGA) and nitrates in processed potatoes decreased (Rytel 2012). TGA decreased most after peeling (30 %), blanching (28 %) and pre-drying (25 %). Nitrate content decreased significantly after blanching (21 %) and after pre-drying (18 %). During peeling of raw potatoes, the losses were about 20 % of the total content of both glycoalkaloids α -solanine and α -chaconine (factor = 0.80) (Ostrý et al. 2010). Cooking of raw peeled potatoes until edible stage in salted water resulted in 20 % loss (factor = 0.80). Combining both factors (for peeling and

cooking) led to a combined loss of 36 % (factor = 0.64) of total glycoalkaloids.

Phytochemicals in Baked Potatoes

Forty-two volatile compounds, mostly pyrazines and aliphatic aldehydes, were characterised in whole baked potatoes (Buttery et al. 1973). They stated the components most important to baked potato aroma included 2-ethyl-3,6-dimethylpyrazine, 3-methylmercaptopropanal (methional), deca-*trans,trans*-2,4-dienal and possibly 2-ethyl-3,5-dimethylpyrazine. Comparison of the volatile oils obtained from the baked potato skins and the potato pulp showed a considerably greater ratio of pyrazines to aldehydes in the skins indicating that the pyrazines were probably formed largely in the skins.

Pareless and Chang (1974) found that a combination of 2-isobutyl-3-methylpyrazine; 2,3-diethyl-5-methylpyrazine and 3,5-diethyl-2-methylpyrazine had an odour closer in character closer to baked potato than any other single compound. Eight other pyrazines were identified: 2-ethyl-3,5,6-trimethylpyrazine; isoamyl-methylpyrazine; trimethylisobutylpyrazine; a diethylmethylpyrazine, two alkylpyrazines (Mw 164), a tetra-substituted alkylpyrazine (mw 178) and olefinic pyrazines (mw 148 and 178).

The following pyrazines, 2,3,5-trimethylpyrazine; 2,3,6-trimethyl-5-hydroxy-cyclopentapyrazine; 2,3-diethyl-5-methylpyrazine; 2,3-diethylpyrazine; 2,3-dimethyl-5-butylpyrazine; 2,3-dimethylpyrazine; 2,5-dimethyl-3-butylpyrazine; 2,5-dimethylpyrazine; 2,6-dimethyl-3-butylpyrazine; 2,6-dimethylpyrazine; 2-butyl-3-methylpyrazine; 2-butyl-6-methylpyrazine; 2-ethyl-3,5,6-trimethylpyrazine; 2-ethyl-3,5-dimethylpyrazine; 2-ethyl-3,6-dimethylpyrazine; 2-ethyl-3-methylpyrazine; 2-ethyl-5-methylpyrazine; 2-ethyl-6-methylpyrazine; 2-ethyl-6-propylpyrazine; 2-ethyl-6-vinylpyrazine; 2-isobutyl-2,5-dimethylpyrazine; 2-isobutyl-3-methylpyrazine; 2-isopropyl-3-methoxypyrazine; 2-methyl-6,7-dihydro-5*H*-cyclopentapyrazine; 3,5-diethyl-2-methylpyrazine; 3,5-

dimethyl-6,7-dihydro-5*H*-cyclopentapyrazine; 3-butyl-2,5-dimethylpyrazine; 3-ethyl-2,5-dimethylpyrazine; 3-isoamyl-2,5-dimethylpyrazine; 3-isobutyl-2,5-dimethylpyrazine; 5,7-dimethyl-1,2,3,4,7,8-hexahydroquinoxaline; 5-butyl-2,3-dimethylpyrazine; 5-methyl-6,7-dihydro-5*H*-cyclopentapyrazine; ethylpyrazine; and methylpyrazine, and three thiazoles, 2,5-dimethyl-4-ethylthiazole; 2,5-dimethyl-4-butylthiazole and 2,5-dimethyl-4-methylthiazole, were identified in the volatile flavour of baked potatoes (Coleman and Ho 1980). Fourteen halogen compounds were identified in volatile flavour constituents of baked potatoes: 1,1,1-trichloroethane; tetrachloroethylene; trichloroacetic acid; 2-chloropropane; chloroform; 1-chloroheptane; 1,1-dichloroheptane; 1-chloro-2-methylbutane; *o*-chloroaniline; 2-chlorobiphenyl; 2-bromo-5-ethylnonane; *p*-chloroaniline; 1-iodooctadecane; and 1-chlorohexadecane (Ho and Coleman 1981).

A total of 228 compounds were identified in the volatiles of baked Idaho russet Burbank potatoes comprising aldehydes, alcohols, ketones, acids, hydrocarbons, esters, lactones, ethers, furans, halogenated compounds, pyrazines, oxazoles, thiazole, thiophenes and miscellaneous heterocycles (Coleman et al. 1981). The compound included aldehydes: (2-methylpropanal; 2-methyl-2-propanal; 3-methyl-1-butenal; 2-methyl-2-butenal; 3-methyl-2-butenal; pentanal; 2-pentenal; 4-methyl-2-phenyl-2-pentenol; hexanal; 2-ethylhexanal; 5-methyl-2-phenylhexanal; 3-hexenal; heptanal; nonanal; undecanal; *trans,trans*-2,4-decadienal; octadecanal; benzaldehyde; phenylacetaldehyde; ethylbenzaldehyde; 2,5-dimethylbenzaldehyde; methoxycinnamaldehyde; salicylaldehyde), alcohols: (methanol, ethanol; 2-butanol; 2-pentanol; 2-methyl-2-pentanol; 3-methyl-1-pentanol; 4-methyl-1-pentanol; 2,4-dimethyl-3-pentanol; 4-methyl-4-pentenol; 2-methyl-3-penten-2-ol; 2-methyl-1-penten-3-ol; heptanol; 3,6-dimethyl-3-octanol; 2-isobutyloctanol; 1-octen-3-ol; benzyl alcohol; dodecanol; hexadecanol; cyclohexanol; 2-ethylcycloxyethanol; hexahydrofarnesol; trimethylbenzyl alcohol; 3-methoxy-4-isopropylbenzyl alcohol; and naphthol), ketones: (acetone; 1-phenyl-1,2-propanedione; 4-methyl-2-pentanone; 5-methoxy-2-pentanone; cyclopentanone; 2,5-

dimethyl-1-cyclopentanone; 4-methyl-3-penten-2-one; 2,6-dimethyl-3-penten-2-one; hexanone; 2-acetyl-3,3-dimethylcyclohexanone; heptanone; 2-heptanone; 4-heptanone; 2-methyl-4-heptanone; 2-methyl-2-hepten-6-one; 3-octen-2-one; 4-decanone; and methyl acetophenone), acids: (acetic acid; propanoic acid; butanoic acid; pentanoic acid; hexanoic acid; heptanoic acid; 2-methylhexanoic acid; 2-methylpentanoic acid; 2-methylpropanoic acid; 3-methylbutanoic acid; 3-methylpentanoic acid; 4-methylpentanoic acid; 2-ketoadipic acid), esters: (1-methylpropyl acetate; 2-methylbutyl acetate; 2-methylbutyl pentanoate; allyl hexanoate; butyl acetate; diethyl phthalate; diisobutyl phthalate; diisobutyl isophthalate; ethyl acetate; hept-1-enyl-2-acetate; methyl-2-methylpropanoate; methyl hexanoate; methyl nonanoate; methyl octanoate; methyl pentanoate; pentyl acetate; phthalic anhydride), lactones: (4-pyridoxic lactone), hydrocarbons: (2-methyltetradecane; 2,6,10,14-tetramethylpentadecane; 5,7-dimethylhexadecane; 7,9-dimethylhexadecane; 2,6,11,15-tetramethylhexadecane; 2,4-dimethylheptane; 9-octylheptadecane; cyclodecane; 2,6,9-trimethylundecane; 2,6,10-trimethylundecane; 4,6-di-*n*-propyldodecane; 1-cyclopentyl-4-octyldodecane; 3,5,5-trimethyl-1-hexene; 2-ethyl-3-octene; 4-ethyl-3-octene; 1-octadiene; 1,4-dimethyl-4-vinylcyclohexene; diphenylmethane; 1-methylindan; 4,5,7-trimethylindan; limonene; α -pinene; 3-carene; benzene; methylbenzene (toluene); 1,2-dimethylbenzene; 1,3-dimethylbenzene; 1,4-dimethylbenzene; isopropylbenzene; trimethylbenzene; 3-ethylstyrene; *tert*-butylbenzene; *sec*-butylbenzene; 1,2,3,4-tetramethylbenzene; hexamethylbenzene; 1-methyl-4-ethylbenzene; nonylbenzene; biphenyl; diphenylmethane; 1,2-dimethylnaphthalene; 1,3-dimethylnaphthalene; 2,7-dimethylnaphthalene; 1,3,8-trimethylnaphthalene; 1,4,5-trimethylnaphthalene; 1,4,6-trimethyl-1,2,3,4-tetrahydronaphthalene; 2-isopropylnaphthalene; 3-methyleicosane; methylcyclopentane; γ -humulene; myrcene; cymene; *trans*, *trans*-farnesene; phellandrene), halogens: (chloroform; 1,1,1-trichloroethane; tetrachloroethylene; 1,1-dichloroheptane; 1-chloroheptane; 1-chlorobiphenyl; 2-chlorophenyl; 2-chloro-2-methylbutane; 1-chlorohexadecane; 2-

chloropropane; *o*-chloroaniline; *p*-chloroaniline; trichloroacetic acid; 2-bromo-5-ethylnonane; 1-ioda-octadecane), pyrazines: (methylpyrazine; ethylpyrazine; 2,3,5-trimethylpyrazine; 2,3,5-trimethyl-5-hydroxycyclopentapyrazine; 2,3-diethyl-5-methylpyrazine; 2,3-diethylpyrazine; 2,3-dimethyl-5-butylpyrazine; 2,3-dimethylpyrazine; 2,5-dimethyl-3-butylpyrazine; 2,6-dimethyl-3-butylpyrazine; 2,5-dimethylpyrazine; 2,6-dimethylpyrazine; 2-butyl-3-methylpyrazine; 2-butyl-6-methylpyrazine; 2-ethyl-3,5,6-trimethylpyrazine; 2-ethyl-3,5-dimethylpyrazine; 2-ethyl-3,6-dimethylpyrazine; 2-ethyl-3-methylpyrazine; 2-ethyl-5-methylpyrazine; 2-ethyl-6-methylpyrazine; 2-ethyl-6-propylpyrazine; 2-ethyl-3,5,6-trimethylpyrazine; 2-ethyl-6-propylpyrazine; 2-ethyl-6-vinylpyrazine; 2-isobutyl-3-methylpyrazine; 3,5-diethyl-2-methylpyrazine; 2-methyl-6,7-dihydro-5*H*-cyclopentapyrazine; 3,5-dimethyl-6,7-dihydro-5*H*-cyclopentapyrazine; 5-methyl-6,7-dihydro-5*H*-cyclopentapyrazine; 5-butyl-2,3-dimethylpyrazine; 3-butyl-2,5-dimethylpyrazine; 3-ethyl-2,5-dimethylpyrazine; 2,3,6-trimethyl-5-hydroxycyclopentapyrazine; 5,7-dimethyl-1,2,3,4,7,8-hexahydroquinoxaline), pyridines: (2-aminopyridine; 2-acetylpyridine), pyrroles: (2-acetylpyrrole; 2-acetyl-1-pyrroline; *N*-methyl-2-formylpyrrole), furans: (2-furaldehyde; 2-pentylfuran; 2-acetylfuran; 2-propionylfuran; 2-methylfurfural; furfural; *trans*-2-(2-pentenyl)furan; methyl furoate; 2,5-dimethyltetrahydrofuran; 2-methyltetrahydrofuran-3-one; 2-methyl-3-(2*H*)-furanone), ethers: (methyl ether; ethyl isopropyl ether; ethyl pentyl ether; ethyl nonyl ether; diethylene glycol diethyl ether; 1-ethoxy-1-propoxyethane; 1,1-diethoxyisopentane), thiazoles: (2,5-dimethyl-4-ethylthiazole; 2,5-dimethyl-4-butylthiazole; 2,5-diethyl-4-methylthiazole), thiophenes: (thiopene; 2-formylthiophene; 2-butyl-6-ethylthiophene), oxazoles: (2,4,5-trimethyloxazole; 5-acetyl-2,4-dimethyloxazole), sulphur compounds: (2-ethylhexyl mercaptan), nitrogen-containing compounds: (2-isopropylbenzimidazole; diethylformamide; diethylacetamide; diphenylamine; cyanobenzene; 2-amino-4-nitrotoluene; 2-aminopentane) and miscellaneous heterocycles: (2-propyl-1,3-dioxolane; 2,4,6-trimethyl-1,3,5-

trioxane). The following compounds were deemed most important to baked potato aroma: 2-ethyl-3-6-dimethylpyrazine; methional, *trans,trans*-2,4-decadienal; and possibly 2-ethyl-3-5-dimethylpyrazine (Coleman et al. 1981).

The following flavour components were identified in the volatiles of baked potatoes of four cultivars: 2-methyl-2-butenal; pentanal; pentenal; 2-pentenal; hexanal; 2-hexenal; heptanal; 2-heptenal; octanal; 2-octenal; nonanal; 2-nonenal; 2,4-heptadienal; 2,4-nonadienal; benzaldehyde; phenylacetaldehyde; methional; furfural; 2-methylbutanol; 3-methylbutanol; hexanol; 2-ethyl-hexanol; 3-hexen-1-ol; 1-octen-3-ol; linalool; 2,3-pentadione; 2-heptanone; 6-methyl-5-hepten-2-one; 4-octen-3-one; 2,3-octadione; methyl-2-methylbutanoate; methylbutanoate; 2,2,4,6,6-pentamethylheptane; copaene; limonene; α -pinene; β -pinene; 3-carene; benzene; toluene; ethylbenzene; 1,2-dimethylbenzene; 1,3-dimethylbenzene; 1,4-dimethylbenzene; trimethylbenzene; propylbenzene; 2-methylvinylbenzene; methylpropylbenzene; naphthalene; myrcene; cymene; 2,5-dimethylpyrazine; 2,6-dimethylpyrazine; 2-isopropyl-3-methoxypyrazine; 3-ethyl-2,5-dimethylpyrazine; methylpyrazine; 2-ethylfuran; 2-pentylfuran; 2-methyl-3(2*H*)-furanone; methyl-*N*-pentyl disulphide; dimethyl disulphide; dimethyl trisulphide; and dimethyl tetrasulphide (Oruna-concha et al. 2001). Eighty flavour components were identified in eight potato cultivars baked in microwave oven: hexanal; 2-heptenal; nonanal; decanal; undecanal; 2-undecanal; 2-dodecanal; hexadecanal; 2,4-decadienal; 2,4-heptadienal; 2,4-nonadienal; benzaldehyde; phenylacetaldehyde; methional; 2-furfural; 5-methylfurfural; 5-methyl-2-furfural; 5-methyl-2-thiophenecarboxaldehyde; 3-methylbutanol; 1-octen-3-ol; hexadecanol; 2-methoxyphenol; eugenol; 4-vinyl-2-methoxyphenol; 2-methoxy-4-vinylphenol; 3-ethylcyclopentanone; 2-pentadecanone; 3,5,5-trimethyl-3-cyclohexene-1-one; 2,3-octadione; 3,5-octadien-2-one; solavetivone; methyl hexadecanoate; methyl octadecanoate; methyl tetradecanoate; octadecyl acetate; cycloheptane; undecane; limonene; ethylbenzene; propylbenzene; 2-methylnaphthalene; 2,3,5-trimethyl-6-(3-methylbutyl)pyrazine; 2,3-diethyl-5-methylpyrazine; 2,5-

dimethyl-3(2-methylpropyl)pyrazine; 2,5-dimethyl-3-(3-methylbutyl)pyrazine; 2,5-dimethyl-3-propenylpyrazine; 2,5-dimethylpyrazine; 2,6-dimethyl-3-(2-methylbutyl)pyrazine; 2,6-dimethylpyrazine; 2-ethenyl-5-methylpyrazine; 2-ethenyl-6-methylpyrazine; 2-ethyl-3,6-dimethylpyrazine; 2-ethyl-3-methylpyrazine; 2-ethyl-5-methylpyrazine; 2-ethyl-6-methylpyrazine; 2-isopropyl-3-methoxypyrazine; 2-methyl-5-propenylpyrazine; 3,5-diethyl-2-methylpyrazine; 3,5-diethyl-2-(2-methylpropyl)pyrazine; 3-ethyl-2,5-dimethylpyrazine; ethylpyrazine; methylpyrazine; trimethylpyrazine; pyridine; 2-acetylpyrrole; 2-acetyl-1-pyrroline; 1-methyl-1(*H*)-pyrrole; 1-(2-furanylmethyl)-1(*H*)-pyrrole; 2-pentylfuran; 2,5-dihydrofuran; methylpropyl disulphide; methyl-*N*-pentyl disulphide; dimethyl disulphide; dimethyl trisulphide; dimethyl tetrasulphide; ethyl pentyl disulphide; benzyl methyl sulphide; benzyl methyl disulphide; and dipentyl disulphide (Oruna-Concha et al. 2002a). Quantitative and qualitative differences were observed between isolates from flesh and skins and among the four cultivars grown at different sites. Lipid and sugar degradation and/or the Maillard reaction were the main origins of volatiles in flesh. The two main sources of flavour compounds (regardless of cooking procedure) were lipid degradation and the Maillard reaction and/or sugar degradation (Oruna-Concha et al. 2002b). The ratio (yield derived from lipid)/(yield derived from Maillard reaction and/or sugar) decreased from 8.5–9.1 (boiling) to 2.7–3.4 (microwave baking) and to 0.4–1.1 (conventional baking).

The volatile flavour components of baked potatoes were identified as: decanal; 3-methylbutanal; methylpropanal; 2-methylpropanal; 2-methylbutanal; 3-methylbutanal; methional; pentanal; hexanal; heptanal; 2-heptenal; octanal; nonanal; 2-nonenal; undecanal; dodecanal; benzaldehyde; phenylacetaldehyde; 2-furfural; β -damascenone; 2-methylbutanol; 3-methylbutanol; hexanol; 1-octen-3-ol; linalool; butanedione; 2,3-pentadione; butanone; 3-hexanone; 2-heptanone; 5-methyl-5-hepten-2-one; geranyl acetone; solavetivone; ethyl acetate; methylbutanoate; copaene; α -aromadendrene; guaiane; limonene, α -pinene; 3-carene, benzene, toluene; ethyl benzene; 1,2-dimethylbenzene; 1,3-dimethylbenzene; 1,4-dimethylbenzene; styrene; naphthalene;

methylcyclopentane; myrcene; ocimene; cymene; terpinolene; phellandrene; 2,5-diethyl-5-pyrazine; 2,5-dimethylpyrazine; 2-ethyl-3,6-dimethylpyrazine; 2-ethyl-3-methylpyrazine; 2-ethyl-5-methylpyrazine; 2-ethyl-6-methylpyrazine; 3,5-diethyl-2-methylpyrazine; 3,5-dimethyl-2-(2-methylpropyl)pyrazine; 2-ethyl-2,5-dimethylpyrazine; 2-isopropyl-3-methoxypyrazine; 2-isobutyl-3-ethoxypyrazine; 3-isopropyl-2-methoxypyrazine; ethylpyrazine; methylpyrazine; pyridine; 1-methyl-1(*H*)-pyrrole; 2-ethylfuran; 2-pentylfuran; 2-methylfuran; dimethyl disulphide; dimethyl trisulphide; and dimethyl tetrasulphide (Duckman et al. 2001, 2002). Lipid degradation and the Maillard reaction were the main sources of flavour compounds, accounting for 22–69 % and 28–77 %, respectively, of the total yields in baked potatoes (Duckham et al. 2001). Various sulphur compounds, methoxypyrazines and terpenes were also identified at lower levels. Compounds contributing most to baked aroma (relative aroma impact value (RAV >) 10,000 in at least one cultivar) were 2-isobutyl-3-methoxypyrazine, 2-isopropyl-3-methoxypyrazine, β -damascenone, dimethyl trisulphide, decanal and 3-methylbutanal. Of the compounds monitored, those most likely having the greatest flavour impact in baked potatoes were 2-isopropyl-3-methoxypyrazine, 2-isobutyl-3-methoxypyrazine, dimethyl trisulphide, decanal and 3-methylbutanal, with methylpropanal, 2-methylbutanal, methional and nonanal also being probable important contributors to flavour (Duckham et al. 2002).

Phytochemicals in Potato Chips

The following compounds were identified as contributing to potato chip flavour, namely, alcohols (2-butanol; 3-methyl-1-butanol; 1-pentanol; 2-furfuryl alcohol; α -terpineol), aldehydes (2-methylpropanal; 2-methylbutanal; 3-methylbutanal; 2-isopropyl-2-butenal; 4-methyl-2-pentenal; *trans*-2-hexenal; 4-methyl-2-hexenal; *trans*-2,*trans*-4-octadienal; *trans*-2-nonenal; *trans*-2,*trans*-4-nonadienal; benzaldehyde; 2-phenyl-2-butenal; 4-methyl-2-phenyl-2-pentenal; 5-methyl-2-phenylhexanal; 2-octenal, ethanal (acetaldehyde); 2-phenylacetaldehyde;

hexanal; pentanal; 2-heptenal; 2-octenal; propenal; n-butanal; 2-pentenal; 2-hexenal; *n*-heptanal; 2-heptenal; deca-2,4-dienal), ketones (2,3-butanedione; 2-propanone; 2-pentanone), furans (2-butylfuran; 2-pentylfuran; 2-hexylfuran; furfural; 5-methylfurfural; 2-methyldihydro-3(2H)-furanone; 2-acetylfuran; furfuryl alcohol), hydrocarbons (1-decyne), ketones (2-butanone; 2,3-butanedione; *trans*-3-penten-2-one; 2,3-pentanedione; 5-methyl-2,3-hexanedione; *trans*-2-nonen-4-one; 2-decanone; acetophenone), pyrazines (2-methylpyrazine; 2,3-dimethylpyrazine; 2,5,-dimethylpyrazine; 2,6-dimethylpyrazine; 2-ethylpyrazine; 2-ethyl-3-methylpyrazine; 2-ethyl-5-methylpyrazine; 2-ethyl-6-methylpyrazine; 2,3,5-trimethylpyrazine; 2-methyl-5-vinylpyrazine; 2-ethyl, 3,6-dimethylpyrazine; 2-ethyl-3-5-dimethylpyrazine; 2,6-diethylpyrazine; 2-isobutyl-3-methylpyrazine; 2,3-diethyl-5-methylpyrazine; 2-isobutyl-3,6-dimethylpyrazine; 2-methyl-6-vinylpyrazine; 2,5-dimethyl-3-vinylpyrazine; 2,5-dimethyl-6-isopropylpyrazine; 2-isoamyl-5-methylpyrazine; methylethylisobutylpyrazine; 2-isobutenyl-3-methylpyrazine; 2-isoamyl-3,6-dimethylpyrazine; isobutenyldimethylpyrazine), pyridines and pyrroles (pyridine; 2-acetylpyridine; 2-acetylpyrrole) and sulphur compounds ((methylthio)acetaldehyde and methional (3-methylmercaptopropanal)) (Deck and Chang 1965; Mookherjee et al. 1965; Dornseifer and Powers 1965; Buttery et al. 1971; Buttery and Ling 1972; Guadagni et al. 1972; Buttery 1973; Maga 1994; Koehler et al. 1971). Deck and Chang (1965) identified 2,5-dimethylpyrazine in potato chips imparting a typical raw earthy potato flavour at a concentration of approximately 10 ppm. Dornseifer and Powers (1965) reported changes in volatile carbonyls of potato chips during storage; they identified 2,3-butanedione, 2-propanone, ethanal, propenal, n-butanal, 2-pentenal, 2-hexenal, n-heptanal and 2-heptenal. Mookherjee et al. (1965) identified 18 monocarbonyl compounds in fresh potato chips and 19 compounds in stale but not rancid sample. Among saturated aldehydes, the largest increase during storage was in hexanal and next in pentanal; among the 2-alkanones the important increase was in 2-pentanone and next in 2-propanone, and among the 2-enals the largest increase was in

2-heptenal and 2-octenal. Only one 2,4-dienal, viz. 2,4-decadienal, was found in both fresh and stale potato chips; 4-decadienal which had a characteristic deep-fried flavour was greatly reduced during storage. Of the 18 pyrazine and pyridine compounds indentified, 2-ethyl-3,6-dimethylpyrazine was found to be a major contributor to the odour intensity of potato chips (Buttery et al. 1971). Of the 46 compounds identified in non-basic steam volatile components of potato chips, methional, 3-methylbutanal, phenylacetaldehyde and 2,4-decadienal were determined to be important determinants of flavour (Buttery and Ling 1972). Koehler et al. (1971) found 2,ethyl-3,6-dimethylpyrazine to be a significant contributor to potato chip aroma. Guadagni et al. (1972) found 3-methylmercaptopropanal (methional) to be probably one of the most important contributors to potato chip aroma; other compounds that may contribute in varying degrees include deca-2,4-dienal, 2-ethyl-3,6-dimethylpyrazine, 2-acetyl-1,4,5,6-tetrahydropyridine, 2,6-diethylpyrazine, 2-octenal and 2-phenylacetaldehyde. The following volatile compounds were identified from potato chips: heptane; nonane; decane; undecane; tetradecane; 2-methyl-1-butene; limonene; 3-*p*-menthene; α -terpinene; ethylbenzene; 1,2,4-trimethylbenzene; 1-ethyl-3,5-dimethylbenzene; benzaldehyde; phenylacetaldehyde; 2,6-di-*t*-butyl-4-hydroxytoluene; ethanol; acetaldehyde; butanal; pentanal; hexanal; heptanal; 2-heptenal; 2-octenal; hepta-2,4-dienal; deca-2,4-dienal; cyclopentanone; pentanoic acid; hexanoic acid; heptanoic acid; octanoic acid; decanoic acid; 2-methylpropanoic acid; 3-methylbutanoic acid; propyl acetate; butyl acetate; diphenyl ether; dimethyl disulphide; benzylthiobenzoate; 2-ethylpyrazine; 2,5-dimethylpyrazine; 2,6-dimethylpyrazine; 2-ethyl-5-methylpyrazine; 2,5-diethylpyrazine; 2,3,5-trimethylpyrazine; 2-ethyl-3,6-dimethylpyrazine; pyridine; 2-acetylfuran; and furfural (Deck et al. 1973).

Unusual aldehydes, 4-methylpent-2-enal; 4-methylhex-2-enal; 2-isopropylbut-2-enal; 2-methylmercaptomethylbut-2-enal; 2-methylmercaptomethyl-4-methylpent-2-enal; 2-phenylbut-2-enal; 2-phenyl-4-methylpent-2-enal; and 2-phenyl-5-methylhex-2-enal, were identified in potato chips, probably formed during frying by aldol-type condensation

(Buttery 1973). Other compounds characterised included 2-methylhexa-4,5-dione; acetophenone; hepta-*trans,trans*-2-4-dienal; octa-*trans-trans*-2-4-dienal; nona-2,4-dienal; acetylbenzene; 2-isopropyl-2-butenal; 2-phenyl-2-butenal; 4-methyl-2-pentenal; 4-methyl-2-hexenal; 5-methyl-2-hexenal; 2-phenyl-4-methyl-2-pentenal; and 2-phenyl-5-methyl-2-hexenal (Buttery 1973). Taste panel described odour of potato chips as strong potato, baked potato and earthy potato (Maga 1994).

A large number of heterocyclic compounds were identified in baked Idaho Russet Burbank potatoes (Ho and Coleman 1980). This included furans (2-methylketotetrahydrofuran; methylfuroate; 5-methyl-2-furaldehyde; furfural; 2,5-dimethyl-tetrahydrofuran; *trans*-2-(2-pentyl)-furan; 2-acetyl furan; 2-pentyl furan; 2-propionylfuran), oxazoles (2,4,5-trimethyloxazole; 5-acetyl-2,4-dimethyloxazole), thiophenes (2-formylthiophene; 2-butyl-5-ethylthiophene) and pyrroles (2-acetylpyrrole; N-methyl-2-formypyrrole; 1-dioxolane; and 1-trioxane). It was noted that heterocyclic compounds with formyl or acetyl substituents had aromas with nutty characteristics.

The following nitrogen-containing compounds were identified in potato chips head space by comprehensive two-dimensional gas chromatography–time-of-flight mass spectrometry (GC × GC–TOFM): pyrazine; pyrrole; pyridine; 1-ethyl-1*H*-pyrrole; 2-methylpyridine; 2-methylpyrazine; 2-methyl-1*H*-pyrrole; 3-methyl-1*H*-pyrrole; 3-methylpyridine; 2,6-dimethyl pyridine; 2-ethylpyridine; 2,5-dimethylpyrazine; 2,6-dimethylpyrazine; ethyl pyrazine; 2-ethyl-1*H*-pyrrole; 2,3-dimethylpyrazine; ethenylpyrazine; 1-butyl-1*H*-pyrrole; 2-pyridinecarboxaldehyde; 3-ethylpyridine; 2-ethyl-6-methylpyrazine; 2-ethyl-5-methylpyrazine; 2,3,5-trimethylpyrazine; 2-ethyl-3-methylpyrazine; 2-(*n*-propyl)-pyrazine; 1*H*-pyrrole-2-carboxaldehyde; 2-carboxaldehyde; 1-methyl-1*H*-pyrrole; 2-ethenyl-6-methylpyrazine; 2-ethenyl-5-methylpyrazine; *N*-acetyl-4(*H*)-pyridine; acetylpuridine; acetylpurazine; 1-pentyl-1*H*-pyrrole; 1-methyl-2-pyrrolidinone; 2-acetylpurrole; 2-ethyl-3,5-dimethylpyrazine; 2-ethyl-3,6-dimethylpyrazine; 2-pyrrolidinone; 3-acetyl-3-

methylpyrazine; tetramethylpyrazine; 2-methyl-5-(1-propenyl)-(E)-pyrazine; 1-pyrrolidinecarboxaldehyde; 2-acetyl-3-methylpyrazine; (1-methylethenyl)-pyrazine; 2-acetyl-3-methylpyrazine; 2-isobutyl-3-methylpyrazine; 1-(2-pyridynl)-1-propane; 2,3-diethyl-5-methylpyrazine; 3,5-diethyl-2-methylpyrazine; 5-methyl-5H-cyclopenta[b]pyrazine; 3,5-diethyl-2-methylpyrazine; 2-butyl-3-methylpyrazine; 3,5-dimethyl-2-isobutylpyrazine; 2-pyridinecarboxaldehyde; 2-methyl-5-(1-propenyl)-pyrazine; 1-acetyl-1,2,3,4-tetrahydropyridine; 5,6,7,8-tetrahydroquinoxaline; and 2-butyl-3-methylpyrazine (Lojzova et al. 2009).

Chemical composition (g/100 g chips) of fresh potato chips fried in mid-oleic sunflower oil was found to contain: moisture 1.96 g, fat 39.19 g, fatty acid (g/100 g oil from chips), myristic acid (C14:0) 0.35 g, palmitic acid (C16:0) 4.62 g, palmitoleic acid (C16:1n7) 0.08, stearic acid (C18:0) 4.47 g, oleic acid (C18:1n9) 57.73 g, linoleic acid (C18:2n6c) 31.02 g, α -linolenic acid (C18:3n3) 0.31 g, arachidic acid (C20:0) 0.29 g, *cis*-11-eicosenoic acid (C20:1n9) 0.23 g and behenic acid (C22:0) 0.91 g (Lee and Pangloli 2013). Twenty-one flavour volatiles were isolated from potato chips fried in mid-oleic sunflower oil, but only 16 compounds were positively identified: hexanal; *trans*-2-pentenal; heptanal; *trans*-2-hexanal; octanal; *trans*-2-octenal; *trans*-2-heptenal; nonanal; 2-furaldehyde; decanal; benzaldehyde; *trans*-2-nonenal; *trans*-2-decenal; tetradecanal; hexadecanal; and *trans,trans*-2,4-decadienal (Lee and Pangoli 2013).

Phytochemicals in Crisped/French Fried Potatoes

Twenty-four alkyloxazole compounds were identified in the volatiles from French fried potatoes: trimethyl oxazole; 2-ethyl-4,5-dimethyl oxazole; 5-ethyl-2,4-dimethyloxazole; 2-ethyl-4-methyl-5-propyloxazole; 2,4,-dimethyl-5-propyloxazole; 4-ethyl-2-methyloxazole; 4,5-dimethyl-2-isopropyloxazole; 4-n-butyl-2,5-imethyloxazole; 2-methyl-4-butyloxazole; 2-hexyl-4,5-dimethyloxazole; 2-butyl-4,5-

dimethyloxazole; 2-butyl-4-propyl-5-methyloxazole; 2-pentyl-4-methyl-5-ethyloxazole; 2-hexyl-4-methyl-5-ethyloxazole; 2-methyl-4-ethyl-5-propyloxazole; 2-pentyl-4,5-dimethyloxazole; 2-butyl-4,5-diethyloxazole; 2,4-dimethyl-5-butyloxazole; 2-methyl-4-pentyloxazole; 2-pentyl-4-methyloxazole; 2,4,5-trimethyloxazole; 2-isopropyl-4,5-dimethyloxazole; 5-acetyl-2,4-dimethyloxazole; and 2-methyl-4-pentyloxazole (Carlin et al. 1986). Two new S-containing compounds were isolated and identified from French fried potatoes as 3-(methylthio)butanal and 3-(methylthio)heptanal (Carlin et al. 1990).

Among the 48 odour compounds indentified in French fries, potent odorant found from Maillard reaction products included methional; furaneol; sotolone; 2-ethyl-3,5-dimethylpyrazine; 2,3-diethyl-5-methylpyrazine; 3-ethyl-2,5-dimethylpyrazine; dimethyltrisulphide; and 3-methylbutanal and from lipid oxidation products were (*E,E*)-2,4-decadienal; *trans*-4,5-epoxy-(*E*)-2-decenal; (*Z*)-2-nonenal; (*E*)-2-nonenal; and (*E,Z*)-2,4-decadienal (Wagner and Grosch 1997). Methional; 2-ethyl-3, 5-dimethylpyrazine; 2,3-diethyl-5-methylpyrazine; (*E,E*)-2,4-decadienal; 4-hydroxy-2,5-dimethyl-3(2H)-furanone; methanethiol; dimethyltrisulphide; 3-methylbutanal; and 2,3-butanedione (IX) showed high factors of dilution. The concentration of the most potent odorants found in French fries and their attributes were 2,3-diethyl-5-methylpyrazine 400 µg/kg with an earthy attribute; (*E,E*)-2,4-decadienal 900 µg/kg with deep-fried, fatty note; methional 1 µg/kg boiled potato attribute; furaneol 125 µg/kg sweet caramel; and 3-methylbutanal 30 µg/kg with a malty attribute. The deep-fried note (caused by (*E,E*)-2,4-decadienal) predominated when the French fries were nasally evaluated, whereas the deep-fried and boiled potato-like smells (caused by methional) were mainly perceived in the retronasal test. Twenty-one compounds were identified as potent odorants of French fries prepared in palm oil (PO): 2-ethyl-3,5-dimethylpyrazine; 3-ethyl-2,5-dimethylpyrazine; 2,3-diethyl-5-methylpyrazine; 2-ethenyl-3-ethyl-5-methylpyrazine; 3-isobutyl-2-methoxypyrazine; 1-octen-3-one; (*Z*)-2-nonenal; (*E*)-2-nonenal; (*E,E*)-2,4-nonadienal; (*E,Z*)-2,4-decadienal; (*E,E*)-2,4-decadienal; *trans*-4,5-epoxy-(*E*)-2-decenal; 4-

hydroxy-2,5-dimethyl-3(2*H*)-furanone; 3-hydroxy-4,5-dimethyl-2(5*H*)-furanone; methylpropanal; 2-methylbutanal; 3-methylbutanal; 2,3-butanedione; methional; methanethiol; dimethyltrisulphide; 2-ethyl-3,5-dimethylpyrazine; 3-ethyl-2,5-dimethylpyrazine; 2,3-diethyl-5-methylpyrazine; 2-ethenyl-3-ethyl-5-methylpyrazine; 3-isobutyl-2-methoxypyrazine; 1-octen-3-one; (*Z*)-2-nonenal; (*E*)-2-nonenal; (*E,E*)-2,4-nonadienal; (*E,Z*)-2,4-decadienal; (*E,E*)-2,4-decadienal; *trans*-4,5-epoxy-(*E*)-2-decenal; 4-hydroxy-2,5-dimethyl-3(2*H*)-furanone; 3-hydroxy-4,5-dimethyl-2(5*H*)-furanone; methylpropanal; 2-methylbutanal; 3-methylbutanal; 2,3-butanedione; methional; methanethiol; and dimethyltrisulphide (Wagner and Grosch 1998). In addition to these 21 compounds, γ -octalactone, γ -nonalactone, γ -decalactone and δ -decalactone were found in French fries prepared in coconut fat. γ -Octalactone was identified as a major contributor to this note.

Relative amounts (in gas chromatographic (GC) peak area units) of selected flavour compounds formed in potato slices fried in palmolein or silicone fluid were reported, respectively, as: methyl propanal (649.8, 548.9), 3-methylbutanal (941.6, 948.5), 2-methylbutanal (1227.2, 1156.2), phenylacetaldehyde (50.7, 57.3), methional (3.6, 2.9), dimethyl disulphide (196.5, 167.8), dimethyl trisulphide (13, 20.5), pyrazine (1.1, 0.6), methylpyrazine (53.7, 19.1), 2,5(6)-dimethylpyrazine (74.8, 28), ethylpyrazine (22.9, 10.4), 2,3-dimethylpyrazine (9.0, 4.0), vinylpyrazine (3.8, 2.1), 2-ethyl-6-methylpyrazine (16.9, 6.2), 2-ethyl-5(3)-methylpyrazine (54.8, 24.2), 6-vinyl-6-methylpyrazine (9.2, 5.5), 3-ethyl-2,5-dimethylpyrazine (32.4, 15.5), hexanal (40.1, 62.2), (*E,Z*)-2,4-decadienal (40.2, 0.4) and (*E,E*)-2,4-decadienal (10.52, 0.0) (Martin and Ames 2001). Levels of Strecker aldehydes and sulphides in chips fried in the two media were not significantly different, but levels of pyrazines were significantly higher in palmolein-fried chips. Amounts of 2,4-decadienal were also significantly higher in palmolein-fried chips, but there was no significant difference in hexanal levels between the samples.

A total of 31 compounds including hexanal were identified in oxidised potato crisps that resulted mainly from the

degradation/rearrangement of lipids and carbohydrates (Sanches-Silva et al. 2005). Tajner-Czopek et al. (2014) found that blue-fleshed potatoes, Vitelotte variety and red-fleshed Highland Burgundy Red variety could be used for French fries processing due to their low content of TGA (total glycoalkaloids α -solanine and α -chaconine) in unpeeled and peeled potatoes. However, blue-fleshed Blue Congo variety should not be used for French fries processing because of high TGA in unpeeled and peeled potatoes. The peeling of coloured-fleshed potatoes decreased TGA content (α -solanine and α -chaconine) by about 50 %, cutting process by about 53 % and blanching by about 58 % compared with the raw material. The highest decrease in TGA content was caused by the frying process.

Skatole, indole and *p*-cresol were identified as the main volatile components in off-flavoured French fries (Whitfield et al. 1982). It was suggested that *p*-cresol and skatole, the main faecal off odour compounds, might be formed in potatoes by a bacterial degradation of the amino acids tyrosine and tryptophan.

Acrylamide in Potatoes

Mottram et al. (2002) reported acrylamide to be generated from food components during heat treatment as a result of the Maillard reaction between amino acids and reducing sugars. They found that asparagine, a major amino acid in potatoes and cereals, was a crucial participant in the production of acrylamide by this pathway. Acrylamide levels in the products were significantly reduced if tubers were preconditioned before being placed in storage at 2 °C. Acrylamide, a chemical that formed when certain starchy foods were cooked or processed, had been shown to cause cancer in animals (FSANZ 2014; USFDA 2008; Beth and Bussan 2013). Acrylamide is typically found in plant-based foods cooked with high heat (e.g. frying, roasting and baking) not raw plant-based foods or foods cooked by steaming or boiling. Some foods are larger sources of acrylamide in the diet, including certain potato products (especially French fries and potato chips), coffee and cereal-based products (such as breakfast

cereal, cookies, sweet biscuits and toast bread) which are all part of a regular diet. Beth and Bussan (2013) conducted a comprehensive review on acrylamide in processed potato products and health concerns covering animal and epidemiological research studies and mitigation strategic studies conducted to date.

Glucose and fructose concentrations in the tubers were significantly and positively correlated with subsequent acrylamide formation in the products (Silva and Simon 2005). Glucose, fructose, sucrose and asparagine concentrations in tubers increased upon storage at 2 °C. Tuber sucrose and asparagine concentrations did not have an effect on acrylamide levels. Studies by Ohara-Takada et al. (2005) suggested that the content of reducing sugars in potato tubers determined the degree of acrylamide formation in chips after frying. There was strong correlation between the reducing sugar content and acrylamide level, $R^2 = 0.873$ for fructose and $R^2 = 0.836$ for glucose. The sucrose content had less correlation with the acrylamide content. The chip colour, as evaluated by L^* (lightness), was correlated well with the acrylamide content. Matsuura-Endo et al. (2006) found that at storage temperatures <8 °C the contents of reducing sugars increased markedly in all potato cultivars, with similar increases in the acrylamide level and dark brown chip colour. The contents of reducing sugars correlated well with the acrylamide level when the fructose/asparagine molar ratio in the tubers was <2. When the fructose/asparagine ratio was >2 by low-temperature storage, the asparagine content, rather than the reducing sugar content, was found to be the limiting factor for acrylamide formation. High correlations were observed between the acrylamide content in potato chips and glucose and fructose contents in the tubers indicating that the limiting factor for acrylamide formation in potato chips was reducing sugars, not asparagine content in the tubers (Yoshida et al. 2005).

Acrylamide is formed through the Maillard reaction during high-temperature cooking, such as frying, roasting or baking, and the main precursors are free asparagines as in wheat and reducing sugars as in potatoes (Muttucumaru et al. 2008). However, in potatoes, when sugar levels are limiting,

competition between asparagine and the other amino acids for participation in the Maillard reaction determines acrylamide formation. Improvement in parameters such as (1) potato variety, (2) potato storage temperature, (3) process control (thermal input, pre-processing), (4) final preparation and (5) colour had all contributed to a significant overall reduction in the average acrylamide content in French fries and potato crisps (termed ‘chips’ in the USA) (Foot et al. 2007). The use of asparaginase offered potentially significant reduction in certain prefabricated potato products. Halford et al. (2012) reported that glucose and fructose showed the best correlations with acrylamide formation in both crisps and heated flour produced from nine varieties of potatoes grown commercially in the UK in 2009. However, free asparagine and total free amino acid concentrations also correlated with acrylamide formation in French fry varieties. Acrylamide formation, measured in heated potato flour, correlated with glucose and fructose concentration (Muttucumaru et al. 2014b). In French fry potato varieties, containing higher concentrations of sugars, acrylamide formation also correlated with free asparagine concentration, demonstrating the complex relationship between precursor concentration and acrylamide-forming potential in potato. Storage of the potatoes for 6 months at 9 °C had a significant, variety-dependent impact on sugar and amino acid concentrations and acrylamide-forming potential. Asparagine the predominant free amino acid in potato tubers was shown not to play an important role in the transport of nitrogen from leaf to tuber in potato and that the high concentrations of free asparagine that accumulated in potato tubers arose from synthesis in situ (Muttucumaru et al. 2014a). The study demonstrated that glutamine, glutamate and serine were the major transport amino acids from leaf to tubers in potato with alanine, aspartate, GABA, glycine, phenylalanine, proline, threonine and valine also playing a role.

Ye et al. (2011) found that microwaving treatment of potato chips could form more acrylamide from methylglyoxal, the main α -dicarbonyl, compared with frying method. Microwaving treatment promoted the formation of methylglyoxal compared with frying treatment at 160 and 180

°C in potato chips. There was a significant correlation between methylglyoxal and acrylamide in potato chips, thus confirming the important role of dicarbonyls in the formation of acrylamide in potato chips. Miao et al. (2014) found that formation of acrylamide and 5-hydroxymethylfurfural (HMF) in reconstituted potato chips was highly correlated with frying temperature and time. The formation of HMF had significant correlation acrylamide formation. Water activity could also influence the formation of acrylamide and HMF.

Most potato chips and whole potato-based fried snacks sold in Japanese markets showed acrylamide concentration higher than 1000 µg/kg (Yoshida et al. 2005). The concentrations in non-whole potato-based Japanese snacks, including rice crackers and candied sweet potatoes, were less than 350 µg/kg. Those in instant precooked noodles were less than 100 µg/kg with only one exception. Acrylamide concentrations in fresh sliced potato crisps in Europe from 2002 to 2011 based on a dataset of 40,455 samples showed a clear, significant downward trend for mean levels of acrylamide, from 763 ± 91.1 ng/g (parts per billion) in 2002 to 358 ± 2.5 ng/g in 2011; this was a decrease of $53 \% \pm 13.5 \%$ (Powers et al. 2013). The effect of seasonality arising from the influence of potato storage on acrylamide levels was evident, with acrylamide in the first 6 months of the year being significantly higher than in the second 6 months. The proportion of samples containing acrylamide at a level above the indicative value of 1000 ng/g for potato crisps introduced by the European Commission in 2011 fell from 23.8 % in 2002 to 3.2 % in 2011. The limit of detection and limit of quantification of acrylamide found in 32 samples of potato chips purchased on the South Italian market in 2009 were 6 µg/kg and 18 µg/kg, respectively, and recovery values ranged from 90.7 to 96.3 % (Tateo et al. 2010). The relative standard deviation (RSD) ranged between 2.1 % and 5.8 %. The values ranged between 27 and 1400 µg/kg and the arithmetic mean acrylamide content resulted 363 µg/kg. Considering 500 µg/kg as the minimum level possible with the actual available mitigation tools, the number of samples showing an acrylamide level higher than 500 µg/kg resulted to be 22 %.

Maillard reaction had been found to produce melanoidin pigments and a host of aroma and flavour volatiles including heterocyclic compounds such as pyrazines, pyrroles, furans, oxazoles, thiazoles and thiophenes (Mottram et al. 2002; Halford et al. 2012), but if free asparagine participated in the final stages, it resulted in the production of acrylamide, an undesirable contaminant (Muttucumaruet al. 2014b).

Mycotoxins in Diseased Potatoes

Potato tubers artificially infected with *Fusarium sambucinum* were contaminated with the mycotoxin, diacetoxyscirpenol, in concentrations up to 200 µg/tuber (Ellner 2002). The toxin could also be found in tubers without any disease symptoms. *Fusarium graminearum*, causal pathogen of potato dry rot, produced trichothecene mycotoxins in diseased tissues (Delgado et al. 2010). Xue et al. (2013) detected two type A (T-2 and diacetoxyscirpenol) and two type B (3-acetyldeoxynivalenol and Fusarenon X) trichothecenes in potato tubers inoculated with *Fusarium sulphureum*. It was found that T-2, diacetoxyscirpenol, 3-acetyldeoxynivalenol and Fusarenon X could be predominantly detected in diseased lesion, and the toxin could also be identified in tubers without any disease symptoms. Four trichothecenes (Fus-X, 3ADON, DAS and T-2) were detected in potato tubers inoculated with *Fusarium* spp. (Xue et al. 2014). The trichothecenes were found not only in the lesion but also in the adjacent asymptomatic tissue.

Potato Consumption, Nutrition and Health

In a secondary analysis of 24-h dietary recall data from the National Health and Nutrition Examination Survey (NHANES) 2003–2006, Freedman and Keast (2011) found that approximately 35 % of American children and adolescents consumed white potatoes (WP), oven-baked fries (OBF) and French fries (FF) and 18 % consumed FF. Intakes were lower in children compared with adolescents. Among adolescents, more boys than girls consumed FF. Both WP + FF + OBF and FF provided 9–12 % of total daily energy (but was within

energy requirements in the highest consumers); 8–15 % of daily fat (>75 % monounsaturated fatty acids + polyunsaturated fatty acids); ≥ 10 % dietary fibre, vitamin B6 and potassium; 5 % or greater thiamine, niacin, vitamin K, phosphorus, magnesium and copper; and less than 5 % sodium intake, for all sex–age groups. The combination WP + FF + OBF provided 5 % or greater vitamin C for all sex–age groups and 5 % or greater vitamin E and iron for most groups; FF provided 5 % or greater vitamin E intakes for all. They found that approximately 35 % of adults consumed potatoes; 12 % consumed FF (Freedman and Keast 2012). Intakes were lowest in adults aged 51+ years. More males, compared to females, consumed potatoes. In all age–sex groups, potatoes and FF provided 7–11 % of total energy (within daily energy requirements); 3–14 % of daily fat (>75 % MUFA + PUFA); >15 % dietary fibre, >13 % vitamin B6 and potassium; >5 % thiamine, niacin, phosphorus, magnesium and copper; and <5 % sodium. Potatoes provided >10 % vitamin C for all age–sex groups and >5 % vitamin K and iron for most groups; FF provided >5 % vitamin E and folate intakes for all. These cross-sectional data show that WP, including FF, provided shortfall nutrients within energy requirements to children and adolescents and, when consumed in moderate amounts, can be part of healthful diets.

Gibson and Kurilich (2013) found that, in a secondary analysis of 4-day dietary records from the British National Diet and Nutrition Survey 2008–2011, over 92 % of respondents consumed potatoes [oven chips, fried chips, boiled potatoes, mashed potatoes, roast potatoes and jacket (baked) potatoes], 27 % consumed oven chips and 41 % consumed fried chips. Potatoes (including chips) contributed 7 % of total energy, but greater proportions of potassium and vitamin B6 (15 %), vitamin C (14 %), fibre (13 %), folate (10 %) and magnesium (9 %). In contrast, they contributed only 4 % of saturated fatty acids. Among UK adults, potatoes provided in total 7 %, 10 % and 13 % of monounsaturated fatty acid, n-6 polyunsaturated fatty acid and n-3 polyunsaturated fatty acid in the diet, respectively, compared with only 4 % of saturated fatty acid and 6 % of total fatty acids. Fried chips were more popular than oven chips, being

consumed by 41 % of the total sample and half of all teenagers. It was concluded that potatoes, as currently consumed in their various forms, enriched the diet in this population in respect of at least five micronutrients, including potassium, magnesium, folate, vitamin C and vitamin B6, as well as dietary fibre and unsaturated fatty acids, while lowering the dietary concentration of saturated fat. Potatoes can increase the nutrient density of the diet by providing a relatively high micronutrient contribution, compared with energy content, while delivering only modest amounts of saturated fatty acid and sodium. Nutritionally, potatoes and potato products should be seen as a white vegetable, whose consumption should be encouraged alongside other, coloured, vegetable.

Potatoes (*Solanum tuberosum*) are an important food crop worldwide and contribute key nutrients to the diet, including vitamin C, potassium and dietary fibre (McGill et al. 2013). Potatoes and potato components have been shown to have favourable impacts on several measures of cardiometabolic health in animals and humans, including lowering blood pressure, improving lipid profiles and decreasing markers of inflammation.

Antioxidant Activity

Under active oxidation conditions, 20 g soy oil treated with 0.05 g of freeze-dried potato peel extracts attained lower peroxide values (22.0–28.0 meq/kg) than the control oil sample (109.0 meq/kg) indicating very strong antioxidant activities (Onyeneho and Hettiarachchy 1993). The antioxidant activities of these extracts were due to the presence of phenolic acids, namely, chlorogenic, protocatechuic and caffeic acids that were predominant and appeared to be mainly responsible for the strong antioxidant activities of the extracts. Potato peel extracts, at various concentrations, exhibited very strong antioxidant activity in refined soybean oil, which was almost equal to synthetic antioxidants BHT (butyl-hydroxytoluene) and BHA (butyl-hydroxyanisole) (Zia-ur-Rehman et al. 2004). The results suggested that potato peel extract in oils, fats and other food products could safely be

used as natural antioxidant to suppress lipid oxidation. After 4 day storage at 63 °C, 5.00 g of sunflower oil containing either the freeze-dried potato peel waste extract (200 ppm) or BHA (200 ppm) reached peroxide values (PV) of 37.38 and 37.47 meq/kg, respectively (De Sotillo et al. 1994b). The freeze-dried potato peel waste extract was as good as BHA as antioxidant. The freeze-dried potato peel waste extract was as good as BHA as antioxidant. After 16 day storage at 63 °C, 5.00 g of soybean oil containing either the methanolic potato peel extract (800, 1600 ppm) or BHA (200 ppm) and BHT (200 ppm) reached peroxide values (PV) of 37.35, 24.65, 33.20 and 28.88 meq/kg, respectively (Samarin et al. 2012). Also the Rancimat method revealed that TBHQ (t-butylhydroxyquinone) was the best antioxidant, but potato peel extract was as good as BHA and BHT. Potato peel extracted with menthol had the highest amount of phenolic compounds.

The free- and bound-form phenolics in potato peel showed high DPPH radical scavenging activity, while those in the flesh showed low activity (Nara et al. 2006). The total amount of chlorogenic acid and caffeic acid in the free-form phenolics from the peel was highly correlated with the DPPH radical scavenging activity. Ferulic acid was identified as the active radical scavenging compound in the bound-form phenolics from the peel. Studies found that potato peel (PE) was capable of protecting erythrocytes against oxidative damage probably by acting as a strong antioxidant (Singh and Rajini 2008). PE was found to inhibit lipid peroxidation with similar effectiveness in both rat RBCs and human RBC membranes (about 80–85 % inhibition by PPE at 2.5 mg/ml). While PE per se did not cause any morphological alteration in the erythrocytes, under the experimental conditions, PE significantly inhibited the H₂O₂-induced morphological alterations in rat RBCs and was found to offer significant protection to human erythrocyte membrane proteins from oxidative damage induced by ferrous ascorbate. Methanolic extract of potato peels showed potent antioxidant activity in antioxidant assays and under accelerated oxidation conditions using sunflower oil as oxidation substrates for 72 h at 70 °C (Mohdaly et al. 2010, 2013). The potent antioxidant activity of

potato peels could be attributed to its high content of phenolic compounds and flavonoids. The results suggested that potato peels could be used as preservative ingredients in the food and/or pharmaceutical industries. The main phenolic compounds identified in potato peel waste extracts were chlorogenic and ferulic acids; small amounts of gallic and hydroxycinnamic acids were also found (Amado et al. 2014). Potato peel extracts were able to stabilise soybean oil under accelerated oxidation conditions, minimising peroxide, totox and p-anisidine indices. Their results demonstrated potato peel waste to be a good source of antioxidants for effectively limiting oil oxidation while contributing to the revalorisation of these agrifood by-products.

Patatin purified from potato tuber showed antioxidant or antiradical activity by a series of in-vitro tests, including 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical ($IC_{50} = 0.582$ mg/mL) scavenging activity assays, anti-human low-density lipoprotein peroxidation tests and protections against hydroxyl radical-mediated DNA damages and peroxynitrite-mediated dihydrorhodamine 123 oxidations (Liu et al. 2003). It was suggested that cysteine and tryptophan residues in patatin might contribute to its antioxidant activities against radicals. Patatin from potato fruit was found to possess significant antioxidant activities measured by scavenging of the DPPH and superoxide free radicals, notable reducing power, protective effects against hydroxyl radical-induced oxidative DNA damage and lipid peroxidation inhibition (Sun et al. 2013).

Antioxidant activity varied among potato cultivars but was not related to flesh colour or total phenolics (Al-Saikhan et al. 1995). The antioxidant activity for white-flesh cultivars ranged from 65.2 to 88.1 % inhibition relative to control and total phenolics of 369.1–527.1 $\mu\text{g/g}$. The antioxidant activity for yellow-flesh cultivars ranged from 68.6 to 89.2 % inhibition relative to control and total phenolics of 237.7–407 $\mu\text{g/g}$. Antioxidant activity was evenly distributed within tuber parts and/or sections, except for skin tissue which had the greatest antioxidant activity and total phenolic content. Total phenolics varied among cultivars, with some containing twofold higher

concentrations than other cultivars. Phenolic content differences were genotype dependent and not related to flesh colour.

Total anthocyanin ranged from 6.9 to 35 mg per 100 g fresh weight in the red-fleshed and 5.5 to 17.1 in the purple-fleshed clones (Brown et al. 2003). Red-fleshed clones contained predominantly acylated glycosides of pelargonidin, while the purple-fleshed clones contained a more complex content of acylated glucosides of pelargonidin, petunidin, cyanidin and malvidin but had predominantly acylated glycosides of petunidin and peonidin. Oxygen radical absorbance capacity and ferrous reducing ability of plasma revealed that the antioxidant levels in the red- or purple-fleshed potatoes were two to three times higher than white-fleshed potato. In potatoes with total carotenoids ranging from 35 to 795 μg per 100 g FW, the lipophilic extract of potato flesh presented oxygen radical absorbance capacity (ORAC) values ranging from 4.6 to 15.3 nmoles α -tocopherol equivalents per 100 g FW (Brown 2005). The hydrophilic antioxidant activity of solidly pigmented red or purple potatoes was comparable to brussels sprouts or spinach. In red and purple potatoes with solidly pigmented flesh with levels of total anthocyanin ranging from 9 to 38 mg per 100 g FW, ORAC ranged from 7.6 and 14.2 μmole per g FW of trolox equivalents. Potato contained an average 20 mg per 100 g FW of vitamin C, which may account for up to 13 % of the total antioxidant capacity. Potatoes should be considered vegetables that may have high antioxidant capacity depending on the flesh composition. Potato anthocyanins were reported to be potent antioxidants and anti-inflammatory substances (Brown et al. 2008). The level of total anthocyanins is correlated with antioxidant level ($R^2 = 0.94$). Several methods of cooking interacted with genotypes in the antioxidant level remaining after cooking compared to raw potatoes. No method of cooking completely eliminated antioxidant activity, while boiling appeared to increase it compared to raw potato in the case of the most highly pigmented clone.

The main potato antioxidants were reported to be polyphenols, ascorbic acid, carotenoids, tocopherols, α -lipoic

acid and selenium (Lachman and Hamouz 2005). Polyphenolic antioxidants found in potatoes were L-tyrosine, caffeic acid, scopolin, chlorogenic and cryptochlorogenic acid and ferulic acid. In addition, red and purple potatoes contained acylated anthocyanins and pigmented potatoes displaying two to three times higher antioxidant potential in comparison with white-fleshed potato. Red potato tubers contained glycosides of pelargonidin and peonidin, and purple potatoes contained glycosides of malvidin and petunidin. Anthocyanins containing petunidin showed greater antioxidant potential than those with malvidin, peonidin or pelargonidin. Total anthocyanins (TAC) in coloured-fleshed potato cultivars ranged from 248.5 to 2257.8 mg/kg dry matter (Lachman et al. 2012). Cold storage (4 °C) influenced TAC differentially. In the Violette and Highland Burgundy Red cultivars, TAC increased by 18.5 % and 12.1 %, respectively, and in the Valfi cultivar, it decreased by 33.9 %. Baking increased TAC 3.34 times, whereas cooking in boiled water increased it 4.22 times. Correlation between antioxidant activity (AOA) and TAC ($R^2 = 0.659$) was found. Violette, Vitelotte and Highland Burgundy Red cultivars with the highest TAC showed high AOA, and the Shetland Black cultivar and the cultivars Salad Blue and Blue Congo with a marbled texture showed the lowest TAC and AOA.

Total anthocyanin (ACY) and total phenolic (PHEN) contents of different purple- and red-fleshed potato genotypes ranged from 11 to 174 mg cyanidin-3-glucoside/100 g fresh weight and from 76- to 181-mg chlorogenic acid/100 g fresh weight, respectively, and were genotype and location dependent (Reyes et al. 2005). Although ACY and PHEN concentrations in potato peel were 0.9- to 1.6-fold higher than in potato flesh, overall contribution of the peel to ACY and PHEN contents of a potato slice was ~20 %. High positive correlations between antioxidant capacity and ACY and PHEN suggested that these compounds were mainly responsible for the antioxidant capacity. The hydrophilic oxygen radical absorbance capacity (ORAC) and antioxidant capacity of 74 potato genotypes ranged from 28.25 to 250.67 μmol of trolox equiv/g of DW (Andre et al. 2007a). Total phenolic content

varied between 1.12 and 12.37 mg of gallic acid equiv/g of DW, total carotenoid content between 2.83 and 36.21 µg/g of DW and total vitamin C content between 217.70 and 689.47 µg/g of DW. The hydrophilic antioxidant capacity and the total phenolic content were highly and positively correlated ($R^2 = 0.91$). The iron content ranged from 29.87 to 157.96 µg/g of dry weight (DW), the zinc content from 12.6 to 28.83 µg/g of DW and the calcium content from 271.09 to 1092.93 µg/g of DW. A strong relationship between iron and calcium contents was also found ($R^2 = 0.67$). Total anthocyanin of 38 native potato cultivars from South America ranged from zero to 23 mg cyanidin equivalents/100 g fresh weight (FW) (Brown et al. 2007). The cultivars consisted of 23 diploids, seven triploids and eight tetraploids. Total carotenoid ranged from 38 to 2020 µg zeaxanthin equivalents/100 g FW. Oxygen radical absorbance capacity (ORAC) was measured for the anthocyanin (hydrophilic) and carotenoid (lipophilic) extracts. The hydrophilic ORAC ranged from 333 to 1408 µm trolox equivalents/100 g FW. The lipophilic ORAC ranged from 4.7 to 30 nM α -tocopherol equivalents/100 g FW. Total carotenoids were negatively correlated with total anthocyanins. Total anthocyanins were correlated with hydrophilic ORAC. Among clones with less than 2 mg cyanidin equivalents/100 g FW, total carotenoid and lipophilic ORAC were correlated, but this was not true for analysis of all 38 clones.

Total antioxidant activity (AA) of Texas specialty (coloured) potato selections ranged from 157 µg trolox equivalents (TE)/gfw to 832 µg TE/gfw and 810 µg TE/gfw to 1622 µg TE/gfw using the DPPH and ABTS assays, respectively (Reddivari et al. 2007a). TP total phenolic content (TP) ranged from 221 µg chlorogenic acid equivalents (CGAE)/gfw to 1252 µg CGAE/gfw. Selection COH2F2-2P/P had the highest AA and TP. Purple flesh selections had the highest AA and TP, followed by red-flesh and yellow-flesh selections. Selections with similar flesh colour did not differ significantly in AA and TP. A significant positive correlation was observed between AA and TP. Chlorogenic acid, gallic acid, catechin, caffeic acid and malvidin-3-(p-coumaryl

rutinoside)-5-galactoside were the major polyphenols identified. Chlorogenic acid accounted for 50 to 70 % of TP, followed by catechin, gallic acid and caffeic acid. Chlorogenic acid contributed 28 to 45 % to AA, followed by gallic acid, catechin and caffeic acid. Reddivari et al. (2007b) found that the antioxidant activity (AOA), total phenolics (TP) and total carotenoids (TC) of 25 potato genotypes differed significantly with genotype (G), Texas location (L) and year (Y). Phenolic composition differed significantly among genotypes and between locations. The AOA, TP and chlorogenic acid content were significantly correlated with one another. Genotypic effects were significant for all parameters measured and were larger than location and year effects. Interaction effects (G x L and G x L x Y) were significant for most parameters, but were relatively smaller than genotypic effects. Lutein and violaxanthin were the major carotenoids identified, and genotypes differed significantly in their carotenoid content.

Potatoes pan-fried in sunflower oil, olive oil and refined palm oil enriched with olive leaf polyphenols were found to have higher DPPH radical scavenging capacity and higher total polyphenols, tocopherols, phytosterols and squalene content than those pan-fried in the non-supplemented oils (Chiou et al. 2009). Oleuropein as well as other polyphenol compounds were detected in all French fries cooked in enriched oils (Chiou et al. 2007). Polyphenol intake by consuming French fries pan-fried in the enriched oils was calculated to be 6 to 31 times higher than that in the case of French fries fried in non-enriched commercial oils, being dependent on the frying oil type.

Antioxidant capacity of potato was influenced by potato variety and cooking conditions; however, cooked potatoes retained 68–97 % oxygen radical absorbance capacity assay (ORAC) value depending on cooking procedure and variety (Xu et al. 2009). Chlorogenic acid and its isomers dominated the phenolic composition of each variety involved in this study. ORAC and total phenolics were highly and positively correlated ($R^2 = 0.9119$). Principal component analysis that showed different cooking processes did not influence the trend of the antioxidant profile of the eight potato varieties, but

specific compounds exerted influence on the antioxidant capacity. The effects of drought stress on dietary antioxidant and glycoalkaloid contents in potato tubers of five native Andean cultivars were highly cultivar specific (Andre et al. 2009). The antioxidant contents of the yellow tuber-bearing cultivars (Sipancachi and SS-2613) were weakly affected by the drought treatment, whereas the pigmented cultivars demonstrated highly cultivar-dependent variations. A drastic reduction of anthocyanins and other polyphenols was observed in the red- (Sullu) and purple-fleshed (Guincho Negra) cultivars, whereas an increase was shown in the purple-skinned and yellow-fleshed cultivar (Huata Colorada). The hydrophilic antioxidant capacity (evaluated by Folin-Ciocalteu and H-oxygen radical absorbance capacity assays) was highly correlated with the polyphenol content and followed, therefore, the same behaviour upon drought. Carotenoid contents, including β -carotene, as well as vitamin E, tended to increase or remain stable following drought exposure, except for the cultivar Sullu, in which the level of these lipophilic antioxidants was decreased. Vitamin C contents were not affected by drought with the exception of Guincho Negra, in which the level was increased. These variations of health-promoting compounds were associated with increased or stable levels of the toxic glycoalkaloids, α -solanine and α -chaconine. Storage at 10 °C for 4 months tended to decrease the concentrations of all dietary antioxidants, except those of vitamin E. This storage also reduced the drought-induced variations observed in freshly harvested tubers.

The total equivalent antioxidant capacity (TEAC) was higher in the extracts of early potato cultivars in Racale, and a highly positive linear relationship ($R^2 = 0.8193$) between TEAC values and total phenolic content was observed (Leo et al. 2008). There was a considerable variation in carotenoid content and weak differences in the ascorbic acid concentration of the examined cultivars of 'early potato' and between the harvested locations (Racale and Monteroni). Chlorogenic acid and catechin were the major phenols present in potato tuber extracts; a moderate amount of caffeic acid and ferulic acid was also detected. A highly significant linear

correlation ($R^2 = 0.9613$) between total antioxidant capacity (as a sum of peroxy radicals + peroxynitrite) and total phenol content of methanol/water extracts was established. Chlorogenic acid was the most abundant phenolic and ranged from 22 to 473 mg/100 g dry weight in 50 potato genotypes (Navarre et al. 2011). Rutin and kaempferol-3-rutinoside were the most abundant flavonols. Total phenolics ranged from 1.8 to 11 mg/g DW and antioxidant capacity ranged from 27 to 219 $\mu\text{mol TE/g DW}$. Total phenolics and antioxidants in these high-phytonutrient potatoes compared favourably to 15 other analysed vegetables. Total phenolic content of native Chilean potatoes varied in the peeled potato samples from 191 to 1864 mg/100 g DM and from 345 to 2852 mg/100 g DM in unpeeled samples (Kong et al. 2012). Antioxidant activity was higher in unpeeled potatoes and was the highest in the unpeeled NG-6 or 'Bruja' native potato.

Purple-fleshed potato cultivars showed higher total phenol (TP content) (by 60 %) than yellow-fleshed cultivars; antioxidant activity (AA) in purple-fleshed cultivars was twice as high as in yellow-fleshed potatoes (Lachman et al. 2008). A medium linear correlation between TP and AA was found ($R^2 = 0.747$). Average TP content in yellow-fleshed cultivars was 2.96 GAE (g of gallic acid per kg dm); in purple-fleshed cultivars, it was 4.68 GAE. Average AA in yellow-fleshed cultivars was 11.26 AAE (mg of ascorbic acid equivalent per 100 g dm) and in purple-fleshed cv. 24.79 AAE. Purple potatoes exhibited the highest antioxidant activity; peels were more potent than the flesh and contained higher phenolic content (Albishi et al. 2013). Bound and esterified phenolics contributed as much or even more than the free phenolics to the antioxidant activity of the peels. HPLC data showed the presence of chlorogenic, caffeic, *p*-coumaric and ferulic acids.

All cooking treatments (boiling, baking and microwaving) of white-, yellow-, red- and purple-fleshed potatoes reduced ascorbic and chlorogenic acid contents, total glycoalkaloids, α -chaconine and α -solanine with the exception of total anthocyanins (Lachman et al. 2014). The losses of ascorbic and chlorogenic acids were minimised with boiling and total anthocyanin levels retained the highest. Boiling of peeled

tubers decreased contents of total glycoalkaloids (α -chaconine and α -solanine) and appeared as the most favourable among the three tested methods. Moreover, due to higher initial levels, red- and purple-fleshed cultivars retained higher amounts of antioxidants (ascorbic acid, chlorogenic acid and total anthocyanin) after boiling and may be healthier as compared with white or yellow cultivars.

Both red and purple-fleshed potato varieties contained high levels of total polyphenols (227–845 mg/100 g dry weight) and anthocyanins (21–109 mg/100 dry weight) (Kita et al. 2013). The process of frying caused degradation of anthocyanin compounds (38–70 %); pelargonidin and malvidin derivatives were more stable during frying than petunidin derivatives. Although frying process affected the anthocyanin and polyphenol levels, the obtained potato crisps exhibited bright intensive colour and good antioxidant activity as evaluated by 2,2'-azino-bis-3-ethylbenzothiazoline-6-sulphonic acid (ABTS) and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical as well as ferric reducing ability of plasma (FRAP) assays. In a recent study, they reported both red- and purple-fleshed potato varieties contained higher content of total polyphenols (250–526 mg/100 g DW) and anthocyanins (16–57 mg 100/g DW) (Kita et al. 2014). The higher content of polyphenols was directly related to higher antioxidant activity of tested potatoes. The process of frying caused almost total degradation of anthocyanin compounds, while polyphenols exhibited quite good stability (especially in chips obtained from red-fleshed potatoes). The antioxidant activity decreased significantly in chips obtained from purple-fleshed potatoes. Red-fleshed varieties exhibited better stability after long-term storage and gave chips with better properties.

Anticancer Activity

Among the *Solanum* steroidal glycoalkaloids tested, only solasodine (from solasonine) and α -chaconine exhibited strong cytotoxicity against tested cancer cells in-vitro (Nakamura et al. 1996). Growth inhibition GI_{50} values (μ g/ml) of solasodine (from solasonine) and α -chaconine against the tested cancer

cells were, respectively, as follows: PC-6 (lung cancer) 4.6; 1.83 $\mu\text{g/ml}$, MCF-7 (breast cancer) 1.62, 1.54 $\mu\text{g/ml}$, SW620 (colon cancer) 3.50, 1.46 $\mu\text{g/ml}$, NUGC-3 (stomach cancer) 1.47, 1.43 $\mu\text{g/ml}$, P388 (mouse leukaemia) 2.18, 1.58 $\mu\text{g/ml}$; α -Chacocine was more superior than solasodine and α -solanine against all cancer cell lines. Solanidine α -L-rhamnopyranosyl-(1 $\rightarrow$ 2)- β -D-glucopyranoside was weaker than α -chacocine and solasodine.

Glycoalkaloids and metabolites of potato inhibited the growth of human colon (HT29) and liver (HepG2) cancer cells (Lee et al. 2004). Four concentrations each (0.1, 1, 10 and 100 $\mu\text{g/mL}$) of the potato trisaccharide glycoalkaloids α -chaconine and α -solanine; the disaccharides β (1)-chaconine, β (2)-chaconine and β (2)-solanine; the monosaccharide γ -chaconine and their common aglycone solanidine; the tetrasaccharide potato glycoalkaloid dehydrocommersonine and the potato aglycone demissidine were all antiproliferative, with the glycoalkaloids being the most active and the hydrolysis products less so. The effectiveness against the liver cells was greater than against the colon cells. Potency of α -chaconine at a concentration of 1 $\mu\text{g/mL}$ against the liver carcinoma cells was higher than those observed with the anticancer drugs doxorubicin and camptothecin. Because α -chaconine and α -solanine also inhibited normal human liver HeLa (Chang) cells, safety considerations should guide the use of these compounds as preventative or therapeutic treatments against carcinomas. Pure α -chaconine and α -solanine from Dejima potatoes and TGA (glycoalkaloids) from five fresh potato varieties (Dejima, Jowon, Sumi, Toya and Vora Valley) tested reduced the numbers of the following human cell lines: cervical (HeLa), liver (HepG2), lymphoma (U937), stomach (AGS and KATO III) cancer cells and normal liver (Chang) cells (Friedman et al. 2005). The results showed that (a) the effects of the glycoalkaloids were concentration dependent in the range of 0.1–10 $\mu\text{g/mL}$ (0.117–11.7 nmol/mL); (b) α -chaconine was more active than α -solanine; (c) some mixtures exhibited synergistic effects, whereas other produced additive ones; (d) the different cancer cells varied in their susceptibilities to destruction; and (e) the destruction of

normal liver cells was generally lower than that of cancer liver cells.

CO112F2-2 potato cultivar extracts and their anthocyanin fraction at 5 µg chlorogenic acid eq/ml were more active and inhibited cell proliferation and increased the cyclin-dependent kinase inhibitor p27 levels in both LNCaP (androgen dependent) and PC-3 (androgen independent) prostate cancer cells (Reddivari et al. 2007c). Potato extract and its anthocyanin fraction were found to be cytotoxic to both prostate cancer cells via activation of caspase-independent apoptosis. The apoptosis induced by whole potato extracts in prostate cancer cell lines may be in part due to α -chaconine and gallic acid (Reddivari et al. 2010). α -Chaconine (5 µg/ml) and gallic acid (15 µg/ml) exhibited potent antiproliferative properties and increased cyclin-dependent kinase inhibitor p27 levels in both cell lines. Both α -chaconine and gallic acid induced poly[adenosine diphosphate (ADP)] ribose polymerase cleavage and caspase-dependent apoptosis in LNCaP cells; however, caspase-independent apoptosis through nuclear translocation of endonuclease G was observed in both LNCaP and PC-3 cells. The proliferation of human mammalian cancer (MCF-7) cells was significantly inhibited in a dose-dependent manner after exposure to 'early potato' cultivar extracts (Leo et al. 2008).

HepG₂ human hepatocarcinomatic cell lines treated with solanine showed typical signs of apoptosis (Gao et al. 2006). Solanine opened up the permeability transition channels in HepG₂ mitochondrial membrane by lowering the membrane potential, leading to Ca²⁺ being transported down its concentration gradient, which in turn led to the rise of the concentration of Ca²⁺ in the cell, turning on the mechanism for apoptosis.

The proliferation of colon cancer and liver cancer cells was significantly inhibited by potato antioxidant extracts (Wang et al. 2011). The highest antiproliferative activity was observed in extracts of *Solanum pinnatisectum* and the lowest in potato cv. Northstar. *S. pinnatisectum* had the highest antioxidant activity, total phenolic and chlorogenic acid content. An

inverse correlation was found between total phenolics and the EC_{50} of colon cancer cell ($R^2 = 0.9303$), as well as liver cancer cell proliferation ($R^2 = 0.8992$). The relationship between antioxidant activity and EC_{50} of colon cancer/liver cancer cell proliferation was significant ($R^2 = 0.8144$; $R^2 = 0.956$, respectively). A significant difference in inhibition of cancer cells existed between the 3 polyphenols: chlorogenic acid, pelargonidin chloride and malvidin chloride, suggesting that chlorogenic acid was a critical factor in the antiproliferation of colon cancer and liver cancer cells.

The results of studies by Madiwale et al. (2011) suggested that although the antioxidant activity and phenolic content of potatoes were increased with storage, the antiproliferative and pro-apoptotic activities against early, HCT-116 and advanced stage, HT-29 human colon cancer cell lines were suppressed. Purple-fleshed potatoes were more potent in suppressing proliferation and elevating apoptosis of colon cancer cells compared with white- and yellow-fleshed potatoes. The extracts from both fresh and stored potatoes (10–30 $\mu\text{g/mL}$) suppressed cancer cell proliferation and elevated apoptosis compared with the solvent control, but these anticancer effects were more pronounced with the fresh potatoes. Storage duration had a strong positive correlation with antioxidant activity and percentage of viable cancer cells and a negative correlation with apoptosis induction. Ethanolic extracts of baked and chipped samples suppressed proliferation and elevated apoptosis in human colon HCT-116 (p53 wild type; ras mutated) and HT-29 (p53 mutated; ras wild type) human colon cancer cell lines (Madiwale et al. 2012). Antiproliferative and pro-apoptotic properties of baked potatoes were similar to that of fresh potatoes, while chipping caused a significant suppression. Phenolic content and antioxidant activity of purple-fleshed potatoes, after baking, were comparable with those of anthocyanin-rich berries. When compared with unprocessed samples, baking or chipping led to significant losses in the phenolic and anthocyanin content and antioxidant activity of the potatoes. However, with storage, total phenolic and anthocyanin content and antioxidant activity increased in baked samples, while in the chipped samples they

remained constant. Hence, purple-fleshed potatoes could be a healthier choice for consumers as they were found to possess greater levels of bioactive compounds and anticancer properties even after processing as compared with their white- and yellow-fleshed counterparts.

Patatin from potato fruit was identified as a potent antiproliferative agent against mouse melanoma B16 cells, causing cell cycle arrest in the G1 phase (Sun et al. 2013). Assays of apoptotic cells also showed that patatin treatment at concentrations of 20 mg/mL resulted in a marked reduction of viable cells.

Heated potato fibre (Potex) containing melanoidin complexes inhibited C6 glioma cell proliferation in a dose-dependent manner (Langer et al. 2011). High molecular weight components present in initial extract were responsible for stronger antiproliferative effect compared with low molecular weight fraction. It was observed that the activity of melanoidins present in heated Potex was linked to dysregulated MAPK and Akt signalling pathways, as well as to cell cycle cessation. In a subsequent study, they reported that both heated potato fibre Potex extract (180 °C for 2 h) and melanoidins isolated from the extract exert growth-inhibiting activity in human LS180 colon cancer cells in-vitro (Langner et al. 2013). Roasted potato fibre extract (AM4) as well as with high (HMW) and low (LMW) molecular weight fractions (containing melanoidins) isolated from the extract, at concentration of 1000 µg/ml, reduced cell growth down to 45 %, 69 % and 54 %, respectively. Besides deregulation of ERK1/2 signalling upon treatment, multiple alternations in cell cycle regulators activity were found (i.e. cyclinD1, cyclin-dependent kinase 4 and 6, p21, p27, p53, pRb) leading to cell cycle cessation in G0 phase.

Epidemiologic health studies had shown a reduction in cancer risk in individuals and populations consuming high amounts of dietary fibre and vegetables (Cummins et al. 1992; Faivre et al. 1993). Recently, a strong inverse association between starch consumption and incidence of large bowel cancer was reported. Starch being the predominant form of carbohydrate found in potatoes, an appreciable amount of

which called resistant starch (RS) had been reported to escape digestion in the small intestine, depending on physical inaccessibility, type of granule and food processing. Starch and dietary fibre together were reported as the principal substrates controlling the pattern of fermentation in the colon and, thus, the metabolism of compounds like bile acids, nitrate and enzyme activities (bacterial and antioxidant enzymes), which had been implicated in carcinogenesis (Cummings et al. 1992; Hylla et al. 1998; Raban et al. 1994). This resistant starch had been reported to have similar physiological effects and health benefits of fibre in that it provides bulk, gives protection against colon cancer, increases glucose tolerance and insulin sensitivity, reduces plasma cholesterol and triglyceride concentrations, enhances satiety and may even reduce fat storage.

Antiviral Activity

The infectivity of herpes simplex virus type I in tissue culture was inhibited by prior incubation with aqueous suspensions of glycoalkaloids in order of activity α -chaconine greater than α -tomatine greater than α -solasanine but not by the corresponding aglycones, solanidine, tomatidine and solasodine (Thorne et al. 1985). The glycones, but not the aglycones, showed cytopathic effects on cellular membranes of Vero cells and erythrocytes; therefore, it was suggested that inactivation of virus results from insertion of the glycones into the viral envelope.

Anti-inflammatory Activity

In a randomised study of free-living healthy men (18–40 years old), consumption of pigmented-fleshed potato was found to alter oxidative stress, DNA damage and inflammatory damage (Kaspar et al. 2011). Compared with the white-fleshed potato (WP) group, the yellow-fleshed potato (YP) group had higher concentrations of phenolic acids and carotenoids, whereas the purple-fleshed potato (PP) group had higher concentrations of phenolic acids and anthocyanins. Men who consumed YP and PP tended to have lower plasma interleukin IL-6 compared

with those consuming WP. The PP group tended to have a lower plasma C-reactive protein concentration than the WP group. The plasma 8-hydroxydeoxyguanosine concentration was lower in men who consumed either YP or PP compared with WP. Studies showed that potato glycoalkaloids α -chaconine, α -solanine and solanidine, along with potato peel extracts, possessed anti-inflammatory effects in-vitro (Kenny et al. 2013). α -Chaconine and solanidine significantly reduced interleukin-2 (IL-2) and interleukin-8 (IL-8) productions in Con A-induced Jurkat cells. In LPS-stimulated RAW macrophages, α -solanine, solanidine and two potato peel extracts significantly reduced induced NO production. Oral administration of *Solanum tuberosum* var. Vitelotte (SV) extract to NC/Nga mice resulted in the inhibition of the development of atopic dermatitis (AD)-like skin lesions induced by the topical application of 2,4-dinitrochlorobenzene (shim and Choung 2014). SV extract has attenuated AD-like skin lesion, ear thickening and scratching behaviour and alleviated infiltrated inflammatory cells in tissue. Production of Th1 and Th2 cytokines was inhibited in splenocyte cultures. Additionally, reduced levels of IgE and IgG1/IgG2a ratio in serum and expression of AD-related mRNAs in lesional skins were observed in SV-treated mice compared with control group. The chloroform fraction of the peel of Jayoung (CFPJ), a color-fleshed potato, inhibited the expressions of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) at the transcription level and attenuated the transcriptional activity of nuclear factor- κ B (NF- κ B) by reducing the translocation of NF- κ B depending on degradation of inhibitory κ B- α (I κ B- α) in lipopolysaccharide (LPS)-induced RAW 264.7 macrophages (Lee et al. 2014). Additionally, CFPJ attenuated the phosphorylations of mitogen-activated protein kinase 3/6 (MKK3/6) and of p38. Administration of CFPJ to mice with dextran sulphate sodium-induced colitis significantly reduced the severity of colitis and the productions and protein levels of pro-inflammatory mediators in colonic tissue.

Antidiabetic Activity

Potato peel (PP) powder supplementation in diet was found to effectively attenuate diabetic alterations in rats (Singh et al. 2005a). Streptozotocin diabetic rats fed with PP powder-supplemented diet for 4 weeks showed a significant decrease in blood glucose levels. Incorporation of PP powder reduced significantly the hypertrophy of both the liver and kidney of streptozotocin (STZ)-diabetic rats and also normalised the activities of serum ALT and AST, hepatic and renal MDA and GSH, as well as activities of various antioxidant enzymes in the liver and kidney of diabetic rats. Furthermore, PP powder in the diet also appeared to attenuate the eye lens damage associated with the diabetic condition. They also reported that in a 4-week feeding trial, incorporation of potato peel powder (5 and 10 %) in the diet of diabetic rats was found to significantly reduce the plasma glucose level and also reduce drastically the polyuria of STZ diabetic rats (Singh et al. 2005b). The total food intake was significantly reduced in the diabetic rats fed 10 % PP powder compared to the control diabetic rats. However, the body weight gain over 28 days was nearly four times greater in PP powder-supplemented diabetic rats (both at 5 and 10 %) compared to the control diabetic rats. PP powder in the diet also decreased the elevated activities of serum transaminases (ALT and AST) and nearly normalised the hepatic MDA and GSH levels as well as the activities of specific antioxidant enzymes in the liver of diabetic rats.

Calystegines A₃ and B₂ purified from potatoes were found to inhibit maltase and sucrose, α -glucosidases contributing to human carbohydrate degradation in the small intestine (Jocković, et al. 2013). Calystegine A₃ showed low in-vitro enzyme inhibition; calystegine B₂ inhibited mainly sucrose activity. Both compounds were not transported by Caco-2 cells indicating low systemic availability. The authors suggested that vegetables rich in calystegine B₂ should be further investigated as possible components of a diet preventing a steep increase in blood glucose after a carbohydrate-rich meal.

Feeding mice with polyphenolic-rich potato extracts (PRPE) of cultivars Onaway and Russet Burbank for 10 weeks attenuated weight gain in male and female mice by as much as

63.2 %, which was associated mostly with a reduction in adiposity (Kubow et al. 2014). Mice receiving PRPE showed enhanced capacity for blood glucose clearance. Sex differences regarding the impact of HFD and PRPE on plasma levels of insulin, ghrelin, leptin, gastric inhibitory peptide and resistin were observed. PRPE may serve as part of a preventative dietary strategy against the development of obesity and type 2 diabetes.

Starch in foods may be classified into rapidly digestible starch (RDS), slowly digestible starch (SDS) and resistant starch (RS) (Englyst et al. 1992). RS may be further divided into three categories according to the reason for resistance to digestion. Studies conducted showed that the replacement of digestible starch with RS resulted in significant reductions in postprandial glycaemia and insulinemia and in the subjective sensations of satiety (Raban et al. 1994). The amount of resistant starch found in potatoes was highly dependent upon preparation methods. Cooking and then cooling potatoes significantly increased resistant starch. For example, cooked potato starch contained about 7 % resistant starch, which increased to about 13 % upon cooling (Englyst et al. 1992). Cooked potatoes were found to have high levels of digestible starch (DS) (García-Alonso and Goñi 2000). Starch digestibility is improved after processing and it is affected by the cooking methods. Boiled and mashed potatoes showed the highest rate of digestion; on the contrary raw potato was hardly digested. The estimated glycaemic index (GI) from the degree of starch hydrolysis within 90 min was in accordance with the reported GI values, for potatoes processed in the same way. Results of studies demonstrated that degree of gelatinisation (DG) of starch strongly affected its digestibility in-vitro and may influence the postprandial glycaemic response (Parada and Aguilera 2009). DG was closely related with heating temperature ($R^2 = 0.997$), size parameters of granules (measured by image analysis), in-vitro digestion and in-vivo glycaemic response (R^2 of adjusted models > 0.9). Shape parameters of granules were not related with the degree of gelatinisation. Seven potato cultivars tested had a wide range of GI values (53–103) (Ek et al. 2014). The Carisma

cultivar was classified as low GI and the Nicola cultivar (GI = 69) as medium GI, and the other five cultivars were classified as high GI according to ISO guidelines. The GI values were strongly and positively correlated with the percentage of in-vitro enzymatic hydrolysis of starch in the cooked potatoes. Amylose, dietary fibre and total starch content were not correlated with either in-vitro starch digestibility or GI.

Recently, it was reported that hydrolysis of the potato protein isolates (breaking down of the compound by reacting with water) produced proteins with an increased activity for ACE (angiotensin-I-converting enzyme) inhibition and radical scavenging activity. ACE inhibitors act by inhibiting the conversion of angiotensin I to the potent vasoconstrictor, angiotensin II, thereby improving blood flow and blood pressure. The study suggested that potato was a promising source for the production of bioactive compounds as ingredients for developing functional foods with a beneficial impact on cardiovascular health. ACE inhibitors made by drug companies have been found to be beneficial in treating hypertension, particularly in patients with type 1 or type 2 diabetes, and also appear to provide good cardiovascular and renal protection.

On the negative side, potato is regarded as high glycaemic index (GI) food and is avoided by people following a 'low GI' eating regimen. The GI of potatoes can vary considerably depending on the potato variety (i.e. red vs. russet vs. white vs. Prince Edward), preparation methods (i.e. cooking method, whether it is eaten hot or cold, whether it is mashed or cubed or consumed whole, etc.) and with what is consumed (i.e. the addition of various high fat or high protein toppings). US Russet potatoes have only a moderately high glycaemic index. Individuals who wish to minimise dietary glycaemic index can be advised to precook potatoes and consume them cold or reheated (Fernandes et al. 2005). Boiled potatoes were more satiating than French fries on an energy-equivalent basis, the effect being most prominent in the early postprandial phase, whereas no difference in satiety could be seen on a carbohydrate-equivalent basis. French fries resulted in a significantly lower glycaemic response (glycaemic index (GI)

= 77) than boiled potatoes either with or without the addition of oil (Leeman et al. 2008). It was also shown that the high glycaemic and insulinaemic features commonly associated with potato meals can be reduced by the use of vinegar dressing and/or by serving cold potato products.

Clinical Studies

In a study of ten healthy, normal-weight, young males, after administration of a meal of 50 g raw potato starch (54 % resistant starch (RS)) together with 500 g artificially sweetened syrup, postprandial plasma concentrations of glucose, lactate, insulin, gastric inhibitory polypeptide (GIP), glucagon-like peptide-1 and epinephrine were significantly lower compared with after the meal of 50 g pregelatinised starch (0 % RS) together with 500-g artificially sweetened syrup (Raben et al. 1994). It was concluded that replacement of digestible starch with resistant starch resulted in significant reductions in postprandial glycaemia and insulinemia and in the subjective sensations of satiety. In a subsequent study of 11 healthy, normal-weight, young men, they compared two chemically modified starches—a 1–2 % acetylated potato starch and a starch enriched with 2 % β -cyclodextrin—and a native, unmodified potato starch (control) (Raben et al. 1997). The meal was given in the morning after a 2-day carbohydrate-rich, weight-maintenance diet. After the modified-starch meals, response patterns for plasma glucose, insulin, gastric inhibitory polypeptide, subjective satiety and fullness were significantly different from response patterns after the meal with the control starch. A flattening of the glucose curve, a lower insulin and gastric inhibitory polypeptide response and higher fullness ratings were observed after the meal with the β -cyclodextrin starch. Satiety ratings were higher after both meals with modified starch than after the meal with the control starch. It was concluded that a minor modification insulinaemic (1–2 %) of native potato starch improved the glycaemia, insulinaemic and satiating properties of a meal. In a study of 10 healthy volunteers, potatoes, regardless of variety, cooking method and maturity, were found to have exceptionally high glycaemic index (GI)

values (Soh and Brand-Miller 1999). Mean GI values ranged from 65 for canned new potatoes to 10 for boiled Desiree potatoes. The relative lower values of new potatoes were attributed to differences in starch structure. Cold storage and addition of vinegar reduced acute glycaemia and insulinaemia in healthy subjects after a potato meal (Leeman et al. 2005). Cold storage of boiled potatoes increased resistant starch (RS) content significantly. The results showed that the high glycaemic and insulinaemic features commonly associated with potato meals could be reduced by use of vinegar dressing and/or by serving cold potato products. Precooked Russet potatoes elicited lower area under the curve than day cooked in human subjects, while precooking had no effect on boiled white potatoes (Fernandes et al. 2005). The glycaemic index values of potatoes varied significantly, depending on the variety and cooking method used ranging from intermediate (boiled red potatoes consumed cold: 56) to moderately high (roasted California white potatoes: 72; baked US Russet potatoes: 77) to high (instant mashed potatoes: 88; boiled red potatoes: 89). In studies of healthy subjects, boiled potatoes induced higher subjective satiety than French fries when compared on an energy-equivalent basis (Leeman et al. 2008). French fries elicited the lowest early glycaemic response and was less satiating in the early postprandial phase (area under the curve (AUC) 0–45 min). No differences were found in glycaemic or satiety response between boiled or mashed potatoes. In a second study, French fries resulted in a significantly lower glycaemic response (glycaemic index (GI) = 77) than boiled potatoes either with or without the addition of oil (GI = 131 and 111, respectively). No differences were found in subjective satiety response between the products served on carbohydrate equivalence.

In a randomised block design study of 9 healthy volunteers, administration of pigmented potatoes resulted in no significant differences in areas under the curve (AUC) for blood glucose response or insulin among the various potatoes studied (Ramdath et al. 2014). Although the mean GI values for the potato types varied (purple = 77.0; red = 78.0; yellow = 81.0; and white = 93.0), these differences were not significantly different. The mean polyphenol content (mg

GAE/100 g DW) was 234, 190, 108 and 82 for purple, red, yellow and white potatoes, respectively. There was a significant inverse correlation between polyphenol content and GI of the potatoes ($R^2 = -0.825$). In-vitro, polyphenol extracts of red and purple potatoes inhibited α -glucosidase by 37.4 % and 28.7 %, respectively. The GI of coloured potatoes was significantly related to their polyphenol content, possibly mediated through an inhibitory effect of anthocyanins on intestinal α -glucosidase.

Hepatoprotective Activity

Administration of red potato extract (RPE) protected liver damage in D-galactosamine (GalN)-intoxicated rats (Han et al. 2006a). Increases in serum aspartate aminotransferase, alanine aminotransferase and lactate dehydrogenase activities, all of which were induced by GalN injection, decreased in RPE-administered rats, suggesting that RPE acted as a functional food showing anti-hepatotoxicity. Purple potato flakes were found to have antioxidant functions with regard to DDPH radical scavenging activity and inhibition of linoleic acid oxidation, and they improved the antioxidant potentials in rats by enhancing hepatic Mn-SOD (superoxide dismutase), Cu/Zn-SOD and glutathione peroxidase (GSH-Px) mRNA expression (Han et al. 2006b). In another study, Han et al. (2007b) found serum thiobarbituric acid-reactive substances concentration and hepatic superoxide dismutase mRNA level in rats fed red potato flakes (RPF) were significantly lower and higher, respectively, than those in control rats. The results suggested that RPF might improve the antioxidant system by enhancing hepatic SOD mRNA.

Supplementation with anthocyanin-rich purple potato (cv. Shadow Queen) flakes in F344 rats fed a cholesterol-rich diet was found to enhance the antioxidant status (Han et al. 2007a). Thiobarbituric acid-reactive substance (TBARS) levels in the serum and liver of rats fed Shadow Queen were significantly lower than those in the control and white potato (cv. Toyoshiro) groups. The hepatic glutathione levels and activities of hepatic glutathione reductase and glutathione S-transferase in the Shadow Queen were significantly higher in

the Shadow Queen group than in the control group. The results showed that enhancement of antioxidant enzymes and oxidative status in the serum and liver by the purple potato flake diet (Shadow Queen) containing polyphenols/anthocyanins may play an important role in the protection against adverse effects related to oxidative damage in rats fed a high-cholesterol diet.

Antihypercholesterolemic Activity

Feeding rats a potato-enriched diet for 3 weeks led to a significant decrease in cholesterol and triglyceride levels in plasma and cholesterol level in the liver (Robert et al. 2006). Antioxidant status was also improved by potato consumption. TBARS levels in the heart were decreased and vitamin E/triglycerides ratio in plasma was improved. Robert et al. (2008) found that the consumption of complex carbohydrates (provided as cooked potatoes) by rats for 3 weeks, in combination with different antioxidant micronutrients, may enhance the antioxidant defences and improve lipid metabolism, when compared with starch (complex carbohydrates) and to sucrose consumption (source of simple sugar). Feeding rats a potato-based diet for 3 weeks led to a decrease in cholesterol (−37 %, potato vs. control, and −32 %, potato vs. sucrose) and triglycerides (−31 %, potato vs. control, and −43 %, potato vs. sucrose) concentrations in triglyceride-rich lipoprotein (TGRLP) fractions. The antioxidant status was decreased by sucrose consumption and improved by potato consumption. These effects limited oxidative stress and reduced the risk of developing the associated degenerative diseases, including cardiovascular disease, and could have potential in cardiovascular disease prevention.

Hypotensive Activity

In a crossover study, 18 hypertensive subjects with an average body mass index (BMI) of 29 and administration of six to eight small microwaved purple potatoes twice daily for 4 weeks elicited a significant decrease in diastolic and systolic

blood pressures (Vinson et al. 2012). There was no significant effect of potato on fasting plasma glucose, lipids or HbA1c. There was no significant body weight increase. In a comparative single-dose study six to eight microwaved potatoes with skins and comparable amount of refined potato starch as cooked biscuits given to eight normal fasting subjects, potato caused an increase in plasma and urine antioxidant capacity, whereas refined potato starch caused a decrease in both, i.e. it acted as a pro-oxidant.

Wound Healing Activity

Compared with treatment with plain gauze dressings for burn wounds, the application of the potato peel dressing reduced or eliminated desiccation, permitted the survival of superficial skin cells and hastened epithelial regeneration (Keswani et al. 1990). Bacteriological studies showed that the potato peels had no intrinsic antibacterial activity, the wounds beneath both dressings showing either no growth or, on most occasions, the same bacterial species. The easy availability of potato peels and gauze bandages on to which they can be affixed, the simplicity of the preparation of this dressing, the ease of sterilisation and its low cost of production make this the dressing of choice for burn wounds in developing country. In a series of experiments, full thickness skin defects in 68 rats were covered with dressings made of boiled potato peels, the wounds closed within 14 days, and histologically complete repair of epidermis was found (Dattatreya et al. 1991). The cork layer of the potato peel prevented dehydration of the wound and protected against exogenous agents. Experiments with homogenates revealed that a complete structure of the peel was necessary. Steroidal glycosides may have contributed to the favourable results. In the 50 patients treated with honey, 90 % of burn wounds were rendered sterile within 7 days (Subrahmanyam 1996). In the 50 patients treated with boiled potato peel dressings, persistent infection was noted within 7 days. Of the burn wounds treated with honey, 100 % healed within 15 days as against 50 % in the wounds treated with boiled potato peel dressings (mean 10.4 vs. 16.2 days).

Cholesterol Metabolism

Hashimoto et al. (2011) reported that rats fed a potato pulp (PP)-supplemented diet for 4 weeks improved both cecal conditions and cholesterol metabolism, suggesting that potato pulp had prebiotic effects. Rats fed with the PP-supplemented diet showed increased cecal ratios of *Lactobacillus* and *Clostridia* and decreased cecal ratios of *Bacteroides* and *Proteobacteria* with slightly negative and positive correlations with plasma T-cholesterol levels, respectively. Mandimika et al. (2008) found that PI3K/AKT, JNK and ERK pathways were not crucial for the induction of cholesterol biosynthesis gene SREBP-2 transcription in intestinal caco-2 epithelial cells following treatment with the potato glycoalkaloid α -chaconine.

Pharmacokinetic Studies

Potato glycoalkaloids, α -solanine and α -chaconine, were detected in all blood serum samples collected from seven volunteers 1–25 h after a meal of potatoes (Hellenäs et al. 1992). Their aglycone, solanidine, was detected in some samples, but there were no traces of the mono- or diglycosides. The average apparent biological half-lives for α -solanine and α -chaconine were 11 and 19 h, respectively. In a randomised, controlled double-blinded, crossover pilot study of three men, consumption of zeaxanthin-rich mashed potatoes significantly increased chylomicron zeaxanthin concentrations suggesting that potentially such potatoes could be used as an important dietary source of zeaxanthin (Bub et al. 2008). There were no significant differences in the concentrations of other major potato carotenoids such as lutein and β -carotene in chylomicrons after consumption of genetically modified and wild-type control potatoes.

Miranda et al. (2013) found that iron uptake, as evaluated by a ferritin assay, by intestinal human cells was decreased after incubation with the intestinal phase of in-vitro digestion, presumably due to the presence of polyphenols (chlorogenic acid and derivatives and rutin) from potatoes and sweet potatoes.

Trypanocidal Activity

The glycoalkaloids α -chaconine, α -solanine, α -solanine, solasonine, sycophantine and tomatine, as well as the aglycones demissidine, solanidine, solanocapsine, solasodine, tomatidine and veratrine, were tested as growth inhibitors of *Trypanosoma cruzi*, strain EP (Chataing et al. 1998).

Glycoalkaloids containing α -chacotriose, namely, α -chaconine, and the aglycone solanidine showed trypanolytic activity against the epimastigote form and trypanocidal activity against the bloodstream and metacyclic trypomastigote form of *Trypanosoma cruzi* in culture medium in micromolar concentrations.

Toxicological Studies

Rabbits fed on greened potatoes became dull and showed reduction in body weight after 30 days of feeding (Azim et al. 1982). They had comparatively enlarged livers and also showed a significant difference in relative size of heart. Blood samples collected from these animals after 30 days showed an increase in the concentration of cholesterol and sugars in blood plasma and a decrease in protein. Plasma electrolytes showed an increase in Ca^{2+} and a decrease in Na^+ and K^+ . There was a decrease in protein content of the liver, kidney, heart and intestine. The glycogen content of liver and kidney was also decreased though glycogen concentration increased in heart tissue. Cholesterol levels were increased in each of these organs. There was a decrease in Ca^{2+} content in the four organs but K^+ content was significantly increased in kidney and intestinal muscles though its concentration was decreased in liver and heart muscles. Na^+ content significantly increased in the heart muscles but decreased in other organs. The results illustrated the toxic nature of the glycoalkaloids in greened potatoes.

Compared to controls, *Solanum elaeagnifolium* and *Solanum dulcamara* fruit, containing appreciable amounts of an unknown spirosolane, an aglycone provisionally identified as soladulcidine, both induced a high percentage incidence of

deformed hamster litters with congenital craniofacial malformations (20.4 and 16.3, respectively) that was statistically significant, while percentage incidence of deformed litters induced by *Solanum sarrachoides* and *Solanum melongena* fruit containing mainly solasodine glycosides (9.5 and 7.6 respectively) were both higher than controls (3.4 %), in neither case was the incidence statistically significant (Keeler et al. 1990). Deformed litter incidence induced by sprouts of *Solanum tuberosum*, containing mainly solanidane glycosides, was 24.0 %. Oral administration of the steroidal alkaloid glycosides α -solanine and α -chaconine from potato var. Kennebec sprouts and their aglycone solanidine was shown to induce craniofacial malformations (exencephaly, encephalocele and anophthalmia) in Syrian hamsters (Gaffield and Keeler 1996). Malformation induction was observed in litters upon dosing both the non-toxic aglycone solanidine and the derivative solanidine N-oxide at higher levels. The relatively high teratogenicity of non-toxic solanidine, compared to the glycosides, demonstrated that terata induction by solanidanes was not due to maternal toxicity nor was the oligosaccharide portion of steroidal alkaloid glycosides required to facilitate passage of the teratogen to the foetus.

Aqueous potato leaf extracts containing glycoalkaloids (PGA) (α -solanine and α -chaconine) were cytotoxic to Chinese hamster ovary cells and lysed human, rat and hamster blood cells with no difference in sensitivity among species (Phillips et al. 1996). Oral administration of potato tops to rats, mice and Syrian hamsters had no adverse effects at the highest practicable dose. A mixture of α -solanine and α -chaconine (1:1, w/w) given orally at doses of up to 50 mg/kg body weight to hamsters had no effect, but a single i.p. injection of 25 mg/kg body weight or greater was lethal, with bleeding in the gut. High concentrations of cytotoxic PGA were found in some potato tops, but their effect in laboratory animals was minimal. The authors concluded that the consumption of moderate quantities of potato tops (2–5 g/kg body weight/day) was unlikely to represent an acute health hazard to humans.

Feeding non-pregnant mice for 14 days on a diet containing 2.4 mmol/kg of aglycone solanidine (derived by

hydrolytic removal of the carbohydrate side chain from the potato glycoalkaloids α -chaconine and α -solanine) resulted in significantly greater ratios of % liver weights to body weights (%LW/BWs) 25 than those of the control values (Friedman et al. 2003a). The corresponding increase in pregnant mice was 5.3 for solanidine. For pregnant mice, (a) body weight gain –36.1 for solanidine was less than with control, solanidine; (b) litter weight with solanidine –27.0 was less than control; and (c) the average weight of the foetuses for solanidine –11.2 was less than the control. Abortion of foetuses occurred in five of 24 pregnant mice on the solanidine diet. In in-vitro assays for estrogenic activity, solanidine at 10- μ M concentration exhibited an increase in the MCF-7 human breast cancer cell proliferation.

In an acute animal toxicity study, daily doses of potato α -solanine (100 mg/kg body weight (BW)) induced death in two of four hamsters within 4 days, when administered by gavage to female Syrian hamsters (Langkilde et al. 2008). Doses of 100 mg of α -chaconine alone or α -solanine and α -chaconine combined in a ratio of 1:2.5, in doses of 75 or 100 mg/kg BW, induced death in one of four hamsters within the same period. Animals dosed with α -solanine alone or in combination with α -chaconine suffered from fluid-filled and dilated small intestines. The glycoalkaloid (GA) administration had no effect on acetylcholinesterase (AChE) or butyrylcholinesterase (BuChE) activity in plasma or the brain. In addition, metabolomics gave direct evidence of glycolytic metabolism of the GA with the β 1, β 2 and γ GAs detected in the urine and, to a lesser extent, the faeces. Doses from 75 mg/kg BW of α -chaconine, α -solanine or the two compounds combined were potentially lethal within 4–5 days in the Syrian Golden hamster. However, the cause of death in these studies could not be established. No synergistic effects of α -solanine combined with α -chaconine were evident. In another study, doses of up to 33.3-mg total glycoalkaloids/kg body weight were applied in ratios of 1:3.7 and 1:70 (α -solanine/ α -chaconine) to Syrian Golden hamster by gavage for 28 days (Langkilde et al. 2009). Administration of the highest doses of both ratios resulted in distended and fluid-filled small intestines and stomach. Animals receiving the ratio with the

reduced content of α -solanine were less affected compared to those receiving the other ratio. In a 90-day feeding trial with the Syrian Golden hamster, administration of 60 % freeze-dried potato powder of a GM potato line (SGT 9–2) with reduced α -solanine content, and the parental control line (Desiree wild type) with a traditional α -solanine/ α -chaconine ratio, did not raise concerns related to nutritional value or safety (Langkilde et al. 2012). Results of the feeding trials showed a low number of significant differences between potato lines with different α -solanine/ α -chaconine ratio, but none were considered to raise safety concerns with regard to human (or animal) consumption.

In a clinical study, human volunteers were administered one of 6 treatments of solutions with TGA (total glycoalkaloid) doses of 0.30, 0.50 or 0.70 mg/kg body weight (bw) or 4–6 mashed potatoes with TGA doses of 0.95, 1.10 or 1.25 mg/kg bw (Mesinga et al. 2005). Mashed potatoes contained TGA level of nearly 200 mg/kg fresh weight (presently recognised as upper limit of safety). The administered single dose of up to 90.2 mg TGA (1.25mgTGA/kg body weight) did not induce acute systemic effects. In one subject at the highest level of exposure (1.25mgTGA/kg body weight), some vomiting was experienced possibly due to local glycoalkaloid toxicity. The results also showed that the clearance of glycoalkaloids took more than 24 h, thus allowing the substance to accumulate in the body. They asserted that additional studies were required to establish an adequate based no observed adverse effect level (NOAEL).

The toxicological monograph produced by the JointFAO/WHO Expert Committee on Food Additives (JECFA) in 1993 stated that glycoalkaloids were not acutely toxic by the oral route in laboratory animals even at very high doses (up to 1 g/kg bodyweight) in some species. The committee considered that the evidence implicating glycoalkaloids in potato poisoning cases was not convincing. JECFA concluded that levels of α -solanine and α -chaconine normally found in potatoes (20–100 mg/kg) were not of toxicological concern. Nevertheless, JECFA and others have

expressed concern about glycoalkaloids in skin-on potato products, such as crisps, that became widely available in the mid-1990s. Glycoalkaloid concentrations of up to 720 mg/kg were found in green-skinned crisps, compared with a maximum of 150 mg/kg in normal crisps.

Freeze-dried potato peel aqueous extract was found to be non-mutagenic using the in-vitro *Salmonella typhimurium*–*Escherichia coli* microsome assay; plate counts revealed <10 CFU/g (De Sotillo et al. 1998). It was effective only at high concentration against Gram-negative and one Gram-positive bacteria but it was bacteriostatic. In the frog embryo teratogenesis assay—*Xenopus* (FETAX), α -chaconine was teratogenic and more embryotoxic than α -solanine; in terms of the median lethal concentration (LC₅₀) after 96 h of exposure, the concentration inducing gross terata in 50 % of the surviving frog embryos (96-h EC₅₀, malformation) and the minimum concentration needed to inhibit the growth of frog embryos (Friedman et al. 1991). The aglycones demissidine, solanidine and solasodine were less toxic than the glycosides α -chaconine and α -solanine.

The glycol–alkaloid extracts were also reported active against *Microsporum gypseum* and *Cryptococcus neoformans*, *Artemia salina nauplii* and *Trypanosoma cruzi* and showed intraperitoneal subacute toxicity in mice.

Adverse Toxicity Issues

The total glycoalkaloid content (TGA) of potato tubers had been reported to vary widely; values between 2 and 410 mg/100 g of fresh weight (FW) had been reported (Lisinska and Leszczynski 1989), but in most cases the TGA concentration in whole tubers was between 10 and 150 mg/100 g of FW (Gelder et al. 1988). Cooking and frying had been reported to not destroy the glycoalkaloids (Maga 1994). The widely accepted safety limit for the level of total glycoalkaloids (TGA) in tubers was stated as 200 mg/kg of FW (Boemer and Mattis 1924; Smith et al. 1996). Mild clinical symptoms of glycoalkaloid poisoning include abdominal pain, vomiting and diarrhoea (Friedman and

McDonald 1997). Severe glycoalkaloid poisoning caused symptoms ranging from gastrointestinal disorders through confusion, hallucination and partial paralysis to convulsions, coma and death (Smith et al. 1996). Evidence suggested that human susceptibility to glycoalkaloid poisoning was high and very variable: oral doses in the range of 1–5 mg/kg of body weight were marginally to severely toxic to humans (Hellenäs et al. 1992, whereas 3–6 mg/kg of body weight could be lethal (Morris and Lee 1984). Glycoalkaloids (α -solanine and α -chaconine) had been reported to contribute flavour to potatoes but at higher concentrations (>200 mg/kg) caused bitterness (Friedman 2006) and were toxic to humans (Ostrý et al. 2010). α -Solanine and α -chaconine appeared to have two main toxic actions, one on disruption of cell membranes (Roddick et al. 1990; Keukens et al. 1992, 1995, 1996) and another one on acetylcholinesterase (Huxtable 1992). Symptoms of α -solanine/ α -chaconine poisoning involve an acute gastrointestinal upset with diarrhoea, vomiting and severe abdominal pain (Friedman 2006). The steroidal glycoalkaloid solamargine caused significant disruption of phosphatidylcholine/cholesterol liposomes at a concentration >50 μ M, whereas the normally co-occurring glycoalkaloid solasonine was ineffective at up to 150 μ M (Roddick et al. 1990). In combination, the two compounds produced a marked synergism. Synergistic effects were also observed with certain combinations of these and potato glycoalkaloids, viz. solamargine and solanine and also solasonine and chaconine.

Keukens et al. (1992) found that glycoalkaloids α -solanine, α -chaconine, α -tomatine and the aglycone solanidine were able to interact strongly with sterol containing membranes, thereby causing membrane disruption. The order of potency of the glycoalkaloids was α -tomatine > α -chaconine > α -solanine. The plant sterols β -sitosterol and fucosterol showed higher affinity for glycoalkaloids as compared to cholesterol and ergosterol. The mode of action of the glycoalkaloids was proposed to consist of three main steps: (1) insertion of the aglycone part in the bilayer, (2) complex formation of the glycoalkaloid with the sterols present and (3) rearrangement of the membrane caused by the formation of a network of sterol–glycoalkaloid complexes resulting in a transient disruption of

the bilayer leading to leakage. They found that the most important properties for sterols to interact with glycoalkaloids turned out to be a planer ring structure and a 3 β -OH group, whereas for α -chaconine the 5–6 double bonds and the 10-methyl group were also of importance. The importance of sugar–sugar interactions was illustrated by the high synergistic effect between α -chaconine and α -solanine, the leakage enhancing effect of glycolipids and the almost complete loss of activity after deleting one or more monosaccharides from the glycoalkaloids (Keukens et al. 1995). They further found that these glycoalkaloids specifically induced membrane disruptive effects of cholesterol-containing membranes as was previously reported in model membrane studies (Keukens et al. 1996). In addition, α -chaconine was found to selectively decrease gap-junctional intercellular communication. Furthermore, the glycoalkaloids were more potent in permeabilising the outer membrane of mitochondria compared to digitonin at the low concentrations used.

Studies by Friedman et al. (1996) found that feeding of potato, tomato and eggplant alkaloids affected food consumption and body and liver weights in mice. The relative liver weights (liver weight/body weight $\times$ 100, %LW/BW) were lower than that of controls in mice fed the potato glycoalkaloid α -chaconine (–10 %) for 7 days with the 2.4 mmol/kg diet dose. Under these same conditions, %LW/BW was greater than that of controls in mice fed two aglycones: solanidine (27 %) and solasodine (8 %). Relative liver weight increases induced by the aglycones were determined under time and dose conditions in which differences in body weight and food consumption were not significant (2.4 mmol/kg diet for 28 days). Under these conditions, the observed %LW/BW increases relative to the controls were as follows: solanidine (32 %), solasodine (22 %) and dehydroepiandrosterone (DHEA) (16 %). Solanidine, solasodine and DHEA were equally potent and were more potent than tomatidine. Storage of potatoes at 5 °C increased the proportions of the 4-*O*- α -D-galactoside of calystegine B₂ and the trihydroxylated calystegine A₃ (Watson et al. 2000). Mice treated with calystegine A₃ showed vacuolation of Kupffer cells with

minimal vacuolation in other histiocytic cells. The microflora in rumen fluid removed from sheep previously fed hay reduced calystegines B₁ and B₂ to undetectable levels, but the concentrations of calystegine A₃ and the control compound swainsonine were not affected. There was no effect on the overall respiratory rate of the microbial population by any of these alkaloids.

Exposure of T84 cultured intestinal epithelial monolayers to potato glycoalkaloids (solanine and chaconine) permeabilised the cholesterol-containing membranes, with chaconine/solanine 1:1 mixture > chaconine > solanine, and led to the disruption of epithelial barrier integrity in a concentration-dependent fashion (Patel et al. 2002). In-vivo oral feeding experiments demonstrated that chaconine/solanine ingestion, at physiologic concentrations, aggravated histologic colonic injury in mice genetically predisposed to developing inflammatory bowel disease (IBD). Iablokov et al. (2010) demonstrated that consumption of deep-fried potato skins containing glycoalkaloids by interleukin 10 gene-deficient mice significantly elevated levels of ileal interferon IFN- γ relative to controls. Mice in the dextran sodium sulphate colitis IBD model that were fed the same strain of potatoes demonstrated significantly elevated levels of pro-inflammatory cytokines IFN- γ , TNF- α and IL-17 in the colon in addition to an enhanced colonic permeability. They concluded that consumption of potato skins containing glycoalkaloids could significantly aggravate intestinal inflammation in predisposed individuals.

Studies by Wang et al. (2005) concluded that exposure of bovine oocytes to potato steroidal glycoalkaloids (α -solanine and α -chaconine) during in-vitro maturation inhibited subsequent pre-implantation embryo development. This effect was significant during the later pre-implantation embryo development period as indicated by fewer numbers of expanded and hatched blastocysts produced in the media containing these alkaloids. They suggested that ingestion of *Solanum* species containing toxic amounts of glycoalkaloids may have negative effects on pre-implantation embryonic survival.

Hansen (1925) reported the fatal case of two members of a family of seven after a cooked meal of greened potatoes, and symptoms sustained included extreme exhaustion, restlessness, rapid breathing and loss of consciousness; the loss of six pigs due to eating sprouted, uncooked potatoes and the death of 30 chickens that died after consuming a large quantity of green potato sprouts. He also cited Macfayden who demonstrated that old sprouted potatoes were poisonous to horses. McMillan and Thompson (1979) reported an outbreak of suspected solanine poisoning in 78 schoolboys who became ill after eating cooked old potato at lunch. They suffered from diarrhoea, vomiting and circulatory, neurological and dermatological problems, with 17 of the boys being hospitalised. The amount of solanine in potato waste recovered after the meal was excessive as assessed by its anticholinesterase activity. The amount of α -solanine and α -chaconine in the flesh and peel of potatoes from a bag known to have been left from the previous term was high. Hellenäs et al. (1995a) reported that in Sweden, there were no indications of serious or widespread adverse health effects in consumers consuming potatoes with high glycoalkaloid levels, although there was circumstantial evidence that a few cases of temporary gastrointestinal disturbances were caused by consumption of Magnum Bonum potatoes with glycoalkaloid concentrations in the range 310–1000 mg/kg.

Traditional Medicinal Uses

Fomentations of potato juice followed by an application of liniment and ointment have been employed to relieve acute pain in cases of gout, rheumatism and lumbago (Grieve 1971). Sprains and bruises have also been successfully treated by the potato-juice preparations, and in cases of synovitis rapid absorption of the fluid has resulted. Hot potato water has in years past been a popular remedy for some forms of rheumatism, fomentations to swollen and painful parts, as hot as can be borne. Uncooked, peeled potatoes, pounded in a mortar and applied cold, have been found to make a very soothing plaster to parts that have been scalded or burnt. The mealy flour of baked potato, mixed with sweet oil, is a very

healing application for frostbites. In Derbyshire, hot boiled potatoes are used for corns. In Rwanda, potato tuber and carrot are pounded and the extract taken orally to treat dyspepsia and as a laxative (Kayonga and Habiyaemye 1987). In Ethiopia, the leaf extract is used against bacteria species causing tonsillitis (Desta 1993). In Morocco, a slice of potato is used to treat bruises, sprain and blisters and a poultice of potato used to treat fever and sunstroke (Bellakhdar 1997). In Cameroon, a mixture of potato tuber, avocado and honey is used as a poultice topically for injuries and wounds, and a decoction of carrot, potato tuber, orange fruit and green clay and honey is taken orally for cough, asthma and sinusitis (Nnomo et al. 2009).

Other Uses

The tubers are also used as animal feed in parts of Eastern Europe. Potato starch is used in the textile, cosmetic, pharmaceutical and paper industries and in the production of derived substances such as ethanol glucose (Graves 2001).

Both the potato peel waste and PPW fermentation residue had shown potential based on properties to be converted into crude biofuel via thermochemical processes (Liang and McDonald 2014).

Although young potatoes contain no citric acid, the mature tubers yield enough even for commercial purposes, and ripe potato juice is an excellent cleaner of silks, cottons and woollens (Grieve 1971).

In pure form, both potato glycoalkaloids, α -solanine and α -chaconine, deterred snail (*Helix aspersa*) feeding, with chaconine being the more active compound (Smith et al. 2001). In combination, authentic solanine and chaconine interacted synergistically in their inhibition of feeding. Comparison of data from peel extracts of all three potato varieties and authentic glycoalkaloids indicated that the level of feeding inhibition by the extracts was, at least in part, a consequence of a synergism between solanine and chaconine.

Studies by Okeke and Frankenberger (2005) found that potato peel waste in combination with amylolytic microorganisms (*Citrobacter* sp. S4, *Streptomyces* sp. S2, *Flavobacterium* sp. S6, *Pseudoxanthomonas* sp. S5, *Streptomyces* sp. S7 and *Aeromonas* sp. S8) and *Dechlorosoma* sp. could be economically used to achieve complete perchlorate removal from water.

Comments

The leading potato-producing countries in the world based on 2013 production (tonnes) (FAOSTAT 2014) are China, 88,925,000; India, 45,343,600; Russian Federation, 30,199,126; Ukraine, 22,258,600; USA, 9,843,919; Germany, 9,669,700; Bangladesh, 8,603,000; France, 6,975,000; Netherlands, 6,801,000; Poland, 6,334,200; United Kingdom, 5,580,000; and Iran, 5,560,000.

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Tropaeolum tuberosum

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Scientific Name

Tropaeolum tuberosum Ruiz and Pavón

Synonyms

Tropaeolum mucronatum Meyen, *Tropaeolum suberosum* Walp., *Trophaem denticulatum* Kuntze, *Trophaem tuberosus* (Ruiz & Pav) Kuntze

Family

Tropaeolaceae

Common/English Names

Anu, Anyu, Bulbous Nasturtium, Capucine, Edible Nasturtium, Mashua, Patagonian Capucine, Peruvian Capucine, Peruvian Nasturtium, Tuber Nasturtium, Tuberous Nasturtium, Tuberous Rooted Nasturtium

Vernacular Names

Argentina: Sisaño (Aymara), Añu, Isaño (Spanish);

Boliva: Isau, Isañu, Kkayacha, Mishwa (Aymara), Añu, Isaño, Ocaquisaño (Quechua), Añu, Apilla, Apiña Mama, Isaño, Isañu, Mafua, Majua, Mashua, Mashuar, Mauja, Mashwa, Maxua (Spanish)

Brazil: Capuchinha-Tuberosa (Portuguese)

Chinese: Kuai Jing Lzan Hua

Columbia: Pane (Guambiano), Puel (Paez), Cubios, Mafua, Majua, Mashua, Mashuar, Mauja, Mashwa, Maxua, Navios, Navos (Spanish)

Czech: Lichořeřišnice Hlíznatá

Danish: Anu

Dutch: Knof, Oostindische Kers

Eastonian: Mugul-Mungalill

Ecuador: Mafua, Majua, Mashua, Mashuar, Mauja, Mashwa, Maxua (Spanish)

French: Capucine Tubéreuse

German: Knollige Kapuzinerkresse, Knollenkresse, Peruanische Kapuzinerkresse, Peruanische Knollenkresse

Italian: Nasturzio Tuberosa, Tropeolo del Peru

Japanese: Toropaeorumu Chuuberosumu

Peru: Añu, Apiñu, Apiña-Mama, Isaño, Mashua, Mashwa (Quechua), Añu, Anyú, Isaño, Mafua, Majua, Mashua, Mashuar, Mauja, Mashwa, Maswallo, Maxua, Mazuko, (Spanish), Allausu

Polish: Nasturcja Bulwiasta

Spanish: Añu, Magua, Mashau

Swedish: Knölkrasse

Origin/Distribution

Tropaeolum tuberosum apparently originated from the central Andes (latitude 10° to 20°S) (Arbizu and Tapia 1994). Its cultivation is thought to have been spread by pre-Columbian

migrations to Colombia (latitude 8°N) and northern Argentina and Chile (latitude 25°S). Mashua is cultivated in the Andes of Bolivia, Peru, Ecuador, Columbia and Venezuela (Gibbs et al. 1978), northern Argentina and Chile (Arbizo and Tapia 1994). It is also being grown experimentally in New Zealand and the Pacific Northwest to evaluate its potential for worldwide cultivation (Soria et al. 1998). The tubers of *T. tuberosum* are an important source of food for around 9 million people living at elevations of 2500–4000 m throughout the Andes (King and Gershoff 1987).

Agroecology

Mashua is a cool temperate species and a native of the high Andean altitudes which are typified by steep terrain, strong winds, shallow soil and bare rock surfaces with a high water run-off. It is grown in the Andes in the latitudinal range of 8°N to 24°S and altitudinal range from 2400 to 4300 m, most frequently from 3000 to 3800 m, where mean annual temperature ranges from 8 to 11 °C (Arbizo and Tapia 1994; Grau et al. 2003). It is tolerant to light frost and to high temperature of 30 °C for brief durations. Being a short-day plant, it grows and tuberize well in areas of 10 to ≤ 12 h day length. In the absence of irrigation practices, it thrives best in areas that receive 700–1400 mm rainfall per year and has been reported to tolerate short, dry spells. It grows on a wide range of soils including marginal and rocky soils, but thrives best in fertile organic soils and has a wide tolerance to soil pH of 5.3–7.5 (NRC 1989; Torres et al. 1992).

Edible Plant Parts and Uses

Mashua tubers are usually consumed boiled or cooked. Mashua tubers contain isothiocyanates (mustard oils) that give them a sharp, peppery taste reminiscent of hot radishes when eaten raw (Soria et al. 1998). Mashua tubers are often boiled with meat, green vegetables, corn, potatoes and herbs to form a stew or eaten alone as a baked or fried vegetable (King and Gershoff 1987). The tubers are also soaked in molasses and eaten as sweets. In Bolivia and some parts of Peru, the tubers

are coated with molasses and frozen to make a special dessert (NRC 1989). In Bolivia, ñu is eaten in a stew, as a roast or occasionally preserved in a drying process similar to the production of chuno from potatoes to prepare a product called *thayacha*; for this preparation, the tubers are exposed overnight to frost and are eaten the following day soaked in syrup-cane syrup (Fernandez 1973; Arbizu and Tapia 1994; Cárdenas 1989). In addition, the tender young leaves can be eaten as a boiled green vegetables and the flowers are also eaten (NRC 1989).

Botany

A herbaceous erect (bushy) or prostrate climbing annual or perennial, 0.5–2 m high, with slender, cylindrical, aerial, green or reddish-green stems that can twine or climb over other plants by tactile petioles (Plate 1). The tubers are produced on axillary stolons which enlarge to form terminal, elongate, conical or ellipsoid tubers 5–15 cm long and 3–6 cm wide at the distal end, with waxy surface, which are slightly roughened from enlarge scale leaves, generally deeply furrowed, each furrow containing a bud (‘eye) from which it produces aerial stem and adventitious roots. The tubers variable in colour, white, yellow, red, pink or purple often striped or mottled red or purple, especially underneath the eyes (Plates 2 and 3). The flesh of the tuber is usually yellow or white or pale lilac depending on cultivars. Leaves alternate, sub-orbicular, peltate, obtuse or rounded three- to five-lobed, glabrous, 4–6 cm by 5–7 cm, dark grey-green on the upper surface and pale green on the lower with marked purple venation. The flowers are solitary, axillary, zygomorphic, tubular, hypogynous and hermaphrodite and borne on 15–25 cm long peduncles; calyx with five-lobed sepals, mostly red or reddish sometime yellow, sepals fused at the base forming a nectar containing spur (called calcar) funnel shaped with a straight or curved appendix at the base; corolla of five free petals commonly yellow or pale orange with darker veins, sometimes light lilac or reddish, posterior petals unguiculate, anterior petals elliptical, unguiculate; stamens eight, ovary superior, three-carpellate with three locules, each locule with

one axial ovule; style simple with trifid stigmata. The fruit is a schizocarp, dehiscing into three mericarps with ribbed and rugose surface each containing one seed.



Plate 1 Drawing of mashua plant © International Potato Center (CIP)



Plate 2 Mashua tubers © International Potato Center (CIP)



Plate 3 Mottled and variegated mashua tubers

Nutritive/Medicinal Properties

The nutritional value of tubers is high. Proximate nutrient values of mashua tubers (per 100 g fresh weight edible portion) was reported by Sperling and King (1990) as: moisture 87 %, protein 1.5 g, carbohydrate 9.7 g, fat 0.1 g, crude fibre 0.8 g, ash 0.5 g and energy 45.7 Kcal. Dry tubers were reported to contain 14–16 % protein, almost 80 % carbohydrate, about 9 µg/100 g β-carotene and almost 480 mg vitamin C/100 g (Vaughn and Geissler 1997). The nutritional composition (dry weight basis) of mashua tubers was reported as: protein 6.9–15.7 %, carbohydrate 69.7–79.5 %, fat 0.1–0.4 %, ash 4.0–6.5 %, fibre 7.8–8.6 %, moisture 78.3–92.4 % and energy 342–350 cal/100 g (King and Gershoff 1987). They also contained all of the essential amino acids (mg/g protein): lysine 35–41 mg, threonine 22–24 mg, valine 25–46 mg, isoleucine 25–37 mg, leucine 35–43 mg, phenylalanine + tyrosine 14–37 mg, tryptophan 4.7–5.3 mg and methionine + cystine 12–15 mg. Mashua was reported to contain 11 % carbohydrate, on a dry basis the protein content varied between 6.9 and 15.9 % (NRC 1989). According to Barrera et al. (2004), mashua possessed the highest amount of vitamin C (77.37 mg/100 g of fresh matter) among all tubers. The provitamin A content, expressed as retinol equivalents (RE), identified mashua as the most carotene-rich species of tuber, with an average level of 73.56 RE/100 g fresh matter (Barrera et al. 2004). The nutritional content of mashua is good when compared with other staple root and tuber crops eaten around

the world; however it is not as palatable as other tubers and tends to be abandoned more readily when people have access to other foods. Mashua with its tubers being rich in carbohydrates as well as other nutrients and its foliage rich in protein had been suggested to have potential to be grown for livestock feed (NRC 1989).

Chemical composition of mashua tuber was reported as: protein 9.21 %, lipid 0.92 %, soluble fibre 5.04 %, insoluble fibre 10.55 %, total sugar 27.70, starch 41.35 %, mineral residues 5.10 % and moisture 90.84 % (Valcárcel-Yamani et al. 2013). Chemical composition of mashua tuberous starch was reported as: protein n/d, lipid 0.02 %, starch 99.56 %, amylase 27.44 %, mineral residues 0.28 % and moisture 8.44 % (Valcárcel-Yamani et al. 2013). Mashua starch granules were predominantly truncated spherical or oval forms and smaller dimensions (up to 16.29 μm) for mashua starch granule. The physical, chemical and functional characterization of starches from Andean tubers oca, mashua and ulluco suggested that these starches could be used in food systems and other industrial applications, in products that require easy cooking, hot high viscosity, stability under refrigeration and do not need to be frozen. Starch granule size could influence digestion; in this sense, mashua, with its comparatively smaller granules, could be a highly digestible starch. The absence of protein in the isolated starches indicated the utility of these starches for preparing syrups with high glucose content. The starches were found to cook easily and to have a high degree of swelling and solubility, high viscosity, low stability to stirring and cooking or mechanical action and a low tendency towards retrogradation. These starches showed high clarity, but with high syneresis when subjected to freeze-thaw cycle.

Seeds, tubers, leaves and flowers of *T. tuberosum* subsp. *tuberosum* produced *p*-methoxybenzyl isothiocyanate (Johns and Towers 1981). *N, N*-Di(4-methoxybenzyl)thiourea was detected in tuber extracts of subsp. *tuberosum*. *T. tuberosum* subspecies *silvestre* produced benzyl- butylisothiocyanate, 2-propyl- butylisothiocyanate and 2-butyliothiocyanates. *T. tuberosum* subsp. *tuberosum* was found to contain *p*-

methoxybenzyl glucosinolate as its major secondary metabolite (Johns et al. 1982). Studies indicated that the glucosinolate content of mashua tuber was highly dependent on both the variety and the time of harvest (Ramallo et al. 2004). Only one glucosinolate (*p*-methoxybenzyl glucosinolate) was found in the six domestic varieties analysed; its concentration varied between 36.5 and 90.0 $\mu\text{mol/g}$ dry matter. Dark coloured tuber varieties showed higher levels than 'light' coloured tuber varieties at normal harvest time. Of the two varieties on which the effect of delayed harvest was studied, one showed increasing and then decreasing changes until 44 days after maturity, while the other did not show any significant change with time. Postharvest cold stored samples showed similar changes to tubers kept in soil, and glucosinolate levels in dried blanched tubers did not differ significantly from those in fresh samples. Freeze-dried extract of mashua tubers had 3.7 g/100 g of benzyl glucosinolate (Cárdenas-Valencia et al. 2008).

The main glucosinolates detected in cultivated and feral accessions of mashua were aromatic: 4-hydroxybenzyl glucosinolate (glucosinalbin), benzyl glucosinolate (glucotropaeolin) and *m*-methoxybenzyl glucosinolate (glucolimnathin) (Ortega et al. 2006). The total amount of glucosinolate observed ranged from 0.27 to 50.74 $\mu\text{Mol/g}$ of dried tuber tissue. Most of the low-content glucosinolate accessions were distributed within the cultivated population with a total glucosinolate concentration lower than 5.00 $\mu\text{Mol/g}$ of dried tuber tissue. The highest total and specific glucosinolate contents (more than 25.00 $\mu\text{Mol/g}$ of dried tuber tissue) were observed in the feral population with a few exceptions. In addition, only six different glucosinolate profiles were found: only glucolimnathin; only glucotropaeolin; glucosinalbin and glucotropaeolin; glucosinalbin and glucolimnathin; glucotropaeolin and glucolimnathin; and glucosinalbin, glucotropaeolin and glucolimnathin. Volatile compounds emitted from mashua plants were: benzaldehyde, benzyl-alcohol, benzyl-nitrile, benzyl-isothiocyanate and 4-methoxy-benzyl-isothiocyanate (Gonzalez et al. 2009). They also reported the glucosinolates present in different mashua plant parts as follows in μmoles

per gram of dry matter: 4-hydroxy-benzyl glucosinolate 0.6 μ moles in leaves, 0.9 μ moles in stem, 2.4 μ moles in tubers, 0.3 μ moles in roots; methoxy-hydroxy-benzyl glucosinolate 0.07 μ moles in leaves, 0.17 μ moles in stem, 0.45 μ moles in tubers, 0.3 μ moles in roots; 4-methoxy-benzyl glucosinolate 17.9 μ moles in leaves, 46.3 μ moles in stem, 117.1 μ moles in tubers, 62.93 μ moles in roots; benzyl glucosinolate 0.15 μ moles in leaves, 1.01 μ moles in stem, 1.16 μ moles in tubers, 0.43 μ moles in roots.

Eleven different anthocyanins were found in the purple tubers of three mashua genotypes (Chirinos et al. 2006). The two major pigments (56.4–73.0 % total area range at 520 nm) were identified as delphinidin 3-glucoside-5-acetylramnoside and delphinidin 3-sophoroside-5-acetylramnoside. Other pigments were delphinidin 3-glucoside-5-ramnoside, delphinidin 3-sophoroside-5-ramnoside, delphinidin 3-glucoside, cyanidin 3-sophoroside and cyanidin 3-sophoroside-5-ramnoside. Cyanidin 3-glucoside and cyanidin 3-rutinoside were only found in two genotypes, while pelargonidin 3-sophoroside and pelargonidin 3-sophoroside-5-ramnoside were only found in the third one. Phenolic compounds in the tubers of three different coloured mashua genotypes were analysed by separating them into four main fractions (Chirinos et al. 2008a). Fraction I revealed the presence of gallic acid, gallocatechin, procyanidin B2 and epigallocatechin and other phenolic compounds such as hydroxycinnamic and hydroxybenzoic acid derivatives, rutin and/or myricetin derivatives. Fraction II was mainly composed of epicatechin, hydroxycinnamic and hydroxybenzoic acid derivatives. Fraction III presented mainly anthocyanins for the purple coloured mashua tubers and rutin, hydroxycinnamic acid and hydroxybenzoic acid derivatives for the yellow coloured genotype. Alkaline and acid hydrolysis of the different fractions revealed the presence of gallocatechin, epicatechin, *p*-coumaric acid, *o*-coumaric acid, cinnamic acid, protocatechuic acid, rutin and quercetin as the main phenolic moieties present.

Two antimicrobial proteins were purified from mashua tubers (Guimarães 2004). These proteins, a β -1,3-glucanase

(32 kDa) and an osmotin-like protein (22 kDa), acted synergistically to inhibit the growth and spore formation of *Trichoderma harzianum*, a major pathogen of edible mushrooms; however, unlike ocatin, these two proteins were present in relatively small amounts and were restricted to select morphotypes (Guimarães 2004).

Antioxidant Activity

Mashua tubers showed the highest antioxidant capacity and phenolic, anthocyanin and carotenoid content compared with other crops i.e. native potato (*Solanum* sp.), oca (*Oxalis tuberosa*) and ulluco (*Ullucus tuberosus*) (Campos et al. 2006). For mashua tubers, the hydrophilic antioxidant capacity (HAC) and lipophilic antioxidant capacity (LAC) as determined by ABTS (2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid)) ranged from 955 to 9800 µg TE/g and 93–279 µgTE/g respectively. HAC expressed on a phenolic basis, ranged from 729 to 3052 mg TE/g chlorogenic acid equivalent. Mashua tubers presented HAC higher than those observed for blue-berries. HAC in mashua was related to total phenolic and total anthocyanin content. Total phenolic content for mashua tubers ranged from 0.92 to 3.37 mg/g with purple tuber having higher content than yellow tubers. Total anthocyanin content of mashua pigmented tubers ranged from 0.5 to 2.05 mg/g and total carotenoid contents ranged from 1 to 25 µg β-carotene/g. The lipophilic fraction contributed 2–19 % to the total antioxidant capacity values for mashua tuber. According to the results obtained, the HAC range values for the crops studied followed the descending order mashua ≥ oca ≥ native potato ≥ ulluco.

Another study found anthocyanins and other phenolics to be the major contributors to purple mashua tubers high 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) antioxidant activity as anthocyanins were found for only one of the three genotypes (Chirinos et al. 2006). Mashua anthocyanins, total phenolics and 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) antioxidant activity ranged from 45.5 to 131.9 mg of cyanidin 3-glucoside equivalents/100 g fresh weight (FW), 174.9–275.5 mg of

gallic acid equivalents/100 g of FW and 16.2–45.7 micromol of Trolox equivalents/g of FW, respectively. No significant differences in total phenolic recovery and ORAC values of mashua genotypes tubers were observed when 90 % methanol or methanol/acetone/water (45:45:10), both with 0.1 % HCl, were used (Chirinos et al. 2007). In contrast, the 90 % methanol solution with 0.1 % HCl extracted the highest level of anthocyanins, whereas the solvent mixture extracted the highest level of flavanols. The purified extracts from the mashua genotypes presented total phenolics and ORAC contents within the ranges 14.4–18.7 mg gallic acid equivalents/g mashua dry matter (DM) and 221–359 μ mol of trolox equivalents/g mashua DM, respectively. In another subsequent study, they found that the proanthocyanidin fractions were the major contributors to the ORAC antioxidant activity of the mashua tubers for two of the three genotypes (34.7–39.2 %) (Chirinos et al. 2008a). The results obtained confirmed that mashua tubers constitute a promising source of antioxidant phenolics and could potentially be considered as a functional food with beneficial health effects. In another study, purified mashua extracts (PME) from four different coloured mashua genotypes displayed good antioxidant properties against oxidative damage in biological materials rich in polyunsaturated fatty acids (Chirinos et al. 2008b). In the presence of 5 μ M of gallic acid equivalents (GAE), inhibitions of LDL (low density lipoprotein) oxidation for the PME ranged from 29.1 to 34.8 % and from 51.8 to 58.1 % when the TBARS and conjugated dienes assays were performed, respectively. PME inhibited the haemolysis of erythrocytes within the range 20.8–25.1 %. Thus, mashua phenolic extracts are capable of scavenging peroxy radicals, as well as chelating redox metal ions in-vitro. ORAC and LDL protection (TBARS and conjugated dienes assays) showed good correlations with total phenolics and total flavonoids suggesting that these compounds have a good ability to protect LDL molecules under the employed conditions. In contrast, inhibition of hemolysis did not show any correlation with the evaluated phenolic assays (total phenolics, total anthocyanins and total flavonoids) or with any of the evaluated oxidative LDL assays. The displayed antioxidant properties could be

applied in the field of food or cosmetic industry. In a recent study, Betalleluz-Pallardel et al. (2012) found that after 15 days of storage, better effects were evidenced against soybean oil oxidation at 300 and 600 ppm of ethyl acetate fraction of mashua tuber in comparison to 200 ppm butylated hydroxytoluene and the control (no antioxidant added). The ethyl acetate fraction at 200 ppm showed the highest efficacy against soybean oil oxidation in terms of polar compound values, free fatty acids and conjugated dienes and trienes in comparison to the oil containing 200 ppm tert-butylhydroquinone and control. The results provided strong evidence related to the excellent protective effects against soybean oil oxidation by mashua phenolics.

Antifertility Activity

Mashua is considered an antiaphrodisiac and many Andean men refuse to consume it because they believe it produces impotence and infertility (Johns et al. 1982). Experimental animals and controls showed equal capability in impregnating females, although male rats fed *T. tuberosum* showed a 45 % drop in their blood levels of testosterone/dihydrotestosterone (Johns et al. 1982). This decrease appeared to be related to the presence of isothiocyanates in the tubers. *p*-Methoxybenzyl glucosinolate was found to be its major secondary metabolite. Feeding studies of female guinea pigs and in-vitro studies to test the 17β -estradiol binding inhibition of plant extracts and of pure isothiocyanates failed to substantiate any estrogenic activity of these taxa. However, preliminary results suggested that N, N-di-(methoxy-4-benzyl)thiourea competitively inhibited estradiol binding and may have estrogenic activity.

Studies showed that administration of mashua to rats reduced testicular function after one spermatogenic cycle by reducing spermatid and sperm number, daily sperm production and epididymal sperm transit time from 12 to 42 days of treatment (Cárdenas-Valencia et al. 2008). Mashua-treated rats showed lower values of daily sperm production, epididymal and vas deferens sperm count and sperm motility; meanwhile, mashua increased the percentage of abnormal sperm morphology and epididymal sperm transit rate (Leiva-Revilla

et al. 2012). Further, it was demonstrated that the reduction in reproduction function in male rats treated with mashua was reversible 24 days after cessation of the treatment. Results of studies by Vásquez et al. (2012) suggested that the administration of *T. tuberosum* hydroalcoholic extract to male mice for 21 days had a direct action on the male reproductive system decreasing spermatogenic parameters (sperm count and sperm motility) without exerting toxic effects on the mice.

Antimicrobial Activity

Inhibition assays performed with different isothiocyanates showed that benzyl isothiocyanate and 4-methoxy-benzyl isothiocyanate had the lowest IC₅₀ values against *Candida albicans* (Gonzalez et al. 2009). Two related proteins, isolated from mashua tubers, were shown to confer potent antifungal activity against *Trichoderma harzianum* (green mould) is a major pathogen of mushroom crops, especially *Agaricus bisporus*, and may cause health hazards for humans (Guimarães 2004).

Traditional Medicinal Uses

The antibiotic, insecticidal, nematocidal and diuretic properties of isothiocyanates substantiate several uses of mashua in Andean folk medicine (Johns 1981; Johns et al. 1982). Mashua is considered an anaphrodisiac and many Andean men refuse to consume it because they believe it produces impotence and infertility (Johns et al. 1982a). It has been recorded by the Spanish chronicler Cobo that mashua was fed to their armies by the Inca Emperors, “that they should forget their wives”. Mashua is used in Andean folk medicine to treat kidney ailments, skin ulcers, kidney stones and to kill parasites (Ortega et al. 2006) and to reduce reproductive function in men (Cárdenas-Valencia et al. 2008). In Bolivia, *T. tuberosum* is believed to induce menstruation and is employed in popular medicine as emmenagogue (Johns et al. 1982).

Other Uses

In Colombia, mashua is planted as a companion crop to repel pests in potato fields. Its extraordinary resistance to insect, nematode and bacterial pests is attributed to high levels of isothiocyanates (Ortega et al. 2006). It has also been suggested that mashua be grown as feed for livestock because of its highly nutritious vegetative parts (NRC 1989).

Comments

Mashua has been vegetatively propagated for thousands of years and viable seeds are only occasionally produced. Mashua is propagated vegetatively using whole tubers selected from storage. Small tubers are preferred for planting in Peru because they are less valuable for food use (Sperling and King 1990).

Two subspecies of *T. tuberosum* has been recognised: a wild and cultivated subspecies *T. tuberosum* subsp. *silvestre* and *T. tuberosum* subsp. *tuberosum* respectively (Sparre 1973; Sparre and Andersson 1991), the former is smaller and slender in all parts; this subspecies classification was also confirmed by chemotaxonomic studies (Johns and Towers 1981).

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Typha angustifolia

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Scientific Name

Typha angustifolia L.

Synonyms

Massula angustifolia (L.) Dulac, *Typha angustifolia* var. *calumetensis* Peattie, *Typha angustifolia* var. *elator* (Boenn.) Nyman, *Typha angustifolia* var. *elongata* Wiegand, *Typha angustifolia* f. *foveolata* (Pobed.) Mavrodiev, *Typha angustifolia* var. *longispicata* Peck, *Typha angustifolia* var. *spathacea* Borbás, *Typha angustifolia* f. *submersa* Glück, *Typha elator* Boenn., *Typha foveolata* Pobed., *Typha glauca* Seg.-Vianna (illeg.), *Typha gracilis* Rchb. (illeg.), *Typha media* C.C.Gmel., *Typha minor* Curtis, *Typha pontica* Klokov f. & Krasnova

Family

Typhaceae

Common/English Names

Cattail, Lesser Bulrush, Lesser Reed-Mace, Nail-Rod, Narrow-Leaf Cattail, Narrowleaf Cattail, Reed-Mace, Small Reed-Mace, Small Bulrush.

Vernacular Names

Arabic: Bardî, Bût, Hhafâ'

Argentina: Totorá

Australia: Cumbungi (Aboriginal)

Belgium: Kleine Lisdodde;

Brazil: Taboa

Colombia: Enea

Dominican Republic: Enea

Chinese: Pu Huang, Shui Zhu

Czech: Orobincem Úzkolistým, Orobinec Úzkolistý

Danish: Smalbladet Dunhammer

Dutch: Kleine Lisdodde

Esperanto: Tifao Malgranda, Tifao Mallarĝfolia

Estonian: Ahtalehine Hundinui

Fiji: Deniruve, Denisoqe;

Finnish: Kapeaosmankäämi, Kapealehtinen
Osmankäämi, Osmankaeami

French: Chandelle, Massette À Feuilles Étroites,
Massette Des Étangs, Quenouilles, Quenouille À Feuilles
Étroites

Gaelic: Coigeal Chaol

German: Schmalblättriger Rohrkolben, Schmalere
Rohrkolben

India: Hogla, Pater

Indonesia: Purun

Italian: Lisca A Foglie Strette, Mazza Sorda, Schianze,
Stiancia Minore, Tifa A Foglie Strette

Japanese: Hime Gama, Himegama

Nepalese: Khar, Pater

Malaysia: Banat

Norwegian: Smal Dunkjevele, Smalbladet Dunkjevele, Smalt Dunkjevele

Philippines: Homa-homay (Bisaya), Lampakanay, Tubal-tubal (Cebu bisaya), Kaidked (Pampangan), Balangot (Samar-Leyte Bisaya), Balangot (Tagalog)

Polish: Pałka Wąskolistna, Rogózka

Portuguese: Tabua-Estreita

Russian: Rogoz Uzkolistnyj

Slovascina: Rogoz Ozkolistni

Spanish: Anea, Espadaña, Espadaña Común, Espadaña Estrecha, Espadona, Junco De La Pasion, Macio De Hoja Estrecha, Mazio, Paja De Estera, Paja De Sillas, Totorá, Tutuvaco, Vato

Swedish: Smalkaveldum

Thailand: Kok Chaang, Thoup Susi

Turkish: Su Kamış

Uruguay: Totorá

Venezuela: Enea

Vietnam: Bồn Bồn, Cỏ Nén, Thủy Hương

Welsh: Cynffon Y Gath Culddail, Cynffon Y Gath Leiaf, Ffon Y Plant, Ffynwewyr Ellyllon, Ffynwewyr Y Plant, Hesgen Felfedog, Hesgen Felfedog Goraidd, Hesgen Felfedog Leiaf, Rhodell, Rholbren, Tapr Y Dŵr

Origin/Distribution

T. angustifolia is distributed throughout the temperate northern hemisphere, occurring in at least 56 countries (Holm et al. 1977).

Agroecology

The species grows in shallow fresh water of lakes, rivers, ponds, marshes and ditches in valley marshes, coastal sites at low elevation.

Edible Plant Parts and Uses

Several parts of the plant are edible, including dormant sprouts on the roots and bases of the leaves, ripe pollen, the stem and the starchy roots (Schmeda-Hirschmann et al. 1999; Elias and Dykeman 2009).

The roots are edible raw or cooked (Uphof 1968). They can be boiled and eaten like potatoes or macerated and then boiled to yield a sweet syrup (Facciola 1990). The roots can also be dried, ground into a powder and then used as a thickener in soups, etc. or added to cereal flours (Elias and Dykeman 2009), and this protein rich powder is used to make biscuits, etc. (Facciola 1990). Young shoots are eaten in spring raw or cooked (Hedrick 1972; Facciola 1990). The base of the mature stem is also edible raw or cooked (Elias and Dykeman 2009). The tender, young flowering stem is also edible raw, cooked or prepare into a soup (Facciola 1990). The pollen is edible raw, cooked or processed into a protein rich additive to flour used in making bread, porridge, etc. (Tanaka 1976; Facciola 1990). The small seed is edible roasted or cooked (Facciola 1990) and an edible oil can be obtained from the seed (Harrington 1974).

Botany

T. angustifolia is a slender perennial aquatic emergent plant, growing to 1.5–2 m tall (Plate 1). It has branched creeping rhizomes, 2–4 cm in diameter, commonly 70 cm or even longer, with dense fibrous root masses occurring at the base of stems and at rhizome nodes. Stems are unbranched and cylindrical, 100–200 cm, with long (60–100 cm), linear, narrow leaves, 5–10 mm wide and deep green. Leaves are plano-concave or plano-convex or strongly convex on the back, numbering <10 per stem, sheathing at the base and commonly overtopping the inflorescence. The inflorescence is

a thin, dense crowded cylindrical spike of male flowers (brown to yellowish) above a similar spike of female flowers (reddish to dark brown), with a gap of approximately 0.5–8 cm between the two. Pistillate flowers subtended by a linear bract, the bract swollen at the top; fertile flowers pediceled, the stipe densely long-hairy, the style long, slender, bearing a dark brown, linear stigma; sterile flowers long-stipitate with a broad, flat-topped, inflated, terminal, aborted ovary with a rudimentary style, much longer than the functional ovary; stamens on branched filaments, or sometimes sessile, often 2 or 3 to a cluster, the anthers opening by longitudinal slits, the connective clavate, pollen one-celled, single-grain, lemon-yellow. Fruit, a dry, dehiscent, ellipsoid follicle with long hairs containing large numbers of small pendulous seeds, with a straight, narrow embryo.



Plate 1 Narrowleaf cattail plant habit

Nutritive/Medicinal Properties

Alkaloids, sterols, sugars, flavonoids and tannins were present in different extracts (petroleum ether, benzene, chloroform, methanol and water) of *T. angustifolia* rhizome, leaf, shoot and pollens (Shukla et al. 2013).

Five flavonoid glycosides were isolated from the alcoholic extract of *Typha angustifolia* pollen: isorhamnetin-3-*O*-(2^G- α -L-rhamnopyranosyl)- α -L-rhamnopyranosyl- (1 $\rightarrow$ 6)- β -D-glucopyranoside named typhaneoside, and four known compounds kaempferol-3-*O*-(2^G- α -L-rhamnosyl) rutinoside, isorhamnetin-3-*O*-neohesperidoside, kaempferol-3-*O*-rhamnosylglucoside and quercetin-3-*O*-neohesperidoside (Jia et al. 1986). Five aliphatic compounds were isolated from *Typha angustifolia* pollen and identified as: 7-methyl-4-triacontanone, 6-tritriacontanol, pentacosane, β -sitosterol palmitate and an unknown (Jia et al. 1990). Three polysaccharides TAA, TAB, TAC were isolated and purified from *T. angustifolia* pollen (Ping et al. 1990). TAA was mainly composed of α -L-arabinofuranose, β -D-galactose and α -D-galacturonic acid. TAC backbone mainly composed of (1 $\rightarrow$ 5)-linked-L-arabinosyl residue.

Two new nonacosanetriols, 7,8,10-nonacosanetriol and 7,9,10-nonacosanetriol, were isolated from the pollens (Tao et al. 2010a). Nucleosides and nucleobases were determined in the pollen of *T. angustifolia* (Tao et al. 2012). The content of flavonoid glycoside especially of quercetin and isorhamnetin in the pollen was reduced after carbonization (Chen et al. 2012). Compared with the crude pollen typhae (Puhuang), the contents of two flavonoids typhaneoside and isorhamnetin-3-*O*-neohesperidoside decreased by 40.22 % and 49.87 %, respectively, in the stir-fried product (Liu and Lu 1998). Typhaneoside and isorhamnetin-3-*O*-neohesperidoside were not detected in the carbonized product. Ahlers et al. (2000) found that the greater part of oxygen found in sporopollenin from the pollen of *Typha angustifolia* originated from hydroxyl groups derived from aliphatics and not from aromatics. They found that not only aromatics and long

unbranched aliphatics but also poly-hydroxyl aliphatic components were involved in the complex structure of the polymer. Furthermore, they found it most probable that the monomers of the sporopollenin skeleton were linked by ether- and not by ester-linkage. From the HETCOR and COSY spectra of the silylated and the acetylated sporopollenin from the pollen of *Typha angustifolia* samples, the occurrence of aliphatic polyhydroxy compounds as well as phenolic OH groups became evident (Ahlers et al. 2003). Two flavonoids typhaneoside and isorhamnetin-3-*O*-neohesperidoside were identified in the pollen (Fu et al. 2004). Two new cerebrosides, 1-*O*-(β -D-glucopyranosyloxy)-(2S,3S,4R,8Z)-2-[(2'R)-2'-hydroxytricosanoylamino]-8-nonadecene-3,4-diol (1) and 1-*O*-(β -D-glucopyranosyloxy)-(2S,3R,4E,8Z)-2-[(2'R)-2'-hydroxynonadecanoylamino]-4,13-nonadecene-3-diol (2), were isolated from *Typha angustifolia* pollen (Tao et al. 2010b). The following flavonoids were determined from *T. angustifolia* pollens: isorhamnetin; isorhamnetin-3-*O*-(2G- α -L-rhamnosyl)rutinoside; isorhamnetin 3-*O*-neohesperidoside; kaempferol; kaempferol-3-*O*-(2G- α -L-rhamnosyl)rutinoside; kaempferol-3-*O*-neohesperidoside; naringenin; quercetin; quercetin 3-*O*-(2G- α -L-rhamnosyl)rutinoside; quercetin 3-*O*-neohesperidoside (Tao et al. 2011). The following eight flavonoids were isolated from Pollen Typhae (*Typha angustifolia*, Puhuang) by Han et al. (2012): naringenin, isorhamnetin 3-*O*-(2^G- α -L-rhamnosyl)-rutinoside, isorhamnetin 3-*O*-neohesperidoside, isorhamnetin, quercetin 3-*O*-(2^G- α -L-rhamnosyl)-rutinoside, quercetin 3-*O*-neohesperidoside, kaempferol and quercetin. Seven compounds were isolated and identified from active analgesic parts of the pollen as naringenin; 4-hydroxy cinnamic acid; 3-methoxy-4-hydroxy cinnamic acid; vanillic acid; isorhamnetin-3-*O*- α -L-rhamnose-based(1 $\rightarrow$ 2)- β -D-glucoside; typhaneoside and β -sitosterol (Feng et al. 2012a, b). Components from *Typha* pollen identified from the vinegary and aqueous extract of Shixiao San herbal medicine: 3,3'-methylquercetin-4'-glucoside; kaempferol-3-*O*-glucoside; quercetin-3-*O*-(2G- α -L-rhamnosyl)-rutinoside; quercetin-3-*O*-neohesperidoside; kaempferol-3-*O*-galactoside; isorhamnetin-3-*O*-neohesperidoside; kaempferol-3-*O*-(2G- α -L-rhamnosyl)-

rutinoside; kaempferol-3-*O*-neohesperidoside; isorhamnetin-3-*O*-rutinoside; Isorhamnetin-3-*O*-(2*G*- α -L-rhamnosyl)-rutinoside; quercetin-3-*O*-glucoside; naringenin, isorhamnetin, quercetin, kaempferol, quercetin -3, 3'-dimethyl ether and β -sitosterol (Wang et al. 2014).

Studies showed that processing altered the flavonoid contents of *T. angustifolia* pollens (Xi and Li 2000). The contents of flavonoids changed as follows: (1) unprocessed pollens, (2) > pollens stir fried with yellow wine, (3) > pollens stir fried with vinegar, (4) > pollens dried at 140 °C, (5) > parched pollens, (6) > pollens dried at 180 °C, (7) > scorched pollens, (8) > pollens dried at 220 °C and (9) > charcoal pollens.. The statistic analysis showed that the flavonoid contents in raw pollens were significantly different from those in the different processed products except for 2. The polysaccharide contents increased in 4, 5, 6 and 7 significantly and decreased in 9 significantly. As compared with the polysaccharide contents in 1, no significant changes occurred in those in processed pollen products 2 and 8.

Stearic acid propanetriol ester, quercetin and naringenin were isolated from *T. angustifolia* (Chen et al. 2008b). Six flavonoids were isolated from *Typha angustifolia* leaves and identified as quercetin-3,3'-dimethyl ether; isorhamnetin; quercetin; quercetin-3,3' dimethyl ether-4'-*O*- β -D-glucoside; isorhamnetin-3-*O*- β -galactoside and isorhamnetin-3-*O*-neohesperidoside (Liao et al. 1990). Dried *Typha angustifolia* powdered extract showed the presence of alkaloids, sterols and flavanoids (Varghese et al. 2009). Two compounds were isolated from methanolic extract and identified as nonacosanol and lupeol acetate. Mineral content determined in lower part of the leaf (mg/kg Dm) was: N 4620 mg, P 1201 mg, K 3738 mg, Ca 7803 mg, Mg 1340 mg, Fe 104 mg, Zn 12.7 mg, Mn 205 mg, Cu 3.69 mg, Ni 0.98 mg, Pb 4.83 mg and Cd 0.016 mg (Klink et al. 2013). Mineral content determined in top part of the leaf was: N 19,775 mg, P 3239 mg, K 7847, mg Ca 5951 mg, Mg 1447 mg, Fe 81.3 mg, Zn 16.7 mg, Mn 477 mg, Cu 3.01 mg, Ni 1.16 mg, Pb 2.88 mg and Cd 0.015 mg. Six compounds were isolated from the dried leaves and identified as quercetin-3,3'-dimethyl ether-4'-*O*- β -D-glucoside; 5,7-

dihydroxy-3'-methoxy-flavonoid-4'-O- β -D-glucoside; quercetin-3,3'-dimethyl ether; hexacosanoic acid; β -sitosterol; and β -sitosterol-3-O- β -D-glucopyranoside (Liang et al. 2007). 3 β -hydroxy-25-methylenecycloartan-24-ol was isolated from the whole plant ethanol extract (Zhang et al. 2013).

Mineral content (mg/kg DM) of *T. angustifolia* rhizome was determined as: N 14,922 mg, P 5833 mg, K 15,522 mg, Ca 5248 mg, Mg 2673 mg, Fe 476 mg, Zn 29.3 mg, Mn 146 mg, Cu 4.22 mg, Ni 1.32 mg, Pb 7.60 mg and Cd 0.040 mg (Klink et al. 2013).

Anti-Inflammatory Activity

Both aqueous and 70 % methanolic extracts of pollen grains of *T. angustifolia* showed significant dose-dependent inhibition of carrageenan-induced paw edema as compared to the control (Varpe et al. 2012). It was observed that both the extracts at dose of 125 mg/kg inhibited the granuloma formation by 44.30 % which was higher than at dose of 500, 250 mg/kg, thus causing a significant non-dose-related inhibition of granuloma formation. The results indicated that extracts of pollen grains of *T. angustifolia* were effective in the treatment of both acute and chronic inflammatory conditions and thus supported its traditional utilization.

Dietary supplementation with 10 % cattail (*Typha angustifolia*) rhizome flour and its combination with prednisolone prevented trinitrobenzenesulphonic acid (TNBS)-induced colonic and intestinal inflammation damage in rats, but no synergistic effects were observed (Fruet et al. 2012). Cattail rhizome flour showed the best effects at reducing the extension of the lesion, the colon weight ratio, adherences to adjacent organs and diarrhoea. These effects were related to inhibition of myeloperoxidase (MPO) and alkaline phosphatase (AP) activities and an attenuation of glutathione (GSH) depletion. The prevention of TNBS-induced colon damage was associated with an improvement in intestinal oxidative stress, which likely resulted from the antioxidant properties of the active compounds (saponins, flavonoids, coumarins) detected in the cattail rhizome.

Antiatherogenic Activity

Of 12 components isolated from Pollen Typhae, four of them showed different evident antiatherogenic effects (Zhao et al. 1990). (1) Isorhamnetin-3-O-rhamnosyl-glucoside could stimulate porcine aortic endothelial cell to produce tPA and PGI; (2) Quercetin-3-O-neohesperidose could protect endothelial cell from injury by fibrin, as well as raise tPA activity; (3) β -Sitosterol palmitate could inhibit smooth muscle cell proliferation; and (4) β -Sitosterol glucoside showed an inhibitory effect on platelet aggregation. β -Sitosterol palmitate from the pollen showed significant effect in lowering the serum cholesterol (Jia et al. 1990). Two cerebrosides from the pollen exhibited effect on the proliferation of cultured vascular smooth muscle cell (VSMCs) induced by fetal bovine serum (Tao et al. 2010b).

Pollen typhae had been reported to possess various pharmacological functions, such as improving the microcirculation, raising cAMP level, preventing and curing of coronary heart disease, hyperlipidemia and myocardial infarction and to have little side effect (Wang et al. 1998).

Antitumour Activity

The components of pollen typhae were found to inhibit both the growth of implanted Lewis lung carcinoma and Lewis lung carcinoma in C57BL/6 mice (Chen et al. 2008a). The tumour weight of each treatment group decreased compared with the control group, and pollen typhae water extract 100 and 200 mg/kg/day dose groups had significant difference.

Immunomodulatory Activity

Ethanol extract of *T. angustifolia* pollen exerted immunosuppressive effect activity by significantly suppressed concanavalin A (Con A)- and lipopolysaccharide (LPS)-stimulated splenocyte proliferation in-vitro in a concentration-dependent manner (Qin and Sun 2005). The extract also significantly suppressed Con A-, LPS- and OVA (ovalabumin)-induced splenocyte proliferation in the OVA-

immunized ICR mice in a dose-dependent manner. Moreover, the OVA-specific total IgG, IgG1 and IgG2b levels in the OVA-immunized mice were significantly reduced by the extract.

Analgesic Activity

Cattail pollen exhibited strong analgesic effects to the pain caused by irritation of heat or chemical substance (Ge et al. 2002). The hot plate method showed the same analgesic effects of the morphine and cattail pollen but the latter had longer effect. The chemical irritation method showed that analgesic effect of cattail pollen was some weaker than that of the morphine. *T. angustifolia* pollen was found to have analgesic effect and seven bioactive compounds were isolated from the analgesic parts (Feng et al. 2012a).

Antithrombotic Activity

Two new nonacosanetriols, 7,8,10-nonacosanetriol and 7,9,10-nonacosanetriol, isolated from the pollens exhibited weak activity of antiplatelet aggregation in-vitro (Tao et al. 2010a). *T. angustifolia* pollen extract significantly reduced prothrombin time (PT), activated partial prothrombin time (APTT) and recalcification time (Ohkura et al. 2011). Pollen extract directly activated factor XII in the coagulation cascade and the acidic polysaccharide in the pollen was the causative agent of factor XII activation. In the mouse tail bleeding, model oral administration of the pollen extract significantly decreased tail bleeding. It was found that the activation of the intrinsic coagulation pathway by the acidic polysaccharide contributed to the external haemostatic property of Pollen Typhae and the action of components such as flavonoids that possessed anticoagulant activity were the causative agent when orally administered. Pollen typhae extract was found to inhibit thrombosis in rats (Zhao and Zhu 2011). It decreased the wet weight of thrombus and inhibited the rate of thromboembolism and prolonged prothrombin time, thromboplastin time and thrombin time. The aqueous and methanol leaf extracts of *T. angustifolia* possesses

thrombolytic properties in an in-vitro thrombolytic model as well as cytotoxicity effects in the Brine Shrimp Lethality Bioassay (Umesh et al. 2014). The aqueous, methanol and chloroform extracts exhibited brine shrimp lethality with LC₅₀ value of 40 µg/ml, 30 µg and 104 µg/ml, respectively.

Antihyperlipidemic Activity

The vinegary and aqueous extracts of Shixiao San, a classical TCM (traditional Chinese Medicine) formula containing two component herbs Typha Pollen and Faeces Trogopteron, were found to enhance antihyperlipidemic activity in a rat hyperlipidemia model (Wang et al. 2014). Boiling was found to enhance the antihyperlipidemic effect of the vinegary extract.

Antidiabetic Activity

T. angustifolia pollen total flavones (PTF) was found to increase insulin sensitivity by increasing glucose transportation and consumption in the 3 T3-L1 adipocytes as well as decreasing the efflux of free fatty acid from adipocytes (He et al. 2006). With its function as an insulin sensitizer, PTF was found to enhance the PPAR- α and PPAR- γ mRNA expressions in 3 T3-L1 adipocytes. Compared with the normal control group, the transportation rate of glucose of C2C12 skeletal muscle cells in untreated group was decreased 30.43 % after 16 h palmitate culture and was increased 32.39 % in the Pollen Typhae total flavones (PTF)-treated group (Lou et al. 2008a). Compared with the untreated group, the levels of interleukin IL-6 mRNA expression in the skeletal cells and IL-6 protein secretion in supernatant were significantly decreased in the PTF-treated group. PTF inhibited interleukin the IL-6 mRNA expression and IL-6 protein secretion via nuclear factor-kappa B pathway in C2C12 skeletal muscle cells, which may be one of its mechanisms in relieving inflammation conditions and insulin resistance in C2C12 skeletal muscle cells. More recent studies by Feng et al. 2012b) found that PTF improved insulin-induced glucose uptake via the β -arrestin-2-mediated signalling in C2C12 myotubes.

Antimicrobial Activity

Methanolic extract and isolated compounds nonacosanol and lupeol acetate were found to possess potent antibacterial and antifungal activity against *Aspergillus flavus*, *Serratia*, *E. coli*, *Listeria* and *Staphylococcus aureus* (Varghese et al. 2009). *T. angustifolia* leaf extract exhibited antibacterial activity against *Enterobacter aerogenes*, *Salmonella typhimurium*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa* and *Escherichia coli* with minimum inhibitory concentration (MIC) ranging from 0.78 mg/ml to 12.5 mg/ml (Londonkar et al. 2013). The methanol extract strongly inhibited the growth of *S. typhimurium*, *P. aeruginosa* and *E. coli*.

Insecticidal Activity

The ethanol extract of *T. angustifolia* whole grass exhibited toxicity against the micrergates of red imported fire ants, *Solenopsis invicta* (Zhang et al. 2013). Mortality was 100 % after the micrergates were treated with 2000 mg/mL of ethanol extract for 72 h. After 48 h of treatment, LC₅₀ values of ethanol extract and petroleum ether fraction were 956.85 and 398.73 mg/mL, respectively. After 120 h, LC₅₀ values of the same substances were 271.23 and 152.86 mg/mL, respectively. The bioactive component, 3 β -hydroxy-25-methylenecycloartan-24-ol, also exhibited strong toxicity against the micrergates of red imported fire ants, thereby eradicating all of the tested ants treated with 240 mg/mL for 120 h. LC₅₀ values of the compound at 48 and 120 h were 316.50 and 28.52 mg/mL, respectively.

Pharmacokinetic Study

Typhaneoside and isorhamnetin-3-*O*-neohesperidoside were simultaneously found in rat plasma after oral administration of pollen typhae extract (Cao et al. 2015).

Traditional Medicinal Uses

In India, the species is used as a refrigerant, an aphrodisiac and a cure for dysuria (Chopra et al. 1986; Nadkarni 2001). *Typha angustifolia* is mainly used in folk remedies for the treatment of tumours, as anticoagulant, astringent, sedative and tonics (Varghese et al. 2009). According to Guerrero (1921), the whole inflorescence is employed in the healing of wounds. Stuart (1979) stated that the stamens (without the pollen) are used in China as an astringent for dysentery and for haemorrhage of the bowels. The stamens, with the pollen, are also used as an astringent and styptic. De Grosourdy (1864) reported that in the Antilles the pollen was used as substitute for powder of licopodio and that the hairs or seeds were used against burns. The pollen is diuretic, emmenagogue and haemostatic (Yeung 1985). The dried pollen is said to be anticoagulant, but when roasted with charcoal it becomes haemostatic (Bown 1995). It is used internally in the treatment of kidney stones, internal haemorrhage of almost any kind, painful menstruation, abnormal uterine bleeding, post-partum pains, abscesses and cancer of the lymphatic system (Bown 1995; Chevallier 1996). It should not be prescribed for pregnant women (Bown 1995). Externally, it is used in the treatment of tapeworms, diarrhoea and injuries (Bown 1995).

In North America, the Malecite and Mimac tribes used the roots for treatment of kidney stones (Moerman 1998). Watt and Breyer-Brandwijk (1962) stated that the Zulus use a decoction of the root in the treatment of venereal diseases and the Xosas use it to aid in the expulsion of placenta.

T. angustifolia was listed one of several traditional Chinese medicinal herbs used for the treatment of dysmenorrhea through the use of combination-herbal-formula therapeutics with minimal side effects (Jia et al. 2006). Pharmacological studies suggested Chinese herbal dysmenorrhea therapies may decrease prostaglandin levels, modulate nitric oxide, increase plasma β -endorphin (β -EP) levels, block calcium-channels and improve microcirculation.

The pollen of *Typha angustifolia* has been used traditionally for the treatment of dysmenorrhea, stranguria and metrorrhagia in China (Tao et al. 2012). Shixiao San, a classical TCM formula containing two component herbs

Typha Pollen and Faeces Trogopteroni, was originally recorded in *the Complete Collection of Prescriptions* (Taiping Huimin Heji Ju Fang), written in Song Dynasty of ancient China by Imperial Medical Service (Wang et al. 2014). In modern clinical therapies, Shixiao San plays a vital role in treatment of cardiovascular disease, such as hyperlipidemia, atherosclerotic, thrombosis, coronary heart disease and angina pectoris.

Other Uses

The stem and leaves have been used for thatching, making paper and woven into mats, chairs, hats, etc. (Triska 1975). The plant is a good source of biomass, making a superior addition to the compost heap or used as a source of fuel, etc. The hairs of the fruits are used for stuffing pillows (Hill 1952). They have good insulating and buoyancy properties. The female flowers make excellent tinder and can be lit from the spark of a flint. The pollen is highly inflammable and is used in making fireworks (Craighead et al. 1963).

Studies found *T. angustifolia* to be a root accumulator for Cd, Cr, Cu, Fe, Ni and Pb (Chandra and Yadav 2011). Among heavy metals, Fe was accumulated the most, i.e., >1000 µg/g by the plant. The results suggested that *T. angustifolia* could be used for heavy metal phytoremediation from metal containing industrial wastewater. The trends of lead and cadmium accumulation by *T. angustifolia* for all soil–water microcosms suggested interaction effects as decreased soil lead concentrations and increased water cadmium concentrations over time (Panich-Pat et al. 2010). Cadmium uptake in shoot and root biomass slightly decreased when lead was initially added to the soil but cadmium uptake in root biomass increased after 30 days. Data suggested an interaction between lead and cadmium and possible that lead uptake was inhibited when cadmium was present.

Weed control by allelopathic flavonoids from *T. angustifolia* was reported by (Yongvanich et al. 2002; Sethuraman and Sanjayan 201). Various concentrations of *T. angustifolia* extract were then tested for their effects on the

growth of *Mimosa pigra*, with 0.5 g per petridish of extracted flavonoids from the flowers, leaves and rhizomes exerting 100 % inhibitory effect on seed germination (Yongvanich et al. 2002). Complete inhibition of *M. pigra* germination and growth was obtained from the application of 50 ml of 3200 mg/ml crude extract to 500 g of soil, with lesser effects at lower concentrations. From among *T. angustifolia* plant parts tested, the extract of the inflorescence showed the maximum percentage reduction (48 %) in germination of *Vigna mungo* and this was dose-dependant (Sethuraman and Sanjayan 2013). The least effect on germination (20 %) was recorded for tests with the rhizome extract, whereas with the leaf extract, a 29 % reduction effect was observed. Besides impacting germination, the extracts also effected the growth of the shoot and root in terms of reduction in their lengths as well as fresh and dry weights. Although the inflorescence extract appeared to be the best in reducing the growth of the root and shoot, the rhizome extract impacted the root and shoot growth more than the leaf.

Comments

The species is a declared aquatic or terrestrial noxious weed and/or noxious-weed seed in many states in USA (GRIN 2014).

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Typha domingensis

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Scientific Name

Typha domingensis Pers.

Synonyms

Typha abyssinica Rchb.f. ex Rohrb., *Typha aequalis* Schnizl., *Typha aethiopica* Kronf., *Typha americana* Rich. ex Rohrb., *Typha angustata* Bory & Chaub., *Typha angustata* var. *abyssinica* (Rchb.f. ex Rohrb.) Graebn., *Typha angustata* subsp. *aethiopica* (Rohrb.) Kronf., *Typha angustata* var. *aethiopica* Rohrb., *Typha angustata* var. *gracilis* Nyman, *Typha angustata* var. *leptocarpa* Rohrb., *Typha angustifolia* subsp. *angustata* (Bory & Chaub.) Briq., *Typha angustifolia* var. *australis* (Schumach.) Rohrb., *Typha angustifolia* subsp. *australis* (Schumach.) Kronf., *Typha angustifolia* var. *brownii* (Kunth) Kronf., *Typha angustifolia* var. *domingensis* (Pers.) Griseb., *Typha angustifolia* subsp. *domingensis* (Pers.) Rohrb., *Typha angustifolia* var. *domingensis* (Pers.) Hemsl., *Typha angustifolia* subsp. *javanica* (Schnizl. ex Rohrb.) Graebn., *Typha angustifolia* var. *virginica* Tidestr., *Typha australis* Schumach., *Typha basedowii* Graebn., *Typha bracteata* Greene, *Typha brownii* Kunth, *Typha daniattica* Ehrenb. ex Rohrb., *Typha domingensis* var. *australis* (Schumach.) Gèze, *Typha domingensis* var. *javanica* (Schnizl. ex Rohrb.) Gèze, *Typha domingensis* var. *sachetiae* Fosberg, *Typha domingensis*

f. *strimonii* Cheshm. & Delip., *Typha ehrenbergii* Schur ex Rohrb., *Typha essequiboensis* G.Mey. ex Rohrb., *Typha gigantea* Schur ex Kunth, *Typha gracilis* Schur (illeg.), *Typha javanica* Schnizl. ex Rohrb., *Typha macranthelia* Webb & Berthel., *Typha maxima* Schur ex Rohrb., *Typha media* Bory & Chaub.(illeg.), *Typha salgirica* Krasnova, *Typha tenuifolia* Kunth, *Typha truxillensis* Kunth

Family

Typhaceae

Common/English Names

Bulrush, Cattail, Indian Reed Mace, Narrow-leaf Cattail, Narrow-leaved Cumbungi, Lesser Reed Mace, Santo Domingo Cattail, Southern Cattail, Southern Reed Mace, Tall Cattail, Tule

Vernacular Names

Arabic: Bardi, Berdi, Halfa

Argentina: Wana'yuk, Wana (Chulupi), Akho (Lengua), Fapu' (Maká), Jwi'na (Mataco), Chi'na (Pilagá), Chii'na, Chien Á, Cheen Á, Na'ate, Nat/Á/* (Toba), Chi'na (Toba-Pilagá)

Australia: Cumbungi, Yangeti (Aboriginal), Narrow-leaved Cumbungi

Brazil: Partasana, Taboa, Tabua (Portuguese)

Chinese: Chang Bao Xiang Pu

Czech: Orobinec Domingský

French: Canne De Jonce, Chandelle, Manette, Massette Australe, Quenouille, Roseau Des Étangs

Hebrew: Suf

India: Pater (Hindi), Apine Thene, Apu, Dodda Jambu Hullu, Jambu Hullu, Jambuhullu (Kannada), Eraka,

Panalavhala, Rambaana (Marathi), Gundra, Guntha (Sanskrit), Anaikkoria, Anaippul (Tamil), Enuga Jammu, Enugajamu, Jammu Gaddi, Jammugaddi, Kandra (Telugu)

Japanese: Kama, Kama (Okinawa), Hime-Gama

Portuguese: Espadana, Foguetes, Murrão Dos Fogueteiros, Tabúa Estreita, Tabua-Estreita

Spanish: Espadaña, Espadaña De México, Piripepe, Pirivevyi, Totorá

Vietnamese: Hương Bồ Đài Hoa Dài

Yoruba: Ewu Egungun

Origin/Distribution

The species is widespread in the tropics and subtropics and warm temperate regions spanning Europe, Asia, Africa, Australia and North and South America.

Agroecology

The species grows in shallow lakes, ponds, rivers, swamps, streams, irrigation channels and drains. It is reasonably salt tolerant. The species thrives under eutrophic conditions and artificially stabilised hydroperiods, but in undisturbed, low-nutrient wetlands, *T. domingensis* often grows sparsely and does not appear to reduce diversity. It aggressively invades and forms nearly pure stands in brackish or nutrient-enriched wetlands and can become problematic in irrigation channels and drains. When invasive, the species can replace other valuable aquatic plant commodities.

Edible Plant Parts and Uses

The rhizome, tender stalks and flower of *T. domingensis*, *T. angustifolia* and *T. latifolia* are used as food (Yanosky 1936). The tender inner core of the stems (called Cossack asparagus) is eaten raw or cooked (Scholfield 1989). The peeled white core is sliced and added to green salads and potato salads.

They also can be pickled, steamed or stir-fried. The immature, green flower spikes are harvested, boiled in water dipped in heated butter and garlic in a sauce pan and eaten like corn on the cob. The pollens from male spikes are collected, sift and added to pancakes, muffins and biscuits or dried and stored for later use. The wet flour extracted from the rhizome is used immediately in baking or dried and stored for later use. The sprouts on the rhizomes are added to salads as well as Chinese stir-fries. The chosen starch ball at the base of the stem also adds texture and flavour to dishes. It can be sliced and prepared like pan-fried potatoes. American Indian tribes utilised cattail pollens in cakes and mush as well as in ceremonial rites for adolescent girls and the dried ground rhizome-furnished meal (Scholfield 1989). The down blended with tallow was once used as chewing gum. The Yuki, Pomo and Yokio Indians of California utilised cattail roots extensively for food. The roots and the stem bases were harvested and processed in an unspecified manner (Chesnut 1902). The Cahuilla of southern California gathered cattail roots, dried them and ground them into a meal. They also collected the pollen for consumption (Bean and Saubel 1972). In other areas, the Western Apache dug the roots, and the base of the tule stemmed out of the water and roasted them for food. Tule pollens were eaten as they have a highly concentrated caloric content. The White Mountain Apache and the Northern Tonto ate the white tips of young tule shoots. The Cibecue ate the cattail flower buds raw. The White Mountain, San Carlos, and Cibecue ate the white stem bases as well. The Navajo ate the white young stalks and rhizomes raw in the summer (Vestal 1952).

In Argentina, the pollen is eaten by seven ethnic groups – Chulupi, Lengua, Maka, Mataco, Pilaga, Toba and Toba-Pilaga (Arenas and Scarpa 2003). Pollen is used as flour, for baking bread, making gruel, thickening soup and colouring rice yellow and in confectionery (mixed with honey). In some cases, the pollen is mixed with wheat or corn flour (Linskens and Jorde 1997; Morton 1975). The pollens contain a protein-rich additive to flour used in making bread, porridge, etc. (Tanaka 1976; Facciola 1990).

The roots are rich in starch and protein and can be eaten raw or cooked (Tanaka 1976; Facciola 1990). Roots can be boiled and eaten like potatoes or macerated and then boiled to yield a sweet syrup. The roots can also be dried, ground into a powder and then used as a thickener in soups and porridge or added to cereal flours or the flour used to make biscuits, bread and cakes. In parts of DR Congo, the stems and rhizomes are eaten throughout the year (Bosch 2011). In other countries, for instance, Nigeria, the rhizome is eaten as a famine food. Immature leafy spikes are eaten as a vegetable, and the soft core of these spikes is appreciated as a sweet snack. Australian aboriginals eat the roots after pounding the white rhizomes to remove the fibrous parts (Low 1991) and then mould the remaining paste and roast it into cakes that taste like asparagus (Anonymous 2014). They also eat the core of the stem and young flowering spikes but not the hard core of the spike (Anonymous 2014).

The seeds are also edible cooked. An edible oil is obtained from the seed, but due to the small size of the seed, this is probably not a very worthwhile crop (Fern 1997).

Botany

Typha domingensis is a robust, emergent, monoecious, glabrous, aquatic, perennial herb (Plate 1), with erect, unbranched, stout stem, 1.5–4 m high and 2 cm across and long, creeping, submerged rhizome, 20 mm in diameter. Leaves are in two rows (distichous), mostly basal and sub-basal (Plate 2); leaf sheath is membranous, with sloping shoulders, purple spotted within; lamina is flat, up to 1.5 m × 8–13 mm, narrow at the base and obtuse at the apex. Inflorescence is a cylindrical spike (Plate 3), with the male part superposed on the female part; the two parts are separated by a 1–3 cm long bare stalk; flowers are numerous and closely packed; bract at the base of each part is leaf like, caduceus. Male spike is 15–35 cm long and 5–10 mm diameter; flowers are unisexual with 2–3 flattened, forked or thinly lobed bracts surrounding the stamens; filaments are white and connate; anthers are basifixed; and pollens are shed as single grains.

Mature female spike is usually 12–40 cm long, < 20 mm diam. and cinnamon to brown with numerous spatulate (usually 4–8 cells across) floral bracts; female flower with fusiform ovary borne on a thin stalk surrounded by a whorl of hairs at the base; style is distinct, short and thin; stigma is flattened and linear to spatulate; sterile female flowers are similar to fertile ones but with undeveloped ovary. Fruit is a very small fusiform follicle, falling off before dehiscence together with its one-seeded stalk. Seed is striated.



Plate 1 Bulrush plant habit



Plate 2 Distichous leaves



Plate 3 Bulrush inflorescence

Nutritive/Medicinal Properties

The amounts of various water-soluble vitamins, viz. niacin (0.323 and 0.28 mg/g spikes), folic acid (0.062 and 0.08 mg/g) and ascorbic acid (33.0 and 24.0 mg/g), were found in male and female spikes of *T. domingensis*, respectively (Dahot et al. 2007). A considerable amount of macro- as well as microelements were also detected in male and female spikes. Nutrient composition (per g) of dry pollen (mean values) is the following: dry weight, 0.842 g; ash, 0.032 g; protein, 0.142 g; fats, 0.029 g; total sugars, 0.141 g; reducing sugars, 0.017 g; starch, 0.114 g; fibre, 0.134 g; vitamin C, 1.735 mg; P, 4.632 mg; Ca, 1.296 mg; Fe, 0.063 mg; Mg, 0.628 mg; K, 1.181 mg; energy, 3.041 Kcal; and Ca/P ratio, 0.28 (Arenas and Scarpa 2003). The coumarin umbelliferone was isolated from *T. domingensis* (Vasconcelos et al. 2009).

From *T. domingensis*, phytotoxins identified as essential fatty acids (linoleic acid and α -linolenic acid) and phenolic compounds of known phytotoxic activity (caffeic acid from the aqueous extracts; caffeic, *p*-coumaric and gallic acid from the leachates) were isolated (Gallardo-Williams et al. 2002). Both extracts and the phytotoxins in the extracts had the potential of inhibiting the growth and chlorophyll production of several ecologically relevant species.

Antioxidant Activity

The pollen methanol extract was found to have high reducing power and total phenolic contents with high metal chelating activity and possessed considerable potential to be utilised as a natural antioxidant (Khan 2014).

Phenolic contents decreased in the following order: fruit > female flower > male flower of *T. domingensis* (Chai et al. 2014). Superoxide scavenging half-maximal effective concentration (EC₅₀) of fruit, female flower and male flower extracts was 3.5, 4.8 and 28.2 mg dry matter (DM)/ml, respectively, while nitric oxide scavenging EC₅₀ of fruit, female flower and male flower extracts was 0.16, 0.65 and

0.95 mg DM/ml, respectively. On the other hand, iron chelating EC₅₀ of female flower, male flower and fruit extracts was 4.86, 6.43 and 10.88 mg DM/ml, respectively. Only the fruit and female flower extracts exhibited anti-glucosidase activity, with EC₅₀ of 0.75 and 5.07 mg DM/ml, respectively. The fruit and female flower extracts of *T. domingensis* were found to be promising sources of natural antioxidants, iron chelators and glucosidase inhibitors

Antiallergic Activity

Treatment with umbelliferone (60 and 90 mg/kg), a coumarin isolated from *Typha domingensis* caused a marked reduction of cellularity and eosinophil numbers in bronchoalveolar lavage fluids from ovalbumin-induced asthmatic BALB/c mice (Vasconcelos et al. 2009). In addition, a decrease in mucus production and lung inflammation was observed in mice treated with umbelliferone. A reduction of interleukin IL-4, IL-5 and IL-13, but not of IFN- γ , was found in bronchoalveolar lavage fluids of mice treated with umbelliferone, similar to that observed with dexamethasone. The results demonstrated that umbelliferone attenuated the alteration characteristics of allergic airway inflammation.

Antiglycemic Activity

Intraperitoneal administration of streptozotocin (STZ)-diabetic rats with umbelliferone (10, 20 and 30 mg/kg of body weight) and glibenclamide (600 μ g/kg of body weight) for 45 days produced significantly decreased levels of blood glucose and HbA(1c) and activities of glucose-6-phosphatase and fructose-1,6-bisphosphatase, while elevating levels of plasma insulin, Hb and liver glycogen and activities of glucokinase and glucose-6-phosphate dehydrogenase to near normal levels in STZ-diabetic rats when compared with normal control rats (Ramesh and Pulandi 2006). Normal rats treated with umbelliferone (30 mg/kg of body weight) also showed a significant effect on glycemic control. Thus, their results showed that umbelliferone at 30 mg/kg of body weight

possessed a promising antihyperglycemic effect that was comparable with glibenclamide.

Wound-Healing Activity

The extract of female inflorescence of *T. domingensis* had been shown to promote wound healing in mice and rats, but the extract of male inflorescence was ineffective (Akol et al. 2011). It was hypothesised that the wound-healing effect of the female inflorescence of *T. domingensis* was due to the antioxidant activity of its phenolic constituents. The wound-healing effect was found comparable to that of reference ointment Madecassol[®].

Traditional Medicinal Uses

The leaves (Duke and Ayensu 1985) and rootstock (Chopra et al. 1986) are deemed diuretic. The pollen is astringent, desiccant, diuretic, haemostatic and vulnerary (Yeung 1985; Duke and Ayensu 1985) and employed in the treatment of nose bleeds, haematemesis, haematuria, uterine bleeding, dysmenorrhoea, postpartum abdominal pain and gastralgia, scrofula and abscesses. It is contraindicated for pregnant women (Yeung 1985). The seed down is haemostatic (Duke and Ayensu 1985). Mature female cattail flowers are traditionally mashed and formulated into a salve for cuts and burns (Schofield 1989). The sticky juice found between cattail leaves are rubbed on the gums as a novocaine substitute. The Chinese value cattail pollen for its astringent and styptic properties; they use it in the treatment of dysentery. Ashes from the burnt spikes were sprinkled on infant's navels to stop bleeding by American Indian tribes. In traditional medicine in Uganda, the whole plant is burnt and the ash is licked to cure coughing (Bosch 2011). Elsewhere, it is burnt to obtain salt for cooking or for making soap. In North America, the Mescalero Apache used cattail pollen as a general curative agent (Basehart 1960). The Cahuilla, Omaha and Pawnee used the root in poultice or powdered form as a topical ointment for burns and bleeding wounds (Bean and Saubel 1972; Gilmore

1919). The down from the flowering stalk was used as a powder for chafing (Gilmore 1919).

Other Uses

Cattail leaves are used as materials for baskets, summer houses and beddings (Schofield 1989). Soaked in oil, the spikes were torches. Cattail down from mature female spikes yielded insulation, dressings for wounds, bedding for cradle boards and diaper material. During World War I, the down was in great demand for use as filling material in life preservers and insulation material for quilts. According to Schofield (1989), cattail down is still prized as fillings for children's toys and as stuffing for herbal dream pillows. The leaves have long been used as canning material for chairs; cattail-caned chairs have been known to survive a century of use. Leaves have also served as caulking material in pioneer cabins. The stalks have yielded arrows and hand drills. The brown flower spikes afford a delightful accent in dried flower arrangement; spraying with hair spray or varnish will prevent the explosion of the downy seeds. In camping, the dried flower heads soaked in fuel can be lighted as torches. The down provides tinder for starting fire and is used as stuffing material in gloves and socks to prevent frostbites and stuffing material in cloth sacks as pillows.

In North America, Havasupai and the Kawaiisu used cattail leaves for thatching roofs and walls of houses (Zigmond 1981). The Northern Paiute used cattail leaves in such diverse applications as construction of shelters, fabrication of sandals and other clothing and construction of boats (Fowler 1990). The Pima wove the leaves into mats and used the split flower stalks for weaving baskets (Curtin 1984:64–65). The Pawnee, Dakota and Kawaiisu used the down from the flowers for bedding (Gilmore 1919; Zigmond 1981). The Ramah Navaho used cattail leaves for storage and medicine baskets, bed mats and coiled mats. The plant and flower are also used in ritual by the North American Indians. The Pima used the pollen as decoration for the face, chest and back (Curtin 1984). Cattail pollen was also used for face paint by the Seri (Felger and

Moser 1985). The Ramah Navajo used the whole plant as a ceremonial emetic, and pollen was used in an unspecified manner, both for the Lightning Way ceremony in which they made an interesting connection between cattail and lightning. They made mats and hung them up in the hogan to protect it from lightning; a square mat (male) was hung up on the east side of the hogan and a round mat (female) on the west side (Vestal 1952).

In Tropical Africa, the leaves are widely used for making mats, hats and baskets (Bosch 2011). In Gabon, they are used as ties in vegetable cultivation. They are recorded to be used for thatching in Ethiopia. The leaves are sometimes used for caulking barrels and to plug seams of canoes. They are also used as bedding for domestic animals and can be used for making paper. The stems are made into mats and fences. In Nigeria, the stems are used for making house screens. In Kano, State of Nigeria, the stems were made into single-person boats. The mature silky female florets are used for stuffing pillows. In Australia, the aboriginals extract fibre from the roots for making strings, and dried fibres are used as fire balls (Low 1991).

Typha domingensis has extensive root system that makes it very good for stabilising wet soil and is planted in basins for phytoremediation of wastewater treatment in Tanzania, Kenya and in Australia and central and south America. Hadad et al. (2010) found *T. domingensis* to be highly adaptable and a promising species in a constructed wetland for metallurgical effluent treatment. Studies by Hegazy et al. (2011) indicated that *Typha domingensis* was capable of accumulating the heavy metal ions (aluminium, iron, zinc and lead) preferentially from wastewater than from sediments. The accumulation of metals in plant organs attained the highest values in roots, rhizomes and old leaves. Rhizofiltration was found to be the best mechanism to explain *Typha domingensis* phytoremediation capability. Studies by Shehzadi et al. (2014) found enhanced degradation of textile effluent in constructed wetland system using *Typha domingensis* and textile effluent-degrading endophytic bacteria. Significant reductions in COD (chemical oxygen demand) (79 %), BOD (biological oxygen

demand) (77 %) TDS (total dissolved solids) (59 %) and TSS (total suspended solids) 27 %) were observed by the combined use of *T. domingensis* and bacteria *Microbacterium arborescens* TYSI04 and *Bacillus pumilus* PIRI30 within 72 h. The resultant effluent met the wastewater discharge standards of Pakistan and could be discharged into the environment without any risks. Studies by Gomes et al. (2014) found *T. domingensis* to be a promising species for the phytoremediation of water contaminated with mercury in constructed wetlands.

Comments

Typha domingensis can be invasive causing serious aquatic weed problems in irrigation channels and waterways. Short-term *Typha* control is provided by cutting, burning or grazing, each followed by flooding, or herbicide, but re-growth from rhizomes and a vast soil seed bank complicate eradication.

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Alpinia conchigera

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Scientific Name

Alpinia conchigera Griff. (Plate 2)

Synonyms

Alpinia humilis Teijsm. & Binn. nom illeg., *Alpinia laosensis* Gagnep., *Alpinia sumatrana* (Miq.) K.Schum., *Languas conchigera* (Griffith) Burkill, *Languas sumatrana* (Miq.) Merr., *Strobidia conchigera* (Griff.) Kuntze, *Strobidia oligosperma* Kuntze, *Strobidia sumatrana* Miq.,

Family

Zingiberaceae

Common/English Names

Joint-whip Ginger, Lesser *Alpinia*, Mussel Galangal

Vernacular Names

Bangladesh: Khetranga

Chinese: Jie Bian Shan Jiang

German: Muschelgalgant

Khmer: Romdeng

Malaysia: Chengkenam, Jerunang, Lengkuas Padang, Lengkuas Padi, Lengkuas Kecil; Lengkuas Ranting, Langkuas Genting, Rumpit Kelemoyang

Myanmar: Pade-Gaw

Thai: Khaa Ling

Vietnamese: Riêng Rùng

Origin/Distribution

The species is indigenous to East India, Bangladesh, Myanmar, Thailand, Laos, Cambodia, Vietnam, China (Yunnan), Peninsular Malaysia and Sumatra.

Agroecology

In its native tropical/subtropical range, it thrives in shaded and moist environment of valleys and humid rainforest from 600 to 1000 m elevation. This species is also semiwild, common in open wet grounds such as edges of rice fields and streams, as well as under the shade of palm oil and rubber trees (Ibrahim et al. 2009). It is the most cold tolerant of the ginger species.

Edible Plant Parts and Uses

In Indochina, the rhizome is used for flavouring rice spirit and food, while its fruits are eaten and medicinal (Burkill 1966). Slender rhizomes are used to flavour food and in native medicine for treating rheumatism, arthritis and a variety of ailments (Wong et al. 2005); the sour fruit is edible. Young shoots are eaten raw or cooked in curries in Thailand. The rhizome is used as a condiment in the northern states of Peninsular Malaysia and occasionally in folk medicine along the east coast to treat fungal infections (Ibrahim et al. 2000; Aziz et al. 2013). In some states of Peninsular Malaysia, the rhizomes are consumed as a post-partum medicine, and the young shoots are prepared into a vegetable dish. In Thailand, the rhizomes are used in traditional Thai medicine to relieve

gastrointestinal disorders and in the preparation of Thai food dishes (Matsuda et al. 2005). The Malays traditionally used *Alpinia conchigera* rhizome to treat infection and rashes and as a health drink (Sulaiman et al. 2010).

Botany

Alpinia conchigera is a slender perennial herb with 0.6–2 m high pseudostem and woody, slender, aromatic rhizome cream coloured in cross section. Leaves are shortly petiolated (5 mm long), lanceolate-oblong, glabrous, dark green and 30 cm by 9 cm; apex is acuminate; and base is cuneate (Plates 1 and 3). Inflorescence is erect, 20–25 cm long (Plate 4) and sometimes 1–2 branched; secondary branches have many cincinni; and bract is small. Flowers are small, 1.5 cm across; calyx is cupular; apex is 3-cleft; lobes are 5–7 mm; corolla lobes are white to greenish-yellowish; labellum is strongly concave, obovate and cream to pinkish white with red stripes; lateral staminodes are red and quadrate; filament is pale yellowish to pinkish, 5 mm long and slender; and anther is 2 mm. Ovary is pyriform and glabrous. Fruit is small and capsule like, glabrous, globose 8 mm across, green (Plate 3) ripening to red, containing 3–5 seeds and strongly aromatic.



Plate 1 Lesser *Alpinia* young plant



Plate 2 *Alpinia conchigera* plant label



Plate 3 Leaves, flowers and fruits



Plate 4 Lesser *Alpinia* inflorescence

Nutritive/Medicinal Properties

Yu et al. (1988) reported the presence of nonacosane, β -sitosterol, 1'-acetoxychavicol acetate and 1'-acetoxyeugenol acetate in the fruit, the two phenylpropanoid derivatives showing anti-inflammatory activity. Athamaprasangsa et al. (1994) reported the presence of 12 components from *A. conchigera* rhizome essential oil from Thailand including four known phenylpropanoids (chavicol acetate, 1'-hydroxychavicol acetate, 4-acetoxycinnamyl alcohol and 4-acetoxycinnamyl acetate from the aqueous fraction of fresh rhizomes), five diarylheptanoids (1,7-diphenyl-3,5-heptanedione; 1,7-diphenyl-5-hydroxy-3-heptanone; 5-hydroxy-7-(4'-hydroxy-3'-methoxyphenyl)-1-phenyl-3-heptanone; 1,7-diphenylhept-4-en-3-one and 7-(4'-hydroxy-3'-methoxyphenyl)-1-phenylhept-4-en-3-one) and two flavonoids (3,5,7-trihydroxyflavone and 3,5,7-trihydroxy-4'-methoxyflavone from the n-hexane and dichloromethane extracts of the dried rhizomes). Sirat and Nordin (1995) reported 34 essential oil components from *A. conchigera* rhizomes from the southern Peninsular Malaysia, among which β -sesquiphellandrene (20.5 %), β -bisabolene (12.1 %) and 1,8-cineole (11.6 %) were found to be the major constituents. They also reported the presence of α -thujene; δ -2-carene; (Z)- β -ocimene; *p*-mentha-1,5,8-triene; *p*-cymenol; *trans*-carvyl acetate; neryl acetate; methyl eugenol; δ -selinene; farnesol; γ -elemene; 2,4-di(tert-butyl)phenol; 1-hexadecene and heptadecane. Wong et al. (2005) reported 50 components in the rhizome oil from northern Malaysia. The major chemical class was terpenoids, with β -bisabolene (28.9 %), 1,8-cineole (15.3 %) and β -caryophyllene (10.0 %) as the major components. Other minor components included camphene, α -phellandrene, (*E*)- β -ocimene, *p*-cymenene, bornyl acetate, tridecane, thymyl acetate, pentadecane, τ -muurolol, α -bisabolol, heptadec-1-ene, (*E,E*)-farnesyl acetate and nonadec-1-ene. Phan et al. (2005) isolated β -sitosterol, stigmasterol and three flavonoids: cardmomim, alpinetin and naringenin 5-methyl ether from the rhizomes from Vietnam. Lê et al. (2007) isolated β -sitosterol, stigmasterol, cardamomin, chalconaringenin 2'-*O*-methyl ether, alpinetin and naringenin 5-*O*-methyl ether from methanolic rhizome extract. Giang et al. (2008) isolated flavokawin B, β -sitosterol,

stigmasterol, alpinetin, (3*S*,5*S*)-*trans*-3,5-dihydroxy-1,7-diphenyl-1-heptene, β -D-fructopyranose, β -D-fructofuranose and 2-*O*-Me β -D-fructofuranose from the fruits of *Alpinia conchigera* from Vietnam.

More than 40 components were detected in *Alpinia conchigera* rhizome oil, in which 4,11, 11-trimethyl-8-methylene-bicyclo-undec-4-ene (15.65 %), 12-methyl-1,5,9,11-tridecatetraene (10.97 %), 3,3,7,7-tetramethyl-5-(2-methyl-1-propenyl)-tricycloheptane (6.49 %) and (+)-nerolidol (7.72 %) were the major constituents (Anita et al. 2000). The minor components above 1 % were guaiol acetate (3.96 %), α -farnesene (3.3 %), unidentified (2.72 %), α -bisabolol (2.60 %), (*Z*)- β -farnesene (2.01 %), isocaryophyllene (1.61 %), 4-allylphenyl acetate (1.42 %), α -zingiberene (1.29 %), linalool acetate (1.19 %), unidentified (1.17 %), ledane (1.12 %) and δ -elemene (1.11 %). The minor components below 1 % included α -phellandrene, *trans*- β -ocimene, β -pinene, β -myrcene, 2-carene, 4-ethyl-1,2-dimethyl-benzene, limonene, γ -terpinene, terpinolene, 4-decenal, decenal, capryl acetate, isotetradecane, 5-methyl-2-[1-methyl] phenol acetate, geranyl isobutyrate, 2,3,4,6-tetramethyl phenol, (*Z,E*)- α -farnesene, 1ar[1ar α ,4b,4ab,7a,7ab]-decahydro-1,1,4,7-tetramethyl-1H-cyclo azulen-4-ol, (-)- β -elemene, (-)-bisabolene, unidentified, bisabolol, elemol, 1,5,5,8-tetramethyl-12-oxabicyclo 9.1.0 dodeca-3,-diene, (-)- δ -cadiol, nonadienal and dodecane. A total of 17 components were found in the leaf of which (+)- β -bisabolene (24.18 %), (+)-nerolidol (9.68 %), isocaryophyllene (8.25 %), 3,3,7,7-tetramethyl-5-(2-methyl-1-propenyl)-tricycloheptane (3.99 %) and (*Z,E*)- α -farnesene (3.61 %) were the major components (Anita et al. 2000). The minor components included α -pinene; β -pinene; limonene; 4-allylphenyl acetate; (-)- β -elemene; α -farnesene; 4,11, 11-trimethyl-8-methylene- bicyclo undec-4-ene; α -cadrene; decahydro-1,1,4,7-tetramethyl-1H-cyclo azulen-4-ol; levomenol; patchulane and δ -cadinol.

Bhuiyan et al. (2010) reported that the rhizome essential oil contained 74 compounds with eucalyptol (25.85 %), chavicol (25.08 %), α -caryophyllene (10.33 %), β -pinene (6.71 %) and caryophyllene (3.38 %) as the major components.

Other components (above 1 %) included α -pinene (2.59 %), 4-terpineol (2.91 %), sabinene (2.01 %), camphene (1.54 %), γ -terpinene (1.36 %), 3-buten-2-ol, 4-(2, 6, 6-trimethyl-1-cyclohexen-1-yl) (1.13 %) and eugenyl acetate (1.04 %). Components of 0.1–1 % were (+) -4-carene; (+) globulol; 14-methyl-8-hexadecyn-1-ol, 2-methylnorbornane, 3,4-dihydrocoumarin, 4,4-dimethyl-6-hydroxy, 4-chroman-5-ol, 5-nonanol, 5-methyl, 8-heptadecene, β -bisabolene, β -elemene, bergamotol, *Z*, α -*trans*, bicyclo [3,1,0] hexan-2-ol, 2-methyl-5-(1-methylethyl), bicyclo (5,2,0) nonane, 4-methylene-2,8,8-trimethyl-2-vinyl, β -linalool, β -myrcene, caryophyllene oxide, cinnamyl acetate, *cis* -L-bisabolene, germacrene D, eugenol, α -bergamotene, α -bisabolol, *trans*-muurolol, α -linalool, α -panasinsen, α -selinene, α -thujene, neryl acetate, *O*-cymol, terpinolene, ethyl acetate, *trans*-nerolidol, *trans*-carveol and valencene. Constituents of < 0.01 % included δ -cadinene; 1,6,10-dodecatriene, 7,11-dimethyl-3-methylene; citral, (*Z*) 2-decen-2-ol; 3,7-cycloundecadien-1-ol; 1,5,5,8-tetramethyl; 3-octen-1-ol (*Z*); benzene; carvyl acetate; cinerone; *cis*-carvyl acetate; *cis* -*p*-mentha-2,8-dien-1-ol; *cis*-piperitol; *cis*-verbenol; cycloisolongifolene, 4,5-dehydro; dihydrochavicol; fenchol; isoborneol; isoborneol acetate; juniper camphor; α ,4-dimethylstyrene; α -durenol; α -muurolene; α -phellandrene; methyleugenol; ningidrin; ocimene; pseudolimonene and *trans-trans*-farnesal.

Essential oil constituent of fresh leaves and leaves air dried for 1, 2, 3 and 7 days (% area) was, respectively, as follows: bicyclo(3.1.1)hept-2-ene, 2,6,- trimethyl (10.6, 3.05, 2.84, 4.68, 2.49 %), β -pinene (3.36, 10.32, 9.83, 14.78, 7.41), cyclohexene, 4-ethyl-3,4-methyl-3-(1-methylethenyl)-1-(1-methylethyl) (0.65, 0.93, 1.13, 0.66, 0 %), phenol, 4-(2-propenyl)-acetate (0, 0.44, 0.37, 0, 0 %), dodecanal (0.063, 0, 0, 0 %), bicyclo(7.2.0)undec-4-ene, 4,11,11-trimethyl-8-methylene (16.92, 19.76, 18.32, 16.42, 13.49 %), germacrene D 1,6-cyclodecadiene, 1-methyl-5-methylene-8-(1-methylethyl) (2.36, 2.48, 2.50, 1.62, 1.13 %), 1,6,10-dodecatriene, 7,11-dimethyl-3-methylene (1.90, 1.80, 2.16, 1.74, 54.79 %), α -caryophyllene (1.07, 1.59, 1.30, 1.47, 1.27 %), cyclohexene, 1-methyl-4-(5-methyl-1-methylene-4-hexenyl) (61.19, 47.89, 50.47, 48.58, 0 %), cyclohexene, 3-

(1,5-dimethyl-4-hexenyl)-6-methylene (4.32, 3.94, 4.96, 3.33, 4.68 %), 1,6,10-dodecatriene-3-ol, 3,7,11-trimethyl (0.72, 1.07, 0.76, 0, 0 %), α -bisabolol (0.72, 1.07, 0.76, 0, 0 %) and phytol (0.84, 0, 0, 0, 0, %), with a total yield of 0.12, 0.085, 0.22, 0.16 and 0.3 % (Faridah et al. 2010). Essential oil constituent of fresh rhizome and rhizomes air dried for 1, 2, 3 and 7 days (% area) was, respectively, as follows:

bicyclo(3.1.1)hept-2-ene, 2,6,- trimethyl (4.92, 3.69, 4.75, 6.26, 5.57 %), β -pinene (18.44, 18.70, 15.74, 17.09, 16.99 %), β -myrcene (1.25, 0, 0, 1.62, 1.23 %), benzene, 1-methyl-3-(1-methylethyl) (0, 1.54, 5.28, 0.35, 0 %), cyclohexene, 1-methyl-4-(1-methylethynyl) (1.13, 2.38, 0, 1.46, 0.67 %), eucalyptol (0, 0, 0, 42.70, 45.07 %), 1,4-cyclohexadiene, 1-methyl-4-(1-methylethyl) (0.86, 0, 0, 0.61, 0.91 %), bicyclo(3.1.1)heptan-3-ol, 6,6-dimethyl-2-methylene (0, 0, 4.56, 0, 0 %), bicyclo(3.1.1)hept-2-ene-2-methanol, 6,6-dimethyl (0, 0, 3.34, 0, 0 %), 3-cyclohexen-1-ol, 4-methyl-1-(1-methylethyl) (2.25, 0, 0, 0, 1.80 %), α -terpineol (p-menth-1-en-8-ol) (0, 0, 0, 0, 0.99 %), 3-cyclohexeno-1-methanol, α,α 4-trimethyl (1.80, 0, 0, 0.61, 0 %), bicyclo(3.1.1)hept-3-en-2-one, 4,6,6-trimethyl (0, 0, 6.76, 0, 0 %), cyclohexene, 4-ethyl-3-4-methyl-3-(1-methylethenyl)-1-(1-methylethyl) (0, 0, 0, 0, 0.28 %), phenol, 4-(2-propenyl)-acetate (0, 0.83, 0, 1.90, 2.92 %), 2,6-octadien-1-ol, 3,7-dimethyl-acetate (0, 0, 0, 0.42, 0.25 %), 2,6,10-dodecatrien-1-ol, 3,7,11-trimethyl (0, 5.05, 0, 0, 0.41 %), bicyclo(7.2.0)undec-4-ene, 4,11,11-trimethyl-8-methylene (5.63 %, 0, 0, 4.92, 4.53 %), α -caryophyllene (5.64, 0, 0, 4.92, 4.53 %), 1-dodecanol (0, 0, 0, 0.32, 0 %), 1,6,10-dodecatriene, 7,11-dimethyl-3-methylene (7.67, 0, 1.23, 0.40, 0.24 %), 1H-cycloprop(e)azulene, decahydro-1,1,7-trimethyl-4-methylene (0, 0, 0, 0.94, 0 %), naphthalene, 1,2,3,5,6,7,8,8a-octahydro-1,8a-dimethyl-7-(1-methylethenyl) (1.25, 1.11, 0.80, 0, 0.73 %), n-hexadecanoic acid (0, 4.61, 0, 0 %), cyclohexene, 1-methyl-4-(5-methyl-1-methylene-4-hexenyl) (0, 28.44 %, 2.89, 11.51, 6.70 %), phenol, 2-methoxy-4-(2-propenyl)-acetate (0, 0, 0, 0, 0.31 %), cyclohexene, 3-(1,5-dimethyl-4-hexenyl)-6-methylene (0.63, 1.01, 0, 0.82, 0.62 %), T-murolol (0.72, 0, 0, 0, 0.50 %), α -bisabolol (0.58, 1.05, 0, 0.51, 0.41 %) and α -cadinol (0, 0, 0, 0.47, 0 %), with a total yield of 0.078, 0.112, 0.078, 0.162 and 0.145 % (Faridah et al.

2010). The post-harvest drying period had a positive effect on the oil yield of both leaf and rhizome. The highest oil yield was obtained from leaves dried for 7 days (0.300 v/w) and rhizomes dried for 3 days (0.162 v/w). The study suggested that the yield and content of essential oils from the leaves and rhizomes of *A. conchigera* could be increased by drying leaves and rhizomes for 7 and 3 days, respectively.

Aziz et al. (2013) isolated the following compounds from the pseudostem and rhizome, respectively: from the n-hexane, namely, mixture of stigmasterol and β -sitosterol (0.31, 0.25 %), chavicol acetate (0, 0.08 %), caryophyllene oxide (0, 0.05 %), *p*-hydroxycinnamaldehyde (0.07, 0.59 %), 1'*S*-1'-acetoxychavicol acetate (0.15, 40.07 %), *trans-p*-coumaryl diacetate (0.68, 0.19 %), 1'*S*-1'-acetoxyeugenol acetate (0, 0.12 %), 1'-hydroxychavicol acetate (0, 0.15 %), 4-hydroxybenzaldehyde (0.13, 0.61 %) and *p*-hydroxycinnamyl acetate (0.20, 0.12 %), and from the dichloromethane extract, mixture of stigmasterol and β -sitosterol (0, 0.14 %), chavicol acetate (0, 0 %), caryophyllene oxide (0, 0 %), *p*-hydroxycinnamaldehyde (0.18, 0.20 %), 1'*S*-1'-acetoxychavicol acetate (9.08, 25.25 %), *trans-p*-coumaryl diacetate (0.95, 0.80 %), 1'*S*-1'-acetoxyeugenol acetate (0, 0.03 %), 1'-hydroxychavicol acetate (0.37, 0.19 %), 4-hydroxybenzaldehyde (0.48, 0.12 %) and *p*-hydroxycinnamyl acetate (1.10, 0.92 %).

The leaf, pseudostem and rhizome essential oils of *A. conchigera* afforded 40, 33 and 39 constituents, respectively (Ibrahim et al. 2009). Among the compounds identified were 17 monoterpenes (25.7 %), 15 sesquiterpenes (31.8 %), three esters (0.8 %), two aldehydes (3.2 %), one hydrocarbon (0.6 %) and one phenol (2.9 %) from the rhizome; 18 monoterpenes (15.8 %), 15 sesquiterpenes (36.2 %), three esters (1.0 %), two aldehydes (1.3 %), one hydrocarbon (1.9 %) and one phenol (7.5 %) from the leaf oil; and 15 monoterpenes (8.0 %), 11 sesquiterpenes (51.1 %), three esters (1.3 %), two aldehydes (0.2 %), one phenol (2.4 %) and one hydrocarbon (3.0 %) from the pseudostem oil. The most abundant components in the rhizome oil were 1,8-cineole (17.9 %), β -bisabolene (13.9 %), β -sesquiphellandrene (6.8 %)

and β -elemene (4.0 %), β -caryophyllene (3.6 %), ethylbenzaldehyde (3 %) and β -pinene (3.3 %). The major components in the leaf oil were β -bisabolene (15.3 %), β -pinene (8.2 %), β -sesquiphellandrene (7.6 %), chavicol (7.5 %) and β -elemene (6.0 %), while β -bisabolene (19.9 %), β -sesquiphellandrene (11.3 %), β -caryophyllene (8.8 %) and β -elemene (4.7 %) and 3-tetradecen-5-yne (3 %) were the main components in the pseudostem. The minor components found in the rhizome oil included α -pinene, sabinene, myrcene, δ -3 carene, *p*-cymene, (*E*)-2-octenal, γ -terpinene, terpinolene, linalool α -phellandrene epoxide, camphor, terpinene-4-ol, myrtenal, α -terpineol, chavicol, bornyl acetate, eugenol, δ -elemene, geranyl acetate, α -copaene, (*Z*)-cyclodecene, germacrene D, (*E*)- α -bergamotene, α -humulene, (*Z*)- β -farnesene, zingiberene, β -selinene, (*E*)- β -farnesene, eugenyl acetate, β -elemol, β -nerolidol and 3-tetradecen-5-yne. Also, these compounds plus 1,8-cineol and limonene together with β -caryophyllene and ethylbenzaldehyde occurred as minor components in the leaf oil. Most of these compounds plus (*E*)-2-decenal were also found as minor components except for sabinene, δ -3-carene, terpinolene, camphor, δ -elemene, α -copaene, β -selinene and (*E*)-nerolidol which were absent in the pseudostem essential oil. Five new 8-9' linked neolignans conchigeranals A–E together with three known compounds galanganal, galanganols A and B (Xu et al. 2013a) and three unusual sesquineolignans conchignans A, B and C together with two known compounds vanillin and phloroglucinol (Xu et al. 2013b) were isolated from the whole plant of *Alpinia conchigera*.

Antitumour Activity

The crude hexane, dichloromethane and ethyl acetate extracts of *A. conchigera* rhizome exhibited very strong activity in cytotoxic screening test against HL-60 cell line (human promyelocytic leukaemia) with IC₅₀ values <5 μ g/mL (Sukari et al. 2007). 1'S-1'-acetoxyeugenol acetate (AEA), an analogue of 1'S-1'-acetoxychavicol acetate (ACA), isolated from *Alpinia conchigera* exhibited cytotoxic and apoptotic effect on human breast cancer cells (Hasima et al. 2010). Data

from MTT cell viability assays indicated that AEA induced both time- and dose-dependent cytotoxicity with an IC₅₀ value of 14.0 µM within 36 h of treatment on MCF-7 cells, but not in normal human mammary epithelial cells (HMEC). Data from MTT cell viability assays indicated that 1'-(S)-1'-acetoxychavicol acetate (ACA), from *A. conchigera*, induced both time- and dose-dependent cytotoxicity on breast adenocarcinoma (MCF-7), oral squamous carcinoma (HSC-2 and HSC-4), hepatocyte carcinoma (HepG2) and epidermoid cervical carcinoma (CaSki) cell lines tested and had no adverse cytotoxic effects on normal cells (Awang et al. 2010). Total mortality of the entire tumour cell population was achieved within 30 h when treated with ACA at 40.0 µM concentration. The apoptotic effects of ACA were confirmed via the DNA fragmentation assay, in which consistent laddering of genomic DNA was observed for all tumour cell lines after a 24 h post-treatment period at the IC₅₀ concentration of ACA. Also ACA induced cell cycle arrest at the G(0)/G(1) phase, in the tumour cells.

Murakami et al. (1993) found 1'-acetoxychavicol acetate, a superoxide anion generation inhibitor, to potently inhibit tumour promotion by 12-*O*-tetradecanoylphorbol-13-acetate in ICR mouse skin. In et al. (2011) found 1'S-1'-acetoxyeugenol acetate (AEA) isolated from *A. conchigera* rhizome to induce apoptosis in MCF-7 human breast cancer cells but not in normal human mammary epithelial cells. The induction of tumour cell death through apoptosis was modulated through dysregulation of the nuclear factor-kappaB (NF-κB) pathway. Also AEA inhibited phosphorylation levels of the inhibitor of κB-kinase complex, resulting in the elimination of apoptotic resistance. Another compound, 1'S-1'-acetoxychavicol acetate (ACA), isolated from *A. conchigera* rhizome, inhibited growth of oral squamous cell carcinoma (SCC) via apoptosis in in-vitro using MTT assays and in-vivo using *Nu/Nu* mice and further potentiated the effect of standard cisplatin treatment by modulation of proinflammatory microenvironment (In et al. 2012). The effects of ACA also correlated with a downregulation of NF-κB-regulated gene (FasL and Bim), including proinflammatory (NF-κB and

COX-2) and proliferative (cyclin D1) biomarkers in tumour tissue. Results of in-vitro studies showed that conchigeranals D and E, galanganols A and B, from *A. conchigera* plant, exhibited cytotoxicity against A549 cancer cell line with the IC₅₀ values of 12.36, 9.72, 10.26 and 13.05 µg/ml, respectively, and 1–8 against Hela cancer cell line with the IC₅₀ values from 1.53 to 5.29 µg/ml (Xu et al. 2013a).

Antimicrobial Activity

Crude hexane, dichloromethane and ethyl acetate extracts of *A. conchigera* rhizome strongly inhibited *Salmonella choleraesuis* in-vitro (Sukari et al. 2007). The hexane extract showed mild inhibition on *Aspergillus ochraceus* and *Saccharomyces cerevisiae*, while ethyl acetate extract was active towards *S. cerevisiae* as well. The essential oils from *A. conchigera* leaves, pseudostems and rhizomes exhibited weak in-vitro inhibitions against four bacteria, namely, *Pseudomonas aeruginosa*, *Pseudomonas cepacia*, *Staphylococcus aureus* and *Staphylococcus epidermidis*, and three dermatophytic fungi, namely, *Microsporum canis*, *Trichophyton mentagrophytes* and *Trichophyton rubrum*, compared to standard antibiotic cycloheximide for the fungi and streptomycin sulphate for the bacteria (Ibrahim et al. 2009).

The dichloromethane (DCM) extract of *A. conchigera* rhizome exhibited potent in-vitro antifungal activity against *Candida albicans*, *Microsporum canis* and *Trichophyton rubrum* with MIC values: 625 µg/ml, 156 µg/ml and 156 µg/ml, respectively, which were lower than the control antifungal antibiotic, cycloheximide (Aziz et al. 2013). Among the isolated compounds, the lowest inhibition observed was of 1'S-1'-acetoxyeugenol against the fungal dermatophytes (MIC:313 µg/ml) followed by *trans-p*-coumaryl diacetate against both dermatophytes and *Candida* (MIC:625 µg/ml). Neither anticandidal nor anti-dermatophyte activity could be detected at the high concentration of 2500 µg/ml from 1'S-1'-acetoxychavicol acetate, the major compound present in the DCM extracts. In contrast, the DCM extract exhibited weak

inhibitory activity (1250 µg/ml) against the non-mutant *Staphylococcus aureus*. However, significant inhibitory activity with MIC values between 17.88 and 35.75 µg/ml was observed against the MSSA (methicillin-sensitive strain), MRSA (methicillin-resistant strain) and remaining isolate of *Staphylococcus aureus*. The compound *p*-hydroxycinnamyl acetate strongly inhibited VISA (vancomycin-intermediate resistant strain) with MIC of 39 µg/ml followed by *trans-p*-coumaryl diacetate and 10-hydroxychavicol acetate with MIC value of 156 µg/ml as compared to the antibiotic oxacillin (313 µg/ml). In contrast, VRSA (vancomycin-resistant strain) was most affected by 1'S-1'-acetoxychavicol acetate with MIC value of 313 µg/ml. The crude rhizome extract showed moderate antimicrobial activity in-vitro against *Vibrio cholera* and weaker activity against *Staphylococcus aureus*, *Bacillus subtilis* and *Salmonella typhi* (Talukder et al. 2013).

Antiviral Activity

Kondo et al. (1993) reported 1'-acetoxychavicol acetate to be a potent inhibitor of tumour promoter-induced Epstein–Barr virus activation. Liu et al. (2007) found 1'-acetoxychavicol acetate to be a HIV-1 viral regulatory protein, Rev-transport inhibitor from the nucleus to cytoplasm.

Antinociceptive Activity

Alpinia conchigera rhizome ethanol extract (30, 100 and 300 mg/kg) given intraperitoneally (i.p.) exhibited antinociceptive activity in the acetic acid-induced writhing, hot plate and formalin tests in mice and rats (Sulaiman et al. 2010). The range of percentage of analgesia obtained for all doses of extract in the writhing test was 50–92 % and in the early and late phases of the formalin test was 25–62 % and 63–98 %, respectively. In addition, naloxone (5 mg/kg) given subcutaneously (s.c.) was found to reverse the extract (300 mg/kg)-induced antinociceptive activity in the writhing, hot plate and formalin tests. The results suggested that *A. conchigera* rhizomes possessed a peripheral and central antinociceptive activity that was mediated, in part, via the

opioid receptor. Similar antinociceptive activity of the ethanolic leaf extract was found using the acetic acid-induced abdominal writhing test, the hot plate test and the formalin test (Sulaiman et al. 2009). The antinociceptive effect of the leaf extract in the acetic acid-induced writhing and hot plate tests was reversed by naloxone, suggesting that this activity was mediated through activation of the opioid system.

Anti-inflammatory Activity

Alpinia conchigera rhizome ethanol extract (30, 100 and 300 mg/kg) given intraperitoneally (i.p.) exhibited anti-inflammatory activity in carrageenan-induced paw oedema in mice and rats (Sulaiman et al. 2010). Similar anti-inflammatory activity in carrageenan-induced paw oedema was observed for the ethanolic leaf extract (Sulaiman et al. 2009). 1'S-1'-acetoxychavicol acetate inhibited nitric oxide (NO) production in lipopolysaccharide-activated mouse peritoneal macrophages with an IC₅₀ value of 2.3 µM (Matsuda et al. 2005).

Gastroprotective Activity

The methanolic extract (1.56–50 mg/kg, *p.o.*) of *A. conchigera* significantly inhibited gastric mucosal lesions in rats induced by ethanol, 0.6 M HCl and indomethacin with ED₅₀ values of 2.7, 9.8 and 16.5 mg/kg (*p.o.*), respectively, partly by the involvement of endogenous prostaglandins and sulfhydryl compounds (Pongpiriyadacha et al. 2008).

Antithrombotic Activity

Among the plant extracts studied, *Alpinia conchigera* showed significant percent of clot lysis (24.50 %) compared to streptokinase (81.08 %) (Sultana et al. 2012).

Traditional Medicinal Uses

According to Burkill (1966), a poultice of boiled leaves or leaves and rhizomes is applied for rheumatism and an infusion

used for bathing in Peninsular Malaysia. A rhizome poultice is rubbed on the body for bone pains and a pounded leaves used as a poultice for confinement. The Temuan tribe in Ayer Hitam Selangor, Malaysia, used a root decoction as shampoo to rid hairs of lice, pounded leaves as poultice for boils and swellings on stomach after childbirth, pounded rhizome as rub for inside bone pain and powdered rhizome mixed with water as poultice for stomach ache (Ibrahim and Hamzah 1999). According to Ibrahim et al. (2000, 2007), Wong et al. (2005), rhizome juice mixed in water is drank for dysmenorrhoea; ground rhizome mixed with vinegar or kerosene is rubbed on fungal skin infection; *A. conchigera* essential oil is applied topically for muscle pains and strains; rhizome juice and fresh milk are drank in the morning as health drink and treatment for lethargy. In Indochina, the rhizome is deemed stimulating, diaphoretic and employed for treating bronchitis, headache, jaundice and vertigo (Ibrahim 2002). In Thailand, the rhizomes are used for indigestion and abscesses, and rhizome and leaves are poulticed and used for ringworm infections. In China, the roots and body are used in treating chest and abdominal pain and digestive disorders. In Myanmar, rhizomes are used in traditional medicine for cold, gout and digestion (Awale et al. 2006). Traditionally, it is used in gastric pain, diarrhoea and dysentery in the southeast region of Bangladesh (Rahman et al. 2007; Talukder et al. 2013). To stop abdominal pain, 2 teaspoonfuls of juice of *A. conchigera* rhizome and *Carex continua* root are taken thrice daily. *Alpinia conchigera* is used to treat diabetes mellitus in Thailand (Chuakul and Boonpleng 2003). *Alpinia conchigera* rhizomes are extensively used as spice for flavouring food and also used in Thai traditional medicine for the treatment of various diseases, such as carminative, stomachic, antifatulent, skin disease, venereal disease and bronchitis or as appetiser, digestive stimulant, analgesic and anti-inflammatory in Vietnam (Vo 1997). Juice from boiled rhizomes and leaves is used to treat abdominal pain, indigestion and spleen, and water from boiled leaves are used for bathing, while burned leaves are used for rheumatic pains (Nguyen et al. 2014).

Other Uses

Alpinia conchigera oil possessed insecticidal activity. *Alpinia conchigera* oil caused complete mortality of maize weevil (*Sitophilus zeamais*) at 222 $\mu\text{L/L}$ after 24 h, whereas 593 $\mu\text{L/L}$ for 24 h was required for complete mortality of flour beetle (*Tribolium castaneum*) (Suthisut et al. 2010). *Sitophilus zeamais* adults (LC_{50} 114–129 $\mu\text{L/L}$) were more susceptible to the essential oil than *T. castaneum* (LC_{50} 203–369 $\mu\text{L/L}$). In contact toxicity by topical application to insect thorax, *S. zeamais* adults (LC_{50} 18–40 $\mu\text{g/mg}$) had the same mortality as *T. castaneum* (LC_{50} 28–47 $\mu\text{g/mg}$). In repellancy test, *A. conchigera* in 100 % ethanol repelled *T. castaneum* more than *S. zeamais*. Via topical applications, the rhizome oils of *Alpinia conchigera*, *Zingiber zerumbet* and *Curcuma zedoaria* exerted similar toxicity against *Sitophilus zeamais* (LD_{50} 18–24 $\mu\text{g oil/mg insect}$) (Suthisut et al. 2011). *Tribolium castaneum* had similar sensitivity to all three oils (LD_{50} 35–58 $\mu\text{g/mg}$), and it was less sensitive than *S. zeamais*. The LD_{50} values of synthetic *A. conchigera* and synthetic *Z. zerumbet* oils were similar to those of their corresponding extracted essential oils. *Sitophilus zeamais* and *T. castaneum* were sensitive to the rhizome oil constituents terpinen-4-ol and isoborneol in contact toxicity tests. In antifeedant tests, the three extracted oils were able to decrease the consumption of flour disks. Only terpinen-4-ol deterred feeding in both insects. In repellency tests, *A. conchigera* oils at highest concentration repelled *S. zeamais* and *T. castaneum*. None of the synthetic essential oils repelled *S. zeamais* (315 $\mu\text{l/cm}^2$) and *T. castaneum* (31 $\mu\text{l/cm}^2$). Only terpinen-4-ol showed repellent activity against both insects.

Comments

This ginger is propagated by rhizome division or seeds.

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Alpinia galanga

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Scientific Name

Alpinia galanga (L.) Willdenow

Synonyms

Alpinia alba (Retz.) Roscoe, *Alpinia bifida* Warb., *Alpinia carnea* Griff., *Alpinia galanga* var. *galanga*, *Alpinia galanga* var. *pyramidata* (Blume) K. Schum., *Alpinia pyramidata* Blume, *Alpinia rheedei* Wight, *Alpinia viridiflora* Griff., *Amomum medium* Lour., *Amomum galanga* (L.) Lour., *Galanga major* Garsault invalid, *Galanga officinalis* Salisb., *Heritiera alba* Retz., *Hellenia alba* (Retz.) Willd., *Languas galanga* (L.) Stuntz, *Languas pyramidata* (Blume) Merr., *Languas vulgare* Koenig, *Maranta galanga* L. (basionym), *Zingiber galanga* (L.) Stokes, *Zingiber medium* Stokes, *Zingiber sylvestre* Gaertn

Family

Zingiberaceae

Common/English Names

Blue Ginger, Chinese Ginger, False Galangal, Galangal, Galangal Root, Greater Galangal, Java Galangal, Languas,

Laos Root, Siamese Galangal, Siamese Ginger, Spice Ginger,
Thai Galangal, Thai Ginger

Vernacular Names

Arabic: El-Galangal, El-Adkham, Khulanjane-Qasbi, Khulanjan-E-Kabir, Khulanjan Kabeer, Khowlanjan, Khulanjan, Khulanjanekabir, Khulanjaneqasbi, Khulanjane-Kabir

Brazil: Alpinia

Bosnian: Aflidžan, *Galanga*, Galgan, Galgant, Kalgan, Sundska Galangal

Burmese: Pa De Gaw Gyi, Padagoji

Chinese: Da Gao Liang Jiang, Hong Dou Kou

Croatian: Aflidžan, *Galanga*, Galgan, Galgant, Kalgan, Sundska Galanga

Czech: Galgán, Galgan Obecný, Kalkán, Galgán Veliký, Galgán Větší

Danish: Galanga, Stor Galanga, Stor Galangarod

Dutch: Galgant, Galigaan, Grote Galanga, Lengoewas

Esperanto: Galango

Estonian: Suur Kalganirohi

Finnish: Galangajuuri

French: Galanga, Grand Galanga, Galanga De l'Inde, Galanga Majeur, Herbe Indienne, Galanga, Souchet Long, Souchet Odorant

German: Galgant, Großer Galgant, Siam-Ingwer, Siamesische Ingwerlilie

Greek: Galagkē, Galanki

Hebrew: Galangal

Hungarian: Galangagyökér, Galangál, Sziámi Gyömbér

India: Karphul (Assamese), Kulinjan (Bengali), Kolinjan (Gujerati), Pun-nagchampa, Bara-Kulanjan, Barakalijan,

Barakulanjan, Barakulinjan, Kulanajn, Kulanjan,
Kulinjan, Saphed-Panaki-Jhad, Bara-Kalijan (Hindi),
Dhumarasmī, Doddadumprashme, Dumbarasme, Dumpa-
Rasmi, Dumrashta, Rasmi, Sugandhavachi,
Dumparaasme, Raasmi, Sughandavachi, Dumpa Rasme,
Rasmini, Sugandhavaci, Doopparaasme, Dumbaraasme,
Dumbraashta, Gandhamoola, Kulinjana (Kannada),
Aratta, Chitta-Ratta, Cittaratta, Pera-Ratta, Perasatta,
Peraratta (Malayalam), Kanghoo (Manipuri),
Koṣṭkuliñjan, Koshtkulinjan, Kolinjan, Kulimjan
(Marathi), Aichal (Mizoram), Tikshnamula (Oriya),
Aruna, Dhumala, Dhumparastma, Dumparastma,
Elaparni, Gandhamula, Gandhavaruni, Kapidruma,
Koraja, Kulangana, Kulanja, Kulanjana, Kulin-Jana,
Kulinjana, Mahabaravach, Mahabharavacha, Mahabhari
Vaca, Mahabharivaca, Malayavaca, Nakuli, Patala,
Purusha, Raktapushpa, Rasna, Sthulagranthi, Sugandha,
Sugandhamula, Sugandhavacha, Sugandhayoga,
Tikshnamula (Sanskrit), Anandam, Arattai, Ardubam,
Attumam, Pera-Rattai, Kandanaguliyam, Perarathi,
Thumbrashtagam, Perarattai, Tumparattam, Canna
Rastakam, Tumras Takam, Periareta, Perarathai,
Oramrundu, Sattiradji, Sugandam, Araddai, Peraraddai,
Akkulati, Anaivacampu, Anantam, Anantatam, Ananti,
Aracanam, Arppatumam, Arttupam, Arttuvam, Artupam,
Atitipam, Attumam, Atumam, Cakunam, Caramarutam,
Cattiratci, Cattiratti, Cencaram, Cerukkampam,
Cikamatakikam, Cikamatam, Cirenki, Citakampam,
Cukantam, Curacam, Curatakku, Curatakkutam,
Elaparani, Erarattai, Iracana, Iracanacikam,
Iracanakikam, Iracina, Iratanai, Irattaputpam, Irattarenu,
Kantamulam, Kantanakuliyam, Katiyastakam, Kattiratci,
Kentacamakan, Kentakanarani, Kottakarai, Kulancam,
Ormaruntu, Pavanam, Purantam, Putakani,
Tiritosavatakacakkini, Tittikam, Tittipam, Tittiram,
Tittiyam, Tummarastakam, Tumpakam, Tumparastakam,
Tumparattakam, Tumpurastakam, Tumpurattakam,
Tumpurattam, Turani, Mitintarattai, Mitintu,
Mulatiracam, Mutical, Nakuli, Narayanam, Natanatam,
Uttamam, Vamanaci, Perearetei (Tamil),

Sannadumparāṣṭramu, Dumparashtraamu, Kachoramu,
Pedda-Dhumpa, Pedda-Dumpa-Rashtrakam,
Peddadumparashtrakamu, Rash-Trakam,
Dumparaashtrakamu, Peddadumparaashtrakmu (Telugu),
Kulanjan, Khulanjan, Badi Khulanjan, Khulanjan Nim
Kofta (Urdu)

Indonesia: Lengkuwas (Java), Laos (Sundanese), Laja,
Lawas, Langkuweh, Lengkuwas (Sumatra)

Italian: Galanga Maggiore

Japanese: Garanga, Nankyo

Khmer: Madeng, Pras Sva, Romdeng, Rumdeng

Korean: Gal-Ren-Gal, Kallengal

Laotian: Kha Ta Deng

Lithuanian: Alpinija

Malaysia: Lengkuas, Langkuas, Lengkuas Benar, Puar,
Mengkanang

Nepal: Tontha (Bhotia), Sarra (Nepali).

Norwegian: Stor Galanga, Stor galangal, Stor galangarot,
Uekte galanga

Pakistan: Kulanjan, Khulanjan, Badi Khulanjan,
Khulanjan Nim Kofta (Urdu)

Persian: Xuz Rishe, Djus Rishe, Jouz Rishe, Khusrave-
Durue-Kalan, Khusrodaru-E-Kalan, Khurduwara,
Khusravedruekalan, Khusrave-Darue-Kalan

Philippines: Palla (Tagalog), Langkawas, Langkuas

Polish: Galanga

Portuguese: Galanga Maior, Gengibre Do Laos,
Gengibre Tailandés

Russian: Al'piniia Galangal

Serbian: Aflidžan, Galanga, Galgan, Galgant, Kalgan,
Sundska Galanga

Slovak: Alpínia Galangová, Alpínia Liečivá, Galgán Lekársky, Galgán, Galgán Lekársky

Slovenian: Langvas

Spanish: Calanga, Garengal, Galanga, Galanga Grande, Galanga Mayor, Jengibre de Siam

Swedish: Galangarot, Oäkta galangal, Siamingefära, Stor galangarot

Thai: Dok kha, Ginza, Khaa; Khaa-ling

Tibetan: Sga-Skya

Turkish: Büyük havlıcan, Galanga, Havlıcan

Vietnamese: Cao Lương Khương, Cao Khương Hương, Hồng Dầu Khâu, Một Loại Gừng, Riềng ầm, Riềng Nếp, Sown Nai

Origin/Distribution

Wild distribution of *A. galanga* occurs from India, to Southeast Asia (Indonesia, Malaysia, Myanmar, Thailand, Laos and Vietnam) to Southern China (Fujian, Guangdong, Guangxi, Hainan, Yunnan) and Taiwan.

Agroecology

A shade-loving tropical plant. Its natural habitat is in forests, scrub or grasslands, from 100 to 1300 m altitude. Widely cultivated and prefers a rich, well-drained soil high in organic matter and grows well in shade or partial shade. It cannot tolerate waterlogged soils or drought.

Edible Plant Parts and Uses

Galangal rhizome is extensively used as spice. The rhizome is a common ingredient in soups and curries and is used fresh, frozen, dried or in powder form. The fresh rhizome of *A. galanga* has a characteristic fragrance as well as pungency; hence, its rhizome is used as an essential component in Thai curry paste (Prakatthagomol et al. 2011). Fresh galanga has a

pure and refreshing odour and a mildly spicy flavour; it is the galanga of choice for all Thai foods. The rhizome is a common ingredient in Thai soups like *Tom yam*, *Tom Khaa* and Thai, Malaysian and Indonesian curries, where it is used fresh in chunks or thin slices, mashed and mixed into curry paste, or dried and powdered. The spice is commonly used in Indonesian fried rice, *Nasi Goreng*. Malaysian and Indonesian beef *rendang* is usually spiced with galangal. There are many different recipes of *rendang*. Essentially *rendang* comprises chunks of beef cooked in thick coconut milk together with dried chillies, garlic, turmeric, ginger, salam leaves (*Syzygium polyanthum*) and galangal. Some recipes used these together with cinnamon, black pepper and even fennel (*adas*). Galangal is used as flavouring in bean curd in Java and also used in sauces. Essential oil from the rhizome is used to flavour ice cream, alcoholic drinks, liqueurs, cakes and pastries. In Russia and India, it is used as a flavouring for beverages and spirit including *nastoika*, a liquor in Russia (Burkill 1966). Flower buds, leaves and young shoots are also eaten as spice or vegetable. Fruits occasionally used as substitute for cardamom.

Botany

Alpinia galanga is a vigorous, tillering perennial herb with tuberous underground, much-branched rhizome (Plate 1). Rhizomes are subterete, 3–5 cm in diameter, fibrous, hard, shiny pink, greenish, red or pale yellow and aromatic (Plates 3, 4, 5, and 6). Pseudostems erect formed by the rolled leaf sheaths (Plates 2, 3, and 4). Leaves alternate in two rows with suborbicular ligule and 1 cm long hairy petiole. Leaf blade is oblong lanceolate, 25–60 long by 6–15 cm wide, glabrous or abaxially pubescent, base attenuate, apex acute or acuminate (Plate 1). Panicles terminal may be flowered racemes ca. 20 × 30 cm in size; is rachis glabrous or pubescent; with many branches, 2–4 cm, 2–6-flowered; bracts and bracteoles persistent; and bracteoles lanceolate, 5–8 mm. Flowers are yellowish-white to greenish-white (Plate 7) and fragrant with tubular calyx and corolla. Labellum is white with red lines, obovate-spatulate, with a deeply bi-cleft apex and purple

subulate or linear lateral staminodes at the base of the labellum. Stamen is single and erect with incurved anther. Capsule is globose to ellipsoid, 1–1.5 cm by 0.7 cm, green turning to orange brown or red (Plates 8 and 9), with 3–6 seeds.



Plate 1 Cluster of tillering galangal plants



Plate 2 Bases of pseudostems



Plate 3 Pseudostems with attached *red* rhizomes



Plate 4 Harvested pseudostems with attached white rhizomes



Plate 5 White, pink, red galangal rhizomes



Plate 6 Close-up of white and green coloured rhizomes



Plate 7 Galangal inflorescence



Plate 8 Green galangal fruits



Plate 9 Ripe orange galangal fruits

Nutritive/Medicinal Properties

Rhizome Nutrients/Phytochemicals

Nutrient composition of the raw rhizome per 100 g edible portion was reported as energy 51 cal, moisture 85.9 g, protein 1.0 g, fat 0.4 g, total carbohydrates 11.7 g, dietary fibre 3.1 g, ash 1.1 g, Ca 31 mg, P 25 mg, Fe 2.1 mg, β -carotene equivalent 1520 μ g, thiamin 0.05 mg, riboflavin 0.02 mg, niacin 1.1 mg, and ascorbic acid 26 mg (Leung et al. 1972).

Another nutritive composition of *K. galanga* rhizomes was determined as energy 348.9 cal/100 g, moisture 12.5 %, crude protein 4.44 %, carbohydrate 78.9 %, crude fat 1.14 %, crude fibre 18.6 %, ash 3.04 %, K 1525 ppm, Ca 348.3 ppm, Na 31.80 ppm, Mg 968.0 ppm, Fe 17.23 ppm, Mn 12.44 ppm, Zn 6.038 ppm, Cu 0.485 ppm, Ni 0.328 ppm and Cr 0.283 ppm (Indrayan et al. 2009). Tee et al. (1997) reported the nutrient composition of edible portion per 100 g of galangal as energy

13 kcal, water 0.6 g, protein 1 g, fat 0.2 g, carbohydrate 1.6 g, fibre 0.4 g, ash 0.1 g, Ca 7 mg, P 15 mg, Fe 0.6 mg, Na 2 mg, K 30 mg, carotenes 4 µg, vitamin A 1 µg RE, vitamin B1 0.01 mg, vitamin B2 0.01 mg and niacin 4.4 mg. Mineral composition in the rhizomes (g/100 g) was reported by Kasarkar and Kulkarni (2012) as N 0.44 g, NO³⁻ 0.045 g, P 0.10 g, K 0.17 g, Ca 0.85 g, S 0.15 g, Na 0.9 g, Zn 0.27 g, Fe 8.43 g, Cu 0.15 g, Mo 0.0055 g, B 0.19 g, Mg 0.22 g and Mn 1.0 g.

Total arsenic contents (dry weight basis) in six edible Zingiberaceous rhizomes, namely, *Alpinia galanga* (Khaa), *Boesenbergia rotunda* (Kra-chaai), *Curcuma longa* (Khamin-chan), *Curcuma zedoaria* (Khamin-oi), *Zingiber cassumunar* (Plai) and *Zingiber officinale* (Ginger) were found to be 92.4, 103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively (Ubonnuch et al. 2013). Total inorganic arsenic are 92.4, 103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively. All investigated amounts of total and inorganic arsenic were much lower than limits recommended by Thai Food and Drug Administration.

From the rhizomes, the following compounds were isolated: *p*-hydroxycinnamaldehyde and [di-(*p*-hydroxy-*cis*-styryl)] methane (Barik et al. 1987); *trans-p*-coumaryl diacetate; *trans-coniferyl* diacetate; [1'*S*]-1'-acetoxychavicol acetate; [1'*S*]-1'-acetoxyeugenol acetate and 4-hydroxybenzaldehyde (Noro et al. 1988); the diterpene (*E*)-8β, 17-epoxylabd-12-ene-15, 16-dial (Haraguchi et al. 1996); (1'*S*)-1'-acetoxychavicol acetate and two related compounds acetoxyl-1-(2-acetoxylphenyl)-2-propene and (±)-1-acetoxyl-1-(4-acetoxylphenyl)-3-butene (Ando et al. 2005); 1'-acetoxychavicol acetate (Latha et al. 2009); galangogalloside (Jaju et al. 2009a); a flavonoid ganlangoflavonoside (Jaju et al. 2009b); a steroidal glycone, β-sitosterol diglucosyl caprate with the structure β-sitosterol-3-β-D-glucopyranosyl (2 → 1'')-β-D-glucopyranosyl 6''-*N*-decanoate (Jaju et al. 2010); methyl eugenol, *p*-coumaryl diacetate, 1'-acetoxychavicol acetate, 1'-acetoxyeugenol acetate, *trans-p*-acetoxycinnamyl alcohol, *trans*-3,4-dimethoxycinnamyl alcohol, *p*-hydroxybenzaldehyde, *p*-hydroxycinnamaldehyde, *trans-p*-

coumaryl alcohol, galangin, *trans-p*-coumaric acid and galanganol B (Kaur et al. 2010); tannins, coumarins, flavonoids, sterols, glycosides and 5-(hydroxymethyl) furfural (Iyer et al. 2013).

From the 80 % aqueous acetone rhizome extract, three 8–9' linked neolignans, galanganal (0.0048 %), galanganols A (0.0011 %) and B (0.0010 %), and a sesquineolignan, galanganol C (0.0015 %), were isolated together with *p*-hydroxybenzaldehyde (0.0047 %) and nine known phenylpropanoids 1'*S*-1'-acetoxychavicol acetate (1.10 %), 1'*S*-1'-acetoxyeugenol acetate (0.038 %), 1'*S*-1'-hydroxychavicol acetate (0.048 %), chavicol β-*D*-glucopyranoside (0.023 %), methyl eugenol (0.0006 %), *trans-p*-hydroxycinnamaldehyde (0.028 %), *trans-p*-coumaryl alcohol (0.052 %), *trans-p*-hydroxycinnamyl acetate (0.021 %), and *trans-p*-coumaryl diacetate (0.015 %) (Morikawa et al. 2005). A new phenylpropanoid was isolated from galangal rhizome, and its structure was established as 4, 4'[(2*E*, 2'*E*)-*bis*(prop-2-ene)-1, 1'-oxy]-diphenyl-7, 7'-diacetata (Zhu et al. 2009). The major constituents identified in *Alpinia galanga* rhizomes were 5-hydroxymethyl furfural (59.9 %), 9-octadecenoic acid (6.45 %), 2,3-dihydro-3, 5-dihydroxy-6-methyl-4*H*-pyran-4-one (7.44 %) and hexadecanoic acid (5.5 %) (Rao et al. 2010). Other constituents identified included furfuraldehyde (4.95 %), carotol (2.50 %), methyl cinnamate (1.26 %), 1,2 benzenedicarboxylic acid (1.44 %) and 1,8-cineole (1.96 %). Two compounds, (*E*)-*p*-acetoxycinnamyl alcohol and (*E*)-*p*-coumaryl alcohol ethyl ether, were identified in the rhizome hexane extract (Sukhirun et al. 2011). Six phenylpropanoids were obtained from galangal rhizome, and their structures were identified as (*S*)-1'-ethoxy chavicol acetate, (*E*)-4-acetoxy cinnamyl ethyl ether, (*E*)-4-hydroxycinnamaldehyde, (*E*)-4-acetoxy cinnamyl alcohol, 4-acetoxy cinnamyl acetate and 4, 4'[(2*E*, 2'*E*)-*bis*(prop-2-ene)-1, 1'-oxy]-diphenyl-7, 7'-diacetate (Zhao et al. 2012). Nine phenylpropanoids, (1'*S*)-1'-acetoxychavicol acetate, *p*-coumaryl diacetate, (1'*S*)-1'-acetoxyeugenol acetate, *trans-p*-coumaryl alcohol (4), *p*-hydroxybenzaldehyde, 1'*S*-1'-hydroxychavicol acetate, *p*-methyl benzaldehyde, and *trans-p*-hydroxycinnamyl acetate,

were isolated from galangal rhizome extract (Chourasiya et al. 2013).

Composition of essential oil steam distillation of fresh, finely comminuted rhizomes was prepared in low yield 0.04–0.15%, and the major components were α -pinene, 1,8-cineole, bornyl acetate, geranyl acetate, α -bergamotene, *trans* β -farnesene and β -bisabolene in relative equal proportions and mostly imparting camphoraceous, floral, fruit or spicy notes to the aroma (De Pooter et al. 1985). The composition of essential oil of fresh rhizome extraction of steam distillate with dichloromethane (yield 0.4 %) were 1,8-cineole 58.5 %, *trans*- β -farnesene 8.1 %, β -bisabolene 3.9 %, β -sesquiphellandrene 3.2 %, methyl eugenol 3.6 %, eugenyl acetate 2.3 %, 4-terpineol 2.2 %, geranyl acetate 1.4 %, α -bergamotene 1.7 %. Other compounds <1 % included 2-methylpropyl acetate, butyl acetate, α -pinene, β -pinene, *p*-cymene, γ -terpinene, linalool, borneol, borneol acetate, citronellyl acetate, β -caryophyllene, *ar*-curcemenene; compounds in traces included: camphene, sabinene, terpinolene, carveol I, carveol II, chavicol, neryl acetate and branched C-hydrocarbon. The components of *A. galanga* rhizome essential oil included borneol, bornyl acetate, camphene, cineole, *p*-cymene, geranyl acetate, limonene, linalool, α -pinene, β -pinene, sabinene, γ -terpinene, α -terpineol, terpinolene, 3-carene, citronellol, α -fenchone, α -fenchol, geraniol, geranial, isoborneol, *p*-menth-2-en-1-ol, myrcene, β -ocimene, α -phellandrene, β -phellandrene, sabinene hydrate, α -terpinene, α -thujene and β -thujone (Scheffer et al. 1981). From the rhizome essential oil, terpinen-4-ol, and from the *N*-pentane/diethyl ether extract of dried rhizomes, 1'-acetoxychavicol acetate, 1'-acetoxyeugenol acetate and 1'-hydroxychavicol acetate were identified (Janssen and Scheffer 1985).

Twelve compounds were characterised in the oil obtained from the rhizome and leaves of *Alpinia galanga* (Charles et al. 1992). The major compound in the rhizome oil was myrcene (94.51 %). The main constituents identified in galangal rhizome oil were 1,8-cineole (39.4 %) and β -pinene (11.9 %) (Raina et al. 2002). Galangal rhizome oils from Bangalore and Hyderabad respectively contained limonene (3.7 % and 3.5

%), 1,8-cineole (33.0 % and 30.2 %), camphor (5.0 % and 14.0 %), α -terpineol (9.3 % and 2.3 %), α -fenchyl acetate (12.7 % and 1.1 %) and (E)-methyl cinnamate (5.3 % and 2.6 %) as the major constituents (Mallavarapu et al. 2002). The main constituents of galangal rhizome essential oil are 8-cineole (28.4 %), α -fenchyl acetate (18.4 %), camphor (7.7 %), (E)-methyl cinnamate (4.2 %) and guaialol (3.3 %), α -terpineol (2.58 %), camphene (2.55 %), borneol (2.48 %), α -fenchol (2.21 %) (Jirovetz et al. 2003). Other minor compounds included ethyl acetate, hexanol, tricyclene, α -pinene, fenchene, 1-octen-3-ol, sabinene, β -pinene, myrcene, α -terpinene, *p*-cymene, limonene, β -phellandrene, benzyl alcohol, (Z)- β -ocimene, (E)- β -ocimene, γ -terpinene, *trans*-sabinene hydrate, *cis*-linalool oxide, *trans*-linalool oxide, fenchone, α -*p*-dimethyl styrene, terpinolene, linalool, *cis*-sabinene hydrate, β -fenchol, nonanal, *cis*-*p*-menth-2-en-1-ol, β -thujone, *trans*-pinocarveol, β -terpineol, isoborneol, isopulegol, β -terpineol, isoborneol, isopulegol, *p*-cymen-8-ol, terpinene-4-ol, myrtenal, verbenone, *trans*-carveol, *cis*-carveol, carvone, pulegone, geraniol, linalyl acetate, *cis*-sabinyl acetate, 2-hydroxy-1,8-cineole, isobornyl acetate, bornyl acetate, terpinen-4-yl acetate, myrtenol, pinocarvone, (Z)-methyl cinnamate, eugenol, α -cubebene, α -copaene, β -patchoulene, β -bourbonene, β -elemene, α -gurjunene, α -bergamotene, (Z)- β -farnesene, α -guaiene, alloaromadendrene, α -humulene, germacrene D, β -selinene, viridiflorene, γ -muurolene, valencene, α -muurolene, α -selinene, γ -elemene, β -bisabolene, γ -cadinene, D-cadinene, elemol, (E)-nerolidol, β -chamigrene, carotol, spathulenol, caryophyllene oxide, globulol, ledol, viridiflorol, cubenol, γ -eudesmol, τ -cadinol, τ -muurolol, α -cadinol, β -eudesmol, α -bisabolol, β -bisabolol, α -eudesmol, (Z)- α -bergamotol, (Z,E)-farnesol, (E,E)-farnesol and nootketone.

The hydro-distilled volatile oil from *A. galanga* rhizome was found to contain 11 components of which 10 constituents, comprising 98.5 %, were identified (Akhtar et al. 2004). The most abundant class of compounds were 4 monoterpenes comprising about 74 % of the total volatiles. The predominant monoterpene was 1,8-cineole (57 %) followed by geranyl acetate (10.2 %), citronellyl acetate (3.4 %) and linalool (3.1

α -terpinolene 0.44 %, 1-undecene 0.20 %, (–)-borneol 0.72 %, *p*-cymen-8-ol 3.06 %, α -terpineol 0.20 %, *Z*-citral 1.23 %, (–)-bornyl acetate 0.39 %, piperitenone 33.31 %, α -cubebene 0.15 %, decanoic acid 1.31 %, β -elemene 1.91 %, α -gurjunene 0.20 %, *trans*- β -caryophyllene 3.38 %, *trans*- β -farnesene 0.42 %, β -selinene 0.46 %, δ -selinene 0.31 %, pentadecane 5.62 %, α -amorphene 3.01 %, 7-*epi*- α -selinene 0.83 %, *trans*- γ -bisabolene 2.25 %, α -cadinol 0.61 %, γ -selinene 0.40 %, β -bisabolene 0.84 %, apiol 0.65 % and α -*trans*-bergamotol 0.30 % (Prakatthagomol et al. 2011). Five major constituents were identified in galangal rhizome oil, 1,8-cineole, phenol 4-(2-propenyl)-acetate, DL-limonene, α -pinene and α -terpineol (Tadtong et al. 2014).

Sixteen oxygenated aroma compounds were identified in galangal, and among them 1'-acetoxychavicol acetate was identified as an aroma constituent of galanga (Mori et al. 1995). It appeared that the high proportion of 1,8-cineol and other phenolic compounds of galanga had a great influence on the difference of the aroma quality from ginger. Five compounds, 1,8-cineol (49.56 %, cool camphoraceous), linalool (0.29 %, floral), geranyl acetate (0.68 % sour, floral), eugenol (0.2 %, clove-like), chavicol acetate (1.51, cool, mint-like), were determined as the potent odorants of galanga. In addition, acetic acid (1.78 %, sour), bornyl acetate (0.155 %, pine-like), citronellyl acetate (0.15 %, floral, rosy), 2-acetoxy-1,8-cineol (1.77 %, earthy, musty) and the isomer (17.26 %, woody, musty), methyl eugenol (0.56 %, floral fruity) and 1'-acetoxychavicol acetate (13.97 %, cool, earthy), chavicol (2.74 %, camphoraceous), 4-terpineol (1.18 %, lemon-like) thymol acetate (0.34 %, camphoraceous) and α -terpineol (1.33 %, weakly odorous) were also selected as the following important components. Three hydroxy-1,8-cineole glucopyranosides (1*R*, 2*R*, 4*S*)-*trans*-2-hydroxy-1,8-cineole β -D-glucopyranoside, (1*S*, 2*S*, 4*R*)-*trans*-2-hydroxy-1,8-cineole β -D-glucopyranoside and (1*R*, 3*S*, 4*S*)-*trans*-3-hydroxy-1,8-cineole β -D-glucopyranoside, possible precursors of acetoxy-1,8-cineoles as unique aroma components, were isolated from galangal rhizomes (Someya et al. 2001). The pungent principal of galangal rhizomes was isolated and identified as 1'-acetoxychavicol acetate (galangal acetate) (Yang and Eilerman

1999). Galangal acetate was reported to elicit a unique pungent sensation, which was less intense than that of capsaicin and without a lingering effect and were found to have various applications in beverages, sweet goods, dressings and personal care products where galangal acetate was preferred to other pungent ingredients. It could be used as an alcohol enhancer or an alcohol replacer in alcohol and alcohol-free beverages.

Forty-eight compounds, constituting about 89.4 % of the oil, were identified in *A. officinarum* oil, of which five were present in trace amount (<0.05 %) (Rana et al. 2010). The main compounds were 1,8-cineole (28.3 %), α -fenchyl acetate (15.2 %), carotol (8.9 %), α -terpineol (6.7 %), α -eudesmol (4.5 %), (*E*)-methyl cinnamate (4.0 %), camphor (3.4 %), β -pinene (3.1 %), camphene (2.3 %), borneol (1.7 %), α -pinene (1.2 %) and terpinen-4-ol (1.2 %), along with 31 minor (0.8–0.1 %) 2-heptanol; myrcene; α -phellandrene; α -terpinene; (*Z*)- β -ocimene; (*E*)- β -ocimene; γ -terpinene; *cis*-sabinene hydrate; linalool, α -fenchol; camphene hydrate; methyl thymol; methyl carvacrol; bornyl acetate; α -terpinyl acetate; β -elemene; β -caryophyllene; *trans*- α -bergamotene; valencene; α -humulene; (*E*)- β -farnesene; γ -cadinene; β -sesquiphellandrene; elemol; germacrene B; (*E*)-nerolidol; caryophyllene oxide; γ -eudesmol; β -eudesmol; α -bisabolol and hexadecanoic acid and five trace (<0.05 %) compounds tricyclene, α -thujene, *p*-cymene, limonene and linalyl acetate.

The main components of the essential oil of *A. galanga* rhizome were identified to be eucalyptol (22.63%), (1*S*)-(1)- β -pinene (14.36%), 1*R*- α -pinene (10.89%), α -terpineol 8.59 %) and L(-)-borneol (8.41 %) followed by (-)-camphor (4.21 %), camphene (4.14 %), 4-carvomenthenol (3.76 %); 2,4(8)-*p*-menthadiene (2.14 %), 1-bornyl acetate (1.29 %), (*Z*)-geraniol (1.13 %), 1, 2-isopropyltoluene (1.74 %), fenchol (1.72 %), γ -terpinene (1.15 %) and camphene hydrate (1.07 %) (Wu et al. 2014). Other minor components were β -terpinene; α -phellandrene; 1-methyl-3-(1'-methylcyclopropyl)cyclopentene; 2,2-dimethylheptane; undecane; linalool; 2-methyloctane; fenchene; myrtenol; (+)-sabinol; fenchyl acetate; citronellyl formate; benzylacetone; *p*-

menth-1-en-3-one; thymyl acetate; benzalacetone; nerol acetate; caryophyllene; α -caryophyllene; methyl isoeugenol; dihydro-*cis*- α -copaene-8-ol; aciphyllene; 2-methyl-decane; 3,7,1-trimethyl-3-hydroxy-6,10-dodecadien-1-yl-acetate; 1-methylene-2 β -hydroxymethyl-3,3-dimethyl-4 β -(3-methylbut-2-enyl)-cyclohexane; 2-(1,1-dimethylethyl)-6-(1-methylethyl)phenol; 1-formyl-2,2-dimethyl-3-*trans*-(3-methylbut-2-enyl)-6-methylidene-cyclohexane; methyltrans-2-phenyl-1-cyclopropanecarboxylate; bicyl[6.1.0]non-1-ene; 2-methyl-3-(3-methylbut-2-enyl)-2-(4-methyl-pent-3-enyl)-oxenane; bornylane; sycetalone; 3-ethyl-3-methyl-decane; 9-oxononanoic acid; and 2-(fench-2-yl)fenchane. Major compounds identified in the rhizome oils of *A. galanga* and *A. officinarum* were 1,8-cineole (63.4 and 44.2 %), α -terpineol (2.8 and 6.3 %), α -pinene (1.9 and 2.0 %), β -pinene (0.8 and 5.7 %) and terpinen-4-ol (2.8 and 4.5 %), respectively (Raina et al. 2014). Some additional compounds identified in *A. officinarum* oil were camphor (4.0 %) and α -fenchyl acetate (8.9 %), while chavicol (0.9 %), (*E*)- β -farnesene (8.4 %), β -sesquiphellandrene (2.6 %), β -bisabolene (0.3 %) and eugenol acetate (3.3 %) were present in *A. galanga* oil.

Ethyl *trans*-cinnamate and ethyl 4-methoxy-*trans*-cinnamate were isolated from galangal root oil (Zheng et al. 1993). Galangal root oil (I) was found to have fenchyl acetate (30.5 %) along with 1,8 cineole and limonene (Menon 2006). The root essential oil contained α -fenchyl acetate (40.9 %), 1,8-cineole (9.44 %), borneol (6.3 %), bornyl acetate (5.4 %) and elemol (3.1 %), α -fenchol (2.8 %), carotol (2.64 %), camphene (2.43 %), myrcene (1.8 %), terpinen-4-ol (1.25 %), camphor (1.24 %), guaialol (1.16 %), *p*-cymene (1.1 %), valencene (1.07 %) and spathulenol (1.07 %) and other compounds were < 1 % (Jirovetz et al. 2003). The major constituent identified in *Alpinia galanga* roots was benzyl alcohol (57.67 %) (Rao et al. 2010). Other constituents identified included hexadecanoic acid (4.79 %), 9-octadecenoic acid (3.77 %), carotal (2.83 %), 1,2-benzene dicarboxylic acid (2.36 %), β -fenchyl acetate (1.70 %) and 5-tetradecene (1.14 %). *Alpinia galanga* rich in bioactive compounds was genetically transformed using different strains of *Agrobacterium rhizogenes*, viz., LBA 9402, A(4), 532,

2364 and PRTGus (Rao et al. 2012). Even though a higher growth rate was obtained with the LBA 9402 strain, maximum acetoxychavicol acetate accumulation (ACA) was seen in the PRTGus transformant. PRTGus root line present 10.1-fold higher ACA content in comparison to the control roots. The lowest ACA production was shown by the A(4) transformant (4.9 fold). The quantification of ACA in the transformed roots was found to be in the order of PRTGus > LBA 9402 > 2364 > 532 > A(4).

Four isomers of acetoxycineoles, *trans*-2-acetoxy-1,8-cineole; *cis*-2-acetoxy-1,8-cineole; *trans*-3-acetoxy-1,8-cineole; and *cis*-3-acetoxy-1,8-cineole, were identified as the odorous components of the rhizomes of greater galangal (Kubota et al. 1998). The concentration of *trans*-3-acetoxy-1,8-cineole was the highest among the isomers. The isomers presented individual odour features: the (*trans* and *cis*)-2 isomers respectively exhibited woody and sweet aromas, while the (*trans* and *cis*)-3 isomers respectively showed sweet floral and camphoraceous aromas. Of these, *trans*-2-acetoxy-1,8-cineole seemed to have the strongest qualitative effect on the characteristic flavour of greater galangal. (*S*)-(+)-*O*-methylmandelate esters of *trans*- and *cis*-1,3,3-trimethyl-2-oxabicyclo[2.2.2]octan-5- and 6-ols (2- and 3-hydroxy-1,8-cineoles) of *A. galanga* rhizomes were prepared, and eight diastereomers were separated (Kubota et al. 1999b). The enantiomeric purity of *trans*- and *cis*-1,3,3-trimethyl-2-oxabicyclo[2.2.2]octan-5- and 6-yl acetates in the aroma concentrate from the rhizomes of *Alpinia galanga* was determined as 93.9 (5*S*), 19.4 (5*R*), 63.5 (6*R*) and 100 (6*R*) % *ee* (enantiomeric excess), respectively. I'-Acetoxychavicol acetate was present in the optically active 5-configuration in the essential oil of the rhizomes (Kubota et al. 1999a). Only the (*S*)-enantiomer possessed the characteristic cool, woody and ginger-like odour, in contrast of no odour of the (*R*)-enantiomer which played an important role in the odour of the fresh rhizomes, because this compound was degraded during cooking. Among the eight isomers of acetoxyl,8-cineoles, (1*R*, 4*S*, 6*R*)- 1,3,3-trimethyl-2-oxabicyclo[2,2,2]oct-6-yl acetate (*trans*-2-acetoxyl,8-cineole) which presented a woody and

galanga-like odour was the most important odour constituent in the rhizomes of greater galangal.

Yang et al. (2009) reported the isolation of dihydrogalangal acetate in galangal roots. This compound had a taste sensation similar to galangal acetate, the pungent principle of galangal but was more stable in food and beverage applications. Dihydrogalangal acetate was reported to provide many advantages as a flavour ingredient for alcohol enhancement and taste modification. Dihydrogalangal acetate was present in approximately 0.0005 % of fresh roots and in about 0.004 % of dried roots. (*S*)-Dihydrogalangal acetate was found as the main optical isomer in galangal roots (98 %), while its minor (*R*)-isomer was less abundant (2 %). (*R*)-Galangal acetate had a very faint woody and sweet aroma, and (*R*)-dihydrogalangal acetate was almost odourless, while (*S*)-galangal acetate had strong and (*S*)-dihydrogalangal acetate had weak pungent and woody notes.

Seed Phytochemicals

Two potent antiulcer principles, 1'-acetoxychavicol acetate and 1'-acetoxyeugenol acetate, three sesquiterpenes, caryophyllene oxide, caryophyllenol-I and caryophyllenol-II, along with *n*-pentadecane, *n*-7-heptadecene, *p*-hydroxybenzaldehyde, 4-acetoxy-3-methoxy- α -vinylbenzyl alcohol and fatty acid methyl esters, *p*-propyl-phenol acetate, DL-1-acetoxychavicol acetate, vanillin acetate and DL-1'-acetoxyeugenol acetate were isolated from galangal seeds (Mitsui et al. 1976). Two skeletal diterpenes galanal A, galanal B and a new labdane-type diterpene with spectral data identical to labda8(17),12-diene-15,16-dial and (*E*)-8,17-epoxylabd-12-ene-15,16-dial were isolated from galangal seeds (Morita and Itokawa 1986). Two skeletal diterpenes, named galanal A and B, and two new labdane-type diterpenes, named galanolactone and (*E*)-8(17),12-labddiene-15,16-dial, were isolated from *Alpinia galanga* seeds together with (*E*)-8 β (17)-epoxylabd-12-ene-15,16-dial (Morita and Itokawa 1988). From galangal seeds, three new norsesterpenoid racemic mixtures, galanols A–C were isolated, along with three known sesquiterpenoids, namely, (1*S*,6*S*)-1 α -hydroxy-bisabol-2,10-diene-14-al, 1 β -

hydroxyeudesma-4,11-dien-3-one and 15-hydroxybisabolene-1-one (Bian et al. 2014a). Ten flavonoids were isolated from the 95 % ethanol seed extract of *Alpinia galanga* and elucidated as (2*R*, 3*S*)-pinobaksin-3-cinnamate, (2*R*, 3*R*)-pinobaksin-3-cinnamate, pinocembrin, pinobaksin, 3-*O*-acetylpinobaksin, galangin, galangin-3-methylether, kumatakenin, 3-methylkaempferol and (2*R*, 3*R*)-3, 5-dihydroxy-7-methoxyflavanone (Bian et al. 2014b).

Leaf Phytochemicals

Mineral composition in the leaves (g/100 g) was reported by Kasarkar and Kulkarni (2012) as N 0.56 g, NO³⁻ 0.046 g, P 0.11 g, K 0.18 g, Ca 0.70 g, S 0.13 g, Na 1.3 g, Zn 0.82 g, Fe 9.81 g, Cu 0.78 g, Mo 0.0059 g, B 0.14 g, Mg 0.18 g and Mn 8.53 g. The major constituents identified in *Alpinia galanga* leaves were 1,8-cineole (15.65 %), methyl cinnamate (9.42 %), 1,2 benzenedicarboxylic acid (8.93 %), 2,6,10-trimethyl, 14-ethylene-14-pentadecene (8.64 %) and 3-phenyl-2-butanone (8.5 %) (Rao et al. 2010). Other constituents identified included γ -cadinene (6.60 %), 3-phenylpropionaldehyde (5.24 %), benzenemethanol (4.67 %), neophytadiene (3.75 %), hexadecanoic acid (3.69 %) and hexahydrofarnesyl acetone (2.35 %). 1,8-Cineole, α -terpineol, (*E*)-methyl cinnamate, camphor, terpinen-4-ol, and α -pinene and β -pinene were the major constituents commonly distributed in leaf and flower essential oils (Padalia et al. 2010).

Twelve compounds were characterised in the oil obtained from the rhizome and leaves of *Alpinia galanga* (Charles et al. 1992). The major compound in the leaf oil was myrcene 52.34 %. The major constituents of the leaf oils from Bangalore and Hyderabad were respectively α -pinene (6.6 % and 6.3 %), camphene (5.0 % and 5.1 %), β -pinene (21.5 % and 23.5 %), 1,8-cineole (34.4 % and 30.7 %) and camphor (7.8 % and 12.8 %) (Mallavarapu et al. 2002). Galangal leaf oil contained 1,8-cineole (32.5 %), β -pinene (22.7 %) and camphor (12.8 %), as major constituents (Raina et al. 2002). The essential oil of *A. galanga* leaves from India was found to be rich in 1,8-cineole (28.34 %), camphor (15.6 %), β -pinene (5.0 %), β -pinene

(4.97 %), (*E*)-methyl cinnamate (4.63 %), bornyl acetate (4.3 %), *trans*-pinocarveol (3.37 %), guaiol (3.5 %), camphene (2.75 %), myrtenal (2.18 %) and myrtenol (2.05 %) (Jirovetz et al. 2003). Other compounds included (*E*)-2-hexenal, (*E*)-2-hexenol, hexanol, methyl isobutyl ketone, α -thujene, tricyclene, α -pinene, fenchene, sabinene, myrcene, α -phellandrene, δ -3-carene, *p*-cymene, limonene, β -phellandrene, (*Z*)- β -ocimene, (*E*)- β -ocimene, γ -terpinene, *trans*-sabinene hydrate, *cis*-linalool oxide, *trans*-linalool oxide, fenchone, α -*p*-dimethyl styrene, terpinolene, linalool, *cis*-sabinene hydrate, α -fenchol, *cis*-*p*-menth-2-en-1-ol, β -thujone, β -terpineol, isoborneol, isopulegol, borneol, *p*-cymen-8-ol, terpinen-4-ol, α -terpineol, verbenone, *trans*-carveol, α -fenchyl acetate, *cis*-carveol, carvone, pulegone, geraniol, linalyl acetate, isopulegyl acetate, *cis*-sabinyl acetate, 2-hydroxy-1,8-cineole, isobornyl acetate, terpinen-4-yl acetate, pinocarvone, (*Z*)-methyl cinnamate, eugenol, α -cubebene, α -copaene, β -patchoulene, β -bourbonene, β -elemene, α -gurjunene, α -bergamotene, (*Z*)- β -farnesene, (*E*)- β -farnesene, α -guaiane, alloaromadendrene, α -humulene, germacrene D, *ar*-curcumene, viridiflorene, γ -muurolene, valencene, γ -elemene, β -bisabolene, γ -cadinene, δ -cadinene, elemol, (*E*)-nerolidol, β -chamigrene, carotol, spathulenol, caryophyllene oxide, globulol, ledol, viridiflorol, cubenol, γ -eudesmol, τ -cadinol, τ -muurolol, α -cadinol, β -eudesmol, α -bisabolol, β -bisabolol, α -eudesmol, (*Z*)- α -bergamotol, (*Z,E*)-farnesol, (*E,E*)-farnesol and nootkatone. The major constituents of galangal leaf oils were fenchyl acetate (20.7 % leaf oil-I) and β -caryophyllene (40.5 % leaf oil-II) along with β -farnesene, caryophyllene oxide and 1,8-cineole (Menon 2006).

Stem Phytochemicals

The stem essential oil contained 1,8-cineole (31.12 %), camphor (11.0 %), (*E*)-methyl cinnamate (7.44 %), guaiol (4.9 %), bornyl acetate (3.63 %) and β -pinene (3.29 %), and

α -terpineol (3.26 %), carotol (2.84 %), *trans*-pinocarveol (2.26 %), elemol (1.94 %), myrtenal (1.76 %), 2-hydroxy-1,8-cineol (1.35 %), β -elemene (1.69 %), β -caryophyllene (1.665), camphene (1.61 %), myrtenol (1.53 %), nootkatone (1.35 %),

α -copaene (1.02 %), borneol (1.0 %) and other compounds were < 1 % (Jirovetz et al. 2003). The main constituent of galangal stem oil (I) was cubenol (28.4 %) followed by humulene (5.1 %), germacrene (4.9 %) and cadinene (2.5 %) (Menon 2006).

Plant Phytochemicals

Alpinia galanga was reported to contain, among other components, essential oils, tannins, phenol, glycosides, monoterpenes and carbohydrates (Kaushik et al. 2011). In the last few years, new compounds such as gallic acid glycoside, galangoisoflavonoid, β -sitosterol, galangin, alpinin, zerumbone and kampferide had been isolated from various parts of *A. galanga*.

Rapid direct regeneration was obtained from the rhizome explants (15.66 shoots) on MS media supplemented with zeatin at a concentration of 2 mg/l (Rao et al. 2011). The callus cultures of *A. galanga* were initiated from the rhizome explants on MS media supplemented with 2 mg/l each of BAP, 2,4-D and NAA. The regenerated (indirect) plants presented 1.6-fold higher acetoxychavicol acetate (ACA) content (1.253 %) when compared to the control plant (0.783 %).

Antioxidant Activity

Alpinia galanga extracts showed higher antioxidative stability at neutral than at acidic pH ranges (Juntachote and Berghofer 2005). Galangal extracts exhibited strong superoxide anion scavenging activity, Fe^{2+} chelating activity and reducing power in a concentration-dependent manner. Antioxidant activity of the extracts correlated well with reducing power. Furthermore, ethanolic extracts of galangal acted as radical scavenger and also as lipoxygenase inhibitor. The ethanolic extracts galangal showed good heat stability (80 °C, 1 h). The rhizome was reported to have antioxidant index 3.24 as evaluated by β -carotene bleaching method and to contain 7.87 mg% vitamin C, 0.0042 mg% vitamin E, 0.64 mg% total carotenes, 1.05 mg% total xanthophylls, 17.7 mg% tannins and 63.4 mg/% phenolics (Chanwitheesuk et al. 2005). The

ethanolic galangal extract showed the highest DPPH free radical scavenging ability as well as the highest ORAC value when compared to the water extract and the essential oil (Mahae and Chaiseri 2009). The IC₅₀ values of the galangal ethanolic extract (10.66 mg/ml), water extract (55.48 mg/ml) and essential oil (455.43 mg/ml) were higher than those of α -tocopherol (1.45 mg/ml) and butylated hydroxyanisole (BHA; 0.41 mg/ml). The results indicated that the antioxidant activities of galangal extracts were lower than that of BHA, the commercial synthetic antioxidant generally used in food. The ethanolic extract contained the highest concentrations of total phenolic compounds (31.49 mg GAE/g) and flavonoids (13.78 mg CE/g). The water extract and the essential oil had a total phenolic content of 8.25 and 5.01 mg GAE/g and a total flavonoid content of 1.48 and 0.20 mg CE/g, respectively. Antioxidants in the galangal essential oil, namely, methyl eugenol (4130.38 μ g/g), chavicol (2390.45 μ g/g) and eugenol (728.30 μ g/g), were found in its volatile fraction. The water extract contained mainly myricetin (14.60 mg/g extract) and an unknown phenolic compound. The major antioxidants in the ethanolic extract were 1'-acetoxycavichol acetate (10.56 mg/g extract), catechin (1.74 mg/g extract) and three unknown substances. In addition to the phenolic compounds, 1'-acetoxycavichol acetate (ACA) could play an important role in the antioxidant activity of galangal.

Alpinia galanga leaf extract exhibited dramatic ferrous ion-chelating (FIC) activity which was more than 20 times higher than that of rhizomes (Chan et al. 2008). Leaves of *A. galanga* had total phenolic content (TPC) of 392 mg GAE/100 g and ascorbic acid equivalent antioxidant capacity (AEAC) of 90 mg AA/100 g and rhizome TPC of 214 mg GAE/100 g and AEAC of 168 mg AA/100 g (Chan et al. 2008). The percentage yield of methanolic extracts from leaves and rhizomes of *A. galanga* was 6.0 and 5.5 %, and the percentage yield of non-polymeric phenolic (NP) and polymeric tannin (PT) fractions from leaves and rhizomes of *A. galanga* was 74, 0.5, 66 and 6.0 % (Chan et al. 2011). In *A. galanga*, total phenol content (TPC) of leaves was significantly higher than that of rhizomes. However, AEAC (ascorbic acid equivalent antioxidant capacity) values were comparable. In *A. galanga*

leaves, TPC and AEAC of the NP fraction were comparable to those of the PT fraction. In rhizomes, values of the PT fraction were significantly higher than the NP fraction.

The antioxidant activity of galangal extract as evaluated by the β -carotene bleaching method was 70.3 % (Mayachiew and Devahastin 2008). The total phenolic contents of galangal extract as determined by the Folin–Ciocalteu method was 40.9 mg/g plant extract (in GAE). *A. galanga* showed better free radical scavenging activity against DPPH and ABTS⁺ radicals with an IC₅₀ value of 21.26 and 25.54 μ g/mL, respectively, than *A. calcarata* (56.51 and 62.35 μ g/mL, respectively) (Nampoothiri et al. 2015). The antioxidant activity of *A. galanga* may be due to higher amounts of phenolic compounds present in the extract; gallic acid and ellagic acid were the major phenolic compounds in both extracts.

Anticancer Activity

In-Vitro Studies

From *Alpinia galanga*, 1'-acetoxychavicol acetate and 1'-acetoxyeugenol acetate were isolated as antitumour principles against sarcoma 180 ascites in mice (Itokawa et al. 1987). 1'-acetoxychavicol acetate (ACA) treatment resulted in changes in morphology and a dose-dependent suppression of Ehrlich ascites tumour cell viability (Moffatt et al. 2000). Apoptosis, characterised by nuclear condensation, membrane blebbing, cell shrinkage and a significant induction of caspase-3-like protease activity at 8 h, was observed. Formation of apoptotic bodies was preceded by lowering of intracellular polyamines, particularly putrescine, and both dose- and time-dependent inhibitory and activation effect by ACA on ornithine decarboxylase (ODC) and spermidine/spermine N(1)-acetyltransferase (SSAT), respectively. The findings suggested that the anticarcinogenic effects of ACA might be partly due to disturbance of the polyamine metabolic pathway and triggering of caspase-3-like activity, which resulted in apoptosis. Further, they found that apoptosis of Ehrlich ascites tumour cells induced by 1'-acetoxychavicol acetate (ACA) was associated with protein tyrosine phosphorylation and

reduction of cellular sulfhydryl groups, the targets of ACA cytotoxicity in tumour cells (Moffatt et al. 2002). Xu et al. (2010) found correlations among a decrease in cell viability, intracellular glutathione (GSH) levels and the activity of glutathione reductase in Ehrlich ascites tumour cells treated with the various ACA analogues.

Mori et al. (2001) reported that 1'-acetoxychavicol acetate (ACA) induced apoptosis and inhibited cell proliferation of human colorectal cancer cells (Colo 320). Zheng et al. (2002) reported that 1'-acetoxychavicol acetate (ACA) exerted antiproliferative effects in human colorectal cancer cell lines by inducing apoptosis in a concentration- and time-dependent manner and a reduction replicating DNA synthesis.

Thai *Alpinia galanga* exhibited stronger cytotoxicity against two human cancer cell lines, COR L23 lung cancer cell line and MCF7 breast cancer cell line, and the non-cancer MCF5 cell line than Malaysian *A. galanga* samples (Lee and Houghton 2005). This was shown to be due to the relatively high amounts of 1'-acetoxychavicol acetate present in the Thai sample. 1'-acetoxychavicol acetate (48 h exposure against COR L23 cells, IC_{50} 7.8 μ M against MCF7 cells, IC_{50} 23.9 μ M) was isolated as the major cytotoxic component of the *Alpinia* species. Low-dose ACA dramatically inhibited cellular growth of NB4 promyelocytic leukemic cells by inducing apoptosis via a mitochondrial- and Fas-mediated dual mechanism (Ito et al. 2004). Ito et al. (2005a) found that 1'-acetoxychavicol acetate (ACA) induced apoptosis of myeloma cells via induction of TNF-related apoptosis-inducing ligand (TRAIL). Azuma et al. (2006) found that the essential moieties of 1'-acetoxychavicol acetate (ACA) for apoptotic activity against human leukaemia HL-60 cells were both the presence of a 4-acetoxyl group and an unsaturated double bond between C-2' and C-3' and that the configuration at the 1'-position is unrelated to activity. 1'-acetoxychavicol acetate (ACA) significantly decreased cell viability of human breast carcinoma-derived MCF-7 and MDA-MB-231 in a time- and dose-dependent manner, with effective concentrations 10–50 μ M (Campbell et al. 2007). Apoptosis was confirmed by morphological examination of cells. Unahara et al. (2007)

found that in Ehrlich ascites tumour cells, cell growth inhibition elicited by ACA involved decreases in Rb and p27(kip1) phosphorylation and an increase in nuclear localisation of p27(kip1) and these events were dependent on the cellular thiol status. Wang et al. (2013) reported that 1'-acetoxychavicol acetate (ACA) exhibited anticancer effects against human head and neck cancer HN4 cells through downregulation of miR-23a, which could repress tumour suppressor PTEN (phosphatase and tensin homolog) gene.

Treatment of RAW 264.7 cells, a murine monocytic cell line with RANKL (receptor activator of nuclear factor-kappaB (NF-kappaB) ligand) activated NF-kappaB, and coexposure of the cells to 1'-acetoxychavicol acetate (ACA) completely suppressed RANKL-induced NF-kappaB activation in a time- and concentration-dependent manner (Ichikawa et al. 2006). The suppression of NF-kappaB by ACA was mediated through suppression of RANKL-induced activation of IkappaBalpha kinase, IkappaBalpha phosphorylation and IkappaBalpha degradation. Additionally, incubation of monocytic cells with RANKL-induced osteoclastogenesis, and ACA suppressed it. Inhibition of osteoclastogenesis was maximal when cells were simultaneously exposed to ACA and RANKL and minimum when ACA was added 2 days after RANKL. ACA also inhibited the osteoclastogenesis induced by human breast cancer MCF-7 cells, multiple myeloma MM1 cells and head and neck squamous cell carcinoma LICR-LON-HN5 cells. The results indicated ACA to be an effective blocker of RANKL-induced NF-kappaB activation and of osteoclastogenesis induced by RANKL and tumour cells, suggesting its potential as a therapeutic agent for osteoporosis and cancer-associated bone loss.

The ethanolic extracts of *Curcuma longa* and *Alpinia galanga* were found to be toxic with LD₅₀ of 33 and 109 µg/ml, respectively, in the brine shrimp lethality bioassay (Khattak et al. 2005). In one study, six different human cell lines including normal and p53-inactive fibroblasts, normal epithelial and tumour mammary cells and a lung adenocarcinoma cell line displayed a broad range of cytotoxicity to the crude aqueous extract of galangal rhizome

(Muangnoi et al. 2007). It was found that p53-active cell lines may be more sensitive than their p53-inactive counterparts. The contribution of apoptosis to total cell mortality was only appreciable after exposure to 300 µg/mL of extract. Apoptosis appeared to be independent of p53 expression. Exposure to as little as 100 µg/mL galangal extract generated a significant level of DNA single-strand breaks. The three major UV-absorbing compounds in the aqueous extract were identified by mass spectrometry as 1'-acetoxychavicol acetate and its deacetylated derivatives. However, when tested in A549 human lung adenocarcinoma cells, these compounds were not responsible for the cytotoxicity induced by the complete aqueous extract. The ethanolic extract of *Alpinia galanga* inhibited growth in-vitro of prostate cancer PC-3 cell line (Suja and Chinnaswamy 2008). This was supported by DNA fragmentation where a characteristic DNA laddering was noticed in treated tumour cell line and not in the control.

4'-Hydroxycinnamaldehyde (4'-HCA) isolated from *A. galanga* rhizome was cytotoxic to human leukemic HL-60 and U937 cells by induction of apoptosis through a combination of mitochondrial and endoplasmic reticulum stress pathways (Banjerdpongchai et al. 2011). 4-Acetoxy cinnamyl acetate, a phenylpropanoid compound from galangal rhizome, exhibited selective cytotoxic activity against human lung adenocarcinoma cell A549 (IC₅₀ 19.35 µmol/L) (Zhao et al. 2012). The phenylpropanoids from galangal rhizome, *trans-p*-coumaryl alcohol and *trans-p*-hydroxycinnamyl acetate exhibited potent anticancer activity in-vitro against human cancer cell lines A549 (lung cancer), Colo-205 (colon cancer), A431 (skin cancer), NCI H460 (lung cancer), PC-3 (prostate cancer) and HT-29 (colon cancer) with IC₅₀ values ranging from 1.8 to 13.4 and 5.6 to 19.9 µg/ml respectively (Chourasiya et al. 2013). Ethanol galangal rhizome extract decreased cell viability of malignant human breast carcinoma cell line (MCF-7) in a concentration- and time- dependent manner (Samarghandian et al. 2014). The IC₅₀ values against MCF-7 were determined at 400 and 170 µg/ml after 48 and 72 h respectively. *Alpinia galanga* induced apoptosis in MCF-7 cells, as determined by flow cytometry.

In-Vivo Studies

Ethyl *trans*-cinnamate and ethyl 4-methoxy-*trans*-cinnamate from galanga root oil were found to have anticarcinogenic activity based on their capacity to induce the activity of the detoxifying enzyme, glutathione *S*-transferase (GST), in several tissues of female A/J mice (Zheng et al. 1993). Both compounds exhibited significant activity in the mouse liver and intestines. 1'-acetoxychavicol acetate (ACA) exerted an inhibitory effect on N-nitrosobis(2-oxopropyl)amine (BOP)-induced cholangiocarcinogenesis in Syrian hamsters (Miyachi et al. 2000). 1'-acetoxychavicol acetate (ACA) potently inhibited tumour promotion by 12-*O*-tetradecanoylphorbol-13-acetate (TPA) in ICR mouse skin (Murakami et al. 1996). Topical application of ACA (160 nmol) markedly reduced the average number of tumours per mouse and the ratio of tumour-bearing mice: inhibition ratios 90 % and 42 %, respectively. ACA potently inhibited TPA-induced superoxide (O₂⁻) generation in differentiated HL-60 cells (IC₅₀ = 4.3 µM) and suppressed the lipid hydroperoxide formation by 42 % in the ethyl linoleate autoxidation test. Incorporation of ACA in the CDAA (choline-deficient, L-amino acid-defined) diet of male Fischer 344 rats for 12 weeks prevented CDAA diet-associated induction of putative preneoplastic lesions in the liver by reduction of oxidative DNA damage but did not affect their subsequent growth (Kobayashi et al. 1998).

In-vivo studies showed that 1'-acetoxychavicol acetate (ACA) could inhibit the development of development of azoxymethane-induced colonic aberrant crypt foci in rats through its suppression of cell proliferation in the colonic mucosa, indicating that ACA might be a possible chemopreventive agent against colon tumourigenesis (Tanaka et al. 1997b). In another study, ACA inhibited the development of azoxymethane-induced colon tumourigenesis in rats through its suppression of cell proliferation in the colonic mucosa and its induction of glutathione *S*-transferase (GST) and quinone reductase (QR) in the liver and colon (Tanaka et al. 1997a). The results confirmed previous finding

that ACA feeding effectively suppressed the development of colonic aberrant crypt foci. Dietary feeding of 1'-acetoxychavicol acetate (ACA) (500 ppm) was effective in inhibiting the development of oesophageal tumours induced by N-nitrosomethylbenzylamine (NMBA) when given during the initiation or post-initiation phase, and such inhibition was related to suppression of cell proliferation in the oesophageal epithelium (Kawabata et al. 2000). ACA exerted an inhibitory effect on NF-kappaB and induced the apoptosis of myeloma cells in-vitro and in-vivo (Ito et al. 2005b). In myeloma cells, incubation with ACA induced G0-G1 phase cell cycle arrest, followed by apoptosis. In-vivo, ACA treatment of RPMI8226-transplanted NOD/SCID mice significantly reduced tumour weight. Azuma et al. (2011) found that incorporation of 1'-acetoxychavicol acetate (ACA) in water-soluble inclusion complexes with cyclodextrins improved the solubility and stability of ACA in water. One preparation of HP β -CD · ACA maintained high levels of antitumour activity in human epithelial carcinoma HeLa cells and murine adenocarcinoma colon26 cells. In addition, HP β -CD · ACA and Me β -CD · ACA showed suppressive effect for the transcription factor NF- κ B activation on LPS-activated murine macrophage RAW264.7 cells, and the former was the more active complex. Furthermore, HP β -CD · ACA inhibited the in-vivo tumour growth of tumour-bearing mice, although the activity was slightly weak compared with that of free ACA.

In a 2-week study in which wild-type (WT) and K5.Stat3C mice were co-treated with either vehicle, 1'-acetoxychavicol acetate (ACA), galanga extract or fluocinolone acetonide (FA) and tetradecanoyl phorbol acetate (TPA), only the galanga extract and FA suppressed TPA-induced skin hyperproliferation and wet weight (Clifford and Kleiner-Hancock 2012). None of these agents were effective at suppressing p-Tyr705Stat3 expression. However, ACA and FA showed promising inhibitory effects against skin tumourigenesis in K5.Stat3C mice. ACA also suppressed phospho-p65 NF- κ B activation.

Galangal extract suppressed tetradecanoyl phorbol acetate (TPA)-induced skin hyperproliferation and wet weight, while

ACA showed promising inhibitory effects against skin tumourigenesis in K5.Stat3C mice (Batra et al. 2012). ACA also suppressed phospho-p65 NF- κ B activation, suggesting a potential mechanism for its action. Pang et al. (2011) found that 1'-acetoxychavicol acetate (ACA) suppressed prostate tumour growth and angiogenesis by targeting vascular endothelial growth factor (VEGF)-mediated Src-FAK-Rho GTPase-signalling pathway. ACA suppressed vascular endothelial growth factor (VEGF)-induced proliferation, migration, adhesion and tubulogenesis of primary cultured human umbilical vascular endothelial cells (HUVECs) in a dose-dependent manner. Further, treatment of human prostate cancer cells (PC-3) with ACA resulted in decreased cell viability and suppression of angiogenic factor production by interference with dual Src/FAK kinases. After subcutaneous administration to mice bearing human prostate cancer PC-3 xenografts, ACA (6 mg/kg/day) markedly inhibited tumour volume and tumour weight and decreased levels of Src, CD31, VEGF and Ki-67. 1'-Acetoxychavicol acetate inhibited growth of human oral carcinoma xenograft in mice and potentiated cisplatin effect by downregulation of NF- κ B regulated gene (FasL and Bim), including pro-inflammatory (NF- κ B and COX-2) and proliferative (cyclin D1) biomarkers in tumour tissue (In et al. 2012).

Antiviral Activity

Galangal rhizome extract potently inhibited tumour promoter Epstein–Barr virus (EBV) activation, and the active inhibitor component was elucidated as 1'-acetoxychavicol acetate (Kondo et al. 1993). In-vitro studies found that upon esterase blockade in Raji cells, (1'*R,S*)-1'-acetoxychavicol acetate (ACA) from galangal rhizomes suppressed tumour promoter teleocidin B-4-induced Epstein–Barr virus (EBV) activation, suggesting that ACA bearing two acetoxyl groups is an intracellular structure prerequisite for activity exhibition (Murakami et al. 2000). Studies reported that 1'*S*-1'-acetoxychavicol acetate (ACA), a small molecular compound isolated from *Alpinia galanga* rhizomes at a low concentration, inhibited Rev, an HIV-1 viral regulatory

protein, transported by binding to chromosomal region maintenance 1 and accumulating full-length HIV-1 RNA in the nucleus, resulting in a block in HIV-1 replication in peripheral blood mononuclear cells (Ye and Li 2006). Additionally, ACA and didanosine acted synergistically to inhibit HIV-1 replication. Thus, 1'-S-1'-acetoxychavicol acetate may represent a novel treatment for HIV-1 infection, especially in combination with other anti-HIV drugs. 1'-acetoxychavicol acetate (ACA, 1) was isolated from *A. galanga* roots as a new inhibitor for nuclear export of Rev, an HIV-1 viral regulatory protein (Tamura et al. 2009). Crucial portions of the compound were established for Rev-export inhibitory activity. Four more potent and robust halogenated analogues of 1'-acetoxychavicol acetate (ACA), the Rev-export inhibitor from *Alpinia galanga*, were reported (Tamura et al. 2010). In particular, the difluoroanalog 20d exhibited approximately fourfold potent activity as compared with ACA. 1'-acetoxychavicol acetate (ACA) from *Alpinia galanga* was reported as potent inhibitors for the influenza virus replication (Watanabe et al. 2011). Six aqueous extracts from *Alpinia galanga*, *Alpinia oxyphylla*, *Celosia cristata*, *Houttuynia cordata*, *Ophioglossum vulgatum* and *Selaginella tamariscina* showed significant antiviral effects against bovine viral diarrhoea virus (BVDV), a flavivirus used here as a surrogate in-vitro model of hepatitis C virus, without toxic effects on host embryonic bovine trachea (EBTr) cells (Herrmann et al. 2011).

Antimicrobial Activity

The rhizomes also have antimicrobial activity. The essential oils from fresh and dried rhizomes of *A. galanga* showed an antimicrobial activity against Gram-positive bacteria, a yeast and some dermatophytes (Janssen and Scheffer 1985). Terpinen-4-ol was found most active among the major components. An N-pentane/diethyl ether extract of dried rhizomes was active against *Trichophyton mentagrophytes*. Acetoxychavicol acetate was active against the seven fungi tested, and its MIC (minimum inhibitory concentration) value for dermatophytes ranged from 50 to 250 µg/ml. The diterpene (*E*)-8β, 17-epoxylabd-12-ene-15, 16-dial 1 from galangal

rhizome, synergistically enhanced the antifungal activity of quercetin and chalcone against *Candida albicans* (Haraguchi et al. 1996). Protoplasts of *C. albicans* were lysed by the diterpene, and its membrane permeability was altered. Its antifungal activity was reversed by unsaturated fatty acids. Extracts from several members of Zingiberaceae, especially *Alpinia galanga*, *Curcuma zedoaria* and *Zingiber purpureum*, were found to have pronounced inhibitory activities against a wide variety of human pathogenic fungi, including strains resistant to the common antifungals amphotericin B and ketoconazole (Ficker et al. 2003). The chloroform extracts of *Alpinia galanga* and *Boesenbergia pandurata* had pronounced antifungal activity in-vitro against *Cryptococcus neoformans* and *Microsporum gypseum*, but exhibited weak activity against *Candida albicans* (Phongpaichit et al. 2005). *A. galanga* and *B. pandurata* were found to be excellent candidates for the development of a remedy for opportunistic fungal infections in AIDS patients. Chloroform extract of *Alpinia galanga* demonstrated the greatest inhibition zones of 29.1 and 23.7 mm against *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA), respectively (Voravuthikunchai et al. 2005). The MIC values of this extract against *Staphylococcus aureus* and MRSA were 128 and 256 µg/ml, and the MBC values were 256 and 256 µg/ml, respectively. Its active component, 1'-acetoxychavicol acetate, was identified with MIC values against MRSA and *Staphylococcus aureus* of 64 and 128 µg/ml, respectively. *Alpinia galanga* chloroform extract was inhibitory against most clinical *Staphylococcus aureus* isolates with MIC value of 0.19 mg/mL and MBC value of 1.57 mg/mL (Voravuthikunchai et al. 2006). Significant growth inhibition of methicillin-resistant *S. aureus* (MRSA) was observed in the cultures incubated in the presence of *A. galanga* extract. Galangal extract had the strongest inhibitory effect in-vitro against *Staphylococcus aureus* (Oonmetta-aree et al. 2006). The minimum inhibitory concentration (MIC) of the galangal extract was 0.325 mg/ml and the minimum bactericidal concentration (MBC) at 1.3 mg/ml. The galangal extract caused both outer and inner membrane damage and cytoplasm coagulation. The major compound of the extract was identified

as D,L-1'-acetoxychavicol acetate. The chloroform galangal extract inhibited growth of the pandemic strain of *Vibrio parahaemolyticus* in-vitro (Vuddhakul et al. 2007). The MIC and MBC of a freshly squeezed preparation of galangal were 1:16 and 1:16, respectively. One active component is identified as 1'-acetoxychavicol acetate.

The ethanolic extracts of *Curcuma longa* and *Alpinia galanga* were also found to possess good antifungal activities against *Trichophyton longifusus* (65 % and 60 %, respectively) (Khattak et al. 2005). These extracts were found quite inert in antibacterial bioassay. The growth of a toxigenic strain (Saktiman 3Nst) of *Aspergillus flavus* decreased progressively with increasing concentration of galangal rhizome essential oil incorporated into SMKY liquid medium (Srivastava et al. 2008). The oil significantly arrested aflatoxin B1 elaboration by *A. flavus*; *A. galanga* showed complete inhibition at 500 ppm. The oil combination of *Cinnamomum camphora* and *A. galanga* showed higher efficacy than the individual oils, showing complete inhibition of aflatoxin B1 production even at 250 ppm. Crude ethanolic extracts of *Alpinia galanga* rhizomes exhibited antidermatophytic activity in-vitro in a concentration-dependent manner against selected zoonotic dermatophytes *Microsporum canis*, *Microsporum gypseum* and *Trichophyton mentagrophyte* and the yeast-like *Candida albicans* (Trakranrungsie et al. 2008). The crude acetone extract of *Alpinia galanga* rhizomes exhibited antiplasmid activity against *Salmonella typhi*, *Escherichia coli* and vancomycin-resistant *Enterococcus faecalis* with an efficiency of 92 %, 82 % and 8 % respectively at 400 µg/ml SIC (subinhibitory concentration) (Latha et al. 2009). The principal compound responsible for the activity was identified as 1'-acetoxychavicol acetate. 1'-Acetoxychavicol acetate demonstrated the ability to cure plasmid-encoded antibiotic resistance in various multidrug-resistant bacterial strains of clinical isolates such as *Enterococcus faecalis*, *Salmonella typhi*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Bacillus cereus* with curing efficiency of 66 %, 75 %, 70 %, 32 % and 6 % respectively at SIC of 400–800 µg/ml, thus making the antibiotic treatment more effective.

Leaf extracts and fractions of *A. galanga* and *C. longa* did not show any antibacterial activity against *Staphylococcus aureus*, *Micrococcus luteus* and *Bacillus cereus* (Chan et al. 2011). Rhizome extracts and fractions of *A. galanga* and *C. longa* had no inhibitory effect on *M. luteus* and *S. aureus*, respectively. With the addition of 0.01 mg/ml of EDTA, extracts and fractions of *A. galanga*, *C. longa* and *E. elatior* showed moderate, weak and strong responses, respectively. Strongest antibacterial activity was observed in the PT fraction of *A. galanga* rhizomes with MID of 0.06 mg/disc against all three bacterial species. Galangal extract exhibited potent inhibitory effect against *Staphylococcus aureus* with minimum inhibitory concentration (MIC) of 0.325 mg/ml and minimum bactericidal concentration (MBC) of 1.3 mg/ml (Jirawan et al. 2006). Transmission electron microscopy clearly demonstrated that the galangal extract caused both outer and inner membrane damage, cytoplasm coagulation and release of cell materials including nucleic acid. The major compound of the extract was D,L-1'-acetoxychavicol acetate. Weerakkody et al. (2012) reported that 1'-acetoxychavicol acetate (ACA) affected membrane fatty acid composition and triggered a cell envelope stress response in *Staphylococcus aureus*.

Galangal extract exhibited antimicrobial activity against *Staphylococcus aureus* with minimum inhibitory concentration (MIC) and minimum biocidal concentration (MBC) values of 0.78 mg/ml and 2.34 mg/ml, respectively (Mayachiew and Devahastin 2008). In another study, *A. galanga* rhizome extract exhibited higher antibacterial activity in-vitro against *Staphylococcus aureus* and *Escherichia coli* than against *Bacillus subtilis* and *Pseudomonas aeruginosa* (Indrayan et al. 2009). *A. galanga* hexane and ethanol extracts exhibited strong antimicrobial activity against *Staphylococcus aureus* and/or *Listeria monocytogenes* (Weerakkody et al. 2010). Interestingly the minimal inhibitory concentrations determined using the broth dilution method and the diameter of inhibition zones using the disc diffusion assay were not strongly correlated (R^2 ranged from 0.10 to 0.70) in most extracts, suggesting that choosing just one method for antimicrobial testing may lead to indefinite conclusions. Gels formulated

with varying levels of carbopol 940 (0.5 %, 1.25 % and 2 %) and 1 mL of galangal essential oil showed the effectiveness of antiseptic gels in reducing number of microbial colonies (Kurniawan et al. 2012). The MICs of galangal oil were against *Staphylococcus aureus* 4 % v/v, against *Pseudomonas aeruginosa* >40%v/v, against *Streptococcus bovis* 0.5 % v/v and against *Candida albicans* 0.5 % v/v (Tadtong et al. 2014). Synergistic activity against tested microorganisms was best noted for a combined formulation of lemon grass and galangal oils in the volume ratio 3:7.

Methanol extracts of *A. galanga* leaves, rhizomes and roots exhibited excellent activity against *Bacillus subtilis*, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Staphylococcus aureus* and *Streptococcus epidermis* with MIC and MBC values ranging from 0.04 to 1.28 mg/ml and 0.08–2.56 mg/ml, respectively, compared to the acetone and diethyl ether extracts (Rao et al. 2010). Oven-dried ethanol extract from galangal flower was the most effective against *Staphylococcus aureus* with minimum inhibitory concentration (MIC) ranging from 0.352 to 0.547 mg/mL (Hsu et al. 2010). In contrast, freeze-dried samples extracted with ethanol exhibited the lowest overall antimicrobial activity. *A. galanga* essential oil exhibited strong bactericidal activity against both Gram-negative and Gram-positive bacteria (Prakatthagomol et al. 2011). *A. galanga* oil had antibacterial action probably as a result of its modification of the bacterial cell membrane, disrupting the membrane's permeability. Galangal essential oil exhibited in-vitro inhibitory activity against *Escherichia coli* with minimum inhibitory concentration (MIC) of 4 mg/ml and minimum bacterial concentration (MBC) of 4 mg/ml, *Salmonella typhi* (MIC and MBC 2 mg/ml), *Shigella sonnei* (MIC and MBC 2 mg/ml), and *Staphylococcus aureus* (MIC and MBC 8 mg/ml).

The ethyl acetate extract of *Alpinia galanga* rhizome showed the strongest antibacterial effect against *Propionibacterium acnes*, with minimum inhibitory concentration (MIC) and minimum bactericidal concentration

(MBC) values of 156.0 and 312.0 µg/mL, respectively (Niyomkam et al. 2010). The antibacterial active compound was identified as 1'-acetoxychavicol acetate (1'-ACA). 1'-ACA had a strong inhibitory effect on *P. acnes* with MIC and MBC values of 62.0 and 250.0 µg/mL, respectively. Phenylpropanoid compounds from *A. galanga* rhizome, viz., 1'-S-1'-acetoxychavicol acetate, *trans-p*-coumaryl diacetate and 1'-S-1'-acetoxyeugenol acetate, were found to be potent modulators of efflux pump inhibitory activity and decreased the MIC of ethidium bromide by 64-fold at the concentration of 2.5, 6.25 and 5.0 mg/L respectively (Roy et al. 2012). The crude ethanolic extract of *A. galanga* rhizome inhibited *Corynebacterium* sp., *Staphylococcus aureus* and four strains of *Escherichia coli* in-vitro (Prakatthagomol et al. 2012). The essential oil exhibited dramatically stronger antibacterial activity than the crude extract. The antibacterial activity of only 40 µg of *A. galanga* rhizome essential oil was as effective as 15,000 µg of its crude extract in inhibiting *E. coli*. Eleven Thai herbal formulas used against dental caries (THF-DC) exhibited clear inhibition zones of 7.0–22.5 mm against *Streptococcus mutans* (Joycharat et al. 2012). Subsequent determination of their MIC revealed that the formula containing *Albizia myriophylla*, *Alpinia galanga*, *Avicennia marina* and *Ocimum sanctum* was the most active, with MIC of 250 µg/mL.

The chloroform extract of *Alpinia galanga* rhizomes had strong antimycobacterial effects with MIC values of 0.12 µg/ml; its active component 1'-acetoxychavicol acetate MIC values of 0.024 µg/ml (Phongpaichit et al. 2006). *A. galanga* possessed antimycobacterial activity at a concentration of 250 µg/ml onwards against *Mycobacterium tuberculosis* standard strain H37Rv, clinical isolate of Isoniazid monoresistant and polyresistant isolates (Soundhari and Rajarajan 2013). The extracts were nontoxic to Vero cells with a maximal toxic-free concentration on Vero cells at 300 µg/ml. 1'-S-1'-acetoxyeugenol acetate enhanced the accumulation and inhibited the efflux of ethidium bromide in *Mycobacterium smegmatis* mc² 155 cells. *A. galanga* exhibited anti-*Mycobacterium tuberculosis* activity with multiple modes of

action (Gupta et al. 2014). Since the activity of the extracts was observed under reducing oxygen concentrations, it may be effective in treating the dormant and non-replicating bacteria of latent tuberculosis.

Combinations of galangal with either rosemary (*Rosmarinus officinalis*) or lemon iron bark (*Eucalyptus staigerana*) showed synergistic antimicrobial activity (Weerakkody et al. 2011b). Specifically, galangal and rosemary showed synergistic activity against *Staphylococcus aureus* and *Listeria monocytogenes* only, while galangal and lemon iron bark showed synergistic activity against *Escherichia coli* and *Salmonella typhimurium*. The major chemical components of the galangal and lemon iron bark extracts were 1'-acetoxychavicol acetate (1'ACA) (63.4 %) and neral (15.6 %), respectively, while 1,8-cineole (26.3 %) and camphor (20.3 %) were identified as major chemical components of the rosemary extract. The results showed that galangal, rosemary and lemon iron bark extracts contained components that may have different modes of antimicrobial action and combinations of these extracts may have potential as natural antimicrobials to preserve foods. They reported that various combinations of galangal, rosemary and lemon iron bark extracts could be used to control the growth of spoilage microflora, aerobic bacteria and lactic acid bacteria, *Listeria monocytogenes* and *Staphylococcus aureus*, on cooked, ready-to-eat shrimp (Weerakkody et al. 2011a).

Anti-inflammatory/Antiallergic/Antiasthmatic Activities

Studies demonstrated that two pretreatments with 1'-acetoxychavicol acetate (ACA) (810 nmol) in the activation phase suppressed double 12-*O*-tetradecanoylphorbol-13-acetate (TPA) application-induced H₂O₂ formation in mouse skin (Nakamura et al. 1998). ACA significantly inhibited mouse epidermis thiobarbituric acid-reacting substance formation. Also, ACA inhibited double TPA treatment-induced morphological changes reflecting inflammatory

response, such as oedema formation, leukocyte infiltration, hyperplasia and cell proliferation. Furthermore, pretreatment with ACA but not 1'-hydroxychavicol in the activation phase inhibited double TPA application-induced increases in both number of leukocytes and proliferating cell nuclear antigen index. Studies demonstrate that 1'-acetoxychavicol acetate (ACA) exerted potent inhibitory effects on NO production in murine macrophage cell line RAW264 cells stimulated with lipopolysaccharide or interferon- γ , by suppression of the activation of transcription factors such as NF-kappaB, AP-1 and Stat1 (Ohata et al. 1998). Murakami et al. (2003) found that 1'-acetoxychavicol acetate (ACA) markedly suppressed NOS/COX-2 gene expression mainly by attenuating IkappaB degradation in combined lipopolysaccharide- and interferon- γ -induced IkappaB degradation in RAW264.7 murine macrophages. ACA abrogated ERK1/2 and JNK1/2, as well as the activation and transcriptional activation of NF-kappaB and CREB (cAMP response element-binding protein) in lipopolysaccharide (LPS)-stimulated RAW264.7 murine macrophages (Murakami and Ohigashi 2006). In another study, 1'S-1'-acetoxychavicol acetate from *Alpinia galanga* rhizomes inhibited nitric oxide (NO) production in lipopolysaccharide-activated mouse peritoneal macrophages with an IC₅₀ value of 2.3 μ M (Matsuda et al. 2005). Further, it was found that 1'S-1'-acetoxychavicol acetate inhibited interferon- β (IFN- β) mRNA expression as well as nuclear factor-kappaB (NF-kappaB) activation, and two related compounds, ($\pm$)-1-acetoxy-1-(2-acetoxyphenyl)-2-propene and ($\pm$)-1-acetoxy-1-(4-acetoxyphenol)-3-butene, also inhibited IFN- β mRNA expression (Ando et al. 2005). In addition, 1'S-1'-acetoxychavicol acetate inhibited the production of NO stimulated by poly(I:C) via Toll-like receptor 3. It was found that 1'-acetoxychavicol acetate (ACA) suppressed lipopolysaccharide-induced cyclooxygenase-2 expression in RAW264.7 murine macrophages by inhibiting extracellular signal-regulated kinase (ERK)1/2, c-Jun NH₂-terminal kinase (JNK)1/2 and the activation of activator protein (AP)-1, NF-kappaB and cAMP-responsive element-binding protein (CREB) transcription factors (Murakami et al. 2005). Also, 1'-acetoxychavicol acetate (ACA) had been shown to attenuate

NADPH oxidase (NOX)-derived superoxide generation in macrophages, as well as lipopolysaccharide-induced nitric oxide and prostaglandin E(2) production through the suppression of inducible nitric oxide synthase (iNOS) and cyclooxygenase (COX)-2 (Murakami and Ohigashi 2007).

Phenolic compound such as chavicol analogues, namely, acetoxychavicol acetate and hydroxychavicol acetate from *Alpinia galanga* rhizomes, exhibited potent antioxidant activity and increased cell apoptosis, thereby diminishing cytokine production by Th (T-helper) cells (Min et al. 2009). Although hydroxychavicol acetate had neither antioxidant activity nor pro-apoptotic function, it was shown to increase IL-2 (interleukin-2) production and attenuated IFN γ (interferon- γ) expression in Th cells. In addition, it was demonstrated that hydroxychavicol acetate suppressed T-bet (a transcription factor) expression, which is responsible for IL-2 suppression and IFN γ induction in Th cells and inhibited T-bet-mediated Th1 cell differentiation. The results suggested that hydroxychavicol acetate may be beneficial as therapeutics for treating inflammatory immune disorders caused by extravagant activation of Th1-mediated immune responses.

Another phenylpropanoid compound structure, *p*-coumaryl alcohol- γ -*O*-methyl ether (CAME) similar to *p*-coumaryl diacetate (CDA), was isolated from *Alpinia galanga*. CDA was found to have antioxidant and anti-inflammatory activity (Yu et al. 2009). CAME potently reduced intracellular reactive oxygen species in Th cells, as does CDA. However, although CDA was cytotoxic, CAME selectively and potently suppressed interferon- γ (IFN γ) production in CD4⁺ Th cells, without toxicity. The results suggested that CAME may be an effective, naturally occurring compound for modulating inflammatory immune disorders.

An 80 % aqueous acetone extract of *Alpinia galanga* rhizomes exhibited nitric oxide production inhibitory activities in mouse peritoneal macrophages (Morikawa et al. 2005). From the extract, three 8–9'-linked neolignans, galanganal, galanganols A and B and, a sesquineolignan, galanganol C, were isolated together with nine known phenylpropanoids and

p-hydroxybenzaldehyde. Among them, galanganal ($IC_{50} = 68 \mu M$), galanganols B ($88 \mu M$) and C ($33 \mu M$), 1'S-1'-acetoxychavicol acetate ($2.3 \mu M$), 1'S-1'-acetoxyeugenol acetate ($11 \mu M$), *trans-p*-hydroxycinnamaldehyde (ca. $20 \mu M$), *trans-p*-coumaryl alcohol ($72 \mu M$) and *trans-p*-coumaryl diacetate ($19 \mu M$) inhibited nitric oxide production induced by lipopolysaccharide in mouse peritoneal macrophages. *Alpinia galanga* root extract exhibited anti-inflammatory activity in rats (Ghosh et al. 2011). Inhibition of inflammation (32.22 %) was observed in carrageenan-induced paw oedema, 37.70 % in 5-HT-induced and 35.21 % in bradykinin-induced anti-inflammatory models. In chronic inflammatory model, a progressive inhibition of 34.73 % (3rd day), 37.50 % (5th day), 38.83 % (7th day), 44.66 % (9th day), 49.59 % (11th day) and 55.75 % (13th day) was observed with the extract.

An 80 % aqueous acetone extract of *A. glanaga* rhizomes was found to inhibit release of β -hexosaminidase, as a marker of antigen-IgE-mediated degranulation in RBL-2H3 cells (Matsuda et al. 2003a). Nine known phenylpropanoids and *p*-hydroxybenzaldehyde were isolated from the extract. Among them, 1'S-1'-acetoxychavicol acetate and 1'S-1'-acetoxyeugenol acetate exhibited potent inhibitory activity with IC_{50} values of 15 and $19 \mu M$. In addition, 1'S-1'-acetoxychavicol acetate and 1'S-1'-acetoxyeugenol acetate inhibited ear passive cutaneous anaphylaxis reactions in mice and the antigen-IgE-mediated TNF- α and IL-4 production, both of which participate in the late phase of type I allergic reactions, in RBL-2H3 cells. A more stable and potent analogue of 1'S-1'-acetoxychavicol acetate from galangal against type 1 anti-allergic activity was developed (Yasuhara et al. 2009). This compound also strongly inhibited the antigen-IgE-mediated TNF- α (tumour necrosis factor α) and IL-4 (interleukin 4) production. In-vitro studies showed that *A. galanga* extracts downregulated interleukin-1 β -induced matrix metalloproteinases MMP-1, MMP-3, MMP-13 and Cox-2 expression in human synovial fibroblasts (Pothacharoen et al. 2011). The data suggested that the decrease of gene expression and production of MMPs in synovial fibroblasts against inflammatory stimuli could be due to the effects of the *A.*

galanga extracts and that *A. galanga* extracts might be a promising therapeutic agent for arthritis.

1'-acetoxychavicol acetate (ACA), isolated from *Alpinia galanga* rhizomes, reduced the infiltration of white blood cells (especially eosinophils) and the level of IgE in the lungs of mice with ovalbumin (OVA)-induced asthma and suppressed histopathological changes such as airway remodelling, goblet cell hyperplasia, eosinophil infiltration and glycoprotein secretion (Seo et al. 2013). In addition, ACA inhibited expression of the Th2 cytokines interleukin (IL)-4 and IL-13, and Th1 cytokines IL-12 α and interferon- γ . The results suggested ACA to have promise as an antiasthmatic drug candidate. Studies showed that galangin, from *A. galanga*, abrogated ovalbumin (OVA)-induced airway inflammation in mice by inhibiting the NF- κ B pathway (Zha et al. 2013). Galangin dose dependently inhibited OVA-induced increases in total cell counts, eosinophil counts and interleukin-(IL)-4, IL-5 and IL-13 levels in bronchoalveolar lavage fluid and reduced serum level of OVA-specific IgE. Galangin also attenuated AHR, reduced eosinophil infiltration and goblet cell hyperplasia and reduced expression of inducible nitric oxide synthase and vascular cell adhesion protein-1 (VCAM-1) levels in lung tissue.

Studies showed *p*-hydroxycinnamaldehyde from *A. galanga* to be a potential anti-inflammatory, therapeutic agent for treatment of osteoarthritis (Phitak et al. 2009). *p*-Hydroxycinnamaldehyde and interleukin-1beta (IL-1beta), when incubated in primary human chondrocytes, suppressed loss of uronic acid and reduced release of hyaluronan, sulphated glycosaminoglycans and matrix metalloproteinases (MMPs). The results demonstrated (a) that expression levels of the catabolic genes matrix metalloproteinases, MMP-3 and MMP-13, were suppressed and (b) mRNA expression levels of anabolic genes of collagen II, SOX9 and aggrecan (aggregating proteoglycan) were increased.

Antihyperlipidemic Activity

Oral administration of the rhizome extracts (20 mg/day) of both *A. galanga* and *Kaempferia galanga* effectively lowered the serum and tissue levels of total cholesterol, triglycerides and phospholipids and significantly increased the serum levels of high-density lipoproteins (HDL) in high cholesterol-fed white wistar rats over a period of 4 weeks (Achuthan and Padikkala 1997). The results suggested the potential of these plants in various lipid disorders especially atherosclerosis. The compound 1'-acetoxychavicol acetate (ACA), from *A. galanga* rhizomes, caused a significant decrease in the activity of GPDH in 3 T3-L1 adipocytes without eliciting cell cytotoxicity, and it inhibited cellular lipid accumulation through the downregulation of transcription factors such as PPAR γ and C/EBP α (Ohnishi et al. 2012). ACA also induced a dose-dependent phosphorylation of AMP-activated protein kinase (AMPK). In the animal model, rats fed in high-fat diet (HFD) containing 0.05 % ACA gained less weight than rats fed with HFD alone. The visceral fat mass in rats fed with HFD containing 0.05 % ACA tended to be lower than that in rats fed with HFD alone. Furthermore, a histological examination of livers from rats fed with HFD showed steatohepatitis. The results indicated ACA exerted antiobesity activities both in-vitro and in-vivo and suggested that ACA may have a novel preventive activity against obesity and possibly other metabolic diseases.

Studies showed that administration of the ethanol rhizome extract of *A. galanga* and its chloroform fraction exhibited antihyperlipidemic activity in rats injected with Triton WR 1339 (Iyer et al. 2013). Both dose dependently inhibited the total cholesterol (TC), triglycerides (TG) and low-density lipoprotein (LDL) level and significantly increased HDL level. Phytochemical screening revealed the presence of tannins, coumarins, flavonoids, sterols and glycosides. Phytochemical investigation of the chloroform fraction resulted in the isolation of 5-(hydroxymethyl) furfural. Feeding of female rats with galangin, a flavonol glycoside from galangal rhizome, inhibited increases in body weight, energy intake and parametrial adipose tissue weight induced by cafeteria diet (Kumar and Alagawadi 2013). Galangin exerted a significant decrease in serum lipids, liver weight, lipid peroxidation and

accumulation of hepatic triglycerides. The IC₅₀ value of galangin for pancreatic lipase was 48.20 mg/mL.

Hypoglycaemic Activity

In normal rabbits, powdered galangal rhizome and its methanol and aqueous extracts significantly lowered blood glucose (Akhtar et al. 2002). Gliclazide also produced a significant decrease in blood glucose in the rabbits. The hypoglycaemic effect of *A. galanga* in normal rabbits was comparable to gliclazide. In alloxan-diabetic rabbits, *A. galanga* and its methanol and aqueous extracts did not produce significant reduction in blood glucose. Administration of galangin dose dependently normalised the elevated blood glucose and insulin levels caused by 60-day feeding of high fructose diet (Sivakumar et al. 2010). The minimum effective dose was 100 µg galangin/kg body weight. At this dose, galangin also prevented the development of insulin resistance and exaggerated the response to oral glucose challenge. The oxidant–antioxidant balance was maintained by galangin. Micro-albuminuria and tubular and glomerular changes observed in fructose-treated rats were significantly prevented by galangin (100 µg/kg body weight).

Gastroprotective/Anitulcerogenic Activities

Methanol extract of galangal seeds exhibited significant inhibitory activity against shay ulcers in rats (Mitsui et al. 1976). Two potent antiulcer principles, 1'-acetoxychavicol acetate and 1'-acetoxyeugenol acetate, were isolated from galangal seed extract and showed marked antiulcer activity at a dosage of 1–10 mg/kg. The ethanolic extract of *A. galanga* at a dose of 500 mg/kg significantly reduced the intensity of gastric mucosal damage induced by pyloric ligation and hypothermic restraint stress in rats (Al-Yahya et al. 1990). It produced a significant decrease in gastric secretion in pylorus-ligated rats and a highly significant cytoprotective effect against 80 % ethanol-, 0.6 M HCl-, 0.2 M NaOH- and 25 % NaCl-induced cytodestruction. Pretreatment with the extract significantly prevented hypothermic stress-induced gastric

wall mucus depletion. The results suggested that a significant antisecretory and cytoprotective action of *A. galanga* may be responsible for its antiulcer activity. Phenylpropanoids isolated from *A. galanga* rhizomes, namely, 1'S-1'-acetoxychavicol acetate and 1'S-1'-acetoxyeugenol acetate, markedly inhibited the ethanol-induced gastric mucosal lesions ($ED_{50} = 0.61$ and ca. 0.90 mg/kg) (Matsuda et al. 2003b). Further, 1'S-1'-acetoxychavicol acetate inhibited the lesions induced by 0.6 M HCl ($ED_{50} = 0.73$ mg/kg) and aspirin ($ED_{50} = 0.69$ mg/kg). However, it did not show a significant effect on indomethacin-induced gastric lesions and acid output in pylorus-ligated rats at doses of 0.5 – 5.0 mg/kg. Endogenous prostaglandins and sulfhydryl compounds were suggested to be involved in the gastroprotective effect of 1'S-1'-acetoxychavicol acetate.

Central Nervous System (CNS)/Nueroprotective Activity

The methanolic and ethyl acetate extract of *A. galanga* showed significant central nervous system (CNS) stimulant activity in mice using actophotometer and rotarod test (Saha and Banerjee 2013). CNS stimulation at a dose of 500 mg/kg was comparable with standard drugs caffeine and amphetamine derivative modalart. The extracts did not show any depressant effect in forced swim or tail suspension tests. 1'-Acetoxychavicol acetate (ACA), the main pungent component in galangal, did not activate transient receptor potential cation channel (TRP) subfamily V, member 1 (TRPV1)-expressing human embryonic kidney (HEK) cells, but strongly activated TRP subfamily A, member 1 (TRPA1)-expressing HEK cells (Narukawa et al. 2010). ACA was more potent than allyl isothiocyanate, the typical TRPA1 agonist.

Anti-amnesic effect in mice was exerted by various fractions of *Alpinia galanga* rhizome (Hanish Singh et al. 2011a). Increased habituation memory and decreased escape latency in behavioural parameter were indicative of the cognitive enhancement after treatment with galangal fractions. Increment in Na^+/K^+ -ATPase and antioxidant activity depicted brain membrane integrity improvement and free radical

scavenging property. Acetylcholinesterase level was decreased to improve the cognition by enhancing cholinergic transmission. Among all fractions, preeminent neuroprotection was exerted by chloroform fraction, which contained 1' δ -1'-acetoxyeugenol acetate, and it may be a potential therapeutic agent for Alzheimer's type of amnesia. Results of another in-vivo studies suggested that ethanol extract of *Alpinia galanga* exerted an anti-amnesic effect in A β -induced neurodegeneration in mice through an antioxidant effect (Hanish Singh et al. 2011b). Also the elevated levels of acetylcholinesterase and monoamine oxidase enzymes in amnesia induced mice were attenuated by treatment with galangal ethanol extract.

Immunomodulating Activity

Hot water polysaccharide extract of *A. galanga* markedly enhanced the proliferation of the murine spleen cells in-vitro using two tests (in-vitro and in-vivo effect) (Bendjeddou et al. 2003). The results of the in-vivo effect at doses of 50 and 25 mg/kg showed a stimulation index better than obtained with the in-vitro effect at 50 and 25 μ g/ml for *A. galanga*. Fractions from and *A. galanga* showed a marked stimulating effect on the reticuloendothelial system (RES) and increased the number of peritoneal exudate cells (PEC) and spleen cells of mice.

1'-Acetoxychavicol acetate strongly inhibited phagocytosis of peritoneal macrophages at an IC₅₀ value of 1.2 μ M with negligible effects on pinocytosis and cell viability (Watanabe et al. 1995). Target(s) of 1'-acetoxychavicol acetate was suggested to be downstream of the signal transduction pathway that is mediated by protein kinase C.

Anti-tyrosinase Activity

In-vitro studies demonstrated that *Alpinia galanga* and *Curcuma aromatica* extracts at non-cytotoxic concentrations suppressed ultraviolet A (UVA)-induced tyrosinase activity and mRNA levels and UVA-mediated melanin production in human melanoma cells (Panich et al. 2009). Both extracts were able to protect against UVA-induced cellular oxidant

formation and depletion of catalase and glutathione peroxidase activities and intracellular glutathione content in a dose-dependent manner. The presence of eugenol in *A. galanga* and curcuminoids in *C. aromatica* were found. Two compounds, 1,7-bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one (BHPHTO) and bisdemethoxycurcumin (BDMC) isolated from *Alpinia galanga* rhizomes of *Alpinia galanga*, exhibited antimelanoma and antityrosinase activity in B16-F10 cell line (Lo et al. 2013). The two compounds significantly inhibited the proliferation of human melanoma A2058 cells in the cell viability assay. The essential oil of *Cymbopogon citratus* had the highest level of antityrosinase activity, with an IC₅₀ of 0.5 mg/mL followed distantly by *Curcuma longa*, and *A. galanga* oils with an IC₅₀ of 3.6 mg/mL (Saeio et al. 2011)

Xanthine Oxidase Inhibitory Activity

Xanthine oxidase inhibitors were isolated from *A. galangal* rhizomes and identified as *trans-p*-coumaryl diacetate (1), *trans*-coniferyl diacetate (2), [1'S]-1'-acetoxychavicol acetate (3), [1'S]-1'-acetoxyeugenol acetate (4) and 4-hydroxybenzaldehyde (5) (Noro et al. 1988). The type of inhibition by either 1 or 3 with respect to xanthine as a substrate was uncompetitive.

Nephroprotective Activity

After 40 days of treatment, the alcoholic extract of *Alpinia galanga* rhizomes significantly decreased glycaemia, blood urea nitrogen (BUN) and urinary albumin and increased body weight in streptozotocin-diabetic-nephropathic rats (Kaushik et al. 2013). The extract (200 mg/kg) decreased malondialdehyde and glutathione significantly and increased superoxide dismutase and catalase in the rats, compared with nephropathic control. The extract (100 and 200 mg/kg) lowered total cholesterolemia, blood triglycerides and blood LDL cholesterol, but increased blood HDL cholesterol. Overall, atherogenic index was decreased significantly. The study demonstrated that the rhizomes of *Alpinia galanga*

exhibited significant nephroprotective activities in the tested models.

Lung Protective Activity

Studies demonstrated that galangin, active constituent of *A. galanga*, protected the lungs of male BALB/c mice against lipopolysaccharide-induced acute lung injury by inhibition of inflammation and oxidative stress (Shu et al. 2014). The protective effects of galangin were associated with inhibition of nuclear factor (NF)- κ B and upregulation of heme oxygenase (HO)-1.

Antimalarial Activity

During early malaria infection, the rhizomes extract of *Languas galanga* produced a dose-dependent chemosuppression activity at the different doses employed compared to control (Al-adhroey et al. 2010). Four-day suppressive effects of 29, 49, 63 and 65 % were shown, respectively, for the corresponding dose of the extract (50, 100, 200 and 400 mg/kg/day). In the established malaria infection, galangal extract exhibited dose-dependent curative antimalarial activity, which was statistically significant when compared to control. The mean parasitaemia for the treated groups on the sixth day of infection were 5.80, 3.40, 3.40 and 3.20 for 50, 100, 200 and 400 mg/kg/day, respectively. The mean parasitaemia for the control group was 9.60. Prophylactic activity of the rhizomes extract during the residual malaria infection showed dose-dependent chemosuppression at 50, 100, 200 and 400 mg/kg/day dose levels, exerting 13, 26, 39 and 52 % suppressions, respectively. The methanolic rhizome extract of *Languas galanga* showed moderate DPPH radical scavenging activity. At 1.56–25 μ g/mL, the scavenging abilities of the methanol extract were 10.08, 8.63, 15.64, 29.34 and 37.88, respectively. The acute oral toxicity (LD₅₀) of galangal extract in mice was established to be 4.998 mg/kg.

Antiplatelet Activity

The methanol extract of *A. galanga* rhizome exhibited inhibitory effects on platelet-activating factor (PAF) binding to rabbit platelets with IC₅₀ value of 5.5 µg/ml (Jantan et al. 2005).

Anti-psoriatic Activity

Ethanol extract of *A. galanga* exhibited anti-psoriatic activity in HaCaT keratinocyte cell line by modulating the expression of NF-κB signalling biomarkers (Saelee et al. 2011). It increased the expression of TNFAIP3 and significantly reduced the expression of CSF-1 and NF-κB2. Psoriasis is a chronic inflammatory skin disorder characterised by rapid proliferation of keratinocytes and incomplete keratinisation.

Expectorant Activity

The petroleum ether extract of galangal rhizome and volatile oil exhibited expectorant activity in rabbits (Inamdar et al. 1961). The petroleum extract produced 82.95 % increase in respiratory tract fluid, while the volatile oil produced an increase of 36.55 %. The volatile oil stimulated rabbits bronchial glands directly while the non-volatile extract acted by reflex through gastric mucosa.

Cytochrome Inhibition Activity

Methanol extracts of *Alpinia galanga* rhizome at 0.5 mg/ml exhibited more than 30 % increase of cytochrome increase of CYP2D6 inhibition via erythromycin *N*-demethylation and dextromethorphan *O*-demethylation activities in human liver microsomes (Subehan et al. 2006).

Antileishmanial Activity

Hexane, chloroform and ethyl acetate extracts (100 µg/ml) of *Alpinia galanga* rhizomes exhibited significant activity in-vitro against promastigotes of *Leishmania donovani* (Kaur et al. 2010). Among the 12 active constituents, *p*-coumaryl diacetate, 1'-acetoxychavicol acetate, 1'-acetoxyeugenol

acetate and *trans-p*-acetoxycinnamyl alcohol were found most active in-vitro against promastigotes of *L. donovani* with IC₅₀ values of 39.3, 32.9, 18.9 and 79.9 µM respectively.

Anti-amoebic Activity

The chloroform extracts from *Alpinia galanga* exhibited potent antiamebic activity against *Entamoeba histolytica* strain HTH-56:MUTM and strain HM1:IMSS trophozoites with IC₅₀ 55.2 µg/ml.

Anthelmintic Activity

Alpinia galanga rhizome extract failed to show any activity against *Pheretima posthuma*, but exhibited potent activity in a dose-dependent manner against *Ascaridia galli* which was comparable to that of the standard, albendazole (Subash et al. 2012). At 50 mg/ml, albendazole took 23 min to cause paralysis and 63.33 min to cause death, while galangal extract at 100 mg/ml took 32.83 min for paralysis and 69.33 min for death.

Allergy Issues

Hong and Chang (2006) reported a case of localised contact dermatitis and subsequently generalised erythema multiforme-like eruptions after topical application of herbal galangal. Patch tests showed there was an allergen in fresh and dried *Alpinia galanga*.

Toxicity Studies

In the chronic (90 days, 100 mg/kg/day) study, mice treated with ethanol galangal rhizome extract showed significant weight gain and weight gains of sexual organs, increased sperm motility and sperm counts and a significant rise in the red blood cell level (Quereshi et al. 1992). The extract did not show any spermatotoxic effects. Acute toxicity study of ethanolic extract of *Alpinia galanga* in rodents conducted in accordance with OECD guideline 423 and phytochemical

analysis classified the extract to fall under the hazard category $2000 \text{ mg/kg} < \text{LD}_{50} < 5000 \text{ mg/kg}$ according to globally harmonised classification system and confirmed the safety of ethnobotanical use of *Alpinia galanga* (Subash et al. 2013).

Traditional Medicinal Uses

Alpinia galanga rhizomes have reported wide medical applications in traditional medicine in Southeast Asia. Galangal rhizome has been used for its emmenagogue, aphrodisiac, abortifacient, carminative, expectorant, stomachic, digestive stimulant, antiseptic, antibacterial, antipyretic and anti-inflammatory qualities (Burkill 1966; WHO 1990; Sala 1993; Norhyayti et al. 1999; HMRC 2002; Kaushik et al. 2011). The rhizomes have been in the treatment of various ailments such as fever, cough, hiccups, asthma, bronchitis, heart diseases, chronic enteritis, renal calculus, diabetes, rheumatism, kidney disorders, rheumatism, skin diseases, dyspepsia, colic, flatulence, gastralgia, borborygmus, emesis, dysentery, diarrhoea, scurf, enlarged spleen, cancers of oral cavity and stomach and cholera. The rhizome has also been claimed to be useful for malaria, tinea, tubular glands, pityriasis versicolor and desquamation of the sole and hands (HMRC 2002). It has been used as alternative medicine for antirheumatic activities (Pothacharoen et al. 2011). The red fruit is used in traditional Chinese medicine and has a flavour similar to cardamom. The rhizome has a reputation among the Arabs as aphrodisiac (Burkill 1966). In Indian indigenous medicine, the rhizomes are used in rheumatism and catarrhal affections, especially in bronchial catarrh and in respiratory troubles of children (Indrayan et al. 2009). Hongdoukou, Fructus Galangae, is the dry ripe red fruit of *Alpinia galanga*, which is used in the treatment of various gastric disorders, emesis and diarrhoea (Tang and Eisenbrand 1992). In Vietnam, rhizomes soaked in salt are used to quench thirst during strenuous work, and rhizome soaked in alcohol is used topically for ringworm infection on the skin (Nguyen et al. 2014).

In Ayurvedic medicine, the rhizome is used to improve appetite, taste and voice. It has also been reported to be useful in *vata*, bronchitis and diseases of the heart (Kirtikar and Basu 1996; Chudiwal et al. 2010). In Unani medicine, rhizomes have been employed as stomachic, aphrodisiac, tonic, diuretic, expectorant and carminative and described as useful in treating headache, rheumatic pains, sore throat, sour eructation, stuttering, chest pain diabetes, burning of the liver, tubercular glands and diseases of the kidney. The seeds are considered calefacient, stomachic, sternutatory and beneficial in colic, diarrhoea and emesis in Chinese medicine. In Thai folk medicine, the rhizomes are employed as carminative, antifatulent, antifungal and anti-itching.

Other Uses

Rhizomes also have insecticidal properties. Studies showed that hexane crude extract of galangal rhizome gave the highest control efficiency of adult *Bactrocera dorsalis* (Sukhirun et al. 2010). The 24 h-LC₅₀ values was 4866.06 ppm (hexane), 24,156.66 ppm (dichloromethane), 16,744.73 ppm (ethyl acetate) and 6337.54 ppm (95 % ethanol). The hexane and ethanol rhizome extracts were found to be most effective against adult oriental fruit fly, *Bactrocera dorsalis*, with LC₅₀ = 4866 and 6337 ppm, respectively, after 24 h (Sukhirun et al. 2011). Two compounds, (*E*)-*p*-acetoxycinnamyl alcohol and (*E*)-*p*-coumaryl alcohol ethyl ether, were identified as active ingredients and found to be more active than total hexane extract (LC₅₀ = 3654 and 4044 ppm, respectively, after 24 h). The data suggested that the compounds were not synergistic but may have some additive effect in a mixture. The hexane extract also inhibited detoxification enzymes, carboxylesterase (CE), by 70 %, and glutathione transferase (GST) was not significantly inhibited. The data suggested that inhibition of these insect enzymes by plant allelochemicals could be a useful alternative approach for the management of the pest in the field. 1'-acetoxychavicol acetate and its positional (*meta* and *ortho*) isomers exhibited repellent activity against adults adzuki bean weevil (Lee and Ando 2001). *A. galanga* rhizome

essential oil was found to possess strong contact toxicity against cigarette beetle *Lasioderma serricorne* adults with LD₅₀ value of 12.2 µg/adult and also showed strong fumigant toxicity against *L. serricorne* adults with LC₅₀ value of 3.5 mg/L (Wu et al. 2014). α-Terpineol and eucalyptol showed strong contact toxicity against *L. serricorne* (LD₅₀ = 13.3 and 15.6 µg/adult, respectively) and fumigant toxicity against *L. serricorne* (LC₅₀ = 2.8 and 5.2 mg/L air, respectively). Moreover, the essential oil and eucalyptol also exhibited the strong repellency against *L. serricorne* adults, whereas borneol exhibited weaker repellency relative to the positive control, DEET.

The ethanolic extracts of *Curcuma longa* and *Alpinia galanga* exhibited excellent (100 %) phytotoxic activity against the aquatic weed, *Lemna minor* (Khattak et al. 2005).

Studies showed that *A. galanga* could be used for phytoremediation of waste water by adsorption of lead and zinc (Chairgulprasert et al. 2013). Galangal exhibited a higher adsorption efficiency for lead (95.2 %) than for zinc (66.9 %).

Comments

This species have been categorised into 2 varieties based on certain morphological traits (Wu and Larsen 2000):

Lamina and panicle rachis glabrous—var. *galanga*

Lamina abaxially and panicle rachis pubescent—var. *pyramidata*

Alpinia galanga and can also be categorised into three types based on rhizome colour, red, yellow and white greater galangal (14:5:3 samples), according to their morphological characteristics (Tonwitawat 2008). Almost all agronomic characteristics of red galangal were higher than the others, plant height at 149.5 cm, LAI 8.2, total fresh weight of plant and rhizome, 2.9 and 1.8 kg per plant and the harvest index of 0.4. Also, pink and green rhizome types were also found (see above plates).

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Alpinia latilabris

T. K. Lim¹ 

(1) Canberra, Australia

Scientific Name

Alpinia latilabris Ridley

Synonyms

Alpinia hookeriana Valetton, *Alpinia sericea* Ridley, *Catimbium latilabre* (Ridley) Holttum, *Languas hookeriana* (Valeton) Merr., *Languas sericea* (Valeton) Merr.

Family

Zingiberaceae

Common/English Names

Shell Ginger

Vernacular Names

Borneo: Terebak becuk

Vietnamese: Re, Ry

Origin/Distribution

The species is found from Indochina to West Malesia but is indigenous to the Malay Peninsula.

Agroecology

A tropical species. It is partial shade-loving and prefers moist, well-drained soil. Its natural habitat is usually found in the forest edges in Malaysia. It occurs wild along river banks and canals in South Vietnam.

Edible Plant Parts and Uses

In Vietnam, the acrid, aromatic rhizome is used as spice (Tanaka and Nguyen 2007). The fruit is eaten by the Lundayeh tribe in Ulu Padas, Sabah, East Malaysia.

Botany

Perennial rhizomatous herb is up to 3 m high; rhizomes are terete and branched. Leaves are lanceolate, with pointed apex and tapering base. Its leaf blade is dark shining green, 40–75 cm long with entire, rough margin. Inflorescence 25 cm long with short, lateral branches, bearing 1–3 white petalled shell-like flowers; corolla white with pink apices, 4–5 cm, and thick yellow labellum (lip) with dots and red stripes (Plate 1); ovary pubescent; and capsule –3 carpels with numerous rough-textured coated, brown seeds 5 mm in diameter.



Plate 1 Inflorescence with open flowers and buds

Nutritive/Medicinal Properties

More than 40 and 30 constituents, respectively, were found to be present in the rhizome and root oils of *Catimbum latibre* (Nguyen et al. 1994). The main components in the rhizome oil were 1,8-cineole (25.3 %), linalool (10.9 %) and carotol (9.2 %), while the root oil contained mainly citronellol (30.7 %) and 1,8-cineole (11.6 %). *Alpinia latilabris* rhizomes yielded 33 identified constituents, the majority was terpenoids, but the oil was clearly dominated by methyl (*E*)-cinnamate (89.5 %) (Wong et al. 2005). More than 55 components were found to be present in the seed oil, of which the major ones were β -caryophyllene (25.8 %), camphor (11.2 %), caryophyllene oxide (5.7 %), carotol (5.6 %), δ -elemene (5.0 %), benzylacetone (4.8 %) and α -phellandrene (4.4 %). About 25 compounds were found in the fruit skin oil, the main components being β -pinene (26.1 %), 1,8-cineole (19.6 %) and α -pinene (11.1 %).

More than 55 components were found to be present in the seed oil of *Catimbum latibre*, of which the major ones were β -caryophyllene (25.8 %), camphor (11.2 %), caryophyllene oxide (5.7 %), carotol (5.6 %), δ -elemene (5.0 %), benzyl acetone (4.8 %) and α -phellandrene (4.4 %) (Leclercq et al. 1994). About 25 compounds were found in the fruit skin oil, the main components being β -pinene (26.1 %), 1,8-cineole (19.6 %) and α -pinene (11.1 %). The oil yields (w/w) were 0.08 % for unripe fruits and 0.05 % for ripe fruits of *A. latilabris*, all on a fresh weight-basis (Ibrahim et al. 2014). Forty-five and forty-four constituents were identified in the unripe and ripe fruit oils of *A. latilabris*, respectively. Monoterpenoids (91.7 % and 92.1 %) characterized the oils of the unripe and ripe fruits, respectively, with 1, 8-cineole (34.2 % and 35.9 %), β -pinene (20.2 % and 19.0 %), α -pinene (8.2 % and 8.8 %), camphor (7.4 % and 8.8 %) and camphene (5.1 % and 5.8 %) accounting for more than half of each sample, respectively. The minor components were 2-heptanol (0.8, 0.7 %), tricyclene (0.1, 0.2 %), α -thujene (0, 0.2 %), benzaldehyde (0, 0.1 %), 6-methyl-5-hepten-2-one (0, 0.1 %), myrcene (2.1, 1.6 %), α -phellandrene (2.5, 0.7 %), *p*-cymene (0, 0.1 %), limonene (0.2, 0 %), 2-heptyl acetate (tr, 0 %), *trans*- β -ocimene (0, 0.4 %), γ -terpinene (0.8, 0.3 %), *trans*-linalool oxide (0.1, 0 %), terpinolene (0.3, 0.3 %), 2-nonanone (0.1, 0.1 %), linalool (2.7, 2.3 %), fenchol (tr, 0%), camphene hydrate (0.3, 0 %), isoborneol (0.3, 0.3 %), borneol (1.8, 2.2 %), terpinen-4-ol (1, 1 %), α -terpineol (3.2, 3.1 %), myrtenal (0, 0.3 %), myrtenol (0.1, 0.1 %), β -citronellol (tr, 0.1 %), neral (0.1, 0.1 %), geranial (0.1, 0.2 %), bornyl acetate (0.4, 0.2 %), carvacrol (0, 0.1 %), α -cubebene (tr, 0.1 %), geranyl acetate (0.1, 0 %), β -caryophyllene (1.0, 0.5 %), *trans*- α -bergamotene (0, 0.2 %), α -humulene (0.1, 0.1 %), *trans*- β -farnesene (0, 0.1 %), *allo*-aromadendrene (0.1, 0 %), *ar*-curcumene (0.2, 0.2 %), α -zingiberene (0.1, 0.1 %), *trans*, *trans*- α -farnesene (0.5, 0.4 %), β -sesquiphellandrene (0.5, 0.4 %), α -elemol (0.1, 0 %), *trans*-nerolidol (1.1, 1 %), caryophyllene oxide (0, 0.6 %), γ -eudesmol (0.1, 0 %), β -eudesmol (0.1, 0 %), α -bisabolol (0, 0.2 %), *cis*-*cis*-farnesol (0, 0.5 %) and *trans*-*trans*-farnesol (0, 0.2 %).

The oils of *A. latilabris*, both unripe and ripe fruit, inhibited in-vitro growth of bacteria *Staphylococcus aureus* and *Bacillus subtilis* with MIC values between 2.50 and 5.0 mg/mL (Ibrahim et al. 2014). However, only the ripe fruit oil showed weak activity against *Escherichia coli* and *Pseudomonas aeruginosa* with MIC value of 5.0 mg/mL. Both oils also elicited antifungal activities against the dermatophytes *Microsporum canis*, *Trichophyton mentagrophytes* and *Trichophyton rubrum* with MIC values of 2.50–5.0 mg/mL. In contrast, only the ripe fruit oil showed moderate potency against *Candida glabrata* while the unripe oil was void of activity.

In Vietnam, rhizomes are reported good for digestion, to dispel colds and to relieve pain, treat stomach ache and vomiting (Tanaka and Nguyen 2007). Juice from the boiled rhizome is used to treat gastrointestinal disorders (Nguyen et al. 2014).

Other Uses

Alpinia latilabris is grown as an ornamental plant for its shell-like flower and fragrant leaves.

Comments

Alpinia latilabris reproduces and spreads by rhizome division. It also produces abundant seeds.

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[CrossRef]

Alpinia malaccensis

T. K. Lim¹ 

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Scientific Name

Alpinia malaccensis (Burm.f.) Roscoe (Plate 1)



Plate 1 Plant label

Synonyms

Alpinia malaccensis var. *malaccensis*, *Alpinia nutans* var. *sericea* Baker, *Buekia malaccensis* (Burm.f.) Raeusch., *Catimbium malaccense* (Burm.f.) Holttum, *Costus malaccensis* Koenig, *Languas malaccensis* (Burm.f.) Merrill, *Maranta malaccensis* Burm.f. (basionym)

Family

Zingiberaceae

Common/English Names

Malacca Ginger, Malacca Galangal, Rieng Malacca

Vernacular Names

Bangladesh: Deotara (Bengali)

Chinese: Mao Ban Shan Jiang

German: Malakka-Galgant

India: Kaupat (Assamese), Jangali Adrak (Madhya Pradesh), Gong (Meghalaya), Lisin (Mishing)

Indonesia: Langkuas Malaka (Maluku), Laja Gowah, Polang (Java), Seruleu Gayo Puar

Laos: Mak Kha

Malaysia: Bangle, Puar

Philippines: Simionan (Bukidnon), Punan (Cebu-Bisaya), Barapat, Kalaeug (Igorot), Sigiapag (Negrito), Tagusahis (Panay-Bisaya), Tam-Tamo (Sambali), Birao-Birao (Sulu), Bagumbung, Tagbak-Babae, Tagbak-Lalaki, Tukang-Maya (Tagalog)

Thailand: Kha Pa

Vietnamese: Riêng Malacca

Origin/Distribution

The species occurs from Assam, Myanmar, Thailand, Peninsular Malaysia to China—Xizang and Yunnan. It is cultivated in India, Java and Southern Java.

Agroecology

Alpinia malaccensis thrives in a wet/dry monsoon tropical climate with mean annual rainfall over 1400 mm and mean annual temperature around 25.3 °C from near sea level to 1500 m altitude. In its native range, *A. malaccensis* occurs in full sun to partial shade in secondary vegetation, bamboo and teak forest, brushwood and ravines on soils rich in organic matter from near sea level to 1200 m elevation.

Edible Plant Parts and Uses

In Indonesia and Laos the fruits are eaten. In Laos, both the fruits and the root of this herb can be used as food (Kashio and Johnson 2001). The fruits are mainly collected and sold to Chinese traders; the villagers in Ban Kachet located in a mountainous area, 750 m altitude, in the north-western part of Luang Prabang province, themselves do not use the fruit. The root is for subsistence use as a spice and sold, bringing 50 kip/kg. The plant shoots are a local food item. Mak kha is common in the village area and easy to find. In north-eastern India, the rhizome is occasionally used as a spice and is eaten as a vegetable (Ibrahim 2002). In the Moluccas, the rhizome is chewed with betel nut. Rhizome is cooked as vegetable by the Garo tribe in Meghalaya, India (Singh et al. 2012).

Botany

Alpinia malaccensis is an herbaceous perennial. Pseudostems are up to 3–4 m. Ligule is 2-cleft, up to 1 cm and slightly tomentose; petiole is ca. 2 cm and grooved; leaves are up to 8; leaf blade is oblong-lanceolate or lanceolate, up to 90 × 15 cm and abaxially pubescent; base is acute; apex is acuminate (Plate 2). Racemes erect up to 47 cm; rachis is stout and densely yellow pubescent; bracteoles are white, broadly elliptic and 3.5–4 cm. Pedicel is ca. 7 mm and densely yellow pubescent. Calyx is campanulate, 1.5 cm, densely sericeous and red-tipped. Corolla is white and sericeous; tube is 1 cm; lobes are oblong-lanceolate and 2.5–3 cm. Lateral staminodes are absent. Labellum is yellow with red stripes, ovate, large and 3.5 cm; apex is emarginate. Stamen is ca. 2.4 cm. Ovary is

villous. Capsule is yellow, globose, ca. 2 cm in diameter and dehiscing irregularly.



Plate 2 Foliage of Malacca ginger

Nutritive/Medicinal Properties

Phenylephrine and 2-pentene were found to be the major secondary metabolites present in the methanol and petroleum ether extracts and nerolidol, α -humulene, *cis*-ocimene and α -farnesene in the methanol extract of *A. malaccensis* rhizomes (Benjamin et al. 2009).

The rhizome essential oil was found to be rich in (*E*)-methyl cinnamate (85.7 %) (Nor Azah et al. 2005). The other minor components were α -phellandrene (1.9 %), β -pinene (1.6 %) and 1,8-cineole (1.5 %); *p*-cymene (1.6 %), α -pinene (1.1 %), limonene (1 %) and the following (<1 %) α -thujene, camphene, myrcene, δ -3-carene and terpinolene; linalool, camphor and terpinene-4-ol; α -terpineol; endobornyl acetate; and β -caryophyllene and β -bisabolene. Raj et al. (2013) found that *A. malaccensis* rhizome oil contained the following compounds as the major component α -phellandrene (36.4 %), followed by *p*-cymene (14.9 %), (*E*)-labda-8(17), 12-diene-15,16-dial (5 %), β -pinene (4.5 %) and 13,14,15,16-tetranor-8(17)-labden-12-al (4.3 %). Sirat et al. (2011) identified 20 compounds representing 99.7 % of the rhizome oil of *A. malaccensis*, among which methyl (*E*)-cinnamate (78.2 %)

was the major constituent. More recently, Muchtaridi et al. (2014) reported the rhizome essential oil to contain: α -pinene (14.90 %), β -pinene (12.44 %), 1,8-cineole (9.89 %), camphor (6.22 %), α -terpineol (6 %), γ -terpinene (3.78 %) and α -bisabolol (1 %), and compounds (<1 %) were linalool (0.7 %), α -cadinol (0.58 %), α -terpinolene (0.4 %), fenchone (0.4 %), juniper camphor (0.4 %), hexadecanoic acid (0.3 %), sabinene (0.2 %), β -caryophyllene (0.2 %), viridiflorol (0.2 %), carotol (0.2 %) and patchouli alcohol (0.1 %).

Essential oil of the pseudostem was found to be rich in (*E*)-methyl cinnamate (64.4 %), α -phellandrene (6.3 %), β -pinene (6 %), *p*-cymene (3.5 %), α -pinene (3.3 %), 1,8-cineole (3 %) and limonene (2.1 %) (Nor Azah et al. 2005). The other minor components (<1 %) were α -thujene, camphene, myrcene, δ -3-carene, (*E*)- β -ocimene, γ -terpinene, linalool and terpinene-4-ol; α -terpineol; and *Z*-citral, geraniol and β -bisabolene.

Recently, the pseudostem essential oil was reported to contain methyl cinnamate (30.24 %) as the major component followed by 1,8-cineole (16 %), α -pinene (13 %), β -pinene (12 %), α -terpineol (6 %), nerol (5 %), camphor (1.3 %) and α -cadinol (1.2 %), and compounds (<1 %) were linalool (0.42 %), β -bisabolol (0.23 %), juniper camphor (0.29 %), patchouli alcohol (0.40 %), santalol (0.21 %), stearaldehyde (0.16 %), tetradecanol (0.19 %), decanoic acid (0.27 %), heptadecane (0.14 %), citronellyl acetate (0.17 %), pentadecanone (0.2 %), octadecane (0.10 %), nanodecane (0.14 %), pentadecatriene (0.24 %), isophytol (0.31 %), dodocatretrialal (0.18 %), phytol (0.32 %) and two unknowns (Muchtaridi et al. 2014).

The leaf essential oil was found to be rich in (*E*)-methyl cinnamate (88 %) (Nor Azah et al. 2005). The other minor components were 1,8-cineole (1.8 %); *p*-cymene (1.5 %) and the following (<1 %) benzaldehyde, β -pinene, myrcene, α -phellandrene, δ -3-carene and limonene; γ -terpinene; linalool and terpinene-4-ol; α -terpineol; and geraniol and β -bisabolene.

Forty-seven components were identified in *Alpinia malaccensis* leaf oil; the majority were terpenoids, but the oil was dominated by α -phellandrene (31.80 %), eucalyptol (13.76 %), *O*-cymene (11.45 %), β -pinene (11.34 %) and limonene (6.44 %), β -myrcene (5.65 %), α -pinene (5.55 %),

camphene (2.78 %), linalool (1.65 %) and sabinyl acetate (1.43 %) (Bhuiyan et al. 2010). The other minor constituents included γ -selinene; γ -terpinene; 1,3-dioxane; 1H-cycloprop(e)azulene, decahydro-1,1,7-trimethyl-4-methylene; 2-carene; 2-menthene; 4-terpineol; 5-nonaol, 5-methyl; anethole; β -caryophyllene; benzaldehyde; benzene, 1-methyl-4-(1-methylethyl); biisobutenyl; β -pinene oxide; caryophyllene oxide; *cis*-piperitol; cyclohexane, 2,4-diisopropyl-1,1-dimethyl; cyclohexanone, 2-(1-methyl-2-oxopropyl); *exo*-2-hydroxycineole; geraniol; isothujol, α -bulnesene, α -caryophyllene; ledol; α -selinene; α -terpinene; α -thujene; *m*-cymene; ocimene, piperitone; *p*-menth-4(8)-en-9-ol; sabinene; terpinene-4-acetate; thymol; *trans*-pinocarveol; and *trans*-pulegone oxide. Sahoo et al. (2014) identified ten components in the leaf essential oil accounting for 92.7 % of the oil. The major constituents of the oil were α -phellandrene (43.9 %), β -cymene (31.7 %) and β -pinene (4.6 %). Other components included: β -caryophyllene (3.3 %), α -terpineol (2.2 %), *trans*-pinocarveol (2.2 %), caryophyllene oxide (1.7 %), α -pinene (1.5 %), δ -cadinene (0.8 %) and α -selinene (0.7 %). The major constituents of the oil are α -phellandrene (43.9 %), β -cymene (31.7 %) and β -pinene (4.6 %). Recently, Muchtaridi et al. (2014) reported the rhizome leaf essential oil to contain α -pinene (30.57 %), 1,8-cineole (21.39 %), β -pinene 11.41 %), methyl cinnamate (9.24 %), geraniol (2.42 %), α -terpineol (2.42 %), myrcene (1.95 %) and camphor (1.76 %), and compounds <1 % were sabinene, heptene, octanal, α -terpinene, γ -terpinene, *cis*-sabinene, α -terpinolene, linalool, nonanal, fenchol, 4-terpineol, pinocarveol, isoborneol, naphthalene, cymen-8-ol, piperitol, carveol, cyclohexane, myrtenol, citral, bornyl acetate, geranyl acetate, α -bergamotene, ionone, geranylacetone, α -ionone, γ -caryophyllene, α -humulene, β -ionone, β -seline and aromadendrene.

Antioxidant Activity

Total phenolic content (TPC) and ascorbic acid equivalent antioxidant capacity (AEAC) of *A. malaccensis* leaves were reported as 744 mg GAE/100 g and 800 mg ascorbic acid/100

g, and rhizomes are 564 mg GAE/100 g and 745 mg ascorbic acid/100 g, respectively (Chan et al. 2008). Values were more variable in rhizomes than in leaves. The methanol leaf extract of *Alpinia malaccensis* exhibited antioxidant activity in-vitro, with an IC₅₀ value of 22.5 µg/ml in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical assay, 26.35 µg/ml in 2,2-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid) (ABTS) assay, 72.38 µg/ml in nitric oxide assay and 80 µg/ml in H₂O₂ radical scavenging assay (Sahoo et al. 2012). Additionally, the TPC (total phenolic content) of the extract was found to be 76.25 mg gallic acid equivalent/g extract. The leaf essential oil and leaf methanol extract exhibited significant antioxidant activities with IC₅₀ values of 18.26 µg/ml and 22.5 µg/ml in DPPH assay and 20 µg/ml and 26.23 µg/ml in the ABTS assay, respectively (Sahoo et al. 2014). The results indicated *A. malaccensis* leaves to have promising antioxidant activity and could serve as potential source of natural antioxidants.

Antimicrobial Activity

The methanol extract of *A. malaccensis* showed antimicrobial activity against *Bacillus subtilis*, methicillin-resistant *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans* and *Aspergillus ochraceus* with MIC 250–500 µg/disc (Habsah et al. 2000). The leaf essential oil and methanol leaf extract showed good antimicrobial activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans* and *Aspergillus niger* (Sahoo et al. 2014). The leaf oil exhibited higher activity than the leaf extract. The MIC (minimum inhibitory concentration) of the leaf oil and extract ranged between 1–7 µl/ml and 2–10 µl/ml, respectively.

Locomotor Inhibition Activity

Studies found that 75 min after inhalation of the rhizome and leaf essential oil (0.3–0.5 ml/cage), the average number of mice wheel cage rotations was significantly reduced, and the percent inhibition was 40.53 and 35.27 %, respectively (Muchtaridi et al. 2014). The rhizome essential showed more

potent inhibition than the leaf essential oil. In earlier studies, they found that the essential oil constituents of methyl cinnamate and 1,8-cineole may be responsible for this inhibitory activity (Muchtaridi et al. 2011).

Traditional Medicinal Uses

Fruit is also utilised like the rhizomes medicinally. Rhizomes are crushed and applied to sores, wounds and boils (Burkill 1966). Ripe and unripe fruits are infused with salt and used as an emetic to control vomiting. The fragrant fruits are pounded and used for washing clothes and hairs by Amboinese girls as it leaves a pleasant scent. The oils of *A. conchigera* and *A. malaccensis* have been reported to be used in folk medicine in the treatment of rheumatism and arthritis (Bhuiyan et al. 2010). Rhizomes are used in the treatment of sores by the Mishing tribe in Assam, India (Sharma and Pegu 2011), and in the Hoshangabad district in Madhya Pradesh, India (Abhyankar and Upadhyay 2011). In the Philippines, a decoction of the fruit or crushed seeds is applied on gastralgia with tympanites, and it is used for bathing feverish people (Ibrahim 2002; Bhuiyan et al. 2010). In Sumedang and Subang, West Java, the leaf is used in children as an anti-vomiting, and rhizome oil used as massage oil (Muchtaridi et al. 2014). In Vietnam, juice from boiled rhizomes is used to treat intestinal disorders and crushed rhizomes used topical for scabies (Nguyen et al. 2014).

Other Uses

The plant is cultivated as an ornamental house plant. The aromatic oil, obtained from the leaves or rhizomes, is known by the trade name essence d'Amali or essence of Amali and is commonly used in perfumery.

Comments

The plant is propagated from seeds or division of the rhizome. Plantlets have been successfully developed from tissue

cultures of rhizome buds on Murashige and Skoog medium (Benjamin et al. 2009).

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Alpinia officinarum

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Scientific Name

Alpinia officinarum Hance

Synonyms

Languas officinarum (Hance) Farwell, *Languas officinarum* (Hance) P.H. Hô

Family

Zingiberaceae

Common/English Names

Chinese Ginger, China Root, Colic Root, East India Catarrh Root, Galangal, India Root, Lesser Galanga, Lesser Galangal

Vernacular Names

Arabic: Kulanjan

Chinese: Gao Liang Jiang

Czech: Galgán Lékařský

Danish: Lille Galangal, Galanga, Lille Galangarod

Dutch: Galgant, Kalanswortel

Eastonian: Väike Kalganirohi

French: Galanga Du Chine, Galangal Officinal, Petite Galanga

German: Galgant

Hungarian: Galangál, Kínai Gyömbér

India: Pun-nag-champa (Bengali), Kúlinján (Hindi), Malayavaca (Sanskrit), Cirrarattai, Chitharathai (Tamil)

Italian: Galanga

Korean: Gal Len Gal

Norwegian: Galangarot, Kinarot

Persian: Khusro-Daru

Polish: Galgant Chinski

Russian: Kalgan Lekarstvennyi

Spanish: Galanga

Swedish: Galangarot

Thailand: Kha Ling, Kha Lek

Vietnam: Riêng, Riêng Thuốc, Cao Luong Khuong, Co Kha (Thai), Kim Sung (Dao)

Origin/Distribution

The species is indigenous to southeast China (Guangdong, Guangxi, Hainan) and Indochina. The plant is cultivated in the plains of West Bengal, Assam and Eastern Himalayas in India.

Agroecology

The species is adapted to a warm and humid climate. It prefers shady locations and moist, fertile soil rich in organic matter but will grow in full sun.

Edible Plant Parts and Uses

Alpinia officinarum rhizome is pungent, is aromatic and is used as spice for flavouring food throughout Asian countries (Ly et al. 2003). The rhizome has been used in Europe as a spice for over 1000 years, but it has now largely gone out of use except in Russia and India. Closely resembling ginger, it is used in Russia for flavouring vinegar and the liqueur ‘nastoika’; it is a favourite spice and medicine in Lithuania and Estonia and the Tartars prepare a kind of tea that contains it, and it is used by brewers (Grieve 1971).

Botany

Alpinia officinarum is a perennial rhizomatous herb with elongate, terete, hard, branched, subterranean rhizomes about 2 cm in diameter. Its rhizomes are marked at short intervals by narrow, whitish, somewhat raised rings, which are the scars left by former leaves and are covered with brownish red scales. The inner section shows a dark centre surrounded by a wider, paler layer which becomes darker in drying. Its odour is aromatic, and their taste pungent and spicy. Pseudostems are 40–110 cm high. Leaves are sessile; ligule is lanceolate, entire and membranous (Plate 1). Lamina is linear–lanceolate, 25–40 cm by 2–3 cm wide, glabrous, base attenuate and apex caudate. Inflorescences of its terminal are erect; dense racemes are 10–20 cm long; flowers are numerous; rachis is tomentose; bracteoles are very small, less than 1 cm. Its calyx is tubular and puberulent, and the apex is 3-toothed. Corolla tube is slightly shorter than calyx; lobes are oblong, with the central one hood-like. Its labellum is 2 cm long, white with red streaks and ovate. Ovary is tomentose and is 3-celled. Capsule is red, and globose is 1 cm across.



Plate 1 Lesser galanga plant with pseudostem and leaves

Nutritive/Medicinal Properties

Nutritive composition of *Alpinia officinarum* rhizomes was determined as follows: energy 348.9 cal/100 g, moisture 12.4 %, crude protein 5.25 %, carbohydrate 76.9 %, crude fat 2.26 %, crude fibre 17 %, ash 3.22 %, K 3570 ppm, Ca 438.8 ppm, Na 152.8 ppm, Mg 569.5 ppm, Fe 85.50 ppm, Mn 72.30 ppm, Zn 9.331 ppm, Cu 0.753 ppm, Ni 21.02 ppm and Cr 0.680 ppm (Indrayan et al. 2009).

The following compounds were isolated from the rhizome: 14 flavonoids quercetin, kaempferol, quercetin-3-methylether, isorhamnetin, kaempferid, galangin, galangin-3-methylether, rhamnocitrin and 7-hydroxy-3,5-dimethoxyflavone (Bleier and Chirikdjian 1972); a pungent principle 5-hydroxy-7-(4-hydroxy-3-methoxyphenyl)-1-phenyl-3-heptanone from the root (Inoue et al. 1978); diarylheptanoids 1,7-diphenylhept-4-en-3-one, 7-(4"-hydroxy-3"-methoxyphenyl)-1-phenylhept-4-en-3-one, dihydroyashabushiketol (1,7-diphenyl-5-hydroxy-3-heptanone) and 5-hydroxy-7-(4"-hydroxy-3"-

methoxyphenyl)-1-phenyl-3-heptanone (Itokawa et al. 1981); a diarylheptanoid (3*R*, 5*R*)-1-(4-hydroxyphenyl)-7-phenylheptane-3, 5-diol and known hexahydrocurcumin [1,7-bis(4-hydroxy-3-methoxyphenyl)-1-heptene-3,5-dione] (Uehara et al. 1987); four flavonols, galangin, izalpin, kaempferide and kaempferol; and six diarylheptanoids 7-(4''-hydroxy-3''-methoxyphenyl)-1-phenylhept-4-en-3-one; 1,7-diphenyl-5-hydroxy-3-heptanone; 5-hydroxy-7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3-heptanone; 7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3,5-heptadione; 5-methoxy-7-(4''-hydroxy-3''-methoxyphenyl) 1-phenyl-3-heptanone and 5-hydroxy-7-(4''-hydroxyphenyl)-1-phenyl-3-heptanone (Kiuchi et al. 1992); β -sitosterol, galangin, emodin and quercetin (Luo et al. 1998); β -sitosterol; 1,7-diphenyl-5-ol-3-heptone; 1-phenyl-7-(3'-methoxyl-4'-hydroxyl) phenyl-5-ol-3-heptone; glandin; kaempferol-4'-methylether; 3,4-dihydroxylbenzoic acid and 1-phenyl-7-(3'-methoxyl-4'-hydroxyl) phenyl-5-ol-3-heptone and a new compound 1,7-diphenyl-3,5-heptandiol-phenyl-7-(3'-methoxyl-4'-hydroxyl) phenyl-3,5-heptaxdiol obtained from 1,7-diphenyl-5-ol-3-heptone and 1-phenyl-7-(3'-methoxyl-4'-hydroxyl) phenyl-5-ol-3-heptone via chemical reductions (Bu et al 2000); nine glycosides (1*R*,3*S*,4*S*)-*trans*-3-hydroxy-1,8-cineole β -D-glucopyranoside; benzyl β -D-glucopyranoside; 1-*O*- β -D-glucopyranosyl-4-allylbenzene (chavicol β -D-glucopyranoside; 3-methyl-but-2-en-1-yl β -D-glucopyranoside; 1-hydroxy-2-*O*- β -D-glucopyranosyl-4-allylbenzene; 1-*O*- β -D-glucopyranosyl-2-hydroxy-4-allylbenzene (demethyleugenol β -D-glucopyranoside; 1-*O*-(6-*O*- α -L-rhamnopyranosyl- β -D-glucopyranosyl)-2-hydroxy-4-allylbenzene (demethyleugenol β -rutinoside; 1-*O*-(6-*O*- α -L-rhamnopyranosyl- β -D-glucopyranosyl)-4-allylbenzene (chavicol β -rutinoside; and 1,2-di-*O*- β -D-glucopyranosyl-4-allylbenzene (Ly et al. 2002); four diarylheptanoids, 1,7-diphenylhept-4-en-3-one; dihydroyashabushiketol (1,7-diphenyl-5-hydroxy-3-heptanone); 5-hydroxy-7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3-heptanone; and 5-hydroxy-7-(4''-hydroxyphenyl)-1-phenyl-3-heptanone (Kim et al. 2003); 3-methylether galangin (Shin et al. 2003); 5-hydroxy-7-(4'-hydroxy-3'-methoxyphenyl)-1-phenyl-3-heptanone (Shin et al. 2004); seven phenylpropanoids (*E*)-p-coumaryl alcohol γ -*O*-

methyl ether; (*E*)-*p*-coumaryl alcohol; and stereoisomers of (*4E*)-1,5-*bis*(4-hydroxyphenyl)-1-methoxy-2-(methoxymethyl)-4-pentene (2a and 2b); stereoisomers of (*4E*)-1,5-*bis*(4-hydroxyphenyl)-1-ethoxy-2-(methoxymethyl)-4-pentene (3a and 3b); (*4E*)-1,5-*bis*(4-hydroxyphenyl)-1-[(*2E*)-3-(4-acetoxyphenyl)-2-propenoxy]-2-(methoxymethyl)-4-pentene (4); (*4E*)-1,5-*bis*(4-hydroxyphenyl)-2-(methoxymethyl)-4-penten-1-ol (5); and (*4E*)-1,5-*bis*(4-hydroxyphenyl)-2-(hydroxymethyl)-4-penten-1-ol (Ly et al. 2004); five diarylheptanoids identified as 5-hydroxy-7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3-heptanone; 5-methoxy-7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3-heptanone; 7-(4''-hydroxyphenyl)-1-phenylhept-4-en-3-one; 7-(4''-hydroxy-3''-methoxyphenyl)-1-phenylhept-4-en-3-one; and 1,7-diphenylhept-4-en-3-one (Liu et al. 2005); a glycosidic ester identified as 4'-hydroxy-2'-methoxyphenol- β -D-{6-O-[4''-hydroxy-3'', 5''-dimethoxy (benzoate)]}-glucopyranoside and named as alpinoside A, along with a known compound *n*-butyl- β -D-fructopyranoside (An et al. 2006a); a diarylheptanoid, *trans*-1(3'-methoxy-4'-hydroxyphenyl)-7-phenyl-5-ol-4,6-dien-3-heptanone along with five known diarylheptanoids (An et al. 2006b); two diarylheptanoids [7-(4''-hydroxy-3''-methoxyphenyl)-1-phenylhept-4-en-3-one and 3,5-dihydroxy-1,7-diphenylheptane] and a flavonol constituent (galangin) (Matsuda et al. 2006); galangin and 3-*O*-methyl galangin (Tao et al. 2006); diarylheptanoids 6-hydroxy-1,7-diphenyl-4-en-3-heptanone; 6-(2-hydroxyphenyl)-4-methoxy-2-pyrone; 1,7-diphenyl-4-en-3-heptanone; 1,7-diphenyl-5-methoxy-3-heptanone and apigenin (Fan et al. 2007); four diarylheptanoids (*5S*)-5-hydroxy-7-(3, 4-dihydroxyphenyl)-1-phenyl-3-heptanone; (*5R*)-5-hydroxy-7-(3-methoxy-4, 5-dihydroxyphenyl)-1-phenyl-3-heptanone; (*5R*)-5-hydroxy-1-(3,4-dihydroxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-3-heptanone; and 7-(3,4-dihydroxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)-4-en-3-heptanone (An et al. 2008); a dimeric diarylheptanoid, (*5R,5'R*)-7,7'-(6,6'-dihydroxy-5,5'-dimethoxy[1,1'-biphenyl]-3,3'-diyl)bis[5-methoxy-1-phenylheptan-3-one]; (*4E,6R*)-6-hydroxy-7-(4-hydroxy-3-methoxyphenyl)-1-phenylhept-4-en-3-one; and

(4*E*,6*R*)-6-hydroxy-1,7-diphenylhept-4-en-3-one, together with seven known diarylheptanoids (Sun et al. 2008a); two diarylheptanoids named alpinoid D (1) and E (2), together with 15 known diarylheptanoids (Sun et al. 2008a); four diarylheptanoids 5-hydroxy-1,7-diphenyl-3-heptanone; 7-(4''-hydroxy-3''-methoxyphenyl)-1-phenylhept-4-ene-3-one; 5-hydroxy-7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3-heptanone; and 3,5-dihydroxy-1,7-diphenylheptane and two flavonol constituents (kaempferide and galangin) (Matsuda et al. 2009); a diarylheptanoid bearing flavonol moiety, named officinin A, along with two known compounds galangin and kaempferide (Zhao et al. 2010a); five diarylheptanoids 5-ethoxyl-7-(4-hydroxy-3-methoxyphenyl)-1-phenyl-3-heptanone; 5-hydroxy-1,7-diphenyl-3-heptanone; 5-hydroxy-7-(4-hydroxyl-3-methoxyphenyl)-1-phenyl-3-heptanone; 5-methoxy-7-(4-hydroxy-3-methoxyphenyl)-1-phenyl-3-heptanone; and (*E*)-7-(4-hydroxy-3-methoxyphenyl)-1-phenylhept-4-en-3-one (Zhao et al. 2010b); three diarylheptanoids, officinaruminane A; officinaruminane B; 5(*S*)-acetoxyl-7-(4-dihydroxyphenyl)-1-phenyl-3-heptanone; together with six known ones, (5*R*)-5-hydroxy-1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-3-heptanone; (5*R*)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4,5-dihydroxy-3-methoxyphenyl)-3-heptanone; 1-phenyl-7-(4-hydroxy-3-methoxyphenyl)-4*E*-en-3-heptanone; 1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-4*E*-en-3-heptanone; 1-phenyl-7-(4-hydroxyphenyl)-4*E*-en-3-heptanone; and 3,6-furan-7-(4''-hydroxy-3''-methoxyphenyl)-1-phenylheptane (An et al. 2010); galangin, kaempferide, kaempferide-3-*O*- β -d-glucoside and baicalein (Eumkeb et al. 2010); 23 diarylheptanoids, namely, 5-hydroxy-1-(4-hydroxy-3-methoxylphenyl)-7-(3,4-dihydroxy-5-methoxylphenyl)-3-heptanone; 5-hydroxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-3-heptanone; 5-hydroxy-1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxylphenyl)-3-heptanone; 5-hydroxy-7-(4-hydroxyphenyl)-1-(4-hydroxy-3-methoxylphenyl)-3-heptanone; 5-hydroxy-1,7-bis(4-hydroxy-3-methoxylphenyl)-3-heptanone; 5-hydroxy-1-phenyl-7-(3,4-dihydroxy-5-methoxylphenyl)-3-heptanone; 5-hydroxy-1-

phenyl-7-(3,4-dihydroxyphenyl)-3-heptanone; 3,5-dihydroxy-1-(4-hydroxyphenyl)-7-phenylheptane; 3,5-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-phenylheptane; 1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-4-en-3-heptanone; 5-hydroxy-1-phenyl-7-(4-hydroxyphenyl)-3-heptanone; 5-hydroxy-1-phenyl-7-(4-hydroxy-3-methoxyphenyl)-3-heptanone; 3,5-dihydroxy-1,7-bisphenylheptane; 1-phenyl-7-(4-hydroxyphenyl)-4-en-3-heptanone; 1-phenyl-7-(4-hydroxy-3-methoxyphenyl)-4-en-3-heptanone; 5-hydroxy-1,7-bisphenyl-3-heptanone; 1-(4-hydroxyphenyl)-7-phenylhepta-3,5-dione; 1-(4-hydroxy-3-methoxyphenyl)-7-phenylhepta-3,5-dione; 5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-phenyl-4,6-dien-3-heptanone; 1,7-bisphenyl-4-en-3-heptanone; 1,7-bisphenylhepta-3,5-dione; 5-hydroxy-1,7-bisphenyl-4,6-dien-3-heptanone; and officinaruminane C (Luo et al. 2010); 7-(4'', 5''-dihydroxy-3''-methoxyphenyl)-1-phenyl-4-heptene-3-one; 1,7-diphenyl-5-heptene-3-one and 4-phenethyl-1,7-diphenyl-1-heptene-3,5-dione (Zhang et al. 2010); a dimeric diarylheptanoid, named alpinin A, along with two known compounds, 1,7-diphenyl-5-ol-3-heptanone and 7-(4'-hydroxy-3'-methoxyphenyl)-1-phenyl-4-heptene-3-one (Liu et al. 2012a); a cadinane sesquiterpene, alpiniaterpene A (Xu et al. 2012); a dimeric diarylheptanoid (E)-3-[3-(3-methoxy-4-hydroxyphenyl)prop-1-enyl]-2,4,6-triphenethylpyridine named officinine B (Zhao et al. 2012); four compounds including 5 *R*-hydroxy-7-(4-hydroxy-3-methoxyphenyl)-1-phenyl-3-heptanone, kaempferol-4'-methylether, galangin and 7-(4-hydroxy-3-methoxyphenyl)-1-phenyl-4E-en-3-heptanone (Tan et al. 2013); and two new dimeric diarylheptanoids, named alpinin C and D (2); a new natural product of diarylheptanoid (3) along with three known diarylheptanoids (Liu et al. 2014a); a dimeric diarylheptanoid, named alpinin B, along with three known diarylheptanoids 1,7-diphenyl-3,5-heptanedione; (4*E*)-1,7-diphenylhept-4-en-3-one; and (4*E*)-7-(4-hydroxyphenyl)-1-phenylhept-4-en-3-one (Liu et al. 2014b).

In the fresh rhizome, the main components (over 1.0 % in content) were 1,8-cineole (50.0 %), *exo*-2-hydroxy-1,8-cineole acetate (11.2 %), β -caryophyllene (6.4 %), α - and β -pinenes (1.7 and 2.6 %), β -bisabolene (2.6 %), chavicol (2.0 %),

limonene (2.0 %), 4-terpineol (1.6 %), chavicol acetate (1.2 %), α -terpineol (1.2 %) and methyl eugenol (1.0 %) (Ly et al. 2001). Minor components (<1 %) included verbenol; 2,8-menthadien-1-ol; terpinen-1-ol; *p*-cymen-8-ol; piperitol; *trans*-carveol; chavicol; bornyl acetate; 4-thujen-2 α -yl-acetate; eugenol; citronellyl acetate; geranyl acetate; eugenyl acetate; *trans*-nerolidol; caryophyllene oxide; spathulenol; guaial; 4-hydroxycinnamyl acetate; α -bisabolol; farnesyl acetate and four unknowns. On drying the rhizome, the monoterpene fraction (including hydrocarbon and oxygenated compounds) decreased in content, and the sesquiterpene and aromatic compound fractions increased. Major components of the oil from dried rhizome (over 1.0 % in content) were β -bisabolene (9.6 %), 1,8-cineole (8.2 %), chavicol acetate (5.9 %), chavicol (5.3 %), eugenyl acetate (3.7 %), α -farnesene (3.3 %), methyl eugenol (3.3 %), β -caryophyllene (2.9 %), α -bisabolol (2.6 %), spathulenol (2.5 %), farnesyl acetate (2.4 %), 4-hydroxycinnamyl acetate (2.3 %), 4-terpineol (1.4 %), caryophyllene oxide (1.3 %), guaial (1.2 %), geranyl acetate (1.2 %) and eugenol (1 %). The minor components were linalool; verbenol; 2,8-menthadien-1-ol; terpinen-1-ol; *p*-cymen-8-ol; α -terpineol; piperitol; *trans*-carveol; bornyl acetate; *exo*-2-hydroxy-1,8-cineole acetate; carveol acetate; *trans*-nerolidol; δ -cadinol and 7 unknowns.

From 122.20 mg petroleum ether extract of *A. officinarum*, 5R-hydroxy-7-(4-hydroxy-3-methoxyphenyl)-1-phenyl-3-heptanone (7.37 mg), 7-(4-hydroxy-3-methoxyphenyl)-1-phenyl-4E-en-3-heptanone (9.11 mg) and 1,7-diphenyl-4E-en-3-heptanone (15.44 mg) with purities over 93 % were obtained within 140 min in one-step separation by high-speed countercurrent chromatography under the conditions of a flow rate of 1.5 mL/min and 858 r/min (Ye et al. 2012).

The average recoveries of α -pinene, β -pinene, eucalyptol and α -terpineolin from *A. officinarum* essential oil were 96.2 %, 96.7 %, 98.7 % and 96.7 %, respectively (Zhao et al. 2009). Forty volatile compounds were identified in the rhizome oil extracted by hydrodistillation (Xie et al. 2013). Main compounds were α -farnesene (19.68 %), γ -muurolene (13.33 %), *p*-menth-1-en-8-ol (10.16 %), eucalyptol (6.00 %),

2,6-dimethyl-6-(4-methyl-3-pentenyl)bicyclo[3.1.1]hept-2-ene (5.01 %), isocaryophyllene (3.97 %), cadinol (3.23 %), cadina-1(10),4-diene (3.21 %), caryophyllene (2.76 %), α -calacorene (2.70 %), eudesma-4(14),11-diene (2.67 %) and (Z,Z,Z)-1,5,9,9-tetramethyl-1,4,7-cycloundecatriene (2.62 %). The minor components were 3-carene, camphene, α -pinene, *m*-cymene, limonene, linalool, (1*R*)-endo-(+)-fenchyl alcohol, camphor, borneol, (+)-terpinen-4-ol, fenchyl acetate, benzoic acid, 2-methyl propylester, ylangene, copaene, (–)- β -elemene, phenylethyl butyrate, aristolene, seychellene, 2-isopropenyl-4 α ,8-dimethyl-1,2,3,4,4 α ,5,6,7-octahydronaphthalene, α -muurolene, α -patchoulene, elemene, cubenol, τ -cadinol, τ -muurolol, eudesm-7(11)-en-*p*-ol and *Z*- α -*trans*-bergamotol.

Forty-eight compounds, constituting about 89.4 % of the oil, were identified in *A. officinarum* oil, of which five were present in trace amount (<0.05 %) (Rana et al. 2010). The main compounds were 1,8-cineole (28.3 %), α -fenchyl acetate (15.2 %), carotol (8.9 %), α -terpineol (6.7 %), α -eudesmol (4.5 %), (*E*)-methyl cinnamate (4.0 %), camphor (3.4 %), β -pinene (3.1 %), camphene (2.3 %), borneol (1.7 %), α -pinene (1.2 %) and terpinen-4-ol (1.2 %), along with 31 minor compounds (0.8–0.1 %) 2-heptanol, myrcene, α -phellandrene, α -terpinene, (*Z*)- β -ocimene, (*E*)- β -ocimene, γ -terpinene, *cis*-sabinene hydrate, linalool, α -fenchol, camphene hydrate, methyl thymol, methyl carvacrol, bornyl acetate, α -terpinyl acetate, β -elemene, β -caryophyllene, *trans*- α -bergamotene, valencene, α -humulene, (*E*)- β -farnesene, γ -cadinene, β -sesquiphellandrene, elemol, germacrene B, (*E*)-nerolidol, caryophyllene oxide, γ -eudesmol, β -eudesmol, α -bisabolol and hexadecanoic acid and five trace (< 0.05 %) compounds tricyclene, α -thujene, *p*-cymene, limonene and linalyl acetate. Thirty-two volatile compounds (representing 91.02 % of the total) were identified in the rhizome oil extracted by HS-SPME (headspace solid-phase microextraction) (Xie et al. 2013). The major components included α -farnesene (25.37 %), γ -muurolene (14.02 %), eucalyptol (7.59 %), 2,6-dimethyl-6-(4-methyl-3-pentenyl)bicyclo[3.1.1]hept-2-ene (7.05 %), *p*-m camphor,enth-1-en-8-ol (6.68 %), isocaryophyllene (4.35 %), cadina-1 (10),4-diene (3.89 %), caryophyllene (3.05 %), (Z,Z,Z)-1,5,9,9-tetramethyl-1,4,7-cycloundecatriene (2.73 %),

eudesma-4(14),11-diene (2.67 %) and α -calacorene (2.62 %). The minor components were camphene, linalool, (1R)-endo-(+)-fenchyl alcohol, (1R,2S,3R)-3-isopropenyl-1,2-dimethylcyclopentan-1-ol, borneol, (+)-terpinen-4-ol, fenchyl acetate, benzoic acid, 2-methyl propylester, ylangene, copaene, (-)- β -elemene, phenylethyl butyrate, aristolene, seychellene, 2-isopropenyl-4 α ,8-dimethyl-1,2,3,4,4 α ,5,6,7-octahydronaphthalene, α -muurolene, elemene, cubenol, τ -cadinol and cadinol. Thirty-seven volatile compounds were identified in the rhizome oil extracted by diethyl ether (Xie et al. 2013). The main volatile compounds were as follows: α -farnesene (15.80 %), *p*-menth-1-en-8-ol (13.88 %), benzyl acetone (13.50 %), γ -muurolene (8.91 %), cadinol (4.08 %), eucalyptol (2.95 %), 2,6-dimethyl-6-(4-methyl-3-pentenyl)bicyclo[3.1.1]hept-2-ene (2.44 %), cadina-1(10),4-diene (2.25 %), *Z*- α -trans-bergamotol (2.25) and benzenepropanal (2.20 %). The minor components were camphene, α -pinene, β -phellandrene, γ -terpinene, limonene, terpinene, *p*-mentha-1,4(8)-diene, (1R)-endo-(+)-fenchyl alcohol, camphor, camphene hydrate, borneol, (+)-terpinen-4-ol, benzoic acid, 2-methyl propylester, ylangene, isocaryophyllene, caryophyllene, (*Z,Z,Z*)-1,5,9,9-tetramethyl-1,4,7-cycloundecatriene, α -muurolene, eudesma-4(14),11-diene, butylated hydroxytoluene, α -calacorene, cubenol, τ -cadinol, eudesm-7(11)-en-p-ol, santolol and hexadecanoic acid. Twenty-two common volatile components extracted by hydrodistillation, HS-SPME and diethyl ether extraction were identical. Major compounds identified in the rhizome oils of *A. galanga* and *A. officinarum* were 1,8-cineole (63.4 and 44.2 %), α -terpineol (2.8 and 6.3 %), α -pinene (1.9 and 2.0 %), β -pinene (0.8 and 5.7 %) and terpinen-4-ol (2.8 and 4.5 %), respectively (Raina et al. 2014). Some additional compounds identified in *A. officinarum* oil were camphor (4.0 %) and α -fenchyl acetate (8.9 %), while chavicol (0.9 %), (*E*)- β -farnesene (8.4 %), β -sesquiphellandrene (2.6 %), β -bisabolene (0.3 %) and eugenol acetate (3.3 %) were present in *A. galanga* oil.

Various pharmacological activities of the plant have been reported in scientific studies.

Antioxidant Activity

Methanol aqueous extract of *A. officinarum* was found to have antioxidative activity using Fenton's reagent/ethyl linoleate system (Kim et al. 1997). *Alpinia officinarum* methanol extract using pyrogallol–luminol assay each exhibited better antioxidant activity than the L-ascorbic acid and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Chang et al. 2012). The extract yielded the high total triterpenoid content. Hot and cold hydroalcoholic and methanol extracts of *A. officinarum* rhizome showed a concentration-dependent radical scavenging activity by inhibiting diphenylpicrylhydrazyl (DDPH)-free radical; also the hydroalcoholic extract prepared by hot maceration process showed better reducing and total antioxidant activity (Srividya et al. 2010). *Alpinia officinarum* extract strongly enhanced viability against hydrogen peroxide-induced oxidative apoptosis damage in Chinese hamster lung fibroblast V79-4 cells (Lee et al. 2003). The activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) were dose-dependently enhanced in V79-4 cells treated with the extract.

Seven phenylpropanoids from fresh *A. officinarum* rhizomes included the following: (*E*)-*p*-coumaryl alcohol γ -*O*-methyl ether (1); (*E*)-*p*-coumaryl alcohol (6); and five novel compounds, stereoisomers of (4*E*)-1,5-bis(4-hydroxyphenyl)-1-methoxy-2-(methoxymethyl)-4-pentene (2a and 2b), stereoisomers of (4*E*)-1,5-bis(4-hydroxyphenyl)-1-ethoxy-2-(methoxymethyl)-4-pentene (3a and 3b), (4*E*)-1,5-bis(4-hydroxyphenyl)-1-[(2*E*)-3-(4-acetoxyphenyl)-2-propenoxy]-2-(methoxymethyl)-4-pentene (4), (4*E*)-1,5-bis(4-hydroxyphenyl)-2-(methoxymethyl)-4-penten-1-ol (5) and (4*E*)-1,5-bis(4-hydroxyphenyl)-2-(hydroxymethyl)-4-penten-1-ol (7) which exhibited antioxidative activities against the autoxidation of methyl linoleate in bulk phase (Ly et al. 2003; Ly et al. 2004).

Cytotoxic/Antitumour Activities

The acetone extract of *Alpinia officinarum* rhizome was found to have 5- α -reductase inhibitory activity (Kim et al. 2003). The fraction responsible for the inhibition of the enzyme was purified and analysed, and the active constituents were identified as four diarylheptanoids, 1,7-diphenylhept-4-en-3-one; dihydroyashabushiketol (1,7-diphenyl-5-hydroxy-3-heptanone); 5-hydroxy-7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3-heptanone; and 5-hydroxy-7-(4''-hydroxyphenyl)-1-phenyl-3-heptanone. Thai *Alpinia galanga* and *Alpinia officinarum* exhibited interesting cytotoxicity activity against two human cancer cell lines, COR L23 lung cancer and MCF7 breast cancer cell lines (Lee and Houghton 2005). Following bioassay-guided fractionation, 1'-acetoxychavicol acetate (48-h exposure against COR L23 cells, IC₅₀ 7.8 μ M against MCF7 cells, IC₅₀ 23.9 μ M) was isolated as the major cytotoxic component of the *Alpinia* species. Extracts of *Alpinia officinarum* induced glutathione-S-transferase (GST) activity in cultured hepatocytes, and this was traced to the phenylpropanoids present, especially 1'-acetoxychavicol acetate (Houghton et al. 2007).

Ethanol extracts of *Alpinia galanga* and *Alpinia officinarum* inhibited growth of PC-3 prostate cancer cell line in-vitro (Suja and Chinnaswamy 2008). DNA fragmentation where a characteristic DNA laddering was noticed in treated tumour cell line and not in the untreated control cells.

The methanol rhizome extract of *A. officinarum* exhibited remarkable antitumour-promoting activity on an in-vivo two-stage carcinogenesis test of mice using 7,12-dimethylbenz[*a*]anthracene as an initiator and 12-*O*-tetradecanoylphorbol-13-acetate (TPA) as a promoter (Yasukawa et al. 2008). Seven diarylheptanoids isolated from the active fraction of the methanol extracts showed marked anti-inflammatory effects, with a 50 % inhibitory dose of 0.8–2.7 μ mol/ear. *Alpinia officinarum* methanol extract inhibited human breast cancer cell line MCF-7 cell proliferation in a dose- and time-dependent manner and induced cell apoptosis (Ghil 2013). The extract also inhibited S-phase cell cycle progression by suppressing the expression levels of S-phase cell cycle regulatory proteins, including E2F1, cyclin-

dependent protein kinase 2 and cyclin A. The methanol, chloroform and dichloromethane extracts of *Alpinia officinarum* leaves and rhizomes maintained clear antiproliferative activities on THP-1 AMoL (human acute monocytic leukaemia) cells in-vitro over a 48-h period (Omoriege et al. 2013). Fractions 9 and 16 of the methanol extracts, respectively, showed the greatest antiproliferative activities. *Alpinia officinarum* extract showed cytotoxic activity against human hepatoma SMMC-7721 cells in a dose-dependent manner (Lu et al. 2013).

Diarylheptanoid 7-(3,4-dihydroxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)-4-en-3-heptanone from the rhizome exhibited moderate cytotoxicity against human tumour cell lines, HepG2, MCF-7 and SF-268, while no significant effect was found for the other three diarylheptanoids (An et al. 2008). Sun et al. (2008b) reported that several diarylheptanoids (11, 12 and 14) exhibited potent activities against IMR-32 human neuroblastoma cell line with IC₅₀ values of 0.83, 0.23 and 0.11 µM, respectively. Two diarylheptanoids derived from *Alpinia officinarum*, 7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-4E-hepten-3-one (compound 1) and (5R)-5-methoxy-7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3-heptanone (compound 2), were demonstrated to have potent cytotoxicity (Tabata et al. 2009). Both diarylheptanoids showed significant cytotoxicity against neuroblastoma cell lines (IMR-32, SK-N-SH, NB-39). The compounds induced nuclear shrinkage and fragmentation and activated caspase-3 and caspase-9. They induced S-phase cell cycle arrest concurrently with an increased sub-G1 cell population. Additionally, a low concentration (10 – 8 M) of compound 1 induced significant neurite branching in the NB-39 cell line. The results suggested that the two compounds may be useful for the treatment of patients with neuroblastoma. In another study, the diarylheptanoid 1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)-4E-en-3-heptanone, from *A. officinarum*, exhibited potent cytotoxicity in neuroblastoma cell line SH-SY5Y (Tian et al. 2009). The compound induced S-phase arrest and apoptosis via upregulation of ATF3 and stabilisation of p53 in SH-SY5Y cell line. Alpinin C from the rhizome

showed selective cytotoxicity against human cancer cell lines of MCF-7 and T98G, while diarylheptanoid compound 6 showed significant cytotoxicity to the all HepG2, MCF-7, T98G and B16-F10 tumour cell lines with IC₅₀ in the range from 8.46 to 22.68 µmol/L (Liu et al. 2014a). The diarylheptanoid (4E)-1,7-diphenylhept-4-en-3-one showed cytotoxicity against the human glioblastoma T98G cell line with IC₅₀ of 27 µmol/L (Liu et al. 2014b).

The study by Zhang et al. (2012) demonstrated that galangin, from *A. officinarum*, induced apoptosis in hepatocellular carcinoma cells by activating caspase 8/t-Bid mitochondrial pathway. Su et al. (2013) found that galangin acted as a stimulator of endoplasmic reticulum stress to suppress the proliferation of hepatocellular carcinoma cells and may be used as a potential anticancer agent. This was evidenced by increased protein levels of GRP94, GRP78 and CHOP, as well as increased free cytosolic Ca(2+) concentration. Zhang et al. (2013c) reported that proliferation of melanoma B16F10 cells was suppressed when exposed to various doses of galangin. Galangin suppressed the transcription of focal adhesion kinase (FAK) gene; molecular data showed that both FAK mRNA level and protein level were reduced dose-dependently. The antimetastatic function of galangin was further evident by the fact that it could inhibit the formation of tumour colonies in the lung tissue on C57BL/6 J mouse lung metastatic model using B16F10 melanoma cells. They also found that galangin significantly decreased cell viability of B16F10 melanoma cells and also induced cell apoptosis (Zhang et al. 2013b). Galangin activated apoptosis signalling cascades by cleavage of procaspase-9, procaspase-3 and PARP in B16F10 cells and significantly induced activation of phosphor-p38 MAPK in a time- and dose-dependent manner. Zhang et al. (2013a) found that galangin inhibited proliferation of HepG2 cells by activating adenosine monophosphate-activated protein kinase (AMPK) via increasing the AMP/TAN ratio independent of the liver kinase B1 (LKB1) signalling pathway and inducing autophagy. Ha et al. (2013) found that galangin induced apoptosis and DNA condensation of human colon (HCT-15 and HT-29) cancer

cells in a dose-dependent manner. Galangin increased the activation of caspase-3 and caspase-9 and release of apoptosis-inducing factor from the mitochondria into the cytoplasm and induced human colon cancer cell death through the alteration of mitochondria membrane potential and dysfunction.

Antimicrobial Activity

The 40 % ethanol extract of *A. officinarum* rhizome inhibited *Staphylococcus aureus*, α -haemolytic *Streptococcus*, β -haemolytic *Streptococcus* and *Streptococcus pneumoniae* (Huang et al. 2008). The lesser galangal extract inhibited β -ketoacyl-ACP reductase (FabG), a key enzyme in type II fatty acid synthase system in bacteria, with an IC₅₀ value of only 4.47 μ g/mL, and was more potent than other previously published inhibitors. The lesser galangal ethanol extract could inhibit FabG irreversibly. *Alpinia officinarum* rhizome extract exhibited higher antibacterial activity in-vitro against *Staphylococcus aureus* than against *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* (Indrayan et al. 2009). Hot and cold hydroalcoholic and methanol extract of *A. officinarum* rhizome showed moderate to potent antimicrobial activity against the *Bacillus cereus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* (Srividya et al. 2010). None of the extracts showed antifungal activity against *Aspergillus niger* and *Candida albicans*. *Alpinia officinarum* showed antimicrobial activity against *Escherichia coli*, *Candida albicans* and *Bacillus subtilis* with MIC values of 13.33, 8.33 and 3.33 μ g/mL, respectively (Lu et al. 2013).

The diarylheptanoid (5-hydroxy-7-(4"-hydroxy-3-methoxyphenyl)-1-phenyl-3-heptanone) isolated from *Alpinia officinarum* showed inhibitory and bactericidal activity against enteropathogenic *Escherichia coli* clinical isolates and efficiently suppressed their lipopolysaccharide-induced inflammation in human peripheral blood mononuclear cells (Subramanian et al. 2009). In silico docking analysis revealed that the diarylheptanoid could interact with subunit A of *E. coli* DNA gyrase. Such molecules with bifunctional activities (antibacterial and anti-inflammatory) may be potential

therapeutics for infectious diseases. Three diarylheptanoids, 7-(4'',5''-dihydroxy-3''-methoxyphenyl)-1-phenyl-4-heptene-3-one; 1,7-diphenyl-5-heptene-3-one; and 4-phenethyl-1,7-diphenyl-1-heptene-3,5-dione, isolated from the rhizomes, showed antibacterial activity against *Helicobacter pylori* (Zhang et al. 2010); the three new compounds showed strong antibacterial activity against *Helicobacter pylori* Sydney strain 1 with the MIC values of 9–12 µg/mL and against *Helicobacter pylori* F44 with the MIC values of 25–30 µg/mL. Recent studies by Deveci et al. (2013) found that Ankaferd blood stopper® (ABS), a mixture of plant extracts prepared from *Alpinia officinarum*, *Glycyrrhiza glabra*, *Thymus vulgaris*, *Urtica dioica* and *Vitis vinifera*, is effective in-vitro against *Mycobacterium tuberculosis* strains.

Lee et al. (2008) showed that the combination of galangin with gentamicin exerted a synergistic effect against methicillin-resistant *Staphylococcus aureus*. The fractional inhibitory concentrations (FICs) of galangin, in combination with gentamicin, against 3 test strains were 0.4, 3.9 and 250 µg/ml. The FIC index showed marked synergism in the value range of 0.19–0.25. In another study, synergistic FIC indices were observed in the combination of *A. officinarum* flavonoids (galangin, quercetin and baicalein) and all selected β-lactam antibiotics (methicillin, ampicillin, amoxicillin, cloxacillin, penicillin G and ceftazidime) (FIC index, < 0.02–0.11) (Eumkeb et al. 2010). The combination of ceftazidime at 5 and 5 µg/ml of test flavonoids (galangin, quercetin and baicalein) exhibited synergistic effect by reducing the cfu/ml of *Staphylococcus aureus*-resistant strain to 1×10^3 over 6 and throughout 24 h. Galangin showed marked inhibitory activity against penicillinase and β-lactamase. The combination of galangin and ceftazidime caused damage to the ultrastructures of the cells of this strain. It was concluded that galangin, quercetin and baicalein exhibited the potential to reverse bacterial resistance to β-lactam antibiotics against penicillin-resistant *S. aureus* (PRSA). The results suggested the potential of using galangin, quercetin and baicalein as phytopharmaceuticals in combination with ceftazidime to treat PRSA. Ethanolic leaf extract of *A. officinarum* exhibited

greater inhibition in-vitro against *Proteus vulgaris* followed by *Vibrio cholerae*, and moderate inhibition was noted against *Staphylococcus aureus* and *Klebsiella pneumoniae* (Xavier and Agatheeswaran 2010).

Ray and Majumdar (1975, 1976) reported an antifungal flavonoid from *A. officinarum*. *Alpinia officinarum* rhizome extract exhibited antifungal activity against *Candida albicans* (Klahan et al. 2011). The minimum inhibitory concentration (MIC) and minimal fungicidal concentration (MFC) values were 1.2 mg/ml and 2.0 mg/ml, respectively. SEM analysis showed that the extract induced deformation of *Candida albicans*. The treated cells had coarse surface and changed from oval to rounder shape. The result suggested that the extract damaged cell wall, causing *Candida albicans* to form spheroplast. The ethanol, acetone and hexane extracts of *A. officinarum* inhibited growth in-vitro of the fungus, *Candida albicans*, pathogen of mycotic vaginitis, by more than 50 % (Liu et al. 2012b).

Antiviral Activity

Ten diarylheptanoids exhibited potential antiviral activity against influenza virus in-vitro; in particular, the influenza virus was more susceptible to 7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-4*E*-hepten-3-one and (5*S*)-5-hydroxy-7-(4''-hydroxyphenyl)-1-phenyl-3-heptanone than the other diarylheptanoids (Sawamura et al. 2010b). In further studies, they found that 7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-4*E*-hepten-3-one had a different anti-influenza virus action to that of oseltamivir and was verified to show anti-influenza activity in-vitro and in-vivo (Sawamura et al. 2010a). At 100 mg/kg, it was significantly effective in reducing the body weight loss and prolonging survival times of infected mice without toxicity. It exhibited anti-influenza virus activity against all viruses used such as wild types of influenza viruses A/PR/8/34 (H1N1), oseltamivir-resistant A/PR/8/34 (H1N1), A/Bangkok/93/03 (H1N1), A/Ishikawa/7/82 (H3N2), A/Fukushima/13/43 (H3N2), B/Singapore/222/79 and B/Fukushima/15/93 strains in-vitro.

Seven of the nine diarylheptanoids isolated from *A. officinarum* rhizomes exhibited potential antiviral activity against respiratory syncytial virus (RSV), and most of the diarylheptanoids with anti-RSV activity, including two diarylheptanoids without anti-RSV activity, were also effective against poliovirus, measles virus and/or herpes simplex virus type 1 (HSV-1) in-vitro (Konno et al. 2011). Konno et al. (2013) synthesised an enantiomer (5*R*)-5-hydroxy-7-(4-hydroxyphenyl)-1-phenylhept-3-one (AO-0503) of (5*S*)-5-hydroxy-7-(4-hydroxyphenyl)-1-phenylhept-3-one (AO-0011) and racemate(5*RS*)-5-hydroxy-7-(4-hydroxyphenyl)-1-phenylhept-3-one (AO-0504) of (5*S*)-5-hydroxy-7-(4-hydroxyphenyl)-1-phenylhept-3-one (AO-0011) and an enantiomer (5*R*)-5-methoxy-1,7-diphenylhept-3-one (AO-0514) of (5*S*)-5-methoxy-1,7-diphenylhept-3-one (AO-0016). The three stereoisomers (AO-0503, AO-0504 and AO-0514) and AO-0011 exhibited significant anti-RSV activity in a plaque reduction assay using human epidermoid carcinoma cells. All four diarylheptanoids with anti-RSV activity in-vitro were also significantly effective in reducing virus titers in the lungs of RSV-infected mice. In the histopathological analysis of RSV-infected lungs, the oral administration of even AO-0514, which showed the lowest reduction of virus titers in the lungs, was significantly effective in reducing the infiltration of lymphocytes and in reducing the interferon- γ level, a marker of severity of pneumonia due to RSV infection, in bronchoalveolar lavage fluids prepared from RSV-infected mice. All four diarylheptanoids examined were suggested to ameliorate pneumonia and to have a potential anti-RSV activity in-vivo.

Anti-inflammatory Activity

Hot aqueous *Alpinia officinarum* rhizome extract significantly inhibited prostaglandin biosynthesizing enzyme (PG synthetase) (Kiuchi et al. 1992). Its chloroform fraction inhibited PG synthetase by 99 % at 150ug/ml concentration. Four flavonols, galangin, izalpin, kaempferide and kaempferol, and six diarylheptanoids 7-(4''-hydroxy-3''-methoxyphenyl)-1-phenylhept-4-en-3-one; 1,7-diphenyl-5-

hydroxy-3-heptanone; 5-hydroxy-7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3-heptanone; 7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3,5-heptadione; 5-methoxy-7-(4''-hydroxy-3''-methoxyphenyl)-1-phenyl-3-heptanone and 5-hydroxy-7-(4''-hydroxyphenyl)-1-phenyl-3-heptanone were isolated from the active chloroform fraction. The compounds were also active against arachidonate 5-lipoxygenase, an enzyme of leukotriene biosynthesis.

The diarylheptanoid 7-(4'-hydroxy-3'-methoxyphenyl)-1-phenylhept-4-en-3-one from *A. officinarum* significantly inhibited lipopolysaccharide (LPS)-stimulated nitric oxide (NO) production in mouse macrophage cell line (RAW 264.7) (Yadav et al. 2003). This compound also inhibited the release of LPS-induced pro-inflammatory cytokines interleukin-1 β (IL-1 β) and tumour necrosis factor- α (TNF- α) from human peripheral blood mononuclear cells (PBMCs) in-vitro. The inhibition of pro-inflammatory mediators was via inhibition of mitogen-activated protein kinase, p44/42 and transcription factor nuclear factor- κ B. Two diarylheptanoids [7-(4''-hydroxy-3''-methoxyphenyl)-1-phenylhept-4-en-3-one and 3,5-dihydroxy-1,7-diphenylheptane] and a flavonol constituent (galangin) substantially inhibited lipopolysaccharide-induced NO production in mouse peritoneal macrophages with IC₅₀ values of 33–62 μ M (Matsuda et al. 2006). Six diarylheptanoids were isolated from *A. officinarum* rhizome as inhibitors of nitric oxide (NO) production in the lipopolysaccharide-activated macrophage cell line RAW 264.7 (Lee et al. 2006). In addition, the active diarylheptanoids suppressed expression of the inducible NO synthase protein and mRNA. The results implied that the traditional use of *Alpinia officinarum* rhizome as anti-inflammatory drug may be partially explained by the inhibition of NO production in activated macrophages.

An 80 % ethanolic *A. officinarum* rhizome extract showed acute anti-inflammatory activity; it reduced the oedema volume in carrageenan-stimulated arthritis in rats and inhibited NO generation in LPS-induced RAW 264.7 cells (Lee et al. 2009). Further this extract showed chronic antirheumatic and analgesic activities by suppressing the swelling volume, by

recovering the paw withdrawal latency and by inhibiting the flexion scores in complete Freund's adjuvant (CFA)-induced arthritis. The extract also displayed an anti-psychiatric effect through control of the expression of the c-Fos protein of the brain hippocampus in CFA-stimulated arthritis.

Hypolipidemic/Antihyperlipidemic Activity

In-Vitro Studies

A pancreatic lipase inhibitor, 5-hydroxy-7-(4'-hydroxy-3'-methoxyphenyl)-1-phenyl-3-heptanone (HPH), from *A. officinarum* rhizome exhibited antihyperlipidemic activity (Shin et al. 2004). HPH inhibited a pancreatic lipase with an IC_{50} value of 1.5 mg/ml (triolein as a substrate). HPH significantly lowered the serum TG level in corn oil feeding-induced triglyceridemic mice and reduced serum triglyceride (TG) and cholesterol in Triton WR-1339-induced hyperlipidemic mice. However, HPH did not show hypolipidemic activity in high-cholesterol diet-induced hyperlipidemic mice.

Another study showed that *A. officinarum* extract (GE) could potentially inhibit fatty acid synthase (FAS) (Li and Tian 2003). The inhibition consisted of both reversible inhibitions with an IC_{50} value of 1.73 μ g dried GE/ml and biphasic slow-binding inactivation. The inhibition of FAS by galangin, quercetin and kaempferol, which are the main flavonoids present in the extract, namely, galangin, quercetin and kaempferol, exhibited no obvious slow-binding inactivation, but quercetin and kaempferol had potent reversible inhibitory activity.

Animal Studies

Aqueous rhizome extract and its ethyl acetate fraction significantly inhibited the serum triglyceride level in corn oil feeding-induced triglyceridemic mice and serum triglyceride and cholesterol in Triton WR-1339-induced hyperlipidemic mice (Shin et al. 2003). 3-Methylether galangin was isolated from the fraction as an inhibitor of pancreatic lipase with an

IC₅₀ value of 1.3 mg/ml (triolein as a substrate). However, this compound and the ethyl acetate fraction did not show hypolipidemic activity in high-cholesterol diet-induced hyperlipidemic mice. The results suggested that the hypolipidemic activity of extract and 3-methylethergalangin was due to the inhibition of pancreatic lipase. Animal studies showed that intake of *A. officinarum* ethanolic extract significantly lowered compared to rats fed with a high-fat diet (HFD) (Xia et al. 2010). The extract also improved the lipid profile in serum and the pathological changes in liver and adipose tissue and decreased the relative weights of epididymal and perirenal white adipose tissues. The extract improved lipid profile by lowering serum total-C, TG and LDL-C concentrations, leptin content and the atherogenic index compared with the HFD group. The HDL-C concentration and the ratio of HDL-C/total-C significantly increased compared with those of the HFD rats. Beattie et al. (2011) found that increased adiposity in the high-fat control mice group, compared with the low-fat control group, was significantly reduced in the mice administered with *A. officinarum* rhizome extract, without food intake being affected. Acetyl-coenzyme A acyltransferase 1 and enoyl-CoA hydratase, which participate in the β -oxidation of fatty acids, were significantly increased by consumption of phytochemical-supplemented diets.

Jung et al. (2012) reported that *A. officinarum* ethanol extract dose-dependently suppressed lipid accumulation during differentiation of 3 T3-L1 preadipocytes by downregulating CCAAT (cytidine–cytidine–adenosine–adenosine–thymidine) enhancer-binding protein- α (C/EBP α), sterol regulatory element binding protein-1 (SREBP-1) and peroxisome proliferator-activated receptor- γ (PPAR- γ) genes. Galangin, a major component of *A. officinarum*, had been reported to have antiadipogenic effects in 3T3-L1 cells. Supplementation of the extract in mice fed with a high-fat diet (HFD) revealed that the extract significantly decreased HFD-induced increases in body, liver and white adipose tissue weights and decreased serum insulin and leptin levels. It was found that *Alpinia* extract efficiently suppressed protein expressions of C/EBP α ,

fatty acid synthase, SREBP-1 and PPAR- γ in the liver and adipose tissue and may have potential for use as an antiobesity therapeutic agent.

Clinical Studies

In a study of 69 obese and 103 nonobese participants, after treatment of peripheral blood mononuclear cells with *A. officinarum* extract, macrophage migration inhibitory factor (MIF) expression differed according to MIF genotype (Mirzaei et al. 2012). The extract was found to be major modulator of MIF-dependent pathologic conditions in obesity and was consistent with mounting evidence that defined a regulating role for MIF in cytokine production in an inflammatory state in in-vitro studies.

Antiplatelet Activity

All three diarylheptanoids from the rhizome, 6-hydroxy-1,7-diphenyl-4-en-3-heptanone; 1,7-diphenyl-4-en-3-heptanone; and 1,7-diphenyl-5-methoxy-3-heptanone, exhibited potent PAF (platelet-activating factor) receptor binding inhibitory activities with an IC₅₀ of 1.3, 5.0 and 1.6 μ M, respectively (Fan et al. 2007).

Anti-acetylcholinesterase Activity

Among all the tested flavonoids, galangin, a flavonol isolated from *Alpinia officinarum* rhizome, showed an inhibitory effect on acetylcholinesterase activity with the highest inhibition by over 55 % and an IC₅₀ of 120 μ M and an enzyme-flavonoid inhibition constant (K_i) of 74 μ M (Guo et al. 2010). The results suggested that flavonoids from *A. officinarum* could be potential candidates for further development of new drugs against Alzheimer's disease.

Antiemetic Activity

Alpinia officinarum was reported to possess antiemetic constituents, namely, a flavonoid, several diarylheptanoids and

a steroid (Shin et al. 2002). A new compound determined as 5-hydroxy-7-(4-hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)-3-heptanone also displayed antiemetic activity in a copper sulphate-induced emesis assay in young chicks.

Melanogenesis Inhibitory/Antityrosinase Activity

The flavonoid mixture of *A. officinarum* and galangin reduced melanin content in B16 mouse melanoma cells to 1.276 $\mu\text{g}/10^5$ cell and 1.61 $\mu\text{g}/10^5$ cell, respectively, while the melanin control was 1.632 $\mu\text{g}/10^5$ cell (Lu et al. 2007). Both flavonoid mixture and galangin reduced melanin production with an inhibition of 21.81 % and 28.86 % at a concentration of 26.5 $\mu\text{g}/\text{mL}$ and 29 $\mu\text{g}/\text{mL}$ (107.4 μM), respectively. Tyrosinase inhibition by the flavonoid mixture and galangin was higher at lower concentrations, and galangin showed competitive inhibition at a concentration less than 21.23 $\mu\text{g}/\text{mL}$ which was soluble. In addition, the flavonoid mixture and galangin showed a broad absorption band at 270 ~ 290 nm related to the UV-B area. The observations suggested that galangin may be a whitening agent and a promising candidate for prevention of skin cancer.

The 80 % aqueous acetone rhizome extract of *Alpinia officinarum* inhibited melanogenesis in theophylline-stimulated murine B16 melanoma 4A5 cells (Matsuda et al. 2009). Among the constituents isolated, four diarylheptanoids [5-hydroxy-1,7-diphenyl-3-heptanone, 7-(4(")-hydroxy-3(")-methoxyphenyl)-1-phenylhept-4-en-3-one, 5-hydroxy-7-(4(")-hydroxy-3(")-methoxyphenyl)-1-phenyl-3-heptanone and 3,5-dihydroxy-1,7-diphenylheptane] and two flavonol constituents (kaempferide and galangin) inhibited melanogenesis with IC_{50} values of 10–48 μM . Further, 7-(4(")-hydroxy-3(")-methoxyphenyl)-1-phenylhept-4-en-3-one, kaempferide and galangin inhibited mRNA expression of tyrosinase and tyrosinase-related proteins 1 and 2 and the protein level of a microphthalmia-associated transcription factor.

Anti-vitiligo Activity

Studies showed that 30-day treatment with galangin, the main active component of *Alpinia officinarum*, was able to improve vitiligo induced by hydroquinone in mice, with the ameliorative activity related to increased concentrations of tyrosinase, expression of tyrosinase protein and decreased activity of malondialdehyde and content of cholinesterase (Huo et al. 2014). The number of skin basal layer melanocytes and melanin-containing epidermal cells had also increased significantly with the application of 4.25 mg/kg of galangin.

Antigenotoxic Activity

Galangin from *A. officinarum* with antioxidative and free radical scavenging activities was found capable of modulating enzyme activities and suppressing the genotoxicity of chemicals (Heo et al. 2001).

Percutaneous Permeation-Enhancing Activity

Alpinia officinarum rhizome essential oil (1 %, 3 %) was found to effectively enhance the permeation and percutaneous absorption of 5-fluorouracil (Shen et al. 2000).

Antihaemorrhagic Activity

Ankaferd blood stopper (ABS) is a traditional folkloric medicinal product that has been approved in the management of external haemorrhage and dental surgery bleedings in Turkey (Kosar et al. 2009). It is a herbal mixture of six plant ingredients *Thymus vulgaris*, *Glycyrrhiza glabra*, *Vitis vinifera*, *Alpinia officinarum* and *Urtica dioica*. Their studies showed that in acetylsalicylic acid-treated animals, topical ABS reduced both the duration and also the amount of bleeding volume by 68.4 and 54.6 %, respectively. It was also effective in shortening the duration of bleeding (30.6 %) and decreasing the amount of bleeding (32.8 %) in enoxaparin-treated animals. Purnak et al. (2011) successfully treated

endoscopically a case of upper gastrointestinal bleeding in a patient with defective haemostasis with Ankaferd blood stopper as an adjunctive medicine. According to Beyazit et al. (2011), Ankaferd blood stopper (ABS) offers a successful candidate for gastrointestinal bleeding. ABS was found to modulate the cellular apoptotic responses to hemorrhagic stress, as well as haemostatic hemodynamic activity. Through its effects on the endothelium, blood cells, angiogenesis, cellular proliferation, vascular dynamics and wound healing, ABS could become an effective alternative haemostatic medicine for gastrointestinal bleedings. Studies by Karabıyık et al. (2012) found that ABS had dual diverse dynamic reversible effects on endothelial cell protein C receptor (EPCR) and plasminogen activator inhibitor type-1 (PAI-1) expression in human umbilical vein endothelial cells (HUVECs) in the presence and absence of lipopolysaccharides (LPSs). Recent clinical studies by Eyi et al. (2013) on pregnant women found that the application of 4 ml of ABS instead of isotonic saline solution lessened bleeding during episiotomy. Phase I randomised, double-blinded, crossover, placebo-controlled clinical studies on the management of critical bleedings due to haemorrhagic diathesis in healthy volunteers indicated the safety of ABS (Turgut et al. 2011; Balcik et al. 2012). Studies in Wistar albino rats showed that Ankaferd (Ankaferd blood stopper®, ABS) may support colon anastomotic healing in septic conditions (Cancan et al. 2014). Topical ABS application controlling the mucosal bleeding at the cut ends of the colon may also improve the anastomotic wound healing by means of increasing mechanical strength and positively affecting angiogenesis.

Erectile Dysfunction Ameliorating Activity

Alpinia officinarum extract was one of the several Iranian plants with aphrodisiac effect for erectile dysfunction exhibiting significant dose-dependent cAMP and cGMP phosphodiesterase inhibitory activities in comparison to control and sildenafil (Khanavi et al. 2012).

Traditional Medicinal Uses

Alpinia officinarum has been used both in Ayurvedic and Chinese medicine since very early times (circa AD 500 in China) and in Europe since the Middle Ages (Bown 1995). The rhizome is reported to be a very effective herb that acts mainly on the digestive system, also relieves pain, lowers fevers and controls bacterial and fungal infections. It is given to young children to make them talk early. Lesser galangal has been known in Europe for centuries as a spice and medicine (Grieve 1971). It is a stimulant and carminative. It is especially useful in flatulence, dyspepsia, vomiting and sickness at stomach, being recommended as a remedy for sea sickness. It tones up the tissues and is sometimes prescribed in fever. Homoeopaths use it as a stimulant. The powder is used as a snuff for catarrh. Gao liang jiang, *Rhizoma Alpinia officinarum*, is the dry root stock of *A. officinarum* Hance collected in late summer and early fall; it is used for the treatment of dyspepsia, gastralgia and emesis (Tang and Eisenbrand 1992).

Alpinia officinarum, a well-known traditional Chinese medicine, has been used as an aromatic stomachic, analgesic and antiemetic in Asia (Tao et al. 2006). As a traditional Chinese herb, the rhizome of *Alpinia officinarum* has been used in China for relieving stomach ache, treating colds, invigorating the circulatory system and reducing swelling (Luo et al. 2010). The dry root and rhizome of *Alpinia officinarum* has long been used in traditional Chinese medicine for its antioxidation, antidiabetic, antiulcer, antidiarrhoea, antiemetic, analgesia, anti-inflammatory and anticoagulation effects (Xie et al. 2013). *Alpinia officinarum* has been used in traditional medicine for the treatment of several conditions, such as abdominal pain, emesis, diarrhoea, impaired renal function and dysentery (Jung et al. 2012). Its rhizomes are used as stomachic, analgesic and antiemetic (Zhao et al. 2012). In Vietnam juice from the boiled rhizome is used to stimulate digestion and treat stomach ache and malaria (Nguyen et al. 2014). Crushed rhizome in wine or vinegar is used topically for ringworm skin infections.

Other Uses

The reddish-brown powder from the rhizome is used as snuff, and in India the oil is valued in perfumery.

Comments

The plant is propagated by division of rhizomes and seeds.

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Alpinia zerumbet

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ScientificName

Alpinia zerumbet (Pers.) B. L. Burtt and R. M. Smith

Synonyms

Alpinia cristata Griff., *Alpinia fimbriata* Gagnep., *Alpinia fluvialis* Hayata, *Alpinia nutans* var. *longiramosa* Gagnep., *Alpinia schumanniana* Valetton, *Alpinia speciosa* (J. C. Wendl.) K. Schum. nom. illeg., *Amomum nutans* (Andrews) Schult., *Catimbium speciosum* (J.C.Wendl.) Holttum, *Costus zerumbet* Pers. (Basionym), *Languas schumanniana* (Valetton) Sasaki, *Languas speciosa* (J.C.Wendl.) Small, *Renealmia nutans* Andrews, *Renealmia spectabilis* Rusby, *Zerumbet speciosum* J.C.Wendl.

Family

Zingiberaceae

Common/English Names

Bright Ginger, Butterfly Ginger, Light Galangal, Pink Porcelain Lily, Pink Shell *Heliconia*, Shell Flower, Shell Ginger, Shell Plant, Variegated Ginger, Variegated Shell Ginger

Vernacular Names

Brazil: Colônia

Chinese: Chui hu Shaina jiang, Da Cao Kou, Yàn Shānjiāng, Yuetao

Cook Islands: Kaopu‘I, Kaopui, Kōpī ‘Ehua (Maori)

French: Atoumau (Martinique)

German: Martinique-Ingwer, Porzellan-Ingwerlilie

Hawaiian: Awapuhi-Leheluhe

India: Punag Champa (Bengali), Banada, Narkchur (Hindi), Mailanchi (Malayalam), Stulagrandhi, Vanardraka (Sanskrit)

Indonesia: Galoba Merah, Goloba Koi, Langkuas Laki-Laki (Moluccas)

Japanese: Gettō, Sannin (Okinawan)

Malaysia: Tepus Kampong

Philippines: Langkawas Na Pula, Langkuas Na Pula (Tagalog)

Russian: Al’piniia Prekrasnaia

Samoa: Kōpī ‘Ehua; Teuila

Swedish: Jättegalarangrot

Thai: Kha Khom

Tonga: Kavapui, Kōpī ‘Ehua; Teuila

Vietnamese: Gừng âm, Riêng âm, Riêng Đẹp, Sẹ Nước

Origin/Distribution

The species is native to eastern Asia—South Japan to Taiwan and South China to Northern Peninsula, Malaysia (Govaert et al. 2010).

Agroecology

In its native range, it occurs in humid natural forests, riparian zones and wetlands. It thrives in full sun to partial shade. The plant can tolerate cold winter temperatures but need warmth and humidity in summer and well-drained, humus-rich, moist soils. Frost and sub-zero temperatures are detrimental and can burn or kill the plant. The plant will grow in slightly alkaline to acidic soils on clays, sands or loams. It is moderately drought tolerant but has poor salt tolerance.

Edible Plant Parts and Uses

Alpinia zerumbet rhizome is used as spice like *Alpinia galanga* (Seidemann 2005). It has a high value all over the world as a spice in culinary preparations and for its medicinal properties (Victório et al. 2009b). Pith of the young stem near the rhizome is commonly eaten in some parts of Malaysia (Burkill 1966). Aromatic leaves are used to wrap rice or fish for cooking in Ambon, Indonesia. The plant's long leaf blades are still used for wrapping *zongzi* (Wikipedia, 2013). In Okinawa, Japan, *A. zerumbet* is known in the local dialect as *sannin* or in Japanese as 'getto'. Its leaves are sold as herbal tea and are also used to flavour noodles and wrap mochi rice cakes. Gettou soba is soba which has getto, which is well liked by Okinawans, kneaded into it. *A. zerumbet* is used as food preservative in Okinawa (Liao et al. 2000).

Botany

Alpinia zerumbet is a robust, rhizomatous, clump-forming evergreen, herbaceous perennial 1–3 m high. It has broad, lanceolate, bright green, shining leaves up to 600 mm long and 200 mm wide sheathing the stems and prominent white midrib (Plate 1). Flowers are borne in pendant showy and fragrant racemes up to 400 mm long, and its main axis is very hairy; white, waxy and pink-tinged ovate bracteoles enfold the buds. Flowers are orchid-like and funnel-formed; calyx and corolla are tubular, corolla is white, and its labellum is up to 40 mm, crinkled and yellow, with red and brown stripes (Plate 1). Stamens are 3 but only 1 is functional, and it has 2 staminodes.

Its ovary is inferior and 3-loculed. Fruit is a red, globose capsule with many striations.



Plate 1 Flowers and leaves of *A. zerumbet*

Nutritive/Medicinal Properties

Rhizome Nutrients/Phytochemicals

The nutritive composition of *Alpinia zerumbet* rhizomes was determined as follows: energy 344.6 cal/100 g, moisture 9.11 %, crude protein 5.64 %, carbohydrate 76.0 %, crude fat 2.01 %, crude fibre 8.60 %, ash 7.21 %, K 2166 ppm, Ca 681 ppm, Na 285.9 ppm, Mg 575.2 ppm, Fe 54.80 ppm, Mn 9.49 ppm, Zn 1.66 ppm, Cu 1.872 ppm, Ni 0.3280.140 ppm and Cr 0.242 ppm (Indrayan et al. 2009).

A dihydrochalcone, dihydroflavokawin B, was isolated together with six known phenolic compounds from the rhizomes (Itokawa et al. 1981). Sesquiterpenes, β -eudesmol, nerolidol, humulene epoxide II and 4 α -hydroxydihydroagarofuran, were isolated from the rhizomes (Morita et al. 1996). The main components in the rhizome oil were dihydro-5,6-dehydrokawain (DDK) and methyl cinnamate (Elzaawely et al. 2007b). The highest DDK content was found in the hexane extract of fresh rhizomes. Masuda et al.(2000) isolated two ferulic glycoside esters from the rhizomes. Upadhyay et al. (2011) and Chompoo et al. (2012a) isolated 6-dehydrokawain (DK), dihydro-5,6-dehydrokawain (DDK) and 8(17),12-labdadiene-15,16-dial (labdadiene) from

the rhizomes. The following steroidal compounds were found in the rhizomes: sitosterol and cholest-8-ene-3,6-diol (Chompoo et al. 2012b). *Alpinia zerumbet* rhizome oil was found to be rich in 1,8-cineole (28.1 %), terpinen-4-ol (41.4 %) and β -pinene (4.0 %) (Ali et al. 2002).

The presence of endo-fenchyl acetate, exo-fenchyl acetate and endo-fenchol was the unique feature of rhizome essential oils of *A. galanga*, *A. calcarata* and *A. speciosa* (Padalia et al. 2010b). *A. speciosa* root oil was characterised by endo-fenchyl acetate (40.1 %), 1,8-cineole (11.8 %), camphene (7.8 %), bornyl acetate (6.9 %) and borneol (5.8 %) (Padalia et al. 2010a). Moreover, endo-fenchyl acetate, exo-fenchyl acetate and endo-fenchol were characteristic of *A. speciosa* root oil. Eighteen constituents were found in the rhizome essential oil terpinen-4-ol (52.26 %), the major component, followed by α -terpineol (12.83 %), α -eudesmol (3.96 %), *trans*-piperitol (2.59 %), borneol (2.36 %), carotol (2.24 %), 10-epi- γ -eudesmol (1.01 %), ethyl isoborneol, endo-ethyl fenchila and five unknowns (Jezler et al. 2013).

Plant Phytochemicals

Major components of *A. speciosa* essential oil were 4-terpineol (20.40 %), 1,8-cineole (14.87 %), γ -terpinene (9.48 %) and *p*-cymene (9.38 %) (Luz et al. 1984). Other components included sabinene (5.97 %), α -thujene (4.59 %), limonene (2.97 %), β -caryophyllene (2.48 %), β -pinene (2.35 %), α -terpinene (1.67 %), α -pinene (1.54 %), α -terpineol (1.07 %), myrcene (0.72 %), α -terpinolene (0.98 %), linalool (0.62 %), α -phellandrene (0.23 %) and camphene (0.13 %). The oils extracted from different plant parts of *A. speciosa* of Amazonian origin were found to have the same major component (terpinen-4-ol) present in 10–50 % concentration (Prudent et al. 1993). The oils of the stem and the flower were devoid of monoterpene hydrocarbons but contained large amounts of sesquiterpenoids. All of these oils were found to be rich in terpene alcohols.

Ethyl acetate extract of copper sulphate-treated *A. zerumbet* plants contained increased levels of total phenolics

(Elzaawely et al. 2006). Contents of DDK, vanillin and cinnamic acid were significantly higher in chloroform and ethyl acetate extracts of *A. zerumbet* plants following exposure to copper. Volatile components that increased after copper treatment include 1,8-cineol, camphor, borneol and terpinen-4-ol.

Stem Phytochemicals

The following steroidal compounds were found in the stem: cholestane, sitosterol, stigmasterol, cholest-8-ene-3,6-diol and campesterol (Chompoo et al. 2012b).

Leaf Phytochemicals

Dihydro-5,6-dehydrokawain (DDK) was isolated from the leaves (Tawata et al. 1996). 4-Hydroxy-6-(2-phenylethyl)-2H-pyran-2-one was prepared by hydrolyzing DDK. Three dihydro-5,6-dehydrokawain derivatives were synthesised by reacting compound 3 with phosphoric agents. Among the synthesised compounds, dimethyl [6-(2-phenylethyl)-2-oxo-2H-pyran-4-yl]phosphorothionate had the strongest antifungal activity of 91 % at 100 ppm against *Corticium rolfsii*. The flavonoids identified from the leaves, rutin, kaempferol-3-*O*-rutinoside, kaempferol-3-*O*-glucuronide, (+)-catechin and (–)-epicatechin, are well-known substances that could contribute to the hypotensive, diuretic and antiulcerogenic activity of the aqueous extract of the plant, while the kava pyrones dihydro-5,6-dehydrokawain and 5,6-dehydrokawain had been described as antiulcerogenic and antithrombotic (Mpalantinos et al. 1998). The main constituents identified in the leaf oil were limonene (25.1 %), terpinen-4-ol (22.7 %) and γ -terpinene (17.4 %) (Zogbhi et al. 1999). The main components in the leaf oil were 1,8-cineol, camphor and methyl cinnamate (Elzaawely et al. 2007b). Ferulic and *p*-hydroxybenzoic acids were the major phenolics present in the leaves (Elzaawely et al. 2007b).

Monoterpenoids were the major oil constituents identified. 1,8-Cineole, α -terpineol, (E)-methyl cinnamate, camphor, terpinen-4-ol and α -pinene and β -pinene were the major

constituents commonly distributed in leaf and flower essential oils of *Alpinia galanga*, *Alpinia calcarata*, *Alpinia speciosa* and *Alpinia allughas* (Padalia et al. 2010b). Monoterpenoids composed 89.6 % of the total identified constituents of *A. speciosa* leaf oil, out of which 59.3 % were oxygenated, represented mainly by terpinen-4-ol (28.4 %) and 1,8-cineole (19.2 %) (Padalia et al. 2010a). *Alpinia zerumbet* leaf oil was found to be rich in 1,8-cineole (13.2 %), terpinen-4-ol (40.9 %) and β -pinene (10.0 %) (Ali et al. 2002). Seventeen compounds were identified in the leaf essential oil from Okinawa (Murakami et al. 2009a). Monoterpenic constituents predominated representing 95 % of the essential oil. *p*-Cymene was the most abundant compound, followed by 1,8-cineole, terpinen-4-ol, α -pinene, β -pinene and limonene. The amount of sesquiterpenic content of the essential oil was small, mostly represented by β -caryophyllene and α -caryophyllene. One of the phenylpropanoid derivatives, methyl cinnamate, was also detected. The content rates of *p*-cymene were abundant in summer, were still high in late autumn and early winter and decreased in midwinter and early spring. In contrast, the contents of terpinen-4-ol and 1,8-cineole were high in winter, but decreased around summer. (+)-Terpinen-4-ol had a tendency to decrease in high temperatures and huge precipitations. It was also suggested that (–)- α -pinene was more sensitive to climate change than (+)- α -pinene. In another instance, Murakami et al. (2009b) reported the identification of five major compounds, *p*-cymene (28.0 %), 1,8-cineole (17.9 %), terpinen-4-ol (11.9 %), limonene (6.3 %) and camphor (5.2 %) in the leaf essential oil. The main constituents in the leaf essential oil were terpinen-4-ol, 1,8 cineole and γ -terpinene (Victório et al. 2009a). Other compounds identified were linalool, *trans*-sabinene hydrate, *cis*- β -terpineol, *p*-cymenol, α -terpineol, bornyl acetate, β -caryophyllene, α -humulene, cubebol, caryophyllene oxide and cubenol. In both leaf essential oils obtained by simultaneous distillation–extraction (SDE) and hydrodistillation (HD), the main constituents were terpinen-4-ol, 1,8-cineole, sabinene and λ -terpinene together with caryophyllene and caryophyllene oxide sesquiterpenes (Victório et al. 2009b). However, individual percentage values of compounds varied between the

methods. The components camphene (0.3 %), *p*-2-mentha-4(8)-diene (1.4 %) and *trans*-sabinene hydrate (1.0 %) were obtained only by SDE. Static headspace (S-HS) was for the first time used to analyse the aroma from fresh leaves of *A. zerumbet*. Sabinene, 1,8 cineole and λ -terpinene were the main terpenes detected through static headspace. In April, the main constituents identified in leaf oil of *A. zerumbet* were terpinen-7-al (40.5 %) and sabinene hydrate (15.4 %); in August, the major components identified were terpinen-4-ol (29.4 %) and 1,8-cineole (23.1 %) (Victório et al. 2010b). Camphor (31.6 %), sabinene (9.4 %), γ -terpinene (8.0 %), 1,8-cineole (5.6 %), terpinen-4-ol (5.3 %) and α -pinene (5.1 %) were the main components of the leaf oil (Ho 2010). Other components found were (*Z*)-hex-3-enol (0.1 %), 4-carene (0.2 %), α -thujene (0.1 %), camphene (0.3 %), β -pinene (1.9 %), myrcene (1.2 %), α -phellandrene (0.2 %), carene (0.6 %), (*Z*)- β -ocimene (trace), terpinolene (0.2 %), linalool (3.9 %), menth-2-en-1-ol (0.2 %), β -terpineol (0.5 %), pinocarvone (0.1 %), borneol (1.5 %), 2-nonen-4-yn-1-ol (2.4 %), α -terpineol (1.0 %), myrtenal (0.2 %), *trans*-carveol (0.25 %), *cis*-carveol (0.2 %), cuminaldehyde (1.2 %), α -phellandral (0.2 %), *trans*-decalone (0.2 %), 4-*tert*-butyl phenol (0.1 %), thymol (0.4 %), α -caryophyllene (2.1 %), linalyl isovalerate (3.3 %), δ -cadinene (0.1 %), γ -cadinene (0.2 %), nerolidol (3.4 %), α -bisabolol (2.8 %), terpinyl pentanoate (0.1 %), α -muurorol (0.5 %) and cadinol (trace).

Twenty constituents were found in the leaf essential oil terpinen-4-ol (55.72 %), the major component, followed by 1,8-cineol (10.84 %), γ -terpinene (5.71 %), α -terpineol (4.21 %), *p*-cymene (4.11 %), caryophyllene oxide (3.83 %), *cis-p*-menth-2-en1-ol (2.34 %), *trans-p*-menth-2-en1-ol (1.74 %), linalool (1.76 %), terpinolene (1.24 %) and β -cariofilene (1.12 %), and minor components (<1 %) were β -pinene, α -terpinene, limonene, *trans*-sabinene hydrate, *trans*-piperitol, ethyl isoborneol, dauceno and α -eudesmol (Jezler et al. 2013)

The relative concentration of phenolics from the hydroalcoholic extracts of plantlets cultured in control MS medium reached 100 % compared with plantlets treated with growth regulators indol-3-acetic acid (IAA), thidiazuron

(TDZ) and 6-benzylaminopurine and donor plants (80 %) (Victório et al. 2010a). The in-vitro rutin production was more pronounced than the other flavonoids. While no direct relation between the content of phenolic compounds and increased flavonoid production was observed, the combination of IAA + TDZ enhanced the production of rutin (83.2-microg/g dried leaves) and kaempferol-3-*O*-glucuronide (29-µg/g dried leaves), compared with growth regulators used alone. Their findings suggested the value of in-vitro cultivation as a means of enriching phenolic and flavonoid production in medicinal plants. The leaf aroma of field-grown donor plants was found to be a complex mixture, mainly consisting of sabinene, α and γ-terpinene, 1,8-cineole and caryophyllene; volatile analyses from most of the in-vitro plant samples only revealed the presence of sabinene and caryophyllene (Victório et al. 2011). Many alkanes were found in the aromas after treating plantlets with cytokinins (indole-3-acetic acid, thidiazuron, benzyladenine or kinetin). Secretory cells found in the epidermis and mesophyll showed a strong positive reaction to lipophilic compounds. The findings demonstrated how in-vitro conditions may alter the quality of volatiles in micropropagation systems, while leaf anatomy analysis revealed a large quantity of oil cells in the mesophyll as a constant feature responsible for the production of volatile compounds in both donor and in-vitro-grown plants.

Ethanol 70 % was more efficient for flavonoid extraction from *A. zerumbet* leaves than water (Victório et al. 2009c). No significant yielding variation was found for ultrasonic, microwave and stirring methods using ethanol 70 % (11–14 %). The relative concentration of rutin and kaempferol-3-*O*-glucuronide, respectively, was higher by ultrasonic (1.5- and 5.62-mg/g dried leaves, respectively) and by microwave (1.0- and 6.64-mg/g dried leaves) methods using ethanol. Significantly high dihydro-5,6-dehydrokawain (DKK) content was recovered from leaves extracted with boiling water or oven drying at 70 °C (Elzaawely and Tawata 2011). However, autoclaving and boiling gave significantly higher amounts of phenolic compounds (*p*-hydroxybenzoic acid, syringic acid, vanillin, *p*-coumaric acids, ferulic acid and cinnamic acid) than ethanol extraction. The following steroidal compounds

were found in the leaf: sitosterol; 5 α -ergost-8(14)-ene; 9,19-cyclolanostan-3-ol; and cholest-8-ene-3,6-diol (Chompoo et al. 2012b).

Flower Phytochemicals

The volatile oil of *Alpinia speciosa* flowers (shell flower oil) was found to contain more than 35 constituents, of which β -pinene (34.0 %), α -pinene (14.8 %) and β -caryophyllene (10.8 %) were the main compounds (Nguyen et al. 1994). The oil obtained from flowers of *A. speciosa* was dominated by 1,8-cineole (23.1 %), terpinen-4-ol (20.4 %) and sabinene (14.5 %) (Zogbhi et al. 1999). *Alpinia zerumbet* pollen was found to contain 22.76 % protein and 19.12 soluble sugar % and was rich in amino acids, mineral elements and vitamins (Liu et al. 1994).

1,8-Cineol, camphor, methyl cinnamate and borneol were the major constituents in flower oils (Elzaawely et al. 2007a). HPLC analysis indicated that *p*-hydroxybenzoic acid, ferulic acid and syringic acid were the predominant phenolics in the ethyl acetate extract of flowers. The hexane extract of flowers contained a significantly higher quantity of dihydro-5,6-dehydrokawain (DDK) than that of seeds. Flower oil was extracted by hydrodistillation method, and the major components identified were 1,8-cineole (15.5 %), λ -terpinene (13.1 %) and terpinen-4-ol (42.3 %) (Victório et al. 2009b). There was a predominance of monoterpenes. The flower oil was dominated by oxygenated monoterpenoids (68.9 %), viz. terpinen-4-ol (26.0 %), 1,8-cineole (24.4 %) and linalool (6.1 %), along with the monoterpene hydrocarbon, sabinene (11.3 %) (Padalia et al. 2010a). The following steroidal compounds were found in the flower: cholest-5-en-3-ol, stigmasterol and campesterol (Chompoo et al. 2012b). Twenty-three constituents were found in the flower petals' essential oil, terpinen-4-ol (60.66 %), the major component, followed by α -terpineol (9.06 %), linalool (5.11 %), 1,8-cineol (3.37 %), β -cariofilene (2.49 %), γ -eudesmol (2.33 %), α -eudesmol (1.94 %), caryophyllene oxide (1.63 %), *cis-p*-menth-2-en1-ol (1.73 %), *trans-p*-menth-2-en1-ol (1.52 %), (*E*)-nerolidol (1.12 %) and ethyl isoborneol (1.06 %), and minor components (<1 %)

were borneol, *p*-cymene, γ -terpinene, camphor, δ -terpineol, *trans*-piperitol, α -humulene, γ -cadinene, elemol and carotol (Jezler et al. 2013).

Pericarp (Fruit) Phytochemicals

The following steroidal compounds were found pericarp: cholestane; 3 α ,7 β -dihydroxy-5 β ,6 β -epoxycholestane; ergost-5-en-3-ol; sitosterol; cholestenone; cholest-4-en-3-ol; stigmasterol; and 4,22-stigmastadiene-3-one (Chompoo et al. 2012b).

Seed Phytochemicals

Cardamonin and alpinetin (Krishna and Chaganty 1973); a labdane-type diterpene zerumin (Xu et al. 1995); and two labdane-type diterpenes, zerumin A and zerumin B, together with two known compounds, (*E*)-15,16-bisnorlabda-8(17),11-diene-13-one and coronarin E, were isolated from the seeds (Xu et al. 1996). The main components in seeds oil were α -cadinol, T-muurolol, α -terpineol, δ -cadinene and terpinen-4-ol (Elzaawely et al. 2007a). HPLC analysis indicated that *p*-hydroxybenzoic acid, syringic acid and vanillin were the major phenolics in seeds. Hexane extract of seeds contained lower quantity of dihydro-5,6-dehydrokawain (DDK) than the flowers. The following steroidal compounds were found in the seed: 3 α ,7 β -dihydroxy-5 β ,6 β -epoxycholestane and cholest-4-ene-3,6-dione (Chompoo et al. 2012b).

Alpinia zerumbet seeds were found to contain 0.51 % essential oils, made up of monoterpenoids, oxygenated monoterpenoids, sesquiterpenoids, oxygenated sesquiterpenoids, aldehydes, acid and esters (Lin et al. 2008). Most of the monoterpenes and sesquiterpenes were recoverable in pentane eluent, while the oxygenated monoterpenoids and sesquiterpenoids remained in ether eluent. The seeds also contained high contents of rutin, quercetin and polyphenolics in the ethanolic extract.

Camphor (19.3 %), sabinene (15.1 %), (*Z*)- β -ocimene (7.9 %), terpinen-4-ol (6.6 %), α -terpineol (5.5 %), cadinol (4.6 %)

and α -pinene (4.6 %) were the main components of the seed oil (Ho 2010). Other components found were camphene (0.2 %), β -pinene (4.4 %), myrcene (1.1 %), α -phellandrene (0.2 %), 1,8-cineole (3.5 %), terpinolene (0.1 %), linalool (2.1 %), fenchyl alcohol (0.3 %), menth-2-en-1-ol (0.3 %), β -terpineol (0.4 %), pinocarvone (0.3 %), pinocamphone (1.3 %), 2-nonen-4-yn-1-ol (1.8 %), myrtenal (0.5 %), 4-methylphenyl acetone (0.2 %), cuminaldehyde (0.3 %), thymol (0.5 %), geranyl acetate (0.1 %), α -caryophyllene (0.8 %), linalyl isovalerate (3.0 %), α -selinene (0.3 %), δ -cadinene (0.1 %), γ -cadinene (0.6 %), nerolidol (2.8 %), caryophyllene oxide (2.2 %), carotol (0.1 %), α -bisabolol (2.8 %), α -muurorol (0.3 %) and palmitic acid (1.4 %).

An agglutinin with a molecular mass of 130 kDa was isolated from the seeds of *Alpinia zerumbet* cv. 'Variegata' (Wong et al. 2010a). It was composed of four identical 32-kDa subunits with substantial N-terminal sequence similarity to chitinase and yieldin.

Studies showed that *Alpinia zerumbet* had antioxidant, hypolipidemic, hepatoprotective, cardiovascular, antihypertensive, antimicrobial and antinociceptive attributes.

Antioxidant Activity

The rhizome was reported to have antioxidant index 3.0 as evaluated by β -carotene bleaching method and to contain 5.87 mg% vitamin C, 0.0209 mg% vitamin E, 1.29 mg% total carotenes, 4.23 mg% total xanthophylls, 17.7 mg% tannins and 79.3 mg/% phenolics (Chanwitheesuk et al. 2005). The ethyl acetate extract of flowers and seeds possessed a high antiradical activity and prevented the bleaching of β -carotene (Elzaawely et al. 2007a). Total phenolic contents of flower and seed extracts were measured as 56.7- and 13.7-mg gallic acid equivalent per gram extract, respectively. The HPLC analysis indicated that *p*-hydroxybenzoic acid, ferulic acid and syringic acid were the predominant phenolics in the ethyl acetate extract of flowers, while *p*-hydroxybenzoic acid, syringic acid and vanillin were the major phenolics in seeds.

Ethyl acetate extract of copper sulphate-treated *A. zerumbet* plants contained increased levels of total phenolics and had higher antioxidant activity assayed by DPPH and β -carotene bleaching methods (Elzaawely et al. 2006). Ethyl acetate extracts from leaves showed higher 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activities than those from rhizomes (Elzaawely et al. 2007b). Ethyl acetate extract from wastewater of leaves possessed the strongest inhibition to β -carotene oxidation. Ferulic and *p*-hydroxybenzoic acids were the major phenolics present in these extracts. The results indicated that disposed wastes produced during essential oil production from *A. zerumbet* leaves or rhizomes may be utilised in foodstuffs as a cheap source of natural antioxidants. *Alpinia zerumbet* rhizome extract was found to have 15.5-mg/g total phenols, 53.8 % antioxidant capacity, 59.4 % DPPH-free radical scavenging activity and 0.47 reducing power (absorbance 700 nm) (Chen et al. 2008). High antioxidant activities shown in leaves of *A. zerumbet*, *A. zerumbet* cv. 'Variegata' and *A. purpurata* by using DPPH and reducing power assays were associated with high total phenolic content values (Wong et al. 2009). The rhizome was reported to have antioxidant index 10.9 as evaluated by β -carotene bleaching method and to contain 5.87 mg% vitamin C, 0.0065 mg% vitamin E, 1.27 mg% total carotenes, 0.54 mg% total xanthophylls, 1.18 mg% tannins and 83.9 mg% phenolics (Chanwitheesuk et al. 2005).

The methanol and aqueous extracts of the seed and leaf showed remarkable antioxidant activity using DPPH hydroxyl radical, chelating effect on Fe²⁺ ions and reducing actions assays (Ho 2010). The most active free radical scavengers measured by the DPPH decoloration assay was the polar extracts. At 1-mg/mL condition, seed methanol, seed aqueous, leaf methanol and leaf aqueous extract exhibited 96.0 %, 95.0 %, 99.4 % and 94.0 % inhibitions effect, respectively. The highest Fe²⁺ ions chelating effect was found from seed aqueous and leaf methanol extracts (95.8 and 86.3 % at 2 mg/mL). This chelating effect could be attributed to the presence of the phenolic compounds. The seeds and leaves showed a moderate effect towards the reducing actions assay,

with nearly 0.4–1.5 absorption. The polar extracts of *A. speciosa* could, thus, be used as natural antioxidants in place of synthetic ones.

Total phenolic content (TPC) and ascorbic acid equivalent antioxidant capacity (AEAC) of *A. zerumbet* leaves reported are 1990 mg GAE/100 g and 2180 mg ascorbic acid/100 g (Chan et al. 2008). Leaves of *A. zerumbet* showed higher inhibition of β -carotene oxidation and radical scavenging activity than did rhizomes. All methods of thermal drying (microwave, oven and sun-drying) of *Alpinia zerumbet*, *Etlingera elatior*, *Curcuma longa* and *Kaempferia galanga* leaves resulted in drastic declines in total phenolic content (TPC), ascorbic acid equivalent antioxidant capacity (AEAC) and ferric-reducing power (FRP), with minimal effects on ferrous ion-chelating ability and lipid peroxidation inhibition activity (Chan et al. 2009). Thermal drying of *A. zerumbet* leaves resulted in significant loss of total phenolic content (TPC) and ascorbic acid equivalent antioxidant capacity (AEAC) values (Wong et al. 2010b). Both oven and microwave drying of *A. zerumbet* leaves resulted in the decline of antioxidant properties; TPC and AEAC declined by 53 %, and 71 %, during oven drying and during microwave drying by 57 % and 61 %, respectively. Air-dried leaves of *A. zerumbet* showed drastic losses in AOP, while freeze-dried leaves had significant gains. Freeze-dried leaves yielded significantly higher values of TPC, AEAC and ferric-reducing power (FRP) than fresh leaves. The freeze-dried tea of *A. zerumbet* was superior to the commercial tea for all antioxidant properties tested.

Two ferulic glycoside esters from the rhizomes showed greater antioxidant activity than that of trolox in the TLC method; however, one of the compounds showed weaker inhibitory activity than that of trolox and epicatechin against 2,2'-azobis(2,4-dimethylvaleronitrile) (AMVN)-induced methyl linoleate oxidation (Masuda et al. 2000).

Disposed wastes of *A. zerumbet* may be utilised in foodstuffs as a cheap source of natural antioxidants. An extraction protocol to obtain essential oils, dihydro-5,6-dehydrokawain (DDK) and enriched antioxidant phenolic

extracts from fresh leaves or rhizomes of *Alpinia zerumbet* and its waste was developed by Tawata et al. (2008). Getto (*A. zerumbet*) herbal tea was found to have 854 mg GAE/100 g total phenolic content, ascorbic acid equivalent antioxidant capacity of 536 mg ascorbic acid/100 g, ferric-reducing power value of 3.5 mg GAE/g and chelating activity of EC₅₀ 0.9 mg/ml (Chan et al. 2010).

Antihypertensive Activity

Treatment with the essential oil of *A. zerumbet* (EOAZ) in either anaesthetised or conscious rats induced an immediate and significant hypotension, an effect that could be partially attributed to the actions of terpinen-4-ol (Lahoul et al. 2002). In both pentobarbitone-anaesthetised and conscious rats, intravenous bolus injections of EOAZ (1 to 20 mg/kg) elicited immediate and dose-dependent decreases in mean aortic pressure. In anaesthetised rats, EOAZ decreased heart rate only at higher doses (10 and 20 mg/kg), while changes of this parameter were not uniform in conscious rats. Hypotensive responses to EOAZ were of the same order of magnitude or duration, irrespective of whether the animal was under general anaesthesia. Treatment with either EOAZ or its main constituent, terpinen-4-ol, dose-dependently decreased blood pressure in conscious deoxycorticosterone acetate (DOCA)-salt hypertensive rats, and this action was enhanced when compared with uninephrectomised controls (Lahoul et al. 2003). Hypotensive responses to terpinen-4-ol were significantly greater than those evoked by the same doses of EOAZ (1–10 mg/kg). This enhancement could be related mainly to an increase in essential oil-induced vascular smooth muscle relaxation rather than to enhanced sympathetic nervous system activity in this hypertensive model. The data further support the previous hypothesis that hypotensive effects of EOAZ were partially attributed to the actions of terpinen-4-ol. Further studies showed that EOAZ besides being very active on excitable tissues, such as smooth muscle, also exhibited its effects on the compound action potential (CAP) of rat sciatic nerve (Leal-Cardoso et al. 2004). At 60 µg/ml, the essential oil induced no demonstrable effect. Conduction velocity of CAP

was significantly reduced at 180 min of preparation exposure to 100 µg/ml of the essential oil. At 300, 600 and 2000 µg/ml doses of, the peak-to-peak amplitudes of CAPs following 180-min exposure of the nerve to the drug were reduced significantly, to 75.3 %, 50.45 % and 0 %, respectively, of control value. Conduction velocity was reduced significantly by 300, 600 and 2000 µg/ml of the oil, at 180 min, to 83.61 %, 64.06 % and 22.7 %, respectively, of control value. All these effects developed slowly and were reversible upon a 180-min wash.

The hydroalcoholic extract of *A. zerumbet* was found to have hypotensive effect on rat arterial blood pressure and on the isolated human saphenous vein Soares de Moura et al. (1998). In further studies, they confirmed that the hydroalcoholic leaf extract of *A. zerumbet* exhibited vasodilation and antihypertensive effects (Soares de Moura et al. (2005). In mesenteric vascular bed, precontracted with norepinephrine, the extract induced a long-lasting endothelium-dependent vasodilation that was not reduced by indomethacin. Inhibition of NO synthase by L-NAME and ODQ reduced its vasodilatory effect. In vessels precontracted with norepinephrine, the vasodilator effect of the extract was not changed by 4-aminopyridine, by glibenclamide or by charybdotoxin plus apamin. Concentrations of atropine, pyrilamine and yohimbine that significantly reduced the vasodilatory effect of acetylcholine, histamine and clonidine, respectively, did not change the vasodilator effect of the extract. *Alpinia zerumbet* (aerial parts) essential oil (0.01–3000 µg/ml) induced significant but incomplete relaxation of the phenylephrine-induced contraction of isolated rat aorta preparation, an effect that was abolished by removal of vascular endothelium (Pinto et al. 2009). At similar concentrations, its main constituent, 1,8-cineole, induced complete vasorelaxant effects ($IC_{50} = 663.2 \mu\text{g/ml}$) that were significantly reduced in endothelium-denuded rings ($IC_{50} = 1620.6 \mu\text{g/ml}$). Neither the oil nor its main constituent affected the basal tonus of isolated aorta. The results corroborated the popular use of *A. zerumbet* for the treatment of hypertension.

Alpinia speciosa (leaf/flower) essential oil decreased rat left atrial force of contraction with an EC₅₀ of 292.2 µg/ml (Santo et al. 2011). Sinus rhythm was diminished by the oil with an EC₅₀ of 595.4 µg/ml. The oil at 25 µg/ml decreased L-type Ca²⁺ current I (Ca_L) by 32.6 %, and at 250 µg/ml it decreased by 89.34 %. Thus, inhibition of L-type Ca²⁺ channels was found to be involved in the cardiodepressive effect elicited by the essential oil of *Alpinia speciosa* in rat heart.

The methanol fraction of *A. zerumbet* essential oil relaxed phenylephrine and KCl-induced contraction of either endothelium-intact or endothelium-denuded Wistar rat aortic rings in a concentration-dependent manner (da Cunha et al. 2013). Preincubation with the methanol fraction (100 and 300 µg/mL) in Ca²⁺-free Krebs solution attenuated phenylephrine- or caffeine-induced contraction. Preincubation with NG-nitro-L-arginine methyl ester (L-NAME), 1H-[1,2,4]-oxadiazolo-[4,3-a]quinoxalin-1-one (ODQ), wortmannin, atropine, indomethacin, catalase, SOD (superoxide dismutase), TEA (tetraethyl ammonium), 4-aminopyridine, glibenclamide, apamin, charybdotoxin or iberiotoxin did not affect the methanol fraction-induced relaxation. The intragastric administration of the methanol fraction induced an antihypertensive effect.

Spasmolytic Activity

Sesquiterpenes isolated from *Alpinia speciosa* and *Alpinia japonica* rhizomes and their derivatives were found to inhibit histamine- or barium chloride-induced contraction of excised guinea pig ileum (Morita et al. 1996). Major spasmolytic principles contained in those extracts were the sesquiterpenes, β-eudesmol, nerolidol, humulene epoxide II and 4α-hydroxydihydroagarofuran. Twenty derivatives were prepared from β-eudesmol by combining oxidation, reduction, acetylation, dehydroxylation, etc. Spasmolytic activity of a tigloyl derivative (15-hydroxyeudesm-11-yl-tiglate) was the strongest of all the sesquiterpenes. Monohydroxyl derivative (β-eudesmol, nerolidol, dihydroeudesmol, hinesol) and those

derivatives with one hydroxyl group and acetyl groups (15-hydroxyeudesm-11-yl-acetate; 4 β -hydroxy-15-noreudesm-11-yl-acetate; 11-hydroxy-15-noreudesm-4 β -yl-acetate; 11-acetoxyeudesm-4(14)-ene) possessed stronger activities than those of the sesquiterpene hydrocarbons. Those with two (4-epi-eudesma-4 β ,11-diol; 15-noreudesma-4 β ,11-diol; eudesma-11,15-diol; cryptomeridiol) or three hydroxyl groups (eudesma-4 α ,11,15-triol; 4-epi-eudesma-4 β ,11,15-triol) were weaker than those of monohydroxyl derivatives.

Sesquiterpenes with no hydroxyl group (γ -selinene, β -selinene) showed weak spasmolytic activity. No hydroxyl group containing compounds such as 15-noreudesm-4 β ,11-yl-diacetate and humulene epoxide II with one double bond showed strong activity, and compound 4 α ,15-epoxyeudesm-11-ol with one epoxy group showed weak activity.

Alpinia speciosa essential oil (0.1 μ g/mL) reversibly relaxed ileal basal tonus on rat ileum (Bezerra et al. 2000). Submaximal contractions induced by 60-mM KCl or acetylcholine were concentration dependently inhibited by the oil with similar IC₅₀ values (approximately 44 and 48 μ g/mL, respectively). The results showed that *Alpinia speciosa* essential oil possessed both relaxant and antispasmodic actions in the ileum.

Antinociceptive Activity

Animal studies showed that the essential oil from *A. zerumbet* possessed antinociceptive activity (de Araújo et al. 2005). In the acetic acid-induced writhing test, *A. zerumbet* essential oil was effective at all doses (30-, 100- and 300-mg/kg body weight). In the hot plate test, it significantly increased the latency at doses of 100- and 300-mg/kg body weight, but not at 30-mg/kg body weight. In the formalin test, it significantly reduced paw licking time in the second phase of the test at 100-mg/kg body weight, but decreased it in both phases at 300-mg/kg body weight. The data showed that orally administered *A. zerumbet* essential oil promoted a dose-dependent antinociceptive effect in male Swiss mice with a

mechanism of action which probably involved the participation of opiate receptors.

Antiatherogenic Activity

Among the acetone extracts of *A. zerumbet* rhizomes, stems, leaves, pericarps and seeds, the seed extract exhibited the strongest activity against tyrosinase, pancreatic lipase, 15-lipoxygenase and LDL oxidation activities (IC_{50} = 2.30, 5.00, 1.29 and 15.40 $\mu\text{g/mL}$, respectively) (Chompoo et al. 2012b). Most of the extracts showed partial agonistic properties towards estrogenic activity. All plant-part samples (500 $\mu\text{g/mL}$) except the stem showed partial agonistic properties. Cholest-4-ene-3,6-dione, a steroid present only in the seed extract, appeared to be the compound responsible for these antiatherogenic activities. The results showed that cholest-4-ene-3,6-dione had similar ability to curcumin and quercetin against pancreatic lipase and LDL oxidation (IC_{50} = 19.50 and 16.12 $\mu\text{g/mL}$, respectively). Furthermore, cholest-4-ene-3,6-dione (IC_{50} = 34.21 $\mu\text{g/mL}$) had higher inhibition against 15-lipoxygenase than quercetin (IC_{50} = 54.79 $\mu\text{g/mL}$).

Cardiovascular diseases, especially hyperlipidemia and atherosclerosis, are often accompanied by endothelial dysfunction. Endothelial dysfunction often accompanies cardiovascular diseases, especially hyperlipidemia and atherosclerosis, and studies by Shen et al. (2012) found that essential oil of *A. zerumbet* fruits protected endothelial cells against oxidised low-density lipoprotein (ox-LDL)-induced injury, by ameliorating the redox status. The essential oil ameliorated the oxidative stress by elevating the activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px) and increasing the reduced glutathione (GSH) levels, in addition to attenuating the malondialdehyde (MDA) contents.

Hypolipidemic Activity

Alpinia zerumbet seed powder and seed oil were reported to be effective hypolipidemics with amazingly potent high-density

lipoprotein cholesterol (HDL-C) elevating capabilities (Lin et al. 2008). The high contents of rutin, quercetin and polyphenolics in ethanolic extract of its seeds exhibited moderate antilipoperoxidative but potent DPPH-free radical scavenging bioactivities. Eight-week feeding studies of high-fat Sprague Dawley showed that faecal neutral cholesterol excretion was increased, and the serum total triglyceride (TG) was significantly reduced to 114.3–119.8 mg/daily when fed with *A. zerumbet* seed essential oil, to 116.3–147.9 mg/daily by *A. zerumbet* seed powder and to 116.2–145.3 mg/daily by *A. zerumbet* seed husk (Chuang et al. 2011). The level of arachidonic acid was raised to 0.50–0.60 % by *Alpinia* oil, compared with 0.37 % in the high-fat group. More importantly, the significant reduction in hepatic TG and total cholesterol (TC) implicated a crucial liver protective effect. The hypolipidemic effect was attributed to the combined effect of the essential oil and the crude fibre.

Diuretic Activity

In a placebo-controlled trial of 10 healthy volunteers (5 men and 5 women), acute administration of *A. speciosa* tea at a dose 0.8 g/100 ml which was five times normally taken at 7-day intervals induced slight diuresis and also lowered the diastolic and systolic blood pressures (Laranja et al. 1991;1992). No effect on electrolytes Na, K, Ca, P and uric acid excretions or renal function parameters was observed, and this probably excluded any renal tubular or glomerular effect from the tea.

Antityrosinase Activity

The seed and leaf oil exhibited concentration-dependent inhibition of mushroom tyrosinase, giving 74 and 81 % inhibition at 1000 ppm, respectively (Ho 2010). Among the acetone extracts of *A. zerumbet* rhizomes, stems, leaves, pericarps and seeds, the seed extract inhibited the tyrosinase enzyme at $IC_{50} = 2.30 \mu\text{g/mL}$ stronger than the other parts (Chompoo et al. 2012b). On carrying out inhibition with steroidal compounds, cholest-4-ene-3,6-dione ($IC_{50} = 75.11$

μg/mL) from the seed showed higher inhibitory effect than sitosterol, stigmasterol and campesterol ($IC_{50} = 187.77, 259.25$ and 283.78 μg/mL, respectively). However, cholest-4-ene-3,6-dione showed lower inhibitory effect than quercetin and kojic acid ($IC_{50} = 4.92$ and 4.20 μg/mL, respectively).

Antiplatelet Activity

5,6-Dehydrokawain (DK) and dihydro-5,6-dehydrokawain (DDK) from the rhizome inhibited the aggregation and ATP release of rabbit platelets induced by arachidonic acid and collagen, without affecting those induced by adenosine diphosphate (ADP), platelet-activating factor (PAF) and thrombin (Teng et al. 1990). This inhibition was reversible and in a concentration-dependent manner. The IC_{50} of DK and DDK on arachidonate-induced platelet aggregation were calculated to be about 10 and 60 μg/ml, respectively.

Thromboxane B₂ formation caused by arachidonic acid was also suppressed by both antiplatelet compounds. DK inhibited the intracellular calcium concentration elevated by arachidonic acid, but not that by collagen or thrombin. DK also inhibited the secondary but not the primary aggregation of human platelet-rich plasma induced by ADP and epinephrine. It was concluded that the antiplatelet effect of both DK and DDK was due to the inhibition of thromboxane A₂ formation.

Hemagglutinating Activity

An agglutinin with a molecular mass of 130 kDa was isolated from the seeds of *Alpinia zerumbet* cv. 'Variegata' (Wong et al. 2010a). The agglutinin exhibited hemagglutinating activity towards rabbit erythrocytes which could not be inhibited by simple sugars. The hemagglutinating activity of *A. zerumbet* agglutinin was stable up to 80 °C and was not affected by the presence of a variety of salts. The agglutinin stimulated [methyl-(3)H]-thymidine uptake by mouse splenocytes.

Anxiolytic/Depressant Activity

The leaf essential oil exerted anxiolytic-like activity in mice in the elevated plus-maze task (Muraki et al. 2009b). Inhalational administration of the oil (8.7 ppm) induced unique jumping behaviours in mice. Studies showed that inhalation of *Alpinia zerumbet* essential oil in mice exerted a positive anxiolytic effect as evaluated by the light and dark box test (LD), open field test (OF) and elevated plus-maze test (EPM) (Satou et al. 2010). This was especially evident in the EPM (time spent in the open arms), where anxiolytic effects were clearly observed. The oil components (α -pinene, *p*-cymene, 1,8-cineole and limonene) chiefly accumulated in the kidney. However, α -pinene accumulated in the brain at almost the same rate as in the liver. The amount of α -pinene in the brain and liver was twofold greater after mixed-component inhalation than that after single-component inhalation (Satou et al. 2013). In a comparison of the components of the mixed inhalation, the ratio of α -pinene increased to about three times that of 1,8-cineole.

Depressant/Antipsychotic Activity

Mice treated once with 50 or 100 mg/kg of *A. zerumbet* leaf essential oil showed a dose-related decrease on locomotor activity (open field) and apomorphine-induced stereotypy (de Araújo et al. 2009). There was a decrease to the order of 55 % of the grooming behaviour with both doses studied. The essential oil 100 mg/kg increased cataleptic activity (167 %) and the immobility time in the forced swimming and tail suspension tests. No alterations in the elevated plus-maze test were registered. Pretreatment with haloperidol (0.2 mg/kg, i.p.) alone also decreased locomotion and increased cataleptic activity and immobility time in the tail suspension test. The results suggested that *A. zerumbet* leaf essential oil had depressant and possible antipsychotic activity, since it could reverse the stereotypy induced by apomorphine, presenting effects comparable with those obtained with haloperidol treatment.

Animal studies suggested that *A. zerumbet* essential oil possessing antipsychotic and antioxidant effects may have promising efficacy for the treatment of schizophrenia (de

Araújo et al. 2011). The essential oil at doses of 100 and 200 mg/kg prevented ketamine hyperlocomotion, as did haloperidol (0.2 mg/kg i.p). The essential oil at a dose of 200 mg/kg decreased sleep latency, while all doses increased sleeping time. There was no effect on motor coordination. The in-vitro antioxidant capacity of the oil caused a decrease in lipid peroxidation and increase in GSH levels. The essential oil also prevented the decrease in nitrite content caused by oxidative stress.

Antidiabetic Activity

5,6-Dehydrokawain (DK), dihydro-5,6-dehydrokawain (DDK) and 8(17),12-labdadiene-15,16-dial (labdadiene) from *A. zerumbet* rhizomes inhibited advanced glycation end products (AGEs), major factors responsible for the complications of diabetes (Chompoo et al. 2011). Labdadiene ($IC_{50} = 51.06 \mu\text{g/mL}$) had similar activity to rutin and quercetin against fructosamine adduct. The inhibition of α -dicarbonyl compound formation by labdadiene was significantly higher than that of DK and DDK. The results indicated labdadiene to be a potent antiglycation agent which was found to inhibit AGEs formation in three different steps in the pathway.

Porphyryn Photosensitivity Inhibition Activity

Laio et al. (2000) found that *Alpinia speciosa* used as a food preservative had an activity similar to that of β -carotene in exhibiting defence mechanism against porphyryn photosensitivity. The inhibitory effect of *A. speciosa* on lipid peroxide (LPO) formation was confirmed when the addition of increasing concentrations of *A. speciosa* extract led to a decrease in the amount of LPO formed from a hematoporphyrin-containing rat liver microsomal suspension irradiated with visible light. It was found that the extract effectively inhibited the formation of singlet oxygen. The extract was found to contain dihydro-5,6-dehydrokawain, a water-soluble compound, with singlet oxygen quenching activity. They synthesised five derivatives of kawain and

found that dimethyl[6-(2-phenylethyl)-2-oxo-2H-pyran-4-yl]phosphorothionate had the strongest singlet oxygen quenching activity.

Antimicrobial Activity

Alpinia speciosa leaf oils were found to have antimicrobial activity against bacteria and six fungi with minimum inhibitory concentration around 2000 ppm for both the fungi and the Gram-positive bacteria (Prudent et al. 1993). *Alpinia zerumbet* leaf essential oil significantly inhibited in-vitro growth of *Cryptococcus neoformans* and also inhibited growth *Candida albicans*, *Escherichia coli*, *Staphylococcus aureus* and *Staphylococcus epidermis* (Victório et al. 2009a). Similar growth inhibition was found in *E. coli* and *C. albicans* tested with stem oil from *A. zerumbet* collected in Egypt that revealed the same major constituents: terpinen-4-ol (16 %), 1,8 cineole (11.5 %) and γ -terpinene (8.2 %) (De Pooter et al. 1995). *Alpinia speciosa* essential oil was found to be active in-vitro against dermatophyte strains of *Trichophyton*, *Epidermophyton* and *Microsporum* species isolated from patients with dermatophytosis, inhibiting 80 % of the dermatophyte strains tested (Lima et al. 1993). Ethyl acetate extract of copper sulphate-treated *A. zerumbet* plants contained increased levels of total phenolics and exhibited higher antibacterial activity against *Bacillus cereus* than that of non-treated plants (Elzaawely et al. 2006).

The ethanol extracts of five Taiwanese folk medicinal plants including *Alpinia speciosa* demonstrated strong anti-*Helicobacter pylori* activity with MIC values of 0.64–10.24 mg/ml (Wang and Huang 2005). *Alpinia zerumbet* rhizome extract exhibited moderate antimicrobial activity in-vitro against *Escherichia coli*, *Salmonella enterica*, *Staphylococcus aureus* and *Vibrio parahaemolyticus* (Chen et al. 2008).

Antiviral Activity

The aqueous extracts of leaves and rhizomes of *A. zerumbet* exhibited HIV-1 integrase inhibitory activity with IC₅₀ values of 30 and 188 μ g/mL, whereas against neuraminidase they

showed 50 % inhibition at concentrations of 43 and 57 $\mu\text{g/mL}$, respectively (Upadhyay et al. 2011). Its constituents, 5,6-dehydrokawain (DK) and dihydro-5,6-dehydrokawain (DDK), strongly inhibited HIV-1 integrase with IC_{50} of 4.4 and 3.6 $\mu\text{g/mL}$, respectively. Against neuraminidase, DK, DDK and labdadiene exhibited mixed type of inhibition with respective IC_{50} values of 25.5, 24.6 and 36.6 μM and K(i) values ranging from 0.3 to 2.8 μM . The results suggested that *A. zerumbet* could be used as a source of bioactive compounds against HIV-1 integrase and neuraminidase and that DK and DDK may have possibilities in the design of drugs against these viral diseases AIDS and influenza.

Antiulcer Activity

Dihydro-5,6-dehydrokawain and 5,6-dehydrokawain isolated from the rhizome were found to have antiulcer effect in experimental ulcers (Hsu 1987).

Skin Enzyme Inhibitory Activity

Studies showed that aqueous extract of *Alpinia zerumbet* rhizome exerted greater inhibitory effects than the others on both antioxidant and skin disease-related enzymes (Chompoo et al. 2012a). Its constituents 5,6-dehydrokawain (DK) showed higher inhibitory activities on DPPH, ABTS and PMS-NADH scavenging (IC_{50} = 122.14, 110.08 and 127.78 $\mu\text{g/mL}$, respectively). DK also had stronger inhibitory activities against collagenase, elastase, hyaluronidase and tyrosinase (IC_{50} = 24, 19.41, 19.48 and 76.67 $\mu\text{g/mL}$, respectively) than the other constituents dihydro-5,6-dehydrokawain (DDK) and 8(17),12-labdadiene-15,16-dial (labdadiene). Thus, DK could be used as a potent inhibitor and be further exploited to be used in anti-skin disease formulations.

Longevity-Enhancing Activity

Using animal model, *Alpinia zerumbet* leaf extract (AZL) was found to have longevity-promoting activity (Upadhyay et al. 2013). AZL extract significantly increased mean lifespan of

Caenorhabditis elegans by 22.6 %, better than the positive control resveratrol. Further, both under thermal and oxidative stressed conditions, AZL increased the survival rate significantly better than quercetin. Further studies indicated that the significant longevity-extending effects of AZL on *C. elegans* could be attributed to its in-vitro free radical scavenging effects and its upregulation of stress-resistance proteins, including superoxide dismutase 3 (SOD-3) and heat-shock protein (HSP-16.2). The results suggested that phytochemical compounds in *A. zerumbet* had beneficial effects on the lifespan of *C. elegans* and that they could be used as a source of dietary supplements for ageing and age-related diseases.

Erectile Dysfunction Ameliorating Activity

Alpinia zerumbet extract was one of the several Iranian plants with aphrodisiac effect for erectile dysfunction that exhibited significant dose-dependent cAMP and cGMP phosphodiesterase inhibitory activities in comparison to control and sildenafil (Khanavi et al. 2012).

Larvicidal Activity

A. speciosa essential oil exhibited larvicidal activity against *Aedes aegypti* larvae with LC₅₀ value of 0.94 µl/ml and LC₉₀ value of 1.2 µl/ml (Freitas et al. 2010). The seed oil exhibited the larvicidal activity against *Aedes aegypti* with 2 h and 24 h LC₅₀ value of 125 and 87 ppm, respectively, while the leaf oil exhibited larvicidal activity with 2 h and 24 h LC₅₀ value of 64 and 32 ppm, respectively (Ho 2010). The results suggested the seed and leaf oil of *A. speciosa* to be a potential natural mosquito larvicide.

Anti-amoebic Activity

Studies found that chloroform extract of *A. zerumbet* exhibited anti-giardial activity against trophozoites of *Giardia intestinalis* with IC₅₀ of <100 µg/ml (Sawangjaroen et al. 2005).

Anthelmintic Activity

Alpinia zerumbet decoction exhibited inhibitory activity on *Haemonchus contortus* larvae hatching and exsheathing (Macedo et al. 2012).

Genotoxicity Studies

Alpinia zerumbet leaf essential oil at non-toxic concentrations (50–300 µg/mL) did not induce genotoxicity in human leukocytes (Cavalcanti et al. 2012). However, at the highest concentration (500 µg/mL) tested, it caused a reduction in cell proliferation and viability and an increase in DNA damage. Further, in-vivo experiments showed that the oil (400 mg/kg) did not exert mutagenicity on peripheral blood cells and bone marrow in mice. In DPPH test, the essential oil showed scavenging effects against DPPH radicals and other free radicals (determination of intracellular GSH and lipid peroxidation assays). It was able to reduce the intracellular levels of ROS and prevented leukocyte DNA against oxidative damage. The ability of the oil to reduce H₂O₂ toxicity was observed only when cells were treated with the oil during and after exposure to H₂O₂. With the co- and post-treatment procedures, the oil decreased the frequency of apoptotic and micronucleated leukocytes as well DNA strand breaks. However, a synergistic effect was observed in cultures exposed to 500 µg/mL oil. It was concluded that the oil at concentrations up to 300 µg/mL or doses up to 400 mg/kg were not mutagenic in leukocytes and in mice and had antioxidative and protective effects against the cytotoxicity and clastogenesis induced by H₂O₂.

Traditional Medicinal Uses

Alpinia zerumbet is used in the northeast and southeast of Brazil as infusions or decoctions as a diuretic, antihypertensive and antiulcerogenic (de Moura et al. 2005). In northeastern Brazil, it has been used widely in folk medicine as teas and infusions for the treatment of intestinal and cardiovascular diseases and as hypotonic agent for arterial hypertension (Luz

et al. 1984; Leal-Cardoso et al. 2004) and for its anti-inflammatory, bacteriostatic and fungistatic properties (Zoghi et al. 1999). *Alpinia zerumbet* is popularly used as a diuretic, antihypertensive, antiulcerogenic and sedative (de Araújo et al. 2009). In phytotherapy, the essential oil from the leaves of *Alpinia zerumbet* is used for neuropsychiatric symptoms, such as depression, stress and anxiety, and chronic problems that are associated with reproductive hormone imbalances in women (Murakami et al. 2009b). In Chinese folkloric medicine, *Alpinia zerumbet* has been popularly recognised as an excellent hepatoprotector (Lin et al. 2008). The essential oil from fructus *Alpinia zerumbet* is widely used in Miao folk herbs in Guizhou province for the treatment of gastrointestinal and cardiovascular diseases (Shen et al. 2012). The plant has been used as a medicine against venoms of snakes and spiders in India. In Vietnam, juice from boiled rhizomes, leaves, flowers and seeds is used to treat fever, stomach ache, bloating, indigestion and diarrhoea (Nguyen et al. 2014).

Other Uses

It is a popular ornamental plant in home gardens and public areas. There is an ornamental cultivar with variegated leaves. The plant has been used as source of fibre and the digested pulp has been used for making paper (Burkill et al. 1966).

The plant has been reported to have allelopathic activity. Dihydro-5,6-dehydrokawain (DDK) isolated from the leaves was found to have plant growth inhibitory activity (Fujita et al. 1994). DDK caused a 35 % reduction in hypocotyl length of lettuce seedling compared to the control at 25 ppm, etiolation at 100 ppm and necrosis at 200 ppm. Among some synthesised related compounds, 4-methoxy-6-(*m*-chlorophenethyl)-2H-pyran-2-one was much more active, causing a 66 % growth retardation at 25 ppm.

Comments

A. zerumbet reproduces and spreads by rhizome division. It also produces abundant seeds.

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Boesenbergia rotunda

T. K. Lim¹ 

(1) Canberra, Australia

Scientific Name

***Boesenbergia rotunda* (L.) Mansfield**

Synonyms

Boesenbergia cochinchinensis (Gagnep.) Loes., *Boesenbergia pandurata* (Roxb.) Schlecht., *Curcuma rotunda* L. (basionym), *Gastrochilus panduratus* (Roxb.) Ridl., *Gastrochilus rotundus* (L.) Alston, *Kaempferia cochinchinensis* Gagnep., *Kaempferia ovata* Roscoe, *Kaempferia pandurata* Roxb.

Family

Zingiberaceae

Common Names

Chinese Keys, Chinese Ginger, Fingerroot, Lesser Ginger, Resurrection Lily, Sweet Thai Ginger, Tropical Crocus

Vernacular Names

Chinese: Ao Chun Jiang, Lap Seuh Geung, Cu Dia, Mau Cam, Suo Shi

Czech: Číňan Zázvor

Dutch: Temoe Koentji

French: Petits Doigts

German: Chinesischer Ingwer, Fingerwurz, Gewürzlilie

Hungarian: Kínai Gyömbér

India: Yai Macha (Manipuri);

Indonesia: Kunci, Temu Kunci (Java), Konchi, Temmo Konci (Madurese), Tumbu Konci (Maluku), Temu Kunci (Sundanese)

Japanese: Gajutu

Khmer: Khchiey

Korean: Pinggeo-Rutu, Pinngo-Rutu

Laos: Houo Ka Sai, Kas'a:Y, Ne: Gngx Kiengz, Neng Kieng

Lithuanian: Besenbergija, Kiniškas Imbieras

Malaysia: Temu Kunci

Russia: Bëzenbergiia Kruglaia

Singapore: Yao Shi, Suo Shi

Thai: Ka-Aen (Northern), Gra Chai, Kra Chaai, Krachai, Krachai Dam (General), Khao Chae Won-Prathit (Bangkok);

Vietnamese: Bồng Nga Truật, Cú Ngái, Ngai Num Kho

Origin/Distribution

The species is native to China (S. Yunnan) to West Malaysia. It is widely cultivated in Southeast Asia.

Agroecology

In its native sub-temperate to tropical range, it occurs in dense forests up to 1000-m elevation. It thrives in rich, alluvial soil

or well-drained woodland soil in filtered shade; it will tolerate deep shade. It is frost sensitive.

Edible Plant Parts and Uses

It is a culinary and medicinal herb. The rhizomes, young leaves and heart of the spurious stem are edible.

In Java, rhizomes are popularly used in ‘sayor masak tetege’ or in side dishes such as ‘sambal petis’, or made into pickle ‘acar’ or eaten raw as ‘lalap’ with rice (Ochse and van den Brink 1980). The heart of the pseudostem is likewise used. Young unfolded leaves and pseudostem are cut up fine and added to ‘sayor’ or ‘urab’. They are also used together with the rhizome (all cut up) with young coconut, salt and minced green chilli, wrapped in banana leaves and steamed to make the ‘botok kunci’ dish. The roots are also sold in a pickled form in Indonesia and Thailand.

Fingerroot assumes an important role in flavouring many Thai dishes such as ‘kaeng tai pla’, fish curries, fish soups and vegetable stews. The rhizomes are used in ‘kroeung’ pastes in Cambodian cuisine.

Botany

Boesenbergia rotunda is a perennial herb growing up to 30–70 cm. Rhizome is small, robust, ovoid globose, 1.5–2 cm in diameter, jointed or fused and strongly aromatic, bearing slender, 5–10 cm long, 1.0–1.5 cm thick, swollen, tapering or fusiform tuberous roots like a bunch of fingers (Plate 1). Both the colour of the central rhizome and the tubers are dependent on the variety. The yellow variety produces bright yellow rhizomes, while other varieties produce red and black rhizomes. Leaves 3–7; erect, biseriate, alternate; leaf sheath red; ligule 2-cleft, broadly deltoid; petiole 7–16 cm, channelled forming a short pseudostem; leaf blade green on both surfaces, ovate-oblong or elliptic-lanceolate, 25–50 × 7–12 cm, glabrous except for sparsely hairy midvein abaxially, base rounded to cuneate, apex apiculate (Plate 2). Inflorescences are terminal on pseudostems, appearing from

within apical leaf sheaths, and are subsessile; bracts are lanceolate. Flowers are aromatic, exerted arising from the axil of an outer bract and a similar oblong-lanceolate bracteole. The calyx is shortly tubular, 1.5–2 cm; the apex is 2-cleft. Corolla is pink to scarlet; corolla tube is 4.5–5.5 cm; lobes are oblong, 1.5–2 cm. Lateral staminodes are light pink and obovate. Labellum is patent, white or pink with purple stripe, fiddle shaped, 2.5–3.5 cm. and concave, margin is slightly crisped, and apex is entire. The filament is short; connective appendage is reflexed, 2-cleft and 1–3 mm. The fruit is not known.



Plate 1 Fingerroot roots



Plate 2 Foliage of fingerroot

Nutritive/Medicinal Properties

Nutrient composition of the raw rhizome per 100-g edible portion was reported as: energy 38 cal, moisture 89.5 g, protein 1.1 g, fat 0.8 g, total carbohydrates 7.3 g, ash 1.3 g, Ca 28 mg, P 40 mg, Fe 2.0 mg, β -carotene equivalent 3 μ g, thiamine 0.08 mg and riboflavin 0.02 mg (Leung et al. 1972).

Pinostrobin and alpinetin were isolated from the rhizome of *B. pandurata* (Mongkolsuk and Dean 1964). From yellow rhizomes, 5-hydroxy-7-methoxyflavanone (pinostrobin), 5,7-dihydroxyflavanone (pinocembrin), 2',6'-dihydroxy-4'-methoxychalcone (pinostrobin chalcone), 2',4'-dihydroxy-6-methoxychalcone (cardamonin) and boesenbergin A were isolated (Jaipetch et al. 1982). From the black rhizomes, the following flavonoid compounds were isolated: 5-hydroxy-7-methoxyflavanone (pinostrobin); 5,7-dimethoxyflavanone; 5-hydroxy-7-methoxyflavone; 5-hydroxy-7,4'-dimethoxyflavone; 5,7-dimethoxyflavone; 5,7,4'-

trimethoxyflavone; 5,7,3',4'-tetramethoxyflavone; 5-hydroxy-3,7-dimethoxyflavone; 5-hydroxy-3,7,4'-trimethoxyflavone; 3,5,7-trimethoxyflavone; 5-hydroxy-3,7,3',4'-tetramethoxyflavone (Jaipetch et al. 1983); three flavones 3,5,7,3',4'-pentamethoxyflavone, 3,5,7,4'-tetramethylflavone and 5-hydroxy-7,4'-dimethoxy flavone; and two chalcones 2'-hydroxy-4',6'-dimethoxychalcone and 2'-hydroxy-4,4',6'-trimethoxychalcone (Herunsalee et al. 1987). Fourteen flavonoids (flavones, flavanones and chalcones) were isolated from the yellow and black rhizomes: 5,6-dimethoxyflavone; 5-hydroxy-7-methoxyflavone; 3,5,7-trimethoxyflavone; 5-hydroxy-3,7-dimethoxyflavone; 5,7,4'-trimethoxyflavone; 3,5,7,4'-tetramethoxyflavone; 3,5,7,3',4'-pentamethoxyflavone; 5,7-dimethoxyflavanone; 5-hydroxy-7-methoxyflavanone; 5,7-dihydroxyflavanone; 2,4,6-trimethoxychalcone; 2,6-dihydroxy-4-methoxychalcone; 2-hydroxy-6-methoxychalcone; and acetylsalicylic acid (Panthong et al. 1994). From the rhizomes, the following compounds were isolated: boesenbergin B and panduratin A (Mahidol et al. 1984); 1'RS, 2'SR, 6'RS-(2, 6-dihydroxy-4-methoxy-phenyl)-[3'-methyl-2'-(3"-methylene-2"-enyl)-6'phenylcyclohex-3'-enyl] methanone (panduratin A), pinostrobin and two chalcones boesenbergin A and rubranine from red rhizomes (Tuntiwachwutiikul et al. 1984); (-)-panduratin B1; (-)-panduratin B2 from red rhizomes (Pancharoen et al. 1987); pinostrobin, pinocembrin, alpinetin and panduratin A (Phuwapraisirisan et al. 2000); 2',4',6'-trihydroxychalcone (pinocembrin chalcone); cardamonin; pinocembrin; 5-hydroxy-7-methoxyflavanone; (2,4,6-trihydroxyphenyl)-[3'-methyl-2'-(-methylbutenyl)-6'-phenylcyclohex-3'-enyl]methanone (4-hydroxypanduratin A); panduratin A (Trakoontivakorn et al. 2001); (-)-4-hydroxypanduratin A; (-)-panduratin A; 5,4'-dihydroxy-7-methoxyflavanone (sakuranetin); 5-hydroxy-7-methoxyflavanone; 5,7-dihydroxyflavanone; dihydro-5,6-dehydrokawain from red rhizomes (Tuchinda et al. 2002); flavonoids, pinostrobin, pinocembrin, alpinetin and cardamonin (Tewtrakul et al. 2003, 2006); camphor, geraniol, methyl cinnamate and geranial (*E*-citral) (Zaeoung et al. 2005); panduratin C, panduratin A, 4-hydroxypanduratin A,

helichrysetin, 2',4',6'- trihydroxydihydrochalcone (propiophenone) and uvangoletin (Cheenpracha et al. 2006); 5-hydroxy-7-methoxyflavanone; (–)-panduratin A; 5,7-dihydroxyflavone, pinostrobin chalcone, cardamonin and (–)-4-hydroxypanduratin A (Shindo et al. 2006); (2S)-6-geranylpinostrobin; geranyl-2,4-dihydroxy-6-phenethylbenzoate; 2',4'-dihydroxy-3'-(1''-geranyl)-6'-methoxychalcone; (1'r,2's,6'r)-2-hydroxyisopanduratin A; (2R)-8-geranylpinostrobin; (±)-6-methoxypanduratin A; (2S)-7,8-dihydro-5-hydroxy-2-methyl-2-(4''-methyl-3''-pentenyl)-8-phenyl-2H, 6H-benzo[1,2-b:5,4-b']dipyran-6-one; (–)-pinostrobin; tectochrysin; 5,6-dehydrokawain; cardamonin; (–)-alpinetin; flavokawain c; (–)-7,4'-dihydroxy-5-methoxyflavanone; (–)-6-geranylpinocembrin; boesenbergin A; panduratin A; boesenbergin B; (±)-isopanduratin a1; (–)-pinocembrin; (–)-4-hydroxypanduratin A; nicolaioidesin B; panduratin C; isopanduratin A2 (Win et al. 2007); six secondary metabolites, panduratin D-I, together with known diastereomers and panduratin B1 and B2 isolated from the non-polar fraction (Win et al. 2008); three flavones pinostrobin pinocembrin, alpinetin and two chalcones cardamonin; boesenbergin A (Yap et al. 2007; Sukari et al. 2008); prenylchalcones (+)-krachaizin A, (–)-krachaizin A, (+)-krachaizin B, (–)-krachaizin B, (+)-panduratin A, (–)-panduratin A, (+)-4-hydroxypanduratin A, (–)-4-hydroxypanduratin A, (+)-isopanduratin A and (–)-isopanduratin A; prenylflavonoids rotundaflavone Ia, rotundaflavone Ib, rotundaflavone IIa and rotundaflavone IIb; flavanones and others (12)—pinostrobin; pinocembrin; alpinetin; 7,4'-dihydroxy-5-methoxyflavanone; 5,7-dihydroxy-8-geranylflavanone; 7-methoxy-5-hydroxy-8-geranylflavanone; cardamonin; 2,6-dihydroxy-4-methoxydihydrochalcone; 2,4-dihydroxy-6-phenethyl-benzoic acid methyl ester; geranyl-2,4-dihydroxy-6-phenylbenzoate; 5,6-dehydrokawain; geraniol (Morikawa et al. 2008)—and pinostrobin, alpinetin and pinocembrin chalcone (Wangkangwan et al. 2009).

The flavonoids levels (µg/g DW) in *B. rotunda* rhizomes, callus and cell suspension were determined as follows: alpinetin (1139.34, 4.50, 0.30 µg), pinocembrin (2613.77,

17.76, 1.02 μg), cardamonin (57.20, 1.63, 0.24 μg), pinostrobin (8220.72, 96.30, 3.15 μg), panduratin A (944.58, 0.42, 0.20 μg) and total flavonoids (12975.52, 120.61, 4.91 μg), respectively (Yusuf et al. 2013a).

Essential oil of the rhizomes contained the following compounds: camphor, linalool, camphene, α -pinene, α -terpineol, α -phellandrene, γ -terpinene, methyl 3-phenylpropionate, geranyl formate, geranyl propionate, geraniol, neral, myrcene, isoborneol, β -pinene, neryl acetate, geranial, β -thujaplicin, (*E,E*)- α -farnesene, borneol, tricyclene, terpinen-4-ol, terpinolene, myristicin, allo-ocimene, α -thujene, (*Z*)- β -ocimene, sabinene, (*E*)- β -ocimene, (*Z*)-nerolidol, *cis*-linalool oxide, 3-carene, δ -elemene, (*Z*)- β -farnesene, γ -elemene and β -elemene (Jantan et al. 2001).

The rhizome oil of *B. pandurata* consisted mainly of the oxygenated monoterpene derivatives camphor (57.97 %) and *trans*-geraniol (6.25 %) (Sukari et al. 2008). Other compounds were *trans*-2-hexenyl-*n*-propionate (5.59 %), *trans*-caryophyllene (3.42 %), cyclohexyl-*n*-propionate (2.72 %), 1,8-cineole (2.60 %), guaiacol (2.60 %), borneol (1.99 %) and neryl acetate (1.17 %). The other minor compounds isolated in concentrations of <1 % were *trans*-ocimene, β -pinene, β -citronellol, bicycle(2.2.1)heptan-2-ol, methyl-*n*-nonanoate, 2-cyclohexylethylacetate, 3,4-dimethoxyacetophenone, rosephenone, terpinyl *n*-valerate, *n*-hexyl angelate, 1-3-tetradecadiene, *n*-hexanal, 2-isopropyl-4,5-dimethyloxazole, 2-*n*-propyl-4,5-dimethylthiazole, ethyl benzoate, guaiacol *n*-caproate, geranyl benzoate, *n*-butyl-*n*-pentadecanoate, *n*-eicosane and cinnamyl cinnamate. Composition of *B. pandurata* rhizome oil was reported as geraniol (56.68 %), camphor (38.03 %), linalool (2.36 %), α -terpineol (1.28 %) and unknown (1.65 %) (Taweechaisupapong et al. 2010).

Total arsenic contents (dry weight basis) in six edible zingiberaceous rhizomes, namely, *Alpinia galanga* (Khaa), *Boesenbergia rotunda* (Kra-chaai), *Curcuma longa* (Khamin-chan), *Curcuma zedoaria* (Khamin-oi), *Zingiber cassumunar* (Plai) and *Zingiber officinale* (ginger), were found to be 92.4, 103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively (Ubonnuch et al. 2013). Total inorganic arsenic are 92.4,

103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively. All investigated amounts of total and inorganic arsenic were much lower than limits recommended by Thai Food and Drug Administration.

Panduratin A and its regioisomer isopanduratin A were synthesised in four steps from (*E*)-ocimene to [(*E*)-3,7-dimethyl-1,3,6-octatriene] via a Diels–Alder cycloaddition reaction (Chee et al. 2010).

Antioxidant Activity

Leaves of *Boesenbergia rotunda* had a total phenolic content (TPC) of 260 mg GAE/100 g, ascorbic acid equivalent antioxidant capacity (AEAC) of 157 mg AA/100 g, rhizome TPC of 197 mg GAE/100 g, and AEAC of 89 mg AA/100 g (Chan et al. 2008). The rhizome was reported to have antioxidant index 0.91 as evaluated by β -carotene bleaching method and to contain 0.98 mg% vitamin C, 0.0032 mg% vitamin E, 0.64 mg% total carotenes, 0.52 mg% total xanthophylls, 4.48 mg% tannins and 20.5 mg/% phenolics (Chanwitheesuk et al. 2005). *B. rotunda* ethanolic extract exhibited antioxidant activity as evaluated by the ferric reducing/antioxidant power (FRAP) and DPPH free radical scavenging activity (Jitvaropas et al. 2012). Boesenbergin A, from *B. rotunda*, exhibited considerable antioxidant activity, when the results of ORAC assay were reported as Trolox equivalents (Isa et al. 2012). Boesenbergin A (20 μ g/mL) and quercetin (5 μ g/mL) were equivalent to a Trolox concentration of 11.91 and 160.32 μ M.

Panduratin A, from *Boesenbergia rotunda* rhizomes, had less potent DPPH radical scavenging effect and antioxidant activity than ascorbic acid and quercetin but similar to that of the reference drug silymarin at the low and medium concentrations 1 and 10 μ g/mL but not at the high concentration 100 μ g/mL (Salama et al. 2013b). Treating thioacetamide-induced, oxidative-injured embryonic cell line WRL-68 with panduratin A significantly reduced malondialdehyde (MDA) level and increased the cell viability, comparable to SI. The activities of superoxide dismutase

(SOD), catalase (CAT) and glutathione peroxidase (GPx) were significantly elevated in the Panduratin A-treated cells in a dose-dependent manner and again similar to silymarin.

Anticancer Activity

In-vitro studies showed that pinostrobin, from *K. pandurata* rhizome, inhibited activity of DNA topoisomerase I isolated from human tumour suggesting that this could be a possible mechanism of pinostrobin for the cytotoxicity observed in cell culture of human mammary carcinoma (Sukardiman et al. 2000). Cardomin, from *B. pandurata*, was identified as the active antitumour constituent in the tumour promoter-induced Epstein–Barr virus (EBV) activation test (Murakami et al. 1994). It showed more potent inhibitory activities than the representative antitumour promoters such as β -carotene or quercetin. *K. pandurata* extract showed potent inhibitory activity in-vitro against human MCF-7 and HT-29 cancer cells (Kirana et al. 2003). Panduratin A, a chalcone derivative isolated from *B. pandurata*, was found to inhibit the growth of MCF-7 human breast cancer and HT-29 human colon adenocarcinoma cells with an IC₅₀ of 3.75 and 6.56 μ g/ml, respectively (Kirana et al. 2007). Panduratin A arrested cancer cells in the G0/G1 phase and induced apoptosis in a dose-dependent manner. Feeding male rats with AIN diet containing ethanolic extracts prepared from the equivalent of 4 % by weight of dried rhizomes of *B. pandurata* and *C. longa* prior to challenge by azoxymethane mutagen found the extracts were not toxic. Total aberrant crypt foci were slightly reduced by *B. pandurata* extract compared to control group but not significantly different.

The rhizome extracts and pure compounds pinostrobin, pinocembrin, alpinetin, cardamonin and boesenbergin A, isolated from the rhizome, were active against human promyelocytic leukaemia (HL-60) cancer cell lines (Sukari et al. 2007). The chloroform extract and boesenbergin A showed the most potent cytotoxic activity. The chloroform rhizome extract demonstrated marked preferential cytotoxicity against human pancreatic PANC-1 cancer cells in nutrient-deprived

medium (NDM) (Win et al. 2007). All the isolated compounds, i.e. four secondary metabolites and twenty known compounds, showed varying degrees of in-vitro preferential cytotoxicity against human pancreatic PANC-1 cells. Nicolaoidesin B and panduratin A were most potent, each showing a PC_{100} (the concentration at which 100 % cancer cell death occurred preferentially in NDM) at 2.5 μ M. Panduratin D, E, G, H and I and panduratin B1 and B2, isolated from the rhizome, exhibited mild activity against human pancreatic PANC-1 cancer cells under nutrient-deprived medium (NDM) with PC_{100} values of 128 mM, whereas panduratin F showed a weaker activity (PC_{100} = 256 mM) (Win et al. 2008). Of four *Boesenbergia* species, *B. rotunda* showed significant inhibitions in-vitro towards all the cancer cell lines breast cancer (MCF-7), non-hormone-dependent breast cancer (MDA-MB-231), ovarian cancer (CaOV₃), colon cancer (HT-29) and cervical cancer (Hela) cell lines tested with IC_{50} ranging from 51.0 to 71.0 μ g/mL (Ling et al. 2011). In cell-cycle analysis, *B. rotunda* crude extract arrested cell at sub-G1 phase. Petroleum ether and chloroform extracts of *B. rotunda* rhizomes exhibited in-vitro cytotoxicity against the hormone-independent, highly metastatic human breast cancer cell MDA-MB-231 cells with IC_{50} of 9.21 and 10.25 μ g/mL (Chew et al. 2012). Both extracts exhibited strongly active antiproliferative activity against MDA-MB 231 and had anti-mitigation activity against the cancer cells. Also, both extracts were cytotoxic to human lung fibroblast cell line MRC-5 with IC_{50} of 12.78 μ g/mL for the petroleum ether extract and 13.22 μ g/mL for the chloroform extract.

The methanol rhizome extract exhibited inhibitory effect on tumour necrosis factor- α (TNF- α)-induced cytotoxicity in L929 cells (IC_{50} = 6.1 μ g/mL) (Morikawa et al. 2008). Among the constituents, (+)-krachaizin B, (-)-krachaizin B, (+)-4-hydroxypanduratin A, (-)-4-hydroxypanduratin A, (+)-isopanduratin A, (-)-isopanduratin A, alpinetin, cardamonin and 2,6-dihydroxy-4-methoxydihydrochalcone significantly inhibited TNF- α -induced cytotoxicity in L929 cells at 10 μ M. In addition, (+)-krachaizin B, (-)-krachaizin B, (+)-

panduratin A, (–)-panduratin A, (+)-4-hydroxypanduratin A, (–)-isopanduratin A and geranyl-2,4-dihydroxy-6-phenylbenzoate were found to show strong inhibitory effects on aminopeptidase N activity. C-6 and C-8 prenylated derivatives of pinostrobin (5-hydroxy-7-methoxyflavanone) from fingerroot showed cytotoxic activity towards SK-BR-3, MCF-7, PC-3 and Colo-320DM human tumour cell lines, and all of them had significantly lower IC₅₀ (μM) values than pinostrobin (Poerwono et al. 2010). Boesenbergin A, from *B. rotunda*, exhibited cytotoxicity on non-small cell lung cancer (A549), prostate adenocarcinoma (PC3), human hepatocellular carcinoma (HepG2), colon adenocarcinoma (HT-29) and normal hepatic cells (WRL-68) with IC₅₀ of 20.22, 10.69, 20.31, 94.10 and 9.324 μg/mL (Isa et al. 2012).

Panduratin A, isolated from *Kaempferia pandurata*, exhibited cytotoxicity in human colon cancer cells HT-29 with an IC₅₀ value of 28 μM (Yun et al. 2005). The cytotoxic effects of panduratin A were found to be accompanied by the dose-dependent induction of apoptosis and resulted in cleavage of poly(ADP-ribose) polymerase (PARP) with a concomitant decrease in procaspase-3 protein. Panduratin A is protected against tert-butylhydroperoxide (t-BHP)-induced cytotoxicity in a human hepatoma cell line, HepG2 (Sohn et al. 2005). Panduratin A significantly reduced the cell growth inhibition caused by t-BHP. Further, it ameliorated lipid peroxidation, as demonstrated by a reduction in MDA formation, and attenuated glutathione (GSH) depletion in a dose-dependent manner. The results strongly suggested panduratin A to have significant protective ability against oxidative damage caused by reactive intermediates. Panduratin A induced apoptosis and G₂/M cell-cycle arrest in androgen-independent human prostate cancer cells PC3 and DU145 (Yun et al. 2006). Panduratin A-mediated apoptosis was accompanied with upregulation of Fas death receptor and TNF-related apoptosis-inducing ligand (TRAIL). In both cell lines panduratin A treatment resulted in a dose-dependent (i) induction of p21^{WAF1/Cip1} and p27^{Kip1}; (ii) downregulation of cdk2, 4 and 6; and (iii) decrease in cyclins D1 and E. Panduratin A (PA), from the rhizome displayed, marked

antiangiogenic activity in-vitro and in-vivo, suggestive of its potential for development as an antiangiogenic agent for cancer therapy (Lai et al. 2012). In-vitro, it suppressed VEGF-induced survival and proliferation of human umbilical vein endothelial cells (HUVECs). It significantly inhibited endothelial cell migration, invasion and morphogenesis or tube formation in a time- and dose-dependent manner. PA also suppressed matrix metalloproteinase-2 (MMP-2) secretion and attenuated its activation to intermediate and active MMP-2 and suppressed F-actin stress fibre formation to prevent migration of the endothelial cells. In-vivo, PA inhibited neo-vessels formation in murine Matrigel plugs and angiogenesis in zebra fish embryos. Panduratin A, isolated from *Boesenbergia rotunda*, exhibited cytotoxicity with an IC₅₀ value of 4.4 µg/mL (10.8 µM) and dose-dependent apoptosis on A549 human non-small cell lung cancer cells (Cheah et al. 2011). Panduratin A arrested cancer cells labelled with bromodeoxyuridine (BrdU) and phospho-histone H3 in the mitotic phase. Further, panduratin A significantly inhibited nuclear factor-kappa beta (NF-κB) translocation from cytoplasm to nuclei activated by tumour necrosis factor-α (TNF-α). Panduratin A (PA) induced apoptotic cell death A549 in human non-small cell lung cancer cells through the activation of caspase-3 leading to PARP cleavage (Cheah et al. 2013). Treatment of A549 cells with PA resulted in a strong inhibition of NF-κB activation, which was consistent with a decrease in nuclear levels of NF-κB/p65 and NF-κB/p50 and the elevation of p53 and p21. Also, PA significantly inhibited the invasion of A549 cells in a dose-dependent manner through reducing the secretion of MMP-2 of A549 cells.

Boesenbergin A, from *B. rotunda*, was found to have the highest toxicity towards leukaemic CEMss cancer cells (IC₅₀ = 8 µg/ml) (Ng et al. 2013). The morphology of CEMss cells after treatment showed evidence of apoptosis that included blebbing and chromatin condensation and DNA fragmentation during late apoptosis. Also, boesenbergin A was able to induce G2/M phase arrest in CEMss cells. The activity of caspases -3/7, -8 and -9 was increased after treatment indicating both

intrinsic and extrinsic pathways were induced during apoptosis.

Antimutagenic Activity

Six compounds 2',4',6'-trihydroxychalcone (pinocembrin chalcone; 1), 2',4'-dihydroxy-6'-methoxychalcone (cardamonin; 2), 5,7-dihydroxyflavanone (pinocembrin; 3), 5-hydroxy-7-methoxyflavanone (pinostrobin; 4), (2,4,6-trihydroxyphenyl)-[3'-methyl-2'-(3''-methylbut-2''-enyl)-6'-phenylcyclohex-3'-enyl]methanone (5) and (2,6-dihydroxy-4-methoxy-phenyl)-[3'-methyl-2'-(3''-methylbut-2''-enyl)-6'-phenylcyclohex-3'-enyl]methanone (panduratin A; 6) isolated from fresh rhizomes showed strong antimutagenicity towards 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1) in *Salmonella typhimurium* TA98 (Trakoontivakorn et al. 2001). The antimutagenic IC₅₀ values of compounds 1–6 were 5.2, 5.9, 6.9, 5.3, 12.7, and 12.18 µM in the preincubation mixture, respectively. They also similarly inhibited the mutagenicity of 3-amino-1-methyl-5H-pyrido[4,3-b]indole (Trp-P-2) and 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP). All of them strongly inhibited the N-hydroxylation of Trp-P-2. Thus, the antimutagenic effect of compounds 1–6 was ascribed to the inhibition of the first step of enzymatic activation of heterocyclic amines. Incorporation of 5 Asian species galangal (*Alpinia galangal*), fingerroot (*Boesenbergia pandurata*), turmeric (*Curcuma longa*), cumin (*Cuminum cyminum*) and coriander seeds (*Coriandrum sativum*) into beef patties at 0.2 % before cooking at 204 °C (400 °F) for 10 min inhibited the formation of mutagenic heterocyclic amines (HCA) like 2-amino-3,8-dimethylimidazo [4,5-f]quinoxaline (MeIQx) and 2-amino-1-methyl -6-phenylimidazo [4,5-b]pyridine (PhIP) (Puangsombat et al. 2011). The average HCA content of the control patties was 7 ng/g MeIQx and 6.53 ng/g PhIP. Turmeric (39.2 % inhibition), fingerroot (33.5 % inhibition) and galangal (18.4 % inhibition) significantly decreased HCAs compared with the control. But, only turmeric and fingerroot were as effective as rosemary in preventing HCA formation. The HCA inhibition in patties containing spices was significantly correlated to the total phenolic content ($R^2 =$

0.80) and the scavenging activity ($R^2 = 0.84$) of the spices as measured by the 2,2-diphenyl- β -picrylhydrazyl assay.

Antiviral Activity

Cheenpracha et al. (2006) found that of the compounds isolated from the rhizome, hydroxy panduratin A possessed the most potent anti-HIV-1 protease activity with an IC_{50} value of 5.6 μ M, followed by panduratin A ($IC_{50} = 18.7 \mu$ M), whereas other compounds panduratin C, helichrysetin, 2',4',6'-trihydroxyhydrochalcone and uvangoletin exhibited only mild activity. *Boesenbergia pandurata* rhizome, chloroform extract, showed the most potent inhibitory activity against HIV-1 PR, followed by the methanol extract with inhibition of 64.92 % and 51.92 %, respectively (Tewtrakul et al. 2003). The flavonoid cardamonin exhibited an appreciable anti-HIV-1 protease activity with an IC_{50} value of 31 μ g/ml (Tewtrakul et al. 2003). The chloroform, methanol and water extracts of *B. pandurata* rhizomes at concentration of 100 μ g/ml exhibited HIV-I integrase activity with percent inhibition of 51.42 %, 28.71 % and 13.02 %, respectively (Tewtrakul et al. 2006). *Boesenbergia rotunda* cyclohexenyl chalcone derivatives, 4-hydroxy panduratin A and panduratin A, demonstrated good competitive inhibitory activities towards dengue-2 virus NS3 protease with the K_i values of 21 and 25 μ M, respectively, while those of pinostrobin and cardamonin were observed to be non-competitive (Tan et al. 2006). Frimayanti et al. (2011–2012) used a fragment-based molecular approach based on 4-hydroxy panduratin A, panduratin A (natural product extracts) and 246 DA (synthesised compound) to develop new dengue virus Den2 NS2b/NS3 inhibitors. All three ligands were found to be competitive inhibitors for the active proserine protease sites in dengue virus. The new ligands were bound by linking and redocking them into the active site of serine protease. *B. rotunda* rhizome extract exhibited antiviral activity against the foot and mouth disease virus (FMDV) in-vitro (Chungsamarnyart et al. 2007). Panduratin A and its regioisomer isopanduratin A were found to be inhibitors of dengue-2 viral activity (Chee et al. 2010).

Antimicrobial Activity

K. pandurata methanol extract exerted fast killing bactericidal effect against the cariogenic bacterium *Streptococcus mutans* in 2 min at 50 µg/ml of extract concentration (Hwang et al. 2004b). Isopanduratin A, from *K. pandurata*, completely inactivated cariogenic *Streptococcus mutans* at 20 mg/l in 1 min (Hwang et al. 2004a). The minimum inhibitory concentration (MIC) of isopanduratin A was 4 mg/l which was much lower than that of some other natural anticariogenic agents such as sanguinarine (12 mg/l), green tea extract and carvacrol (125 mg/l), thymol (250 mg/l) and isoeugenol and eucalyptol (500 mg/l). Significant inhibitory activity of isopanduratin A was also observed against *Streptococcus sobrinus*, *Streptococcus sanguinis* and *Streptococcus salivarius* with an MIC of 4 mg/l. The chloroform extracts of *Alpinia galanga* and *Boesenbergia pandurata* had pronounced antifungal activity in-vitro against *Cryptococcus neoformans* and *Microsporum gypseum* but exhibited weak activity against *Candida albicans* (Phongpaichit et al. 2005). *A. galanga* and *B. pandurata* were found to be excellent candidates for the development of a remedy for opportunistic fungal infections in AIDS patients. Ethanolic fingerroot extracts at 5–10 % (vol/vol) inhibited most *Listeria monocytogenes* strains for 24 h in the agar dilution assay (Thongson et al. 2005). In the enumeration-over-time assay, a 5 % fingerroot ethanol extract reduced ca. 4 log CFU/ml *Listeria* by around 2 log in 24 h, while 10 % inactivated the microorganism in 9 h. Fingerroot essential oil (EO) inhibited five strains of *Listeria monocytogenes* and four strains of *Salmonella enterica* ssp. *enterica* serovar *Typhimurium* DT104 at ≤ 0.4 % (v/v). Fingerroot EO at 0.2 % inactivated 4 log CFU/ml *L. monocytogenes* in 6–9 h. It was concluded that fingerroot EO and extract have potential for inhibiting pathogens in food systems. The application of high-intensity ultrasound-assisted (HI-US) extraction reduced the time of extraction to 5 min, compared with the 24 h required for conventional extraction and maintained antimicrobial activity of ginger, fingerroot and turmeric against *Salmonella typhimurium* but slightly reduced activity against *Listeria monocytogenes* (Thongson et al.

2004). Fingerroot extracted with isopropanol hexane and without HI-US had the best antilisterial effect, while HI-US-isopropanol fingerroot extract had the greatest antimicrobial efficacy against *S. typhimurium*.

Boesenbergia pandurata essential oil inhibited growth in-vitro of *Escherichia coli*, *Staphylococcus aureus*, *Bacillus cereus* and *Listeria monocytogenes* (Norajit et al. 2007). *Boesenbergia pandurata* extract at $\frac{1}{2}$ MIC (7.81 $\mu\text{g/mL}$) inhibited biofilm formation by *Streptococcus pyogenes* but did not show inhibition on quorum sensing (Limsuwan and Voravuthikunchai 2008). Pinostrobin, from *B. pandurata* rhizome, exerted inhibitory activity on the Ca^{2+} signals involved in the control of G2/M phase cell-cycle progression in *Saccharomyces cerevisiae* (Wangkangwan et al. 2009).

B. pandurata extract exerted an inhibitory effect on the ability of *Candida albicans* to adhere to denture acrylic and could be employed as an antifungal agent for preventing denture stomatitis (Sroisiri and Boonyanit 2010). *B. pandurata* rhizome ethanol extract (BPE) and oil (BPO) exhibited antimicrobial activity against oral pathogens in-vitro (Taweechaisupapong et al. 2010). BPE had MBC (minimum bactericidal concentration)/MFC (minimum fungicidal concentration) of 2.5, 1.25, 0.04 and 1.25 mg/ml against *Aggregatibacter actinomycetemcomitans*, *Streptococcus mutans*, *Lactobacillus* sp. and *Candida albicans*, respectively. BPO had MIC (minimum inhibitory concentration) of 0.5, 2, 1, 0.5 mg/ml against *Aggregatibacter actinomycetemcomitans*, *Streptococcus mutans*, *Lactobacillus* sp. and *Candida albicans*, respectively, and MBC/MFC of 1, 2, 2, 0.5 mg/ml against *Aggregatibacter actinomycetemcomitans*, *Streptococcus mutans*, *Lactobacillus* sp. and *Candida albicans*, respectively. BPO was the most effective extract against *C. albicans*. It was also demonstrated that the BPO possessed potent anti-*Candida* biofilm activity in-vitro and could be considered as a natural antifungal agent against *Candida* infections.

The growth of all clinical enterococci *Enterococcus faecalis* and *E. faecium* isolates ($n = 23$) were inhibited by panduratin A at a concentration of 2 $\mu\text{g/ml}$ (Rukayadi et al. 2010).

Panduratin A was able to kill all clinical enterococci isolates with a MBC of 8 µg/ml. The time-kill curves demonstrated that the bactericidal endpoint for clinical enterococci was reached after 30 min of incubation at a panduratin A concentration of 4x MIC. The growth of biofilm-producing enterococcal strains were inhibited and eradicated by panduratin A at concentrations of $< \text{or } = 4 \text{ µg/ml}$ and $< \text{or } = 16 \text{ µg/ml}$, respectively. The antibacterial activity of panduratin A against all clinical enterococci isolates was generally more potent than commonly used antimicrobials. Panduratin A exhibited stronger activity against biofilm-producing enterococcal strains than daptomycin and linezolid. Panduratin A exhibited strong antistaphylococcal activity in-vitro (Rukayadi et al. 2009b). Panduratin A had an MIC at which 90 % of clinical staphylococcal isolates methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-susceptible *S. aureus* (MSSA), methicillin-resistant coagulase-negative staphylococci (MRCNS) and methicillin-susceptible coagulase-negative staphylococci (MSCNS) were inhibited at 1 µg/ml. It was generally more potent than commonly used antimicrobials such as ampicillin, erythromycin, gentamicin, levofloxacin, linezolid, oxacillin, tetracycline, thymol and vancomycin. Studies showed that panduratin A was efficacious in preventing and reducing oral biofilm formation by *Streptococcus mutans*, *Streptococcus sanguis* and *Actinomyces viscosus* (Rukayadi et al. 2009a; Yanti et al. 2009d). Panduratin A showed an MIC of 1 µg/ml for multispecies strains. At $8 \times \text{MIC}$, panduratin A was able to prevent biofilm formation by $>50 \%$. Biofilm mass was reduced by $>50 \%$ after exposure to panduratin A at 10 µg/ml for 15 min. The results suggested that panduratin A could be applicable as a natural anti-biofilm agent to eliminate oral bacterial colonisation during early dental plaque formation.

B. rotunda ethanolic extract displayed potential antimicrobial and antifungal activities by inhibiting the gram-positive bacteria *Staphylococcus aureus*, *S. epidermidis* and *Bacillus subtilis* and the yeasts *Candida albicans* and *Saccharomyces cerevisiae* (Jitvaropas et al. 2012). Minimum inhibitory concentration (MIC) and minimum microbicidal concentration (MMC) values varied from 0.04 to 25 mg/mL

and from 0.16 to 25 mg/mL, respectively. *Escherichia coli* strains were found to be susceptible to the methanol extract of *B. rotunda* rhizome with MIC and MBC values of 0.019–2.5 mg/ml and 0.039–5 mg/ml (Zainin et al. 2013).

K. pandurata rhizome ethanol extract exhibited antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant coagulase-negative *Staphylococci* (MRCNS), methicillin-sensitive *Staphylococcus aureus* (MSSA), *Bacillus subtilis* and *Salmonella typhi* (Sukandar et al. 2014). The MIC of the extract was 16 ppm for both *Bacillus subtilis* and MRSA, 8 ppm for both MSSA and *Salmonella typhi* and 4 ppm for MRCNS.

Antigingivitis Activity

Treatment with *K. pandurata* extract (1–10 µg/ml) dose-dependently suppressed the activity, secretion and protein expression of matrix metalloproteinase-2 (MMP-2) in human gingival fibroblast-1 (HGF-1) exposed to *Porphyromonas gingivalis* via downregulation of phosphorylation of c-Jun N-terminal kinase (JNK) and cyclic AMP response element-binding protein (CREB) signalling pathways (Yanti and wang 2010). Due to its efficacy in inhibiting MMP-mediated periodontal destruction, *K. pandurata* might represent a new, potent periodontal therapy.

Gastroprotective/Antiulcer Activity

Crude extract of *B. rotunda* was reported to have chemopreventive and anti-*H. pylori* activities (Bhamarapravati et al. 2003). Pinostrobin and red oil from roots of *B. rotunda* exhibited anti-*Helicobacter pylori* activity in-vitro (Bhamarapravati et al. 2006). Pinostrobin and red oil had MIC of 125 and 150 µg/mL and MBC of 150 and 175 µg/mL, respectively. Both had antibacterial activity in the same range of that of drug currently used in the treatment of peptic ulcer. Minimum inhibitory concentration (MIC) of 95 % ethanol extract of *B. rotunda* against 6 CagA⁺ strains of *Helicobacter pylori* was determined as 3.125 µg/ml (Mahady et al. 2006). In

Mongolian gerbils, fingerroot significantly reduced *H. pylori* bacterial load, acute and chronic mucosal and submucosal inflammation, cryptitis, as well as epithelial cell degeneration, and erosion induced by *H. pylori* infection. Importantly, the extract did not increase morbidity or mortality of the animals.

Pretreatment with methanolic extract of *B. rotunda*, pinostrobin or omeprazole protected the gastric mucosa as seen by reduction in ulcer area and mucosal content, reduced or absence of submucosal oedema and leucocytes infiltration (Abdelwahab et al. 2011). Pinostrobin significantly lowered the elevated TBARS level in the gastric homogenate. Pinostrobin did not produced significant in-vitro inhibition of NO from LPS/IFN- γ -activated rodent cells nor cox enzymes. It was concluded that the extract possessed antiulcer activity, which could be attributed to indirect antioxidant mechanism of pinostrobin but not to the intervention with nitric oxide and COX inflammation pathways.

Anti-inflammatory Activity

Flavonoids (fourteen) isolated from *B. pandurata* rhizomes that exhibited anti-inflammatory activity by inhibiting carrageenan-induced paw oedema in male rats were found to possess methoxy groups at C5 and C7 of ring A and the pyrano ring of the flavonoid molecule (Panthong et al. 1994). Negligible or low anti-inflammatory activities were found in the chalcone derivatives. (-)-Hydroxypanduratin A and (-)-panduratin A, isolated from red rhizome, showed significant topical anti-inflammatory activity in the assay of TPA-induced ear edema in rats (Tuchinda et al. 2002). Panduratin A strongly inhibited both NO (IC₅₀: 0.175 μ M) and PGE₂ (IC₅₀: 0.0195 μ M) production and suppressed both iNOS and COX-2 enzyme expression without any appreciable cytotoxic effect on RAW264.7 cells in a dose-dependent manner (Yun et al. 2003). Panduratin A also suppressed the phosphorylation of inhibitor kappaB α (IkappaB α) and degradation of IkappaB α associated with nuclear factor kappaB (NF-kappaB) activation. Furthermore, panduratin A inhibited LPS-induced NF-kappaB transcriptional activity in a dose-

dependent manner suggesting it is potential as an anti-inflammatory agent. Compounds from *B. pandurata*, panduratin A, displayed the most potent NO inhibitory effect with an IC₅₀ value of 5.3 µM, followed by hydroxypanduratin A, IC₅₀ = 13.3 µM, and cardamonin, IC₅₀ = 24.7 µM (Tewtrakul et al. 2009). Panduratin A and hydroxypanduratin A showed strong activity against prostaglandin E₂ (PGE₂) with IC₅₀ values of 10.5 and 12.3 µM, respectively, and a moderate effect on tumour necrosis factor-α (TNF-α) production (IC₅₀ = 60.3 and 57.3 µM), respectively. Boesenbergin A exhibited significant anti-inflammatory at 12.5 to 50 µg/mL and without any significant cytotoxicity for the murine macrophage cell line RAW 264.7 at 50 µg/mL (Isa et al. 2012). Study by Boonjaraspinyo et al. (2010) found that fingerroot clearly reduced the inflammatory cells in hamsters that were administered N-nitrosodimethylamine (NDMA) but not in the case of liver fluke *Opisthorchis viverrini* infection. The decrease of direct bilirubin levels in hamsters treated with fingerroot suggests that fingerroot may enhance biliary contraction.

Kaempferia pandurata significantly decreased MMP-9 expression at both protein and mRNA levels in human oral epidermoid KB cells in a dose-dependent manner (Yanti et al. 2009a). It interfered *Porphyromonas gingivalis* supernatant-induced MMP-9 expression in KB cells by downregulating MAPK phosphorylation (extracellular signal-related kinase 1/2, p38 kinase and c-Jun N-terminal kinase), inhibiting transcriptional expression (Elk1, c-Jun and c-Fos) and blocking AP-1 and NF-kappaB activities. The results suggested *Kaempferia pandurata* could be employed as a candidate for MMP-9 inhibitor with therapeutic potential for treatment of periodontal inflammation. Also, panduratin A, from *K. pandurata*, exhibited inhibitory activity against MMP-9 secretion from *Porphyromonas gingivalis* supernatant-induced human oral epidermoid KB cells (Yanti et al. 2009c). MMP-9 protein and mRNA levels were significantly decreased after panduratin A treatment. Panduratin A also suppressed urokinase-type plasminogen activator (uPA) mRNA expression. These results suggested that panduratin A

could potentially prevent periodontal inflammation by decreasing the levels of MMP-9 protein and mRNA. Further, it was found that c-Jun N-terminal kinase (JNK) and activator protein-1 (AP-1) were the major signalling for *P. gingivalis* supernatant-stimulated MMP-9 expression in KB cells, and panduratin A markedly downregulated MMP-9 expression through inhibition of these signalling (Yanti et al. 2009b). Panduratin A (20 μ M), from *Boesenbergia pandurata*, inhibited secretion of β -hexosaminidase (46.69 %), histamine (34.32 %) and Ca^{2+} influx (43.84 %) (Choi et al. 2012). Panduratin A reduced the production of prostaglandin E_2 (47.58 %) and leukotriene B_4 (98.15 %) and the mRNA expression of cyclooxygenase-2, 5-lipoxygenase, interleukin (IL)-4, IL-13 and tumour necrosis factor- α . Furthermore, panduratin A attenuated phosphorylation of Akt, the mitogen-activated protein kinases (MAPK) extracellular signal-regulated kinase (ERK), p38 and c-Jun N-terminal kinase (JNK) expression.

Neuroprotective Activity

Boesenbergia pandurata rhizome was found to possess potent antioxidant activity in a rat brain homogenate model (Shindo et al. 2006). Its bioactive constituents, panduratin A, 4-hydroxypanduratin A and 2',6'-dihydroxy-4'-methoxychalcone, were also found to exert neuroprotective effects.

Hepatoprotective Activity

Oral administration (8 weeks) of *Boesenbergia rotunda* (BR) rhizome ethanolic extract exhibited hepatoprotective activity against thioacetamide-induced liver cirrhosis in rats (Salama et al. 2012, 2013a). BR treatment improved liver histopathology, immunohistochemistry and biochemistry, triggered apoptosis and inhibited cytokines, extracellular matrix proteins and hepatocytes proliferation. In the high-dose (5 g/kg) BR treatment group, the livers of the rats exhibited nearly normal looking lobular architecture, minimal inflammation and minimal hepatocyte damage; the levels of the serum

biomarkers and liver enzymes read nearly normal, and these results were all comparable to those observed or quantified from the normal and silymarin-treated groups.

Antihyperlipidemic/Antihypercholesterolemic/Antiobesity Activity

Panduratin A (PA), an LKB1 (liver kinase B1)-dependent AMP-activated protein kinase (AMPK) stimulator, activated PPAR α/δ and attenuated high-fat diet-induced obesity and dysregulation of lipid metabolism in mice (Kim et al. 2011). PA (50 mg/kg/day) reduced weight gain, fat mass, fatty liver and improved serum lipid profiles in obese mice. Additionally, it reduced ectopic fat accumulation and increased the proportion of slow-twitch myofibres and mitochondria content in skeletal muscle, thereby increasing running endurance. *B. pandurata* extract (BPE) treatment decreased triglyceride accumulation in both 3T3-L1 adipocytes and HepG2 hepatocytes by activating AMP-activated protein kinase (AMPK) signalling and regulating the expression of lipid metabolism-related proteins (Kim et al. 2012). In high-fat diet (HFD)-induced obese mice, oral administration of BPE (200 mg/kg/day for 8 weeks) significantly reduced HFD-induced body weight gain without altering the amount of food intake. Additionally, elevated serum levels of total cholesterol, low-density lipoprotein cholesterol and triglycerides were suppressed by BPE administration. Fat pad masses were reduced in BPE-treated mice, as evidenced by reduced adipocyte size. Furthermore, BPE is protected against the development of non-alcoholic fatty liver by decreasing hepatic triglyceride accumulation. BPE also activated AMPK signalling and altered the expression of lipid metabolism-related proteins in white adipose tissue and liver.

Antiplatelet Activity

B. pandurata extract was one of six Malaysian medical plants that showed significant inhibitory effects on platelet-activating factor (PAF) binding to rabbit platelets with IC₅₀ values ranging from 1.2 to 18.4 μ g/ml (Jantan et al. 2005).

Wound Healing Activity

Studies showed that wounds dressed topical with *B. rotunda* rhizome gel significantly accelerated wound-healing closure in rats (Mahmood et al. 2010). In wound-healing studies, the topical application of *B. rotunda* extract induced a significantly increased percentage of wound contraction on day 12 compared with the control group (Jitvaropas et al. 2012). Histological studies showed complete epidermis and found collagen fibres and hair follicles in the dermis.

Diuretic Activity

The diuretic activity of *B. rotunda* was found to be associated with two of its flavonoid derivatives, pinocembrine and hydroxy panduratin, which were identified as possible active compounds that bound to adenosine A₁ receptor (Yuliana et al. 2013).

Antityrosinase/Skin Whitening Activity

Studies in Korea reported that two chalcone compounds, isopanduratin A and 4-hydroxy panduratin A, isolated from the ethyl acetate fraction of ethanol extract of *Kaempferia pandurata* exhibited inhibitory effect on melanin biosynthesis and tyrosinase activity (Yoon et al. 2007). Compared with phenylthiourea ($IC_{50} = 34.3 \mu M$) as a positive control, the depigmentation IC_{50} values for isopanduratin A and 4-hydroxy panduratin A were $10.6 \mu M$ and $23.2 \mu M$, respectively. The compounds also significantly inhibited the activity of tyrosinase; the IC_{50} values of isopanduratin A and 4-hydroxy panduratin A for tyrosinase were $10.5 \mu M$ and $>30 \mu M$, respectively, while that of phenylthiourea was $47.6 \mu M$. The tyrosinase protein level was also significantly decreased by isopanduratin A and 4-hydroxy panduratin A. The results indicated isopanduratin A and 4-hydroxy panduratin A to be promising compounds that could be useful for treating hyperpigmentation as skin-whitening agents. Panduratin A, isolated from *Kaempferia pandurata*, was found to inhibit melanin biosynthesis in melan-a murine melanocytes (Lee et

al. 2010). The IC_{50} values of panduratin A for melanogenesis and tyrosinase were 9.6 μ M and 8.2 μ M, respectively, while those of arbutin as a positive control were 990 μ M and 660 μ M, respectively. In western blot analysis, panduratin A also significantly decreased tyrosinase, TRP-1 and TRP-2 protein levels. The results suggested the potential of panduratin A to be developed as a skin-whitening agent.

Skin Ageing Prevention Activity

Kaempferia pandurata extract (0.01–0.5 μ g/mL) significantly reduced the expression of matrix metalloproteinase (MMP)-1 and induced the expression of type 1 procollagen at the protein and mRNA levels in a dose-dependent manner (Shim et al. 2009a). Treatment of *K. pandurata* extract in the range of 0.01–0.5 μ g/mL inhibited the UV-induced phosphorylations of ERK, JNK and p38, respectively. Moreover, inhibition of phosphorylated ERK, JNK and p38 by *K. pandurata* extract resulted in decreased c-Fos expression and c-Jun phosphorylation induced by UV light. The results strongly suggested *K. pandurata* to be potentially useful for the prevention and treatment of skin. Studies also showed that 4-hydroxypanduratin A, isolated from *Kaempferia pandurata*, could be a potential candidate for the prevention and treatment of skin ageing brought about by UV (Shim et al. 2009b). 4-Hydroxypanduratin A in the range of 0.001–0.1 μ M significantly reduced the expression of MMP-1 levels and inhibited UV-induced MAPKs activation. Inhibition of MAPKs by 4-hydroxypanduratin A resulted in decreasing c-Fos expression and c-Jun phosphorylation induced by UV, which led to inhibiting AP-1 DNA-binding activity.

Panduratin A in the range of 0.001–0.1 μ M significantly reduced the expression of matrix metalloproteinase MMP-1 and induced the expression of type 1 procollagen at the protein, and mRNA gene levels in cultured human fibroblasts were irradiated with UV (Shim et al. 2008a, b). Panduratin A showed stronger activity than epigallocatechin-3-O-gallate (EGCG) known as a natural anti-ageing agent. The results suggested that panduratin A could be a potential candidate for

the prevention and treatment of skin ageing brought about by UV.

Sexual Behaviour Activity

Animal studies showed that gavage administration of *B. rotunda* ethanolic extract (60 mg/kg) significantly increased the relative testicular weight and the diameter of the seminiferous tubule and relative weight of seminal vesicle but did not affect sexual behaviour nor serum androgenic levels of male Wistar rats (Sudwan et al. 2007). There was no significant difference of courtship behaviour, mount frequency (MF), intromission frequency (IF), mount latency (ML), intromission latency (IL), copulatory efficiency or intercopulatory interval in male rats.

Antiparasitic Activity

The chloroform and methanol extracts of several plants including *Boesenbergia pandurata* were found to be inhibitory to be of *Giardia intestinalis* (AIDS pathogen) with an IC_{50} of $<100 \mu\text{g/ml}$ (Sawangjaroen et al. 2005). The chloroform extracts from *Boesenbergia pandurata* exhibited potent antiamoebic activity against *Entamoeba histolytica* strain HTH-56/MUTM and strain HM1/IMSS trophozoites with IC_{50} $45.8 \mu\text{g/ml}$ (Sawangjaroen et al. 2006). The chloroform and methanol extracts from *Boesenbergia pandurata* exhibited anti-giardial activity against trophozoites of *Giardia intestinalis* in-vitro with an IC_{50} of $<100 \mu\text{g/ml}$ (Sawangjaroen et al. 2005).

Insecticidal Activity (Health Pest)

Results of studies indicated the potential of essential oils extracted from *Boesenbergia rotunda*, *Zingiber zerumbet*, *Litsea petiolata*, *Curcuma zedoaria* and *Zingiber cassumunar* with good repellency against *Aedes aegypti* and *Culex quinquefasciatus* and high biting deterrence for deterred biting (Phukerd and Soonwera 2014). *Boesenbergia rotunda* essential oil provided the best efficiency, in which protection time was

4.3 h equivalent to that provided by the commercial chemical repellents (DEET; N,N-diethyl-3-methylbenzamide).

Drug Metabolism Activities

Short-term treatment of pinocembrin, from *B. pandurata* rhizome, in Wistar rats increased the activity of heme oxygenase but did not affect on the activities of other phase II xenobiotic-metabolising enzymes or the expression of cytochrome P450 enzymes (Punvittayagul et al. 2011).

Detoxification Activity

Boesenbergia pandurata (fingerroot) had been found to have extraordinarily high ability to induce mammalian phase 2 detoxication enzymes such as quinone reductase (Fahey and Stephenson 2002). The quinone reductase-inducing activity had been reported to be high from fresh broccoli, but the potency of fingerroot rhizomes (ca. 110,000 units/g) was even higher than that of broccoli, and the potencies of fingerroot oil and powdered rhizome (ca. 500,000 units/g) rivalled that of broccoli sprouts.

Toxicity Studies

Studies showed that oral administration of ethanol extracts of *B. rotunda* at all doses (60, 120 and 240 mg/KgBW/day) for 60 days elicited no toxic effect on male rats (Saraithong et al. 2010). The extracts had no effect on the body weight, regardless of the dosage used. All haematological parameters, including the total white blood cell count, the differential white blood cell count, packed red cell volume (PCV) and haemoglobin, were the same as those of the control. The kidney and liver functions, including blood urea nitrogen (BUN), creatinine (Crea), aspartate aminotransferase (AST) and alanine aminotransferase (ALT), were within the normal range. No histopathologic changes of the liver or kidney were observed. Studies found pinocembrin and pinostrobin, constituents from *Boesenbergia pandurata*, to be non-toxic and not mutagenic to male Wistar rats (Charoensin et al.

2010). There were no deaths observed following a single oral administration of 500 mg/kg of both compounds. Body weight, vital organ weights and blood biochemistry values of treated rats were not significantly different compared with those of the control group. Neither phytochemical nor mitotic index affected micronucleus formation in liver cells.

Adverse Issues

The results of animal studies suggested that *Citrus hystrix* as well as *B. pandurata* and *Languas galanga* may contain agents augmenting the hepatocarcinogenicity of 2-amino-3,8-dimethylimidazo(4,5-f)quinoxaline in rats (Tiwawech et al. 2000).

Traditional Medicinal Uses

The rhizome is used as an ingredient in post-partum tonic mixtures; as stomachic and carminative; as remedy for coughs, dyspepsia, sprue and colic; as external remedy for ringworm, rheumatic and post-partum muscular pain and swollen abdomen; and as medication for urination problem in children (Ibrahim and Nugroho 1999). In Indonesia, *B. rotunda* is typically used to prepare ‘jamu’, a popular traditional tonic for women after childbirth as well as a beauty aid for teenage girls and to prevent leucorrhoea (Chaudhary and Rafei 2002). In Thailand ‘krachai’ is used for the relief of stomachache, anti-flatulence, the eradication of ringworm and the promotion of appetite (Chomchalow et al. 2003) and as a diuretic (Chuakul and Boonpleng 2003). In Thailand, an alcoholic tincture of krachai dam root is used as aphrodisiac (Chamratpan and Homchuen 2005). *Boesenbergia rotunda* is traditionally used in many Asian countries as medicine for stomach pain and discomfort, viral and bacterial infection, inflammation and diuretic agent (Yuliana et al. 2013).

Other Uses

The rhizome has insecticidal activity. The methanol extract of the rhizomes of *K. rotunda* and (–)-2-acetyl-4-benzoyl-1-

benzoyloxymethyl-1,6-epoxycyclohexan-2,3,4,5-tetrol (2-acetylrotopoxide B) exhibited antifeedant activity against larvae of *Spodoptera littoralis* (Stevenson et al. 2007). (–)-Zeylenol also showed antifeedant activity, whereas (–)-6-acetylzeylenol was inactive.

Comments

Fingerroot is traditionally propagated using a rhizome segment. Studies showed that it can be rapidly propagated from shoot bud explants derived from shoot base callus grown on tissue culture medium (Yusuf et al. 2013b).

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Curcuma aeruginosa

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Scientific Name

Curcuma aeruginosa Roxb.

Synonyms

No synonyms recorded

Family

Zingiberaceae

Common/English Names

Black Ginger, Hidden Lily, Pink and Blue Ginger

Vernacular Names

India: Karimanjil, Neelakua (Malayalam)

Malaysia: Temu Hitam, Temu Ireng

Thai: Kha Min Dam, Wahn Mahamek (Rhizome) Kra-Jeaw (Flowers)

Vietnamese: Nghệ Ten Đồng, Nghệ Đen, Nghệ Xanh, Ngải Tím

Origin/Distribution

The species is indigenous from Indo-China to West Malesia. It is widely cultivated in Malaysia (Sirat et al. 1998a) and Indonesia.

Agroecology

It thrives in a warm, humid environment in the open or partial shade. It grows in various soil types but prefers loose, well-textured and well-drained fertile soils.

Edible Plant Parts and Uses

Rhizomes of *C. aeruginosa* have functional food quality and medicinal and health benefits (Liu et al. 2013).

Tubers/rhizomes are eaten by tribals from Pechiparai Social forest in Kanyakumari district, India (Sujatha and Renuga 2013). Tg Kamazeri et al. (2012) found the rhizome essential oil to have promising antimicrobial properties and to be useful as food preservative. The inflorescences are eaten as vegetables by the Karen people in Thailand (CINE 2008).

Botany

Curcuma aeruginosa is an erect, tillering herb with rhizome up to 16 cm long and 3 cm thick. The rhizome outside is grey and shiny, tips pink, and its inside bluish or blue-green with white cortex. Its spurious stem is green, terminal on ovoid primary rhizome. Leaf sheaths are up to 50 cm long. Leaf blades are elliptical to oblong-lanceolate, 30–80 cm × 9–20 cm, and green with wide purplish-brown suffusion on each side of the midrib on distal half (Plate 1). Inflorescence is terminal on a separate lateral shoot; bracts are pale green and coma bracts red-purple (Plate 2). Flowers are 2–7 in axils of secondary bracts; calyx is half as long as the corolla tube and 3-toothed; corolla is tubular at base, glabrous about 4.5 cm long and deep crimson-pink or red. Labellum is about 17 mm × 17 mm, tip emarginated and yellow with deep yellow median band, ovary 3-celled and pubescent, style long and glabrous, stigma

bilabiate and fimbriated, lateral staminodes longitudinally folded and pale yellow and anther spurred.



Plate 1 Foliage of black ginger



Plate 2 Inflorescence on short leafless scape

Nutritive/Medicinal Properties

Flower Nutrients

Nutrient composition of the flower per 100 g edible portion was reported as follows: moisture 90.4 g, energy 34 Kcal,

protein 1.3 g, fat 0.6 g, carbohydrate 5.8 g, vitamin A 8.7 µg RE or 4.3 µg RAE, β-carotene 52 µg, thiamine 0.07 mg, Ca 43 mg and Fe 1.9 mg (CINE 2008).

Rhizome Nutrients/Phytochemicals

The rhizome was reported to contain total ash 6.1 %, acid-insoluble ash 1.20 %, alcohol-soluble extractives 3.70 %, water-soluble extractives 14.50 %, sugar 20.93 %, starch 41.85 % and tannins 0.68 % (Srivastava et al. 2006). On hydrodistillation, the rhizomes and sessile tubers yielded 0.17 % oil. Sujatha and Renuga (2013) reported the rhizome stock and tubers had 25 % dry matter, 14.06 % starch with granule size 6.60–23 µm, 1.3 % sugar and 0.78 % lipids. Choudhury et al. (2013) found that mature parts of the inner cortex of the rhizome contained higher amount (0.5–1.71 mg/100 g FWT) of curcumin. The flavonoid content in the extracts of the inner cortical part (0.16–0.37 mg/g FWT) was higher than that in the extracts of the outer cortical part of the rhizome (0.05–0.36 mg/g FWT), and the estimated total phenol varied from 2.53 to 3.4 mg/g FWT in the inner cortex, which was higher than the outer cortex (1.84–3.25 mg/g FWT) and accumulated basipetally towards mature tissues. Results of studies suggested that curcumin-glucuronide, dihydrocurcumin-glucuronide, tetrahydrocurcumin-glucuronide and tetrahydrocurcumin were major metabolites of curcumin in mice (Lin and Lin-Shiau 2001).

C. aeruginosa rhizomes were found to contain curcumenol, isocurcumenol and ferulic acid (Zhang et al. 1986); difurocumenone (Shiba et al. 1987); an oxygenated guaiane sesquiterpene aerugidiol (Masuda et al. 1991); two guaiane derivatives, zedoalactones A and B and zedoarondiol (Takano et al. 1995); curcumin (Sirat et al. 1998b); three sesquiterpenes, curcumenol, zedoarol and isocurcumenol, and phytosterol mixtures containing stigmasterol and α-sitosterol (Md Saad 2006); three sesquiterpenes, zedoarol, curcumenol and isocurcumenol (Sukari et al. 2007); camphor 16.85 %, curzerenone 16.81 % and epicurzerenone 3.5 % (Aromdee et al. 2011); and six sesquiterpenes, germacrone, zederone,

dehydrocurdione, curcumenol, zedoarondiol and isocurcumenol (Suphrom et al. 2012).

Twenty-six compounds were identified in the rhizome essential oil of which curzerenone (24.6 %), 1,8-cineole (11 %), camphor (10.6 %), zedoarol (6.3 %), isocurcumenol (5.8 %), curcumenol (5.6 %) and furanogermenone (5.5 %) were the major components (Sirat et al. 1998b). Zwaving and Bos (1992) found *C. aeruginosa* rhizome essential oil to contain isocurcumenol (8.5 %), β -eudesmol (6.5 %), curdione (3.6 %), curcumenol (9.9 %), curcumanolides A and B (11.4 %), dehydrocurdione (9.4 %) and curcumenone (1.9 %). Jantan et al. (1999) reported 1,8-cineole (23.2 %) and curzerenone (28.4 %) the major constituents of the essential oil. In another study, *C. aeruginosa* yielded 0.19 % (fresh weight basis) of essential oil with 37 constituents accounting for 80.67 % of total oil identified (Jarikasem et al. 2005). High amounts of curzerenone (41.63 %), 1,8-cineole (9.64 %) and β -pinene (7.71 %) were found. Other components included α -pinene 1.46 %, camphene 0.34 %, sabinene 0.22 %, myrcene 0.13 %, limonene 0.65 %, 2-heptanol 0.21 %, 2-nonanone 1.10 %, 2-decanone 0.21 %, 2-nonanol 2.04 %, linalool 0.23 %, α -elemene 1.68 %, β -caryophyllene 0.342 %, 2-undecanone 0.76 %, myrtenol 0.43 %, β -elemene 0.21 %, *trans*-pinocarveol 0.19 %, humulene 0.28 %, isoborneol 0.58 %, β -terpineol 0.29 %, α -terpineol 1.31 %, borneol 0.48 %, germacrene D 0.50 %, β -bisabolene 0.22 %, δ -cadinene 0.42 %, β -sesquiphellandrene 0.57 %, *ar*-curcumene 1.01 %, germacrene B 0.51 %, curzerene 1.08 %, caryophyllene oxide 0.32 %, germacrone 0.99 %, *T*-cadinol 0.86 %, *T*-muurolol 1.15 % and α -cadinol 0.83 %.

Tg Kamazeri et al. (2012) identified sixteen compounds in *C. aeruginosa* rhizome essential oil, with sesquiterpenes predominating, accounting for 94.08 % of the oil with cycloisolongifolene, 8,9-dehydro formyl (35.29 %) and dihydrocostunolide (22.51 %) as dominant compounds. Other major compounds present were the sesquiterpenes vellerol (10 %), germacrone (6.5 %), β -elemene (4.75 %), alloaromadendrene oxide-(2) (4.07 %), β -farnesene (2.65 %), aromadendrene oxide-(2) (2.40 %), α -bulnesene (2.14 %) and

eudesma-4(14),11-diene (1.13 %). Oxygenated monoterpenes present included eucalyptol (3.98 %), *L*-camphor (1.32 %) and isoborneol (0.62 %). Small amounts of caryophyllene (1.01 %), β -cubebene (0.92 %) and xanthinin (0.69) were also found.

Twenty-seven compounds were detected in the methyl *tert*-butyl ether extract of *C. aeruginosa* rhizome; the major compounds were methenolone (16.64 %), cycloisolongifolene, 8,9-dehydro-9-formyl- (15.93 %), labd-13-en-15-oic acid, 8,12-epoxy-12-hydroxy- γ -lactone (10.77 %), propiolic acid, 3-(1-hydroxy)-2 isopropyl-1,5-methylcyclohexyl) (7.84 %), 4-oxo- β -isodamascol (5.17 %), velleral (3.11 %) and *Z*- α -farnesene (2.00 %) (Simoh and Zainal 2015). The minor compounds were 3-carene, camphene, 2-thujene, β -pinene, cineole (eucalyptol), acetophenone, camphor (1*R*,4*R*), borneol, terpinene-4-ol, α -terpineol, δ -elemene, caryophyllene, germacrene B, epi-bicyclosesquiphellandrene, curzerene, germacrone, 8,9b-dimethyl, 4a,9b-dihydrodibenzo[b,d]furan-3(4H)-one and cholesta-22,24-dien-5-ol-4,4-dimethyl- β -sitosterol. The most prevailing major compounds identified in the polar fraction of the methanol/chloroform extract were α -*D*-glucopyranoside, 1,3,4,6-tetrakis-*O*-(TMS)- β -*D*-fructofuranosyl 2,3,4,6-tetrakis-*O*-(TMS)- (38.08 %); *d*-glucose, 2,3,4,5,6-pentakis-*O*-(TMS)-, *O*-methyloxime (14.61 %); *D*-fructose, 1,3,4,5,6-pentakis-*O*-(TMS)-, *O*-methyloxime (5.28 %); isocitric acid (TMS) (3.06 %); oxalic acid, bis-(TMS) ester (2.96 %); hexadecanoic acid, TMS ester (2.16 %); citric acid, ethyl ester, tri-TMS (1.91 %); and butanedioic acid, [(TMS)oxy]-, bis-(TMS) ester (1.14 %). Other minor compounds were malonic acid bis-(TMS) ester; butanoic acid, 4-[(TMS)oxy]-TMS ester; *L*-alanine, *N*-octanyl-ethyl ester; myo-inositol, 1,2,3,4,5,6-hexakis-*O*-(TMS)-; 4,4-dimethyl-*N*-(2-phenylethyl)-5 α -androst-2-en-17-amine; stearic acid, TMS ester; tetracosane; 17-hydroxy-3,20-dioxopregna-1,4,9 (11)-trien-21-yl acetate; and triacontane and tetratriacontane. In the non-polar extract, among the major compounds detected were cycloisolongifolene, 8,9-dehydro-9-formyl (15.70 %); propiolic acid, 3-(1-hydroxy-2-isopropyl-5-methylcyclohexyl) (11.09 %); stearic acid, TMS ester (2.78 %); hexadecanoic acid, TMS ester (2.33 %); oleic acid, TMS ester (1.62 %);

curzerene (1.56 %); *Z*- α -farnesene (1.52 %); germacrone (1.41 %); β -elemene (1.33 %); and pregna-1,4,16-triene-3,20-dione,11,22-diacetoxy- (1.11 %). The minor compounds (<1 %) were 3-methyl cyclopentane-1-yl-TMS ether; eucalyptol (cineole); thiosalicylic acid *O*, *S*-di-TMS-; camphor; terpinene-4-ol; α -terpineol; butane-1,3-diol, 1-methylene-3-methyl-bis (TMS) ether; glycine, *N*-(TMS)-, TMS ester; borneol, TMS ether; phenylethanolamine; tris-(TMS) phosphate; *S*-elemene; caryophyllene, β -cubebene; (2,6-ditert-butylphenoxy)(trimethyl)silane; velleral; 2-isopropenyl-2,3-dihydro-7H-furo (3,2-g) chromen-7-one; heptadecanoic acid, TMS ester; linoleic acid, TMS ester; 4 α -methylandrostane-2,3-diol-17-dione; anthiaergostan-5,7,9,22-tetraen-14-ol-15-one; 19-norpregn-4-en-20-yn-3-one, 17 (TMS)oxy; androst-5-en 17-one; and 3,16-bis-[(TMS)oxy], *O*-methyloxime (3 β , 16 α).

The crude homogenate and ammonium sulphate cut fraction of *Curcuma aeruginosa* rhizomes was found to contain a significant level of superoxide dismutase (SOD) activity (Moon-ai et al. 2012). An overall SOD yield of 2.51 % with a specific activity of 812.20 U/mg was obtained. The enriched SOD had an apparent MW of 31.5 kDa and a pH and temperature optima of 4.0 and 50 °C.

Leaf Phytochemicals

More than 25 components are identified from the leaf essential oil, of which curzerene (16.2 %), germacrone (13.6 %), 1,8-cineole (13.5 %) and camphor (5.7 %) were the major ones (Dũng et al. 1995). Fifty components were found in the leaf essential oil from South India (Jirovetz et al. 2000). The major components were 1,8-cineola (17.7 %), curzerenone (10.5 %), furanogermenone (7.8 %), camphor (7.5 %), (*Z*)-3-hexenol (5.8 %), furanodienone (5.1 %), curcumenol (4.3 %), isocurcumenol (3.7 %) and β -elemene (3.3 %).

Antioxidant Activity

The antioxidant activity of *C. aeruginosa* ginger was found to be greater than its curcuminoids curcumin,

demethoxycurcumin and bisdemethoxycurcumin, as assessed by the isothiocyanate and thiobarbituric acid assays (Jitoe et al. 1992). Leaves of *C. aeruginosa* had a total phenolic content (TPC) of 282 mg GAE/100 g and ascorbic acid equivalent antioxidant capacity (AEAC) of 140 mg AA/100 g and rhizome TPC of 145 mg GAE/100 g and AEAC of 55 mg AA/100 g (Chan et al. 2008).

Mature part mainly the inner cortex of *C. aeruginosa* rhizome showed excellent performance of 2,2-diphenyl-1-picrylhydrazyl (PPPH), reducing power and nitric oxide scavenging antioxidant activity (Choudhury et al. 2013). The antioxidant activity increased with rhizome maturity. Total phenol, flavonoid and curcumin contents were obtained higher in the mature part of rhizome. Free radical scavenging activities were highly correlated with total phenol content. In another study, curcumenol and isocurcumenol from the rhizomes were found to have antioxidant activity (MD Saad 2006). The MTT [3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide] antioxidant assay revealed that the extracts of *Curcuma caesia*, *Curcuma zedoaria* and *Curcuma aeruginosa* at 250 µg/ml and isolates at 5 µg/ml demonstrated activity comparable to positive controls vitamin C and *t*-butyl hydroquinone (TBHQ) at 25 µg/ml (Liu et al. 2013).

Anti-inflammatory Activity

Purified superoxide dismutase, from the rhizomes, exhibited inhibitory effects on lipopolysaccharide-induced nitric oxide production in cultured mouse macrophage cell RAW 264.7 in a dose-dependent manner ($IC_{50} = 14.36$ µg protein/ml) (Moonai et al. 2012). *Curcuma caesia*, *Curcuma zedoaria* and *Curcuma aeruginosa* extracts inhibited lipid peroxidation (LPO), by 40 % at 250 µg/ml, whereas pure isolates 1–11 inhibited by about 20 % (Liu et al. 2013). The extracts and isolates inhibited cyclooxygenase COX-1 and COX-2 enzymes between the ranges of 3–56 and 5–30 %, respectively.

Antitumour Activity

The crude chloroform extract of *Curcuma aeruginosa* rhizome was found to be active against CEM-SS cell lines with IC₅₀ value of 6 µg/mL (Md Saad 2006). Chloroform extract from *C. aeruginosa* rhizome showed strong activity against lymphoblastic leukaemia IC cancer cell lines with IC₅₀ of 50 µg/ml (Sukari et al. 2007). Curcumin, a major component of the *Curcuma* species including *C. aeruginosa*, had been shown to have anticarcinogenic activity in animals as indicated by its ability to block colon tumour initiation by azoxymethane and skin tumour promotion induced by phorbol ester TPA (Lin and Lin-Shiau 2001). It is proposed that curcumin may suppress tumour promotion by blocking signal transduction pathways in the target cells.

Uterine Relaxant Activity

In the agonist- and KCl-stimulated rat uteri, the chloroform and methanol rhizome extracts exerted concentration-dependent inhibition of the contractions induced by oxytocin (1 mU/ml), prostaglandin F2alpha (PGF2alpha, 0.5 µg/ml), acetylcholine (3×10^{-6} M) and KCl (40 mM) with the IC₅₀ (inhibition of force) of 31.4, 58.59, 56.21 and 29.28 µg/ml and 57.79, 69.3, 223.8 and 69.19 µg/ml, respectively (Thaina et al. 2009). In contrast in nonstimulated uterus, the two extracts (10–400 µg/ml) had no significant effect. It was speculated that the two plant extracts might inhibit uterine contraction by interrupting the influx of Ca²⁺ probably through voltage-gated L-type calcium channels. Based on the inhibitory effect of the extracts on the oxytocin-induced contraction, it is concluded that the extracts might be useful as tocolytic agents for the prevention of preterm labour. Their effects on the inhibition of PGF2alpha-induced contractions also seem useful for the treatment of dysmenorrhoea. It was also postulated that the uterine relaxant effect of the plant extracts could be due to β -pinene and some sesquiterpene lactone contents.

Anti-androgenic Activity

Studies showed that *Curcuma aeruginosa* extract, a 5 α -reductase antagonist, could be used to treat hair loss (Suphrom et al. 2014). Six sesquiterpenes, germacrone, zederone, dehydrocurdione, curcumenol, zedoarondiol and isocurcumenol, isolated from the rhizomes, inhibited 5 α -reductase which converts testosterone to dihydrotestosterone (DHT) (Suphrom et al. 2012). Germacrone was the most potent (IC₅₀ = 0.42 mg/mL). Germacrone was anti-androgenic in LNCaP cells when proliferation was testosterone induced. The growth of flank gland of male Syrian hamsters was dependent on circulating androgen, and when maintained with testosterone, germacrone (3, 30, 100 μ g) inhibited growth but was ineffective against DHT. The results suggested germacrone to have a potential as lead compound for treatment of androgen-dependent disorders. (*E,E*)-8-Hydroxygermacrene β prepared by ketone reduction of germacrone, a naturally occurring compound from *Curcuma aeruginosa*, showed remarkable in-vitro anti-androgenic activity (IC₅₀ 0.15 mM) applicable to male baldness treatments (Srivilai et al. 2014). Suphrom et al. (2014) found anti-androgenic constituents of *C. aeruginosa* were instable at high temperature and in solid form.

Antiplatelet Activity

C. aeruginosa extract was one of the six Zingiberaceae species found to inhibit platelet-activating factor (PAF) binding to rabbit platelets (Jantan et al. 2005). They showed significant inhibitory effects with IC₅₀ values ranging from 1.2 to 18.4 μ g/ml.

Analgesic/Antinociceptive Activity

Oral administration of the chloroform extract and the methanol extract of *C. aeruginosa* rhizomes (100–400 mg/kg) to rats significantly decreased the number of writhings and stretchings induced by acetic acid (Reanmongkol et al. 2006). Only the chloroform extract suppressed the licking activity of the late phase in the formalin test in mice. All extracts of *C. aeruginosa* rhizomes had no effects on heat-induced pain in

mice, yeast-induced fever and carrageenan-induced edema in rats. These results suggested that the chloroform extract of *C. aeruginosa* rhizome possessed analgesic effect via a different mechanism from that of the aspirin.

Antiviral Activity

The water extract from the rhizome of *C. aeruginosa* effectively inhibited human immunodeficiency virus type I (HIV-1)-infected MT-4 cells (Otake et al. 1995). It also suppressed the formation of syncytia in cocultures of MOLT-4 and MOLT-4/HIV-1 cells.

Antimicrobial Activity

The chloroform extract from *C. aeruginosa* rhizome exhibited moderate activity against *Pseudomonas aeruginosa* and weak activity against *Bacillus subtilis* and the mutant strain and *Staphylococcus aureus* (MRSA strain) (Sukari et al. 2007). However, the petroleum ether and methanol extracts were inactive against all the pathogenic microbes. The purified component isocurcumenol exhibited moderate activity against *Bacillus subtilis* and *Pseudomonas aeruginosa* but was not active against *Bacillus subtilis* mutant. In another study, the ethyl acetate extract of *Curcuma aeruginosa* inhibited in-vitro growth of *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Bacillus subtilis* at concentration of 500 mg/mL, while at 50 mg/mL, its ethyl acetate extract also inhibited *Bacillus subtilis* (Philip et al. 2009). Both hexane and methanolic extract of *Curcuma aeruginosa* showed weak antimicrobial activity against *Pseudomonas aeruginosa* and *Staphylococcus aureus* at concentration of 500 mg/mL, while the hexane extract also inhibited growth of *Pseudomonas aeruginosa* at 50 mg/mL concentration.

Compared to *C. mangga* rhizome oil, *C. aeruginosa* essential oil had moderate antimicrobial activity (Tg Kamazeri et al. 2012). *Staphylococcus aureus* was the most susceptible and *Pseudomonas aeruginosa* was the most resistant. It exhibited moderate activity against *Candida albicans* and weakly inhibited *Cryptococcus neoformans*.

Traditional Medicinal Uses

Rhizome is used medicinally as antidiarrhoeal and antifungal and externally as astringent for wounds in India (Srivastava et al. 2006). *C. aeruginosa* rhizome has been used in Thai traditional medicine for the treatment of inflammations, postpartum uterine and perimenopausal bleeding (Pongboonrod 1979); as carminative, analgesic and anti-inflammatory agent for uterine inflammation (Jarikasem et al. 2005); and as a component of Thai herbal medicinal recipes used for decreasing dysmenorrhoea (Reanmongkol et al. 2006). According to Burkill (1966), it is one of the numerous ingredients in Singapore universal tonic or 'ubat jamu'; it is prescribed for cough and asthma and used externally pounded in coconut oil for scurf and to treat mental derangements. He also reported that its primary use in Indonesia was in childbirth for its purgative action, administered internally as a decoction. Kartasapoetra (1988) listed the use of *C. aeruginosa* extract in Indonesian traditional medicine as local anaesthetics in cold, cough, asthma and other preparation, besides having antispasmodic effect. It is considered to be depurative and used both internally and externally for treating exanthema and also as a poultice for itching (Perry 1980). It also added in a beverage given to women in confinement to accelerate the lochia and decrease pain and inflammation of uterus (Perry 1980; Pongboonrod 1979).

Other Uses

C. aeruginosa was found to have acaricidal activity. *C. aeruginosa* rhizome extracts were found to be efficacious in controlling red spider mite, *Tetranychus urticae* on queen palm, *Livistona rotundifolia* foliage (Svinningen et al. 2010). All the concentrations 5, 10, 15, 20 and 25 g/L except 2 g/L were found to be effective compared to control.

Comments

Choudhury et al. (2013) found that single-node cutting propagation is the best method for ex-situ conservation of the

plant. *C. aeruginosa* rhizome could be successfully propagated through single rhizome nodal cutting and apical tip culture. 100 % germination was observed from longitudinal single-node cutting as well as apical tip culture, and 90 % germination was found from transverse single-node cutting.

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Curcuma longa

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Scientific Name

Curcuma longa L.

Synonyms

Amomum curcuma Jacq., *Curcuma brog* Valetton, *Curcuma domestica* Valetton, *Curcuma longa* var. *vanaharidra* Velay., Pandrav., J.K. George & Varapr., *Curcuma ochrorhiza* Valetton, *Curcuma soloensis* Valetton, *Curcuma tinctoria* Guibourt, *Kua domestica* Medik. (illeg.), *Stissera curcuma* Giseke, *Stissera curcuma* Raeusch.

Family

Zingiberaceae

Common/English Names

Common Turmeric, *Curcuma*, Indian Saffron, Long Rooted Curcuma, Long Turmeric, Turmeric, Turmeric Common, Yellow Ginger

Vernacular Names

Afrikaans: Borrie

Albanian: Shafran I Indisë

Amharic: Ird

Antilles: Arrow-Root De l'Inde, Safran-Cooli, Safran Des Indes, Safran Du Pays

Arabic: Aurukesafur, Auruqussabba-ghin, Auruqussufr, Haldi Zard, Kumkum, Kurkum, Uqdah Safra, Urukessabaghin, Urukessubr, Urukessufr, Zardchaub, Zarsud

Aramaic: Eqar Kurkma

Armenian: Toormerik, Turmerig

Azeri: Sarikök

Belarusian: Kurkuma, Žouty Imbir

Bhutan: Yong La (Dzongkha)

Brazil: Açafrão, Açafrão-da-terra, Açafroeira, Curcuma, Zedoária (Portuguese)

Breton: Kurkuma

Bulgarian: Kurkuma

Burmese: Hsanwen, Sa nwin, Sanae, Nanwin

Catalan: Curcuma

Chakma: Olod;

Chinese: Wòhng Gèung, Wong Keong (Cantonese), Jiang Huang, Huang Jiang, Yu Jin, Yu Chiu (Mandarin)

Croatian: Indijski šafran, Kurkuma

Czech: Indický Šafrán, Japonský Šafrán, Kurkuma, Kurkuma Dlouhá, Žlutý Kořen, Žlutý Zázvor

Egypt: Aqîd Hindî, Hurd, Kurkum, Timmer (Arabic)

Esperanto: Kurkumo

Estonian: Harilik Kurkuma, Kurkum, Pikk Kollajuur, Lõhnav Kollajuur

Danish: Gurgemeje, Gurkemeje, Kurkuma

Dutch: Geelwortel, Indaansche Saffraan, Kurkuma, Kurkuma Geelwortel

Fiji: Haldi

Finnish: Keltajuuri, Kurkuma, Maustekurkuma

French: Curcuma, Curcuma Longue, Rhizome De Curcuma, Safran Des Indes, Souchet Des Indes, Terre-mérite

Galician: Cúrcuma

German: Curcuma, Kurkuma, Gelber Ingwer, Gelbwurz, Gelbwurzel, Gilber Ingwer, Gilbwurzel, Indischer Safran, Javanische Gelbwurz, Kurkuma, Kurkume, Lange Kurkuma

Greek: Kitrinoriza, Kourkoumi, Kourkoumas

Hawaiian: Ōlena

Hebrew: Kurkum

Hungarian: Indiai Kurkuma, Kurkuma, Sáfránygyökér, Sárga Gyömbérgyökér, Sárga Kurkuma

Icelandic: Gullinrót, Kúrkúma, Túrmerik

India: Halodhi, Horidra (Assamese), Halud, Holdi, Holood (Bengali), Andi (Bishnupriya Manipuri), Halde (Bodo), Reen'dhoo (Dhivehi), Bsar, Haldi (Dogri), Holdi (Garo), Haldar, Haldi (Gujerati), Aieng (Hmar), Besvar, Halad, Halda, Haldi, Holeed (Hindi), Arasina, Arishina, Arisina, Haladi, Haldi (Kannada), Shynrai (Khasi), Kuva, Manjal, Manjella-kua, Mannal, Manyal, Marinalu, Marinnala, Paccamannal, Varattumannal (Malayalam), Hared, Hardi (Maithili), Yaingang, Machu (Manipuri), Halad, Halede (Marathi), Ai-eng (Mizo), Injaikaraim (Naga, Rongmei), Yaingang (Naga, Tangkhu), Haladi (Oriya), Haldi (Punjabi), Aneshta, Bahula, Bhadra, Dirgharaga, Dosa, Gandhapalashika, Gauri, Gharshani, Haladi, Haladika, Haridra, Haridrakam, Harita, Hemaragi, Hemaragini, Hridvilasini, Jayanti, Jvarantika, Kanchani, Kaveri, Krimighni, Ksanada, Kshanada, Kshapa, Lakshmi, Marmarii, Mangalaprada, Mangalya,

Mehaghni, Nisa, Nisha, Nishakhya, Nishavha, Nisi,
Paimanjal, Pavitra, Pinga, Pinja, Pita, Pitaka, Pitavaluka,
Pitika, Rabhangavasa, Rajani, Ranjani, Ratri,
Ratrinamika, Shifa, Shivashobhana, Shyma, Siva,
Subhagavhaya, Suvarna, Suvarnavarna, Tamasani, Uma,
Vara, Varangi, Varavarnini, Varnadatri, Varnavat,
Varnavati, Varnini, Varvarini, Yamini, Yoshitapriya,
Yositpriya, Yuvati (Sanskrit), Sasang (Santali),
Akkinicaruman, Akkinicekaram, Alar, Amparam,
Ancarakam, Anmancal, Aran, Aranmaki, Aranmakiceti,
Ari, Aricam, Aricanam, Aricanattuvayam, Aricatti, Arici,
Aritaram, Arittira, Arittiramancal, Arittirapam,
Atavapitan, Cakiyam, Cankocam, Caruvari, Conitam,
Cuvarnavarnan, Ilekini, Iracani Irattankam, Irattiri,
Kacamaram, Kacarppam, Kacayar, Kakacani,
Kaleyakam, Kallaram, Kanakavarni, Kanatteru, Kancani,
Kancini, Kantapalacikam, Kappu Mancal, Karccurakam,
Karimancal, Katampam, Katankateri, Katuppu, Kauram,
Kaviram, Kilankumancal, Kirucan, Kirucanatitam,
Lankali, Mamam, Mancal, Mancatkottu, Manjal, Munjil,
Muntan, Mutiyakkilanku, Mutiyarikam, Muttan,
Muttanmancal, Nakainokkam, Nakali, Nanmancal,
Naravati, Nicaram, Nicatu, Nicatukam, Nici, Nicikam,
Niku, Nompuvirali, Nompuviraliceti, Novu, Pacappu,
Pattirai, Picunam, Pitai, Pitakaveram, Pitam, Pitani, Pitar,
Talapattiri, Tamaniti, Tami, Tanavaka, Tapanarkanci,
Taparkanci, Tecani, Tecanikakkompu, Tekani, Tekavarni,
Teni, Tipakam, Tipanam, Tiralarakam, Tiralarakamancal,
Tirkkaracikai, Tokaimukapusanam, Tokaimukaputanam,
Tunkam, Turu, Turukakkompu, Ulokitam, Uluttiram,
Umai, Urittiram, Uruttiram, Uttiram, Vaccani, Vaccanir,
Vaivaccutam, Vallikam, Valliyam, Varam, Varanki,
Varavannini, Varnam, Vattiyaputpam, Veram, Vilacini,
Visakinacam (Tamil), Haridra, Pampi, Pasupu (Telugu),
Manjalu (Tulu), Haladi, Haldi, Haldi Biryani, Haldi Nim
Kfota, Zard Chob (Urdu)

Indonesia: Kunir, Kunir Bentis, Temu Kuning
(Javanese), Kunyir, Koneng, Koneng Temen (Sundanese)

Italian: Croco Indiano, Curcuma, Curcuma Di Levante, Curcuma Lunga, Radice Gialla, Zafferano Delle Indie

Japanese: Ukon, Tamerikku

Kashmiri: Ladar

Khmer: Lamiet, Lomiet, Romiet

Korean: Kang-hwang, Keolkuma, Kolkuma, Sim-hwang, Teomerik, Tomerik, Tumerik, Ulgeum, Ulgum, Ulgumun

Laotian: Khamin, Khamin Khune, Khimin, Khi Min Khun

Latvian: Kurkuma

Lithuanian: Ciberžolė, Dažinė Ciberžolė, Kurkuma

Malaysia: Kunyit, Temu Kunyit (Malay), Tius (Semang), Renet (Sakai)

Nepal: Besar, Haldi, Hardi (Nepali), Halu (Newari, Nepalbhasa)

Norwegian: Gurkemeie, Gurkemeje, Kurkuma

Papua New Guinea: kawawara;

Persian: Dar-Zard, Darzard, Darzardi, Zard-chob, Zard-Chobah, Zardchobah, Zardchubah

Philippines: Salampauyan (Bagobo), Kalabaga, Kalauag, Kinamboi (Bisaya), Kunik (Ibanag), Kulyau, Kunig (Iloko), Parak (Kuyonon), Kalauag (Manobo), Angai, Pangas, Kulalo (Pampangan), Lampuyang (Panay Bisaya), Dulau (Samar Leyte Bisaya), Lauag (Subanum), Dilau, Dilaw, Luyang-Dilau (Tagalog)

Polish: Kłącze Kurkumy, Kurkuma, Kurkuma Długa, Ostryż Długi

Portuguese: Açafroa, Açafrão-da-Índia, Açafrão-da-terra, Cúrcuma, Gengibre Amarelo, Gengibre Dourada, Turmérico

Romanian: Curcumă

Russian: Imbir Zhyoltyj, Imbir Zheltyj, Koren Kurkumy, Kurkuma

Serbian: Žutnjak, Zerdečaf, Kurkuma, Žuti ingver

Slovak: Kurkuma

Slovenian: Kurkuma

Somali: Haruut

Spanish: Azafrán De La India, Azafrán De Las Indias, Cúrcuma, Rizoma Dos Índios Cúrcuma Larga, Terra Merita, Turmérico

Sri Lanka: Kaha (Sinhala)

Swahili: Manjano

Swedish: Gurkemeja, Gurkmeja

Tajik: Zard Chova

Thai: Kha Mîn, Khamin, Kha Mîn Chan (Central Thailand), Kha Mîn Hua (Chiang Mai)

Tibetan: Ha Ri Da Dro, Ha Ri Dra, Rtsi Ser, Ser-Po, Sga Ser, Skyer-Rtsa, Yun Ba, Yun-Ba

Tigrinya: Herud

Turkish: Hind Zafrani, Kurkim, Kurkum, Safran kökü, Sarı boya, Sarı kölk, Zerdali, Zerdé Djavé, Zerdeçal, Zerdeçöp, Zerdecube

Ukrainian: Kurkuma

Vietnamese: Bột Nghệ, Củ Nghệ, Nghệ, Uất Kim, Khương Hoàng

Welsh: Tyrmerig

Yiddish: Kurkume

Origin/Distribution

Turmeric is native to tropical South Asia (India) or Southeast Asia and has been cultivated over many centuries and is now extensively cultivated in tropical Asia and some areas in Africa, with India and Southeast Asia being the areas of largest cultivation. It is cultivated almost throughout India,

particularly in Punjab, West Bengal, Maharashtra, Karnataka, Tamil Nadu and Kerala.

Agroecology

Turmeric thrives in a warm and wet tropical climate with high annual rainfall of 1500–2000 mm and temperatures of 18–30 °C. It is hygrophilous and grows in full sun or partial shade on well-drained, sandy–clayey loam in low altitudes below 1500 m.

Edible Plant Parts and Uses

Turmeric rhizome is used as a culinary spice in Asian cuisine, being an important ingredient of curry powder; dried rhizome and powdered form are also used. The rhizomes are boiled for several hours and then ground into a deep orange-yellow turmeric powder. In non-Indian recipes, turmeric is used as a colouring agent and flavouring agent in processed foods. Turmeric is used in baked products, yellow cakes, cake icings, sweets, cereals, biscuits, sauces, mustards, gelatins, cheese, margarine, ice cream, yogurt, popcorn colour, dairy products, orange juice and canned beverages. Turmeric is also used to give a yellow colour to some prepared mustards, canned chicken broths and other foods. Turmeric is used in combination with annatto seeds (*Bixa orellana*) and has been used to colour cheeses, yogurt, dry mixes, salad dressings, winter butter and margarine. It is also used as a food additive and used to protect food products from sunlight. The oleoresin is used for oil-containing products. The curcumin/polysorbate solution or curcumin powder dissolved in alcohol is used for water-containing products. Overcolouring using turmeric, such as in pickles, relishes and mustard, is sometimes used to compensate for fading. In Java a flour is made from the rhizome in the same way as from cassava and arrowroot, which is used for all kinds of dainties.

Young shoots and young rhizome are also used fresh as a spicy vegetable. Turmeric inflorescences are also cooked and eaten. The aromatic leaves of *C. longa* and *C. mangga* are also

used for flavouring steamed and baked fish (Liu and Nair 2012).

Botany

Curcuma longa is a perennial, erect, glabrous herb 0.6–1 m high, forming dense clumps (Plates 1–2). Rhizome is stout and much branched with cylindrical, aromatic tubers (3 m across) and orange, orange-red or golden yellow inside with carrot-turmeric odour (Plates 3–4). Leaves are radical, distichous, entire and long sheathed. Leaf blade is green, oblong or elliptic, 30–50 cm long by 10–25 cm wide and glabrous; base is attenuate, and apex is shortly acuminate (Plates 1–2). Petiole and sheath are sparsely to densely pubescent. Inflorescences are terminal on scape. Spike is cylindric, 15–20 cm long and 5–11 cm across; fertile bracts are white to pale green, ovate or oblong and 5–6 cm long; apex is obtuse; coma bracts are spreading, white and green and sometimes slightly tinged reddish purple; apex is acute (Plates 5, 6, and 7). The flowers are not exerted beyond the bracts. Calyx is white and puberulent, and apex is unequally 3-toothed. Corolla is white to yellowish white; tube is up to 3 cm long; lobes are deltoid and central one larger; apex is mucronate. Lateral staminodes are shorter than labellum. Labellum is obovate, 1.22 cm long and yellowish white with yellow median band (Plate 7). Anther is spurred at the base. Ovary is sparsely hairy. Capsule is 3-celled, and ellipsoid is with arillate seeds.



Plate 1 Young turmeric plants



Plate 2 Dense clump of mature turmeric plant



Plate 3 Turmeric rhizomes on sale



Plate 4 Close-up of turmeric rhizome



Plate 5 Turmeric inflorescences lateral view



Plate 6 Turmeric inflorescences top view



Plate 7 Turmeric flower—labellum with distinct yellow median strip

Nutritive/Medicinal Properties

Rhizome/Root Nutrient/Phytochemicals

Turmeric is a good source of phosphorus, potassium, magnesium, manganese, selenium and iron, choline, betaine, vitamin B, vitamin E, vitamin K and phytosterols.

The proximate nutrient value per 100-g edible portion of ground turmeric spice powder was reported as: water 11.36 g; energy 312 kcal (1305 kJ); protein 9.68 g; total lipid 3.25 g; ash 7.08 g; carbohydrate 67.14 g; total dietary fibre 22.7 g; total sugars 3.21 g (sucrose 2.38 g, glucose 0.38 g, fructose 0.45 g); minerals (Ca 168 mg, Fe 55 mg, Mg 208 mg, P 299 mg, K 2080 mg, Na 27 mg, Zn 4.50 mg, Cu 1.30 mg, Mn 19.80 mg); Se 6.2 µg; vitamins (vitamin C 0.7 mg, thiamine 0.058 mg, riboflavin 0.233 mg, niacin 1.350 mg, pantothenic acid 0.542 mg, vitamin B6 0.107 mg, total folate 20 µg, total choline 49.2 mg, betaine 9.7 mg, vitamin A 370 IU, vitamin E (α -tocopherol) 4.43 mg, β -tocopherol 0.01 mg, γ -tocopherol 0.72 mg, vitamin K (phylloquinone) 13.4 µg); total saturated fatty acids 1.838 g (8:0 (caprylic acid) 0.003 g, 10:0 (capric acid) 0.8448 g, 12:0 (lauric acid) 0.003 g, 14:0 (myristic acid) 0.395 g, 16:0 (palmitic acid) 0.155 g, 17:0 (margaric acid) 0.335 g, 18:0 (stearic acid) 0.003 g, 20:0 (arachidic acid) 0.097 g); total monounsaturated fatty acids 0.499 g, 14:1 (myristoleic acid) 0.154 g, 17:1 undifferentiated (heptadecanoic acid) 0.164 g, 18:1 undifferentiated (oleic acid) 0.131 g, 18:1c 0.075 g, 18:1 t 0.056 g); total polyunsaturated

fatty acids 0.756 g, 18:2 undifferentiated (linoleic acid) 0.672 g, 18:3 undifferentiated (linolenic acid) 0.084 g, 18:3 n-3 c,c,c (ALA) (α -linolenic acid) 0.003 g, 18:3 n-6 c,c,c (γ -linolenic acid) 0.081 g); total *trans*-fatty acids 0.056 g, total *trans*-monoenoic fatty acids 0.056 g; and amino acids (tryptophan 0.170 g, threonine 0.330 g, isoleucine 0.470 g, leucine 0.810 g, lysine 0.380 g, methionine 0.140 g, cystine 0.150 g, phenylalanine 0.530 g, tyrosine 0.320 g, valine 0.660 g, arginine 0.540 g, histidine 0.150 g, alanine 0.330 g, aspartic acid 1.860 g, glutamic acid 1.140 g, glycine 0.470 g, proline 0.480 g and serine 0.280 g) (USDA-ARS 2014). Turmeric was found to contain 9.45 % proteins (Das et al. 2014). The amino acid patterns of these isolated proteins comprised essential amino acids such arginine (2.48 %), histidine (1.80 %), isoleucine (7.58 %), leucine (2.53 %), lysine (12.73 %), methionine (3.28 %), threonine (2.87 %) and valine (1.53 %) and non-essential amino acids such as alanine (2.55 %), aspartic acid (5.05 %), glutamic acid (8.75 %), glycine (3.42 %), serine (2.29 %) and tyrosine (3.68 %). Pepsin digestibility of the isolated protein found was 96.13 %. β -turmerin, a 34-kDa hydrophobic antioxidant glycoprotein, was purified and characterised from turmeric (*Curcuma longa*) waste grits (Smitha et al. 2009). Turmerin, a water-soluble 5-kDa antioxidant peptide, was isolated from turmeric (Srinivas et al. 1992). It was found to be a heat-stable, noncyclic peptide containing 40 amino acid residues, with a blocked N-terminal and leucine at the C-terminal, and insensitive to trypsin and pepsin, heat and UV radiation. Turmerin contained three residues of methionine which were partly responsible for its antioxidant activity. Turmerin, a protein from turmeric, was purified and found to have a relative molecular mass of 14 kD (Chethankumar and Srinivas 2008; Chethankumar et al. 2010b). An antioxidant protein with apparent molecular mass of approximately 20 kDa was isolated from turmeric peel waste (Chethankumar et al. 2010a).

Proximate nutrient composition (per 100 g) of *C. longa* rhizome was reported by Trinidad et al. (2012) as moisture 82.7 %, ash 1.4 g, fat 0.6 g, protein 1.7 g, carbohydrate 13.6 g, dietary fibre 6.1 g, β -carotene 2 μ g, Fe 2.4 mg, Zn 22.6 mg, Ca 8.2 mg, phytic acid 18.4 mg and tannic acid 3 mg. *Curcuma*

longa had higher content of ash, fat, protein, carbohydrates and dietary fibre, while *Zingiber officinale* had greater moisture and β -carotene (Trinidad et al. 2012). Both samples were good sources of dietary fibre, and when fermented in-vitro, the only short-chain fatty acid produced was propionate. *Z. officinale* had significantly greater iron and calcium content. The availability of zinc (11.9 %) and calcium (56.9 %) for absorption was significantly higher in *C. longa* but not iron (1.7 %). Iron availability was significantly greater in *Z. officinale* (21.5 %). Microwave vacuum drying (3500–4000 W; 27–30 min) of turmeric optimised the quality of dried turmeric in terms of colour (L, a*, b*), moisture content, water activity (aw), ash, antioxidant activity (2,2-diphenyl-1-picrylhydrazyl; DPPH), total phenolic content and curcuminoid content and suppressed the enzymatic formation of brown pigments and increased the phenol substrates (Hirun et al. 2014).

Isolated turmeric and ginger starches had purity of approximately 77 and 85 %, respectively (Braga et al. 2006). The turmeric starch (B type) demonstrated more resistance under the pressure than ginger starch (C type), in spite of its lower amylopectin content (52 %) as compared to ginger starch (66 %). The chemi-physico composition of turmeric starch before SFE (supercritical fluid extraction) and after SFE were starch purity (76,77 %), total protein (0.6, 0.5 %), ash (1.5, 1.43 %), reducing sugars (tr, tr), moisture (11.8, 12.1 %), onset temperature (69.3,66.3 °C), peak temperature (79.2, 81 °C), conclusion temperature (96, 97 °C), enthalpy of gelatinisation (19, 18 J/g), pasting temperature (85,86 °C), peak time (7, 7 min), viscosity peak (1951,1632 cP), breakdown (199,116 cP), final viscosity (3631, 3045 cP), setback (1879, 1529 cP), amylose (48, 48 %), amylopectin (52, 52 %), swelling factor (2.3, 2.11) and turbidity (ABS absorbance) (2.93, 2.43).

A glycan, named ukonan A, was isolated from the hot water extract of turmeric rhizomes (Tomoda et al. 1990). The glycan possessed an α -L-arabino-3,6- β -D-galactan structure. α -1,3-Linked L-arabinopyranose, β -3,4-branched D-xylose, α -1,4-linked D-glucose, α -2,4-branched L-rhamnose and α -1,4-

linked *D*-galacturonic acid residues were also identified as the component sugar units. Three polysaccharides, named ukonan A, ukonan B and ukonan C, were isolated from *Curcuma longa* rhizomes (Gonda et al. 1990). They were found to compose *L*-arabinose, *D*-xylose, *D*-galactose, *D*-glucose, *L*-rhamnose and *D*-galacturonic acid in the molar ratios of 12:4:12:1:4:10 (ukonan A), 12:4:12:1:2:4 (ukonan B) and 8:3:6:14:2:3 (ukonan C), in addition to small amounts of peptide moiety. Ukonan B had acidic arabinogalactan-type structural units. The polysaccharide ukonan C was composed of *L*-arabinose, *D*-xylose, *D*-galactose, *L*-rhamnose and *D*-galacturonic acid in the ratio 8:3:6:14:2:3 (Gonda and Tomoda 1991). It mainly comprised α -*L*-arabino- β -3,6-branched *D*-galactan-type and α -4,6-branched *D*-glucan-type structural units (Gonda et al. 1992b). The core structural features of ukonan A include a backbone chain mainly composed of β -1,3-linked *D*-galactose, β -1,4-linked *D*-xylose and α -1,2-linked *L*-rhamnose residues. All of the galactose units in the backbone carry side chains composed of α -*L*-arabino- β -*D*-galactosyl or β -*D*-galactosyl residues at position 6. The arabino core of ukonan C includes a backbone chain composed of β -1,3-linked *D*-galactose and β -1,4-linked *D*-xylose (Gonda et al. 1993). All of the galactose units in the backbone carry side chains composed of β -1,6-linked *D*-galactosyl residues with or without terminal α -*L*-arabinose units at position 3. A neutral polysaccharide, named ukonan D, was isolated from *Curcuma longa* rhizome (Gonda et al. 1992a). Ukonan D is composed of *L*-arabinose, *D*-galactose, *D*-glucose and *D*-mannose in the molar ratio of 1:1:12:0.2, in addition to small amounts of peptide moiety. Its structural features included mainly both α -1,5-linked *L*-arabino- β -3,6-branched *D*-galactan-type and α -4,6-branched *D*-glucan-type structural units. A 28-kDa glycoprotein isolated, purified and characterised from boiling water extract of turmeric powder was named as BGS-Haridrin (Ramadas and Srinivas 2011).

A new curcuminoid, cyclocurcumin, was isolated from the nematocidally active fraction of turmeric rhizome, together with three known curcuminoids, curcumin, demethoxycurcumin and bisdemethoxycurcumin (Kiuchi et al.

1993). Two new pigments 1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)-1,6-heptadiene-3,5-dione and 1,7-bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one were isolated from fresh *Curcuma domestica* rhizomes (Nakayama et al. 1993). The levels of curcuminoid pigments of turmeric cultivated in eight different cities in the state of Minas Gerais, Brazil, varied from 1.4 to 6.14 g/100 g and of volatile oil from 0.97 to 7.55 mL/100 g (dry basis) (Souza and Glória, 1998). Composition (g/100 g DW) of the oil was determined as protein 4.69–8.18 g, fibre 6.82–8.00 g, ash 5.39–9.55 g, starch 32–47.78 g and ethyl ether extract 4.57–13.25 g. A higher yield of pigment in the flavour-free oleoresin was obtained using the combination of water vapour and ethanol or acetone. The oleoresin so obtained was free of flavour and could be used in a wider range of food applications. Curcumin, the yellow colour pigment of turmeric, is produced industrially from turmeric oleoresin (Negi et al. 1999; Jayaprakasha et al. 2001). The mother liquor after isolation of curcumin from oleoresin was found to contain approximately 40 % oil. Four compounds were isolated from turmeric rhizome curcumin, demethoxycurcumin and bisdemethoxycurcumin, including a gingerdione and 1-dehyrdogingerdione, and from turmeric oil, *ar*-turmerone 0.41 %, (-)-caryophyllene oxide 0.4 % and α -turmerone 23.42 % were identified (Demerdash et al. 2012).

Diarylheptanoid dihydrocurcumin was isolated from the rhizome (Ravindranath and Satyanarayana 1980). The presence of two turmerones α -turmerone and β -turmerone in turmeric was demonstrated, and their structures were defined as 2-methyl-6-(4-methylcyclohexa-2,4-dien-1-yl)hept-2-en-4-one (' α -turmerone') and 2-methyl-6-(4-methylenecyclohex-2-en-1-yl)hept-2-en-4-one (' β -turmerone') (Golding et al. 1982). Two insect repellents from *C. longa* were identified as 2-methyl-6-(4-methylphenyl)-2-hepten-4-one (*ar*-turmerone) and 2-methyl-6-(4-methyl-1,4-cyclohexadien-1-yl)2-hepten-4-one (turmerone) (Su et al. 1982). Turmerone was unstable thermally and also at ambient temperature in the presence of air yielding its dimer or the more stable *ar*-turmerone. A new sesquiterpenoid, curlone, was isolated from the rhizome and its structure elucidated as (6*S*)-2-methyl-6-[(1*S*)-4-methylene-2-cyclohexen-1-yl]-2-hepten-4-one (Kiso et al. 1983a).

Antioxidative components in the methanol extract of *Curcuma longa* rhizome were identified as curcumin, 4-hydroxycinnamoyl(feruloyl)methane and bis(4-hydroxycinnamoyl)methane (Toda et al. 1985). Five new sesquiterpenes, germacrone-13-al; 4-hydroxybisabola-2,10-diene-9-one; 4-methoxy-5-hydroxybisabola-2,10-diene-9-one; 2,5-dihydroxybisabola-3,10-diene; and procurcumadiol, were isolated along with curcumenone, dehydrocurdione, (4*S*,5*S*)-germacrone-4,5-epoxide, bisabola-3,10-diene-2-one, α -turmerone, bisacumol, bisacurone, curcumenol, isoprocumumenol, zedoaronediol, procumumenol, epiprocumumenol and 4,5-dihydroxybisabola-2,10-diene from *Curcuma longa* (Ohshiro et al. 1990). Two new phenolic sesquiterpene ketones named turmeronol A and turmeronol B were isolated from dried turmeric rhizome (Imai et al. 1990). Their structures were determined to be 2-methyl-6-(3-hydroxy-4-methylphenyl)-2-hepten-4-one and 2-methyl-6-(2-hydroxy-4-methylphenyl)-2-hepten-4-one, respectively. Two new natural phenolics 1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-(1*E*,4*E*)-1,4-dien-3-one and 1-(4-hydroxy-3-methoxyphenyl)-5-(-4-hydroxyphenyl)-penta-(1*E*,4*E*)-1,4-dien-3-one were isolated from *Curcuma domestica* rhizomes along with four known curcuminoids (Masuda et al. 1993). The compounds responsible for the pigment yellow colour of turmeric were attributed to curcumin [1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione] and two curcuminoids [demethoxycurcumin (DMC) and bis(demethoxy)curcumin (BDMC)] (Taylor and McDowell 1992). Five major compounds were isolated from fresh turmeric curcumin (diferuloylmethane), demethoxycurcumin, bisdemethoxycurcumin, *ar*-turmerone and curlone (He et al. 1998). From *Curcuma longa*, two novel compounds, 4''-(3'''-methoxy-4'''-hydroxyphenyl)-2''-oxo-3''-enebutanyl,3-(3'-methoxy-4'-hydroxyphenyl) propenoate (calebin A) and 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,4,6-heptatrien-3-one, and seven known compounds, 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione (curcumin); 1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)-1,6-heptadiene-3,5-dione (demethoxycurcumin); 1,7-bis(4-hydroxyphenyl)-1,6-heptadiene-3,5-dione

(bisdemethoxycurcumin); 1-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)-6-heptene-3,5-dione; 1,7-bis(4-hydroxyphenyl)-1-heptene-3,5-dione; 1,7-bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one and 1,5-bis(4-hydroxy-3-methoxyphenyl)-1,4-pentadien-3-one, were isolated (Park and Kim 2002). From *Curcuma longa* rhizomes, one new compound, cyclodocosalactone (1), and ethyl ferulate (2), 6-methyl-7-(3-oxobutyl)-bicyclo[4.1.0]heptan-3-one (3), isocurcumenol (4), curcumenol (5), ferulic acid (6), curcumin (7), demethoxycurcumin (8), bisdemethoxycurcumin (9) and daucosterol (10) were isolated (Yi et al. 2003). Diterpenoids (*E,E,E*)-3,7,11,15-tetramethylhexadeca-1,3,6,10,14-pentaene; 2,6,11,15-tetramethylhexadeca-2,6,8,10,14-pentaene; and 1,6,10,14-hexadecatetraen-3-ol, 3,7,11,15-tetramethyl-, (*E,E*)-[16c] and triterpenoids hopenone I; hop-17(21)-en-3 β -ol; and hop-17(21)-en-3 β -yl acetate were isolated and identified from *C. longa* (Mohamed et al. 2003). The dried rhizomes of *C. longa* yielded four curcuminoids, curcumin, demethoxycurcumin, bisdemethoxycurcumin and tetrahydrocurcumin (Park et al. 2005). The rhizomes of *Curcuma domestica* afforded curcumin; bisacurone, a mixture of *ar*-turmerone, *p*-turmerone and α -turmerone; and *ar*-curcumyl alcohol (Ragasa et al. 2005).

A novel compound named *Curcuma*-J (Wu et al. 2008) and a novel sesquiterpene named curcumin L (Liu et al. 2007) were isolated from *C. longa* roots. Eight characteristic compounds including β -caryophyllene, *ar*-curcumene, zingiberene, β -bisabolene, β -sesquiphellandrene, *ar*-turmerone, α -turmerone and β -turmerone were identified in turmeric rhizome 'Jiang Huang' and tuberous roots 'Yujin' (Qin et al. 2007). Four components such as *ar*-curcumene, *ar*-turmerone, α -turmerone and β -turmerone were optimised as markers for quality control of rhizome ('Jiang Huang') and tuberous root ('Yujin'), two traditional Chinese medicines from *Curcuma longa*.

One novel sesquiterpene with new skeleton, (6*S*)-2-methyl-6-(4-hydroxyphenyl-3-methyl)-2-hepten-4-one, two new bisabolane sesquiterpenes, (6*S*)-2-methyl-6-(4-hydroxyphenyl)-2-hepten-4-one and (6*S*)-2-methyl-6-(4-

formylphenyl)-2-hepten-4-one, and two calebin derivatives, 4''-(4'''-hydroxyphenyl-3'''-methoxy)-2''-oxo-3''-butenyl-3-(4'-hydroxyphenyl)-propenoate and 4''-(4'''-hydroxyphenyl)-2''-oxo-3''-butenyl-3-(4'-hydroxyphenyl-3'-methoxy)-propenoate, were isolated along with five known bisabolane sesquiterpenes 5-hydroxyl-*ar*-turmerone, turmeronol B, bisabolene, bisabolene-4-one and turmeronol A, from *Curcuma longa* (Zeng et al. 2007b). Six sesquiterpenes were isolated from *C. longa* and identified as turmeronol A, turmeronol B, bisabolene, 8-hydroxyl-*ar*-turmerone, bisabolene-9-one and (6S)-2-methyl-6-[(1R,5S)-(4-methene-5-hydroxyl-2-cyclohexen)-2-hepten-4-one] (Zeng et al. 2007a). One new quinoline alkaloid 2-(2'-methyl-1'-propenyl)-4,6-dimethyl-7-hydroxyquinoline (1) and seven known bisabolane sesquiterpenes, 2,5-dihydroxybisabola-3,10-diene (2), 4,5-dihydroxybisabola-2,10-diene (3), turmeronol A (4), bisacurone (5), bisacurone A (6), bisacurone B (7) and bisacurone C (8), as well as dehydrozingerone (9) and zingerone (10), were isolated from *Curcuma longa* rhizome (Wang et al. 2008a); and diaryl derivatives 1,7-bis-(4-hydroxyphenyl)-1,4,6-heptatrien-3-one and 1,5-bis-(4-hydroxyphenyl)-penta-(1E,4E)-1,4-dien-3-one were isolated from turmeric rhizomes (Wang et al. 2008b). The rhizome ethanol extract afforded two new sesquiterpenes, 2-methoxy-5-hydroxybisabola-3,10-diene-9-one and 2,8-epoxy-5-hydroxybisabola-3,10-diene-9-one; one new monoterpene, 2-(2,5-dihydroxy-4-methylcyclohex-3-enyl)propanoic acid, together with five known sesquiterpenes bisacurone; bisacurone A; 4-methylene-5-hydroxybisabola-2,10-diene-9-one; 2-methyl-6-(4-hydroxy-3-methylphenyl)-2-hepten-4-one; and turmeronol (Li et al. 2009b). The following curcuminoids were isolated from *Curcuma longa* rhizomes: 1,5-dihydroxy-1,7-bis(4-hydroxyphenyl)-4,6-heptadiene-3-one; 1,5-dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)-4,6-heptadiene-3-one; 1,5-dihydroxy-1-(4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-4,6-heptadiene-3-one; 3-hydroxy-1,7-bis-(4-hydroxyphenyl)-6-heptene-1,5-dione; 1-(4-hydroxyphenyl)-7-(3,4-dihydroxyphenyl)-1,6-heptadiene-3,5-dione; 1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)-1,6-heptadiene-3;

1,5-dihydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)-4,6-heptadiene-3-one; and 1-(4-hydroxy-3-methoxyphenyl)-5-(4-hydroxyphenyl)-1,4-pentadiene-3-one (Li et al. 2009c).

Terpecurcumins A-I, together with three known analogues, were isolated from turmeric rhizomes (Lin et al. 2012).

Fourteen novel terpene-conjugated curcuminoids, terpecurcumins J–W (1–14), were isolated from *C. longa* rhizomes (Lin et al. 2013). Among them, terpecurcumins J–Q and V represented four unprecedented skeletons featuring an unusual core of hydrobenzannulated[6,6]-spiroketal (1 and 2), bicyclo[2.2.2]octene (3–7), bicyclo[3.1.3]octene (8) and spiroepoxide (13), respectively.

Three new bisabolocurcumin ethers, named bisabolocurcumin ether, demethoxybisabolocurcumin ether and didemethoxybisabolocurcumin ether, along with two known compounds, (1*E*,4*E*)-1,5-bis-(4-hydroxyphenyl)penta-1,4-diene-3-one and (1*E*,4*E*,6*E*)-1,7-bis (4-hydroxyphenyl)hepta-1,4,6-trien-3-one, were isolated from the rhizome ethyl extract (Xiao et al. 2012). A new skeleton bisabolane-type sesquiterpene curcuminoid, bisabocurcumin, along with five known compounds, curcumin, demethoxycurcumin, bide-methoxycurcumin, (1*E*,4*E*)-1,5-bis(4-hydroxy-3-methoxyphenyl)-penta-1,4-dien-3-one and (1*E*,4*E*)-1-(4-hydroxy-3-methoxyphenyl)-5-(4-hydroxyphenyl)-penta-1,4-dien-3-one, was isolated from turmeric rhizomes (Xiao et al. 2011). Two new bisabolane derivatives were isolated from the rhizome (Zhang et al. 2014).

Of the turmeric varieties grown in Maharashtra, India, the highest range of curcumin content was observed from 3.584 to 7.730 % in Pratibha variety followed by Salem variety from 2.169 to 5.932 %, Rajapuri 2.812 to 4.366 % and Krishna 1.599 to 3.520 %, respectively (Kamble et al. 2011). The highest amount of curcumin was extracted by HPLC method in comparison to solvents ethanol, acetone and hexane. The range of curcumin extracted by HPLC method was found as 2.308 to 5.662 % from boiled turmeric and 3.520 to 5.932 % from steam cooked turmeric, respectively. Niranjana et al. (2013) used a simple, rapid and sensitive high-performance liquid chromatography photodiode array (HPLC-PDA) method

for simultaneous determination of curcuminoids, namely, a mixture of curcumin, demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC) in rhizomes of *C. longa*. The amount of curcumin varied from 0.46 to 2.17 %, DMC from 0.13 to 0.92 % and BDMC from 0.06 to 0.52 %. Total phenolic content in rhizomes ranged from 14.12 to 27.72 mg/g. The chemical composition of rhizome essential oil showed large variations in major compounds like *ar*-turmerone (7.31–38.66 %), β -curcumene (1.58–24.53 %) and curlone (1.55–15.97 %). All the chemical components identified included α -pinene, β -pinene, myrcene, δ -3-carene, α -phellandrene, limonene, β -phellandrene, sabinene, *p*-cymene, α -terpinene, 2-carene, terpinene-4-ol, citral, camphor, α -terpineol, *p*-cymen-8-ol, *trans*- α -bergamotene, thymol, β -caryophyllene, β -farnesene, α -caryophyllene, zingiberene, *ar*-curcumene, β -sesquiphellandrene, *E*-nerolidol, γ -elemene, *trans*-sesquisabinene hydrate, camphene, turmerone, α -bisabolol, caryophyllene oxide, dihydrocurcumene, α -santalol, β -curcumene, β -atlantone, *ar*-turmerone, curlone, α -atlantone, β -bisabolene and corymbolone.

Total arsenic contents (dry weight basis) in six edible Zingiberaceous rhizomes, namely, *Alpinia galanga* (Khaa), *Boesenbergia rotunda* (Kra Chaai), *Curcuma longa* (Khamin Chan), *Curcuma zedoaria* (Khamin oi), *Zingiber cassumunar* (Plai) and *Zingiber officinale* (ginger) were found to be 92.4, 103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively (Ubonnuch et al. 2013). Total inorganic arsenic contents were 92.4, 103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively. All investigated amounts of total and inorganic arsenic were much lower than limits recommended by Thai Food and Drug Administration.

The rhizome oil of Chinese turmeric had high contents of turmerone (24.07 %) and *ar*-turmerone (18.38 %), *ar*-curcumene and γ -curcumene (12.17 %), cardione (11.58 %) and zingiberene (8.14 %) (Chen et al. 1983). Other constituents included 1,8-cineole (2.92 %), γ -terpinene (2.72 %), curzerenol (2.13 %), curzerenone (2.04 %), curzerendiol (1.19 %), α -pinene (0.53 %), β -pinene 0.27 %, eugenol (0.21 %), limonene (0.20 %), linalool (0.16 %), camphor (0.06 %)

and borneol (0.02 %). It was found that 5-month-old turmeric plant gave the highest % volatile oil (9.79 %) in cultivar (cv.) 'Nakorn Pathon' and 11.98 % for cv. 'Prachuap Khiri Khan' (Chavalittumrong and Jirawattanapong 1992). The major components identified were curcuminoids curcumin, desmethoxycurcumin, bisdesmethoxycurcumin, *ar*-curcumene, *dl*-turmerone and curcumol. Turmeric rhizome oil from India did not contain β -pinene but had all the other components of the leaf oil in different proportions (McCarron et al. 1995). Interestingly, the rhizome volatiles included car-3-ene, α -terpinene, γ -terpinene and terpinolene. The volatile oil of Chinese turmeric contained α -curcumene (major constituent), *ar*-curcumene, α -zingiberene, 1,8-cineole and zerumbone, but 1-(3-cyclopentylpropyl)-2,4-dimethylbenzene, β -sesquiphellandrene and germacrene were also found (Hu et al. 1998). Some of the major volatile compounds identified by GC/MS in turmeric essential oils from commercial samples of dry turmeric and samples γ -irradiated at a dose of 10 kGy were α -phellandrene, *p*-cymene, 1,8-cineol, β -caryophyllene, *ar*-curcumene, zingiberene, β -sesquiphellandrene, nerolidol, turmerone, *ar*-turmerone, curlone and dehydrozingerone (Chatterjee et al. 2000). No detectable differences were observed between the aroma impact compounds of the irradiated and commercial samples. The curcuminoid content of fresh, peeled, turmeric rhizomes was slightly increased by γ -irradiation (Dhanya et al. 2011). No statistically significant changes were observed due to irradiation in majority of the volatile oil constituents. The major components (approximately 60 %) of the extracted turmeric oil were identified as turmerone and *ar*-turmerone (Gopalan et al. 2000). Other compounds present were caryophyllene, germacrene D, β -sesquiphellandrene, α -curcumene, xanthorrhizol, linalool, nerol, citronella pentanoate, citronellal, α -pinene, menthofuran, α -terpineol, carvone, phellandro and *p*-cymene. The highest yields of essential oil (0.46 wt%) and curcuminoid pigment (0.16 wt%) expressed as curcumin, demethoxycurcumin and bisdemethoxycurcumin, as well as *ar*-turmerone and (α and β)-turmerone, were extracted from *C. longa* (Manzan et al. 2003). The mass spectra obtained for the predominant volatile compounds indicated the presence of *ar*-

curcumene, *ar*-turmerone, zingiberene, β -sesquiphellandrene, sabinene, 1,8-cineol and 1,4-terpineol in turmeric (Mata et al. 2004).

Turmeric rhizome oil from plains of northern India contained 84 constituents, comprising 100 % of the oil (2.2 % yield), of which the major ones were 1,8-cineole (11.2 %), α -turmerone (11.1 %), β -caryophyllene (9.8 %), *ar*-turmerone (7.3 %) and β -sesquiphellandrene (7.1 %) (Raina et al. 2002). Fifty-two constituents were identified from rhizome oil representing 98.6 % of the oil from the lower Himalayan region of Northern India (Raina et al. 2005). The major constituents of the oil were α -turmerone (44.1 %), β -turmerone (18.5 %), α -phellandrene (9.4 %), *ar*-turmerone (5.4 %), zingiberene (2.3 %), 1,8-cineole (1.9 %), β -sesquiphellandrene (1.8 %), viridiflorol (1.6 %), T-cadinol (1.5 %), *p*-cymene (1.2 %), terpinolene (1.2 %) and (*E*)- α -atlantone (1.1 %). Other minor constituents (tr- <1 %) included octane, α -thujene, camphene, α -pinene, β -pinene, sabinene, 2-octanol, δ -3-carene, α -terpinene, limonene, γ -terpinene, linalool, *trans*-*p*-menth-2-en-1-ol, camphor, *p*-cymen-8-ol, myrtenal, *cis*-sabinol, neral, sabinyl acetate, tetradecane, γ -elemene, β -farnesene, *ar*-curcumene, α -selinene, β -curcumene, β -sesquiphellandrene, geranyl butyrate, (*E*)-nerolidol, *ar*-turmerol, caryophyllene oxide, epicurzerenone, *trans*-sesquisabinene hydrate, humulene epoxide II, 10-epi- γ -eudesmol, germacrone, geranyl hexanoate, furanodienone, heptyl salicylate and cinnamyl cinnamate.

Vietnamese turmeric rhizome essential oil was found to contain α -turmerone (30 %), *ar*-turmerone 10 %), β -turmerone (10 %), β -sesquiphellandrene (3 %), *ar*-curcumene (1.5 %), zingiberene (1.5 %), curzerenone (1 %), terpinolene (0.9 %), β -caryophyllene (0.9 %), α -humulene (0.5 %), β -bisabolene (0.2 %), α,α,p -trimethylbenzyl alcohol (0.15 %), 1,8-cineole (0.1 %), *p*-cymene (0.05 %), limonene (0.05 %) and terpinene-4-ol (0.05 %) (Phan et al. 1987). Another analysis of Vietnamese turmeric essential oil reported the following 13 chemical compositions identified out of 36 volatiles: *ar*-turmerone (30.33 %), α -turmerone (14.14 %), β -sesquiphellandrene (4.42 %), α -zingiberene (3.44 %), β -

caryophyllene (3.02 %), *ar*-curcumene (3.02 %), terpinolene (1.87 %), 1,8-cineole (0.45 %), benzene (0.19 %), α -humulene (0.79 %), β -bisabolene (0.72 %), di-epi- α -cedrene (0.15 %), zingiberene (0.2 %) and others (37.19 %) (Nguyen et al. 2010).

Fourteen components were found in turmeric rhizome essential oil of South India, and eight were identified as limonene, 1,8-cineol, curcumene, zingiberene, bisabolene, sesquiphellandrene, *ar*-turmerone and turmerone (Gopalam and Ratnambal 1987). The rhizome oil of *C. longa* from northern plains of India was reported to contain 59.7 % of *ar*-turmerone (Nigam and Ahmad 1990), while the rhizome oil of another Indian chemotype was characterised by *ar*-turmerone (24.7 %), turmerone (29.5 %), turmerol (20 %) and α -atlantone (2.4 %) (Zwaving and Bos 1992). Twenty-one constituents were identified in turmeric rhizome essential oil from Bhutan, and the major ones identified were α -turmerone (32 %), *ar*-turmerone (25.7 %), β -turmerone (18.4 %), β -sesquiphellandrene (1.9 %), zingiberene (1.5 %), α -curcumene (1.4 %), *ar*-turmerol (1.3 %), (*E*)- α -atlantone (1.1 %), α -phellandrene (1.1 %) and the rest (<1 %), and traces included (*E*)- β -farnesene, β -bisabolene, curcuphenol, 1-bisabolene, toluene, α -pinene, myrcene, *p*-cymene, limonene, 1,8-cineole, γ -terpinene and α -terpineol (Sharma et al. 1997). The volatile oil of Chinese turmeric contained α -curcumene (major constituent), α -zingiberene, 1,8-cineole and zerumbone, but 1-(3-cyclopentylpropyl)-2,4-dimethylbenzene, β -sesquiphellandrene and germacrene were also found (Hu et al. 1998). The effect of plant maturity on the composition of turmeric rhizome oil from Sri Lanka revealed that sesquiterpenes (*ar*-turmerone and turmerone) increased while monoterpenes (1,8-cineole and α -phellandrene) declined with maturity (Cooray et al. 1988). Monoterpene content was lower in the mother sets during the early stages of growth. Curcumin content was highest followed by bisdemethoxycurcumin and demethoxycurcumin. Maturity did not affect the ratio of curcumins to any great extent. The main volatile constituents of the rhizome were reported as myrcene (81.4 %), β -pinene (10.4 %), (*E*)- β -ocimene (2.7 %) and α -pinene (1.6 %) (Jantan et al. 1999). The oil content of rhizomes from 27 accessions of

C. longa grown in the climatic conditions of northern Indian plains varied between 0.16 % and 1.94 % on a fresh weight basis (Garg et al. 1999). The accessions could be classified into two types: (a) those in whose essential oils the sum of the seven major terpenes (β -pinene, *p*-cymene, α -curcumene, β -curcumene, *ar*-turmerone, α -turmerone and β -turmerone) was in the range 58–79 % and (b) those in whose oils this sum was 10–22 %. The rhizomes of all the accessions were also evaluated for their curcumin content, which was found to vary from 0.61 to 1.45 % on a dry weight basis. Composition (%wt) of turmeric essential oil obtained by SCFE (supercritical fluid extraction) with CO₂ and ethanol was reported by Chassagnez-Mendez et al. (2000) as (*Z*)- γ -atlantone 20.3 %, (*E*)- γ -atlantone 15.6 %, *ar*-turmerone 15 %, β -sesquiphellandrene 7.7 %, α -zingiberene 6.4 %, α -phellandrene 4.1 %, 1,8-cineole 4.0 %, *ar*-curcumene 3.6 %, β -bisabolene 1.7 %, *ar*-turmerol 1.5 %, *p*-cymene 1.5 %, terpinolene 1.3 % and the following compounds (<1 %): α -pinene, myrcene, α -terpinene, limonene, γ -terpinene, 4-terpineol, thymol, carvacrol, α -*cis*-bergamotene, caryophyllene, α -humulene, γ -curcumene, β -germacrene, (6*S*, 7*R*)-bisabolene and (*E*)- α -atlantone. Essential oil yield from the rhizome was 3.8 % with the major components identified as *ar*-turmerone (31.1 %), curlone (10.6 %), turmerone (10.0 %), *ar*-curcumene (6.3 %), *p*-cymene (3 %), β -sesquiphellandrene (2.6 %), 1,8-cineole (2.4 %), dihydrocurcumenone (2.2 %) and β -bisabolene (1.3 %) (Leela et al. 2002). Other minor components (<1 %) were α -pinene, myrcene, α -phellandrene, terpinolene, *p*-cymen-8-ol, α -terpineol, carvacrol, γ -curcumene, curcuphenol and 6*S*,*SR*-bisabolene, and very minor compounds (traces) were α -zingiberene, *p*-methylacetophenone, β -phellandrene and β -pinene. Other identified compounds were 27.8 %. The highest yields of turmeric essential oil (0.46 wt%) and pigment (0.16 wt%) expressed as curcumin, demethoxycurcumin and bisdemethoxycurcumin as well as *ar*-turmerone and (α and β)-turmerone were obtained at an autoclave pressure of 1.0×10^5 Pa and a distillation time of 2 h (Manzan et al. 2003). *ar*-Turmerone (44.4 %), β -turmerone (26.5 %) and α -turmerone (20.8 %) were the main components in turmeric rhizome oil (Ajaiyeoba et al. 2008). Hydrodistillation of turmeric rhizomes

from northern Indian plains resulted in the isolation of 0.36 % of oil (w/v) FWB and in the identification of 73 constituents comprising 95.2 % of the oil, of which the major ones were *ar*-turmerone (31.7 %), α -turmerone (12.9 %), β -turmerone (12.0 %), (*Z*)- β -ocimene (5.5 %), 1,8-cineol (2.6 %), τ -cadinol (2.4 %), caryophyllene oxide (2.1 %), elemicin (2 %), humulene epoxide II (1.9 %), viridiflorol (1.7 %), (*E*)- α -atlantone (1.5 %), β -curcumene (1.3 %), zingiberene (1.3 %), α -cadinene (1.2 %) and δ -elemene (1 %), and the rest were < 1 % and traces and included n-heptane, isobutyl acetate, n-octane, n-nonene, camphene, sabinene, myrcene, α -phellandrene, *p*-cymene, α -fenchol, *trans*-*p*-menth-2-en-1-ol, *p*-methyl acetophenone, camphor, borneol, terpinene-4-ol, myrtenal, myrtenol, 2-decanol, *cis*-carvotanacetol, *cis*-carveol, carvone, geraniol, linalyl acetate, isobornyl acetate, undecane, geranyl formate, carvacrol, undecanol, thymol acetate, geranyl acetate, β -patchoulene, tetradecane, caryophyllene, α -guaiene, α -patchoulene, germacrene D, *ar*-curcumene, β -bisabolene, geranyl butyrate, *cis*-sesquisabinene hydrate, 10-epi- γ -eudesmol, β -eudesmol, α -bisabolol, germacrone, curdione, 1-bisabolene, geranyl hexanoate, furanodienone and n-heptyl salicylate (Awasthi and Dixit 2009). The following constituents were detected in turmeric essential oil: eucalyptol, *D*-camphor, β -elemene, β -caryophyllene, α -caryophyllene, α -curcumene, zingiberene, β -bisabolene, β -sesquiphellandrene, *ar*-turmerone, α -turmerone, curdione, germacrone, β -turmerone, neocurdione, 1-actyl-4,6-8-trimethylazulene and four unknowns (Jiang et al. 2013b).

Pulverised *Curcuma longa* rhizome, grown in north central Nigeria, on hydrodistillation, afforded an oil yield of 1.24 % v/w comprising mainly of monoterpenes (46.9 %) (Usman et al. 2009). The major constituents of the oil were β -bisabolene (13.9 %), *trans*-ocimene (9.8 %), myrcene (7.6 %), 1,8-cineole (6.9 %), α -thujene (6.7 %) and thymol (6.4 %); others were car-2-ene (4 %), α -pinene (2.8 %), β -pinene (2.4 %), β -phellandrene (3.1 %), limonene (5.3 %), *cis*-ocimene (2.6 %), iso-artemisia ketone (1.1 %), γ -terpinene (2.6 %), borneol (3.3 %), terpineol (2.1 %), α -terpineol (2.0 %), neral (tr), geranial (tr), zingiberene (5.2 %), sesquiphellandrene (5.2 %) and turmerone (3.5 %). The main components of turmeric rhizome

essential oil grown in Iran were *ar*-turmerone 68.9 % and α -turmerone 20.9 %, followed by α -phellandrene 2.2 %, terpinolene 1.5 %, α -zingiberene 1.5 % and β -sesquiphellandrene 1.3 %, and minor components were *ar*-curcumin 0.8 %, β -caryophyllene 0.6 %, *p*-cymene 0.4 %, 1,8-cineol 0.4 %, β -bisabolene 0.4 % and α -terpinene 0.2 % (Asghari et al. 2009). The curcuminoids were detected as curcumin, desmethoxycurcumin, and bisdesmethoxycurcumin. The turmerone in harvested rhizome accounted for almost 90 % of the oil composition. Rhizome dry weight and curcumin content increased with plant maturity; rhizomes were harvested after 6-month maturity. Eighteen major components were isolated from turmeric essential oil from samples collected in different geographical regions in China: 1,8-cineole; α -terpinolene; β -; β -caryophyllene; α -humulene; *ar*-curcumene; α -zingiberene; β -bisabolene; β -sesquiphellandrene; caryophyllene oxide; *ar*-turmerone; germacrone; α -turmerone; curdione; neocurdione; (6*R*,1'*R*)-6-(1',5'-dimethylhex-4'-enyl)-3-methylcyclohex-2-enone; (+)- α -atlantone; and an unknown (Li et al. 2009a). Large proportions of turmerones (circa 37 %), zingiberene (11.8 %), β -sesquiphellandrene (8.1 %) and terpinolene (15.8 %) were found in the rhizome oil of *C. longa* grown in the Reunion Island (Chane-Ming et al. 2002). Six new sesquiterpenes, curculonone A, curculonone B, curculonone C, curculonone D, 6 α -hydroxycurcumanolide A and 1,10-dehydro-10-deoxy-9-oxozedoarondiol, were isolated from the rhizome of *Curcuma longa*, together with 19 known compounds comprising eight sesquiterpenes, (S)-(+)-*ar*-turmerone, bisacurone, curlone, β -atlantone, (6*R*)-[(1*R*)-1,5-dimethylhex-4-enyl]-3-methylcyclohex-2-en-1-one, zedoarondiol, curcumanolide A and curcumanolide B; three curcuminoids, curcumin, demethoxycurcumin and bisdemethoxycurcumin; six benzenoids, vanillin, vanillic acid, (*E*)-ferulic acid, (*Z*)-ferulic acid, (*E*)-4-(4-hydroxy-3-methoxyphenyl) and but-3-en-2-one, 1,5-bis-(4-hydroxy-3-methoxyphenyl)-(1*E*,4*E*)-1,4-pentadien-3-one; and mixed steroids β -sitosterol and stigmasterol (Chen et al. 2010d).

The major chemical constituent curcuminoids, a group of diarylheptanoid compounds and major mono- and

sesquiterpenoids were identified and quantified in turmeric from in-vitro micropropagated and conventional greenhouse cultivation (Ma and Gang 2006). The chemicals identified included linoleic acid; 8,11-octadecadienoic acid; methyl ester; palmitic acid; oleic acid; stearic acid; phytol; hexadecane-1,2-diol; β -elemene; corymbolone; curcuphenol; γ -bisabolene; α -oxobisabolene; *R*-citronellene; cineole; β -pinene; sylvestrene; piperitone epoxide; *p*-meth-8-en-2-one; *p*-cymen-8-ol; *o*-cymene; γ -terpineol; terpinene-4-ol; and *p*-mentha-1,4-(8)-diene. The following constituents were identified in the rhizome essential oil of micropropagated and conventionally propagated turmeric: α -phellandrene, eucalyptol, β -farnesene, *ar*-curcumene, β -sesquiphellandrene, clionasterol, *ar*-turmerone, curlone, methyl-3-methyl-2-phenyl-2-butanol and *trans*-2-methyl-2-pentenoic acid (Singh et al. 2010b). The major constituents in fresh turmeric rhizome oil were *ar*-turmerone (24.4 %), α -turmerone (20.5 %) and β -turmerone (11.1 %) and in dry rhizome oil *ar*-turmerone (21.4 %), α -santalene (7.2 %) and *ar*-curcumene (6.6 %) (Singh et al. 2010a), whereas, in oleoresins, the major components were α -turmerone (53.4 %), β -turmerone (18.1 %) and aromatic turmerone (6.2 %) in fresh and aromatic turmerone (9.6 %), α -santalene (7.8 %) and α -turmerone (6.5 %) in dry rhizome. Results showed that α -turmerone, a major component in fresh rhizomes, is only a minor one in dry rhizomes. Also, the content of β -turmerone in dry rhizomes was less than the half amount found in fresh rhizomes.

Fifty-four compounds identified from turmeric yellow rhizome type of which the major compounds were *ar*-turmerone (27.78 %), turmerone (17.16 %), curlone (13.82 %), 2-carene (4.78 %), zingiberene (4.37 %), β -sesquiphellandrene (5.57 %), *ar*-curcumene (3.29 %), α -bisabolol (2.04 %), bicyclo[7.2.0]undecane,10,10-dimethyl-2,6-bis(methylene) (1.44 %) and 1,4-dimethyl-2,4-dimethylbenzene (1.19 %) (Chowdhury et al. 2008). Other components (<1 %) were γ -gurjunenpoxide-(1); 2,5-octadiene,3,4,5,6-tetramethyl-; aristolene; 4,7-methanobenzofuran,2,2'-oxybis[octahydro-7,8,8-trimethyl; acoradiene; 1,1'-bicyclohexyl,4-(methoxymethyl)-4'-propyl-; di-epi- α -cedrene; naphthalene,1,2,3,4,4a,5,6,8a-octahydro-4a,8-dimethyl-2-(1-

methylethylidene)-; benzene,1,4-dimethyl-2-(2-methylpropyl)-; α -santolol; caryophyllene oxide; dicumyl peroxide; (1,2,3-trimethyl-cyclopent-2-enyl)-methanol; γ -elemene; 2-oxabicyclo[9.1.0]dodeca-3,7-diene,1,5,5,8-tetramethyl-; elixine; 2,3,5-trimethylfuran; teresantalol; benzene, 1-methyl-4-(1-methylpropyl)-; *cis*- α -bisabolene, α -himachalene, α -caryophyllene, β -santalene; decahydroquinoline 243a; caryophyllene; α -santalene; α -bergamotene; *p*-cymen-8-ol; menthol; borneol; camphor; β , β -dimethylstyrene; (*E*)-3,7-dimethyl,1,3,6-octatriene; eucalyptol; limonene; *m*-cymene; α -terpinene; 3-carene; α -phellandrene; β -pinene; camphene; and α -pinene. The red rhizome type contained 39 compounds with carvacrol (21.14 %), citral (13.91 %), methyl eugenol (7.31 %), geraniol (6.99 %), menthol (5.11 %), caryophyllene oxide (4.14 %), 2,6,11,15-tetramethylhexadeca-2,6,8,10,14-pentaene (2.91 %), 7-nonadien-2-ol,4,8-dimethyl- (2.39 %), piperitone (2.27 %), geranic acid (2.24 %), neric acid (2.29 %), citronellol (1.89 %), geranyl acetate (1.82 %), neryl acetate (1.53 %), 2,6-octadiene,4,5,-dimethyl (1.18 %), 6-octadiene-1,8-diol, 2,6-dimethyl- (1.05 %), 1,6,10,14-hexadecatetraen-3-ol, 3,7,11,15-tetramethyl-, (*E,E*)- (1.76 %), (*E,E,E*)-3,7,11,15-tetramethylhexadeca-1,3,6,10,14-pentaene (1.65 %), 2,2,4-trimethyl-3-(3,8,12,16-tetramethyl-heptadeca-3,7,11,15-tetraenyl)-cyclohexanol (1.17 %), nerolidyl propionate (1.07 %), α -farnesene (1 %) and 6,11-dimethyl-2,6,10-dodecatrien-1-ol (1.16 %) as major constituents. Other components (<1 %) included linalool; 6-nonenal,3,7 dimethyl-; cyclohexyl formate; α -selinene; juniper camphor; cyclohexanol, 3,3,5-trimethyl-, acetate; *cis*-, *trans*-nerolidol; 8-oxabicyclo[3.2.1]oct-6-en-3-one,2,4-dimethyl-; 3-bornanone; adoxal; 2-cyclohexene-1-carboxaldehyde,2,6-dimethyl-6-(4-methyl-3-pentenyl)-; bicyclo[3.3.1]nonan-9-one,2,4-dimethyl-3-nitro- (exo)-; 5,9-undecadien-2-one,6,10-dimethyl-, (*Z*)-; gitoxigenin; pyrazolo[1,5-a]pyridine,3,3a,4,7-tetrahydro-3,3-dimethyl-, (3a*S*); 20-oxopregn-16-en-12-yl acetate; and 6,10-dodecatrien-1-ol,3,7,11-trimethyl-. Nineteen diarylheptanoids were identified in fresh turmeric rhizome extract including curcumin, demethoxycurcumin and bisdemethoxycurcumin (Jiang et al. 2006).

Major volatiles identified in turmeric rhizomes included α -thujene (3-thujene); α -pinene; sabinene (4(10)-thujene); β -pinene; myrcene; α -phellandrene; 3-carene; α -terpinene; limonene; β -phellandrene; 1,8-cineole (eucalyptol); (*E*)- β -ocimene; γ -terpinene; *p*-mentha-1,4(8)-diene (terpinolene); *p*-menth-1-en-8-ol (α -terpineol); unknown (7-epi-sesquithujene-like); (*E*)-caryophyllene (β -caryophyllene); (*E*)- α -bergamotene; α -humulene (α -caryophyllene); (*E*)- β -farnesene; γ -curcumene; *ar*-curcumene; (–)- α -zingiberene; β -bisabolene; (–)- β -sesquiphellandrene; (*E*)- γ -bisabolene; β -curcumene; unknown (*cis*-sesquisabinene hydrate-like); (*E*)-nerolidol; unknown (*trans*-sesquisabinene hydrate-like1); unknown (*trans*-sesquisabinene hydrate-like2); unknown (*trans*-sesquisabinene hydrate-like3); (+)- α -turmerone; epi- α -bisabolol/ α -bisabolol; (+)- β -turmerone; (*Z*)- α -atlantone; α -oxobisabolene; and (*E*)- α -atlantone (Koo and Gang 2012).

Non-polar extracts identified from turmeric hexane extract included *ar*-turmerone (19.5 %), α -turmerone (201.1 %) and β -turmerone (17.6 %) as major compounds (>5 %) and cineole (<1 %), α -terpinolene (<1 %), *Z*- β -farnesene (<1 %), β -himachalene (<1 %), *ar*-curcumene (2.3), α -zingiberene (2.3 %), β -bisabolene (<1 %) and β -sesquiphellandrene (4.1 %) as minor compounds (Herebian et al. 2009). Also polar metabolites were identified as TMS (trimethylsilyl)/methoxime derivatives from turmeric methanol extract: glycerol, malic acid, citric acid, fructose 1, fructose 2, glucose 1, glucose 2 and sucrose as major compounds (5–50 %); lactic acid, *L*-alanine, oxalic acid, monoethyl phosphate, malonic acid, *L*-valine, phosphoric acid, succinic acid, glyceric acid, fumaric acid, *L*-aspartic acid, 5-oxo-proline, erythritol, *L*-threonic acid, *L*-glutamic acid, xylitol, *p*-hydroxycinnamic acid, vanillic acid, *p*-coumaric acid, glucitol, gulonic acid, *trans*-ferulic acid and myo-inositol as minor compounds (<5 %); and 2-hydroxypyridine, 1,3-propandiol, acetic acid, *L*-leucine, hydroxylamine, carbonic acid, *L*-valine, *L*-serine, *L*-serine, *L*-glycine, *L*-threonine, *p*-hydroxybenzoic acid, *p*-hydroxyphenylacetate, ribitol, 6-deoxy-galactose, α -glycerophosphate, *L*-tyrosine, dihydroferulic acid, β -alanine, citramalic acid, *N*-acetyl-*L*-serine, *L*-asparagine, aconitic acid, tetroneic acid, ribonic acid,

shikimic acid, *L*-tryptophane, uridine, trehalose, *L*-isoleucine and *N*-acetylglucosamine as trace compounds. Some volatile metabolites detected in non-polar turmeric extracts by gas chromatography–time-of-flight mass spectrometry (GC/TOF MS) included (*Z*)- β -farnesene, β -cedrene, α -curcumene, germacrene D, β -bisabolene, β -sesquiphellandrene, α -patchoulene, cedr-9ene, *ar*-turmerone, turmerone, curlone and four unknowns (Lee et al. 2014a). Also curcuminoids curcumin, demethoxycurcumin and bisdemethoxycurcumin were detected by ultrahigh-performance liquid chromatography–quadrupole time-of-flight mass spectrometry (UPLC/Q-TOF MS).

Composition (%) of the turmeric extracts (volatile fraction) obtained by supercritical fluid extraction (SFE) at 300 bar pressure using ethanol, isopropyl alcohol and ethanol/isopropyl alcohol co-solvents, hydrodistillation (HD), Soxhlet extraction (Soxhlet) and low-pressure solvent extraction (LPSE) were respectively determined as follows: (*Z*)- γ -atlantone 24.7, 39.5, 36.2, 44, –, 33.4 %; (*E*)- γ -atlantone 19.8, 18.0, 17.1, 18.3, –, 18.7 %; *ar*-turmerone 26.9, 15.1, 15, 18, –, 21.6 %; *ar*-curcumene 2.0, 1.0, 0.–, 1.5 %; β -sesquiphellandrene 2.6, 2.0, 1.9, 1.0, –, 2.9 %; α -zingiberene 1.9, 2.4, 2.2, 2.4, –, 2.5 %; *ar*-turmerol 1.0, 0.8, 0.7, 1.1, 6.5, tr%; *ar*-turmerol isomer 1.1, 0.8, 0.8 %, – tr; 6*S*,7*R*-bisabolene 1.1,0.9, 0.9–0.6, – 0.8 %; β -bisabolene 0–.5, 0.4, 0.4, tr, –, 0.7 %; α -pinene tr, tr, tr, 2.7, –, –%; 1,8-cineol tr, tr, tr, 1.4, –, – %; *trans*-caryophyllene tr, 0.4, 0.4, tr, –, tr%; (*Z*)- α -atlantone 0.5,0.4,1.7, 0.6, 17, 0.8 %; (*E*)- α -atlantone tr, 0.7, 0.9, 0.6, –, 0.3 %; dihydro-*ar*-turmerone tr, 0.4, 0.4, tr, –, tr%; 1-epicubenol 0.7, 0.6, 0.6, 0.6, –, tr%; and unidentified 15.6, 16.1, 19.4, 4.9, 76.5,16.8 % (Braga et al. 2003). 86 % pure *ar*-turmerone was extracted from *C. longa* by supercritical carbon dioxide and liquid–solid chromatography (Cheng et al. 2012). Three active components curcumin, demethoxycurcumin and bisdemethoxycurcumin in *Curcuma longa* were separated with high sensitivity using HPLC coupled with electrochemical detection (Long et al. 2014). Good linearity was obtained in the range of 0.208–41.6, 0.197–39.4 and 0.227–114 μ M for curcumin, demethoxycurcumin and bisdemethoxycurcumin, respectively.

The main constituent of turmeric essential oil was found to be *ar*-turmerone (61.79 %), curlone (12.48 %), *ar*-curcumene (6.11 %), phenol (3.45 %), zingiberene (2.98 %), α -sesquiphellandrene (2.81 %), 1-ethyl-4-isobutylbenzene (2.61 %) and other components α -bisabolene (1.48 %), benzene (1.48 %), benzaldehyde (1.44 %), 1,2,3,5-tetramethylbenzene (1.42 %), 4-methyl-carbonitrile (1.09 %) and silane (0.84 %) (Liju et al. 2011).

Tsai et al. (2011) reported the composition of the rhizome essential oil (yield 9.85 mg/g) as follows: *ar*-turmerone 49.04 %, humulene oxide 16.59 %, β -selinene 10.18 %, caryophyllene oxide 5.6 %, α -humulene 3.41 %, α -selinene 3.14 %, α -terpineol 2.9 %, 1,8-cineol 2.85 %, curcumenol 1.45 % and minor components (<1 %) which include α -pinene, β -pinene, limonene, *p*-cymene, 2-heptanol, linalool oxide, 2-nonanol, camphor, linalool, β -elemene, 4-terpineol, caryophyllene, δ -cadinene and dodecanoic acid. Singh et al. (2011b) reported the rhizome essential oil to contain *ar*-turmerone 41.9 %, curlone (β -turmerone) 16.8 %, α -phellandrene 5.3 %, *ar*-curcumene 3.5 %, eucalyptol 2.6 %, β -sesquiphellandrene 1.7 %, β -caryophyllene 0.8 %, β -farnesene 0.6 %, β -bisabolene 0.6 % and δ -3-carene 0.3 %. Lee et al. (2011) reported the following major components of *C. longa* essential oil: α -turmerone (35.59 %), germacrone (19.02 %), α -zingiberene (8.74 %), *ar*-turmerone (6.31 %), *trans*- β -elemenone (5.65 %), curlone (5.45 %) and β -sesquiphellandrene (4.73 %). *ar*-Turmerone, β -turmerone, zingiberene, β -elemene, α -curcumene, α -turmerone, germacrone and β -sesquiphellandrene were identified in *Curcuma* volatile oil (Jiang et al. 2012a). Yield of oil for fresh, dried and cured turmeric rhizomes was 3.5, 3.0 and 4.5 %, respectively (Gounder and Lingamallu 2012). Major components were *ar*-turmerone (21.0–30.3 %), α -turmerone (26.5–33.5 %) and β -turmerone (18.9–21.1 %).

Chemical constituents (totalling 96.3 %) identified in the rhizome oil of *C. domestica* were *ar*-turmerone (45.8 %), curcumenol (18.2 %), (*Z*)-dihydromyrcene-1,6-diol (3.6 %), geranyl acetate (2.5 %), α -eudesmol acetate (2.3 %), β -sesquiphellandrene (1.9 %), zingiberene (1.7 %), γ -eudesmol

acetate (1.6 %), β -elemene (1.5 %), zerumbone (1.4 %), β -eudesmol (1.3 %), (E)-dihydromyrcene-1,6-diol (1.3 %), *ar*-curcumene (1.2 %), α -phellandrene (1.1 %), γ -curcumen-15-al (1.1 %), *ar*-dihydro-turmerone (1 %), α -*cis*-bergamotene (0.9 %), 1-epicubenol (0.8 %), β -curcumene (0.8 %), 8-cedren-14-ol acetate (0.8 %), γ -curcumene (0.4 %), 10-epi- γ -eudesmol (0.4 %), hinesol (0.4 %), 15-hydroxy-9-epi-(E)-caryophyllene (0.4 %), 1,8-cineole (0.3 %), terpinolene (0.3 %), (E)-caryophyllene (0.3 %), (Z)-isoeugenol acetate (0.3 %), *ar*-turmerol (0.3 %), caryophyllene oxide (0.3 %), geranyl isovalerate (0.3 %), cubenol (0.3 %), β -bisabolene-12-ol (0.3 %), (E)- β -farnesene (0.2 %), α -terpinene (0.2 %), *p*-cymene (0.2 %), β -bisabolene (0.2 %), γ -eudesmol (0.2 %), 14-hydroxy- α -humulene (0.2 %), α -amyl-cinnamyl acetate (0.2 %) and α -humulene (0.1 %) (Jantan et al. 2012).

Essential oil of rhizome reported by Ferreira et al. (2013) comprised *ar*-turmerone 33.2 %, α -turmerone 23.5 %, β -turmerone 22.7 %, (6*R*,7*R*)-bisabolone (3.1 %), *ar*-curcumene 2.6 %, β -sesquiphellandrene 2.4 %, vinyl propionate 1.7 %, *ar*-turmerol 1.5 %, (E)- α -atlantone (1.4 %), α -cadinol (1.3 %); other minor compounds (<1 %) were α -pinene, *p*-cymene, 1,8-cineole, camphor, α -terpineol, β -caryophyllene, γ -curcumene and α -zingiberene. Five compounds were identified in the rhizome essential oil with an ester, 3-methyl-2-butenic acid and 3-phenyl-2-propenyl ester (45.64 %) constituting the bulk of the oil, followed by a ketone, known as curlone (26.84 %), and a carboxylic acid, 9-octadecenoic acid (16.78 %) (Uchegbu et al. 2014). Other compounds identified were 3,5-di-*tert*-butylphenol (5.37 %) and turmerone (5.37 %).

Essential oil yield from the root was 4.3 % with the major components identified as *ar*-turmerone (46.8 %), *ar*-curcumene (7 %), dihydrocurcumenone (4.3 %), *p*-cymene (3.3 %), β -bisabolene (2.3 %), *p*-cymen-8-ol (1.5 %) and 6*S*,*SR*-bisabolene (1.2 %) (Leela et al. 2002). Other minor components (<1 %) were α -pinene, β -pinene, α -phellandrene, 1,8-cineole, terpinolene, linalool, α -terpineol, thymol carvacrol, γ -curcumene, curlone and curcuphenol, and very minor compounds (traces) were myrcene, *p*-methylacetophenone, α -zingiberene and β -sesquiphellandrene.

Other identified compounds were 30.3 %. Major volatiles identified in turmeric roots included tricyclene; α -thujene (3-thujene); α -pinene; β -pinene; myrcene; α -phellandrene; 3-carene; α -terpinene; limonene; 12, β -phellandrene; 1,8-cineole (eucalyptol); (*E*)- β -ocimene; γ -terpinene; *p*-mentha-1,4(8)-diene (terpinolene); bornyl acetate; β -elemene; unknown (7-epi-sesquithujene-like); (*E*)-caryophyllene (β -caryophyllene); (*E*)- α -bergamotene; α -humulene (α -caryophyllene); (*E*)- β -farnesene; γ -curcumene; *ar*-curcumene; (–)- α -zingiberene; β -bisabolene; (–)- β -sesquiphellandrene; (*E*)- γ -bisabolene; unknown (*cis*-sesquisabinene hydrate-like); (*E*)-nerolidol; unknown (*trans*-sesquisabinene hydrate-like¹); unknown (*trans*-sesquisabinene hydrate-like³); (+)- α -turmerone; (+)- β -turmerone; (*Z*)- α -atlantone; and α -oxobisabolene (Koo and Gang 2012).

Curcuma longa rhizome lectin had been reported to have antifungal, antibacterial and α -glucosidase inhibitory activities, forming a homodimer with high thermal stability as well as acid tolerance (Biswas and Chattopadhyaya 2014). Size exclusion chromatography and dynamic light scattering showed it to be a dimer at pH 7, but at near pH 2, it was converted to a monomer. Unfolding experiments, temperature-dependent circular dichroism and dynamic light scattering for the dimer at pH 7 indicated its higher stability than for the monomer at pH 2.

Solvent extraction was found to be a more suitable method to extract the essential oil of *Curcuma longa* compared to steam distillation and Soxhlet extraction because solvent extraction did not require heat (Ching et al. 2014). Sample extracts showed that the *Curcuma longa* contained high amount of curcumin in all samples (40 °C, 50 °C, 60 °C and 70 °C curcumin extracts). Curcumin extract at 40 °C showed 90.477 % area of peak, 50 °C curcumin extract with 92.304 %, 60 °C curcumin extract with 90.428 % and 70 °C curcumin extract showed 92.053 % area of peak. The 50 °C curcumin extract showed the highest antioxidant activity with 24.968 IC₅₀ value, while the lowest was 70 °C curcumin extract with 111.93 IC₅₀ value.

Ramirez-Ahumada Mdel et al. (2006) identified curcuminoid synthase and hydroxycinnamoyl-CoA thioesterases involved in the biosynthesis of curcuminoids in turmeric and gingerols in ginger. Assays for enzymes in the phenylpropanoid pathway identified the corresponding enzyme activities in protein crude extracts from leaf, shoot and rhizome tissues from ginger and turmeric. These enzymes included phenylalanine ammonia lyase, polyketide synthases, *p*-coumaroyl shikimate transferase, *p*-coumaroyl quinate transferase, caffeic acid *O*-methyltransferase and caffeoyl-CoA *O*-methyltransferase. The results of polyketide synthase assays showed detectable curcuminoid synthase activity in the extracts from turmeric with the highest activity found in extracts from leaves. However, no gingerol synthase activity could be identified. Two novel type III polyketide synthases were proposed to be involved in the pathway for curcuminoid biosynthesis in herb *C. longa* (Katsuyama et al. 2009a). One of the type III polyketide synthases, named diketide-CoA synthase (DCS), catalysed the formation of feruloyldiketide-CoA by condensing feruloyl-CoA and malonyl-CoA. The other, named curcumin synthase (CURS), catalysed the in-vitro formation of curcuminoids from cinnamoyldiketide-*N*-acetylcysteamine (a mimic of the CoA ester) and feruloyl-CoA. Co-incubation of DCS and CURS in the presence of feruloyl-CoA and malonyl-CoA yielded curcumin at high efficiency, although CURS itself possessed low activity for the synthesis of curcumin from feruloyl-CoA and malonyl-CoA. Two additional type III polyketide synthases, named CURS2 and CURS3, associated with curcuminoid synthesis, were identified and characterised in *C. longa* (Katsuyama et al. 2009b). In-vitro analysis revealed that CURS2 preferred feruloyl-CoA as a starter substrate and CURS3 preferred both feruloyl-CoA and *p*-coumaroyl-CoA. The results suggested that CURS2 synthesises curcumin or demethoxycurcumin and CURS3 synthesises curcumin, bisdemethoxycurcumin and demethoxycurcumin. Koo and Gang (2012) reported the identification and functional characterisation of 13 mono- and 11 sesquiterpene synthases from turmeric. Novel terpene synthases, (-)-caryolan-1-ol synthase and α -zingiberene/ β -sesquiphellandrene synthase, which is responsible for the

formation of the major sesquiterpenoids in ginger and turmeric rhizomes, were also discovered. The most abundant and most important sesquiterpenoids in turmeric rhizomes, (+)- α -turmerone and (+)- β -turmerone, are produced from (-)- α -zingiberene and (-)- β -sesquiphellandrene, respectively, via α -zingiberene/ β -sesquiphellandrene oxidase and a still unidentified dehydrogenase. Hydroxycinnamoyl-CoA thioesterases had been found to be present in turmeric tissues (Flores-Sanchez and Gang 2013).

Of several brands of turmeric and curry powders analysed, pure turmeric powder had the highest curcumin concentration, averaging 3.14 % by weight (Tayyem et al. 2006). The curry powder samples, with one exception, had relatively small amounts of curcumin present, and the variability in content was great.

Flower Phytochemicals

Essential oil yield from flowers was 0.3 % with the major components identified as *p*-cymen-8-ol (26 %), terpinolene (7.4 %), 1,8-cineole (4.1 %), *ar*-curcumene (1.9 %), *p*-cymene (1.6 %), linalool (1.1 %), α -terpineol (1.1 %), β -sesquiphellandrene (1.1 %), (*E*)-nerolidol (1.1) and turmerone (1.0 %) (Leela et al. 2002). Other minor components (<1 %) were α -pinene, myrcene, β -pinene, δ -3-carene, α -terpinene, 1,3,8-paramenthatriene, *p*-methylacetophenone, α -zingiberene, β -bisabolene, curlone and 6*S*,*SR*-bisabolene, and very minor compounds (traces) were β -phellandrene, γ -curcumene and curcuphenol.

Leaf/Aerial Part Phytochemicals

Hexane extract from the turmeric leaves yielded labda-8(17),12-diene-15,16-dial (Roth et al. 1998). Oguntimein et al. (1990) found turmeric leaf oil from Nigeria to contain mainly monoterpenes; α -phellandrene (47.7 %) and terpinolene (28.9 %) were the major components. With the exception of the absence of myrcene, turmeric leaf oil from India largely resembled the Nigerian counterpart (McCarron et al. 1995). Forty-nine constituents were identified in turmeric leaf

essential oil from Bhutan, and the major ones identified were α -phellandrene (18.2 %), 1,8-cineole (14.6 %), *p*-cymene (13.3 %), terpinolene (11.6 %), β -pinene (7.2 %), limonene (3.3 %), α -pinene (2.6 %), *p*-cymen-8-ol (2.4 %), myrcene (1.8 %), linalool (1.2 %), *cis*-sabinol (1 %), γ -terpinene (1 %) and the rest <1 %, and traces included toluene, α -thujene, camphene, sabinene, δ -3-carene, α -terpinene, (*Z*)- β -ocimene, (*E*)- β -ocimene, dehydro-*p*-cymene, camphor, borneol, terpinene-4-ol, myrtenal, α -terpineol, myrtenol, *cis*-carvotanacetol, piperitone, cinnamaldehyde, thymol, cavarol, 5-hydroxy-*p*-menth-6-en-2-one, 6-hydroxy-*p*-menth-6-en-3-one, caryophyllene, α -humulene, (*E*)- β -farnesene, α -curcumin, zingiberene, β -bisabolene, β -sesquiphellandrene, elemicin, (*E*)-nerolidol, caryophyllene oxide, *ar*-turmerone, α -turmerone, germacrone, β -turmerone and curdione (Sharma et al. 1997).

More than 20 components were identified from the leaf oil from Vietnam, of which monoterpenes α -phellandrene (24.5 %), 1,8-cineole (15.9 %), *p*-cymene (13.2 %) and β -pinene (8.9 %) were the major ones (Nguyen et al. 1995). Essential oil yield from leaves was 1.3 % with the major components identified as α -phellandrene (32.6 %), terpinolene (26 %), 1,8-cineole (6.5 %), *p*-cymene (5.9 %), β -phellandrene (3.2 %), β -pinene (2.8 %), myrcene (2.3 %), α -pinene (2.1 %), α -terpinene (1.5 %) and δ -3-carene (1.1 %) (Leela et al. 2002). Other minor components (<1 %) were (*Z*)- β -ocimene, (*E*)- β -ocimene, linalool, 1,3,8-paramenthatriene, *p*-methylacetophenone, *p*-cymen-8-ol, α -terpineol, thymol, carvacrol, γ -curcumene, *ar*-curcumene, α -zingiberene, β -sesquiphellandrene, (*E*)-nerolidol, *ar*-turmerone, turmerone, curlone and 6*S*,*SR*-bisabolene, and the very minor compound (traces) was curcuphenol. Other identified compounds were 9 %. Turmeric leaf oil (2.2 % yield) from plains of northern India contained 83 components, comprising 97.4 % of the total oil, of which the main constituents were terpinolene (26.4 %), 1,8-cineole (9.5 %), α -phellandrene (8 %) and terpinen-4-ol (7.4 %) (Raina et al. 2002). The leaf oil of *C. longa* from northern Indian plains, India, consisted mainly of monoterpenoids, monoterpene hydrocarbons (57 %), oxygenated monoterpenes (10 %), sesquiterpene hydrocarbons

(3.3 %) and oxygenated sesquiterpenes (2.1 %) (Garg et al. 2002). The major constituents of the oil were *p*-cymene (25.4 %) and 1,8-cineole (18 %), followed by *cis*-sabinol (7.4 %) and β -pinene (6.3 %). The major components of turmeric leaf volatile oil were *ar*-turmerone (63.4 %), α -turmerone (13.7 %) and β -turmerone (12.6 %) (Ajaiyeoba et al. 2008). The oils of turmeric leaves and flowers were chemically similar and particularly rich in terpinolene: 76.8 % and 67.4 %, respectively (Chane-Ming et al. 2002). The same sesquiterpenoids were found in all three oils, but in higher amounts in the rhizomes.

Sixty-one constituents were identified from turmeric leaf oil representing 99.8 % of the oil from the lower Himalayan region of Northern India, and the main constituents were α -phellandrene (53.4 %), terpinolene (11.5 %), 1,8-cineole (8.5 %), *p*-cymene (4.8 %), α -pinene (2.3 %), 2-octanol (3 %), γ -terpinene (2.2 %), limonene (2 %), β -pinene (1.8 %) and α -terpinene (1 %) (Raina et al. 2005). Other minor constituents (tr- <1 %) included α -thujene, camphene, sabinene, myrcene, (*Z*)-3-hexenyl acetate, δ -3-carene, (*Z*)- β -ocimene (*E*)- β -ocimene, *cis*-linalool oxide, linalool, *trans*-*p*-menth-2-en-1-ol, *p*-methyl acetophenone, camphor, *p*-cymen-8-ol, terpinene-4-ol, myrtenal, α -terpineol, myrtenol, *cis*-sabinol, 2-decanol, *cis*-carvotanacetol, *cis*-carveol, neral, perilla ketone, linalyl acetate, geranial, isobornyl acetate, geranyl formate, undecanol, geranyl acetate, β -patchoulene, β -elemene, β -caryophyllene, γ -elemene, α -bergamotene, β -farnesene, germacrene D, zingiberene, α -selinene, β -sesquiphellandrene, *ar*-turmerol, caryophyllene oxide, viridiflorol, *trans*-sesquisabinene hydrate, humulene epoxide II, T-cadinol, *ar*-turmerone, germacrone, (*E*)- α -atlantone and heptyl salicylate (Raina et al. 2005).

Hydrodistillation of turmeric leaves from northern Indian plains resulted in the isolation of 0.53 % of oil (w/v) FWB and in the identification of 75 constituents comprising 77.5 % of the oils; the major ones were α -phellandrene (9.1 %), terpinolene (8.8 %), 1,8-cineole (7.3 %), undecanol (7.1 %), *p*-cymene (5.5 %), sabinyl acetate (3.5 %), methyl eugenol (3 %), cinnamaldehyde (1.9 %), tetradecane (1.8 %), isobornyl

acetate (1.8 %), myrcene (1.6 %), *cis*-sabinol (1.5 %), α -terpineol (1.4 %), β -elemene (1.2 %), geranyl butyrate (1.1 %), geranyl acetate (1.0 %) and the rest (<1 %), and traces included isobutyl acetate, n-octane, 3-buten-2-ol, *cis*-3-hexenol, n-nonene, α -pinene, camphene, sabinene, β -pinene, 2-nonanol, α -fenchol, *trans*-*p*-menth-2-en-1-ol, *p*-methyl acetophenone, borneol, *cis*-carvotanacetol, *cis*-carveol, carvone, perilla ketone, geraniol, safrole, undecane, geranyl formate, thymol, carvacrol, linalyl propionate, *cis*-carvyl acetate, δ -elemene, thymol acetate, capric acid, β -patchoulene, caryophyllene, γ -elemene, α -cadinene, (*E*)- β -farnesene, germacrene D, α -selinene, β -curcumene, β -sesquiphellandrene, *ar*-turmerol, viridiflorol, *trans*-sesquisabinene hydrate, humulene epoxide II, 10-epi- γ -eudesmol, τ -cadinol, *ar*-turmerone, α -turmerone, α -bisabolol, germacrone, β -turmerone, curdione, 1-bisabolene, geranyl hexanoate, (*E*)- α -atlantone, furanodienone, n-heptyl salicylate and cinnamyl acetate (Awasthi and Dixit 2009). Turmeric leaf oil of Kerala contained α -phellandrene (24.35 %), *p*-cymene (11.07 %) and terpinolene (13.10 %) as the major components (Sindhu et al. 2011). Other components included 1,8-cineole (7.04 %), dl-limonene (4.61 %), β -pinene (4.72 %), β -myrcene (4.03 %), α -pinene (3.49 %), γ -terpinene (1.83 %), δ -3-carene (1.45 %), linalool (1.42 %), cuminol (1.14 %) and α -terpinene (1.05 %).

Nine compounds were isolated from the methanol leaf extract: 8,12-epoxygermacra-1(10),4,7,11-tetraen-6-one (1); 8,12-epoxygermacra-1(10),4,7,11-tetraene (2); cyclohexanecarboxylic acid methyl ester (3); isopulegol (4); 2-menthen-1-ol (5); menth-1-en-9-ol (6); octahydrocurcumin (7); labda-8(17)-12-diene-15,16-dial (8); and coronadiene (9) (Liu and Nair 2012). Nine out of 25 constituents were identified from the leaf essential oil of *Curcuma longa* Kasur variety grown in Pakistan (Parveen et al. 2013). Eucalyptol (10.27 %) was the major component; others included α -pinene (1.50 %), β -phellandrene (2.49 %), β -pinene (3.57 %), limonene (2.73 %), 1,3,8-*p*-menthatriene (1.76 %), ascaridole epoxide (1.452 %), 2-methylisoborneol (2.92 %) and 5-isopropyl-6-methyl-hepta-3,dien-2-ol (2.07 %).

Major volatiles identified in turmeric leaves included α -thujene (3-thujene); α -pinene; β -pinene; myrcene; α -phellandrene; 3-carene; α -terpinene; limonene; β -phellandrene; 1,8-cineole (eucalyptol); (*E*)- β -ocimene; γ -terpinene; (*Z*)-sabinene hydrate; *p*-mentha-1,4(8)-diene (terpinolene); linalool; myrtenal; (*E*)-caryophyllene (β -caryophyllene); α -humulene (α -caryophyllene); (*E*)- β -farnesene; (–)- α -zingiberene; (*E,E*)- α -farnesene; (–)- β -sesquiphellandrene; (*E*)-nerolidol; caryophyllene oxide; (+)- α -turmerone; and (+)- β -turmerone (Koo and Gang 2012).

Activity-guided fractionation of the ethanol extract of turmeric aerial parts led to the isolation of two phenolic compounds, 1,2,3,4,6-penta-*O*-galloyl- β -*D*-glucopyranoside and gallic acid, as antioxidant compounds (Ahn et al. 2012).

In addition to well-known curcuminoids, three coloured metabolites identified as dihydro derivatives of curcuminoids, dihydrocurcumin (dihydroCurc) with the structure, dihydrobisdesmethoxycurcumin (dihydroBDMC) and dihydrodesmethoxycurcumin-a (dihydroDMC-a), were isolated from cultured cell clumps derived from buds on turmeric rhizomes (Kita et al. 2009). The structures were defined as 5-hydroxy-1,7-*bis*(4-hydroxy-3-methoxyphenyl)-4,6-heptadiene-3-one; 5-hydroxy-7-(4-hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)-4,6-heptadiene-3-one; and 5-hydroxy-1,7-*bis*(4-hydroxyphenyl)-4,6-heptadiene-3-one, respectively. The cell clumps did not contain dihydroDMC-b, an isomer of dihydroDMC-a. Unlike rhizomes, the cell clumps, leaves and roots contained dihydrocurcuminoids as the major coloured constituents. Whereas dimethoxy compounds, curcumin and dihydrocurcumin, respectively, were most abundant in the rhizomes and leaves, one of the monomethoxy derivatives, dihydroDMC-a, was found most abundantly in the cell clumps and roots. While both dihydroDMC-a and dihydroDMC-b were detected in the rhizomes, dihydroDMC-b was not detectable in the cell clumps, leaves or roots.

Assays for enzymes in the phenylpropanoid pathway of the biosynthesis of curcuminoids and gingerols identified the corresponding enzyme activities in protein crude extracts from

leaf, shoot and rhizome tissues from ginger and turmeric (Ramirez-Ahumada et al. 2006). These enzymes included phenylalanine ammonia lyase, polyketide synthases, p-coumaroyl shikimate transferase, p-coumaroyl quinate transferase, caffeic acid *O*-methyltransferase and caffeoyl-CoA *O*-methyltransferase. All crude extracts possessed activity for all of these enzymes, with the exception of polyketide synthases. The results of polyketide synthase assays showed detectable curcuminoid synthase activity in the extracts from turmeric with the highest activity found in extracts from leaves. However, no gingerol synthase activity could be identified.

Pharmacological Activities/Review Studies

Innumerable studies had reported that turmeric and its curcuminoids especially curcumin exhibited a diverse range of pharmacological properties: antioxidant and anti-inflammatory, antibacterial, antifungal, antitumourous, anticarcinogenic, antithrombotic, cytotoxic, antiangiogenic, antivenom, antiatherosclerotic, antinociceptive, hypolipidaemic, anticataractogenic, nematocidal, anti-apoptotic, anti-atherogenic, cardioprotective, antidiabetic, hepatoprotective, antirheumatic, antihepatotoxic, antiviral, antiparasitic, antispasmodic, thymolytic and anti-human immunodeficiency virus.

Curcumin has been shown to exhibit antioxidant, anti-inflammatory, antiviral, antibacterial, antifungal, and anticancer activities and thus has a potential against various malignant diseases, diabetes, allergies, arthritis, Alzheimer's disease and other chronic illnesses (Aggarwal et al. 2007). Studies had indicated that turmeric oil, present in turmeric, could enhance the bioavailability of curcumin and that curcumin-free turmeric (CFT) components possess numerous biological activities including anti-inflammatory, anticancer and antidiabetic activities (Aggarwal et al. 2006a; 2013). The authors reviewed the anticancer and anti-inflammatory activities exhibited by CFT and by some individual components of turmeric, including turmerin, turmerone, elemene, furanodiene, curdione, bisacurone, cyclocurcumin,

calebin A and germacrone. Curcumin, a natural antioxidant, had been shown to have many pharmacological activities such as anti-inflammatory, antimicrobial, anticancer and anti-Alzheimer in both preclinical and clinical studies (Naksuriya et al. 2014). Moreover, curcumin has hepatoprotective, nephroprotective, cardioprotective, neuroprotective, hypoglycaemic, antirheumatic and antidiabetic activities, and it also suppresses thrombosis and protects against myocardial infarction. Tetrahydrocurcumin, from turmeric rhizome, had been demonstrated to prevent oxidative stress and inflammation, to act against neurodegeneration and to possess anticancer activity (Wu et al. 2014). Annadurai et al. (2013) reported the presence of transcripts related to biosynthetic pathways of several anticancer compounds like taxol, curcumin and vinblastine in addition to antimalarial compounds like artemisinin and acridone alkaloids, emphasising turmeric's importance as a highly potent phytochemical. Their data not only provided molecular signatures for several terpenoids but also a comprehensive molecular resource for facilitating deeper insights into the transcriptome of *C. longa*. Turmeric has a role in the treatment of periodontal diseases and oral cancers (Chaturvedi 2009; Nagpal and Sood (2013). Turmeric can also be used as a pit and fissure sealant, mouth wash and subgingival irrigant in different preparations (Nagpal and Sood 2013). It can also be used as a component in local drug delivery system in gel form.

Antioxidant Activity

Turmeric extracts and curcumin showed good antioxidant activity as evaluated by the CUPRAC method (Çıkrıkçı et al. 2008). Aqueous extract of fresh turmeric rhizomes showed higher antioxidant properties as compared to the extracts from dry rhizomes as evaluated by 1,1-diphenyl-2-picrylhydrazyl (DPPH) and β -carotene bleaching radical-generating system (Vankar 2008). A comparison of the long and short varieties in their two different physical states of rhizomes, fresh and dry, showed considerable loss in antioxidant properties in dry powders. The order of reactivity was *Curcuma* long (dry) < dry spice turmeric powder < *Curcuma* long (wet) < *Curcuma* short

(dry) < *Curcuma* short (wet). The loss of antioxidant properties during the dry spice preparation thus indicated that its beneficial pharmacological activities were definitely reduced, thus suggesting that fresh *Curcuma longa* rhizome be preferred for consumption to obtain its maximum benefit. The aqueous and ethanol extracts of two major preparations of turmeric, corresponding to its use in cooking and medicine, showed significant antioxidant abilities (Tilak et al. 2004). The study revealed that the ability of turmeric to scavenge radicals, reduce iron complex and inhibit peroxidation may explain the possible mechanisms by which turmeric exhibited its beneficial effects in relation to its use in cooking and medicine

Emblica officinalis-free (EOFP) and *Emblica officinalis*-bound phenolics (EOBP) showed between four- and tenfold higher levels of antioxidant activity as evaluated by both free radical scavenging and reducing power assays compared to that of *Curcuma longa*-free (CLFP) and *Curcuma longa*-bound phenolics (CLBP) (Kumar et al. 2006). The free and bound phenolics of *E. officinalis* showed high content of phenolic compounds (126 and 3.0 mg/g) compared to that of *C. longa* (29.7 and 1.6 mg/g). Gallic acid and tannic acid were identified as the major antioxidant components in phenolic fractions of *E. officinalis*, while the antioxidant activity of CLFP could be attributed to curcumin and that of CLBP to ferulic acid and *p*-coumaric acid. Further, the extracts of both *E. officinalis* and *C. longa* also exhibited significant protection to DNA against oxidative damage.

Total phenolic content (TPC) and ascorbic acid equivalent antioxidant capacity (AEAC) of crude extract and fractions of *C. longa* rhizomes were determined as follows: crude extract yield 4.1 %, TPC 94 %, AEAC, 59 %, non-polymeric phenol fraction yield 86 %, TPC 92 %, AEAC 53 %, polymeric tannin fraction yield 2 %, TPC 28 % and AEAC 21 % (Chan et al. 2011). Total phenolic content (TPC) and ascorbic acid equivalent antioxidant capacity (AEAC) of crude extract and fractions of *C. longa* leaves were determined as follows: crude extract yield 4.3 %, TPC 59 %, AEAC 39 %, non-polymeric phenol fraction yield 92 %, TPC 57 %, AEAC 39 %, and polymeric phenol fraction yield 1.7 %, TPC 28 %, AEAC 21 %.

polymeric tannin fraction yield 7.4 %, TPC 68 % and AEAC 60 % (Chan et al. 2011).

Turmeric oil and its fractions exhibited antioxidant activity in the β -carotene–linoleate model system and the phosphomolybdenum method (Jayaprakasha et al. 2002). The fraction III showed maximum antioxidant capacity. Turmeric oil contained aromatic turmerone (31.32 %), turmerone (15.08 %) and curlone (9.7 %), whereas fraction III contained aromatic turmerone (44.5 %), curlone (19.22 %) and turmerone (10.88 %) as major compounds. Also, oxygenated compounds (5,6,8–10) were enriched in fraction III. All the fractions and turmeric oil exhibited a markedly antimutagenicity in the Ames test, but fraction III was the most effective. Turmeric essential oil and ethanol oleoresin of fresh rhizomes have higher antioxidant properties as compared to dry ones as assessed by various lipid peroxidation assays as well as DPPH radical scavenging and metal chelating methods (Singh et al. 2010c). Turmeric oil was found to have in-vitro antioxidant activity, and IC_{50} values for scavenging superoxides, hydroxyl radicals and lipid peroxidation were 135 μ g/ml, 200 μ g/ml and 400 μ g/ml, respectively. The ferric-reducing activity for 50 μ g of turmeric essential oil was found to be 5 mM. Intraperitoneal administration of oil was found to inhibit PMA-induced superoxide radicals elicited by macrophages. Oral administration of turmeric oil for 1 month to mice significantly increased superoxide dismutase, glutathione and glutathione reductase enzyme levels in blood and glutathione S-transferase and superoxide dismutase enzymes in the liver. Fresh, dried and cured turmeric rhizome oils showed antioxidant capacity of 358, 686 and 638 mM of ascorbic acid equivalents per 1 mg of oil, respectively (Gounder and Lingamallu 2012). Trolox equivalent antioxidant capacity (TEAC) values were 38.9, 68.0 and 66.9 μ M at 1 mg of oil/ml for fresh, dried and cured rhizome, respectively, in ABTS assay. IC_{50} values for fresh, dried and cured rhizome oil to quench DPPH radicals were 4.4, 3.5 and 3.9 mg of oil/ml, respectively. The rhizome oil shows good reducing potential and was concentration dependent. It was

concluded that the cured rhizomes provided high yield of volatile oil with appreciably high antioxidant potential.

The essential oil combination of *Curcuma longa* and *Zingiber officinale* showed strong antioxidant activity through 2,2-diphenyl-1-picrylhydrazil-free radical scavenging, β -carotene–linoleic acid bleaching and total phenolic content assay (Prakash et al. (2012)).

Effectiveness of antioxidant activity and DPPH scavenging ability of essential oil of three *Curcuma rhizomes* was inversely correlated with their EC₅₀ values (Tsai et al. 2011). EC₅₀ values of antioxidant activities of the essential oils were 3.19–19.63 mg/mL, and the effectiveness was, in descending order, as follows: *Curcuma longa* > *C. sichuanensis* > *C. aromatica*. EC₅₀ values of scavenging abilities on 1,1-diphenyl-2-picrylhydrazyl radicals were 8.29–15.54 mg/mL, and the effectiveness was in a descending order: *C. aromatica* > *C. longa* > *C. sichuanensis*. *Curcuma longa* had significantly greater total polyphenols, flavonoids, anthocyanidins and antioxidant activity than *Zingiber officinale* (Trinidad et al. 2012). For *C. longa* and *Z. officinale*, the total polyphenol content per 100 g was 174, 55-mg gallic acid equivalent; flavonoids 125, 37-mg gallic acid equivalent; anthocyanidins 129, 22-mg catechin equivalent; DPPH % inhibition 54, 32 %; and FRAP 0.63, 0.26-mM reduced Fe, respectively. The methanol extracts and rhizome oils of *C. domestica* and *C. xanthorrhiza* exhibited strong inhibitory activity on copper-mediated oxidation of human low-density lipoprotein (LDL) (Jantan et al. 2012). Curcumin, demethoxycurcumin and bisdemethoxycurcumin, isolated from the methanol extracts of both plants, exhibited stronger activity than probucol (IC₅₀ value 0.57 μ mol/L) as reference, with IC₅₀ values ranging from 0.15 to 0.33 μ mol/L. The major components of *C. domestica*, *ar*-turmerone (45.8 %) and zerumbone (3.5 %), exhibited IC₅₀ values of 10.18 and 24.90 μ mol/L, respectively. The high levels of curcuminoids in the methanol extracts and xanthorrhizol, *ar*-turmerone and zerumbone in the oils, in combination with the minor components, were responsible for the high LDL antioxidant activity of the herbs.

C. domestica exhibited DPPH antioxidant activity; its chloroform extract was found to have the highest total phenolic content of 47.8 µg/mL among Thai edible plants tested (Lee et al. 2014b). Of 10 Zingiberaceous species, *Curcuma longa* and *Zingiber officinale* exhibited the highest free radical scavenging capacity of 270.07 mg/TE/g DW and 266.95 mg/TE/g DW and FRAP assay (Alafiatayo et al. 2014b). *Curcuma longa* and *Zingiber officinale* also gave the highest ferric-reducing power of 231.73 mg/TE/g DW and 176.26 mg/TE/g DW, respectively. For phenolic compounds, *Curcuma longa* and *Curcuma xanthorrhiza* gave the highest values of flavonoid (741.36 mg/NGN/g DW and 220.53 mg/NGN/g DW), phenolic acid (42.71 mg/GAE/g DW and 22.03 mg/GAE/g DW) and polyphenols (39.38 mg/GAE/g DW and 38.01 mg/GAE/g DW). Significant and positive linear correlations were found between total antioxidant capacity and phenolic compounds ($R^2 = 0.65\text{--}0.96$). Compared to *Curcuma xanthorrhiza*, *C. longa* had higher values in all the assays including DPPH (270.1 mg TE/g DW), FRAP (231.7 mg TE/g DW), phenolic acid (42.7 mg GA/g DW) and polyphenols (39.4 mg GA/g DW) (Alafiatayo et al. 2014a). The 90 % methanol extract showed the highest flavonoid content in both species.

The supercritical fluid extraction (SFE) conditions slightly affected the antioxidant activity of turmeric, which varied from 15 to 25 % of inhibition of oxidation for the first hour of reaction, increasing up to 28 and 43 % after 3 h of oxidation reaction (Braga et al. 2003). Despite the absence of curcuminoids in the hydrodistilled extracts, their antioxidant activity were considerably elevated as compared to the SFE extracts, but their antioxidant activity decreased over long reaction periods. The Soxhlet extracts were very effective (elevated antioxidant activity) for short reaction periods, and the antioxidant activity slightly decreased for long reaction periods. The low-pressure solvent extraction (LPSE) extracts were the most effective antioxidant, since their antioxidant activities were larger than 60 % of inhibition of oxidation and increased up to 70 % after 3 h of reaction. However, the ratio of solid to solvent used was too high (1:100) for commercial

utilisation. The results of studies by Kim et al. (2012) indicated that turmeric could effectively suppress the proliferation of tumour cells through the suppression of inflammatory nuclear factor NF- κ B and STAT3 (signal transducers and activators of transcription 3) pathways. Turmeric also inhibited NF- κ B activation induced by RANKL that correlated with the suppression of osteoclastogenesis.

Of the antioxidative curcuminoids, curcumin, 4-hydroxycinnamoyl (feruloyl) methane and *bis*(4-hydroxycinnamoyl) methane, isolated from turmeric rhizome, curcumin was the most active component, and its 50 % inhibitory concentrations for the air oxidation of linoleic acid were $1.83 \times 10^{-2}\%$ (thiobarbituric acid value) and $1.15 \times 10^{-2}\%$ (peroxide value) (Toda et al. 1985). These values of curcumin were superior to those of dl- α -tocopherol. The antioxidant activity of *Curcuma domestica* ginger was found to be greater than its curcuminoids curcumin, demethoxycurcumin and bisdemethoxycurcumin as assessed by the isothiocyanate and thiobarbituric acid assays (Jitoe et al. 1992). Curcumin was found to be the most potent scavenger of superoxide radicals followed by demethoxycurcumin and bisdemethoxycurcumin (Sreejayan and Rao 1996). Acetylcurcumin was inactive. Interaction with DPPH showed a similar activity profile. Curcumin I, curcumin II (monodemethoxycurcumin) and curcumin III (bisdemethoxycurcumin) showed antioxidant activity (Ramsewak et al. 2000). The inhibitions of liposome peroxidation by curcumins I–III at 100 microg/ml were 58, 40 and 22 %, respectively. Curcumin, demethoxycurcumin and bisdemethoxycurcumin showed DPPH radical scavenging effects with IC₅₀ values of 2.8, 39.2 and 308.7 μ M, respectively (Song et al. 2001). L-Ascorbic acid and resveratrol as positive controls exhibited IC₅₀ values of 22.5 and 25.0 μ M, respectively.

Turmeronol A and turmeronol B from dried turmeric rhizome prevented the autoxidation of linoleic acid at a concentration of ca. 200 ppm (Imai et al. 1990). Turmeronol A and turmeronol B inhibited soybean lipoxygenase at the IC₅₀

values of 16 μM and 9 μM , respectively. Turmeric rhizome compounds, curculonone A, curculonone B, 6 α -hydroxycurcumanolide A, zedoarondiol, curcumin, demethoxycurcumin and the benzenoid 1,5-*bis*-(4-hydroxy-3-methoxyphenyl)-(1*E*,4*E*)-1,4-pentadien-3-one, exhibited inhibition ($\text{IC}_{50} \leq 18.22 \mu\text{M}$) of superoxide anion generation by human neutrophils in response to formyl-*L*-methionyl-*L*-leucyl-*L*-phenylalanine/cytochalasin B (fMLP/CB) (Chen et al. 2010d). Compounds 6 α -hydroxycurcumanolide A, zedoarondiol, curcumanolide A, curcumanolide B; curcumin, demethoxycurcumin and benzenoid 1,5-*bis*-(4-hydroxy-3-methoxyphenyl)-(1*E*,4*E*)-1,4-pentadien-3-one inhibited fMLP/CB-induced elastase release with IC_{50} values $\leq 14.28 \mu\text{M}$. Two phenolic compounds, 1,2,3,4,6-penta-*O*-galloyl- β -*D*-glucopyranoside and gallic acid, isolated from the aerial parts showed significant antioxidative effects during the DPPH-free radical scavenging assay and the riboflavin- and xanthine-originated superoxide quenching activity tests (Ahn et al. 2012).

Das and Das (2002) demonstrated that curcumin was able to effectively quench singlet oxygen ($^1\text{O}_2$) at very low concentration in aqueous systems but not effective superoxide or hydroxyl radical scavengers. Curcumin was found to inhibit the $^1\text{O}_2$ -dependent 2,2,6,6-tetramethylpiperidine *N*-oxyl (TEMPO) formation in a dose-dependent manner. Curcumin at 2.75 μM caused 50 % inhibition of TEMP-(1)O(2) adduct formation. In-vitro, curcumin inhibited ferric nitrilotriacetate (Fe-NTA)- and hydrogen peroxide-induced peroxidation of renal microsomal membrane lipids and DNA damage (Iqbal et al. 2003a). It had been reported that curcumin exhibited bifunctional antioxidant properties related to its capability to react directly with reactive oxygen species (ROS) and also to its ability to induce the expression of cytoprotective and antioxidant proteins through the transcription factor nuclear factor-erythroid-2-related factor 2 (Nrf2) (Trujillo et al. 2014). Their review of recent studies suggested a close relationship of this antioxidant with the mitochondrial function.

Leaves of *Curcuma longa* had very low phenolic content (TPC) of 230 mg GAE/100 g and ascorbic acid equivalent antioxidant capacity (AEAC) of 113 mg AA (ascorbic acid)/100 g, and rhizome had TPC of 534 mg GAE/100 g and AEAC of 390 mg AA/100 g (Chan et al. 2008). The methanolic and water extracts of *C. mangga* (CMM and CMW) and *C. longa* (CLM and CLW) leaves, at 100 µg/mL, inhibited lipid peroxidation (LPO) by 78 %, 63 %, 81 % and 43 % (Liu and Nair 2012). The methanolic leaf extract of *C. longa* afforded nine compounds: 8,12-epoxygermacra-1(10),4,7,11-tetraen-6-one (1); 8,12-epoxygermacra-1(10),4,7,11-tetraene (2); cyclohexanecarboxylic acid methyl ester (3); isopulegol (4); 2-menthen-1-ol (5); menth-1-en-9-ol (6); octahydrocurcumin (7); labda-8(17)-12-diene-15,16-dial (8); and coronadiene (9). Compounds 1–9 showed inhibition against LPO enzyme by 11 %, 22 %, 18 %, 39 %, 66 %, 65 %, 87 %, 39 % and 55 %, at 25-µg/mL concentrations, respectively. Compounds 7–9 showed strong LPO inhibition and accounted for the activity exhibited by the extracts. Chan et al. (2009) found that all methods of thermal drying (microwave, oven and sun-drying) resulted in drastic declines in total phenolic content (TPC), ascorbic acid equivalent antioxidant capacity (AEAC) and ferric-reducing power (FRP), with minimal effects on ferrous ion-chelating ability and lipid peroxidation inhibition activity of turmeric leaves. Of the nonthermal drying methods, significant losses were observed in air-dried leaves.

Turmerin, a water-soluble, 5-kDa antioxidant peptide isolated from turmeric, was found to contain three residues of methionine which were partly responsible for its antioxidant activity (Srinivas et al. 1992). At 183 nM turmerin offered 80 % protection to membranes and DNA against oxidative injury. ROS-induced arachidonate release and the mutagenic activity of t-butyl hydroperoxide were substantially inhibited by turmerin. Turmerin was noncytotoxic up to milligram concentrations, as tested by Ames assay and in human lymphocytes. An antioxidant protein with apparent molecular mass of approximately 20 kDa was isolated from turmeric peel waste (Chethankumar et al. 2010a). The protein was stable even after heating at 60°C for 30 min and showed 84 %

antioxidant activity in terms of inhibition of hydroxyl radical formation. The antioxidant activity was significantly reduced at 90°C showing only 22 % inhibition of hydroxyl radical formation. The protein when exposed to UV radiations at 345 nm was stable till 20 min showing 91 % inhibition, and upon increase in exposure time, a significant decrease in the antioxidant activity was observed with only 11 % inhibition of hydroxyl radical formation. Treatment of erythrocyte membranes with ferrous sulphate ascorbate as pro-oxidant inhibited the Na + K + ATPase enzyme activity. There was 82 % decrease in the ATPase activity when compared to the untreated erythrocyte membrane. Incubating the membrane with antioxidant protein restored the ATPase activity by threefold. β -Turmerin, from turmeric waste grits, exhibited antioxidant activities (Smitha et al. 2009). In three different model systems, i.e. linolenic acid micelles, erythrocyte membrane systems and liposomes, β -turmerin at 0.125 μ M offered 70 %, 64 % and 60 % inhibition of lipid peroxidation, which was 3200 times more efficient than the standard antioxidants BHA (400 μ M) and α -tocopherol (400 μ M). β -Turmerin inhibited diene–triene and tetraene conjugation up to 54 %, 72 % and 47 %, respectively. β -Turmerin also effectively scavenged hydroxyl radicals when compared to butylated hydroxyanisole (BHA) and α -tocopherol. β -Turmerin (2.5 μ M) further inhibited the activation of PMNL (polymorphonuclear leukocyte) mediated by fMLP (*N*-formyl-*L*-methionyl-*L*-leucyl-*L*-phenylalanine) up to the extent of 75 %, whereas standard BHA (400 μ M) and mannitol (10 μ M) inhibited the same to 65 % and 55 %, respectively. At 0.125- μ M dose, β -turmerin prevented t-BOOH-induced cell death at all time intervals. In addition to the above properties, it was non-toxic to lymphocytes as it did not affect the viability of cells. Turmerin showed good DPPH (IC₅₀ = 29 μ g/mL) and superoxide (IC₅₀ = 48 μ g/mL) and moderate ABTS (IC₅₀ = 83 μ g/mL) radical scavenging and Fe(II) chelation (IC₅₀ = 101 μ g/mL) activities (Lekshmi et al. 2012b).

In-Vivo Studies

Studies indicated that dietary turmeric lowered lipid peroxidation in liver homogenates and microsomes of rats by enhancing the activities of antioxidant enzymes superoxide dismutase, catalase and glutathione peroxidase (Reddy and Lokesh 1994). The activities of superoxide dismutase, catalase and glutathione peroxidase were higher (by 19, 19 and 20 %, respectively) in liver homogenates of rats fed with the turmeric-containing diet in comparison with the controls. Dietary supplementation of curcumin (2 %, w/v) to male ddY mice for 30 days significantly increased the activities of glutathione peroxidase, glutathione reductase, glucose-6-phosphate dehydrogenase and catalase in the liver and in the kidney as compared with corresponding normal diet-fed control (Iqbal et al. 2003b). Concomitantly, curcumin feeding to mice also resulted in a considerable enhancement in the activity of phase II-metabolising enzymes, viz. glutathione S-transferase and quinone reductase, to 1.7 and 1.8 times in the liver and 1.1 and 1.3 times in the kidney, respectively, as compared with corresponding normal diet-fed control. In general, the increase in activities of antioxidant and phase II-metabolising enzymes was more pronounced in the liver as compared to the kidney.

Cadmium-induced lipid peroxidation was significantly lowered by curcumin pretreatment and was accompanied by significant increase of glutathione (GSH) level in both Cd-treated and Cd plus curcumin-treated group (Eybl et al. 2004). In mice, the Cd-induced lipid peroxidation was abolished by curcumin treatment. Curcumin treatment did not change cadmium (Cd) distribution and did not cause systematic alterations in trace element status. Administration of both curcumin and Mn-curcumin prevented the increase of hepatic lipid peroxidation expressed as MDA level, induced by cadmium intoxication, and attenuated the Cd-induced decrease of hepatic GSH level in male mice (Eybl et al. 2006b). A decreased GSH-Px activity was measured in curcumin- and Mn-curcumin alone-treated mice. Neither curcumin nor Mn-curcumin treatment influenced cadmium distribution in the tissues and did not correct the changes in the balance of essential elements caused by Cd treatment. The treatment with Mn-curcumin increased the Fe and Mn content in the kidneys

of both control and Cd-treated mice and Fe and Cu content in the brain of control mice. In another study, curcumin, resveratrol and melatonin oral pretreatment completely prevented the Cd-induced lipid peroxidation and Cd-induced inhibition of GPx hepatic activity in mice (Eybl et al. 2006a). The decrease in hepatic reduced glutathione (GSH) level was not prevented by curcumin, resveratrol or melatonin pretreatment. In mice treated with antioxidants alone, the level of LP, GSH, GPx or CAT was not different from control levels. The pretreatment with antioxidants did not affect cadmium distribution in the tissues of Cd-intoxicated mice.

Pretreatment of mice inhibited oxidative stress and the activity of ornithine decarboxylase (ODC) as well as histopathological changes induced by ferric nitrilotriacetate (Fe-NTA) in the kidney (Okazaki et al. 2005). Curcumin pretreatment almost completely prevented kidney biomolecules from oxidative damage and protected the tissue against observed histopathological alterations. In further studies, they found that prophylactic feeding of animals with 1.0 % curcumin in diet for 4 weeks completely abolished the formation of (1) 4-hydroxy-2-nonenal (HNE)-modified protein adducts, (2) 8-hydroxy-2'-deoxyguanosine (8-OHdG) and (3) protein reactive carbonyl in the kidneys of ferric nitrilotriacetate (Fe-NTA)-treated animals (Iqbal et al. 2009). The results suggested that curcumin may afford substantial protection against oxidative damage caused by Fe-NTA, and these protective effects may be mediated via its antioxidant properties.

Turmeric oil was found to have in-vitro antioxidant activity, and IC₅₀ values for scavenging superoxides, hydroxyl radicals and lipid peroxidation were 135 µg/ml, 200 µg/ml and 400 µg/ml, respectively (Liju et al. 2011). The ferric-reducing activity for 50 µg of turmeric essential oil was found to be 5 mM. Intraperitoneal administration of oil was found to inhibit PMA-induced superoxide radicals elicited by macrophages. Oral administration of turmeric oil for 1 month to mice significantly increased superoxide dismutase, glutathione and glutathione reductase enzyme levels in blood and glutathione S-transferase and superoxide dismutase enzymes in the liver.

BGS-Haridrin glycoprotein from turmeric scavenged hydroxyl, DPPH radicals and superoxide radicals of about 76–82 % and inhibited lipid peroxidation about 78 % at a maximum dosage of 0.9-nM concentration when compared to BHA, curcumin (400 μ M) and α -tocopherol (400 μ M) (Ramadas and Srinivas 2011). BGS-Haridrin effectively protected H₂O₂ (100 μ M)-induced cell death in human peripheral lymphocytes. Further BGS-Haridrin prevented H₂O₂ (1 mM) that caused calf thymus DNA damage. Studies found that administration of *C. longa* and *Garcinia kola* (kolaviron) ameliorated the adverse biochemical effects (decreased hepatic catalase, superoxide dismutase, glutathione S-transferase, reduced glutathione (GSH) and increased levels of serum urea, creatine kinase and alanine transferase) of NG-nitro-l-arginine methyl-ester (*L*-NAME) in rats (Adaramoye et al. 2012). Both extracts also significantly inhibited lipid peroxidation induction by *L*-NAME and augmented tissues antioxidant indices.

Anticancer Activity

In-Vitro Studies

Curcumin had been demonstrated to interact with multiple molecules and signal pathways, making it a potential adjuvant anticancer agent to chemotherapy (Ye et al. 2012). Apart from transcription factors and apoptosis, other mechanisms such as epidermal growth factor receptor (EGFR), microRNAs (miRNA), autophagy and cancer stem cell-based therapy might be promising mechanisms and targets of curcumin in the therapeutic strategy of lung cancers. Curcumin was reported to bind to soya lipoxygenase in a non-competitive manner in the central cavity of the complex that may impact on the development, metastasis and progression of cancers (Skrzypczak-Jankun et al. 2000, 2003). By the use of X-ray diffraction and mass spectrometry, they found an unoccupied electron mass that appeared to be an unusual degradation product of curcumin (4-hydroxyperoxy-2-methoxyphenol) located near the soybean L3 catalytic site. Sandur et al. (2007) demonstrated that different analogues of curcumin such as

demethoxycurcumin (DMC), bisdemethoxycurcumin (BDMC), tetrahydrocurcumin (THC) and turmerones present in turmeric exhibit variable anti-inflammatory and antiproliferative activities, which do not correlate with their ability to modulate the reactive oxygen species (ROS) status. The relative potency for suppression of tumour necrosis factor (TNF)-induced nuclear factor-kappaB (NF-kappaB) activation was Cur > DMC > BDMC. THC was inactive for suppression of the transcription factor. Turmerones also failed to inhibit TNF-induced NF-kappaB activation. Whether suppression of NF-kappaB or cell proliferation, no relationship of any of the curcuminoid was found with reactive oxygen species (ROS) production. Curcumin was shown to be a strong inhibitor of nuclear factor-kappaB (NF- κ B) activity, and its inhibitory effect on NF- κ B-related pathways often led to cellular apoptotic response in cancer cells (Troselj and Kujundzic 2014).

Studies by Griesser et al. (2011) reported that non-enzymatic degradation of curcumin had been described to yield vanillin, ferulic acid and feruloylmethane through cleavage of the heptadienone chain connecting the phenolic rings, and they provided evidence for autooxidative cyclisation of the heptadienone moiety as a major pathway of degradation. Autooxidative transformation of curcumin was pH dependent with the highest rate at pH 8 and associated with stoichiometric uptake of O² and also catalysed by recombinant cyclooxygenase yielding a quinone methide and the final dioxygenated bicyclopentadione product. When curcumin was added to RAW264.7 cells, the bicyclopentadione was increased 1.8-fold in cells activated by LPS; vanillin and other putative cleavage products were negligible. Oxidation to a reactive quinone methide is the mechanistic basis of many phenolic anticancer drugs. Curcumin and its final dioxygenated bicyclopentadione product, as well as vanillin, ferulic acid and feruloylmethane, had no effect on topoisomerase DNA cleavage, but its oxidative intermediate metabolites, quinone-based compounds (such as quinone methide), were found to act as redox-dependent (as opposed to interfacial) topoisomerase II poisons (inhibitors) (Ketrn et al.

2013). Also, under conditions that promote oxidation, the dietary spice turmeric enhanced topoisomerase II-mediated DNA cleavage. Topoisomerase inhibitors can function as chemopreventive anticancer and antibacterial agents.

Curcumin, curcumin II (monodemethoxycurcumin) and curcumin III (bisdemethoxycurcumin) from *Curcuma longa* showed cytotoxic activity against leukaemia, CNS, melanoma and colon, renal and breast cancer cell lines (Ramsewak et al. 2000). Curcumin has both a Michael acceptor and a Michael donor unit, its analogues dibenzoylmethane (DBM, a component of licorice) and dibenzoylpropane (DBP) have a Michael donor but not a Michael acceptor unit, and the analogue dibenzylideneacetone (DBA) has a Michael acceptor unit (Anand et al. 2011). The authors found that although curcumin and its analogues exhibited activities to suppress inflammatory pathways (TNF-induced NF- κ B activation of NF- κ B-regulated gene products), and cancer cellular proliferation, a lack of Michael acceptor units in DBM and DBP could reduce their activities. For suppression of TNF-induced expression of NF- κ B-regulated gene products such as COX-2 (inflammation marker), cyclin D1 (proliferation marker) and VEGF (angiogenesis marker), DBA and curcumin were more active than DBM. Similarly for suppression of proliferation of leukaemia (KBM-5), T-cell leukaemia (Jurkat), prostate cancer (DU145) and breast (MDA-MB-231) cancer cells, curcumin and DBA were most active and DBP was least active. Of 22 receptors with critical virulent functions in various cancer, curcumin showed the best binding efficiencies, and it exhibited best results towards epidermal growth factor (EGF), virulent protein of gastric cancer, glutathione S-transferase Pi gene (GST-PI), virulent protein for prostate cancer, platelet-derived growth factor α (PDGFA) and virulent protein for mesothelioma and glioma compared with their natural ligands (Mahajanakatti et al. 2014). The calculated binding energies of their docked conformations with curcumin were found to be -7.59 kcal/mol, -7.98 kcal/mol and -7.93 kcal/mol, respectively. It was found that curcumin had better interacting properties towards these cancer targets than their normal ligands and conventional antitumour agents. Their data

provided insight for designing of curcumin as novel inhibitors against various types of cancer.

Curcumin inhibited telomerase activity by downregulating hTERT expression in MCF-7 breast cancer cells (Ramachandran et al. 2002). In MCF-7 cells, telomerase activity decreased with increasing concentrations of curcumin, inhibiting about 93.4 % activity at 100- μ M concentration. Curcumin was found to induce apoptosis of Ehrlich's ascite carcinoma cells by the upregulation of the proto-oncoprotein Bax, release of cytochrome c from the mitochondria and activation of caspase-3 (Pal et al. 2001). The cytolytic effect of the turmeric oil obtained by hydrodistillation extract started at 25 μ g/mL for the breast (MCF-7) and ovary (OVACAR); for the breast expressing the multidrug resistance phenotype (NCIADR), the cytolytic effect started at an extract concentration of 250 μ g/mL (Braga et al. 2003). Therefore, the turmeric volatile oil antitumour activity was lower than that of the supercritical fluid extraction extracts; nonetheless, it was selective. Squires et al. (2003) observed that curcumin inhibited proliferation ($IC_{50} = 1-5 \mu$ M), invasiveness and progression through S/G2/M phases of the cell cycle in the nontumorigenic HBL100 and tumorigenic MDA-MB-468 human breast cell lines, but exerted much more pronounced apoptosis in the tumour line. Their results suggested that while curcumin had several different molecular targets within the p38 mitogen-activated protein kinase (MAPK) and PI3K/PKB signalling pathways that could contribute to inhibition of proliferation and induction of apoptosis, inhibition of basal activity of Akt/protein kinase B (PKB), but not extracellular signal-regulated kinase (ERK), may facilitate apoptosis in the tumour cell line. Lee et al. (2005) found that curcumin inhibited tumour promoter 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced upregulation of cyclooxygenase-2 and matrix metalloproteinase-9 by blocking ERK1/2 phosphorylation and NF-kappaB transcriptional activity in MCF10A human breast epithelial cells which may contribute to its chemopreventive potential. Demethoxycurcumin (DMC), a turmeric curcuminoid, inhibited adhesion, migration and invasion of MDA-MB-231 human breast cancer cells via

downregulation of ECM degradation-associated proteins including matrix metalloproteinase-9 (MMP-9), membrane type I matrix metalloproteinase (MT1-MMP), urokinase plasminogen activator (uPA) and uPA receptor (uPAR), up-regulation of the level of uPA inhibitor (PAI-1) and inhibition of DNA-binding activity of nuclear factor-kappaB (NF-kappaB) (Yodkeeree et al. 2010). Studies showed that the curcuminoids (curcumin, demethoxycurcumin and bisdemethoxycurcumin) and α -turmerone significantly inhibited proliferation of cancer cells in dose-dependent manner (Yue et al. 2010b). The IC₅₀ values of these compounds in cancer cells ranged from 11.0 to 41.8 μ g/ml. α -Turmerone induced MDA-MB-231 cells to undergo apoptosis and DNA fragmentation assay. The caspase cascade was activated as shown by a significant decrease of procaspase-3, procaspase-8 and procaspase-9 in α -turmerone-treated cells. Both α -turmerone and aromatic turmerone showed stimulatory effects on human peripheral blood mononuclear cells (PBMC) proliferation and cytokine production. Studies by Boonrao et al. (2010) showed that curcumin (Cur), demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC) exerted inhibitory effects on matrix metalloproteinase-3 secretion in human invasive MDA-MB-231 breast carcinoma cells. Treatment of the cells with Cur, DMC and BDMC exhibited a significant inhibition of cell invasion and motility with DMC and BDMC being more potent. Oral administration of turmeric showed anticancer activity against the MNU (methylnitrosourea)-induced mammary tumours in a dose-dependent manner, and it was more in pre-induction treatment than in post-induction treatment groups (Annapurna et al. 2011). Topical application of turmeric was found to be more effective in pre-induction treatment, and topical treatment was more effective when compared to oral treatment.

The results of studies by Park et al. (2012c) suggested that *ar*-turmerone suppressed the 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced upregulation of MMP-9 and COX-2 expression by blocking NF- κ B, PI3K/Akt and ERK1/2 signalling in human breast cancer cells (Park et al. 2012c). Further, *ar*-turmerone significantly inhibited TPA-induced

invasion, migration and colony formation in human breast cancer cells. The results of studies by Shieh et al. (2013) revealed that demethoxycurcumin (DMC) demonstrated the most potent cytotoxic effects on breast cancer MDA-MB-231 cells. Compared with oestrogen receptor (ER)-positive or HER2-overexpressing breast cancer cells, DMC demonstrated the most efficient cytotoxic effects on triple-negative breast cancer (TNBC) cells. DMC was shown to inhibit breast cancer cells through a spectrum of anti-TNBC activities including activation of AMPK and targeting multiple AMPK downstream pathways in TNBC cells, suppressing LPS-induced IL-6 production and activation of epidermal growth factor receptor. MTT assay demonstrated that β -cyclodextrin–curcumin complex enhanced curcumin delivery in T47D breast cancer cells (Kazemi-Lomedasht et al. 2013). Also the cyclodextrin–curcumin complex was found to be more effective than free curcumin in the inhibition of telomerase expression. Bisdemethoxycurcumin suppressed MCF-7 cells proliferation by inducing ROS accumulation and modulating senescence-related p53/p21 and p16/Rb pathways (Li et al. 2013c). Curcumin treatment of antioestrogen-resistant breast cancer cell lines MCF-7/LCC2 and MCF-7/LCC9 exerted antiproliferative and pro-apoptotic activities and induced cell cycle arrest at G2/M phase (Jiang et al. 2013d). The combination of curcumin and tamoxifen resulted in a synergistic survival inhibition in MCF-7/LCC2 and MCF-7/LCC9 cells. It was found that curcumin targeted multiple signals involved in growth maintenance and resistance acquisition in endocrine-resistant cells. Terpecurcumins D, F and G and two known analogues 10 and 11, from turmeric rhizomes, showed higher cytotoxic activities ($IC_{50} = 10.3\text{--}19.4\text{ }\mu\text{M}$) than curcumin ($IC_{50} = 31.3\text{--}49.2\text{ }\mu\text{M}$) against human cancer cell lines (breast cancer MDA-MB-231, A549 (lung cancer) and HepG2 (hepatocarcinoma cell) (Lin et al. 2012). Terpecurcumins from *C. longa* rhizomes showed more potent cytotoxic activities than curcumin and *ar*-turmerone or β -turmerone (Lin et al. 2013). Among them, terpecurcumin Q exhibited IC_{50} of $3.9\text{ }\mu\text{M}$ against MCF-7 human breast cancer cells, and mitochondria-mediated apoptosis played an

important role in the overall growth inhibition. Wright et al. (2013) reported that three curcuminoid-containing turmeric extracts differing with respect to the inclusion of additional naturally occurring chemicals (essential oils and/or polar compounds) were equipotent in inhibiting human breast cancer MDA-MB-231 cell growth ($IC_{50} = 10\text{--}16\text{ }\mu\text{g/mL}$) and secretion of osteolytic parathyroid hormone-related protein (PTHrP) ($IC_{50} = 2\text{--}3\text{ }\mu\text{g/mL}$). While curcumin and bisdemethoxycurcumin were equipotent to each other and to the naturally occurring curcuminoid mixture ($IC_{50} = 58\text{ }\mu\text{M}$), demethoxycurcumin did not have any effect on cell growth. However, each of the individual curcuminoids inhibited PTHrP secretion ($IC_{50} = 22\text{--}31\text{ }\mu\text{M}$) to the same degree as the curcuminoid mixture ($IC_{50} = 16\text{ }\mu\text{M}$). Curcumin could suppress expression of pro-growth and anti-apoptosis molecules; induce inactivation of NF- κ B, Src and Akt/mTOR pathways; and downregulate the key epigenetic modifier EZH2. The treatment of MCF-7/Adriamycin (ADR) multidrug-resistant human breast cancer cells with a combination of germacrone (from turmeric rhizome) and ADR resulted in an increase in cytotoxicity compared with that of ADR alone (Xie et al. 2014a). Germacrone promoted cell apoptosis in a dose-dependent manner, while treatment with germacrone plus ADR enhanced the apoptotic effect synergistically. The combined treatment resulted in a reduction of anti-apoptotic protein expression levels (bcl-2) and enhancement of pro-apoptotic protein expression levels (p53 and Bax) in MCF-7/ADR cells compared with the levels achieved by treatment with ADR alone. Furthermore, germacrone significantly reduced the expression of P-glycoprotein via the inhibition of the multidrug resistance 1 (MDR1) gene promoter. Studies by Thulasiraman et al. (2014) demonstrated that suppression of the FABP5/PPAR β/δ pathway by curcumin sensitised retinoic acid-resistant triple-negative breast cancer cells to retinoic acid-mediated growth suppression. Tetrahydrocurcumin (THC), a major metabolite of curcumin, exhibited significant cell growth inhibition by inducing human breast cancer MCF-7 cells to undergo mitochondrial apoptosis and G2/M arrest (Kang et al. 2014). It

was found that p38 MAPK might mediate THC-induced apoptosis and G2/M arrest.

Curcumin inhibited completely cell survival signal protein B/Akt activation in both human prostate cancer LNCaP and PC-3 cells (Chaudhary and Hruska 2003). Results suggested that one of the mechanisms of curcumin inhibition of prostate cancer may be via inhibition of Akt. Treatment of prostate cancer androgen-sensitive LNCaP and androgen-insensitive PC-3 cell lines with curcumin resulted in cell cycle arrest at G1/S phase and the induction of apoptosis by cyclin-dependent kinase inhibitor p21 (WAF1/CIP1) pathway (Srivastava et al. 2007). Studies by Hung et al. (2012) revealed that demethoxycurcumin (DMC) demonstrated the most efficient cytotoxic effects on prostate cancer PC3 cells. It was shown that DMC exerted antitumour effect via AMPK-induced downregulation of heat shock protein (HSP) and epidermal growth factor receptor (EGFR). At 100 µg/mL concentration, *C. longa* leaf water extract showed inhibition against human prostate tumour DU-145 cell line by 46 %, while the methanolic leaf extract showed little or no inhibition (Liu and Nair 2012). Water and methanolic leaf extracts inhibited the growth of prostate tumour cell line LNCaP by 43 % and 34 %, respectively. Similarly, water and methanolic extracts revealed growth inhibition against pancreatic tumour cell line BxPc-3 by 18 % and 36 %, respectively. The methanolic extracts of *C. longa* afforded nine compounds which showed weak inhibition against the human tumour cell lines tested except coronadiene which inhibited the proliferation of prostate cell line LNCaP by 36 % at 25 µg/mL. A mixture of isopropyl alcohol, acetone, water, chloroform and methanol extract of *C. longa* showed significant chemopreventive action against PC-3 M prostate cancer cell line (Rao et al. 2012). The ethyl acetate fraction not only inhibited colony-forming ability of PC-3 M cells but also upregulated cell cycle genes p57(kip2) and Rad9 and further reduced the migration and invasive ability of prostate cancer cells. Kurapati et al. (2012) found that the combined effects of *C. longa* and *Z. officinale* were much greater than their individual effects in inhibiting growth of PC-3 M prostate cancer cell line, suggesting the role of multiple components

and their synergistic mode of actions to elicit stronger beneficial effects.

The data from in-vitro studies showed that curcumin induced cell death in human and rodent transformed as well as normal cells that could be classified as apoptosis-like, and only in HL-60 (human promyelocytic leukaemia) cells could it be deemed as classical apoptosis (Bielak-Zmijewska et al. 2000). Curcumin inhibited the growth of human acute myelogenous leukaemia HL-60 cells (neo) in a dose- and time-dependent manner, whereas Bcl-2- and Bcl-xl-transfected cells were relatively resistant (Anto et al. 2002). The study found that curcumin induced apoptosis through mitochondrial pathway involving caspase-8, BID cleavage, cytochrome c release and caspase-3 activation. The results also suggested that Bcl-2 and Bcl-xl were critical negative regulators of curcumin-induced apoptosis. Curcumin was found to induce apoptosis in human leukaemia cell line K-562 (Chakraborty et al. 2006; Mukherjee Nee Chakraborty et al. 2007). Curcumin inhibited telomerase activity in a dose- and time-dependent manner, the inhibition being due to suppression of translocation of telomerase reverse transcriptase (TERT), a catalytic subunit, from cytosol to nucleus. Most significantly, the inhibition of telomerase activity by curcumin correlated with several parameters of apoptosis. Aratanechemuge et al. (2002) found that selective induction of apoptosis by *ar*-turmerone was observed in human leukaemia Molt 4B and HL-60 cells in a concentration- and time-dependent manner, but not in human stomach cancer KATO III cells. *ar*-Turmerone exhibited potent cytotoxicity on K562 (human erythromyeloblastoid leukaemia cell line), L1210 (murine leukaemia), U937 (human lymphoma) and RBL-2H3 (basophilic leukaemia cell) cancer cell lines (Ji et al. 2004). The IC₅₀ values of *ar*-turmerone on these cell lines were 20–50 µg/ml. DNA fragmentation, a characteristic of apoptosis, induced *ar*-turmerone in a concentration- and time-dependent manner. Curcuminoid mixture and pure compounds curcumin, demethoxycurcumin and bisdemethoxycurcumin 2–4 demonstrated cytotoxic effects on FLT3-overexpressing EoL-1 leukaemic cell line with IC₅₀ values ranging from 6.5 to 22.5

μM (Tima et al. 2014). A significant decrease in FLT3 protein levels was found after curcuminoid treatment with IC_{20} doses, especially with curcuminoid mixture and curcumin, and both showed activity on cell cycle arrest at the G0/G1 phase and decreased the FLT3 and STAT5A protein levels in a dose-dependent manner.

Turmeric exhibited inhibitory activity towards both sulfo- and glucuronosyl conjugations of 1-naphthol at approximately the same levels ($\text{IC}_{50} = 0.24$ and 0.29 mg/ml, respectively) in Caco-2, a human colon carcinoma cell line (Naguma et al. 2006). Ryu et al. (2008) showed that the natural derivatives of curcumin, namely, demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC) and metabolite tetrahydrocurcumin (THC) attenuated the Wnt/ β -catenin pathway by decreasing the amount of the transcriptional coactivator p300. DMC and BDMC suppressed catenin response transcription (CRT) that was activated by Wnt3a-conditioned medium (Wnt3a-CM) without altering the level of intracellular β -catenin and inhibited the growth of various colon cancer cells, with comparable potency to curcumin. THC also inhibited CRT and cell proliferation, but to a much lesser degree than curcumin, DMC or BDMC. Curcumin exhibited a potent apoptotic effect on HT-29 colon cancer cells at concentrations of $50 \mu\text{mol/L}$ and above (Lee et al. 2009). These apoptotic effects were correlated with the decrease in pAkt and COX-2, as well as the increase in p-AMPK. Cell cycle analysis showed that curcumin induced G(1)-phase arrest. It was found that AMPK was crucial in apoptosis induced by curcumin and that the pAkt–AMPK–COX-2 cascade or AMPK–pAkt–COX-2 pathway was important in cell proliferation and apoptosis in colon cancer cells. Yamakoshi et al. (2010) synthesised a series of novel analogues of 1,5-*bis*(4-hydroxy-3-methoxyphenyl)-penta-(1*E*,4*E*)-1,4-dien-3-one (C_5 -curcumin), a natural analogue of curcumin isolated from turmeric rhizomes, and evaluated for their cytotoxicities against human colon cancer cell line HCT-11. They found that (1) *bis*(arylmethylidene)acetone served as a promising skeleton for eliciting cytotoxicity; (2) the 3-oxo-1,4-pentadiene structure was essential for eliciting

cytotoxicity; and (3) as for the extent of the aromatic substituents, hexasubstituted compounds exhibit strong activities, in which 3,4,5-hexasubstitution resulted in the highest potency.

Curcumin induced apoptosis in human gastric carcinoma AGS cells and colon carcinoma HT-29 cells through mitochondrial dysfunction and endoplasmic reticulum stress (Cao et al. 2013). Curcumin inhibited sulfo-conjugation at lower concentrations ($IC_{50} = 9.7 \mu\text{g/ml}$), but only showed weak inhibition towards glucuronosyl conjugation of 1-naphthol in Caco-2 cells. Further, turmeric was found to strongly inhibit in-vitro phenol sulfotransferase (SULT) activity and demonstrated moderate inhibitory effects against UDP-glucuronosyl transferase (UGT) activity in Caco-2 cells ($IC_{50} = 0.17 \text{ mg/ml}$ and 0.62 mg/ml , respectively). Curcumin also strongly inhibited in-vitro phenol sulfotransferase activity with an IC_{50} of $2.4 \mu\text{g/ml}$. Moreover, and in contrast to the moderate inhibition of UGT activity by turmeric and curcumin, both induced the expression of the UGT1A1 and UGT1A6 genes. Studies by Xue et al. (2014) demonstrated that curcumin induced morphological changes and decreased human gastric adenocarcinoma SGC-7901 cell viability. Apoptosis of SGC-7901 cells triggered by curcumin was mediated through the mitochondrial signalling pathways and activation of capase-3.

In-vitro assays showed potent antiproliferative effects of a synthesised curcumin derivative B63 on colon cancer cells (about twofold more effective than curcumin based on IC_{50}) (Zheng et al. 2014a). B63 treatment also induced significant necrosis, apoptosis and S-phase cell cycle arrest in SW620 colon cancer cells. B63 inhibited tumour growth in-vivo more effectively than curcumin in a mouse xenograft model of SW620 cells. The necrotic and apoptotic effects of B63 were mediated by ROS resulting from endoplasmic reticulum (ER) stress and mitochondrial dysfunction.

Prusty and Das (2005) demonstrated that curcumin (diferuloylmethane) could selectively downregulate human papillomavirus HPV18 transcription as well as the AP-1

binding activity in cervical cancer HeLa cells. Curcumin also reversed the expression dynamics of c-fos and fra-1 in this tumourigenic cell line. Divya and Pillai (2006) found that curcumin was cytotoxic to cervical cancer cells in a concentration-dependent and time-dependent manner. The cytotoxic activity was selectively more in HPV16-and HPV18-infected cells compared to non-HPV-infected cells. Curcumin-induced apoptosis in cervical cancer cells was found to be associated with selective inhibition viral oncogenes E6 and E7 and suppression of NF-kB activation and AP-1 translocation. Curcumin reduced proliferation and induced apoptosis in human papillomavirus-positive cervical cancer HeLa, SiHa and Ca Ski cells (Singh and Singh 2009). This was associated with inhibition of human telomerase reverse transcriptase activity and an increase in caspase-3 and caspase-9 activities and upregulation of pro-apoptotic Bax, AIF, release of cytochrome c and downregulation of anti-apoptotic Bcl-2 and Bcl-XL in HeLa and SiHa. In a subsequent study, curcumin counteracted the proliferative effect of oestradiol and induced apoptosis in HPV-positive and HPV-negative cervical cancer cell lines in HeLa, SiHa, CaSki and C33A cells (Singh and Singh 2011). Maher et al. (2011) showed that curcumin suppressed cervical cancer cell growth by altering human papillomavirus (HPV)-associated molecular pathways. It suppressed human papillomavirus oncoproteins; restored p53, Rb and PTPN13 proteins; and inhibited benzo[a]pyrene-induced upregulation of HPV E7. Nine components of turmeric essential oil were identified to have significant cytotoxicity and antitumour effect on HeLa cell line: *ar*-turmerone, *β*-turmerone, zingiberene, *β*-elemene, *α*-curcumene, *α*-turmerone, germacrone and *β*-sesquiphellandrene (Jiang et al. 2012a). Similarly they reported 13 turmeric curcuminoids (Jiang et al. 2012b, 2013b) and 19 turmeric constituents (Jiang et al. 2013c) with similar antitumour activities against HeLa cell line. The essential oil from *Curcuma longa* and its constituents (Jiang et al. 2013b) and six volatile constituents (three terpenes and three ketones) and five non-volatile constituents (five curcuminoids) from turmeric alcohol extract (Jiang et al. 2014b) exhibited marked cytotoxic effects on HeLa cells. The study by Zhao et al.

(2014a) found that curcumin exerted its cytotoxic effects against SKOV3 ovarian cancer cells largely through upregulation of miR-9 and subsequent modulation of Akt/FOXO1 axis. Curcumin caused a significant and dose-dependent increase of miR-9 expression in SKOV3 cells, while significantly impeding cell proliferation and stimulating apoptosis. Curcumin and its different formulations had been shown to display multifunctional mechanisms of anticancer activity, not only in platinum-resistant primary epithelial ovarian cancer but also in multidrug-resistant cancer cell/xenograft models (Terlikowska et al. 2014b). Curcumin administered together with platinum–taxane chemotherapeutics had been reported to demonstrate synergistic effects, sensitise resistant cells to drugs and decrease their biologically effective doses. Curcumin demonstrated the greatest potential for inhibiting cell growth, cell cycle progression and FLT3 expression in EoL-1 cells. Recent studies by Kumar et al. (2014) showed that encapsulating curcumin in hydrophilic polymeric core such as poly(2-hydroxyethyl methacrylate) [PHEMA] nanoparticles improved its efficacy against ovarian cancer cells (SKOV-3) in-vitro. The C-PHEMA-NPs had better tumour cell regression activity than free curcumin, exerting significant reduction in G0/G1 cells followed by apoptosis. Toxicity of PHEMA nanoparticles was studied in zebrafish embryo model, and results revealed the material to be highly biocompatible. Lewinska et al. (2014) showed that curcumin at low 1- μ M range may be effective against human cervical cancer (HeLa) cells. Curcumin caused a decrease in the cell number and viability and increase in apoptotic events and superoxide level. It induced a decrease in AgNOR protein pools, which may be mediated by global DNA hypermethylation.

Turmeric volatile oil inhibited the growth and proliferation of human lung adenocarcinoma A549 cells and induced their apoptosis (Wang and Yang 2005). The antitumour of the curcuminoid mixture used as standard was not specific and started at 25 μ g/mL, except for the lung cell (NCI.460), for which the cytolytic effect was observed at this concentration (Braga et al. 2003). After treatment of human A549 lung adenocarcinoma cells with curcumin, percentage of apoptotic

cells increased dose- and time-dependently, and morphology observation revealed typical apoptotic features (Chen et al. 2010e). The data further indicated that the expression of Bax proteins in A549 cells was increased in a dose-dependent manner, whereas the expression of Bcl-2 was significantly decreased; thus, the ratio of Bax/Bcl-2 was increased. The apoptotic process was accompanied by the change of mitochondrial function and structure which led to the release of the cytochrome c and activation of caspase-9 and caspase-3. Additionally, curcumin also induced a dose-dependent cleavage of poly(ADP-ribose) polymerase (PARP). Studies showed a new 4-arylidene curcumin analogue T63 to be a potent antitumour agent, which could induce cell cycle arrest and apoptosis of lung cancer cells (Liu et al. 2014a).

In cultured human cancer cells, curcumin caused cell death by interfering with mitosis and leading to fragmented nuclei and disrupted microtubules, a process named mitotic catastrophe (Dempe et al. 2008). In Ishikawa and HepG2 cells, curcumin was metabolised to hexahydrocurcumin and small amounts of octahydrocurcumin, whereas the only metabolism in HT29 cells was the formation of curcumin glucuronide. Despite their different metabolism, all three cell systems responded to curcumin with arrest in G2/M phase and mitotic catastrophe. Curcumin inhibited proliferation and induced apoptosis of human hepatocellular carcinoma cells (Xu et al. 2013a). The mechanism involved curcumin's interruption of the Wnt signalling pathway by decreasing β -catenin activity which in turn suppressed the expression of β -catenin target genes (c-myc, VEGF and cyclin D1). Studies showed that curcumin significantly decreased hypoxia-induced hypoxia-inducible factor-1 α (HIF-1 α) protein level in HepG2 hepatocellular carcinoma cells (Duan et al. 2014). Furthermore, cell proliferation, migration and invasiveness, as well as epithelial–mesenchymal transition (EMT) changes associated with HIF-1 α accumulation generated by a hypoxic microenvironment, were eliminated by curcumin. The data indicated that curcumin may be a viable anticancer agent in the treatment of hepatocellular carcinoma. *ar*-Turmerone, volatile from turmeric oil, exhibited significant antiproliferative activity, with 50 % inhibitory concentrations

of 64.8, 102.5 and 122.2 $\mu\text{g/mL}$ against human hepatocellular carcinoma cell lines HepG2, Huh-7 and Hep3B cells, respectively (Cheng et al. 2012). The results suggested that *ar-turmerone*-induced apoptosis in HepG2 cells was through reactive oxygen species (ROS)-mediated activation of extracellular signal-related kinase (ERK) and c-Jun N-terminal kinase (JNK) and triggered both intrinsic and extrinsic caspase activation, leading to apoptosis. Curcumol inhibited the proliferation of human hepatocarcinoma HepG2 cells in-vitro and induce G1 arrest of cell cycle through mechanisms activating p53 and pRB pathways that involve genes of cyclin A1, CDK2, CDK8, p21WAF1 and p27KIP1 (Huang et al. 2013b).

Curcumin caused dose-dependent apoptosis and DNA fragmentation of Caki cells (human renal carcinoma), by inactivating the Akt-related cell survival pathway and release of cytochrome c, providing a new mechanism for curcumin-induced cytotoxicity (Woo et al. 2003). Curcumin significantly enhanced dual PI3K/Akt and mTOR inhibitor NVP-BEZ235-induced apoptosis in human renal carcinoma Caki cells through downregulation of p53-dependent Bcl-2 expression and inhibition of Mcl-1 protein stability (Seo et al. 2014).

Cytotoxicity of curcumin in melanoma cells was dose dependent and the EC_{50} for 24-h incubation was 69 μM (Oelkrug et al. 2014). Saturation was reached at 30 μM for a 48-h incubation. The EC_{50} for 24-h incubation with degraded curcumin solution was 116 μM and that for 48 h was 94 μM . Curcumin induced a strong increase in caspase-3/7 activity at 30–40 μM . It was also demonstrated that sub-toxic doses of curcumin counteracted atrophy in C2C12 muscle cells. The findings indicated not only the positive effects of curcumin on melanoma cells in-vitro but also that curcumin was able to considerably trigger anti-cachectic effects in-vitro. Jiang et al. (2014a) demonstrated that curcumin could induce apoptosis and inhibit proliferation in melanoma cells through mitochondrial pathway and caspase-9 and caspase-3 activation.

The antiproliferative activity of curcumin had been attributed to its ability to induce apoptosis which was found to be mediated through the impairment of the ubiquitin-proteasome system (Jana et al. 2004). Exposure of curcumin to the mouse neuro 2a cells caused a dose-dependent decrease in proteasome activity and an increase in ubiquitinated proteins. Like other proteasome inhibitors, curcumin targets proliferative cells more efficiently than differentiated cells and induces apoptosis via mitochondrial pathways. Addition of curcumin to neuro 2a cells induced a rapid decrease in mitochondrial membrane potential and the release of cytochrome c into cytosol, followed by activation of caspase-9 and caspase-3. Curcumin exerted antiproliferative effect in human LAN5 NB neuroblastoma cells (Picone et al. 2014). Curcumin treatment caused a rapid increase in reactive oxygen species and a decrease in the mitochondrial membrane potential events leading to apoptosis activation. Further, curcumin induced decrease in heat shock protein (Hsp) 60 and hexokinase II mitochondrial protein levels and increase in the pro-apoptotic protein bcl-2-associated death promoter (BAD). They also demonstrated that curcumin modulated antitumour activity through modulation of phosphatase and tensin homologue deleted on chromosome 10 and consequential inhibition of the survival Akt cell-signalling pathway.

Curcumin (diferuloylmethane) downregulated the constitutive activation of nuclear factor-kappaB and IkappaBalpha kinase in human multiple myeloma cells, leading to suppression of proliferation and induction of apoptosis (Bharti et al. 2003). In-vitro studies demonstrated that MG-63 osteosarcoma cells were much more sensitive in terms of cytotoxicity to curcumin, while the healthy human osteoblasts exhibited a higher healthy viability after 24 h of curcumin treatment (Chang et al. 2014). The study showed that at the right concentrations (5–25 μ M), curcumin, along with a proper nanoparticle drug delivery carrier, may selectively kill bone cancer cells over healthy bone cells. Treatment with tetrahydrocurcumin (THC), an active metabolite of curcumin, reduced highly metastatic HT1080 human fibrosarcoma cell invasion and migration in a dose-dependent manner (Yodkeeree et al. 2008). The inhibition of

cancer cell invasion was associated with the downregulation of extracellular matrix (ECM) degradation enzymes, matrix metalloproteinase (MMP)-2, MMP-9 and urokinase plasminogen activator (uPA) secretion and the inhibition of cell adhesion to ECM proteins. The results of in-vitro studies indicated that the differential potency for inhibition of human fibrosarcoma cell invasion was bisdemethoxycurcumin (BDMC) > or = demethoxycurcumin (DMC) > curcumin, whereas cell migration was not affected (Yodkeeree et al. 2009). All three differentially inhibited cancer cell invasion through the downregulation of matrix metalloproteinases MMP-2 and MMP-9 and urokinase plasminogen activator. The data demonstrated that DMC and BDMC showed higher antimetastasis potency than curcumin by the differentially downregulation of extracellular matrix degradation enzymes.

Sikora et al. (1997) found that curcumin (50 μ M) inhibited proliferation of rat thymocytes stimulated with concanavalin A (Con A) as well as that of human Jurkat lymphoblastoid cells in the logarithmic growth phase. The pigment also inhibited apoptosis in dexamethasone-treated rat thymocytes and in UV-irradiated Jurkat cells. The inhibition of apoptosis by curcumin in rat thymocytes was accompanied by partial suppression of AP-1 activity. Complete suppression of AP-1 activity was observed in Con A-treated, proliferating thymocytes. Studies by Piwocka et al. (1999) showed that 50 μ M curcumin by itself induced cell death in Jurkat cells, but its symptoms differ from those observed after a short ultraviolet (UV) irradiation. Curcumin-treated Jurkat cells exhibited DNA splitting into high-, but not low-, molecular-weight fragments. The apoptosis-like pathway was independent of mitochondria and caspases. In human Jurkat cells (cell line used for studying T-cell leukaemia), 50- μ mol/L curcumin severely lowered cell survival and induced initial stage of chromatin condensation (Sikora et al. 2006). It also induced caspase-3-dependent apoptotic pathway but inhibits DNA fragmentation factor 40/caspase-activated DNase endonuclease in human Jurkat cells. Studies by Shidodia et al. (2005) indicated that curcumin inhibited the constitutive NF-kappaB and IKK leading to suppression of expression of NF-kappaB-regulated gene products that resulted in the suppression of proliferation, cell

cycle arrest and induction of apoptosis in human mantle cell lymphoma (MCL), an aggressive B-cell non-Hodgkin's lymphoma. *ar*-Turmerone treatment inhibited human lymphoma U937 cell viability in a concentration-dependent manner, with inhibition exceeding 84 % (Lee 2009). The apoptotic effect of *ar*-turmerone on U937 cell was associated with the induction of Bax and p53 proteins, rather than Bcl-2 and p21.

Studies by Aggarwal et al. (2004) found curcumin to be a potent inhibitor of cell proliferation and an inducer of apoptosis in head and neck squamous cell carcinoma through suppression of IkappaBalpa kinase (IKK)-mediated nuclear factor NF-kappaB activation and of NF-kappaB-regulated gene expression. They also reported that curcumin downregulated expression of cell proliferation and anti-apoptotic and metastatic gene products through suppression of IkappaBalpa kinase and Akt activation (Aggarwal et al. 2006b).

In-Vivo Studies

Animal studies showed that dietary curcumin inhibited the number of papillomas and squamous cell carcinomas of the forestomach as well as the number of adenomas and adenocarcinomas of the duodenum and colon (Huang et al. 1994). Feeding 0.5–2.0 % commercial-grade curcumin in the diet decreased the number of benzo(a)pyrene-induced forestomach tumours per mouse by 51–53 % when administered during the initiation period and 47–67 % when administered during the post-initiation period. Feeding 0.5–2.0 % commercial-grade curcumin in the diet decreased the number of *N*-ethyl-*N*^c-nitro-*N*-nitrosoguanidine-induced duodenal tumours per mouse by 47–77 % when administered during the post-initiation period. Administration of 0.5–4.0 % commercial-grade curcumin in the diet both during the initiation and post-initiation periods decreased the number of azoxymethane (AOM)-induced colon tumours per mouse by 51–62 %. Administration of 2 % commercial-grade curcumin in the diet inhibited the number of AOM-induced colon tumours per mouse by 66 % when fed during the initiation

period and 25 % when fed during the post-initiation period. The ability of commercial-grade curcumin to inhibit AOM-induced colon tumorigenesis was comparable to that of pure curcumin (purity greater than 98 %). In another study, they found that topical application of commercial-grade curcumin, pure curcumin or demethoxycurcumin had an equally potent inhibitory effect on 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced increases in ornithine decarboxylase activity and TPA-induced tumour promotion in 7,12-dimethylbenz[*a*]anthracene-initiated mouse skin (Huang et al. 1995). Also, commercial-grade curcumin, pure curcumin, demethoxycurcumin and bisdemethoxycurcumin had about the same potent inhibitory effect on TPA-induced inflammation of mouse ears, as well as TPA-induced transformation of cultured JB6 (P+) cells. Tetrahydrocurcumin was less active.

Results of in-vivo studies suggested that the induction of hepatic enzymes glutathione S-transferase (GST), rGST 8-8 and glutathione peroxidase may be involved in the detoxification of the electrophilic products of lipid peroxidation in the rat's liver and may contribute to the anti-inflammatory and anticancer activities of curcumin (Piper et al. 1998). Dietary curcumin (commercial grade) inhibited B[a]P-induced forestomach carcinogenesis, *N*-ethyl-*N'*-nitro-*N*-nitrosoguanidine (ENNG)-induced duodenal carcinogenesis and azoxymethane (AOM)-induced colon carcinogenesis, but had little or no effect on 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)-induced lung carcinogenesis and 7,12-dimethylbenz[*a*]anthracene (DMBA)-induced breast carcinogenesis in mice (Huang et al. 1997). Administration of 0.2 % curcumin during both the initiation and post-initiation periods significantly inhibited azoxymethane (AOM)-induced colon tumorigenesis in rats (Kawamori et al. 1999). In addition, administration of 0.2 % and of 0.6 % of the synthetic curcumin in the diet during the promotion/progression stage significantly and dose-dependently suppressed the incidence and multiplicity of noninvasive adenocarcinomas and also strongly inhibited the multiplicity of invasive adenocarcinomas of the colon. Administration of curcumin to the rats during the initiation and post-initiation stages and throughout the promotion/progression stage increased

apoptosis in the colon tumours as compared to colon tumours in the groups receiving azoxymethane (AOM) and the control diet. Systemic administration of curcumin [1,7-*bis*(4-hydroxy-3-methoxyphenyl)1,6-heptadiene-3,5-dione] (20 µg/kg body weight) for 6 consecutive days to rats bearing the highly cachectic Yoshida AH-130 ascites hepatoma resulted in an important inhibition of tumour growth (31 % of total cell number) (Busquets et al. 2001). Both the weight and protein content of the gastrocnemius muscle significantly decreased as a result of tumour growth, and curcumin was unable to reverse this tendency. It was concluded that curcumin, in spite of having clear antitumoural effects, had little potential as an anti-cachectic drug in the tumour model used in the study.

The administration of dietary curcumin significantly reduced the incidence (28.0 %) of diethylstilbestrol (DES)-induced mammary tumours initiated with γ -irradiation in rats (Inano et al. 1999). Multiplicity and Iball's index of mammary tumours were also decreased by curcumin. Rats fed with the curcumin diet showed a reduced incidence of the development of both mammary adenocarcinoma and ER(+)PgR(+) tumours in comparison with the control group. On long-term treatment with curcumin, body weight and ovarian weight were reduced, but liver weight was increased. Compared with the control rats, the curcumin-fed rats showed a significant reduction in serum prolactin, whereas oestradiol-17 β and progesterone concentrations were not significantly different between the two groups. Curcumin did not have any effect on the concentration of free cholesterol, cholesterol ester and triglyceride. Feeding of the curcumin diet caused a significant increase in the concentrations of tetrahydrocurcumin, arachidonic acid and eicosapentaenoic acid and a significant decrease in thiobarbituric acid-reactive substance concentration in serum. Further, they found that curcumin did not have any side effects and was an effective agent for chemoprevention acting at the γ -irradiation-induced initiation stage of mammary tumorigenesis (Inano et al. 2000). In a subsequent study, they found that adding curcumin to the diet for 3 days before and/or 2 days after irradiation reduced the elevated 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels by 50–70 % in female rats (Inano and Onoda 2002). The

evaluation of the protective action of curcumin against the long-term effects revealed that curcumin significantly decreased the incidence of mammary and pituitary tumours. However, the experiments on survival revealed that curcumin was not effective when administered for 3 days before and/or 3 days after irradiation (9.6 Gy). They demonstrated that curcumin could be used as an effective radioprotective agent to inhibit acute and chronic effects, but not mortality, after irradiation.

In in-vivo studies, the combination treatment of a prophylactic immune preparation of soluble proteins from B16-R cells with curcumin resulted in substantial inhibition of growth of B16-R melanoma, whereas each treatment by itself showed little effect (Odote et al. 2004). Moreover, animals receiving the combination therapy exhibited an enhancement of their humoral anti-soluble B16-R protein immune response and a significant increase in their median survival time (>82.8 % vs. 48.6 % and 45.7 %, respectively, for the immunised group and the curcumin-treated group). Curcumin was found to be cytotoxic in-vitro for B16-R melanoma cells resistant to doxorubicin either cultivated as monolayers or grown in three-dimensional (3-D) cultures (spheroids).

Curcumin inhibited paclitaxel-activated NF-kappaB in breast cancer cells through inhibition of IkappaBalpha kinase activation and IkappaBalpha phosphorylation and degradation (Aggarwal et al. 2005). Curcumin also suppressed the paclitaxel-induced expression of anti-apoptotic (XIAP, IAP-1, IAP-2, Bcl-2 and Bcl-xL), proliferative (cyclooxygenase 2, c-Myc and cyclin D1) and metastatic proteins (vascular endothelial growth factor, matrix metalloproteinase-9 and intercellular adhesion molecule-1). It also enhanced apoptosis. In a human breast cancer xenograft model, dietary administration of curcumin significantly decreased the incidence of breast cancer metastasis to the lung and suppressed the expression of NF-kappaB, cyclooxygenase 2 and matrix metalloproteinase-9. Studies demonstrated that low-toxic levels of curcumin could efficiently inhibit migration and invasion of 801D lung cancer cells through inhibition of Rac1/PAK1 signalling pathway and MMP-2 and

MMP-9 expression (Chen et al. 2014b). Through xenograft experiments, they confirmed the connection between Rac1 and the growth and metastasis inhibitory effect of curcumin on lung cancer cells in-vivo. Curcumin diet treatment significantly reduced the growth of melanoma tumours in the flank of C57BL/6 mice (Dahmke et al. 2013). Furthermore, the miRNA expression signature in the melanoma tumours was substantially altered by curcumin intake with mmu-miR-205-5p over 100 times higher expressed when compared to controls. In-vivo studies in human osteosarcoma drug-resistant cell line xenograft-nude mice model showed that curcumin displayed the features of sensitising antitumour drugs and inhibiting the proliferation, invasion and metastasis of osteosarcoma multidrug resistance (MDR) cells (Si et al. 2013). Downregulation of P-glycoprotein (P-gp) and inhibition of the function of P-gp efflux pump may contribute to MDR reversion induced by curcumin in-vitro and in-vivo.

Pisano et al. (2010) demonstrated that the new curcumin-related compound α,β -unsaturated ketone D6 was more effective in inhibiting tumour cell growth when compared to curcumin. Clonogenic assay showed a significant dose-dependent reduction in both melanoma and neuroblastoma colony formation only after D6 treatment. D6 caused tumour cell death by triggering apoptosis, similarly to curcumin, but with a stronger and quicker extent. These apoptotic features appeared to be associated with loss of mitochondrial membrane potential and cytochrome c release. In-vivo, using subcutaneous melanoma and orthotopic neuroblastoma xenograft models, D6-treated mice exhibited significantly reduced tumour growth compared to both control- and curcumin-treated ones.

In an animal colitis model, oral administration of *ar*-turmerone significantly suppressed 2 % dextran sulphate sodium (DSS)-induced shortening of the large bowel by 52–58 % (Murakami et al. 2013). At the low dose, *ar*-turmerone markedly suppressed dimethylhydrazine-initiated and DSS-promoted mouse colon adenoma multiplicity by 73 %, while curcumin at both doses suppressed adenocarcinoma multiplicity by 63–69 %. Interestingly, the combination of

curcumin and *ar*-turmerone at both low and high doses abolished tumour formation. The curcuminoid demethoxycurcumin significantly decreased NO secretion by 35–41 % in our inflamed human intestinal Caco-2 cells (Somchit et al. 2014). Decrease in NO production by demethoxycurcumin was concomitant with downregulation of iNOS at mRNA and protein levels compared to pro-inflammatory cytokine cocktail and LPS-treated controls. The findings suggested that demethoxycurcumin may have potential as a therapeutic agent against inflammation-related diseases, especially in the gut.

Administration of curcumin-free aqueous turmeric extract (CFATE) in the diet of Swiss female albino mice 2 weeks before, during and 2 weeks after the last dose of benzo[a]pyrene (B(a)P) treatment significantly suppressed B(a)P-induced tumorigenesis when compared with the group receiving B(a)P and control diet/drinking water (Deshpande et al. 1997). Among different fractions tested (ethanol turmeric extract (ETE), turmeric powder (T)), CFATE appeared to be more powerful as not only did it reduce the tumour multiplicity to the lowest levels but it also significantly reduced the tumour incidence. The results also indicated the potential of turmeric-derived CFATE as a powerful chemopreventive fraction and also demonstrated the efficacy of lower, i.e. 1/25th and/or 1/5th of the reported, chemopreventive doses of T/ETE (essentially curcumins) in inhibiting B(a)P-induced forestomach tumours in mice. *Curcuma* oil inhibited hepatocellular carcinoma cell growth in-vivo and in-vitro (Li et al. 2014b). Pretreatment with *Curcuma* oil significantly attenuated inflammation and oxidative damage by concanavalin A in mice. Treatment with *Curcuma* oil decreased the incidence of hepatocellular carcinoma. *Curcuma* oil inhibited cell growth and induced cell death in Hepa1-6 cells.

Curcuma longa rhizome in the synergistic preparation by Lou Huang enhanced the antitumour effect of *Rhizoma paridis* saponins (RPS) (Liu et al. 2014b). The median lethal dose (LD₅₀) of Lou Huang in mice was 3410.9 mg/kg by oral acute toxicity test. Lou Huang relieved the inhibition of RPS on the

gastric emptying. In-vitro, Lou Huang exerted high inhibition rate of 57.07 % against murine H22 cancer cells, 43.22 % against sarcoma S180 cells, and 46.8 % against Ehrlich ascites carcinoma cells which were higher than that of RPS. *Curcuma longa* rhizome also reduced the toxicity of RPS. The active components of Lou Huang were Rhizoma paridis saponins and turmeric polysaccharides with the inhibition of 58 % and 47 % on H22 and S180 tumour cells.

Clinical Studies

By regulating multiple important cellular signalling pathways including NF- κ B, TRAIL, PI3 K/Akt, JAK/STAT, Notch-1, JNK etc., curcumin had been known to activate cell death signals and induce apoptosis in precancerous or cancer cells without affecting normal cells, thereby inhibiting tumour progression (Chen et al. 2014a). Several phase I and phase II clinical trials indicated curcumin to be quite safe and may exhibit therapeutic efficacy. In a 3-month prospective phase I study of oral administration of curcumin in patients with one of the following five high-risk conditions: (1) recently resected urinary bladder cancer, (2) arsenic Bowen's disease of the skin, (3) uterine cervical intraepithelial neoplasm (CIN), (4) oral leukoplakia and (5) intestinal metaplasia of the stomach), histological improvement of precancerous lesions was seen in 1 out of 2 patients with recently resected bladder cancer, 2 out of 7 patients of oral leukoplakia, 1 out of 6 patients of intestinal metaplasia of the stomach, 1 out of 4 patients with CIN and 2 out of 6 patients with Bowen's disease (Cheng et al. 2001). Also, curcumin was not toxic to humans up to 8000 mg/day when taken orally for 3 months.

Antiviral Activity

Several studies had shown that curcumin possessed antiviral activity. Curcumin was found as a modest inhibitor of the human immunodeficiency virus HIV-1 ($IC_{50} = 100 \mu M$) and HIV-2 ($IC_{50} = 250 \mu M$) proteases (Sui et al. 1993). Simple modifications of the curcumin structure raised the IC_{50} value, but complexes of the central dihydroxy groups of curcumin

with boron lowered the IC₅₀ to a value as low as 6 µM. The boron complexes were also time-dependent inactivators of the HIV proteases. Mazumder et al. (1995) found that curcumin inhibited human immunodeficiency virus type I (HIV-1) integrase with an IC₅₀ of 40 µM for replication. Mazumder et al. (1997) found that two curcumin analogues, dicaffeoylmethane and rosmarinic acid, inhibited both activities of human immunodeficiency virus type I (HIV-1) integrase with IC₅₀ values below 10 µM. Barthelemy et al. (1998) demonstrated that curcumin used at 10–100 nM inhibited Tat transactivation of type I human immunodeficiency virus (HIV1-LTR lacZ) by 70–80 % in HeLa cells. Several curcumin derivatives were synthesised, and results obtained showed that C1, C2 and C3 curcumin derivatives exerted a significant inhibition (70–85 %) of Tat transactivation.

Vajragupta et al. (2005) reported that curcumin bound preferentially to active binding sites of both HIV-I integrase and protease. Si et al. (2007) found that treatment with curcumin significantly reduced Coxsackie virus B3 viral RNA expression, protein synthesis and virus titre and protected cells from virus-induced cytopathic effect and apoptosis. Their results suggested the antiviral effect of curcumin wherein it potently inhibited Coxsackie virus replication through dysregulation of the ubiquitin-proteasome system. Seven Zingiberaceous rhizomes including *Curcuma domestica* were found to possess inhibitory activity towards Epstein–Barr virus early antigen (EBV-EA) activation, induced by 12-*O*-tetradecanoylphorbol-13-acetate (TPA) (Vimala et al. 1999). The rhizome extracts that exhibited EBV activation inhibitory activity had no cytotoxicity effect in Raji cells. *Curcuma longa* ethanolic extract was found to be cytotoxic in the brine shrimp lethality bioassay with LD₅₀ of 33 µg/ml (Khattak et al. 2005). Kim et al. (2009b) found that turmeric aqueous extract repressed hepatitis B virus (HBV) by inhibiting the transcription of HBx gene by suppressing HBV enhancer I and X promoter through enhancing the level of p53 protein.

Dutta et al. (2009) found that curcumin protected neuronal cells from Japanese encephalitis virus-mediated cell death and also inhibited infective viral particle formation by dysregulation of ubiquitin-proteasome system. Kutluay et al. (2008) reported that curcumin treatment inhibited herpes simplex virus (HSV) immediate-early gene expression, possibly by interfering with the recruitment of RNA polymerase II to immediate-early gene promoters. Kim et al. (2010) reported that curcumin inhibited hepatitis C virus replication via suppressing the Akt-SREBP-1 pathway. Rechtman et al. (2010) found that curcumin inhibited hepatitis B virus gene expression and replication. Chen et al. (2010b) found that treatment of cells with curcumin prior to infection markedly reduced the influenza A virus (IAV) yield at subcytotoxic doses, probably mediated by suppression of NF- κ B cellular signalling pathway. Treatment with 30- μ M curcumin reduced the yield of virus by over 90 % in cell culture. The EC₅₀ determined using plaque reduction assays was approximately 0.47 μ M (with a selective index of 92.5). They demonstrated that curcumin had a direct effect on viral particle infectivity that was reflected by the inhibition of haemagglutination receptor binding activity. Chen et al. (2013b) found that curcumin inhibited the infectivity of enveloped viruses including the influenza virus by inhibition of plaque formation but did not affect nonenveloped enterovirus 71. Three curcumin derivatives including curcumin, gallium curcumin and Cu curcumin exhibited antiviral activity against HSV-1 in zero cell line (Zandi et al. 2010). The CC₅₀ values for curcumin, gallium curcumin and Cu curcumin were 484.2 μ g/mL, 255.8 μ g/mL and 326.6 μ g/mL, respectively, and their respective IC₅₀ values 33.0 μ g/mL, 13.9 μ g/mL and 23.1 μ g/mL. The calculated SI values were 14.6, 18.4 and 14.1, respectively. All 13 curcuminoids isolated from *C. longa* exhibited strong inhibitory effects on the neuraminidases from two influenza viral strains, H1N1 and H9N2, as non-competitive inhibitors with IC₅₀ values ranging from 6.18 to 40.17 μ g/ml and 3.77 to 31.82 μ g/ml, respectively (Dao et al. 2012). Compounds 4, 5 and 13 also exhibited significant inhibitory activity against the

neuraminidases from novel influenza H1N1 (WT) and oseltamivir-resistant novel H1N1 (H274Y mutant) expressed in 293 T cells.

Recent structure–activity relationship analytical studies of functional analogues of curcumin, such as tetrahydrocurcumin (THC) and petasiphenol, showed that the presence of the double bonds in the central seven-carbon chain enhanced the curcumin-dependent anti-influenza virus type A (IAV) activity and also that curcumin might interfere with IAV entry by its interaction with the receptor binding region of viral haemagglutination protein (Ou et al. 2013). Germacrone showed antiviral activity against the H1N1 and H3N2 influenza A viruses and the influenza B virus in a dose-dependent manner (Liao et al. 2013b). The viral protein expression, RNA synthesis and the production of infectious progeny viruses were decreased both in Madine–Darby canine kidney (MDCK) cells and A549 cells treated with germacrone. In a time-of-addition study, germacrone was found to exhibit an inhibitory effect on both the attachment/entry step and the early stages of the viral replication cycle. Germacrone also exhibited an effective protection of mice from lethal infection and reduced the virus titres in the lung. The results suggested that germacrone may have the potential to be developed as a therapeutic agent alone or in combination with other agents for the treatment of influenza virus infection

Antimicrobial Activity

Wessler et al. (2005) demonstrated that curcumin inhibited *Neisseria gonorrhoeae*-induced NF-kappaB signalling and release of pro-inflammatory cytokines/chemokines and attenuated adhesion of bacteria to cells in late infection underlining the high potential of curcumin as an antimicrobial compound without cytotoxic side effects. The ethyl acetate extract of *C. longa* demonstrated a higher antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) than the methanol extract or water extract (Kim et al. 2005). In the checkerboard test, the ethyl acetate extract of *C. longa* markedly lowered the MICs of ampicillin and oxacillin against MRSA. In the bacterial invasion assay, MRSA intracellular

invasion was significantly decreased in the presence of 0.125–2 mg/mL of *C. longa* extract compared with the control group. Of the various fractions, the ethyl acetate fraction of turmeric methanol extract showed the highest inhibitory effect on the microorganisms such as *Bacillus subtilis*, *Streptococcus aureus*, *Escherichia coli*, *Listeria monocytogenes* and *Vibrio parahaemolyticus* at 1,000/disc (Choi 2009). The antimicrobial compound isolated from the fractions was identified as 2,3-dihydrobenzofuran. Turmeric extracts and curcumin showed weak inhibitory activity in-vitro against *Staphylococcus aureus*, *Enterococcus faecalis* and *Candida albicans* but showed no activity against *Escherichia coli* and *Pseudomonas aeruginosa* (Çıkrıkçı et al. 2008). They also exhibited weak activity against *Mycobacterium smegmatis*, *M. simiae*, *M. kansasii*, *M. terrae* and *M. szulgai*.

Haukvik et al. (2009) found that aqueous preparations of DMSO, polyethylene glycol (PEG) and the pluronic block copolymer poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) were the most efficient vehicles for curcumin to exert photokilling of both Gram-positive *Enterococcus faecalis* and *Streptococcus intermedius* and Gram-negative *Escherichia coli* bacteria in-vitro. Changes in post-irradiation incubation time, curcumin concentration, irradiation dose and preparation strongly influenced the phototoxic efficiency of curcumin in-vitro. Despite a higher solubility of curcumin with increasing PEG 400 concentrations, the surfactant reduced the phototoxicity of curcumin against *E. coli* (Haukvik et al. 2010). The obtained phototoxic effect can be increased by increasing the irradiation dose or by choosing an optimal curcumin concentration. *Enterococcus faecalis* was efficiently killed by the lowest concentration of curcumin in combination with the lowest radiant exposure when curcumin was dissolved in certain PEG solutions (< 0.02 % survival), but showed no reduction when exposed to preirradiated curcumin. In a subsequent study, they found that curcumin derivatives demethoxycurcumin (C1) and bisdemethoxycurcumin (C3) were strongly phototoxic towards *E. faecalis* (no surviving bacteria) and showed a lower but significant effect towards *E. coli* (< or = 0.5 log reductions and 1–4 log reductions, respectively) (Haukvik et al. 2011).

Compounds C2 and C4 in combination with blue light reduced the colony-forming ability of *E. faecalis* (approximately 1–4 log reductions). The phototoxic effect of the curcuminoids varied with concentration and further influenced the addition of polyethylene glycol 400 (PEG 400) to the preparations. 2,6-Divanillylidencyclohexanone (C5) showed very low phototoxic potential (< 0.2 log reductions) under the conditions used in the study. The addition of polyethylene glycol 400 (PEG 400) appeared to increase the solubility of compounds C1, C3 and C5 in phosphate-buffered saline. Hegge et al. (2009) found that curcumin had a more than 30-fold higher association constant with hydroxypropyl- γ -cyclodextrin compared to hydroxypropyl- β -cyclodextrin in buffer containing 0.5 % ethanol. They found large variations in the complexation between curcumin and hydroxypropyl- β -cyclodextrin and hydroxypropyl- γ -cyclodextrin, respectively, as a result of various alcoholic co-solvents and alginates in the complexing media. Release of curcumin in its monomeric form was demonstrated in-vitro and found to be dependent on the type and amount of cyclodextrins in the formulation (Hegge et al. 2010). Curcumin was stable during storage, but susceptible to photodegradation in the foams, especially when the formulations contain polyethylene glycol 400 or hydroxypropyl- γ -cyclodextrins. Curcumin did not degrade after γ -sterilisation; however, a decrease in the in-vitro release rate of curcumin and changes in the foams' physical characteristics were detected. Further, they investigated the efficacy of curcumin-loaded alginate foams for application in antimicrobial photodynamic therapy of infected wounds (Hegge et al. 2011). Exposure to the prepared foams in combination with visible light irradiation resulted in >6 log reduction of *Enterococcus faecalis* cells. However, curcumin-mediated photokilling of *Escherichia coli* was ineffective when cyclodextrins were selected as solubiliser of curcumin in the foams. An 81 % reduction in viable *E. coli* cells was detected after treatment with the foam containing polyethylene glycol 400 as the only solubiliser of curcumin combined with visible light irradiation.

Turmeric oil at dilutions of 1:40–1:320 inhibited 15 isolates of dermatophytes and four isolates of pathogenic fungi

at dilutions of 1:40–1:80, but curcumin was inactive (Apisariyakul et al. 1995). In *Trichophyton rubrum*-induced dermatophytosis in guinea pigs, an improvement in lesions was observed in 2–5 days, and the lesions disappeared 6–7 days after the application of turmeric oil. It was found that crude ethanol turmeric extract exhibited inhibitory effects (6.1–26-mm inhibition zones) against 29 clinical strains of dermatophytes (Wuthi-udomlert et al. 2000). There was no inhibition activity from crude curcuminoids, while curcumin, demethoxycurcumin and bisdemethoxycurcumin gave different inhibition zone diameters ranging from 6.1 to 16.0 mm. Although antifungal activity of undiluted freshly distilled turmeric oil and 18-month-old oil revealed some differences, the inhibition zone diameters for both extracts varied within 26.1 to 46.0 mm. The MICs of freshly distilled and 18-month-old turmeric oils were 7.8 and 7.2 mg/ml, respectively. Turmeric oil and its fractions exhibited antifungal activity in-vitro against *Aspergillus flavus*, *A. parasiticus*, *Fusarium moniliforme* and *Penicillium digitatum*, and fraction II was found to be more active (Jayaprakasha et al. 2001). *Curcuma longa* ethanolic extract exhibited good antifungal activities against *Trichophyton longifusus* (65 %) (Khattak et al. 2005). Turmeric rhizome essential oils showed toxicity to seven fungi involved in deterioration of stored agricultural commodities (Dhingra et al. 2007). Depending upon the fungus, in-vitro growth inhibition varied from 36 to 77 % at 0.1 %. *Aspergillus flavus*, *Fusarium semitectum*, *Colletotrichum gloeosporioides* and *C. musae* were most sensitive with growth inhibition of over 70 %. *ar*-Turmerone constituted 87 % of the fungitoxic component of the oil. The purified *ar*-turmerone showed antifungal activity similar to the crude oil. The essential oil combination of *Curcuma longa* and *Zingiber officinale* significantly inhibited the growth and aflatoxin production by the toxigenic food-borne strain of *Aspergillus flavus* LHP-6 at 2.5 and 2.0 $\mu\text{L/mL}$, respectively (Prakash et al. 2012). Turmeric essential oil was found to have inhibitory activity in-vitro against the lipophilic, yeast-like fungus *Malassezia furfur* which causes pityriasis versicolour disease, a common superficial fungal skin disease (Sharma 2012). In the disc diffusion method, it was more inhibitory than standard

antibiotics streptomycin and gentamicin. In the microdilution method, minimum inhibitory concentration (MIC) of turmeric oil was found to be 0.1 µl/ml against *Malassezia furfur*. Turmeric creams containing 6 and 10 % w/w turmeric oil were inhibitory against clinical strains of dermatophytes: *Trichophyton mentagrophytes*, *T. rubrum*, *Epidermophyton floccosum* and *Microsporum gypseum* using broth dilution technique (Jankasem et al. 2013). Minimum fungicidal concentrations of 6 and 10 % w/w turmeric creams were found to be 312 µg/mL. *ar*-Turmerone, a major compound separated from turmeric oil, promoted more effective antidermatophytic activity with the MICs of 1.56–6.25 µg/mL, compared to 3.90–7.81 µg/mL of standard ketoconazole. *C. longa* rhizome essential oil exhibited stronger antifungal activity than curcumin on *Aspergillus flavus* (Ferreira et al. 2013). The essential oil reduced the fungal growth in a concentration-dependent manner. *A. flavus* growth rate was reduced by *C. longa* essential oil at 0.10 %, and this inhibition effect was more efficient in concentrations above 0.50 %. Germination and sporulation were 100 % inhibited in 0.5 % oil. Turmeric leaf oil exhibited significant inhibition of the aflatoxigenic fungus, *Aspergillus flavus* growth as well as aflatoxins B₁ and G₁ production (Sindhu et al. 2011). Turmeric leaf oil exhibited 95.3 % and 100 % inhibition of toxin production, respectively, at 1.0 and 1.5 %. The extent of inhibition of fungal growth and aflatoxin production was dependent on the concentration of essential oil used. LD₅₀ was 0.3 % and LD₉₀ 0.93 %. Turmeric essential oil exhibited stronger antifungal activity than curcumin on *Aspergillus flavus* (Dias Ferreira et al. 2013). The essential oil reduced the fungal growth in a concentration-dependent manner. *A. flavus* growth rate was reduced by turmeric essential oil at 0.10 %, and this inhibition effect was more efficient in concentrations above 0.50 %. Germination and sporulation were 100 % inhibited in 0.5 % oil. Scanning electron microscopy (SEM) of *A. flavus* exposed to oil showed damage to hyphae membranes and conidiophores.

Turmeric oil and its fractions exhibited antibacterial activity in-vitro against *Bacillus cereus*, *Bacillus coagulans*, *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and

Pseudomonas aeruginosa (Negi et al. 1999). Fraction II eluted with 5 % ethyl acetate in hexane was found to be the most active fraction. The turmeric oil, fraction I and fraction II were found to contain *ar*-turmerone, turmerone and curlone as the major compounds along with other oxygenated compounds. Gram-positive bacteria were found to be more sensitive to turmeric oil (Nguyen et al. 2010). *Bacillus cereus* was completely suppressed at the concentration 1 %, and growth of *Micrococcus* sp. was inhibited at this concentration, while *Listonella damsela* growth was inhibited at oil concentration of 3 % only. Growth of *Aspergillus tubingensis* was completely suppressed at 2 % oil concentration, *Aspergillus versicolor* and *Valsa* sp. at 3 % concentration and *Aspergillus japonicus* and *Cladosporium cladosporioides* at 5 % oil concentration. Turmeric essential oil and its curcuminoid extract inhibited the growth of *Bacillus subtilis*, *Bacillus macerans*, *Bacillus licheniformis* and *Azotobacter* sp. in-vitro (Naz et al. 2010). Among all the bacterial strains, *B. subtilis* was the most sensitive to turmeric extracts of curcuminoids and oil. Turmeric rhizome oil showed very good activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans* and *Aspergillus niger* at concentration of 10 μ L except *Pseudomonas aeruginosa* (Singh et al. 2011 b). Very low concentration of 1.95 μ L/mL oil was needed to inhibit the growth of most highly infecting pathogen *Staphylococcus aureus* within 15 min of its exposure in comparison to other microbial strains. The high content of the active ingredient turmerone content (49.76 %) was assigned to be responsible for such excellent antimicrobial activity against the tested pathogens.

C. longa essential oil inhibited the growth and acid production of cariogenic *Streptococcus mutans* at concentrations from 0.5 to 4 mg/mL (Lee et al. 2011). The essential oil also exhibited significant inhibition of *S. mutans* adherence to saliva-coated hydroxyapatite beads at concentrations higher than 0.5 mg/mL. *C. longa* essential oil inhibited the formation of *S. mutans* biofilms at concentrations higher than 0.5 mg/mL. The crude ethanolic extract and essential oil of *C. longa* rhizome inhibited only *Corynebacterium* sp. in-vitro (Prakatthagomol et al. 2012).

Mali et al. (2012) found that chlorhexidine gluconate as well as turmeric mouthwash could be effectively used as an adjunct to mechanical plaque control in prevention of plaque and gingivitis. Both the mouthwashes had comparable anti-plaque, anti-inflammatory and antimicrobial properties. On comparison between chlorhexidine and turmeric mouthwash between 0 and 21st day, percentage reduction of the Plaque Index was 64.207 and 69.072, respectively, percentage reduction of Gingival Index were 61.150 and 62.545, respectively, and percentage reduction of *N*-benzoyl-*L*-arginine-*p*-nitroanilide (BAPNA values) were 42.256 and 48.901, respectively.

Demethoxycurcumin, isolated from turmeric rhizomes, was found to possess antitubercular activity against *Mycobacterium tuberculosis* H(37)Rv strain at 200 µg/mL (Agrawal et al. 2008). Derivatisation of this active principle yielded a potent agent 6, exhibiting considerable activity with a minimum inhibitory concentration (MIC) value of 7.8 µg/mL. Among the highly active curcuminoids against *Mycobacterium tuberculosis*, the isoxazole analogues were the most active group, with mono-*O*-methylcurcumin isoxazole (53) being the most active compound (MIC 0.09 µg/mL) (Changtam et al. 2010b). It was 1131-fold more active than curcumin, the parent compound, and was approximately 18- and 2-fold more active than the standard drugs kanamycin and isoniazid, respectively. Compound 53 also exhibited high activity against the multidrug-resistant *M. tuberculosis* clinical isolates, with the MICs of 0.195–3.125 µg/mL.

Curcumin was a potent inhibitor of sortase A, a bacterial surface protein anchoring transpeptidase, from *Staphylococcus aureus*, with an IC₅₀ value of 13.8 µg/mL (Park et al. 2005). Bisdemethoxycurcumin (IC₅₀ = 31.9 µg/mL) and demethoxycurcumin (IC₅₀ = 23.8 µg/mL) were more effective than the positive control *p*-hydroxymercuribenzoic acid (IC₅₀ = 40.6 µg/mL). The three isolated compounds (1–3) showed no growth inhibitory activity against *S. aureus* strain Newman, with minimum inhibitory concentrations (MICs) greater than 200 µg/mL. Curcumin also exhibited potent inhibitory activity

against *S. aureus* cell adhesion to fibronectin. Curcumin exhibited antimicrobial activity against 10 strains of *Staphylococcus aureus* with MICs of 125 to 250 µg/ml (Mun et al. 2013). In the checkerboard test, curcumin markedly reduced the MICs of the antibiotics oxacillin, ampicillin, ciprofloxacin and norfloxacin used against MRSA (methicillin-resistant *Staphylococcus aureus*). The time-kill curves showed that a combined curcumin and oxacillin treatment reduced the bacterial counts below the lowest detectable limit after 24 h.

Turmeric rhizome compounds bisacurone, *ar*-turmerone, *p*-turmerone, α -turmerone and *ar*-curcumyl alcohol exhibited moderate antifungal activity against *Aspergillus niger*, and all except bisacurone had moderate antibacterial activity against *Pseudomonas aeruginosa* (Ragasa et al. 2005). Curcumin displayed antifungal properties against all tested *Candida* strains, with minimum inhibitory concentrations (MICs) varying from 250 to 2000 µg/mL (Neelofar et al. 2011). At MIC, curcumin inhibited H⁺ extrusion in *Candida albicans* and *Candida glabrata* by 42 % and 32 % in the absence of glucose and by 28 % and 18 % in the presence of glucose, respectively. Ergosterol content decreased by 70 % and 53 % for the two strains following exposure to curcumin at MIC. Curcumin and fluconazole decreased proteinase secretion by 49 % and 53 %, respectively, in *C. albicans* and by 39 % and 46 %, respectively, in *C. glabrata*.

Curcuma longa rhizomes yielded three curcuminoids, which displayed topoisomerase I and II enzyme inhibition activity (Roth et al. 1998). Curcumin III was the most active curcuminoid, inhibiting topoisomerase at 25 µg/mL. Curcumin I and curcumin II inhibited the topoisomerases at 50 µg/mL. Curcumin appeared to inhibit the catalytic activity of lethal factor (LF) the proteolytic component of anthrax toxin produced by the bacterium *Bacillus anthracis*, through a mixture of inhibitory mechanisms, without significant compromise to the binding of oligopeptide substrates (Antonelli et al. 2014). One curcumin derivative, 4-phenylaminocarbonylbisdemethoxycurcumin, inhibited LF with potency comparable with the parent compound, while

also showing improved solubility and stability. Treatment with curcumin inhibited biofilm development of uropathogens such as *Escherichia coli*, *Pseudomonas aeruginosa* PAO1, *Proteus mirabilis* and *Serratia marcescens*, by attenuating quorum sensing-dependent factors, such as exopolysaccharide production, alginate production and swimming and swarming motility of the uropathogens (Packiavathy et al. 2014). Curcumin was shown to possess superior potency to resensitize methicillin-resistant *Staphylococcus aureus* (MRSA) to antibiotics (Mun et al. 2014). Curcumin had a significant effect on the protein level of PBP2a (penicillin-binding protein 2a). After curcumin treatment MRSA showed damage of the cell wall, disruption of the cytoplasmic contents, broken cell membrane and cell lysis. The data indicated a remarkable antibacterial effect of curcumin, with membrane permeability enhancers and ATPase inhibitors, and curcumin did not directly bind to peptidoglycan on the cell wall. The MIC of curcumin was >256 µg/mL against all multidrug-resistant strains of *Acinetobacter baumannii*, while those for epigallocatechin gallate (EGCG) ranged from 128 to 1024 µg/mL (Betts and Wareham 2014). The addition of EGCG reduced the MIC of curcumin by 3- to 7-fold, with the greatest interaction resulting in a CCM MIC of 4 µg/mL. The synergistic combination may have a potential use in medicine as a topical agent to prevent or treat *A. baumannii* infections. The 3'-demethoxy analogue of curcumin inhibited *Escherichia coli* ATP synthase F1 more strongly than curcumin did (Sekiya et al. 2014). Furthermore, these compounds inhibited *E. coli* growth through oxidative phosphorylation, consistent with their effects on ATPase activity. The results suggested that the two compounds affected bacterial growth through inhibition of ATP synthase. Derivatives including bis(arylmethylidene)acetones (C5 curcuminoids) exhibited only weak activity towards ATPase and bacterial growth.

Labda-8(17),12-diene-15,16 dial from the leaf hexane extract exhibited antifungal activity against *Candida albicans* at 1 µg/mL and inhibited the growth of *Candida krusei* and *Candida parapsilosis* at 25 µg/mL (Roth et al. 1998). Turmeric leaf essential oil showed maximum inhibition against *Fusarium miniformes* followed by *Bacillus subtilis*,

Staphylococcus aureus, *Escherichia coli*, *Salmonella typhimurium*, *Enterobacter aerogenes*, *Aspergillus niger*, *A. flavus*, *A. fumigatus*, *A. ficuum* and *A. oryzae* but was less inhibitory towards *Fusarium oxysporum* and *Penicillium digitatum* (Parveen et al. 2013). Compared to standard antibiotics, *C. longa*, *Zingiber officinale* and *Tinospora cordifolia* were more effective in killing *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*, *Bacillus subtilis* and *Proteus mirabilis* as evident from MIC and MBC values (5–125 µg/mL) (Chakraborty et al. 2014). Moreover, *C. longa* had highest antibacterial efficacy compared to *Z. officinale* and *T. cordifolia*. Ethyl acetate and water extracts from *C. domestica* roots showed MIC of 306 µg/mL and 183 µg/mL, respectively, against *Clostridium perfringens* (Lee et al. 2014b).

Anti-inflammatory Activity

Studies in the past decades had shown curcumin to have anti-inflammatory activity by downregulation of the expression of various pro-inflammatory cytokines including TNF (tumour necrosis factor), interleukins IL-1, IL-2, IL-6, IL-8, IL-12 and chemokines, most likely through inactivation of the nuclear transcription factor NF-κB (Kohli et al. 2005; Jagetia and Aggarwal 2007) and inhibition of arachidonic acid metabolism, cyclooxygenase, lipoxygenase and release of steroidal hormones (Kohli et al. 2005). Curcumin was reported to stabilise lysosomal membrane and cause uncoupling of oxidative phosphorylation besides having strong oxygen radical scavenging activity, which was responsible for its anti-inflammatory property. Modulation of the ubiquitin-proteasome system (UPS) pathway by curcumin had been linked to regulation of cancer-linked inflammatory proteins (such as COX-2 and iNOS), transcription factors (NF-κB, STAT3, Sp, AP-1, GADD153/CHOP, HIF-1α), growth factors (VEGF, HER2), apoptotic proteins (p53, Bcl-2, survivin, DNA topoisomerase II, HDAC2, p300, hTERT) and cell cycle proteins (cyclin D1, cyclin E, cyclin B, p21, p27) associated with the prevention and therapy of cancer (Hasima and Aggarwal 2014). Curcumin had been reported to be a potent

inhibitor of COP9 signalosome and associated kinases, casein kinase 2 and protein kinase D, all linked to the ubiquitin-proteasomal system (UPS). Curcumin could also directly inhibit ubiquitin isopeptidases, a family of deubiquitinases (DUBs) that salvaged ubiquitin for reuse by the 26S proteasome system.

In-Vitro Studies

Laboratory studies had identified a number of different molecules involved in inflammation that were inhibited by curcumin including phospholipase, lipoxygenase, cyclooxygenase 2, leukotrienes, thromboxane, prostaglandins, nitric oxide, collagenase, elastase, hyaluronidase, monocyte chemoattractant protein-1 (MCP-1), interferon-inducible protein, tumour necrosis factor (TNF) and interleukin-12 (IL-12) (Chainani-Wu 2003). Curcumin I, curcumin II (monodemethoxycurcumin) and curcumin III (bisdemethoxycurcumin) showed anti-inflammatory activity (Ramsewak et al. 2000). The inhibition of COX-I and COX-II enzymes by the curcumins was observed. Curcumins I–III were active against COX-I enzyme at 125 microg/ml and showed 32, 38.5 and 39.2 % inhibition of the enzyme, respectively. Curcumins I–III also showed good inhibition of the COX-II enzyme at 125 mg/ml with 89.7, 82.5 and 58.9 % inhibition of the enzyme, respectively. Crude organic extracts of turmeric were capable of inhibiting LPS-induced tumour necrosis factor α (TNF- α) (IC₅₀ value = 15.2 μ g/ml) and prostaglandin E2 (PGE2) (IC₅₀ value = 0.92 μ g/ml) production in HL-60 cells (Lantz et al. 2005). Purified curcumin was more active than either demethoxycurcumin or bisdemethoxycurcumin. Fractions and subfractions of turmeric extracts collected via preparative HPLC had differing biological activity, ranging from no activity to IC₅₀ values of < 1 μ g/ml. A combination of several of the fractions that contain the turmeric oils was more effective than the curcuminoids at inhibiting PGE2. While curcumin inhibited COX-2 expression, turmeric oils had no effect on levels of COX-2 mRNA.

Pre-incubation of myelomonocytic U937 cells with curcumin increased glutathione (GSH) content and significantly lowered reactive oxygen species (ROS) production nuclear factor-kappaB (NF-kappaB) activation (-34 %) and tumour necrosis factor α (TNF- α) secretion (-51 %) after LPS exposure (Strasser et al. 2005). The antioxidative effects of curcumin were preceded by an oxidative stimulus, which was time and dose dependent. Excessive concentrations of curcumin may even harm cells, as cell viability was decreased, in spite of elevated GSH contents. There was no clear relationship between intracellular GSH concentrations and the anti-inflammatory effects of curcumin. Among the tested polyphenolic agents curcumin, rosmarinic acid, resveratrol and epigallocatechin gallate, curcumin showed prominent inhibition of major ion channels in lymphocytes, which might contribute to the anti-inflammatory effects of curcumin (Shin et al. 2011). Curcumin inhibited Ca^{2+} -release-activated Ca^{2+} channel (CRAC) and K^{+} channels in Jurkat T cells.

Cyclooxygenase-2 (COX-2) expression in *Porphyromonas gingivalis* fimbria-stimulated RAW 264.7 cells was inhibited by curcumin but not by tetrahydrocurcumin (Murakami et al. 2008). LPS-stimulated COX-2 gene expression was completely inhibited by curcumin, but an increase in the concentration of tetrahydrocurcumin did not cause complete inhibition of COX-2 expression. It was found that calculated chemical hardness (η) for curcumin was clearly smaller, whereas its electronegativity (χ) and electrophilicity (ω) were clearly greater than the corresponding values for the curcumin-related compounds tetrahydrocurcumin, isoeugenol and eugenol. This suggested that the anti-inflammatory activities of curcumin may be related to η -, χ - and/or ω -controlled enzymes. Guimarães et al. (2013) demonstrated that curcumin potently inhibited expression of LPS-induced pro-inflammatory cytokines in RAW 264.7 macrophages via mechanisms that involve modulation of expression and activity of SOCS-1 and SOCS-3 and of p38 MAPK. Antoine et al. (2013) found that curcumin possessed potent modulatory activities on primed or agent-induced

human neutrophils in-vitro and that it possessed important anti-inflammatory activities in-vivo by inhibiting LPS-induced neutrophilic inflammation. Curcumin inhibited formyl-methionyl-leucyl-phenylalanine (fMLP)- or lipopolysaccharide (LPS)-induced suppression of human neutrophil apoptosis by inhibiting LPS-induced cytokine production and LPS-induced NF- κ B activation. In-vivo, intraperitoneal administration of curcumin inhibited LPS-induced neutrophilic infiltration.

Both curcumin and *ar*-turmerone (ATM) inhibited lipopolysaccharide (LPS)-induced expression of inducible forms of both nitric oxide synthase and cyclooxygenase (iNOS and COX-2, respectively) (Murakami et al. 2013). A chase experiment using actinomycin D revealed that ATM accelerated the decay of iNOS and COX-2 mRNA, suggesting a post-transcriptional mechanism. ATM prevented LPS-induced translocation of HuR, an AU-rich element-binding protein that determines mRNA stability of certain inflammatory genes. Treatment of NR-INF-02 (turmeric extract) showed a significant increase of NO, IL-2, IL-6, IL-10, IL-12, interferon (IFN) γ , tumour necrosis factor (TNF) α and MCP-1 production in unstimulated mouse splenocytes and mouse macrophages (Chandrasekaran et al. 2013). Also, NR-INF-02 showed potent inhibitory effect towards release of PGE2 and IL-12 levels in LPS-stimulated mouse splenocytes. Its polysaccharide fraction F1 was found to be more potent than the mother liquor (F2) towards inhibiting PGE2 and IL-12 in LPS-stimulated splenocytes. The methanolic and water extracts of *C. mangga* (CMM and CMW) and *C. longa* (CLM and CLW) leaves, at 100 μ g/mL, inhibited cyclooxygenase enzymes COX-1 by 55 %, 33 %, 43 % and 24 % and COX-2 by 65 %, 55 %, 77 % and 69 %, respectively (Liu and Nair 2012). The methanolic leaf extract of *C. longa* afforded nine compounds: 8,12-epoxygermacra-1(10),4,7,11-tetraen-6-one (1); 8,12-epoxygermacra-1(10),4,7,11-tetraene (2); cyclohexanecarboxylic acid methyl ester (3); isopulegol (4); 2-menthen-1-ol (5); menth-1-en-9-ol (6); octahydrocurcumin (7); labda-8(17)-12-diene-15,16-dial (8); and coronadiene (9). Compounds 1–9 inhibited COX-1 enzyme by 3 %, 4 %, 7 %, 35 %, 29 %, 7 %, 0 %, 8 % and 14 %, and COX-2 by 18 %, 34

%, 0 %, 34 %, 22 %, 20 %, 82 %, 52 % and 42 %, respectively, at 25 µg/mL. The curcuminoid demethoxycurcumin significantly decreased NO secretion by 35–41 % in our inflamed human intestinal Caco-2 cells (Somchit et al. 2014). Decrease in NO production by demethoxycurcumin was concomitant with downregulation of iNOS at mRNA and protein levels compared to pro-inflammatory cytokine cocktail- and LPS-treated controls. The findings suggested that demethoxycurcumin may have potential as a therapeutic agent against inflammation-related diseases, especially in the gut. Turmeric extract and curcumin competitively inhibited lipooxygenase 12/15-LOX from the rat lung cytosolic fraction (Bezáková et al. 2014).

In considering skin immune activation activities, turmeric leaf extract dried by ultrasonication extraction (BU) showed about 10 % higher inhibition of hyaluronidase activity than those of turmeric leaf extract dried by conventional hot air drying (HE) and even higher than that of the turmeric leaf freeze-drying (FE) extract (Choi et al. 2014). Nitric oxide production from macrophage of the BU extract in adding 1.0 mg/mL was increased up to 16.5 µM. The BU extract also showed 53 and 78 % of inhibition of IL-6 and TNF- α production from the human T lymphocytes (T cell), respectively. It was found that the BU extract could effectively suppress the expression levels of skin inflammation-related genes such as COX-2 and iNOS, down to 80 and 85 % compared to the control, respectively.

Animal Studies

The rank order of anti-inflammatory potencies of curcumin (C) and curcumin analogues sodium curcumin (NaC), diacetyl curcumin (DAC), triethyl curcumin (TEC), tetrahydrocurcumin (THC) and ferulic acid (FA) compared to PB in carrageen-induced inflammation rats were NaC > THC > C > PB > TEC (Mukhopadhyay et al. 1982). The curcumin analogues decreased carrageenan-induced paw oedema at low doses; however, at higher doses this effect was partially reversed. FA and DAC were devoid of anti-inflammatory activity.

Turmeric oil showed significant reduction in paw thickness in carrageenan, dextran-induced acute inflammation and formalin-induced chronic inflammation (Liju et al. 2011). Turmeric diet increased the levels of interleukin IL-6 (1.9-fold) iNOS (4.39-fold), IL-8 (3.11-fold) and COX oxygenase COX-2 (2.02-fold) in Sprague Dawley rats suggesting that turmeric either was more bioavailable or had more affect on pro-inflammatory genes compared to curcumin diet (Martin et al. 2012). The results demonstrated the molecular effects of curcumin and turmeric in the role as an anti-inflammatory therapy. Agarwal et al. (2013) reported that topically applied standardised aqueous extract of *C. longa* suppressed endotoxin-induced uveitis in rats by reducing TNF- α activity.

Studies showed that curcuminoids and oil-free aqueous extract (COFAE) of *C. longa* at three dose levels significantly inhibited inflammation in n-xylene-induced ear oedema and cotton pellet granuloma models in albino Swiss mice and albino Wistar rats, as evidenced by reduction in ear weight and decrease in wet as well as dry weights of cotton pellets, when compared to the vehicle control (Bagad et al. 2013). The COFAE of *C. longa* showed considerable anti-inflammatory effects against acute and chronic inflammation, and the effects were comparable to those of curcuminoids and turmerones. The percent inhibition as a measure of paw oedema for turmeric oil and fish oil at 100 mg/kg was 76 % and 31 %, respectively, while the percent inhibition by the combination of the two at 100 mg/kg was 62 %, which was the same as that of aspirin at the same dose (Jacob and Badyal 2014). McCann et al. (2014) found that turmeric extract and several chromatographically separated fractions beneficially affected the variants of solute carrier protein 22 A4 and interleukin IL-10 associated with inflammatory bowel disease, by reducing inappropriate epithelial cell transport (SLC22A4, 503 F) and increasing anti-inflammatory cytokine gene promoter activity (IL-10, -1082A).

Curcumin was found to interact with transient potential vanilloid receptor 1 (TRPV1) to mediate its protective action in inflamed tissues caused by dinitrobenzene sulphonic acid (DNBS)-induced colitis in mice (Martelli et al. 2007).

Subhashini et al. (2013) demonstrated that intranasal curcumin (5.0 mg/kg, i.n.) could effectively be absorbed and detected in plasma and lungs and suppressed airway inflammations at lower doses than the earlier doses used for detection (100–200 mg/kg, i.p.) for pharmacological studies (10–20 mg/kg, i.p.) in a mouse model of asthma. At considerably lower doses, curcumin performed better than the standard drug disodium cromoglycate (DSCG 50 mg/kg, i.p.) by affecting inflammatory cell infiltration and histamine release in mouse model of asthma. Clarithromycin treatment significantly decreased *Klebsiella pneumoniae* bacterial load and other inflammatory components in *K. pneumoniae* lung-infected mice, but animals receiving curcumin alone or in combination with clarithromycin showed a much more significant reduction in neutrophil influx along with reduced levels of various inflammatory parameters (malondialdehyde, myeloperoxidase, nitric oxide, TNF- α) (Bansal and Chhibber 2014). The results showed that curcumin as an adjunct therapy will help to downregulate the exaggerated state of immune response during acute lung infection.

Curcumin pretreatment of male BALB/c mice improved the airway inflammatory cell infiltration and reversed the increasing levels of Notch1/2 receptors and GATA3 (Chong et al. 2014). The results of their study suggested that Notch1 and Notch2 receptor, major Notch1 receptor, played an important role in the development of allergic airway inflammation, and the inhibition of Notch1-GATA3 signalling pathway by curcumin can prevent the development and deterioration of the allergic airway inflammation. Intranasal curcumin administration prevented accumulation of inflammatory cells to the airways, structural alterations and remodelling associated with chronic asthma-like peribronchial and airway smooth muscle thickening, sloughing off of the epithelial lining and mucus secretion in ovalbumin-induced chronic asthma of BALB/c mice (Chauhan et al. 2014). In TLR4^{-/-} mice subjected to weight-drop contusion injury, intraperitoneal injection of curcumin attenuated acute inflammatory injury by inhibiting the TLR4/MyD88/NF- κ B signalling pathway (Zhu et al. 2014a). Similar outcomes were observed in the microglia

and neuron co-culture following treatment with curcumin after lipopolysaccharide (LPS) stimulation. LPS increased TLR4 immunoreactivity and morphological activation in microglia and increased neuronal apoptosis, whereas curcumin normalised this upregulation. The increased protein levels of TLR4, MyD88 and NF- κ B in microglia were attenuated by curcumin treatment.

Clinical Studies

Phenylbutazone and curcumin produced a better anti-inflammatory response than placebo in patients with postoperative inflammation (Satoskar et al. 1986). Turmeric curcuminoids comprising curcumin, demethoxycurcumin and bisdemethoxycurcumin had been reported to possess remarkable anti-inflammatory properties (Panahi et al. 2014a). In a 4-week, randomised double-blind placebo-controlled trial of male subjects who were suffering from chronic sulphur mustard (MS)-induced pulmonary complications, treatment with turmeric curcuminoids was found to be efficacious in suppressing systemic inflammations compared to placebo (Panahi et al. 2014a).

Anti-inflammatory/Anti-arthritic Activity

In-Vitro Studies

In-vitro studies showed that treating synovial fibroblasts obtained from rheumatoid arthritic patients with curcumin resulted in the downregulation of anti-apoptotic Bcl-2 and the X-linked inhibitor of the apoptosis protein as well as the upregulation of pro-apoptotic Bax expression in a concentration-dependent manner (Park et al. 2007). Curcumin-induced apoptosis was also associated with the proteolytic activation of caspase-3 and caspase-9 and the concomitant degradation of poly(ADP-ribose) polymerase protein. Furthermore, curcumin decreased the expression levels of the cyclooxygenase (COX)-2 mRNA and protein without causing significant changes in the COX-1 levels, which was correlated with the inhibition of prostaglandin E(2) synthesis. The results

indicated that curcumin may be a useful new therapeutic pathway against hyperplasia of the synovial fibroblasts in rheumatoid arthritis. Studies by Jackson et al. (2006) found that both curcumin and quercetin inhibited inflammatory processes associated with arthritis; both inhibited neutrophil activation, synoviocyte proliferation and angiogenesis. Curcumin strongly inhibited collagenase and stromelysin expression at micromolar concentration, whereas quercetin had no effect, indicating the potential of curcumin over quercetin in the treatment of crystal-induced arthritis or rheumatoid arthritis. Lev-Ari et al. (2006) found that curcumin augmented the growth inhibitory and pro-apoptotic effects of celecoxib in osteoarthritis synovial adherent cells.

From ground turmeric rhizome, two extracts were isolated: (1) a crude extract containing essential oils and 34 % (by weight) of the three major curcuminoids (curcumin, demethoxycurcumin and bisdemethoxycurcumin) that inhibited in-vitro LPS-stimulated PGE₂ production with a 50 % inhibitory concentration (IC₅₀) of 0.13 µg/ml and (2) an essential oil-depleted fraction containing 41 % curcuminoids with an IC₅₀ of 0.48 µg/ml for in-vitro PGE₂ inhibition (Funk et al. 2006a). Major compounds present in turmeric essential oils (TEO) include *ar*-turmerone, α -turmerone and β -turmerone. Administration of a turmeric fraction depleted of essential oils profoundly inhibited joint inflammation and periarticular joint destruction in a dose-dependent manner in female Lewis rats with streptococcal cell wall-induced arthritis. In-vivo treatment prevented local activation of NF-kappaB and the subsequent expression of NF-kappaB-regulated genes mediating joint inflammation and destruction, including chemokines, cyclooxygenase 2 and RANKL. Consistent with these findings, inflammatory cell influx, joint levels of prostaglandin E₂ and periarticular osteoclast formation were inhibited by turmeric extract treatment. A commercial sample containing 94 % of the three major curcuminoids was more potent in preventing arthritis than the essential oil-depleted turmeric fraction when compared by total curcuminoid dose per body weight (Funk et al. 2006b). The data documented the in-vivo anti-arthritic efficacy of an

essential oil-depleted turmeric fraction and suggested that the three major curcuminoids were responsible for this anti-arthritic effect, while the remaining compounds in the crude turmeric extract may inhibit this protective effect.

Cartilage explants harvested from metacarpophalangeal and metatarsophalangeal joints of eight horses were stimulated with increasing concentrations of the pro-inflammatory cytokine IL-1 β to select effective doses for inducing cartilage degeneration (Clutterbuck et al. (2009). Treatment with curcumin (100 μ mol/L) significantly reduced interleukin IL-1 β -stimulated glycosaminoglycan release in the explants by an average of 20 % at 10 ng/mL and 27 % at 25 ng/mL back to unstimulated control levels. The data suggested that the inflammatory cartilage explant model was useful for studying the effects of curcumin on inflammatory pathways and gene expression in IL-1 β -stimulated chondrocytes. In alginate beads and cartilage explant models, curcumin inhibited the basal and the pro-inflammatory mediators interleukin IL-1 β -stimulated NO, PGE(2), IL-6, IL-8 and metalloproteinase-3 (MMP-3) production by human chondrocytes in a concentration-dependent manner (Mathy-Hartert et al. 2009). In the basal condition, (35)S-glycosaminoglycan release from cartilage explants was decreased by curcumin. The data suggested that curcumin could be useful in the treatment of osteoarthritis. Buhrmann et al. (2010) demonstrated that although curcumin alone did not have chondrogenic effects on mesenchymal stem cells, it inhibited interleukin IL-1 β -induced activation of NF- κ B, activation of caspase-3 and cyclooxygenase-2 in MSCs time and concentration dependently, as it did in chondrocytes. In IL-1 β -stimulated co-cultures, 4-h pretreatment with curcumin significantly enhanced the production of collagen type II, cartilage-specific proteoglycans (CSPGs) and β 1-integrin, as well as activating MAP kinase signalling and suppressing caspase-3 and cyclooxygenase-2. Thus, curcumin treatment may help establish a microenvironment in which the effects of pro-inflammatory cytokines are antagonised, thus facilitating chondrogenesis of MSC-like progenitor cells in-vivo and support the regeneration of articular cartilage. Curcumin effectively blocked interleukin IL-1 β and PMA-induced IL-6

expression both in human synovial fibroblast cell line MH7A and on fibroblast-like synoviocytes (FLS) derived from patients with rheumatoid arthritis (Kloesch et al. 2013). Furthermore, curcumin inhibited activation of NF- κ B and induced dephosphorylation of ERK1/2. Treatment of FLS with high concentrations of curcumin led to a decrease in cell viability and induction of apoptosis.

Animal Studies

In rats with Freud's adjuvant-induced arthritis, oral administration of turmeric significantly reduced inflammatory swelling compared to controls (Arora et al. 1971).

An essential oil-depleted turmeric fraction containing 41 % of the three major curcuminoids was efficacious in preventing joint inflammation when treatment was started before, but not after, the onset of joint inflammation in an animal model of rheumatoid arthritis (Funk et al. 2006b). A commercial sample containing 94 % of the three major curcuminoids was more potent in preventing arthritis than the essential oil-depleted turmeric fraction when compared by total curcuminoid dose per body weight. The data documented the in-vivo anti-arthritic efficacy of an essential oil-depleted turmeric fraction and suggested that the three major curcuminoids were responsible for this anti-arthritic effect, while the remaining compounds in the crude turmeric extract may inhibit this protective effect. In a subsequent study, they found that crude or refined turmeric essential oil (TEO) extracts dramatically inhibited joint swelling (90–100 % inhibition) in female rats with streptococcal cell wall (SCW)-induced arthritis when extracts were administered via intraperitoneal injection to maximise uniform delivery (Funk et al. 2010). However, this anti-arthritic effect was accompanied by significant morbidity and mortality. Oral administration of a 20-fold higher dose TEO was non-toxic, but only mildly joint protective (20 % inhibition). The results did not support the isolated use of TEO for arthritis treatment but, instead, identify potential safety concerns in vertebrates exposed to TEO. Compared with untreated collagen-induced arthritic mice, curcumin-treated mice downregulated clinical arthritis score, the proliferation of

splenic T cells, expression levels of TNF- α and IL-1 β in the ankle joint and expression levels of IgG2a in serum (Moon et al. 2010). Additionally, by altering nuclear factor (NF)- κ B transcription activity in FLSs, curcumin inhibited PGE₂ production, COX-2 expression and MMP secretion. The results suggested that curcumin could effectively suppress inflammatory response by inhibiting pro-inflammatory mediators and regulating humoral and cellular immune responses.

Treatment of collagen-induced arthritic rats with 110-mg/ml/kg turmeric extract showed significant mean difference in the erythrocyte sedimentation rate (ESR), arthritis score and radiological scores on day 28 compared to the vehicle-treated group (Taty et al. 2011). The mean difference for the ESR, arthritis score and radiological scores of this highest turmeric dose group was found to be insignificant compared to the betamethasone-treated group. The results showed that administration of turmeric extract arrested the degenerative changes in the bone and joints of collagen-induced arthritic rats. Turmeric and ginger rhizomes (at dose 200 mg/kg body weight) significantly suppressed (but with different degrees) the incidence and severity of arthritis by increasing/decreasing the production of anti-inflammatory/pro-inflammatory cytokines, respectively, and activating the antioxidant defence system in adjuvant-induced arthritic rats ((Ramadan et al. 2011). The anti-arthritic activity of turmeric exceeded that of ginger and indomethacin (a nonsteroidal anti-inflammatory drug), especially when the treatment started from the day of arthritis induction. The percentage of disease recovery was 4.6–8.3 % and 10.2 % more in turmeric compared with ginger and indomethacin, respectively. In another study, oral administration of ginger–turmeric rhizome mixture was found to be more effective than indomethacin (a nonsteroidal/anti-inflammatory drug) in alleviating the loss in body weight gain; the histopathological changes observed in ankle joints, blood leukocytosis and thrombocytosis; iron deficiency anaemia; serum hypoalbuminaemia and globulinaemia; the impairment of kidney functions; and the risks for cardiovascular disease in adjuvant-induced human rheumatoid arthritic rats (Ramadan

and El-Menshawy 2013). Curcumin dramatically attenuated the progression and severity of collagen-induced arthritis in DBA/1 J mice, accompanied with decrease of BAFF (B-cell-activating factor belonging to the TNF family) production in serum and spleen cells as well as decrease of serum interferon IFN γ and interleukin IL-6 (Huang et al. 2013a). Treatment of B lymphocytes with curcumin suppressed IFN γ -induced BAFF expression, STAT1 (signal transducers and activators of transcription) phosphorylation and nuclear translocation, suggesting that curcumin may repress IFN γ -induced BAFF expression via negatively interfering with STAT1 signalling. In a recent study, oral administration of curcumin reduced inflammation in the first 6 h after experimentally zymosan-induced arthritis in male rats (Nonose et al. 2014). Curcumin was more effective than lower doses of prednisone in the first 6 h after induction of the arthritis.

Clinical Studies

In a randomised controlled study of 107 patients with primary knee osteoarthritis (OA) with pain score of ≥ 5 , patients were randomised to receive ibuprofen (800 mg per day) or *C. domestica* extracts (2 g per day) for 6 weeks; turmeric extract appeared similarly efficacious and safe as ibuprofen for the treatment of knee osteoarthritis (Kuptniratsaikul et al. 2009). In another larger clinical study of 367 primary knee osteoarthritis patients with a pain score of 5 or higher, *C. domestica* extracts were found to be as effective as ibuprofen for the treatment of knee osteoarthritis (Kuptniratsaikul et al. 2014). The side effect profile was similar but with fewer gastrointestinal adverse events (abdominal pain/discomfort) reports in the turmeric extract group. In a clinical study of 28 osteoarthritic patients who completed the study, a formulation containing *Curcuma longa* and *Boswellia serrata* extracts at a dose of 500 mg administered twice a day was more successful than administering celecoxib 100 mg twice a day for symptom scoring and clinical examination (Kizhakkedath 2013). The treatment was well tolerated and did not produce any adverse effect in patients, as judged by the vital signs, haemogram and liver and renal function tests.

In a prospective randomised open end blinded evaluation (PROBE) study of 80 patients with knee osteoarthritis, the ability of curcuminoid from *Curcuma domestica* rhizome extract was not significantly different compared to diclofenac sodium in suppressing the secretion of cyclooxygenase-2 enzyme by synovial fluid's monocytes (Kertia et al. 2012). In a randomised, single-blind, placebo-controlled study of 20 patients (37 males and 83 females) with primary knee osteoarthritis, treatment with a polysaccharide-rich extract of *C. longa*, NR-INF-02, was found to be safe and efficacious as a useful treatment option for patients with primary painful knee osteoarthritis (Madhu et al. 2013). The analysis of post-treatment scores following administration of NR-INF-02 using visual analogue scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale at each clinical visit showed significant decrease compared to placebo. NR-INF-02-treated group showed a significant decrease in the use of rescue medication, along with clinical and subjective improvement compared to placebo.

A recent study in Belgium reported that Flexofytol®, a new preparation of curcumin, could be a potential nutraceutical for the care of patients complaining of joint problems, with excellent tolerance and rapid benefits for articular mobility, pain and quality of life (Appelboom et al. 2014). Within the first 6 weeks of treatment, Flexofytol® improved patient pain, articular mobility and quality of life. Excellent tolerance was reported, and more than half of these patients were able to discontinue analgesic and anti-inflammatory drugs. A multicentre, observational, prospective, open-label study involving 42 patients (36 women; mean age = 67 years) suffering from acute or chronic, degenerative spine or joint pain was conducted to ascertain the efficacy of a complex of three natural anti-inflammatory agents comprising devil's claw (*Harpagophytum procumbens*), turmeric (*Curcuma longa*) and bromelain (AINAT) in eight rheumatology centres (Conrozier et al. 2014). It was found that the improvement of joint pain was clinically relevant in patients treated with AINAT for both acute and chronic osteoarthritis pain. Considering its excellent tolerance profile, the tested complex of three plant extracts with anti-

inflammatory properties may be a valuable and safe alternative to NSAIDs in patients suffering from degenerative joint diseases.

Hypoglycaemic/Antidiabetic Activity

Zhang et al. (2013) reported on recent literature on the applications of curcumin for glycaemia and diabetes-related liver disorders, adipocyte dysfunction, neuropathy, nephropathy, vascular diseases, pancreatic disorders and other complications, and we also discuss its antioxidant and anti-inflammatory properties.

In-Vitro Studies

Turmerin, from turmeric, inhibited α -amylase and α -glucosidase activities with IC_{50} values of 31 and 192 $\mu\text{g/mL}$, respectively. Under the experimental conditions, those values for a standard glucosidase inhibitor, acarbose, were 81 and 296 $\mu\text{g/mL}$, respectively (Lekshmi et al. 2012b). The inhibitory potential showed by turmerin against enzymes linked to type II diabetes, as well as its moderate antioxidant capacity, could rationalise the traditional usage of turmeric rhizome preparations against diabetes. Bisdemethoxycurcumin from turmeric acted as an inhibitor to inactivate human pancreatic α -amylase, a therapeutic target for oral hypoglycaemic agents in type II diabetes (Ponnusamy et al. 2012). It inhibited porcine and human pancreatic α -amylase with an IC_{50} value of 0.026 and 0.025 mM, respectively. Studies showed that curcumin and demethoxycurcumin could significantly restore advanced glycation end product (AGE)-induced apoptosis to normal levels ($IC_{50} = 3.874 \times 10^{-11}$) M for curcumin and $IC_{50} = 6.085 \times 10^{-11}$) M for demethoxycurcumin and reduce dramatically reactive oxygen species generation in mesangial cell (Liu et al. 2012). Additionally, curcumin and demethoxycurcumin dramatically elevated AGE-decreased superoxide dismutase activity while significantly reducing AGE-increased malondialdehyde content in cell culture supernatant. The results suggested that both curcumin and demethoxycurcumin had a significant protective potential to

the prevention of diabetic nephropathy. Turmeric volatile oils inhibited glucosidase enzymes more effectively than the reference standard drug acarbose (Lekshmi et al. 2012a). Drying of rhizomes was found to enhance α -glucosidase ($IC_{50} = 1.32\text{--}0.38\ \mu\text{g/ml}$) and α -amylase ($IC_{50} = 64.7\text{--}34.3\ \mu\text{g/ml}$) inhibitory capacities of volatile oils. *ar*-Turmerone, the major volatile component in the rhizome, also showed potent α -glucosidase ($IC_{50} = 0.28\ \mu\text{g}$) and α -amylase ($IC_{50} = 24.5\ \mu\text{g}$) inhibition.

Bisht et al. (2007) synthesised polymeric nanoparticle encapsulated formulation of curcumin and nanocurcumin utilising the micellar aggregates of cross-linked and random copolymers of *N*-isopropylacrylamide (NIPAAm), with *N*-vinyl-2-pyrrolidone (VP) and poly(ethylene glycol)monoacrylate (PEG-A). Nanocurcumin demonstrated comparable in-vitro therapeutic efficacy to free curcumin against a panel of eight human pancreatic cancer cell lines (MiaPaca2, Su86.86, BxPC3, Capan1, Panc1, E3LZ10.7, PL5 and PL8), as assessed by cell viability and clonogenicity assays in soft agar. Further, nanocurcumin's mechanisms of action on pancreatic cancer cells mirror that of free curcumin, including induction of cellular apoptosis, blockade of nuclear factor-kappa-B (NF- κ B) activation and downregulation of steady-state levels of multiple pro-inflammatory cytokines (IL-6, IL-8 and TNF- α). The antitumour activity of liposome-encapsulated curcumin was equal to or better than that of free curcumin at equimolar concentrations (Li et al. 2005). Liposomal curcumin downregulated the NF-kappaB machinery, suppressed growth and induced apoptosis of human pancreatic cells in-vitro. Encapsulated curcumin in a liposomal delivery system facilitated intravenous administration. In-vivo, curcumin suppressed pancreatic carcinoma growth in murine xenograft models and inhibited tumour angiogenesis.

Kim et al. (2009c) demonstrated that curcuminoids effectively suppressed dexamethasone-induced phosphoenolpyruvate carboxykinase (PEPCK) and glucose 6-phosphatase (G6Pase) in H4IIE rat hepatoma and Hep3B human hepatoma cells. In addition, curcuminoids increased the

phosphorylation of AMP-activated protein kinase (AMPK) and its downstream target acetyl-CoA carboxylase (ACC) in H4IIE and Hep3B cells with 400 times (curcumin) to 100,000 times (THC) the potency of metformin. Curcuminoids did not exert a direct effect on receptor tyrosine kinase activity, 2-deoxyglucose uptake in L6-GLUT4myc cells or intestinal glucose metabolism measured by DPP4/ α -glucosidase inhibitory activity. The results suggested that AMPK-mediated suppression of hepatic gluconeogenesis may be a potential mechanism mediating glucose-lowering effects of curcuminoids. Kang and Kim (2010) found that curcumin could promote glucose uptake and AMPK (AMP-activated protein kinase)/ACC (acetyl-CoA carboxylase) activation, but not PI3-kinase (phosphoinositide 3-kinase)/Akt activation with increased insulin sensitivity in murine muscle cells as a potential antidiabetic therapeutic agent. Co-treatment of insulin and curcumin produced a mutual synergistic activation of both AMPK/ACC and PI3-kinase/Akt pathways.

The accumulation of advanced glycation end products (AGEs) in the body, due to the non-enzymatic glycation of proteins, was reported to be associated with several pathological conditions like ageing and diabetes mellitus (Khan et al. 2014). They found that crude methanolic extracts of fruits of *Capsicum frutescens* and *Curcuma longa* had antiglycation and antioxidation properties. Among the two, *C. frutescens* had more antiglycation ability with a minimum inhibitory concentration (MIC_{50}) of 90 μ g/mL as compared to 324 μ g/mL MIC_{50} of *C. longa*. *Curcuma longa* had the more antioxidation potential, i.e. 35.01, 30.83 and 28.08 % at 0.5 mg, 0.25 mg and 0.125 mg, respectively.

Animal Studies

The turmeric ethanol extract significantly suppressed an increase in blood glucose level in type II diabetic KK-A(y) mice (Kuroda et al. 2005). In an in-vitro evaluation, the extract stimulated human adipocyte differentiation in a dose-dependent manner and showed human peroxisome proliferator-activated receptor (PPAR)- γ ligand-binding

activity in a GAL4–PPAR- γ chimaera assay. The main constituents of the extract were identified as curcumin, demethoxycurcumin, bisdemethoxycurcumin and *ar*-turmerone, which had also PPAR- γ ligand-binding activity. The results indicated turmeric to be a promising ingredient of functional food for the prevention and/or amelioration of type II diabetes and that curcumin, demethoxycurcumin, bisdemethoxycurcumin and *ar*-turmerone mainly contributed to the effects via PPAR- γ activation.

Dietary administration of an aqueous extract of turmeric and abromine (*Abroma augusta*) powder resulted in a significant reduction in blood glucose and oxidative stress and an increase in total haemoglobin in streptozotocin-induced diabetic rats (Ali Hussain 2002). The herbal mixture also restored the other general parameters in diabetic animals. The results indicated that combination of herbal extracts showed better efficacy as compared to individual herbal plant extracts used. Oral administration of tetrahydrocurcumin (THC) (80 mg/kg body weight) to streptozotocin–nicotinamide-induced diabetic rats for 45 days showed a decrease in the level of blood glucose and plasma glycoproteins (Murugan and Pari 2006, 2007; Pari and Murugan 2007a, b). The levels of plasma insulin and tissue sialic acid were increased, whereas the levels of tissue hexose, hexosamine and fucose were near normal in diabetic rats treated with THC. In addition, THC caused significant increase in the activities of superoxide dismutase, catalase, glutathione peroxidase, glutathione S-transferase, reduced glutathione, vitamin C and vitamin E in the liver and kidney of diabetic rats with significant decrease in thiobarbituric acid-reactive substances (TBARS) and hydroperoxide formation in the liver and kidney, suggesting its role in protection against lipid peroxidation-induced membrane damage. Administration of THC and curcumin to diabetic rats showed decreased level of blood glucose, glycosylated haemoglobin and erythrocyte TBARS. In addition the levels of plasma insulin, haemoglobin, erythrocyte antioxidants and the activities of membrane-bound enzymes also were increased in THC- and curcumin-treated diabetic rats. These biochemical observations were supplemented by histopathological examination of liver, pancreas and kidney

sections. They also found that THC prevented brain lipid peroxidation in streptozotocin-induced diabetic rats (Murugan and Pari 2007). THC caused significant increases in the activities of superoxide dismutase, catalase, glutathione peroxidase, glutathione S-transferase and reduced glutathione in the brains of diabetic rats with significant decrease in the lipid peroxidative markers thiobarbituric acid-reactive substances and hydroperoxides in the brain. The antidiabetic and antioxidant effects of THC were more potent than those of curcumin at the same dose. The studies indicated that THC possessed a significant beneficial effect on glycoprotein moiety in addition to its antioxidant and antidiabetic effect.

Feeding of type II diabetic KK-A^y mice with hexane and ethanol turmeric extracts for 4 weeks suppressed the significant increase in blood glucose levels (Nishiyama et al. 2005). Furthermore, the ethanol extract stimulated human adipocyte differentiation, and these turmeric extracts had human peroxisome proliferator-activated receptor- γ (PPAR- γ) ligand-binding activity. Also, curcumin, demethoxycurcumin, bisdemethoxycurcumin and *ar*-turmerone had PPAR- γ ligand-binding activity. The results indicated that both curcuminoids and sesquiterpenoids in turmeric exhibited hypoglycaemic effects via PPAR- γ activation as one of the mechanisms and suggested that ethanol extract including curcuminoids and sesquiterpenoids had the additive or synergistic effects of both components. Weisberg et al. (2008) found that dietary curcumin admixture ameliorated diabetes in high-fat diet-induced obese and leptin-deficient ob/ob male C57BL/6 J mice as determined by glucose and insulin tolerance testing and haemoglobin A1c percentages. Curcumin treatment also significantly reduced macrophage infiltration of white adipose tissue, increased adipose tissue adiponectin production and decreased hepatic nuclear factor-kappaB activity, hepatomegaly and markers of hepatic inflammation. They concluded that orally ingested curcumin reversed many of the inflammatory and metabolic derangements associated with obesity and improved glycaemic control in mouse models of type II diabetes. Oral administration of curcumin to high-fat diet-fed diabetic rats exerted an anti-hyperglycaemic effect

and improved insulin sensitivity, and this action may be attributed at least in part to its anti-inflammatory properties as evident by attenuating TNF- α levels in HFD fed rats, and its anti-lipolytic effect as evident by attenuating plasma-free fatty acids (El-Moselhy et al. 2011). The curcumin effects were comparable to those of rosiglitazone. Turmeric aqueous extract stimulated insulin secretion from mouse pancreatic tissues under both basal and hyperglycaemic conditions (Mohankumar and McFarlane 2011). Turmeric extract induced stepwise stimulation of glucose uptake from abdominal muscle tissues in the presence and absence of insulin, and the combination of turmeric and insulin significantly potentiated the glucose uptake into abdominal muscle tissue.

In diabetic db/db mice, treatment with curcumin increased the expression of AMPK and PPAR- γ , and diminished NF- κ B protein in the liver, suggesting a beneficial effect of curcumin for treatment of type II diabetes mellitus complications (Jiménez-Flores et al. 2014). Antonyan et al. (2014) demonstrated that the complexation of curcumin with ruthenium(II) could be a promising starting point for the development of curcumin-based dipeptidyl peptidase-IV inhibitors. Specifically organometallic ruthenium(II) complexes of general formula $[(\eta(6)\text{-arene})\text{Ru}(\text{curcuminato})\text{Cl}]$, with arene being p-(i)PrC₆H₄Me (1), C₆H₆ (2) and C₆Me₆ (3), were evaluated for their inhibition activity towards the mammalian enzyme. Among them, two suppressed DPPIV activities more potently ($K_i = 20.2 \mu\text{M}$) than 1, 3 or free curcumin, and all complexes showed an antioxidant activity as free curcumin. In alloxan-induced diabetic rats, administration of crude and methanolic extract of *C. longa* significantly improved the levels of serum glucose, serum transaminases and antioxidant activity indicating its protective effect in diabetes especially type I diabetes (Ahmad et al. 2014a).

Clinical Studies

In a crossover study of 14 healthy subjects, the ingestion of 6-g *C. longa* increased postprandial serum insulin levels, but did not appear to affect plasma glucose levels or glycaemic index

(GI), in healthy subjects (Wickenberg et al. (2010). The results indicated that *C. longa* may have an effect on insulin secretion.

Antihypercholesterolaemic/Antihyperlipidaemic Activity

Ramirez-Tortosa et al. (1999) found that oral administration of a turmeric extract inhibited LDL oxidation and exerted hypocholesterolaemic effects in rabbits with experimental atherosclerosis by lowering total plasma cholesterol, phospholipids and triglycerides.

Ingestion of turmeric oleoresin and essential oil inhibited the development of increased blood glucose and abdominal fat mass, while curcuminoids only inhibited the increase in blood glucose in obese diabetic mice (Honda et al. 2006). Turmeric oleoresin ingestion upregulated the expression of genes related to glycolysis, β -oxidation and cholesterol metabolism in the liver of KK-Ay mice, while expression of gluconeogenesis-related genes was downregulated. Curcuminoids were also found to regulate turmeric oleoresin ingestion-induced expression of glycolysis-related genes; thus, curcuminoids and turmeric essential oil acted synergistically to regulate the peroxisomal β -oxidation-related gene expression induced by turmeric oleoresin ingestion. The results suggested that the use of whole turmeric oleoresin was more effective than the use of either curcuminoids or the essential oil alone.

The hydrophilic extracts of turmeric and laurel potently suppressed the incidence of atherosclerosis via a strong antioxidant potential, prevention of apolipoprotein A-I glycation and LDL phagocytosis and inhibition of cholesteryl ester transfer protein (Jin et al. 2011). Consumption of turmeric and laurel extracts exhibited hypolipidaemic and antioxidant activities in a hypercholesterolaemic zebrafish model. The plasma total cholesterol level was significantly lower in the turmeric and laurel groups (48 % and 28 % less, respectively, than in the HCD group). Plasma triglycerides were more markedly reduced in the turmeric and laurel groups

than in the HCD group (68 % and 56 % less, respectively, than the HCD group).

Oral administration of turmeric supplements to rats fed with a high-cholesterol diet caused a significant decrease in total plasma cholesterol and low-density lipoprotein cholesterol but an increase in high-density lipoprotein cholesterol when compared with rats that were fed with a high-cholesterol diet alone (Yiu et al. 2011). Fatty liver developed in hypercholesterolaemic rats with the high-cholesterol diet treatment, and this condition was markedly improved when rats were provided with turmeric supplements at 100 or 300 mg/kg of body mass. The turmeric treatment resulted in a significant decrease in the total amount of hepatic lipid. Histological staining of liver tissues with Sudan III and haematoxylin showed that rats fed with a high-cholesterol diet alone had more and larger granular fat bodies than rats having turmeric extract supplementation in their high-cholesterol diet. The results showed that rats fed with a high-cholesterol diet supplemented with turmeric extract had a significant increase in the expression of cholesterol 7 α -hydroxylase, haem oxygenase 1 and low-density lipoprotein receptors but a significant decrease in 3-hydroxy-3-methyl-glutaryl-CoA reductase level when compared with rats fed a normal or high-cholesterol diet, showing that turmeric prevented hypercholesterolemia and the formation of fatty liver by the modulation of expressions of enzymes important to cholesterol metabolism.

Studies by Neyrinck et al. (2013) found that turmeric extract associated with white pepper decreased high-fat diet-induced inflammation in subcutaneous adipose tissue of mice. This combination did not significantly modify body weight gain, glycaemia, insulinaemia, serum lipids and intestinal inflammatory markers. Tetrahydrocurcumin, but not curcumin, accumulated in the subcutaneous adipose tissue. Importantly, the co-supplementation in *Curcuma* extract and white pepper decreased HF-induced pro-inflammatory cytokine expression in the subcutaneous adipose tissue, an effect independent of adiposity, immune cell recruitment, angiogenesis or modulation of gut bacteria controlling inflammation.

Dietary turmeric curcuminoids and ginger extract for 6 weeks exerted an anti-atherogenic effect in hypercholesterolaemic rabbits (Elseweidy et al. 2014). Ginger extract exerted preferential effects on plasma lipids, reversed cholesterol transport, cholesterol synthesis and inflammatory status. Curcuminoids, however, showed superior antioxidant activity. Curcumin treatment appeared to be effective in reducing liver triglycerides and serum fetuin-A levels in rats fed with a high-fat diet (Öner-İyidoğan et al. 2013). These findings suggested that the reduction of fetuin-A may contribute to the beneficial effects of curcumin in the pathogenesis of obesity. Supplementation of a high-fat diet with curcumin in rats increased hepatic hemoxygenase-1 (HO-1) expression and reduced hepatic lipid accumulation, fibrotic changes and oxidative stress parameters (Öner-İyidoğan et al. 2014). All these contributed to the beneficial effects of curcumin in attenuating the pathogenesis of fatty liver-induced metabolic diseases.

Clinical Studies

The study of Ramirez-Boscá et al. (1995) showed that a 45-day intake (by healthy human individuals ranging in age from 27 to 67 years) of *Curcuma longa* hydroalcoholic extract (at a daily dose equivalent to 20 mg of curcumin) resulted in a significant decrease in the levels of serum lipid peroxides. They also found that a daily oral administration of turmeric hydroalcoholic extract decreased significantly the LDL and apo B and increases the HDL and apo A of healthy subjects (Ramirez-Boscá et al. 2000). In a randomised double-blind placebo-controlled crossover study of 30 obese dyslipidaemic subjects, 4-week supplementation with curcuminoids (1 g/day) did not cause any significant alteration in serum small dense low-density lipoprotein (Moohebbati et al. 2014). In a randomised placebo-controlled trial of 100 patients (treated = 50, placebo = n50), with metabolic syndrome (MS), administration of curcuminoid–piperine combination was found to be an efficacious adjunctive therapy in patients with MS and could modify serum lipid concentrations (Panahi et al. 2014b). Curcuminoids were more effective than placebo in

reducing serum LDL-C, non-HDL-C, total cholesterol, triglycerides and lipoprotein (a) and elevating HDL-C concentrations.

Immunomodulatory Activity

Studies since the last two decades had shown curcumin to be a potent immunomodulatory agent that can modulate the activation of T cells, B cells, macrophages, neutrophils, natural killer cells and dendritic cells (Jagetia and Aggarwal 2007). Curcumin at low doses could also enhance antibody responses. Studies suggested that curcumin's reported beneficial effects in arthritis, allergy, asthma, atherosclerosis, heart disease, Alzheimer's disease, diabetes and cancer might be due in part to its ability to modulate the immune system. Curcumin could also have potential in the therapy for immune disorders.

Three polysaccharides were isolated from *C. longa* rhizomes: ukonan A, ukonan B and ukonan C (Gonda et al. 1990, 1992b, 1993; Tomoda et al. 1990; Gonda and Tomoda 1991), and ukonan D (Gonda et al. 1992a) exhibited remarkable reticuloendothelial system potentiating in a carbon clearance test. Ukonan A, C has marked reticuloendothelial system potentiating, anti-complementary and alkaline phosphatase-inducing activities (Gonda et al. 1992b, 1993). Periodate oxidation and treatment with enzyme caused a decline or disappearance of the polysaccharides' immunological activity, but the controlled Smith degradation product having the core structure of polysaccharide showed considerable restoration of these activities. Studies showed that curcumin could block cyclosporine A-resistant phorbol myristate acetate (PMA) + anti-CD28 pathway of human T-cell proliferation, suggesting that it may have novel adjuvant immunosuppressive properties (Ranjan et al. 1998). In further studies, they found that curcumin had profound immunosuppressive effects mediated via inhibition of interleukin IL-2 synthesis, mitogen and IL-2 induced activation of human lymphocytes (Ranjan et al. 2004). This effect may be mediated via NF-kappaB inhibition. Studies showed that low concentrations of curcumin significantly

downregulated mitogen-induced granulocyte macrophage colony stimulating factor (GM-CSF) mRNA (3- to 5-fold at 3 μ M) in a dose- and time-dependent manner in both T Jurkat CD4⁺ and human peripheral blood mononuclear cell (PBMC) types (Gertsch et al. 2003). In addition, cytotoxic effects and downregulation of mRNAs, including p65 and the house-keeping genes, could only be measured in Jurkat T cells. The findings confirmed the anti-neoplastic potential of curcumin and showed that curcumin differentially modulated the expression profile of Th1 cells and PBMCs. Curcumin completely inhibited OKT3-induced human peripheral blood mononuclear cell (PBMC) proliferation in a dose-dependent manner with an IC₅₀ of 2.8 μ M, while sirolimus, the mTOR inhibitor, could reduce PBMC proliferation dose dependently only to a minimum of 28 % at a concentration of 5 ng/ml (IC₅₀ 1.1 ng/ml) (Deters et al. 2013). Combination of curcumin (1.25–2.5 μ M) with sirolimus (5 ng/ml) showed additive effects. The effects after combination of curcumin at 5 μ M with each sirolimus concentration and sirolimus at 10 ng/ml with each curcumin concentration were presumably antagonistic. It was concluded that the immunosuppressive effects of curcumin and sirolimus in low concentrations were synergistic in OKT3-activated PBMC. Turmeric crude extract was found to attenuate carbon tetrachloride-induced oxidative stress in T-lymphocyte subpopulations (Abu-Rizq et al. 2015). Treatment with the extract of two different doses showed a significant restoration of lymphocyte viability and CD25, CD71 and Con A receptor expression in both immature (PNA+) thymocytes and splenic helper (CD4(+)) T lymphocytes. Turmeric crude extract, at both low and high dose, was found to be more efficient as compared to purified curcumin, suggesting synergistic effect of curcumin with other components of the crude extract.

Curcumin exhibited immunostimulatory activity in BALB/c mice (Antony et al. 1999). Curcumin administration was found to significantly increase the total WBC count and circulating antibody titre (512) against SRBC. Curcumin administration increased the plaque-forming cells (PFC) in the spleen, and the maximum number of PFC was observed on the

6th day after immunisation with SRBC. Bone marrow cellularity and α -esterase-positive cells were also enhanced by curcumin administration. A significant increase in macrophage phagocytic activity was also observed in curcumin-treated animals. Studies showed that *C. longa* polysaccharides exhibited immunostimulatory effects on human peripheral blood mononuclear cells (Yue et al. 2010a). The polysaccharide-enriched fraction modulated cytokine productions (TGF- β , TNF- α , GM-CSF, IL-1 α , IL-5, IL-6, IL-8, IL-10, IL-13, etc.). The findings revealed the potential use of *C. longa* crude extract (containing curcuminoids and polysaccharides) as an adjuvant supplement for cancer patients, whose immune activities were suppressed during chemotherapies.

Exogenous curcumin treatment (100 mg/kg/day) significantly delayed the onset of experimental autoimmune neuritis (EAN) neurological signs, ameliorated EAN neurological severity and reduced body weight loss of EAN rats (Han et al. 2014). In EAN sciatic nerves, curcumin treatment suppressed the inflammatory cell accumulation and the expression of interferon (IFN)- γ , tumour necrosis factor- α , interleukin (IL)-1 β and IL-17. Furthermore, curcumin treatment significantly decreased the percentage of CD4(+) T-helper cells in EAN spleen and suppressed concanavalin A-induced lymphocyte proliferation in-vitro. In addition, curcumin altered helper T-cell differentiation by decreasing IFN- γ (+) CD4(+) Th1 cells in EAN lymph node and spleen.

Neuroprotective and CNS Activity

Recent studies had reported curcumin to possess anti-amyloidogenic, anti-inflammatory, antioxidative and metal chelating properties that may result in potential neuroprotective effects (Chin et al. 2013). Particularly, the hydrophobicity of the curcumin molecule suggested the possibility of blood–brain barrier penetration and accumulation in the brain. However, curcumin exhibits extremely low bioavailability, mainly due to its poor aqueous solubility, poor stability in solution and rapid intestinal first-pass and hepatic metabolism.

In-Vitro Studies

Curcumin was demonstrated to be a potent inhibitor of the inositol 1,4,5-trisphosphate-sensitive Ca^{2+} channel (InsP3 receptor) (Dyer et al. 2002). In porcine cerebellar microsomes, the extent of InsP3-induced Ca^{2+} release (IICR) was almost completely inhibited by 50- μM curcumin ($\text{IC}_{50} = 10 \mu\text{M}$). In addition, curcumin also reduced agonist (ATP)-stimulated Ca^{2+} mobilisation from intact HL-60 cells, indicating that curcumin was cell permeant. However, since it also affected intracellular Ca^{2+} pumps and possibly ryanodine receptors, it may lead to complex Ca^{2+} transient responses within cells, which may well explain some of its putative therapeutic properties. Studies showed that curcumin dose- and time-dependently inhibited rat neuroglial cell proliferation and growth in-vitro (Ambegaokar et al. 2003). Proliferative inhibition was associated with morphological changes, e.g. cell elongation and neurite prolongation, and increased activity of a marker enzyme corresponding to differentiation of oligodendrocytes and with a reduced activity of the marker enzyme for astrocytes. Given neuroglial involvement in anti-inflammatory and antioxidant diseases, the results obtained may provide further explanations of curcumin's preventative–therapeutic role in these diseases.

Studies by Lee et al. (2007) suggested that curcumin-mediated neuroprotective effects may be mostly due to its anti-inflammatory effects. Curcumin did not protect dopamine-directed neuronal cell death and sodium nitroprusside (SNP)-induced NO generation but only blocked activated microglial cell-mediated neuronal cell damage under inflammatory conditions. Curcumin blocked the production of pro-inflammatory and cytotoxic mediators such as NO, $\text{TNF-}\alpha$, IL- 1α and IL-6 produced from A β (25–35)/IFN- γ - and LPS-stimulated microglia, in a dose-dependent manner. A neuroprotective fraction from turmeric rhizome was standardised on the basis of three-marker compound isolated, i.e. *ar*-turmerone, turmerone and curlone (Jain et al. 2007). The composition of marker compounds was found to be 50–60 %, and the content of curcuminoids was found to be 0.32–0.55

% . Theracurmin, a highly bioavailable curcumin, and curcumin, significantly prevented sodium nitroprusside (SNP)-induced cytotoxicity and oxidative stress in primary rat striatal cell culture (Nazari et al. 2013). It was found that Theracurmin and curcumin exerted potent neuroprotective effects against SNP-induced cytotoxicity by free DPPH radical scavenging and iron-chelating activities.

Curcumin protected against 1-methyl-4-phenylpyridinium ion-induced and lipopolysaccharide-induced cytotoxicities in the mouse mesencephalic astrocyte through inhibiting the cytochrome P450 2E1 expression and activity (Gui et al. 2013).

Studies demonstrated that pretreatment of SH-SY5Y dopaminergic cell with curcumin I protected neurons against oxidative damage induced by 6-hydroxydopamine (6-OHDA), as shown by attenuation of p-p38 expression, caspase-3 activation and toxic quinoprotein formation, together with the restoration of p-TH levels (Meesarapee et al. 2014). The results highlighted therapeutic potential of curcumin I in the chemoprevention of oxidative stress-related neurodegeneration. Curcumin was found to act as a neuroprotectant against hemin-induced damage in primary cultures of cerebellar granule neurons (CGNs) of rats (González-Reyes et al. 2013). Pretreatment of CGNs with 5–30 μ M curcumin effectively increased by 2.3–4.9-fold haem oxygenase-1 (HO-1) expression and by 5.6–14.3-fold glutathione (GSH) levels. Moreover, 15- μ M curcumin attenuated by 55 % the increase in reactive oxygen species (ROS) production, by 94 % the reduction of GSH/glutathione disulphide (GSSG) ratio and by 49 % the cell death induced by hemin. Further, it was found that 24 h of incubation with curcumin increased by 1.4-, 2.3- and 5.2-fold the activity of glutathione reductase, glutathione S-transferase and superoxide dismutase, respectively. Additionally, curcumin induced nuclear factor (erythroid-derived 2)-like 2 (Nrf2) translocation into the nucleus. The data suggested that the pretreatment with curcumin induced Nrf2 and an antioxidant response that may play an important role in the protective

effect of this antioxidant against hemin-induced neuronal death.

In-Vivo Studies

Oral administration of curcumin to rats caused a significant reversal in lipid peroxidation, brain lipids and produced enhancement of glutathione, a non-enzymatic antioxidant in ethanol-intoxicated rats, revealing that the antioxidative and hypolipidaemic action of curcumin was responsible for its protective role against ethanol-induced brain injury (Rajakrishnan et al. 1999). Oral administration of turmeric aqueous extracts to the mice from 140 to 560 mg/kg for 14 days elicited dose-dependent relation of immobility reduction in the tail suspension test and the forced swimming test in mice (Yu et al. 2002). The effects of the extracts at the dose of 560 mg/kg were more potent than that of reference antidepressant fluoxetine. The extracts, at the dose of 140 mg/kg or above for 14 days, significantly inhibited the monoamine oxidase A (MAO) activity in mouse whole brain at a dose-dependent manner; however, oral administration of the extract only at a dose of 560 mg/kg produced observable MAO B inhibitory activity in animal brain. Neither the extracts of *C. longa* nor fluoxetine, at the doses tested, produced significant effects on locomotor activity. The results demonstrated that *C. longa* had specifically antidepressant effects in-vivo and may be mediated in part through MAO-A inhibition in mouse brain.

Exposure of rats to lead (50 mg/kg p.o.) for 45 days caused an increase in lipid peroxidation (LPO) and a decrease in reduced glutathione (GSH) levels, SOD and catalase activities in the cerebellum, corpus striatum, hippocampus and frontal cortex and lead levels as compared with controls (Shukla et al. 2003). Cotreatment with curcumin (100 mg/kg p.o.) and lead (50 mg/kg p.o.) for 45 days caused a significant decrease in LPO with concomitant decrease in lead levels in all the brain regions as compared with those treated with lead alone. A significant increase in reduced glutathione (GSH) levels, SOD and CAT activities was also observed in all the four brain regions in rats simultaneously treated with curcumin and lead.

Another study showed that curcumin significantly protected against lead- and cadmium-induced lipid peroxidation in rat brain homogenate and hippocampal cells of male Wistar rats (Daniel et al. 2004). Possible chelation of lead and cadmium by curcumin forming a complex was suggested as one of its mechanism of neuroprotection against such heavy metal insult to the brain. In another study, administration of curcumin by i.p. injections (30 mg/kg body wt) or by supplementation to the AIN76 diet (2.0-g/kg diet) for 2 months significantly attenuated ischaemia-induced neuronal death as well as glial activation in Mongolian gerbils (Wang et al. 2005). Curcumin administration also decreased lipid peroxidation, mitochondrial dysfunction and the apoptotic indices. The biochemical changes resulting from curcumin also correlated well with its ability to ameliorate the changes in locomotor activity induced by cerebral ischaemia/reperfusion. Supplementation of curcumin in the high-fat diet dramatically reduced oxidative damage and normalised levels of BDNF (brain-derived neurotrophic factor), synapsin I and CREB (cAMP response element-binding protein) that had been altered after traumatic brain injury (TBI) in rats (Wu et al. 2006). Additionally, curcumin supplementation counteracted the cognitive impairment caused by TBI. Further, they found that dietary curcumin supplementation counteracted reduction in levels of molecules involved in energy homeostasis after brain trauma in rats caused by mild fluid percussion injury (FPI) (Sharma et al. 2009). The curcumin diet counteracted the effects of FPI and elevated the levels of AMP-activated protein kinase (AMPK), ubiquitous mitochondrial creatine kinase (uMtCK) and cytochrome c oxidase II (COX-2) in curcumin-fed FPI rats as compared to the regular diet-fed sham rats.

The study of Bala et al. (2006) demonstrated the antioxidative, antilipofuscinogenesis and anti-ageing effects of curcumin in the rat brain. Chronic curcumin treatment of both 6- and 24-month-old rats resulted in significant decreases in lipid peroxide and the lipofuscin contents in brain regions; the activities of SOD, GPx and Na(+), K(+) and ATPase, however, showed significant increase in various brain regions. Kumar et al. (2007) found that chronic treatment with curcumin (10, 20

and 50 mg/kg, p.o.) once daily for a period of 8 days beginning 4 days prior to 3-nitropropionic acid (3-NP) administration dose-dependently improved the 3-NP-induced motor and cognitive impairment in rats. Biochemical analysis revealed that curcumin administration significantly attenuated 3-NP-induced oxidative stress (lipid peroxidation estimation, reduced glutathione and nitrite activity) in the brains of rats. It also significantly restored the decreased succinate dehydrogenase activity. Jiang et al. (2007) reported that a single injection of curcumin (1 and 2 mg/kg, i.v.) 30 min after focal cerebral ischaemia/reperfusion in rats significantly diminished infarct volume, improved neurological deficit, decreased mortality and reduced the water content of the brain and the extravasation of Evans blue dye in ipsilateral hemisphere in a dose-dependent manner. In cultured astrocytes, curcumin significantly inhibited inducible nitric oxide synthase (iNOS) expression and NO(x) (nitrites/nitrate contents) production induced by lipopolysaccharide (LPS)/tumour necrosis factor α (TNF(α)). In addition, curcumin prevented peroxynitrite donor SIN-1(3-norpholinosyndnomine)-induced cerebral capillaries' endothelial cell damage. They concluded that curcumin ameliorated cerebral ischaemia/reperfusion injury by preventing peroxynitrite-mediated blood–brain barrier damage.

Xing et al. (2010) demonstrated that curcumin pretreatment had a beneficial role in mitigating acrylonitrile-induced oxidative stress both in the brains and livers of exposed rats, and these effects were mediated independently of cytochrome P450 2E1 inhibition. The results suggested that curcumin should be considered as a potential safe and effective approach in attenuating the adverse effects produced by acrylonitrile-related toxicants. Curcumin (10 μ g/ml) was found to significantly inhibit the apoptosis of pre-oligodendrocytes and expression of either iNOS or NOX in the LPS-activated microglia (He et al. 2010). In-vivo, treatment with curcumin (50 mg/kg/day, i.p.) either 1 h before or immediately after LPS injection significantly ameliorated white matter injury and loss of pre-oligodendrocytes, decreased activated microglia and inhibited microglial

expression of iNOS and translocation of p67phox and gp91phox to the microglial cell membranes in neonatal rat brains following LPS injection. The results suggested that curcumin had a protective effect on infection-driven white matter injury, which was associated with suppression of iNOS and NOX activation. Chronic administration of D-galactose to mice for 6 weeks significantly impaired cognitive function (both in Morris water maze and elevated plus maze), locomotor activity, oxidative defence (raised lipid peroxidation, nitrite concentration, depletion of reduced glutathione and catalase activity) and mitochondrial enzyme complex activities (I, II and III) as compared to vehicle-treated group (Kumar et al. 2011). Curcumin (15 and 30 mg/kg) and galantamine (5 mg/kg) treatment for 6 weeks significantly improved cognitive tasks, locomotor activity and oxidative defence and restored mitochondrial enzyme complex activity as compared to control (D-galactose). Chronic D-galactose treatment also significantly increased acetylcholine esterase activity that was attenuated by curcumin (15 and 30 mg/kg) and galantamine (5 mg/kg) treatment. The data highlighted the therapeutic potential of curcumin against D-galactose-induced senescence in mice.

Oral administration of turmeric ethanol extract for 21 days reduced the duration of mouse immobility in the forced swimming test (Xia et al. 2007). Turmeric extract markedly attenuated swim stress-induced decreases in serotonin, 5-hydroxyindoleacetic acid, noradrenaline and dopamine concentrations as well as increases in serotonin turnover. Furthermore, the ethanolic extract of *Curcuma longa* significantly reversed the swim stress-induced increases in serum corticotropin-releasing factor and cortisol levels. The results suggested that antidepressant properties of turmeric ethanolic extract were mediated through regulations of neurochemical and neuroendocrine systems, and it may be a useful agent against depression. Chronic administration of curcumin significantly improved memory retention in both Morris water maze, elevated plus-maze task paradigms, attenuated oxidative damage, acetylcholinesterase activity and aluminium concentration in aluminium-treated rats (Kumar et al. 2009a). The results suggested that curcumin had

neuroprotective effects against aluminium-induced cognitive dysfunction and oxidative damage. After spinal cord injury (SCI) in rats, 30-mg/kg curcumin was found to improve rats' motor function, and 100-mg/kg curcumin effect was more obvious, especially in promoting the expression of calcitonin gene-related peptide which may be the mechanism of protection of the nervous system (Sun and Xu 2013). Chronic treatment with curcumin significantly reversed the chronic mild stress-induced behavioural abnormalities (reduced sucrose preference and decreased locomotor activity) in stressed rats (Jiang et al. 2013a). Additionally, curcumin effectively inhibited cytokine gene expression at both the mRNA and the protein level and reduced the activation of NF- κ B. The study revealed that curcumin exerted antidepressant-like effects in chronic mild stress rats, partially due to its anti-inflammatory property. Studies in an animal model of traumatic memory formation in post-traumatic stress disorder (PTSD) found that a diet enriched with curcumin impaired fear memory consolidation and reconsolidation processes, findings which may have important clinical implications for the treatment of disorders such as PTSD (Monsey et al. 2014). The study by Xie et al. (2014b) confirmed the antagonistic roles of curcumin to counteract radiation-induced cerebral injury in mice and suggested that the potent Nrf2 activation capability might be important for the protective effects of curcumin against radiation. The results showed that 4Gy heavy ion radiation-induced spatial strategy and memory decline and reduction of brain superoxide dismutase (SOD) activity levels were all consistently improved by curcumin, and the augmentation of cerebral malondialdehyde (MDA) was lowered by curcumin.

The administration of *C. longa* significantly shortened the escape latency in both adult and *D*-galactose-induced aged mice and significantly ameliorated *D*-galactose-induced reduction of cell proliferation and neuroblast differentiation in the subgranular zone of hippocampal dentate gyrus (Nam et al. 2014). Furthermore, the administration of *C. longa* significantly increased the levels of phosphorylated CREB and brain-derived neurotrophic factor in the subgranular zone of dentate gyrus. The results indicated that *C. longa* mitigated *D*-

galactose-induced cognitive impairment, associated with decreased cell proliferation and neuroblast differentiation, by activating CREB signalling in the hippocampal dentate gyrus.

Rastogi et al. (2014) demonstrated the neuroprotective effect of turmeric rhizome curcuminoids, on mitochondrial dysfunctioning in middle-aged and aged female Wistar rat brain. Long-term curcuminoid administration prevented this age-associated loss of mitochondrial enzymes and complex activity in middle-aged rat brain. Among aged rats, curcuminoid treatment specifically elevated isocitrate and NADH dehydrogenase, cytochrome c oxidase, complex I and total ATP content. A significant downregulation of nNOS protein expression along with reduced lipofuscin content was also observed in curcuminoid-treated middle-aged and aged rats. Studies in male Sprague Dawley rats showed that both turmeric curcuminoid mixture and curcumin I lacked hedonic properties and inhibited the reward-facilitating effect of morphine at subthreshold doses (Katsidoni et al. 2014). Their data suggested that curcumin interfered with brain reward mechanisms responsible for the expression of the acute reinforcing properties of opioids and provided evidence that curcumin may be a promising adjuvant for attenuating morphine's rewarding effects in patients who are under long-term opioid therapy. Curcumin was found to stimulate neural stem cell proliferation in-vitro and, in combination with stem cell therapy, synergistically induced profound recovery from severe spinal cord injury as evidenced by improved functional locomotor recovery, increased body weight and soleus muscle mass in rats (Ormond et al. 2014). Also the results indicated that the effect of curcumin extended beyond its known anti-inflammatory properties to the regulation of stem cell proliferation. Turmerone (2.5, 5.0 mg/kg, p.o.) significantly reduced the immobility time of mice in both the forced swimming test and tail suspension test, but it did not significantly affect the ambulatory and total movements of mice. The mechanisms of action of anti-depressive effect of turmerone appeared to involve an increase of the monoamines level decreasing the monoamine oxidase A (MAO-A) activity and the stress of mice.

Clinical Studies

In a 6-week, randomised controlled trial of 60 patients with major depressive disorder (MDD), treatment with curcumin (1000 mg) was found to be as an effective, safe and well-tolerated modality for treatment in patients with MDD without concurrent suicidal ideation or other psychotic disorders (Sanmukhani et al. 2014).

Neuroprotective (Alzheimer's Disease) Activity

According to the review by Ahmed and Gilani (2014), each component of the curcuminoid mixture plays a distinct role in making curcuminoid mixture useful in Alzheimer's disease, and hence, the curcuminoid mixture represents turmeric in its medicinal value better than curcumin alone.

In-Vitro Studies

Alzheimer's disease (AD) is believed to involve increased soluble but toxic β -amyloid ($A\beta$) peptide aggregates, leading to the accumulation of insoluble $A\beta$ deposits, inflammation, oxidative damage, tau pathology and ultimately cognitive deficits (Kim et al. 2001; Lim et al. 2001; Cole et al. 2003; Ringman et al. 2005; Garcia-Alloza et al. 2007). Three turmeric curcuminoids, curcumin, demethoxycurcumin and bisdemethoxycurcumin, were found to protect neuronal PC12 rat pheochromocytoma and normal human umbilical vein endothelial (HUVEC) cells from β -amyloid (βA) (1–42) insult (Kim et al. 2001). ED_{50} values of curcumin, demethoxycurcumin and bisdemethoxycurcumin towards PC12 and HUVEC cells were 7.1, 4.7 and 3.5 $\mu\text{g/ml}$ and 6.8, 4.2 and 3.0 $\mu\text{g/ml}$, respectively. These compounds were better antioxidants than α -tocopherol as determined by DPPH radical scavenging assay. α -Tocopherol did not protect the cells from $\beta A(1-42)$ insult even at $>50\text{-}\mu\text{g/ml}$ concentration. The results suggested that these compounds may be protecting the cells from $\beta A(1-42)$ insult through antioxidant pathway. Lim et al. (2001) found that low (160 ppm) and high doses (500 ppm) of

curcumin significantly lowered oxidised proteins and interleukin-1 β , a pro-inflammatory cytokine elevated in the brains of APPSw mice. With low-dose but not high-dose curcumin treatment, the astrocytic marker GFAP (glial fibrillary acidic protein) was reduced, and insoluble β -amyloid (A β), soluble A β and plaque burden were significantly decreased by 43–50 %. However, levels of amyloid precursor (APP) in the membrane fraction were not reduced. Microgliosis was also suppressed in neuronal layers but not adjacent to plaques. The data suggested curcumin to have promise for the prevention of Alzheimer's disease. It was found that calebin A and its derivatives 21, 28 and 30 protect PC12 rat pheochromocytoma and IMR-32 human neuroblastoma cells from β -amyloid(25–35) insult (Kim and Kim 2001). Turmeric compounds calebin A, curcumin, demethoxycurcumin, bisdemethoxycurcumin and 1,7-bis(4-hydroxyphenyl)-1-heptene-3,5-dione were found to more effectively protect PC12 cells from β -amyloid insult (ED_{50} = 0.5–10 μ /mL) than Congo red (ED_{50} = 37–39 μ g/mL) (Park and Kim 2002). The study by Fiala et al. (2007) found that the curcuminoid bisdemethoxycurcumin could enhance immune defects of AD patients and provide a previously uncharacterised approach to AD immunotherapy. In mononuclear cells of some AD patients, bisdemethoxycurcumin could ameliorate defective phagocytosis of Abeta, the transcription of β -1,4-mannosylglycoprotein 4- β -N-acetylglucosaminyltransferase (MGAT3) and Toll-like receptors (TLRs) and the translation of TLR2-4.

Giri et al. (2003) showed that interaction of Abeta1-40 or fibrillar Abeta1-42 caused activation of nuclear transcription factor, early growth response-1 (Egr-1), which resulted in increased expression of cytokines (TNF- α and IL-1 β) and chemokines (MIP-1 β , MCP-1 and IL-8) in THP-1 monocytes. In subsequent studies, they found that curcumin inhibited activation of Egr-1 DNA-binding activity, amyloid peptide-induced cytochemokine gene expression and CCR5-mediated chemotaxis of THP-1 monocytes by modulating early growth response-1 transcription factor (Giri et al. 2004). The inhibition of Egr-1 by curcumin may represent a potential

therapeutic approach to ameliorate the inflammation and progression of Alzheimer's disease.

The combined NSAID (nonsteroidal anti-inflammatory drug)/antioxidant curcumin was found to be most efficacious in reducing amyloid, oxidative damage, inflammation and synaptic marker loss (Cole et al. 2003). One central mechanism underlying curcumin's reductions in soluble and guanidine-extracted insoluble A β appeared to be the stimulation of phagocytic clearance pathways and exerting net anti-inflammatory activity. Baum and Ng (2004) proposed another possible mechanism for curcumin preventive effect against Alzheimer's disease as metal chelation which may reduce amyloid aggregation or oxidative neurotoxicity. Since curcumin more readily binds the redox-active metals iron and copper than redox-inactive zinc, curcumin might exert a net protective effect against A β toxicity or might suppress inflammatory damage by preventing metal induction of NF- κ B. Pretreatment of neuronal PC12 cells with turmeric water extract (0.5–10 μ g/ml) prior to H₂O₂ exposure significantly elevated the cell survival and antioxidant enzyme (glutathione peroxidase and catalase) activities and decreased the level of malondialdehyde (MDA) (Koo et al. 2004). The above-mentioned neuroprotective effects were also observed with tacrine (THA, 1 μ M), suggesting that the neuroprotective effects of cholinesterase inhibitor might partly contribute to the clinical efficacy in Alzheimer's disease treatment. Curcumin and rosmarinic acid dose-dependently inhibited β -amyloid fibril (fA β) formation from A β (1–40) to A β (1–42), as well as their extension (Ono et al. 2004). In addition, they dose-dependently destabilised preformed fA β s. The overall activities of curcumin, rosmarinic acid and nordihydroguaiaretic acid (NDGA) were similar. The effective concentrations (EC₅₀) of Cur, RA and NDGA for the formation, extension and destabilisation of fA β s were in the order of 0.1–1 μ M.

Curcumin was shown to possess suitable charge and bonding features to facilitate the binding to Abeta (Balasubramanian 2006). In addition, curcumin's anti-inflammatory and antioxidant properties were also attributed

to electronic and structural features. It was shown that the presence of an enolic centre and two phenolic polar groups separated by an essentially hydrophobic bridge of a conjugated network provided both hydrophobic and hydrophilic features to the curcumin pigment, thereby facilitating penetration into the blood–brain barrier through the former property and then binding to Abeta oligomer through the latter property. Zhang et al. (2006) found that after treatment of macrophages with curcuminoids, amyloid- β (A β) uptake by macrophages of three of the six Alzheimer's disease patients was significantly increased. Confocal microscopy of AD macrophages responsive to curcuminoids showed surface binding in untreated macrophages but co-localisation with phalloidin in an intracellular compartment after treatment. Dairam et al. (2008) demonstrated that curcumin significantly curtailed iron (Fe²⁺)- and quinolinic acid (QA)-induced lipid peroxidation and potentially scavenge the superoxide anion generated by 1-mM cyanide in rat brain homogenate. Curcumin bound Fe²⁺ and Fe³⁺ and prevented the redox cycling of iron, suggesting that this may be an additional method through which these agents reduce Fe²⁺-induced lipid peroxidation. The results suggested that curcumin could have important implications in the prevention or treatment of neurodegenerative diseases such as Alzheimer's disease.

Zhang et al. (2008) found that curcumin (Cur), demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC) significantly suppressed nitric oxide (NO) production by LPS-activated microglia, and the relative potency was DMC > BDMC > Cur. All three curcuminoid pigments attenuated the expression of mRNA and proteins of tumour necrosis factor α (TNF- α) in a concentration-dependent manner, and the relative potency was also DMC > BDMC > Cur. It was concluded that Cur, DMC and BDMC were potent microglia activation inhibitors, and DMC exhibited the strongest inhibitory activity on NO and TNF- α production. The results suggested that they may have potential therapeutic implications for various neurodegenerative diseases. All three turmeric extracts, HSS-838, HSS-848 and HSS-888, and the curcuminoids (curcumin,

tetrahydrocurcumin, demethoxycurcumin and bisdemethoxycurcumin) showed dose-dependent inhibition of Abeta fibril (fA β) aggregation from Abeta(1-42) in the cell-free assay, with IC₅₀ values of $\leq$ 5 μ g/mL (Shytle et al. 2009). However, only HSS-888, curcumin and demethoxycurcumin significantly decreased Abeta secretion (approximately 20 %) in human neuronal (SweAPP N2A) cells. Only simple additive effects were observed for the Abeta aggregation inhibition, supporting the notion that the known curcuminoids were not strong inhibitors of this activity. However, HSS-888 showed strong inhibition of Abeta aggregation and secretion, thus indicating that there were novel bioactive molecules in this extract that might be important leads for future Alzheimer's disease drug discovery efforts.

Curcuminoids inhibited acetylcholinesterase (AChE) in the in-vitro assay with IC₅₀ values of 19.67, bisdemethoxycurcumin 16.84, demethoxycurcumin 33.14 and curcumin 67.69 μ M (Ahmed and Gilani 2009). In the ex-vivo AChE assay, curcuminoids and its individual components except curcumin showed dose-dependent (3–10 mg/kg) inhibition in frontal cortex and hippocampus. All compounds at a fixed dose (10 mg/kg) showed significant and comparable effect in scopolamine-induced amnesia. The data indicated that curcuminoids and all individual components except curcumin possess pronounced AChE inhibitory activity and that curcuminoid mixture might possess better therapeutic profile than curcumin for its medicinal use in Alzheimer's disease.

ar-Turmerone significantly suppressed A β -induced expression and activation of MMP-9, iNOS and COX-2, but not MMP-2 in BV2 microglial cells (Park et al. 2012a). The results suggested that *ar*-turmerone impaired the A β -induced inflammatory response of microglial cells by inhibiting the NF- κ B, JNK and p38 MAPK signalling pathways. Lastly, *ar*-turmerone protected hippocampal HT-22 cells from indirect neuronal toxicity induced by activated microglial cells and may have therapeutic potential for the treatment of neurodegenerative disorders. They found that *ar*-turmerone anti-inflammatory effects in LPS-stimulated microglial cells

were mediated by protein kinase A and haem oxygenase-1 signalling (Park et al. 2012b). Curcumin inhibited the AKT/NF- κ B signalling and pro-inflammatory targets including COX-2 and iNOS via CpG demethylation of the promoter and restoration of neprilysin in mouse neuroblastoma N2a cell line (Deng et al. 2014). The results afforded evidence for using curcumin as a therapeutic intervention for Alzheimer's disease.

Animal Studies

Dietary curcumin (2000 ppm), but not ibuprofen, suppressed oxidative damage (isoprostane levels) and synaptophysin loss in Sprague Dawley (SD) rats (Frautschy et al. 2001). Both ibuprofen and curcumin reduced microgliosis in cortical layers, but curcumin increased microglial labelling within and adjacent to Abeta-ir deposits. In a second group of middle-aged female SD rats, 500-ppm dietary curcumin prevented Abeta-infusion-induced spatial memory deficits in the Morris water maze and postsynaptic density (PSD)-95 loss and reduced Abeta deposits. Curcumin inhibited formation of amyloid β -oligomers and fibrils, binds plaques and reduces amyloid in-vitro and in-vivo (Yang et al. 2005). Under amyloid β (A β) aggregating conditions in-vitro, curcumin inhibited aggregation ($IC_{50} = 0.8 \mu\text{m}$) as well as disaggregated fibrillar A β 40 ($IC_{50} = 1 \mu\text{m}$). Curcumin was a better A β 40 aggregation inhibitor than ibuprofen and naproxen and prevented A β 42 oligomer formation and toxicity between 0.1 and 1.0 μm . Curcumin decreased dose-dependently A β fibril formation beginning with 0.125 μm . Alzheimer's disease (AD) and Tg2576 mice brain sections incubated with curcumin revealed preferential labelling of amyloid plaques. In-vivo studies showed that curcumin injected peripherally into aged Tg mice crossed the blood-brain barrier and bound plaques. When fed to aged Tg2576 mice with advanced amyloid accumulation, curcumin labelled plaques and reduced amyloid levels and plaque burden.

Using in-vivo multiphoton microscopy (MPM), Garcia-Alloza et al. (2007) demonstrated that curcumin crossed the

blood–brain barrier and labelled senile plaques and cerebrovascular amyloid angiopathy (CAA) in APP^{swe}/PS1^{dE9} mice. Moreover, systemic treatment of mice with curcumin for 7 days cleared and reduced existing plaques. Curcumin also led to a limited but significant reversal of structural changes in dystrophic dendrites, including abnormal curvature and dystrophy size. Together, the data suggested that curcumin reversed existing amyloid pathology and associated neurotoxicity in a mouse model of Alzheimer's disease. Chronic gavage administration of dietary curcumin and its more stable metabolite tetrahydrocurcumin (TC) to aged Tg2576 APP^{sw} mice or acutely to lipopolysaccharide (LPS)-injected wild-type mice resulted in similar brain levels of both compounds correlating with reduction in LPS-stimulated inducible nitric oxide synthase, nitrotyrosine, F₂ isoprostanes and carbonyls (Begum et al. 2008). In both the acute (LPS) and chronic inflammation (Tg2576), TC and curcumin similarly reduced interleukin-1 β . Despite these similarities, only curcumin was effective in reducing amyloid plaque burden, insoluble β -amyloid peptide (A β) and carbonyls. Curcumin but not TC prevented A β aggregation. The TC metabolite was detected in the brain and plasma from mice chronically fed with the parent compound. TC did reduce neuroinflammation and soluble A β , effects that may be attributable to limiting JNK-mediated transcription. *Curcuma longa* rhizome oil exhibited neuroprotection against experimental cerebral ischaemia in rats (Dohare et al. 2008). *Curcuma* oil treatment showed that the expression of nitric oxide synthase (NOS) isoforms was decreased significantly compared to the untreated ischaemia group. *Curcuma* oil suppressed the elevated protein level of Bax and aided mitochondrial translocation and activation of Bcl-2 by altered mitochondrial membrane potential. It also inhibited the cytosolic release of apoptogenic molecules like cytochrome c and inhibited the activation of caspase-3 and the expression of p53 ultimately inhibiting apoptosis. The results of in-vivo study in rats suggested that the neuroprotective activity of *Curcuma longa* oil against cerebral ischaemia was associated with its antioxidant activities and attenuation of delayed neuronal death via a caspase-dependent pathway (Rathore et

al. 2008). *Curcuma* oil appeared to be a promising agent not only for the treatment of cerebral stroke but also for the treatment of other disorders associated with oxidative stress. Optimised turmeric extract HSS-888 (5 mg/mouse/day) reduced β -amyloid, phosphorylated Tau protein burden and microglial inflammation in Alzheimer's transgenic mice (Shytle et al. 2012).

A 3-month dietary supplementation of 0.2 % curcumin numerically increased adenosine triphosphate concentrations in apolipoprotein APOE3 and significantly in APOE4 mice compared to the respective controls (Chin et al. 2014). Curcumin significantly induced the transcription of peroxisome proliferator-activated receptor (PPAR)- γ and mitochondrial transcription factor A (TFAM) in APOE3, but not in APOE4 mice. Moreover, PPAR- γ coactivator (PGC)-1 α and guanine-adenine repeat binding protein α (GABPa) mRNA were only increased in APOE3 mice. Protein expression of mitochondrial respiratory complexes, especially of complex IV, also appeared to be increased in APOE3 mice. It was concluded that curcumin affected mitochondrial function and gene and protein expression in the murine brain despite its low bioavailability, and carriers of the Alzheimer's disease risk genotype APOE4 may be less responsive to dietary curcumin than APOE3 carriers. Among the curcuminoids from turmeric rhizomes, bisdemethoxycurcumin had the strongest inhibitory activity towards human β -amyloid precursor cleavage enzyme (BACE-1) with 17 μ M IC₅₀, which was 20 and 13 times lower than those of curcumin and demethoxycurcumin, respectively (Wang et al. 2014). Overexpression of APP/BACE-1 resulted in the progressive and measurable defects in morphology of eyes and locomotion. Remarkably, supplementing diet with either 1 mM BDMCCN or 1 mM CCN rescued APP/BACE1-expressing *Drosophila melanogaster* flies and kept them from developing both morphological and behavioural defects. The results suggested that structural characteristics, such as degrees of saturation, types of carbon skeleton and functional group, and hydrophobicity appeared to play a role in determining inhibitory potency of curcuminoids on BACE-1.

Clinical Studies

In a 6-month randomised, placebo-controlled, double-blind, pilot clinical trial of old ethnic Chinese 50 years or older with progressive decline in memory and cognitive function, the lack of cognitive decline on placebo may have precluded any ability to detect a relative protective effect of curcumin which presumably would have appeared as a slower decline rather than an improvement in cognition (Baum et al. 2008). They suggested that a study of longer duration and with more sensitive Alzheimer's disease (AD) assessment testing and less treatment of other AD drugs may show greater deterioration on placebo. They found that although serum $A\beta_{40}$ levels did not differ significantly among doses, serum $A\beta_{40}$ tended to rise on curcumin possibly reflecting an ability of curcumin to disaggregate $A\beta$ deposits in the brain, releasing $A\beta$ for circulation and disposal.

Ringman et al. (2012) were unable to demonstrate clinical or biochemical evidence of efficacy of Curcumin C3 Complex (®) in Alzheimer's disease (AD) in this 24-week randomised, double-blind, placebo-controlled trial of persons with mild-to-moderate AD although preliminary data suggested limited bioavailability of curcumin. Curcumin was generally well tolerated although three subjects on curcumin withdrew due to gastrointestinal symptoms.

In a clinical study of 38 healthy subjects, it was demonstrated that a low dose of a curcumin-lipid preparation (80 mg/day) could produce a variety of potentially health-promoting effects in healthy middle-aged people (DiSilvestro et al. 2012). Curcumin (n19), but not placebo (n19), produced the following statistically significant changes: lowering of plasma triglyceride values, lowering of salivary amylase levels, raising of salivary radical scavenging capacities, raising of plasma catalase activities, lowering of plasma β -amyloid protein concentrations, lowering of plasma sICAM readings, increased plasma myeloperoxidase without increased c-reactive protein levels, increased plasma nitric oxide and decreased plasma alanine amino transferase activities.

Review Studies

Mishra and Palanivelu (2008) reviewed studies conducted on the role of curcumin on Alzheimer's disease (AD). They found a growing body of evidence indicating that oxidative stress, free radicals, β -amyloid and cerebral deregulation caused by bio-metal toxicity and abnormal inflammatory reactions contribute to the key event in Alzheimer's disease pathology. Due to various effects of curcumin, such as decreased β -amyloid plaques, delayed degradation of neurons, metal chelation, anti-inflammatory, antioxidant and decreased microglia formation, the overall memory in patients with AD had improved. Also curcumin's antioxidant, anti-inflammatory and lipophilic action improved the cognitive functions in patients with AD. They concluded that curcumin had a potential role in the prevention and treatment of AD.

Analgesic/Antinociceptive Activity

In-Vitro Studies

In HEK293 (human embryonic kidney 293) cells expressing human TRPA1 (transient receptor potential cation channel, subfamily A, member 1) (hTRPA1-HEK) and native mouse vagal neurons, curcumin caused activation and subsequent desensitisation of native and recombinant TRPA1 nociceptor ion channels.

In-Vivo Studies

Diabetic mice exhibited significant hyperalgesia along with increased plasma glucose and decreased body weights as compared with control mice (Sharma et al. 2006a). Chronic treatment with curcumin (15, 30 and 60 mg/kg body weight; p.o.) for 4 weeks starting from the 4th week of streptozotocin injection significantly attenuated thermal hyperalgesia and the hot plate latencies. Curcumin also inhibited the TNF- α and NO release in a dose-dependent manner. Chronic treatment with insulin (10 IU/kg/day, s.c.) and its combinations with antioxidants (resveratrol 20 mg/kg or curcumin 60 mg/kg,

p.o.) for 4 weeks starting from the 4th week of streptozotocin injection significantly attenuated thermal hyperalgesia and the hot plate latencies in mice (Sharma et al. 2007). There was a significant inhibition of tumour necrosis factor α (TNF- α) and nitric oxide (NO) levels when these drugs were given in combination compared with their effects per se. The results indicated an antinociceptive activity of resveratrol and curcumin and pointed towards the beneficial effect of these combinations with insulin in attenuating diabetic neuropathic pain, possibly through the participation of NO and TNF- α . Curcumin, morphine and naloxone had no effect on the early phase of biphasic pain induced after intraplantar injection of formalin in rats (Tajik et al. 2007). Late phase of pain was suppressed by curcumin at the doses of 100 and 200 mg/kg body weight (BW). Morphine (1 mg/kg BW) reduced, whereas naloxone (1 mg/kg BW) did not affect the late phase of pain. Curcumin did not influence the morphine-induced antinociception but reversed the effect of naloxone on pain. The results indicated that curcumin may produce antinociception by activation of both opioid and non-opioid mechanisms of pain. Tajik et al. (2008) found that in the acetic acid-induced visceral nociception of rats, curcumin may produce an antinociceptive effect, and the endogenous analgesic opioid system was found to be involved in the curcumin-induced antinociception. Curcumin exhibited antihyperalgesic effect against formalin-induced orofacial pain in rats (Mittal et al. 2009). Curcumin produced a dose-dependent inhibition of facial grooming in both acute and tonic phases compared to vehicle and potentiated the subanalgesic dose of diclofenac.

In-vivo studies showed that curcumin produced an antihyperalgesic effect via antagonism of transient receptor potential vanilloid 1 (TRPV1) which plays an important role in nociception (Yeon et al. 2010). Subcutaneous injection of capsaicin in the vibrissa pad area of rats induced thermal hyperalgesia. Intraperitoneally administered curcumin blocked capsaicin-induced thermal hyperalgesia in a dose-dependent manner. Curcumin reduced capsaicin-induced currents in a dose-dependent manner in both trigeminal ganglion neurons

and TRPV1-expressing HEK 293 cells, but did not affect heat-induced TRPV1 currents.

Turmeric oil produced significant antinociceptive activity at all doses studied (Liju et al. 2011). Curcumin (100, 200, 300 mg/kg; i.p.) dose-dependently ameliorated the behavioural deficits associated with pain and depression by restoring behavioural, biochemical, neurochemical and molecular alterations against reserpine-induced pain–depression dyad in rats (Arora et al. 2011). Zheng et al. (2011) found that curcumin ameliorated chronic constrictive injury-induced neuropathic pain in rats attenuating the expression of CX3CR1 in spinal cord dorsal horn and dorsal root ganglia. Chronic, but not acute, curcumin treatment (5, 15 or 45 mg/kg, p.o., twice per day for 3 weeks) alleviated mechanical allodynia and thermal hyperalgesia induced by chronic constriction injury in mice (Zhao et al. 2012). The antinociceptive effect was accompanied by increasing spinal monoamine (or metabolite) contents. The results suggested that the descending monoamine system (coupled with spinal β_2 -adrenoceptor and 5-HT_{1A} receptor) was critical for the modality-specific antinociceptive effect of curcumin in neuropathic pain. Delta- and mu-opioid receptors were likely rendered as downstream targets, accordingly. Combined treatment of curcumin and gliclazide was found to protect against the development of diabetic neuropathy in streptozotocin-induced diabetic rats (Attia et al. 2012). Combined treatment of curcumin with gliclazide significantly increased hot plate and tail flick latencies in comparison with that of the diabetic control group. The threshold of mechanical hyperalgesia was also significantly elevated. Serum glucose and C-peptide levels were significantly increased in the combined treatment compared with the diabetic control group, whereas serum levels of peroxynitrite, lipid peroxide and tumour necrosis factor- α production were significantly decreased. Studies by De Paz-Campos et al. (2012) confirmed curcumin to be an effective antinociceptive agent. Oral curcumin produced a dose-dependent antinociceptive effect in the 1 % formalin test in Wistar rats. Curcumin-induced antinociception appeared to involve the participation of potassium K_{ATP} channels at the

peripheral level, as local injection of glibenclamide prevented its effect. Activation of K_{ATP} channels, however, did not occur by activation of the *L*-arginine-nitric oxide-cGMP- K_{ATP} channel pathway. After 1-week administration, turmerone produced antidepressant-like effects in mice (Liao et al. 2013a). Curcumin (100 mg/kg) injected intraperitoneally 1 h prior to the hot plate test showed significant analgesic activity expressed by both parameters: an increase in latency time and a reduction in rat paw licking as compared to the controls (Haider et al. 2013). Jeon et al. (2013) reported that curcumin during the early stages of peripheral neuropathy could prevent the development of chronic neuropathic pain in rats with peripheral nerve injury. Oral administration of curcumin significantly attenuated the diabetes-induced allodynia and hyperalgesia and reduced the expression of both TNF- α and TNF- α receptor 1 in streptozotocin diabetic rats (Li et al. 2013b). Curcumin appeared to relieve diabetic hyperalgesia, possibly through an inhibitory action on pro-inflammatory tumour necrosis factor α (TNF- α) and TNF- α receptor 1.

Ji et al. (2013) found that curcumin could markedly alleviate nerve injury-induced neuropathic pain in rats by its inhibition of astrocyte hypertrophy in the spinal dorsal horn and phosphorylation of the extracellular signal-regulated kinase (ERK) signalling pathway. Han et al. (2012) demonstrated that intrathecal administration of curcumin decreased inflammatory pain induced by formalin in rats. There was no apparent abnormal behaviour following the administration of curcumin. Acute curcumin treatment (10–40 mg/kg, p.o) significantly and dose-dependently reversed mechanical hyperalgesia in a rat model of postoperative pain (Zhu et al. 2014b). In addition, repeated curcumin treatment significantly facilitated the recovery from surgery. In contrast, repeated treatment with curcumin before surgery did not impact the postoperative pain threshold and recovery rate. All the doses of curcumin did not significantly alter the spontaneous locomotor activity. The analgesic activity measured by the tail flick method showed optimum activities for turmeric oil and fish oil at 60 and 90 min, respectively, whereas the combination of the two decreased the analgesic

activity (Jacob and Badyal 2014). Studies by Zhao et al. (2014b) found that curcumin could normalise the depressive-like behaviours of neuropathic mice, which may be independent of the concurrent analgesic action and possibly mediated via the supraspinal serotonergic system and downstream GABAA receptor. The nociceptive behaviours were examined using Hargreaves test, and the depressive-like behaviours were determined by forced swim test (FST) and tail suspension test (TST). Chronic, but not acute, treatment with curcumin prevented the weight loss and attenuated mechanical allodynia in streptozotocin-induced diabetic rats (Banafshe et al. 2014). Pretreatment with naloxone (1 mg/kg) significantly reduced anti-allodynic effect of chronic curcumin in Von Frey filament test. The results suggested that curcumin could be considered as a new therapeutic potential for the treatment of diabetic neuropathic pain and the activation of opioid system may be involved in the antinociceptive effect of curcumin.

Clinical Studies

In a double-blind, randomised placebo-controlled study of 50 consecutive day-care laparoscopic cholecystectomy patients, prescription of curcumin was found to improve postoperative pain- and fatigue-related patient-reported outcomes (PROs) following laparoscopic cholecystectomy (Agarwal et al. 2011a).

Anxiolytic Activity

Only the higher dose (20 mg/kg, i.p.) of curcumin produced significant antianxiety-like effect in stressed mice (Gilhotra and Dhingra 2010). Pretreatment with aminoguanidine (50 mg/kg; i.p.), an inducible nitric oxide synthase inhibitor, significantly enhanced the anxiolytic-like effect of curcumin in stressed mice as compared to curcumin and aminoguanidine per se in stressed mice. Curcumin (20 mg/kg, i.p.) and aminoguanidine significantly decreased plasma nitrite levels in stressed mice. The combination of aminoguanidine and curcumin significantly decreased the plasma nitrite levels as

compared to curcumin and aminoguanidine per se in stressed mice. Curcumin and aminoguanidine did not produce any significant change in brain GABA contents of the animals. The results suggested the possible involvement of only inducible NOS and not neuronal NOS in antianxiety-like effect of curcumin.

The results of studies by Benammi et al. (2014) showed a noticeable anxiolytic effect of curcumin against lead induced anxiety in Wistar rats, and this may possibly result from modulation of central neuronal monoaminergic neurotransmission, especially serotonin, which had shown a significant reduction of the immunoreactivity within the dorsal raphe nucleus.

Antipyretic Activity

In the animal model of pyrexia, curcumin (100 mg/kg injected intraperitoneally into the rat) exhibited a significant reduction in the rectal temperature after 1, 2, 4 and 5 h of treatment, indicating the antipyretic effect of curcumin (Haider et al. 2013).

Antidyspepsia Activity

In a multicentre, randomised, double-blind trial involving 116 adult patients who had acid dyspepsia, flatulent dyspepsia or atonic dyspepsia, efficacy of turmeric rhizome was compared to a placebo and flatulence (Thamlikitkul et al. 1989). Fifty-three per cent of the patients receiving placebo responded to the treatment, whereas 83 % of the patients receiving flatulence and 87 % of patients receiving turmeric responded to the treatment. The differences in efficacy between placebo and active drugs were statistically significant and clinically important.

Wound Healing Activity

Sidhu et al. (1998) observed faster wound closure of punch wounds in curcumin-treated animals in comparison with untreated controls. Biopsies of the wound showed

reepithelialisation of the epidermis and increased migration of various cells including myofibroblasts, fibroblasts and macrophages in the wound bed. Multiple areas within the dermis showed extensive neovascularisation, and Masson's trichrome staining showed greater collagen deposition in curcumin-treated wounds. Immunohistochemical localisation of transforming growth factor-beta1 showed an increase in curcumin-treated wounds as compared with untreated wounds. Wounds of streptozotocin-induced diabetic mice treated with curcumin (oral or topical) showed earlier reepithelialisation; improved neovascularisation; increased migration of various cells including dermal myofibroblasts, fibroblasts and macrophages into the wound bed; and a higher collagen content (Sidhu et al. 1999). Immunohistochemical localisation showed an increase in transforming growth factor-beta1 in curcumin-treated wounds compared to controls.

Curcumin significantly accelerated healing of punch wounds in rats with or without dexamethasone treatment as revealed by a reduction in the wound width and gap length compared to controls (Mani et al. 2002). Curcumin treatment resulted in the enhanced expression of TGF- β 1 and TGF- β tIrc in both normal and impaired healing wounds. Macrophages in the wound bed showed an enhanced expression of TGF- β 1 mRNA in curcumin treated wounds. However, enhanced expression of TGF- β tIrc by curcumin treatment was observed only in dexamethasone-impaired wounds at the 7th-day post-wounding. iNOS levels were increased following curcumin treatment in unimpaired wounds, but not so in the dexamethasone-impaired wounds. A topical gel formulation of n-hexane fraction of *Curcuma longa* was found to be efficacious in the wound healing of hyperglycaemic mice (Wientarsih et al. 2013). The effect of n-hexane turmeric gel, in terms of decreasing the surface area of wound and histopathological characteristics, was significantly different between the positive control (neomycin sulphate 5 %)-treated group and turmeric gel-treated group. Skin irritant test showed neither rashes, swelling, inflammation, redness, irritation, itching nor any other toxicity symptoms following application of the gel. Based on the observed antimicrobial and wound healing effects, the transdermal drug formulations

containing combination of norfloxacin and *Curcuma longa* could be employed as an alternative to commercial silver sulfadiazine 1 % cream (Dua et al. 2013). This innovative mode of formulation could be employed for making burn wound healing process more effective.

Antiulcer/Gastroprotective/Intestinoprotective Activity

According to the Yadav et al. (2013), in 80 % of the cases, gastric ulcer was caused primarily due to the use of nonsteroidal anti-inflammatory category of drug, 10 % by *Helicobacter pylori* and about 8–10 % by the intake of very spicy and fast food. Although a number of antiulcer drugs and cytoprotectants are available, all these drugs have side effects and limitations. The gastrointestinal problems caused by different etiologies were observed to be associated with the alterations of various physiologic parameters such as reactive oxygen species, nitric oxide synthase, lipid peroxidation and secretion of excessive gastric acid. Gastrointestinal ulcer resulted probably due to imbalance between the aggressive and the defensive factors.

In-Vitro Studies

Huang et al. (2013b) found that a terpenoid C derived from *Curcuma* root could block NF- κ B signal pathway, effectively reducing the secretion of *H. pylori*-induced pro-inflammatory cytokines while increasing the secretion of anti-inflammatory cytokines in *H. pylori*-infected human gastric epithelial gastric cell lines.

Animal Studies

Oral administration of *C. longa* alcoholic extract (600 mg/kg b.w.) significantly reduced the number and severity of induced gastric ulcers in albino rats by lowering ulcer index and ulcer score and increasing healing index indicating its ulcer protective action (Nagle et al. 2012). Studies showed that curcumin protected the rats' gastric mucosa against

indomethacin-induced gastric ulceration possibly, at least in part, by enhancement of the gastric mucosal barrier and reduction in acid secretory parameters in addition to antioxidant and anti-apoptotic activities (Morsy and El-Moselhy 2013). Rats with orally administered curcumin (200 mg/kg) did not show any lesions on the inner lining of the stomach after a 16-h fast, indicating the gastroprotective effects of curcumin as compared to saline- and acetylsalicylic acid-administered rats (Haider et al. 2013). The significantly low ulcer index in curcumin-treated rats following starvation highlighted the gastroprotective characteristics of curcumin. The methanol turmeric extract and curcumin inhibited the growth of all strains of *H. pylori* including *H. pylori* cagA⁺ in-vitro with a minimum inhibitory concentration range of 6.25–50 µg/ml (Mahady et al. 2002). Administration of turmeric essential oil (TEO) and ginger essential oil (GEO) inhibited ethanol-induced ulcer by 84.7 % and 85.1 %, respectively, as seen from the ulcer index and ameliorated ethanol-induced lesions such as necrosis, erosion and haemorrhage of the stomach of rats (Liju et al. 2015). Reduced antioxidant enzymes such as GPx, SOD, catalase and GSH produced by ethanol administration were significantly increased by simultaneous administration of TEO and GEO.

Rats receiving herbal infuse combination of turmeric (*Curcuma domestica*), cardamom pods (*Amomum compactum*) and sembung leaf (*Blumea balsamifera*) exhibited less number and smaller area of gastric ulcers as well as smaller score of mucosal damage in comparison to those of aspirin group (Mutmainah et al. 2014). The number of mast cells and eosinophil of herbal groups was also smaller than that of aspirin group.

In-vivo studies showed that turmeric extract may protect the small intestine of rats from methotrexate-induced damage (severe villous shortening and blunting, inflammatory cell infiltration and haemorrhage in lamina propria, along with epithelial cell necrosis) and oxidative stress (decreased levels of SOD, GSH-Px and CAT) through its antioxidant properties (Moghadam et al. 2013).

Clinical Studies

In a joint Vietnam–Sweden prospective double-blind two-centre study, the herbal remedy of turmeric, in a dosage of 6 g daily as suggested in the Vietnamese pharmacopoeia, was compared with an equal amount of placebo in 118 patients with duodenal ulcer (Van Dau et al. 1998). Turmeric was found not superior to placebo in healing duodenal ulcer either after 4 or 8 weeks of treatment. After 8 weeks, the ulcer healing rate of turmeric was 27 %, while placebo had healed 29 %. In an earlier controlled clinical trial on patients with gastric ulcers in Thailand, turmeric treatment was found not to be superior to placebo and was found to be less effective than antacids (Kositchaiwat et al. 1993). In another study in Thailand on *Helicobacter pylori*-infected gastritis patients, the eradication rate of *H. pylori* in patients that received omeprazole, amoxicillin and metronidazole treatment was significantly higher than the patients that received curcumin (78.9 % versus 5.9 %). (Koosirirat et al. 2010). The decreases of cytokine interleukin (IL)-8, IL-1 β , tumour necrosis factor (TNF)- α and cyclooxygenase (COX)-2 production were not found in the curcumin group. They concluded that curcumin alone may have limited anti-bactericidal effect on *H. pylori* and on the production of inflammatory cytokines. In a clinical study in Jordan of 55 patients with peptic ulcers including 35 patients who were tested positive with *Helicobacter pylori*, consumption of turmeric 2 g/day for 4 and 8 weeks may be beneficial (Aljamal 2011). After 4 weeks of treatment, ulcers were absent in 35 cases and 20 cases were positive with *Helicobacter pylori*. Thirteen cases had absence of ulcer after 8 weeks of treatment, and 8 cases of them were positive with *Helicobacter pylori*. About 7 cases remain positive. Patients with peptic ulcer symptoms both males and females and aged between 16 and 60 years were included in a phase II clinical pilot study to evaluate the therapeutic effects of orally administered capsule-laden turmeric (Prucksunand et al. 2001). The percentages of ulcer healing were 48 % (12cases), 72 % (18 cases) and 76 % (19 cases) after 4, 8 and 12 weeks of treatment, respectively. No serious adverse effects were found in all patients.

Cardiovascular Protective Activity

In-Vitro Studies

Xu et al. (2013b) found that curcumin added before anoxia or immediately prior to reoxygenation exhibited remarkable protective effects against anoxia-reoxygenation-induced oxidative damage to rat heart mitochondria, in concentrations ranging from picomoles to micromoles, with EC₅₀s in the nanomolar range. The results demonstrated the superior antioxidative properties of curcumin and suggested its potential for use in ischaemia/reperfusion injuries and the related free radical-initiated diseases.

Animal Studies

Administration of turmeric extract attenuated oxidative damage in liver mitochondria and microsomes of rabbits fed with a dietary intake of saturated fat and cholesterol (Quiles et al. 1998). Turmeric extract dose-dependently reduced membrane lipid peroxidation, and a concentration of 1.6 mg/kg body weight was found to be an adequate treatment in the therapy of rabbit experimental atherosclerosis. Myocardial infarction produced after ischaemia/reperfusion was significantly reduced in Wistar rats treated with turmeric (Mohanty et al. 2004). Turmeric treatment resulted in restoration of the myocardial antioxidant status and altered haemodynamic parameters as compared to control I/R. Furthermore, I/R-induced lipid peroxidation was significantly inhibited by turmeric treatment. The beneficial cardioprotective effects also translated into the functional recovery of the heart. Cardioprotective effect of turmeric likely resulted from the suppression of oxidative stress and correlates with the improved ventricular function. In another study, they found that chronic treatment with turmeric significantly reduced TUNEL positivity and Bax protein and upregulated Bcl-2 expression in comparison to control IR group (Mohanty et al. 2006). In addition, turmeric demonstrated mitigating effects on several myocardial injury-induced haemodynamic {(+)LVdP/dt, (-) LVdP/dt & LVEDP}

and histopathological perturbations. The study of Singh et al. (2014) found that turmeric oil attenuated arterial injury-induced accelerated atherosclerosis, inflammation and macrophage foam cell formation in male golden Syrian hamsters. Turmeric oil treatment prevented high-cholesterol diet and oxidised LDL (OxLDL)-induced lipid accumulation, decreased the mRNA expression of CD68 and CD36 and increased the mRNA expression of PPAR α , LXR α , ABCA1 and ABCG1 in both hyperlipidaemic hamster-derived peritoneal and THP-1 macrophages. The administration of turmeric oil suppressed the mRNA expression of TNF- α , IL-1 β , IL-6 and IFN- γ and increased the expression of TGF- β in peritoneal macrophages. In THP-1 macrophages, turmeric oil supplementation prevented OxLDL-induced production of TNF- α and IL-1 β and increased the levels of TGF- β .

Oral administration of *Curcuma longa* ethanolic or water extract (200 mg/kg) prior to doxorubicin produced a significant protection against doxorubicin-induced cardiotoxicity which was evidenced by significant reduction in mortality, serum creatine kinase MB (Ck-MB) and lactate dehydrogenase (LDH) activities (Eman et al. 2011). Moreover, they significantly increased glutathione (GSH) markedly and decreased cardiac calcium and cardiac and serum malondialdehyde. In addition, both extracts significantly reduced serum nitric oxide, increased cardiac ascorbic acid and ameliorated the antioxidant enzyme activities. Studies by Yang et al. (2013) demonstrated that curcumin pretreatment of isolated and in-vivo rat hearts and cultured neonatal rat cardiomyocytes attenuated ischaemia/reperfusion (IR) injury by reducing ischaemia/reperfusion-induced mitochondrial oxidative damage through the activation of silent information regulator 1 (SIRT1) signalling pathway.

Ischaemia/reperfusion-induced mitochondrial oxidative damage was markedly attenuated by curcumin treatment as it resulted in a well-preserved mitochondrial redox potential, significantly elevated mitochondrial superoxide dismutase activity and decreased formation of mitochondrial hydrogen peroxide and malondialdehyde. Chen et al. (2013a) found that curcumin pretreatment improved rat cardiac contractility and attenuated myocardial and renal injury through reducing

inflammatory response in the kidney and heart and oxidative stress in the myocardium.

Studies by Manhas et al. (2014) showed that pretreatment and post-treatment of rats with *Curcuma* oil reduced myocardial ischaemia/reperfusion-induced injury (MI/RP) by reducing the endothelial cell-mediated inflammation, specifically in the ischaemic zone of MI/RP rat heart. Results of studies by Zheng et al. (2014b) suggested that hydroxyl acylated curcumin under low-intensity ultrasound had sonodynamic effect on THP-1 macrophages via generation of intracellular singlet oxygen and mitochondria–caspase signalling pathway, indicating that hydroxyl acylated curcumin could be used as a novel sonosensitiser in sonodynamic therapy for atherosclerosis. Curcumin was found to stimulate the apoptotic cell death of H9c2 cardiac myoblasts by upregulating reactive oxygen species (ROS) generation and triggering activation of p38-mitogen-activated protein kinase (p38-MAPK) as well as c-Jun NH2 terminal kinases (JNKs), in a dose- and time-dependent manner (Zikaki et al. 2014). Future studies should assess the appropriate administration conditions of curcumin, so as to optimise its therapeutic potential against cardiovascular pathologies.

Feeding apoprotein E-deficient (apoE(-/-)) mice with a Western diet combined with an herbal mixture of *Artemisia iwayomogi* and *Curcuma longa* (ACE) for 10 weeks reverted the Western diet-elevated serum lipid profiles including total cholesterol (TC), low-density lipoprotein, high-density lipoprotein (HDL), triglyceride and TC/HDL ratio and reverted the elevated glucose, total reactive oxygen species (ROS) and inflammatory cytokines (tumour necrosis factor- α , TNF- α and interleukin-6, IL-6) in the serum levels (Shin et al. 2014). The aortic lesion formation was significantly decreased as were lipid formations by ACE treatment. Moreover, ACE not only caused significant decreases of the lipid drops on the hepatic tissues but also restored the antioxidant components. The gene expression levels including SREBP-1c, FAS, SCD-1, PPAR- α , CPT-1, IL-6, IL-1 β and TNF- α in hepatic tissue were altered by Western diet fed in apoE(-/-) mice, while ACE treatment significantly normalised those alterations.

Hypotensive Activity

In normotensive rats, turmeric methanol extract (10, 20 and 30 mg/kg, i.v.) induced dose-dependent hypotension and pronounced bradycardia (Adaramoye et al. 2009). The extract (1–1000 µg/mL) induced concentration-dependent relaxation of tonic contractions evoked by phenylephrine (Phe) (10 µM) and KCl (80 mM) in mesenteric rings with intact endothelium or denuded endothelium. Also, in a depolarised, Ca^{2+} -free medium, the extract inhibited CaCl_2 (1 µM–30 mM)-induced contractions and caused a concentration-dependent rightward shift of the response curves, indicating that it inhibited the contractile mechanisms involving extracellular Ca^{2+} influx. Additionally the extract inhibited the transient contraction of denuded mesenteric rings constricted with Phe, but not those evoked by caffeine (20 mM). The results demonstrated the hypotensive and bradycardic effects of turmeric methanol extract, as well as its potent vasodilation of rat mesenteric arteries. Curcumin and tetrahydrocurcumin significantly suppressed the blood pressure elevation, decreased vascular resistance and restored vascular responsiveness in rats with *L*-NAME-induced hypertension (Nakmareong et al. 2011). The improvement of vascular dysfunction was associated with reinstating the marked suppression of eNOS protein expression in the aortic tissue and plasma nitrate/nitrite. Both compounds reduced vascular superoxide production, decreased oxidative stress and increased the previously depressed blood glutathione (GSH) and the redox ratios of GSH in *L*-NAME hypertensive rats. The improvement of vascular dysfunction was associated with reinstating the marked suppression of eNOS protein expression in the aortic tissue and plasma nitrate/nitrite. The antihypertensive and some antioxidant effects of tetrahydrocurcumin were apparently more potent than those of curcumin.

Antiplatelet Activity

Intraperitoneal administration of curcumin exerted anti-thromboxane B_2 effect in mice; it protected against collagen-induced paralysis of the hind limbs of mice and reduced

malondialdehyde level (Srivastava et al. 1985). Ethereal extract of turmeric inhibited arachidonate-induced platelet aggregation (Srivastava 1989). Turmeric extract inhibited thromboxane B2 production from exogenous (^{14}C) arachidonic acid (AA) in washed platelets; a simultaneous increase in the formation of lipoxygenase-derived products was observed. Turmeric extract inhibited incorporation of (^{14}C) AA into platelet phospholipids and deacylation of AA-labelled phospholipids on stimulation with calcium ionophore A23187 and alter eicosanoid biosynthesis in human blood platelets. Curcumin inhibited platelet aggregation induced by arachidonate, adrenaline and collagen (Srivastava et al. 1995). This compound inhibited thromboxane B2 (TXB2) production from exogenous ^{14}C arachidonate in washed platelets with a concomitant increase in the formation of 12-lipoxygenase products. Moreover, curcumin inhibited the incorporation of ^{14}C AA into platelet phospholipids and inhibited the deacylation of AA-labelled phospholipids (liberation of free AA) on stimulation with calcium ionophore A23187. Curcumin's anti-inflammatory property may, in part, be explained by its effects on eicosanoid biosynthesis. Curcumin inhibited platelet aggregation mediated by the platelet agonists epinephrine (200 μM), ADP (4 μM), platelet-activating factor (PAF; 800 nM), collagen (20 $\mu\text{g/mL}$) and arachidonic acid (AA 0.75 mM) (Shah et al. 1999). Curcumin preferentially inhibited PAF- and AA-induced aggregation ($\text{IC}_{50} = 25\text{--}20$ μM), whereas much higher concentrations of curcumin were required to inhibit aggregation induced by other platelet agonists. Pretreatment of platelets with curcumin resulted in inhibition of platelet aggregation induced by calcium ionophore A-23187 (IC_{50} 100 μM), but curcumin up to 250 μM had no inhibitory effect on aggregation induced by the protein kinase C (PKC) activator phorbol myristate acetate (1 μM). Curcumin (100 μM) inhibited the A-23187-induced mobilisation of intracellular Ca^{2+} as determined by using fura-2-acetoxymethyl ester. Curcumin also inhibited the formation of thromboxane A2 (TXA2) by platelets ($\text{IC}_{50} = 70$ μM). The results suggested that the curcumin-mediated preferential inhibition of PAF- and AA-induced platelet aggregation

involved inhibitory effects on TXA₂ synthesis and Ca²⁺ signalling, but without the involvement of PKC

ar-turmerone was effective in inhibiting platelet aggregation induced by collagen (IC₅₀, 14.4 μM) and arachidonic acid (IC₅₀, 43.6 μM) (Lee 2006). However, *ar*-turmerone had no effect on platelet-activating factor or thrombin-induced platelet aggregation. In comparison, *ar*-turmerone was significantly more potent platelet inhibitor than aspirin against platelet aggregation induced by collagen.

Hepatoprotective Activity

An extract of the crude drug 'ukon', the rhizomes of *C. longa*, exhibited potent preventive activity against carbon tetrachloride-induced liver injury in-vivo and in-vitro (Kiso et al. 1983b). Curcuminoids from the extract were shown to possess significant antihepatotoxic action against carbon tetrachloride- and galactosamine-produced cytotoxicity in primary-cultured rat hepatocytes. The liver protective effects of some analogues of ferulic acid and *p*-coumaric acid, probable metabolites of the curcuminoids, were also determined.

Turmeric extract exhibited protective effect on carbon tetrachloride-induced liver damage in rats (Deshpande et al. 1998). As compared to CCl₄ group, a short pretreatment of turmeric extract showed reduction in cholesterol, bilirubin, aspartate aminotransferase (AST), alanine amino transferase (ALT) and alkaline phosphatase activity, whereas concurrent treatment of turmeric extract + CCl₄ reduced to a greater extent the levels of all parameters except ALT. Administration of curcumin and *N*-acetylcysteine ameliorated ethanol-induced changes in the levels of prostanoids in the rat organs (Rajakrishnan et al. 2000). Biochemical assessment of liver damage was done by measuring the activities of serum enzymes, which were significantly increased in rats fed with ethanol as evident from the elevated levels serum enzymes (i.e. aspartate transaminase and alkaline phosphatase), whereas the elevated levels of these enzymes were decreased after

curcumin and *N*-acetylcysteine treatment. Also a significant increase in the levels of prostaglandins E₁, E₂, F_{2α} and D₂ was observed in the liver, kidney and brain.

Oral administration of turmeric powder extract attenuated the hepatotoxicity induced by CCl₄ in mice (Pingale 2010). The treatment of turmeric powder considerably restored all the serum and liver parameters to normal levels. Liver histology and biochemistry showed regeneration of liver cells by the turmeric treatment.

Pretreatment with *C. longa* extract exerted protective effects against CCl₄-induced hepatotoxicity in rats, via activities of antioxidant and phase II detoxifying enzymes, and through the activation of nuclear translocated Nrf2 (Lee et al. 2010). Treatment with turmeric ameliorated the biochemical parameters and histological changes associated with fatty liver induced by oxytetracycline in albino rats (Helal et al. 2011). Fatty liver rats showed high significant increase in serum glucose, cholesterol, triglycerides, LDL cholesterol, ALT, AST, GGT, LDH, total protein, albumin, globulin, urea and creatinine, while HDL cholesterol and A/G ratio were significantly decreased compared to control group. In-vivo studies found that oils from *Zingiber officinale* and *C. longa* (200 mg/kg) exhibited hepatoprotective activity in acute ethanol-induced fatty liver by decreasing the activities of serum enzymes, serum triglyceride, serum total cholesterol and hepatic malondialdehyde, while they significantly restored the level of glutathione as well as glutathione S-transferase and superoxide dismutase activities in Wistar rats (Nwozo et al. 2014). Histological examination of rat tissues supported the obtained results. Ginger oil was identified to have better effects than turmeric oil.

Treatment of turmeric extract ameliorated carbon tetrachloride (CCl₄)-induced cellular hepatic damage and oxidative stress in rats (Abu-Rizq et al. 2008, 2015). Treatment with curcuminoid crude extract at two different doses showed a significant cellular recovery among hepatocytes, which was reflected in a reduction of hepatic enzymes and thiobarbituric acid-reactive species (TBAR)

values. A significant restoration of lymphocyte viability and CD25, CD71 and Con A receptor expression in both immature (PNA+) thymocytes and splenic helper (CD4+) T lymphocytes was observed. Turmeric crude extract, at both low and high dose, was found to be more efficient as compared to purified curcumin suggesting synergistic effect of curcumin with other components of the crude extract. Studies showed that turmeric extract had a protective effect against doxorubicin (DOX)-induced cardiac, hepatic and renal toxicity in rats (Mohamad et al. 2009). Biochemical and histopathological findings demonstrated that turmeric extract exerted multiple therapeutic activities that were beneficially protective, and it had an ameliorative effect against DOX-induced cardiac toxicity and hepatotoxicity and blocked DOX-induced nephrosis. Similarly, turmeric extract inhibited the DOX-induced increase in plasma cholesterol and enzymes lactate dehydrogenase and creatine kinase.

Pretreatment with fermented turmeric (FC) drastically prevented the elevated activities of serum AST, ALT, LDH and ALP caused by CCl₄-induced hepatotoxicity in rats and decreased malondialdehyde levels (Kim et al. 2014). Histopathologically evident hepatic necrosis was significantly ameliorated by FC pretreatment. Additionally, FC enhanced antioxidant capacities with higher activities of catalase, glutathione S-transferase, glutathione reductase and glutathione peroxidase and level of reduced glutathione.

Studies found that curcumin attenuated high-fat/cholesterol diet (HFD)-induced hepatic steatosis in obese mice by regulating hepatic lipid metabolism via AMP-activated protein kinase (AMPK) activation, suggesting its use as a therapeutic for hepatic steatosis (Um et al. 2013). Oral administration of curcumin extract dose-dependently reduced inflammation and necrosis in hepatic tissue caused by thioacetamide-induced hepatic encephalopathy in rats (Farjam et al. 2014). Levels of ammonia, alkaline phosphatase (ALP), alanine transaminase (ALT) and aspartate transaminase (AST) enzymes were significantly lower among curcumin-receiving groups when compared with the control group. Curcumin attenuated arsenic-induced hepatic injuries and oxidative stress in

experimental mice through activation of Nrf2 pathway, promotion of arsenic methylation and urinary excretion (Gao et al. 2013).

Curcumin, demethoxycurcumin and bisdemethoxycurcumin showed significant hepatoprotective effects on tetracycline-induced cytotoxicity in human liver-derived HepG2 cells with EC_{50} values of 1–3 as 86.9, 70.7 and 50.2 μ M, respectively (Song et al. 2005). Silybin (EC_{50} = 69.0 μ M) and silychristin (EC_{50} = 82.7 μ M) were used as positive controls.

Tang and Chen (2014) found that curcumin eliminated the effects of advanced glycation end products (AGEs) in hepatic stellate cells (HSC) by interrupting leptin signalling and activating transcription factor NF-E2 p45-related factor 2 (Nrf2), leading to the elevation of cellular glutathione and the attenuation of oxidative stress. They concluded that curcumin eliminated the effects of AGEs on the divergent regulation of gene expression of receptor for AGEs (RAGE) and AGE receptor-1 (AGE-R1) in HSC by interrupting the AGE-caused activation of leptin signalling, leading to the inhibition of HSC activation. Activation of hepatic stellate cells (HSC) was found crucial to the development of hepatic fibrosis.

Renoprotective Activity

The renoprotective effect of curcumin had been evaluated in several experimental models including diabetic nephropathy, chronic renal failure, ischaemia and reperfusion and nephrotoxicity induced by compounds such as gentamicin, Adriamycin, chloroquine, iron nitrilotriacetate, sodium fluoride, hexavalent chromium and cisplatin (Trujillo et al. 2013). It had been shown recently in a model of chronic renal failure that curcumin exerted a therapeutic effect by reverting not only systemic alterations but also glomerular haemodynamic changes. Another recent finding showed the renoprotective effect of curcumin to be associated to preservation of function and redox balance of mitochondria. Trujillo et al. (2013) reported that these studies attributed the protective effect of curcumin in the kidney to the induction of

the master regulator of antioxidant response nuclear factor-erythroid-derived 2 (Nrf2), inhibition of mitochondrial dysfunction, attenuation of inflammatory response, preservation of antioxidant enzymes and prevention of oxidative stress. In their review, Ghosh et al. (2014) reported that curcumin could blunt the generation and action of inflammatory molecules and ameliorate chronic kidney disease CKD as well as associated inflammatory disorders. Recent studies have shown that increased intestinal permeability results in the leakage of pro-inflammatory molecules (cytokines and lipopolysaccharides) from the gut into the circulation in diseases such as CKD, diabetes and atherosclerosis. This change in intestinal permeability is due to decreased expression of tight junction proteins and intestinal alkaline phosphatase (IAP). Curcumin increases the expression of IAP and tight junction proteins and corrects gut permeability. This action reduces the levels of circulatory inflammatory biomolecules.

Turmeric (100 µg/ml) and curcumin (100 µg/ml, 10 µg/ml) exerted as much protection against hydrogen peroxide-induced renal epithelial (LLC-PK1) cell injury as did vitamin E in both chromium release assay and lipid degradation, while turmeric (100 µg/ml) and curcumin (100 µg/ml) gave comparable inhibition of lipid peroxidation (Cohly et al. 1998). Antunes et al. (2001) reported that pretreatment with two dietary antioxidants, curcumin (8 mg/kg body wt.) or selenium (1 mg/kg body wt.), did not offer protection against cisplatin-induced nephrotoxicity and lipid peroxidation in adult Wistar rats. Three days after curcumin or selenium plus cisplatin treatments, the renal damage induced by cisplatin did not recover at a significant statistically level. The administration of curcumin or selenium alone did not increase lipid peroxidation compared to the control group.

Turmerin and 21-aminosteroid showed no protection. Studies found that Adriamycin-induced kidney injury in rats was remarkably prevented by treatment with curcumin (Venkatesan et al. 2000). Treatment with curcumin markedly protected against Adriamycin-induced proteinuria, albuminuria, hypoalbuminaemia and hyperlipidaemia.

Similarly, curcumin inhibited Adriamycin-induced increase in urinary excretion of *N*-acetyl- β -*D*-glucosaminidase (a marker of renal tubular injury), fibronectin and glycosaminoglycan and plasma cholesterol. Curcumin restored renal function in Adriamycin rats, as judged by the increase in glomerular filtration rate. The data also demonstrated that curcumin protected against Adriamycin-induced renal injury by suppressing oxidative stress and increasing kidney glutathione content and glutathione peroxidase activity. Likewise, curcumin abolished Adriamycin-stimulated kidney microsomal and mitochondrial lipid peroxidation. When applied 30 min before transforming growth factor- β (TGF- β), curcumin dose-dependently and dramatically reduced TGF- β -induced increases in plasminogen activator inhibitor-1 (PAI-1), TGF- β 1, fibronectin (FN) and collagen I (Col I) mRNA and in PAI-1 and fibronectin protein (Gaedeke et al. 2004). Prolonged curcumin treatment (> 6 h) significantly reduced TGF- β receptor type II levels (T β RII) and SMAD2/3 phosphorylation in response to added TGF- β . The data suggested that curcumin blocked TGF- β 's profibrotic actions on rat renal fibroblasts through downregulation of T β RII and through partial inhibition of c-Jun activity.

Sharma et al. (2006b) found that chronic treatment with curcumin significantly attenuated both renal dysfunction and oxidative stress in streptozotocin-induced diabetic rats. The nephroprotective action of curcumin was suggested to be attributed to its antioxidative mechanism. Kuhad et al. (2007) demonstrated that curcumin had a protective effect on cisplatin-induced experimental nephrotoxicity, and this effect is attributed to its direct anti-inflammatory and strong antioxidant profile. Curcumin treatment significantly and dose-dependently restored renal function, reduced lipid peroxidation and enhanced the levels of reduced glutathione and activities of superoxide dismutase and catalase. Bayrak et al. (2008) found that curcumin protected rat kidneys against ischaemia/reperfusion (I/R) via its antioxidant effects. Curcumin prevented shock wave lithotripsy-induced renal injury through inhibition of nuclear factor-kappaB and inducible nitric oxide synthase activity in rats (Bas et al. 2009). Curcumin, decreasing expressions of iNOS and p65

and serum nitric oxide levels prevented interstitial, glomerular, tubular epithelial and endothelial cellular injuries.

Administration of turmeric extract protected kidney against acetaminophen-induced tubular necrosis in mice (Khorsandi and Orazizadeh 2008). BUN (blood urea nitrogen), creatine, uric acid and kidney necrosis were reduced significantly in the 1000-mg/kg turmeric-treated group. Studies by Ghosh et al. (2009) found that curcumin ameliorated chronic renal failure in 5/6 nephrectomised rats by its anti-inflammatory property. Curcumin dose-dependently antagonised the TNF- α -mediated decrease in PPAR γ and blocked transactivation of NF-kappaB and repression of PPAR γ . They also reported that curcumin ameliorated renal failure by antagonising inflammation in 5/6 nephrectomised rats (Ghosh et al. 2012). Renal dysfunction in the nephrectomised rats, as evidenced by elevated blood urea nitrogen, plasma creatinine, proteinuria, segmental sclerosis and tubular dilatation, and elevated kidney levels of cytosolic PLA(2), calcium-independent intracellular PLA(2), COX-1 and COX-2, was comparably reduced by curcumin and enalapril, with only enalapril significantly lowering blood pressure. Curcumin, by antagonising inflammatory cytokines, could significantly reduce both phospholipase and cyclooxygenase. Soetikno et al. (2011) found that curcumin administration (100 mg/kg/day for 8 weeks) attenuated diabetic nephropathy by inhibiting PKC- α and PKC- β 1 activities in streptozotocin-induced type I diabetic rats. In further studies, Soetikno et al. (2013) demonstrated that curcumin alleviated oxidative stress, inflammation and renal fibrosis in remnant kidney through the nuclear factor-erythroid-2-related factor 2 (Nrf2)-keap1 pathway in rats. Oral administration of curcumin ameliorated renal injuries induced by gentamicin toxicity in Wistar rats (Manikandan et al. 2011). Curcumin enhanced antioxidant activities and decreased inducible nitric oxide synthase (iNOS) and nuclear factor- κ B (NF- κ B), thereby protecting renal cells against oxidative stress induced by gentamicin. Earlier, the study by Ali et al. (2005) reported that oral administration of curcumin ameliorated the histopathological and biochemical indices of nephrotoxicity induced by gentamicin in rats.

Curcumin pretreatment attenuated $K_2Cr_2O_7$ -induced mitochondrial dysfunction (alterations in oxygen consumption, ATP content, calcium retention and mitochondrial membrane potential and decreased activity of complexes I, II, II–III and V) in rats but was unable to modify renal and mitochondrial Cr(VI) content or to chelate chromium (Molina-Jijón et al. 2011). The findings suggested that the preservation of mitochondrial function played a key role in the protective effects of curcumin against $K_2Cr_2O_7$ -induced renal damage. Curcumin attenuated 5/6 nephrectomy-induced proteinuria, systemic and glomerular hypertension, hyperfiltration, glomerular sclerosis, interstitial fibrosis, interstitial inflammation and increase in plasma creatinine and blood urea nitrogen in 5/6 nephrectomised rats (Tapia et al. 2012). This protective effect was associated with the nuclear translocation of Nrf2 and the prevention of both oxidant stress and the decrease of antioxidant enzymes. They also found that curcumin was able to reverse established oxidant stress glomerular hypertension and hyperfiltration in rats with 5/6 nephrectomy (Tapia et al. 2013). Their data suggested that curcumin may be useful to reverse established haemodynamic alterations and renal injury in patients with chronic renal failure. Curcumin attenuated maleate-induced nephropathy in rats and renal epithelial LLC-PK1 cell injury in-vitro (Tapia et al. 2014). The in-vivo protection was associated with the prevention of oxidative stress and preservation of mitochondrial oxygen consumption and activity of respiratory complex I, and the in-vitro protection was associated with the prevention of ROS production. Pretreatment of turmeric powder for 30 days prior to renal ischaemia/reperfusion operation improved renal function, reduced IR-induced renal inflammatory and oxidative injury and ameliorated histological injuries in Wistar rats (Sefidan and Mohajeri 2013). The results of this study showed that turmeric powder significantly prevented renal IR-induced functional and histological injuries.

Oral administration of C66, a curcumin analogue, daily for 6 weeks, to streptozotocin-induced diabetic rats, prevented renal injury by inhibiting the increased plasma TNF- α levels

and renal inflammatory gene expression, improving histological abnormalities and fibrosis of diabetic kidney, but did not affect the hyperglycaemia in these diabetic rats (Pan et al. 2012). In-vitro C66 pretreatment of primary peritoneal macrophages reduced high glucose-stimulated production of TNF- α and NO and inhibited HG-induced IL-1 β , TNF- α , IL-6, IL-12, COX-2 and iNOS mRNA transcription and the activation of JNK/NF- κ B signalling. Pan et al. (2014) found that the renal protection of C66 in diabetic mice was associated with mitogen-activated protein kinase (MAPK) inactivation and ACE/angiotensin II (Ang II) downregulation. The study indicated C66 to be a potential candidate of diabetic nephropathy therapeutic agents and, more importantly, that reduction in ACE expression by MAPK inhibition appeared to be an alternative strategy for the treatment of diabetic nephropathy. Pan et al. (2013) reported that the administration of another novel curcumin derivative B06 to diabetic rats significantly decreased inflammatory mediators in the serum, kidney and heart and renal macrophage infiltration. This was accompanied with an attenuation of diabetes-induced structural and functional abnormalities in the kidney and heart. In-vitro, pretreatment with B06 at a concentration of 5 μ M significantly reduced the high-glucose-induced overexpression of inflammatory cytokines in macrophages.

Studies by Ademiluyi et al. (2012) found that pretreatment with ginger and turmeric rhizome (2 and 4 %) prior to gentamicin administration significantly protected the kidney and attenuated oxidative stress by modulating renal damage and antioxidant indices in rats. Li et al. (2013a) found that curcumin counteracted TGF- β 1-induced epithelial-to-mesenchymal transition (EMT), a major contributor to tubulointerstitial fibrosis (TIF), in renal tubular epithelial HK-2 cells via ERK-dependent and then PPAR- γ -dependent pathway. Tubulointerstitial fibrosis (TIF) is the final common pathway in the end-stage renal disease.

Studies by Vlahović et al. (2007) found that dietary curcumin did not protect the kidney in glycerol-induced acute renal failure in rats. Rats that received curcumin in addition to glycerol had significantly lower TBARS in serum but not in

the kidney and liver. The activities of kidney cortex enzymes, aminopeptidase N, angiotensinase A and dipeptidyl peptidase IV were reduced in glycerol as well as in curcumin-treated rats. The results obtained in this study provided additional evidence that despite its limited antioxidant activity, curcumin did not protect the kidney in myoglobinuric model of acute renal failure.

Pulmonoprotective Activity

Yeh et al. (2013) found that curcumin pretreatment protected rats against renal ischaemia and reperfusion injury-induced restrictive lung disease most likely through decreasing hydroxyl radical, lipid peroxidation and inflammation in the lungs and improving alveolar vascular permeability. Curcumin and vitamin E (CVE) treatment protected against chlorpyrifos-induced lung oxidative damage in rats (Hassani et al. 2014). CVE treatment led to a decrease in lipid peroxidation in the lungs of the chlorpyrifos-injected animals, caused a significant induction of superoxide dismutase and restored to normalcy catalase and glutathione peroxidase activity. Administration of CVE resulted in apparently normal morphology with a significant decrease in chlorpyrifos-induced lung injuries.

Anti-ageing/Anti-acne Skin-Related Therapeutic Activities

There is growing scientific evidence suggesting curcumin's utility in the treatment of chronic pain, inflammatory dermatoses, acceleration of wound closure, skin infections as well as cosmetic ailments such as dyspigmentation (Nguyen and Friedman 2013). Topical administration of curcumin could directly deliver it to the affected tissue making it useful in treating skin-related disorders. However, limitations still exist such as the cosmetically unpleasing bright yellow-orange colour, its poor solubility and its poor stability at a high pH.

Turmeric extract (at 300 or 1000 mg/kg, twice daily) prevented an increase in skin thickness and a reduction in skin elasticity induced by chronic ultraviolet B (UVB) exposure in

melanin-possessing hairless mice (Sumiyoshi and Kimura 2009). It also prevented the formation of wrinkles and melanin (at 1000 mg/kg, twice daily) as well as increases in the diameter and length of skin blood vessels and in the expression of matrix metalloproteinase-2 (MMP-2). Prevention of UVB-induced skin ageing by turmeric may be due to the inhibition of increases in MMP-2 expression caused by chronic irradiation.

Studies showed that treatment with curcumin during D-galactose-induced ageing in mice exhibited considerable beneficial effects as antioxidant and antiperoxidant (Sarvalkar et al. 2011). Curcumin decreased the accumulation of advance glycation end products and decreased lipofuscin granules in submandibular glands. Curcumin also reduced lipid peroxidation chain reaction as indicated by decreased malondialdehyde levels in treated animals. Lee et al. (2014c) found that curcumin could enhance the production of major structural components of elastic fibres, elastin and fibrillin-1, in normal human fibroblast cells via increasing ELN and FBN1 promoters' activities. With 2- μ M curcumin treatment, the enhanced tropoelastin and fibrillin-1 protein amounts in Detroit 551 skin cells were approximately 134 and 130 % of control, respectively.

The use of turmeric cream was found to be efficacious in decreasing skin sebum secretions of human volunteers from the 4th week onwards, reaching a maximum of 24.8 % at the end of the study period (3 months) (Zaman and Akhtar 2013). The results suggested turmeric preparations to regulate excessive skin sebum secretion in persons suffering from acne and related problems. Arct et al. (2014) found permanent, visible and statistically significant changing of b* component colour of the skin after one application of cosmetic emulsions containing 12 and 25 % of turmeric extract. The change of skin colour remained even after removal of the emulsion. Sensory analysis indicated that the tested emulsions with turmeric extract had a significant impact on skin smoothness, spreadability, cosmetic absorption and pillow effect.

Antispasmodic Activity

Turmeric curcuminoids exerted antispasmodic activity in isolated guinea pig ileum and rat uterus by receptor-dependent and independent mechanism (Itthipanichpong et al. 2003). Curcuminoids at the concentration of 12 µg/ml significantly inhibited the ileum precontracted with acetylcholine and histamine. In potassium depolarising Tyrode solution, curcuminoids 4 and 20 µg/ml reduced the contraction induced by calcium chloride. In rat uterus smooth muscle preparation, curcuminoids 8 and 16 µg/ml significantly reduced force and frequency of contraction induced by oxytocins. Curcuminoids 8 and 16 µg/ml significantly reduced force of contraction induced by KCl. *Curcuma longa* extract had a direct and indirect myorelaxant effect on mouse ileum and colon, independent of the anti-inflammatory effect (Aldini et al. 2012). *Curcuma* extract reduced the spontaneous contractions induced by carbachol in the ileum and colon; the maximal response to carbachol was inhibited in a non-competitive and reversible manner. Similar results were obtained in the ileum and colon from *Curcuma*-fed dextran sulphate sodium-induced colitic mice. The results suggested the use of turmeric extract as a spasmolytic agent.

After 28 days of oral administration in the mouse intestine, turmeric extract appeared as a not competitive inhibitor through cholinergic, histaminergic and serotonergic receptors and showed spasmolytic effect on K(+)-induced contraction at the level of L-type calcium channels (Micucci et al. 2013). No side effect was observed on the bladder, aorta, trachea and heart when used as a dose that was effective on the intestine. Serum liver and lipid parameters were normal, while a slight increase in serum and liver bile acid concentration and a decrease in bile were observed.

Anticonvulsant Activity

Curcumin in a dose of 100 mg/kg significantly increased the seizure threshold in increasing current electroshock (ICES) test on both acute and chronic administration in mice (Bharal et al. 2008). The same dose of curcumin on acute administration showed anxiogenic effect on elevated plus-maze and actophotometer test. However, this anxiogenic effect

of curcumin disappeared on chronic administration. The results suggested that curcumin appeared to possess anticonvulsant activity in mice. Acute oral administration of curcumin (50, 100 and 200 mg/kg, p.o.) dose-dependently suppressed the progression of pentylenetetrazole-induced kindling in mice (Agarwal et al. 2011b). In addition, the increased levels of malondialdehyde (MDA) and glutathione were also reduced by curcumin in kindled animals. Bisabolene sesquiterpenoids from turmeric rhizomes exhibited anticonvulsant activity by inhibiting pentylenetetrazol (PTZ)-induced seizures in both zebrafish and mice (Orellana-Paucar et al. 2012). The study by Akula and Kulkarni (2014) demonstrated that the anticonvulsant effect of curcumin (20–120 mg/kg, p.o.) against pentylenetetrazol (PTZ) seizure threshold was via a direct or indirect activation of adenosine A1 but not A2A receptors in mice. Thus, curcumin may prove to be an effective adjunct in treatment of convulsions. In both pentylenetetrazole and kainate seizure models, curcumol, component of turmeric rhizome oil, suppressed epileptic activity in mice by prolonging the latency to clonic and tonic seizures and reducing the mortality as well as the susceptibility to seizure, presumably by facilitating the activation of γ -aminobutyric acid A (GABAA) receptors (Ding et al. 2014). The results identified curcumol as a novel antiseizure agent which inhibited neuronal excitability through enhancing GABAergic inhibition.

Contractile Activity

In a randomised, double-blind and crossover design study of 12 healthy volunteers (seven males and five females), curcumin administration reduced gall bladder volume which was statistically significant compared to placebo, indicating that curcumin induced contraction of the human gall bladder (Rasyid and Lelo 1999).

Detoxification/Chemopreventive/Antimutagenic Activities

Xenobiotic metabolising enzymes UDP glucuronyl transferase and glutathione S-transferase were significantly elevated in the hepatic tissues of rats fed with turmeric ranging from 0.5 to 10 % in the diet, but no significant differences were seen in the activating enzyme aryl hydrocarbon hydroxylase (Goud et al. 1993). The results suggested that turmeric may increase detoxification systems in addition to its antioxidant properties and could probably mitigate the effects of several dietary carcinogens. In-vitro studies by Singhal et al. (1999) suggested that glutathione S-transferases (GST) played a major role in detoxification of lipid peroxidation products in K562 human leukaemia cells and that these enzymes were modulated by curcumin.

In-vitro incubation of rat liver microsomes with each of the compounds—turmeric curcumin (C), demethoxycurcumin, bisdemethoxycurcumin and phenyl and phenethyl isothiocyanates—showed a dose-dependent decrease in carbon monoxide binding to microsomes and also showed a dose-dependent inhibition of CYP1A1, 1A2 and 2B1 activity (Thapliyal and Maru, 2001). Significantly lower concentrations of curcuminoids than isothiocyanates achieved 50 % inhibition of activity of CYP1A1 and 1A2, and the curcuminoids were also effective inhibitors of CYP2B1 as well. Pretreatment of rats with 1 % turmeric through the diet resulted in a significant decrease in induction of benzo[*a*]pyrene (B(a)P)-induced CYP1A1 and 1A2 and phenobarbitone (PB)-induced CYP2B1 in the liver, lung and stomach, although the extent of the decrease was different. The results suggested that turmeric/curcumin(s) were likely to inhibit activation of carcinogens metabolised by CYP450 isozymes, namely, CYP1A1, 1A2 and 2B1.

In-vitro studies showed that turmeric extract and curcumin prevented the formation of hazardous Maillard reaction products and its mutagenic activity (Kolpe et al. 2002). Turmeric extract and curcumin exhibited dose-dependent inhibition of formation of mutagenic pyrolysates as detected by TA98 with S9 mix. Additionally, turmeric extract and curcumin also inhibited the mutagenicity of lysine + glucose pyrolysed products. Some of the Maillard reaction products

(pyrolysates) are known mutagens/carcinogens; they play an important role in the development and progression of diabetes and age-related degenerative diseases; they also destroy important essential amino acids.

Gastric intubation of rats with curcumin prior to intraperitoneal injection of the mutagen cyclophosphamide (CP) significantly and dose-dependently decreased CP-induced clastogenicity (Shukla et al. 2002). The incidence of aberrant chromosomal cells was found to be reduced by both the doses of curcumin when compared to CP-treated group. The anticytotoxic potential of curcumin towards CP was also evident as the status of mitotic index was found to show increment. The study revealed the antigenotoxic potential of curcumin against CP-induced chromosomal mutations.

Insecticidal Activity (Health Insect Pest)

ar-Turmerone, volatile from the rhizome oil, displayed mosquitocidal activity with an LD₁₀₀ of 50 µg/mL on *Aedes aegypti* larvae (Roth 1998). Also, labda-8(17),12-diene-15,16 dial, isolated from turmeric leaf, displayed 100 % mosquitocidal activity on *A. aegypti* larvae at 10 µg/mL. Turmeric rhizome oil was much more toxic to the malarial vector *Anopheles gambiae* larvae, exhibiting 100 % mortality at 0.125 mg/mL with an LC₅₀ of 0.017 mg/mL than the leaf oil (Ajaiyeoba et al. 2008). The leaf had absolute mortality at 0.500 mg/mL with an LC₅₀ of 0.029 mg/mL. The observed toxicities were also found to be concentration dependent. The turmerone composition, especially the combination of α -turmerone and β -turmerone constituents in the oils, may be responsible for the observed larvicidal toxicities of both essential oils. Both oils displayed overwhelming activities compared with the reference compound *N,N*-diethyl-m-toluamid (DEET) which had an LC₅₀ value of 1.09 mg/mL.

Antiparasitic Activity

Curcumin showed cytotoxicity against African trypanosomes in-vitro with LD₅₀ values of 4.77 µM for bloodstream forms

and 46.52 μM for procyclic forms of *Trypanosoma brucei* *brucei* (Nose et al. 1998). All curcumin concentrations exhibited a cytotoxic effect in *Giardia lamblia* trophozoite inhibiting the parasite growth and adherent capacity, induced morphological alterations and provoked apoptosis-like changes Perez-Arriaga et al. 2006). The parent curcuminoids curcumin, demethoxycurcumin and bisdemethoxycurcumin exhibited low antitrypanosomal activity with EC_{50} values of 2.5, 4.6 and 7.7 μM , respectively, for the drug-sensitive *Trypanosoma brucei brucei* line (WT) (Changtam et al. 2010a). Among 43 curcuminoid analogues and 8 pairs of 1:1 mixture of curcuminoid analogues tested, 8 pure analogues and 5 isomeric mixtures of analogues exhibited high antitrypanosomal activity in submicromolar order of magnitude. Among these highly active analogues, 1,7-bis(4-hydroxy-3-methoxyphenyl)hept-4-en-3-one (40) was the most active compound, with an EC_{50} value of 0.053 μM ; it was about twofold more active than the standard veterinary drug diminazene aceturate (EC_{50} 0.12 μM). Curcumin was shown to be highly effective against the protozoan parasite, *Trichomonas vaginalis*, causal agent of the most common curable sexually transmitted disease, and the susceptibility of the different strains was not affected by an existing resistance to metronidazole (Wachter et al. 2014). After 24 h of incubation, the EC_{50} ranged from 73.0 to 105.8 $\mu\text{g/ml}$ and the EC_{90} from 216.3 to 164.9 $\mu\text{g/ml}$. In all strains tested, a 100 % eradication of all trichomonal cells within 24 h was reached at a concentration of 400 $\mu\text{g/ml}$ curcumin, the 50-fold concentration still being very well tolerated by human mucosa.

Gomes et al. (2002) studied the antileishmanial activity of the curcuminoids and found that the curcumin was more effective than the reference compound, pentamidine isetionate, against *Leishmania amazonensis*. Curcumin was confirmed to be more potent against *Leishmania major* than pentamidine: 100 % of cellular death was observed at 27 μM curcumin (Saleheen et al. 2002). Curcumin exhibited cytotoxicity against *Leishmania major* promastigotes in-vitro with an LD_{50} value of 37.6 μM (Koide et al. 2002). The parent curcuminoids

showed low antileishmanial activity (EC_{50} values of compounds curcumin and demethoxycurcumin for *Leishmania mexicana* amastigotes were 16 and 37 μ M, respectively), while the control drug, pentamidine, displayed an EC_{50} of 16 μ M. Among the active curcuminoid analogues, four compounds exhibited EC_{50} values of less than 5 μ M against *Leishmania major* promastigotes and four against *L. mexicana* amastigotes. No significant difference in sensitivity to curcuminoids between *L. major* promastigotes and *L. mexicana* amastigotes was observed. All the curcuminoids exhibited lower toxicity to human embryonic kidney (HEK) cells than to *Trypanosoma brucei brucei* bloodstream forms, and only one of the tested compounds showed significantly higher activity against HEK cells than curcumin. The selectivity index for *Trypanosoma brucei brucei* ranged from 3-fold to 1500-fold. The selectivity index for the most active analogue, the enone 40, was 453-fold.

Liposomal formulation of turmerone-rich hexane fractions from *Curcuma longa* was found to enhance their antileishmanial activity (Amaral et al. 2014). Parasite growth inhibition was demonstrated to be dose dependent. Important morphological changes as rounded body and presence of several roles on plasmatic membrane could be seen on *Leishmania amazonensis* promastigotes after treatment with subinhibitory concentration (2.75 μ g/mL) of the most active liposomal formulation (LipoRHIC). Curcumin derivatives indium curcumin and gallium curcumin complex showed more antileishmanial activity than curcumin and diacetyl curcumin (Fouladvand et al. 2013). The IC_{50} values for *Leishmania* growth inhibition for curcumin, gallium curcumin, indium curcumin, diacetyl curcumin and amphotericin B were 38 μ g/ml, 32 μ g/ml, 26 μ g/ml, 52 μ g/ml and 20 μ g/ml, respectively.

Adapala and Chan (2008) found that long-term, low-dose, oral consumption of curcumin-activated peroxisome proliferator-activated receptor- γ , deactivated type I response, inhibited inducible nitric oxide synthase and suppressed type I immunity, thus exacerbating the pathogenesis of *Leishmania*

donovani infection in-vivo. These in-vivo effects could be correlated to activities on infected residential macrophages in-vitro. Therefore, when reactive radicals generated from inflammation play the dominant role in elimination of pathogens, excessive use of the antioxidative supplements may compromise microbial defence.

Recent studies had shown that curcumin inhibited chloroquine-sensitive (CQ-S) and chloroquine-resistant (CQ-R) *Plasmodium falciparum* growth in culture with an IC_{50} of $\sim 3.25 \mu M$ (MIC = $13.2 \mu M$) and IC_{50} $4.21 \mu M$ (MIC = $14.4 \mu M$), respectively (Mishra et al. 2008). Several curcumin analogues examined show more effective inhibition of *P. falciparum* growth than curcumin. The most potent curcumin compounds pyrazole curcumin, 3-nitrophenylpyrazole curcumin and 4-(4-hydroxy-3-methoxy-benzylidene) derivative of curcumin were inhibitory to CQ-S *P. falciparum* at IC_{50} of 0.48, 0.87 and $0.92 \mu M$ and CQ-R *P. falciparum* at IC_{50} of $0.45 \mu M$, 0.89 and $0.75 \mu M$, respectively. Pyrazole curcumin exhibited sevenfold higher antimalarial potency against CQ-S and ninefold higher antimalarial potency against CQ-R. Demethoxycurcumin (DMC) was found to inhibit *Plasmodium falciparum* thioredoxin reductase (PfTrxR) (IC_{50} $2 \mu M$) (Munigunti et al. 2014). Both curcumin and DMC were shown to be active against chloroquine (CQ)-sensitive (D6 clone) and moderately active against CQ-resistant (W2 clone) strains of *Plasmodium falciparum*, while no cytotoxicity was observed against Vero cells.

Anthelmintic Activity

Curcuminoids, cyclocurcumin curcumin, demethoxycurcumin and bisdemethoxycurcumin isolated from the nematocidally active fraction of turmeric rhizome, were ineffective when they were applied independently. The nematocidal activity against the dog roundworm *Toxocara canis* increased remarkably when they were mixed, suggesting a synergistic action between them (Kiuchi et al. 1993). *Curcuma longa* and *Zingiber officinale* rhizome extracts and their combination exhibited anthelmintic activity using the earthworm *Pheretima*

posthuma model (Singh et al. 2011a). Both extracts not only paralysed but also killed the earthworms. Among the two herbal extracts, *Curcuma longa* showed maximum vermifuge activity at the concentration of 50 mg/ml, and ginger showed maximum vermucidal activity at the same concentration. *Curcuma longa* extract at the concentration of 10 mg/ml showed the time of paralysis and death of *Pheretima posthuma* at 12.40 min and 34 min, respectively; at concentration of 20 mg/ml, the paralysis and the death time was found to be 7.20 min and 23.40 min, and at the concentration of 50 mg/ml, time was 5.40 min for paralysis and 16.50 min for death (Raul et al. 2012). In the case of combination of the plant extracts (*Curcuma longa* and *Zingiber officinale*), the time of paralysis and death was 10.6 min and 31.8 minutes, respectively, at concentration of 10 mg/ml. At concentration of 20 mg/ml, the time of paralysis and death was 6.8 min and 27 min, respectively, and at 50 mg/ml concentration, the time of paralysis and death was 4.8 min and 16.3 min, respectively. Ginger and curcumin extracts exhibited anthelmintic activity in-vitro against *Ascaridia galli* in a dose- and time-dependent manner (Bazh and El-Bahy 2013). Ginger in all concentrations used exhibited a higher death rate observed than curcumin.

Ocular Ailment Therapy

Various studies demonstrated that curcumin had beneficial effects on several ocular diseases, such as chronic anterior uveitis, diabetic retinopathy, glaucoma, age-related macular degeneration and dry eye syndrome (Pescosolido et al. 2014). A 12-week clinical study of patients suffering from chronic anterior uveitis (inflammation of the iris and middle coat of the eyeball) indicated a possible benefit of oral curcumin supplementation (375 mg of turmeric extract with 95 % curcuminoids three times daily for 12 weeks) for chronic anterior uveitis (Lal et al. 1999). All the patients who received curcumin alone improved, whereas the group receiving antitubercular therapy along with curcumin had a response rate of 86 %. Follow-up of all the patients for the next 3 years indicated a recurrence rate of 55 % in the first group and of 36 % in the second group. The efficacy of curcumin and

recurrences following treatment were comparable to corticosteroid therapy, presently the only available standard treatment for this disease. The lack of side effects with curcumin was its greatest advantage compared with corticosteroids.

Studies demonstrated that the rats treated with naphthalene and kept on a diet supplemented with only 0.005 % (w/w) curcumin had significantly less opacification of lenses as compared to that observed in rats treated only with naphthalene (Pandya et al. 2000b). The study also demonstrated that naphthalene-initiated cataract in lens was accompanied and perhaps preceded by apoptosis of lens epithelial cells and that curcumin attenuated this apoptotic effect of naphthalene. Pandya et al. (2000a) also demonstrated that low levels of dietary curcumin attenuated galactose-induced cataract in rats. Lenses from galactose-fed animals without curcumin were partially opacified with an average intensity of transmitted light (AITL) value of 77 of the controls. The lenses from animals on a curcumin-supplemented galactose diet were significantly clearer than those from animals on galactose only (AITL 90 % of control). Apoptosis was observed in lens epithelia of rats fed with the galactose diet and was attenuated in rats fed with the curcumin-supplemented galactose diet.

Intraperitoneal administration of curcumin inhibited choroidal angiogenesis in laser-induced choroidal neovascularisation in pigmented rats as evidenced by fewer lesion in eyes treated with curcumin compared to eyes treated with vehicle and untreated eyes (Passos et al. 2002). Wistar rat pups treated with curcumin, before being administered with selenium, showed no opacities in the lens (Padmaja and Raju 2004). The lipid peroxidation, xanthine oxidase enzyme levels in the lenses of curcumin and selenium co-treated animals were significantly less when compared to selenium-treated animals. The superoxide dismutase and catalase enzyme activities of curcumin and selenium co-treated animal lenses showed an enhancement. Curcumin co-treatment appeared to prevent oxidative damage and was found to delay the development of cataract.

A decrease in chaperone-like activity of eye lens α H- and α L-crystallins was observed in streptozotocin-treated diabetic rats (Kumar et al. 2005). Curcumin feeding at levels close to dietary consumption prevented the loss of α -crystallin chaperone activity and delayed the progression and maturation of diabetic cataract. α H- and α L-crystallins isolated from curcumin-fed diabetic rat lenses had shown improved chaperone-like activity as compared to α H- and α L-crystallins from untreated diabetic rat lens. In subsequent study, they found that diet supplementation of cumin delayed progression and maturation of streptozotocin (STZ)-induced cataract in rats (Kumar et al. 2009b). Cumin was effective in preventing glycation of TSP and α -crystallin in diabetic lens. The results indicated that cumin had antiglycating properties that may be attributed to the modulation of chaperone activity of α -crystallin, thus delaying cataract in STZ-induced diabetic rat. Studies by Suryanarayana et al. (2003) found curcumin to be effective against galactose-induced cataract only at very low amounts (0.002 %) in the rat's diet. In contrast at and above a 0.01 % level, curcumin appeared to not be beneficial under hyperglycaemic conditions, at least with the animal model of galactose cataract. In another study, Suryanarayana et al. (2005) found that curcumin and turmeric delayed streptozotocin-induced diabetic cataract in rats. Notably, curcumin and turmeric prevented aggregation and insolubilisation of lens proteins due to hyperglycaemia. Also, treatment with turmeric or curcumin appeared to have minimised osmotic stress, as assessed by polyol pathway enzymes. Manikandan et al. (2009) found that curcumin and aminoguanidine suppressed selenium-induced oxidative stress and cataract formation in isolated lens from Wistar rat pups, possibly by inhibiting depletion of enzymatic as well as non-enzymatic antioxidants and preventing uncontrolled generation of free radicals and also by inhibiting iNOS expression. Their results implicated a major role for curcumin and aminoguanidine in preventing cataractogenesis in selenite-exposed lenses, wherein aminoguanidine was found to be more potent. In-vivo studies, they found that curcumin (75 mg/kg body wt) suppressed selenite-induced oxidative stress and cataract formation in rat pups (Manikandan et al. 2010b).

They also found that curcumin was able to prevent selenium-induced oxidative stress leading to activation of Ca^{2+} ATPase and inhibition of lens opacification, thus indicating that curcumin had the potential to function as an anticataractogenic agent, possibly by preventing free radical-mediated accumulation of Ca^{2+} in the eye lens.

Curcumin protected against hyperosmoticity-induced interleukin IL-1 β elevation in human corneal epithelial cells via MAPK (mitogen-activated protein kinases) pathways (Chen et al. 2010c). The results suggested that curcumin might have therapeutic potential for treating dry eye disease. Studies by Alex et al. (2010) found that epigallocatechin gallate (EGCG), resveratrol and curcumin may aid treatment of proliferative vitreoretinopathy (PVR). All three polyphenols tested reduced the absolute number of retinal pigment epithelial (RPE) cells, but had different effects on cell proliferation, apoptosis and necrosis. Resveratrol almost completely suppressed cell proliferation and induced RPE cell necrosis and caspase-3/7- and caspase-8-dependent apoptosis. Curcumin inhibited RPE cell increase exclusively by inducing caspase-3/7-dependent but caspase-8-independent cell death and necrosis. Resveratrol was most potent and EGCG induced the least cell death.

Combined administration of curcumin and vitamin C protected endothelial dysfunction in the iris tissue of streptozotocin-induced diabetic rats (Patumraj et al. 2006). Curcumin was found to enhance the effect of vitamin C in protecting the function of endothelial cells through its antioxidant with hypoglycaemic and hypolipidaemic actions. Kowluru and Kanwar (2007) found that administration of curcumin could prevent the development of retinopathy in streptozotocin-induced diabetic rats. Curcumin administration prevented diabetes-induced decrease in the antioxidant capacity and increase in 8-hydroxy-2'-deoxyguanosine (8-OHdG) and nitrotyrosine; however, it had only partial beneficial effect on retinal GSH (reduced glutathione). Curcumin also inhibited diabetes-induced elevation in the levels of IL-1 β , VEGF and NF- κ B. Topical application of turmeric aqueous extract prior to intravitreal injection of

lipopolysaccharide from *Escherichia coli* exerted potent anti-inflammatory activity against endotoxin-induced uveitis in rabbits as evaluated by grading the clinical signs and histopathologic changes and estimating the inflammatory cell count, protein and TNF- α levels in the aqueous humour (Gupta et al. 2008).

Gupta et al. (2011) found that oral treatment of curcumin (1 g/kg body weight t) prevented streptozotocin-induced diabetic retinopathy in Wistar albino rats through its hypoglycaemic, antioxidant and anti-inflammatory mechanisms.

In an open-label study of patients with acute and chronic central serous chorioretinopathy, oral administration of a curcumin–phospholipid delivery system was found to be effective in the management of central serous chorioretinopathy (Mazzolani and Togni 2013). After 12 months of therapy, no eyes showed further reduction in visual acuity, 39 % showed stabilisation, and 61 % showed statistically significant improvement. Ninety-five percent of eyes showed a reduction in neuroretinal or retinal pigment epithelium detachment and 5 % showed stabilisation. The difference in retinal thickness after 12 months was statistically significant.

Fertility Enhancement Activity

Semen samples were taken from 74 infertile patients and classified in two categories asthenozoospermic (AZ) and oligoasthenozoospermic (OAZ) according to their sperm parameters and treated with alcoholic turmeric extract (Fakhrildin 2011). Results revealed an enhancement of most sperm parameters for control and both treated groups post-in-vitro sperm activation as compared to pre-in-vitro sperm activation. Best results for improvement of sperm parameters were assessed within treated group (5 μ g/mL of turmeric extract). The lower concentration of alcoholic turmeric extraction enhanced human sperm parameters during in-vitro sperm activation without any harmful effects on sperm physiology. Głombik et al. (2014) found that curcumin at low

concentrations (1–50 μM) exhibited protective effects on sperm motility and on di(2-ethylhexyl)phthalate (DEHP)-induced damage of seminiferous tubules in testes and its ability to diminish the decrease in sperm motility in-vivo. In contrast, curcumin used in high concentration (100 μM) decreased sperm motility and viability in-vitro.

Otoprotective Activity

Fetoni et al. (2014) demonstrated that systemic curcumin attenuated cisplatin-induced ototoxicity (hearing loss) in rats by increasing haem oxygenase-1 expression, outer hair cell survival and decreasing toxic aldehyde 4-HNE (4-hydroxy-2-nonenal) expression.

Longevity Activity

The phenolic compound 1,2,3,4,6-penta-*O*-galloyl- β -D-glucose (PGG) isolated from turmeric aerial parts was found to prolong the lifespan and stress resistance of the worm *Caenorhabditis elegans* in normal culture (Ahn et al. 2013). PGG was able to elevate SOD activities of worms and reduce intracellular ROS accumulation in a dose-dependent manner. The results of studies by Shen et al. (2013) suggested that curcumin increased mean lifespan of *Drosophila* via regulating gene expression of the key enzyme superoxide dismutase and reducing accumulation of malondialdehyde and lipid peroxidation.

Antivenom Activity

A potent antivenom against snakebite was isolated from *Curcuma longa* (Ferreira et al. 1992). The fraction consisting of *ar*-turmerone neutralised both the haemorrhagic activity present in *Bothrops jararaca* venom and the lethal effect of *Crotalus durissus terrificus* venom in mice. Immunological studies demonstrated that this fraction also inhibited the proliferation and the natural killer activity of human lymphocytes. Turmerin a protein from turmeric was purified and found to have a relative molecular mass of 14kD, inhibited

the enzymatic activity and neutralised the pharmacological properties, such as cytotoxicity, oedema and myotoxicity of multitoxic phospholipase A₂ (NV-PLA₂) of cobra (*Naja naja*) venom (Chethankumar and Srinivas 2008; Chethankumar et al. 2014b). Turmerin at 1:2 M/M ratio with *Naja naja* venom phospholipase A₂ (NV-PLA₂) showed 89 % inhibition of the enzyme activity. Mice receiving NV-PLA₂ (1 mg/kg body weight) pretreated with turmerin (2 mg/kg body weight) showed 95 % decrement in lipid peroxidation in the plasma. Turmerin was statistically significant in inhibiting lipid peroxide formation in all the organs tested at dose five and seven times less when compared to known antioxidants such as ascorbic acid and α -tocopherol. Turmerin at 1:2 and 1:3 M/M ratio effectively neutralised NV-PLA₂ lethality by 90 %.

Osteogenic/Adipogenic Activity

Curcumin increased alkaline phosphatase activity and osteoblast-specific mRNA expression of Runx2 and osteocalcin when rat bone marrow mesenchymal stem cells (rMSCs) were cultured in osteogenic medium (Gu et al. 2012). In contrast, curcumin decreased adipocyte differentiation and inhibited adipocyte-specific mRNA expression of PPAR γ 2 and C/EBP α when rMSCs were cultured in adipogenic medium. Haem oxygenase (HO)-1 expression was increased during osteogenic differentiation of rMSCs.

Curcumin, physically entrapped and stabilised in silk hydrogel films, was found to enhance adipogenic differentiation of human bone marrow-derived mesenchymal stem cells (hBMSCs) (Li et al. 2014a). The presence of curcumin significantly reduced the silk gelation time and changed the porous morphology of gel matrix, but did not change the formation of the silk β -sheet structure. For hBMSC cultured on silk films containing more than 0.25-mg/ml curcumin, cell proliferation was inhibited, while adipogenesis was significantly promoted. When hBMSCs were cultured in media containing free curcumin, both proliferation and adipogenesis of hBMSC were inhibited when curcumin concentrations exceeded 5 μ M, which was more than 1000

times higher than the level of curcumin released from the films in aqueous solution.

Antisteoporotic Activity

Studies by Yang et al. (2011) suggested that APP/PS1 transgenic mice were susceptible to osteoporosis and that oral administration of curcumin for 12 months could prevent further deterioration of the bone structure and produce beneficial changes in bone turnover. At 12 months, curcumin treatment led to constant increases in the trabecular bone mass of the metaphysis and clearly improved the bone mineral density. The change of inflammation cytokine, including TNF- α and IL-6, may play an important role in the mechanisms of action of curcumin.

Radioprotective Activity

C. longa exerted a beneficial radioprotective effect against γ -irradiation (GR)-induced oxidative stress in male rats by alleviating pathological disorders and modulating antioxidant enzymes (Nada et al. 2012). Exposure of untreated rats to GR resulted in transaminase disorders, lipid abnormalities, elevation of lipid peroxidation, trace element alterations, release of IL-6 and TNF and decrease in glutathione and protein level of superoxide dismutase-1 (SOD-1) and peroxiredoxin-1 (PRDX-1). However, treatment of rats with turmeric extract before and after GR exposure improved antioxidant status and minimised the radiation-induced increase in inflammatory cytokines.

Probiotics-Like Activity

Three lactic acid bacteria (LAB), namely, *Enterococcus faecium*, *Lactococcus lactis* subsp. *lactis* and *Lactobacillus plantarum*, were isolated from turmeric rhizomes (Pianpumepong and Noomhorm (2010). These microorganisms showed similar characteristics as probiotic organisms. They showed high acid and bile salt tolerance (>89 % survival) and exerted antagonistic activity against intestinal

disease-causing bacteria *Escherichia coli*, *Staphylococcus aureus* and *Salmonella* spp. All three LAB species could be used as starter culture to ferment turmeric beverages. Fermentation time and LAB led to dominant amount of TPC and high levels of antioxidant (DPPH radical scavenging) activities. The FRAP (ferric-reducing antioxidant power) value of fermented turmeric beverage increased slightly until the end of fermentation. The absorption of turmeric powder, turmeric powder-mixed encapsulated probiotic (TP) and encapsulated fermented turmeric beverage (TB) in rats was measured in terms of antioxidant activity in the plasma (Pianpumepong et al. 2012). Plasma antioxidant concentration was higher in rats administered fermented turmeric beverage than in those administered turmeric powder with probiotics at all the time points. The maximum concentration (C_{max}) value and area under the plasma concentration versus time curve (AUC) were higher in the rat administered with TB. The value was lower in the plasma of rats administered with turmeric powder and TP.

Antifertility Activity

Incubation of sperm (human and murine) with curcumin caused a concentration-dependent decrease in sperm forward motility, capacitation/acrosome reaction and murine fertilisation in-vitro (Naz 2011). At higher concentrations, there was a complete block of sperm motility and function within 5–15 min. Administration of curcumin, especially intravaginally, caused a significant reduction in fertility. The antifertility effect of curcumin was reversible. The findings suggested that curcumin may constitute a double-edged sword to block conception, infection and cancer, thus providing an ideal contraceptive.

Bioavailability/Drug Delivery Studies

Yallapu et al. (2012) in their review focused on studies conducted on the design and development of nanoparticles, self-assemblies, nanogels, liposomes and complex fabrication for sustained and efficient curcumin delivery to improve curcumin bioavailability and anticancer potential for therapy.

Yue et al. (2012) found that in the presence of α - and aromatic turmerones, the amount of curcumin transported into the Caco-2 cells in 2 h was significantly increased. α -Turmerone and verapamil (a P-gp inhibitor) significantly inhibited the efflux of rhodamine-123 and digoxin (i.e. inhibited the activity of P-gp). It was observed that aromatic turmerone significantly increased the rhodamine-123 efflux and P-gp (MDR1 gene) mRNA expression levels. In a clinical crossover, randomised study of healthy subjects (13 women, 10 men), administration of both the micronised powder and in particular the liquid micellar formulation of curcumin significantly improved its oral bioavailability without altering safety parameters and may thus be ideally suited to deliver curcumin in human intervention trials (Schiborr et al. 2014). Women were found to absorb curcumin more efficiently than men.

O'Toole et al. (2012) found that curcumin delivery for medicinal applications could be enhanced by encapsulating curcumin in submicrometre spray-dried chitosan/Tween 20 particles. Release studies confirmed that curcumin could be released completely from the particles over a 2-h period. Guzman-Villanueva et al. (2013) developed a new nano-microparticulate system for enhanced aqueous-phase solubility of curcumin. Encapsulating the curcumin into the hydrogel nanoparticles yielded a homogenous curcumin dispersion in aqueous solution compared to the free form of curcumin. Also, the in-vitro release profile showed up to 95 % release of curcumin from the developed nano-microparticulate systems after 9 h in PBS (phosphate-buffered saline) at pH 7.4 when freeze-dried particles were used.

Although curcumin possessed remarkable medicinal properties, the bioavailability of curcumin had limited its success in epigenetic studies and clinical trials (Kalani et al. 2015). Curcumin delivered through nanoparticles had been shown to be neuroregenerative, but the use of nanoparticles in the brain had limitations. Curcumin had been shown to be encapsulated in exosomes, nanovesicles (<200 nm), thereby showing its therapeutic effects in brain diseases.

Turmeric oil being volatile, insoluble in water and unstable in certain environments had been reported to encounter difficulties with formulation development and stability of new products (Lertsutthiwong and Rojsitthisak 2011). The use of naturally occurring polysaccharides, chitosan and alginate was reviewed by them as one approach to overcome these problems. The in-vitro skin permeation of turmeric oil from nanocapsules was also discussed. Chu et al. (2014) developed a glycyrrhetic acid-modified curcumin-loaded nanostructured lipid carrier (Cur-GA-PEG-NLC) by the film ultrasound method to improve the tumour-targeting ability. The encapsulation efficiency for various Cur-GA-PEG-NLC was within the range of 90.06–95.31 %, and particle size was between 123.1 and 132.7 nm. An in-vitro MTT assay showed that Cur-GA10%-PEG-NLC had significantly high cellular uptake and cytotoxicity against HepG2 cells compared with other groups.

The main problem associated with the use of curcumin as a chemopreventive agent in humans is its low absorption from the gastrointestinal tract, poor solubility in body fluids and low bioavailability (Terlikowska et al. 2014a). Good results in the prevention and the treatment of breast cancer could be ensured by curcumin nanoparticles coated with albumin, known as nanocurcumin. The low bioavailability of curcumin has limited its application in various ailments, and nanotechnology in drug delivery system is enthusiastically betrothed being pursued in refining the solubility, stability, absorption and therapeutic potential of the curcumin within the diseased tissue and organ (Ahmad et al. 2014b).

Pharmacokinetics Studies

The average recovery of curcumin from plasma and urine was greater than 96 % using high-performance liquid chromatography (Heath et al. 2003). The limit of detection (LOD) and quantification (LOQ) of curcumin in the rat plasma was 1 and 5 ng/ml, respectively (Yang et al. 2007). After curcumin (500 mg/kg, p.o.) administration, the maximum concentration (C_{max}) and the time to reach maximum concentration (T_{max}) were 0.06 µg/ml and 41.7 min,

respectively. The elimination half-life ($t_{1/2 \beta}$) was 28.1 and 44.5 min for curcumin (500 mg/kg, p.o.) and curcumin (10 mg/kg, i.v.), respectively. The oral bioavailability was about 1 %.

Orally administered curcuminoids (curcumin, demethoxycurcumin and bisdemethoxycurcumin) were found to be absorbed from the alimentary tract and present in the general blood circulation after largely being metabolised to the form of glucuronide and glucuronide/sulphate conjugates in rats (Asai and Miyazawa 2000). Hoehle et al. (2007) found that the gastrointestinal tract contributed substantially to the glucuronidation of curcuminoids in humans. The phenolic glucuronidation of the curcuminoids was predominantly catalysed by hepatic UGT1A1 and intestinal UGT1A8 and 1A10, whereas UGT1A9, 2B7 and 1A8 exhibited high activities for hexahydro-curcuminoids. UGT1A9 was able to form the alcoholic glucuronide of each curcuminoid in addition to the phenolic conjugate.

Curcumin glucuronide was the major metabolite of curcumin found in the plasma after oral administration of curcumin in rats (Shoji et al. 2014). They found that the effects of curcumin glucuronide were weaker than those of curcumin and that this difference was related to relative absorption rates of curcumin and curcumin glucuronide into HepG2 cells. Quantitative pharmacokinetic analysis showed that curdione was detected in the plasma, with the lower quantification limit being 6.5 ng/mL, and the recovery from plasma was about 105.2 % (Lv et al. 2014). In order to overcome these pharmacokinetic deficits of curcumin, several strategies, such as the design of synthetic analogues, the combination with specific adjuvants or nanoformulations, had been developed (Teiten et al. 2014).

Herb/Drug Interaction Activity

Curcumin inhibited CYP1A2 (IC_{50} , 40.0 μ M), CYP3A4 (IC_{50} , 16.3 μ M), CYP2D6 (IC_{50} , 50.3 μ M), CYP2C9 (IC_{50} , 4.3 μ M) and CYP2B6 (IC_{50} , 24.5 μ M) (Appiah-Opong et al. 2007). Curcumin showed a competitive type of inhibition towards

CYP1A2, CYP3A4 and CYP2B6, whereas a non-competitive type of inhibition was observed with respect to CYP2D6 and CYP2C9. The inhibitory activity towards CYP3A4, shown by curcumin, may have implications for drug–drug interactions in the intestines, in case of high exposure of the intestines to curcumin upon oral administration. The decomposition products of curcumin (vanillin, vanillic acid, ferulic aldehyde and ferulic acid) showed no significant inhibitory activities towards the CYPs investigated and, therefore, were not likely to cause drug–drug interactions at the level of CYPs.

Incorporation of curcumin into emulsomes results in water-soluble and stable CurcuEmulsome nanoformulations (Ucisik et al. 2013). CurcuEmulsomes showed a significantly prolonged biological activity and demonstrated therapeutic efficacy comparable to free curcumin against HepG2 in-vitro with a delay in response, as assessed by cell viability, apoptosis and cell cycle studies. CurcuEmulsomes not only successfully facilitated the delivery of curcumin into the cell in-vitro but also enabled curcumin to reach its effective concentrations inside the cell. Studies demonstrated that curcumin–cotrimoxazole combination therapy lowered the antimicrobial effectivity of cotrimoxazole in both intrainestinal and extraintestinal organs in mice with typhoid fever induced by *Salmonella typhimurium* (Rahayu et al. 2013). Hsieh et al. (2014) found that oral intake of curcumin significantly decreased the bioavailability of the immunosuppressant everolimus, a probe substrate of P-glycoprotein (P-gp) and cytochrome CYP3A4, mainly through marked activation on CYP3A4. Daveluy et al. (2014) reported a probable interaction between a vitamin K antagonist, fluindione and the herbal medicine turmeric that resulted in the elevation of the international normalised ratio (INR). In a clinical study of six healthy human subjects, administration of turmeric extract with dextromethorphan syrup and the CYP2D6- and CYP3A4-mediated formation of dextromethorphan (DOR) and 3-methoxymorphinan (3-MM) from dextromethorphan were significantly and dose-dependently inhibited by turmeric (Al-Jenoobi et al. 2015). The 100-µg/ml dose of *Curcuma* extract produced highest inhibition, which was about 70 % for DOR and 80 % for 3-MM. *Curcuma*

significantly increases the urine metabolic ratio of DEX/DOR, but the change in DEX/3-MM ratio was statistically insignificant. The results suggested that turmeric significantly inhibited the activity of CYP2D6 in in-vitro as well as in-vivo, indicating its potential to interact with CYP2D6 substrates.

Adverse Effects of Curcumin

Curcumin prevented UV irradiation-induced apoptotic changes, including c-Jun N-terminal kinase (JNK) activation, loss of mitochondrial membrane potential (MMP), mitochondrial release of cytochrome C, caspase-3 activation and cleavage/activation of PAK2 in human epidermoid carcinoma A431 cells (Chan et al. 2003). Curcumin also abolished intracellular oxidative stress caused by UV irradiation. Curcumin prevented photodynamic treatment (PDT)-induced apoptotic events in human epidermal carcinoma A431 cells (Chan and Wu 2004). Curcumin prevented PDT-induced JNK activation, mitochondrial release of cytochrome c, caspase-3 activation and cleavage of PAK2 and abolished PDT-stimulated intracellular oxidative stress. Hsuuw et al. (2005) showed that curcumin inhibited methylglyoxal-induced reactive oxygen species (ROS) generation and various apoptotic biochemical events in embryonic stem cells and blastocysts isolated from pregnant mice. In a more recent study, Chen et al. (2010a) showed that in-vitro exposure of blastocysts to curcumin triggered apoptosis and retarded early postimplantation development after transfer to host mice. In addition, curcumin induced apoptotic injury effects on mouse blastocysts through ROS generation and further promoted mitochondria-dependent apoptotic signalling processes to impair sequent embryonic development.

Curcumin could induce cell death in normal human lymphocytes both quiescent and proliferating, without oligonucleosomal DNA degradation, considered as a main hallmark of apoptotic cell death (Magalska et al. 2006). Taking into account the role of CD8⁺ cells in tumour response, their depletion during chemotherapy could be particularly undesirable. Chan et al. (2006) demonstrated that curcumin

could induce apoptotic changes, including JNK activation, caspase-3 activation and cleavage of PARP and PAK2, at treatment concentrations lower than 25 μ M in human osteoblast cells. In contrast, treatment with 50–200 μ M of curcumin did not induce apoptosis, but rather triggered necrotic cell death in human osteoblasts. Also a dose-dependent decrease in intracellular ATP levels was observed after treatment of osteoblast cells with curcumin. Treating chick limb bud mesenchymal cells with curcumin suppressed chondrogenesis by stimulating apoptotic cell death and downregulating integrin-mediated reorganisation of actin cytoskeleton via modulation of Akt signalling (Kim et al. 2009a). After exposure of human osteoblast-like cells (MG-63), Moran et al. (2012) observed that curcumin abrogated inducible NOS expression and decreased NO levels, inhibiting also cell proliferation. Under osteogenic conditions, curcumin also decreased the level of mineralisation. Curcumin prevented methylglyoxal-induced cell death and apoptotic biochemical changes in human hepatoma G2 cells (Chan et al. 2005). Curcumin abolished methylglyoxal-stimulated intracellular ROS oxidative stress.

Toxicity Studies

In the chronic (90 days, 100 mg/kg/day) study, mice treated with ethanol turmeric rhizome exhibited significant changes in heart and lung weights (Quereshi et al. 1992). A significant fall in the WBC and RBC levels of the *C. longa*-treated animals was observed as compared to the controls. No spermatotoxic effects were observed. Oral administration of 80 mg/kg of *Curcuma longa* extract to 12 healthy rats over 25 days induced changes in urinary metabolic composition (Dall'Acqua et al. 2014). Decreased allantoin urinary levels observed was considered a partial demonstration of the in-vivo effect of curcumin on oxidative stress in a healthy animal model. Such information could be useful to assess its efficacy and safety. The polysaccharide extract of turmeric rhizome (NR-INF-02) up to a dose of 5000 μ g/mL exhibited no mutagenic in the bacterial reverse mutation test (Velusami et al. 2013). The results on chromosome aberration and

micronucleus tests revealed the non-clastogenic activity of NR-INF-02 in a dose range of 250.36 to 2500 µg/mL with and without metabolic activation (S9). In acute oral toxicity study, NR-INF-02 was found to be safe up to 5 g/kg body weight in Wistar rats. The results indicated that polysaccharide extract of *C. longa* was found to be genotoxically safe and also exhibited maximum tolerable dose of more than 5 g/kg rat body weight.

Curcumin had been demonstrated to be safe in six human trials and has demonstrated anti-inflammatory activity (Chainani-Wu 2003). A phase I human trial with 25 subjects using up to 8000 mg of curcumin per day for 3 months found no toxicity from curcumin. Five other human trials using 1125–2500 mg of curcumin per day have also found it to be safe.

The study by Balaji and Chempakam (2010) reported that out of 200 compounds from turmeric, 184 compounds were predicted as toxigenic, 136 compounds were mutagenic, 153 compounds were carcinogenic and 64 compounds were hepatotoxic. To cross validate their results, they chose the popular curcumin and found that curcumin and its derivatives may cause dose-dependent hepatotoxicity.

Traditional Medicinal Uses

Turmeric has been used in traditional Asian folk medicine for centuries. In Ayurvedic medicine, turmeric is a well-documented treatment for various respiratory conditions (e.g. asthma, bronchial hyperactivity and allergy), as well as for liver disorders, anorexia, rheumatism, diabetic wounds, runny nose, cough and sinusitis (Araujo and Leon 2001). In traditional Chinese medicine, it is used to treat diseases associated with abdominal pain (Aggarwal et al. 2004). From ancient times, as prescribed by Ayurveda, turmeric has been used to treat sprains and swelling (Araujo and Leon 2001). In both Ayurvedic and traditional Chinese medicine, turmeric is considered a bitter digestive and a carminative. Unani practitioners also use turmeric to expel phlegm or ‘kapha’, as well as to open blood vessels in order to improve blood circulation.

Artemisia iwayomogi and *Curcuma longa* (ACE) has been popularly used to treat atherosclerosis as well as hyperlipidaemia in the Asian countries (Shin et al. 2014). Herbs are also used traditionally in Ayurvedic medicine as antiseptic, wound healing and anti-inflammatory compounds (Chan et al. 2006). Since the time of Ayurveda (1900 Bc), numerous therapeutic activities have been assigned to turmeric for a wide variety of diseases and conditions, including those of the skin, pulmonary and gastrointestinal systems, aches, pains, wounds, sprains and liver disorders (Aggarwal et al. 2007). In India, turmeric has been used traditionally as a remedy for stomach and liver ailments, as well as topically to heal sores (Chaturvedi 2009). Ancient Indian medicine has touted turmeric as an herb with the ability to provide glow and lustre to the skin as well as vigour and vitality to the entire body. *Curcuma longa* rhizome is used in African traditional medicine to treat palpitation, hypertension or other related blood circulation disorders (Adaramoye et al. 2009, 2012). Turmeric is an Ayurvedic herb that has been traditionally used to treat inflammatory conditions like rheumatoid arthritis (RA) (Taty et al. 2011). Turmeric (rich in curcuminoids) and ginger (rich in gingerols and shogaols) rhizomes have been widely used as dietary spices and to treat different diseases in Ayurveda/Chinese medicine since antiquity (Ramadan et al. 2011).

In Ayurvedic practices, turmeric is thought to have many medicinal properties including strengthening the overall energy of the body, relieving gas, dispelling worms, improving digestion, regulating menstruation, dissolving gallstones and relieving arthritis (Prasad et al. 2011). Many South Asian countries use it as an antiseptic for cuts, burns and bruises and as an antibacterial agent. In Pakistan, it is used as an anti-inflammatory agent and as a remedy for gastrointestinal discomfort associated with irritable bowel syndrome and other digestive disorders. In Pakistan and Afghanistan, turmeric is used to cleanse wounds and stimulate their recovery by applying it on a piece of burnt cloth that is placed over a wound. Indians use turmeric, in addition to its Ayurvedic applications, to purify blood and remedy skin conditions. Turmeric paste is used by women in some parts of India to

remove superfluous hair. Turmeric paste is applied to the skin of the bride and groom before marriage in some parts of India, Bangladesh and Pakistan, where it is believed to make the skin glow and keep harmful bacteria away from the body. Turmeric is currently used in the formulation of several sunscreens. Several multinational companies are involved in making face creams based on turmeric.

In Chinese medicine, turmeric is used to stimulate the production of red blood cells, dissolve blood clots, arrest bleeding and treat jaundice; irregular menstruation; stomach problems; pain in the stomach, chest and back; diarrhoea; and dysentery (Wee and Hsuan keng 1990). *Curcuma longa* is a representative of traditional Chinese medicine and widely used as carminative, laxative and anthelmintic and as a cure for liver ailment (Long et al. 2014).

In the Philippines, the rhizomes with coconut oil are considered stomachic and vulnerary (Stuart 2014). In Malaya, turmeric is used as a carminative, dispelling flatulence and also as antispasmodic in diarrhoea and dysentery (Burkill 1966). It is also used to treat foul ulcers and broken skin, and in India turmeric is a popular remedy for sprains and bruises. The Malays also used turmeric for treating eyes as a magic prescription, but he stated that in Java turmeric is used for sore eyes as in India. Turmeric is pounded into a paste to serve as vehicle for dispensing naphthalene to the abdomen to produce uterine contractions. It is popular as a tea in Okinawa, Japan, to help with stomach problems and other ailments.

In Vietnam, turmeric is used to treat irregular menstruation, amenorrhoea, blood stasis, angina pectoris, post-partum haematometra, contusion, gastric ulcer, furunculosis, impetigo, rheumatism, limb ache and jaundice (NIMM 1999). The rhizome juice is applied topically against furunculosis, phlegmon and impetigo and parasitical dermatosis. Turmeric is also used as a stimulant, tonic, emmenagogue and astringent.

Curcumin preparation (Curcumin C3 Complex®)—a preparation of a mixture of curcuminoids (curcumin, bisdemethoxycurcumin and demethoxycurcumin) and all curcuminoids extracted from the rhizomes of *Curcuma longa*

—has been given a GRAS (generally recognised as safe) status by the Food and Drug Administration of the USA (USFDA 2013).

Other Uses

Main turmeric products include (a) dried whole rhizomes used in medicine, spices and other turmeric processed products; (b) ground turmeric used as spice, curry powder and pastes and dye, in medicine; (c) turmeric oil used as spice and, in medicine, dietary supplements; (d) turmeric oleoresins used in food colouring and medicine dietary supplements; and (e) curcumin (turmeric yellow, kurkum) used in medicine and dietary supplements (Li et al. 2011).

Turmeric is one of the best known of material dyes, being used for dyeing silk, wool and cotton (Burkill 1966). The rhizomes are employed for dyeing mats in the Philippines. In Sudan the rhizome is used as a cosmetic. Turmeric extract can be used as a cheap natural histological dye for staining collagen fibres, cytoplasm, red blood cells and muscle cells (Avwioro et al. 2007). *L*- and *D*-lactic acid could be produced from *Curcuma longa* waste biomass through simultaneous saccharification and cofermentation by *Lactobacillus coryniformis* and *Lactobacillus paracasei*, respectively (Nguyen et al. 2013). The process was simple and efficient and could be utilised by *C. longa* residue-based lactic acid industries without requiring the alteration of plant equipment. Acid hydrolysis of turmeric waste afforded a hydrolysate containing lactic acid and ethanol fermentative sugars (Nguyen et al. 2014).

Turmeric is currently used in the formulation of some sunscreens (Prasad et al. 2011). Turmeric paste is used by some Indian women to keep them free of superfluous hair. Turmeric paste is applied to bride and groom before marriage in some places of India, Bangladesh and Pakistan, on the belief that turmeric promotes glow to skin and keeps some harmful bacteria away from the body.

Results of studies suggested that turmeric extract could enhance resistance against *Eimeria maxima* and *Eimeria*

tenella infections in chickens by attenuating *Eimeria*-induced, inflammation-mediated gut damage (Kim et al. 2013).

Methanol extract of turmeric rhizomes effectively controlled the development of red pepper anthracnose caused by *Colletotrichum coccodes* (Cho et al. 2006). Three antifungal substances curcumin, demethoxycurcumin and bisdemethoxycurcumin were identified from the methanol extract. The curcuminoids in a range 0.4–100 µg/ml effectively inhibited the mycelial growth of three red pepper anthracnose pathogens, *Colletotrichum coccodes*, *C. gloeosporioides* and *C. acutatum*. The curcuminoids also effectively inhibited spore germination of *C. coccodes*, and bisdemethoxycurcumin was the most active. Among the three curcuminoids, only demethoxycurcumin was effective in a greenhouse test in suppressing red pepper anthracnose caused by *C. coccodes*.

Petroleum ether extract of *C. longa* rhizome had been reported to be repellent to *Tribolium castaneum* (Jilani and Su 1983). Hexane extract of *C. longa* rhizome reduced progeny production in *T. castaneum* at 200-ppm concentration (Jilani et al. 1988). Turmeric oil and mustard oil alone did not cause significant adult mortality of red flour beetle *Tribolium castaneum* in stored milled rice (Chander et al. (1992). However, in combination, they offered complete protection. Turmeric oil and sweet flag oil were significantly more repellent against the lesser grain borer *Rhyzopertha dominica* during the first 2 weeks than neem oil and Margosan-O, but thereafter, their repellency decreased more rapidly than that of neem oil or Margosan-O (Jilani and Saxena 1990). Of several turmeric extract, the petroleum ether extract was the most toxic topically causing 94 % mortality at 200 µg/insect to diamondback moth (DBM) (*Plutella xylostella*) (Morallo-Rejesus et al. 1992). This extract was also toxic to brown planthopper (BPH) (*Nilaparvata lugens*). The water extract also caused 87 to 90 % mortalities to DBM by filter impregnation method. Both PE and CE inhibited the feeding behaviour of DBM. Five fractions (A, B, C, D and E) were isolated from the petroleum ether extract, and only B exhibited

contact toxicity to BPH. But all fractions were ovicidal to DBM.

Curcumin I, the major constituent of turmeric powder, was converted to five alkyl ether derivatives and tested along with the parent compounds and other extractives for insect growth inhibitory activity against *Schistocerca gregaria* and *Dysdercus koenigii* nymphs (Chowdhury et al. 2000). At 20 µg per nymph, benzene extract and dibutyl curcumin I were the most active (60 % inhibition) against *S. gregaria*, whereas at 50 µg per nymph, these substances exhibited moderate growth inhibitory activity (45 %) against *D. koenigii* nymphs. At these concentrations, turmeric oil caused 50–60 % nymphal mortality in both test insects. *ar*-Turmerone from *Curcuma longa* rhizome caused 100 and 64 % mortality of *Nilaparvata lugens* female adults, at 1,000 and 500 ppm, respectively (Lee et al. 2001). Against *Plutella xylostella* larvae, the compound gave 100 and 82 % mortality at 1,000 and 500 ppm, respectively. Against *Myzus persicae* female adults and *Spodoptera litura* larvae, *ar*-turmerone at 2,000 ppm was effective, but weak insecticidal activity was observed at 1,000 ppm. At a dose of 2.1 mg/cm², *ar*-turmerone was almost ineffective (<10 % mortality) against adults of *Sitophilus oryzae*, *Callosobruchus chinensis* and *Lasioderma serricorne* as well as larvae of *Plodia interpunctella*.

The leaf essential oil of *Curcuma longa* exhibited contact toxicity against adults of *Rhyzopertha dominica* (lesser grain borer); fumigant toxicity against adult rice weevil, *Sitophilus oryzae* and oviposition-deterrent and ovicidal actions against *Tribolium castaneum* (red flour beetle) (Tripathi et al. 2002). At the concentration of 40.5-mg/g food, the oil totally suppressed progeny production of all the three test insects. Nutritional indices indicated >81 % antifeedant action of the oil against *R. dominica*, *S. oryzae* and *T. castaneum* at the highest concentration tested. *C. longa* rhizome petroleum ether extract was very effective in controlling *Sitophilus zeamais* in stored maize grains and can be incorporated for the control of *S. zeamais* in stored maize grains (Asawalam and Chukwuekezie (2012). *ar*-Turmerone was found to be highly toxic to the maize weevil *Sitophilus zeamais* and fall

armyworm *Spodoptera frugiperda* at low doses (Tavares et al. 2013). *Curcuma longa* essential oil was found to have potent insecticidal activity causing high cell mortality of midgut cell line derived from *Rhynchophorus ferrugineus* (Rizwan-Ul-Haq and Aljabr 2014).

Suppositories weighing 2 g each, containing 0.5 %, 1.0 % and 2.0 % w/w of ethanolic turmeric extract prepared using water-soluble polyethylene glycol base, gave significant and nearly similar observations in breaking test, melting range, disintegration time and dissolution time (Goupale et al. 2012). The release of turmeric extract through the formulations was significant and independent of initial content. It was found that within 60 min complete release was observed.

Curcuma longa ethanolic extract exhibited excellent (100 %) phytotoxic activity against *Lemna minor*, an aquatic weed (Khattak et al. 2005).

Comments

C. longa had been reported to display a certain level of both phenotypic and genotypic variation (Leong-Škorničková et al. 2007), and this variation was definitely higher than in other vegetatively reproducing *Curcuma* species (2n = 63) (Leong-Škorničkov et al. 2008).

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Curcuma mangga

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Scientific Name

Curcuma mangga Valetton and van Zijp

Synonyms

No synonym recorded

Family

Zingiberaceae

Common/English Names

Mango Ginger, Mango Turmeric

Vernacular Names

India: Manga Injee

Indonesia: Temu Mangga, Temu Poh, Temu Bajangan, Temu Putih, Temu Lalab, Kunir Putih (Java); Koneng Lalab, Koneng Joho, Koneng Pare (Sundanese), Temmo Pao, Temmo Pote (Madurese)

Malaysia: Kunyt Mangga, Temu Pauh, Temu Mangga

Origin/Distribution

The species is indigenous to Malesia (Backer and van den Brink 1968) and cultivated in Malaysia, Thailand and Indonesia.

Agroecology

It occurs wild in the teak forest. It thrives in fertile, moist soils rich in organic matter, in full sun or partial shade, from near sea level to 1000 m.

Edible Plant Parts and Uses

The primary use of temu mangga is as a spice vegetable (Burkill 1966; Ochse and Bakhuizen van den Brink 1980). In Indonesia, young tops of rhizomes and young shoots are eaten raw or cooked as ‘lalab’ or ‘kulob’. The rhizomes are finely sliced and mixed with coconut to make ‘Trantjam’. Cooked inflorescences are eaten as ‘sayur lodeh’ or ‘urap’ and eaten with rice. In south India, rhizomes are used for making pickles. Leaves of *Curcuma longa* and *Curcuma mangga* species are used in food preparations (Liu and Nair 2010) in Peninsular Malaysia.

Botany

Curcuma mangga is an erect, tillering, herbaceous perennial, 50–200 cm high (Plate 1) with subterranean rhizome, yellowish-brown outside, white at the top and citron yellow inside and smelled like mango or kwini when sliced or crushed (Plate 2). Main rhizome is hard, globose or ellipsoid, while lateral rhizomes are cylindrical or clavate, smaller and copiously branched. Spurious stems are robust, erect with 2–4 scales or sheaths at the base and with 3–7 leaves higher up. Leaf sheaths are conduplicate and 30–65 cm long. Leaves are 2 seriate, and leaf blades are elliptical oblong to oblong lanceolate, 15–95 cm by 5–23 cm, and green with light or dark

purple-brown zone along the midrib (Plate 1). Inflorescence is lateral, i.e. flowering shoot terminal arises from lateral rhizome, peduncle is slightly hairy, spike is cylindrical and 10–20 cm long with numerous leafy green bracts, flowers are between the bracts in the axils of thinly membranous bracteoles, and coma bract is white at base and purple towards the broad apex. Flower is slender with narrow throat; calyx is with 3 broad, obtuse teeth; corolla is 3–4 cm and white; labellum is obovate and 15–25 mm by 14–128 mm wide with a yellow median band; staminodes are white subelliptical; and anther is with long narrow spur.



Plate 1 Mango ginger plant habit



Plate 2 Mango ginger yellow-fleshed rhizome

Nutritive/Medicinal Properties

Rhizome Nutrients/Phytochemicals

Proximate nutrient composition of rhizome per 100 g edible portion was reported by Ibrahim et al. (2007) as follows: energy 47 kcal, moisture 88.1, protein 0.4 g, fat 1.3 g, carbohydrate 8.6 g, fibre 1.1 g, ash 0.5 g, thiamine 0.03 mg, riboflavin 0.04 mg and ascorbic acid 1.95 mg.

A labdane diterpene glucoside, curcumanggoside, together with nine known compounds, including labda-8(17),12-diene-15,16-dial, calcaratarin A, zerumin B, scopoletin, demethoxycurcumin, *bis*-demethoxycurcumin, 1,7-bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one, curcumin and *p*-hydroxycinnamic acid, were isolated from the rhizomes (Abas et al. 2005). The curcuminoid content (curcumin, demethoxycurcumin and *bis*-demethoxycurcumin) in *C. mangga* rhizomes was determined to be about 0.18–0.47 % (Bos et al. 2007). Demethoxycurcumin was isolated from the chloroform fraction of the rhizome extract, whereas 15,16-bisnorlabda-8(17), 11-dien-13-one and (*E*)-15,15-diethoxylabda-8(17),12-dien-16-al were isolated from the *n*-hexane fraction (Kaewkroek et al. 2010). Chemical investigation from the hexane and ethyl acetate fractions of the methanol rhizome extract resulted in the isolation of seven pure compounds, namely, (*E*)-labda-8(17),12-dien-15,16-dial, (*E*)-15,16-bisnor-labda-8(17),11-dien-13-on, zerumin A, β -

sitosterol, curcumin, demethoxycurcumin and *bis*-demethoxycurcumin (Malek et al. 2011). The methanol and ethyl acetate rhizome extracts yielded bioactive labdane diterpenoids labda-8(17)-12-diene-15,16-dial (1), calcaratarin A (2), communic acid (3), copallic acid (4), zerumin B (5), 14,15,16-trinor-labdan-8,12-diol (6) and two decalins (7–8) (Liu and Nair 2011).

The main volatile constituents of the rhizome were found to be myrcene (81.4 %), β -pinene (10.4 %), (*E*)- β -ocimene (2.7 %) and α -pinene (1.6 %) (Jantan et al. 1999). Another analysis by Wong et al. (1999) identified 44 components in the rhizome essential oil with monoterpene hydrocarbons predominating, accounting for 91.2 % of the oil. The major components were myrcene (78.66 %), (*E*)- β -ocimene (5.1 %), β -pinene (3.7 %) and α -pinene (2.9 %). Thirty compounds were identified in fresh rhizome; the major compounds belonged to the monoterpene group which accounted for 97.46 %, and myrcene (84.61 %) appeared to be the major component followed by α -phellandrene (6.63 %) and *trans*-ocimene (3.85 %) (Makboon et al. 2000). Three non-volatile compounds were found in the rhizome including a labdane-type diterpene, 15-ethoxy-8(17),12-labdadien-15,16-olide, and a norlabdane-type diterpene, 15,16-bisnorlabda-8(17),11-dien-13-one. Additionally β -sitosterol and stigmasterol were detected as a mixture of steroidal compounds. Lolita (2012) reported the identification of the following compounds in the rhizome essential oil: β -myrcene (57.69 %), β -pinene (17.92 %), α -pinene (2.92 %), eucalyptol (2.98 %), *ar*-turmerone (2.75 %) and camphene (0.27 %).

Ninety-seven compounds were identified in *C. mangga* rhizome essential oil, comprising 89.5 % of the total oil; the oil was dominated by 78.6 % of monoterpenes followed by 5.9 % of diterpenes, 4.8 % of sesquiterpenes and 0.2 % of other compounds (Wahab et al. 2011). The major compounds were myrcene (46.5 %) and β -pinene (14.6 %). The minor compounds were perillene (4.2 %), α -pinene (2.5 %), γ -bicyclohomofarnesal (ambrial) (2.3 %), (*E*)- β -caryophyllene (2.2 %), (*E*)- β -ocimene (2 %), (*5E*)-2,6-dimethylocta-1,5,7-trien-3-ol (2.0 %) and *m*-camphorene (1.3 %). The other

compounds were <1 %. Twenty-seven compounds were identified in *C. mangga* rhizome essential oil, comprising 52.67 % sesquiterpenes, 31.44 % monoterpenes and 15.89 % diterpenes (Tg Kamazeri et al. 2012). The major compounds were the sesquiterpene caryophyllene oxide (18.71 %) and caryophyllene (12.69 %), and the main diterpene was 2,6,11,15,-tetramethyl-hexadeca-2,6,8,10,14,-pentaene (8.06 %). Other important components were the monoterpene cyclohexane, 2-ethenyl-1, dimethyl-3-methylene (7.06 %), the oxygenated sesquiterpenes 6-(1-hydroxymethylvinyl)4,8a-dimethyl-3,5,6,7,8,8a-hexahydro-1H-naphthalen-2-one (5.48 %) and *cis*-farnesol (5.14 %), the diterpene 1,6,10,14-hexadecatetraen-3-ol,3,7,11,15-tetramethyl-,(*E,E*)- (4.86 %) and monoterpene cyclohexanol,2-methylene-5-(1-methylethenyl (4.72 %). Small percentages of 2-isopropylidene-3-methylhexa-3,5-dienal (3.71 %), endo-1,5,6,7-tetramethylbicyclo[3.2.0]hept-6-en-3-ol (3.59 %), α -terpineol acetate (3.45 %), (*E,E*)-7,11,15-trimethyl-3-methylene-hexadeca-1,6,10,14-tetraene (2.97 %), α -caryophyllene (2.86 %), but-3-enal, 2-methyl-4-(2,6,6-trimethyl-1-cyclohexenyl)- (2.67 %), α -farnesene (1.84 %), alloaromadendrene oxide-(1) (1.79 %), 2-methyl-4-(2,6,6-trimethylcyclohex-1-enyl)but-2-en-1-ol (1.71 %), longipinane (*E*)- (1.57 %), pentadecanoic acid, 14-methyl-, methyl ester (1.12 %), sabinene (1.08 %), 3-methyl-2-methylene-3-butenyl 2-methylacrylate (0.94 %), (2,4,6-trimethylcyclohexyl) methanol (0.92 %), 1-formyl-2,2-dimethyl-3-*trans*-(3-methyl-but-2-enyl)-6-methylidene-cyclohexan (0.90 %), 5-isopropenyl-1,2-dimethylcyclohex-2-enol (0.69 %), *trans*-chrysanthenyl acetate (0.62 %), germacrone (0.57 %) and 1,3,8 -*p*-menthatriene (0.28 %) were also detected.

Leaf Phytochemicals

8,12-epoxygermacra-1(10), 4,7,11-tetraen-6-one, 8,12-epoxygermacra-1(10), 4,7,11-tetraene, cyclohexanecarboxylic acid methyl ester, isopulegol, 2-menthen-1-ol, menth-1-en-9-ol, octahydrocurcumin, labda-8(17)-12-diene-15, 16-dial and coronadiene were isolated from *C. longa* and *C. mangga* leaves (Liu and Nair 2010).

Antioxidant Activity

The antioxidant activity of *Curcuma mangga* ginger was found to be greater than its curcuminoids curcumin, demethoxycurcumin and *bis*-demethoxycurcumin as assessed by the isothiocyanate and thiobarbituric acid assays (Jitoe et al. 1992). The diarylheptanoids and scopoletin from the rhizome showed significant antioxidant activity (Abas et al. 2005). Studies revealed that ethanol extract of the rhizome exhibited stronger antioxidant activity compared to BHT (butylated hydroxytoluene), and this was attributable to the phenolic compounds in the ethanol extract (Tedjo et al. 2005). Leaves of *C. mangga* had total phenolic content (TPC) of 275 mg GAE/100 g and ascorbic acid equivalent antioxidant capacity (AEAC) of 118 mg AA/100 g and rhizome TPC of 112 mg GAE/100 g and AEAC of 33 mg AA/100 g (Chan et al. 2008). Compounds purified from the methanol and ethyl acetate rhizome extracts, namely, bioactive labdane diterpenoids labda-8(17)-12-diene-15,16-dial (1), calcaratarin A (2), communic acid (3), copallic acid (4), zerumin B (5), 14,15,16-trinor-labdan-8,12-diol (6) and two decalins (7–8), inhibited lipid peroxidation (LPO) by 12–45 % at 25 µg/ml (Liu and Nair 2011).

The methanolic and water extracts of *C. mangga* leaves at 100 µg/mL inhibited lipid peroxidation (LPO) by 78 % and 63 %, respectively (Liu and Nair 2010, 2012).

Anti-inflammatory Activity

Compounds purified from the methanol and ethyl acetate rhizome extracts, namely, bioactive labdane diterpenoids labda-8(17)-12-diene-15,16-dial (1), calcaratarin A (2), communic acid (3), copallic acid (4), zerumin B (5), 14,15,16-trinor-labdan-8,12-diol (6) and two decalins (7–8), exhibited anti-inflammatory activity in-vitro (Liu and Nair 2011). In cyclooxygenase enzyme (COX-1 and COX-2) inhibitory assays, compounds 1–4 showed selective COX-2 enzyme inhibition by 39–55 %, whereas 5–8 showed selectivity to COX-1 between 45 and 53 %. The methanolic and water extracts of *C. mangga* leaves at 100 µg/mL inhibited

cyclooxygenase enzymes COX-1 by 55 % and then 33 % and COX-2 by 65 % and then 55 %, respectively (Liu and Nair 2010, 2012). *Curcuma mangga* rhizome extract and its compounds exerted their anti-inflammatory activity against nitric oxide (NO) and prostaglandin E2 (PGE2) release in RAW 264.7 cells (Kaewkroek et al. 2010). *Bis*-demethoxycurcumin (4), the structure of which was similar to that of 1, was also tested. Of the tested compounds, (E)-15,15-diethoxylabda-8(17),12-dien-16-al (3) exhibited the highest activity against NO release with an IC_{50} value of 9.4 μ M, followed by demethoxycurcumin (1) (IC_{50} = 12.1 μ M), *bis*-demethoxycurcumin (4) (IC_{50} = 16.9 μ M) and 15,16-bisnorlabda-8(17), 11-dien-13-one (2) (IC_{50} = 30.3 μ M). For the effect on PGE2 release, 1 possessed the highest activity (IC_{50} = 4.5 μ M, followed by 4 (IC_{50} = 5.6 μ M), 3 (IC_{50} = 35.3 μ M) and 2 (IC_{50} = 42.5 μ M). The mechanism at transcriptional level revealed that 1, 3 and 4 downregulated the mRNA expressions of iNOS and COX-2 in a dose-dependent manner, whereas 2 had an effect only on iNOS mRNA. *Curcuma mangga* ethanolic rhizome extract (CME) and its fractions, aqueous, chloroform, ethyl acetate and hexane fractions (150 mg/kg, p.o.) showed significant reduction of rat paw oedema (Ruangsang et al. 2010). The order of activity on inhibition of rat paw oedema at 4 h was chloroform fraction > hexane fraction > ethyl acetate fraction > CME > aqueous fraction. When topically applied at 0.5 mg/ear, CME and all fractions suppressed mouse ear oedema induced by croton oil. CME and chloroform fraction showed a greater inhibition by 53.97 and 50.29 %, respectively. The results suggested that CME and its fractions, especially chloroform and hexane fractions, possessed anti-inflammatory activities.

Antinociceptive/Analgesic Activity

Curcuma mangga ethanolic rhizome extract (CME) and its fractions, aqueous, chloroform, ethyl acetate and hexane fractions (200 mg/kg, p.o.) significantly reduced the number of writhings in mice (Ruangsang et al. 2010). Oral administration (p.o.) of CME, chloroform and hexane fractions (200 mg/kg)

significantly prolonged the latency time, whereas aqueous and ethyl acetate fractions were inactive. The activities of CME, chloroform and hexane fractions were abolished by naloxone (2 mg/kg, intraperitoneal (i.p.)). CME and all fractions at similar dose significantly produced antinociception in both early and late phases of the formalin test. CME, chloroform and hexane fractions were more prominent in licking inhibition than those of the aqueous and ethyl acetate fractions. The results suggested that CME and its fractions, especially chloroform and hexane fraction, possessed centrally acting analgesic activity.

Antitumour Activity

Zerumin B, demethoxycurcumin, *bis*-demethoxycurcumin and curcumin from the rhizome exhibited cytotoxic activity against a panel of five human tumour cell lines. Thirty volatile constituents were identified from the fresh rhizome (Abas et al. 2005). Treatment of liver Chang cell culture with 7th and 4th fractions of the ethanol rhizome extract increased the glutathione S-transferase activity when compared to the control (Tedjo et al. 2005). The two fractions were able to prevent oxidative stress resulting from the decrease in glutathione S-transferase activity (cytosolic and microsomal) when Chang cell culture was treated with $\text{H}_2\text{O}_2/\text{Fe}^{2+}$. Studies showed that the mixed volatile oil of *C. mangga* at a concentration of 125 $\mu\text{l/ml}$ produced the highest cytotoxic effect on Raji and myeloma cell lines (Verlianara et al. 2005). The antiproliferation assay showed that *C. mangga* oil inhibited the growth of Raji and myeloma cells. Observation of the cell morphology showed that there was an apoptotic process on the treated myeloma cells and not on the treated Raji cells. The result of the immunocytochemistry assay showed that the *C. mangga* oil induced apoptosis on myeloma cell lines by increasing expression of P53. *C. mangga* essential oil which exhibited selective cytotoxic effect; it exhibited higher cytotoxicity against Raji cancer cell line with IC_{50} of 2.7 $\mu\text{l/ml}$ compared to HeLa 3.0 $\mu\text{l/ml}$, T47D 3.7 $\mu\text{l/ml}$, myeloma 4.1 $\mu\text{l/ml}$ and SiHa 4.5 $\mu\text{l/ml}$ cell lines (Rumiyati et al. 2007). DLBS4847, a standardised bioactive fraction of

Curcuma mangga, inhibited the growth of prostate cancer PC3 cells through downregulation of the 5 α -reductase (5AR) pathway. At the transcription level, 5AR1 and (Karsono et al. 2014) androgen receptor gene expressions were downregulated in a dose-dependent manner. Further, 5AR-1 and dihydrotestosterone expression were also downregulated at the protein level.

The methanolic and water extracts of *C. mangga* leaves at 100 μ g/mL inhibited growth of human pancreatic, prostate and stomach tumour cell lines in-vitro (Liu and Nair 2010). At 100 μ g/mL concentration, water leaf extract of *C. mangga* showed inhibition against prostate cancer DU-145 cell line by 28 %, while their methanolic extract was inactive (Liu and Nair 2012). Water and methanolic extracts of *C. mangga* inhibited the growth of prostate tumour cell line LNCaP by 34 % and 34 %, respectively. Similarly, water and methanolic extracts revealed growth inhibition against pancreatic tumour cell line BxPc-3 by 18 % and 36 %, respectively.

The crude methanol and fractionated extracts (hexane and ethyl acetate) of *C. mangga* rhizome displayed good cytotoxic effects against human cancer cell lines, hormone-dependent breast cell line (MCF-7), nasopharyngeal epidermoid cell line (KB), lung cell line (A549), cervical cell line (Ca Ski) and colon cell line (H-29), but exerted no damage on non-cancer human fibroblast cell line (MRC-5) (Malek et al. 2011). Compounds (*E*)-labda-8(17),12-dien-15,16-dial and zerumin A from the fractions exhibited high cytotoxic effects against all six selected cancer cell lines, while compound (*E*)-15,16-bisnor-labda-8(17),11-dien-13-on showed no antiproliferative activity on the tested cell lines. Compounds purified from the methanol and ethyl acetate rhizome extracts, namely, bioactive labdane diterpenoids labda-8(17)-12-diene-15,16-dial (1), calcaratarin A (2), communic acid (3), copallic acid (4), zerumin B (5), 14,15,16-trinor-labdan-8,12-diol (6) and two decalins (7–8) at 25 μ g/ml, showed some degree of inhibition against NCI-H460 (lung), HCT-116 (colon), AGS (gastric), SF-268 (CNS) and MCF-7 (breast) human tumour cell progression (Liu and Nair 2011).

Antimicrobial Activity

Compared to *Curcuma aeruginosa* and *Zingiber cassumunar*, *C. mangga* rhizome oil had the highest and most broad-spectrum activity by inhibiting all microorganisms tested including four bacteria, *Bacillus cereus*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*, and two fungi, *Candida albicans* and *Cryptococcus neoformans*, with *Cryptococcus neoformans* being the most sensitive microorganism by having the lowest minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) values of 0.1 µl/mL (Tg Kamazeri et al. 2012).

Anti-allergic Activity

The ethanolic extract of *Curcuma mangga* rhizome exhibited anti-allergic effect against antigen-induced β-hexosaminidase release as a marker of degranulation in RBL-2H3 cells, with an IC₅₀ value of 36.1 µg/ml (Tewtrakul and Subhadhirasakul 2007).

Antiviral Activity

Studies showed that the methanol and hexane fractions of *Curcuma mangga* were most potent against the dengue Den2 virus NS2B/NS3 protease activity and may provide potential leads towards the development of antiviral agent for dengue fever (Tan et al. 2006).

Larvicidal Activity

C. mangga rhizome oil was found to have larvicidal activity against 4th instar larvae of *Aedes aegypti*, vector of dengue five with LC₅₀ of 12.51 ppm (Lolita 2012).

Immunomodulatory Activity

Among the methanol extracts studied, *C. mangga*, *Piper nigrum* and *Labisia pumila* var. *alata* showed strong inhibitory activity on lucigenin-amplified oxidative burst of

polymorphonuclear leukocytes (PMNs), with IC₅₀ values ranging from 0.9 to 1.5 µg/ml (Jantan et al. 2011). The results suggested that some of these plants were able to modulate the innate immune response of phagocytes at different steps, emphasising their potential as a source of new immunomodulatory agents.

Traditional Medicinal Uses

In folkloric medicine, the rhizome is deemed stomachic, antitumorous and antibacterial. In Malaysia, the rhizome has traditionally been used as a stomachic, gastric ulcer, for the treatment of chest pains, fever and general debility, as well as to aid womb healing (Burkill 1966; Abas et al. 2005; Wahab et al. 2011). The starch in the rhizome has been used to treat abdominal illness. Rhizomes as a component of a mixture were given to treat continued fever and were chewed to cause the womb to contract after childbirth. The rhizome is eaten raw with rice as a relief for flatulence, stomach ache and colic, and the leaves are used with leaves of other Zingiberaceae species and other herbs as a heated aromatic herbal bath for ladies in confinement (Ibrahim et al. 2007). In Indonesia, the rhizomes have been used for fever and abdominal ailments. *C. mangga* is used traditionally for cancer diseases and colic and as analgesic and hepatoprotective agent in Indonesia (Rumiyati et al. 2007). It is also used to treat skin diseases such as redness and itching and high continuous fever (Hutami and Purnamaningsih 2003).

Other Uses

C. mangga is used for cooking purposes, food decoration as well as vegetable and traditional medicine (Wong et al. 1999). Essential oil containing a high amount of myrcene as the case with mango ginger is widely used as fragrance in cosmetics, as a scent in household products and as flavouring additive in food and alcoholic beverages (Wahab et al. 2011).

Comments

Mango ginger is usually propagated by division of the rhizomes.

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Curcuma zanthorrhiza

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Scientific Name

Curcuma zanthorrhiza Roxburgh

Synonyms

No synonyms recorded;

Curcuma xanthorrhiza Roxb., nom. illeg.

Family

Zingiberaceae

Common/English Names

False Turmeric, Giant Curcuma, Indian Saffron, Java
Turmeric, Javan Turmeric, Javanese Turmeric

Vernacular Names

Chinese: Shu Gu Jiang Huang, Yin Ni E Zhu

Danish: Gurkemeje

French: Curcuma

German: Javanische Gelbwurz, Javanische Gelbwurzel, Kurkuma

Hungarian: Jávai Kurkuma

Indonesia: Temu Raya, Temu Lawak (Java), Koneng Gede (Sudanese), Temo Labak (Madurese)

Malaysia: Temu Lawas, Temu Raya

Polish: Kurkuma Jawajska

Spanish: Temoe-Lawak

Thailand: Wan-Chak-Mod-Luk

Turkish: Zerdecali

Vietnam: Nghệ Rễ Vàng

Origin/Distribution

The species is native to Indonesia—Java, Bali and Moluccas. It is cultivated in Java, Malaysia, Thailand, Vietnam, the Philippines, Yunnan in China and also in India and Surinam.

Agroecology

In its native tropical range, it is found in thickets and teak forest in moist fertile, well-drained, humus-rich soil up to 750-m elevation.

Edible Plant Parts and Uses

Young rhizome tips, inflorescence and centres of spurious stem are aromatic with a strong odour and bitter taste and are eaten as vegetables raw or cooked (Ochse and Bakhuizen van den Brink 1980). The heart of the spurious stems is eaten raw or cooked as lalab. The young tops of the lateral rhizomes are also eaten fresh as lalab, and the inflorescences are eaten cooked with rice, usually as ‘sayur’ or ‘urab’. In Java a soft drink called ‘bir temu lawak’ or ‘wedang temu lawak’ (Javanese) is prepared by cooking dried pieces of the rhizomes which impart a yellow colour and flavour and mixing with

Javanese sugar. The rhizomes yield starch meal which is used in making porridge ('bubur pati temu'); pudding; delicacies like 'dodol temu lawak', 'jenang temu' and 'jenang pati'; and drinks in Java. In the First International Symposium on Temulawak (*Curcuma xanthorrhiza* Roxb.) held in Bogor, Indonesia, on May 27–29, 2008, and the Second International Symposium on Temulawak (*Curcuma xanthorrhiza* Roxb.) in Bogor on December, 2011, various edible and herbal commercial products of temulawak were displayed and sold, among which were 'temulawak' supplements in bubuk, temu lawak gula Jawa, sari temu lawak and other beverages to increase appetite (as natural appetiser) and to revitalise stamina. The rhizome is an important ingredient in various 'jamu' (medicinal health preparations).

Botany

Curcuma xanthorrhiza is an erect, robust, tillering and herbaceous perennial up to 1–2 m tall (Plates 1–2) with creeping, swollen, copiously branched subterranean rhizomes (Plates 3–5) dark yellow to reddish brown outside and orange or orange red inside, paler on younger parts, short and numerous roots with large tubers. Spurious stem is robust and erect, at the base enclosed by 2–3 sheaths and higher up with 2–7 distichous leaves. Ligule is small; petiole is about 10 cm; leaf sheath is up to 75 cm long; leaf blade is green with purple midvein, elliptical oblong to oblong lanceolate, 25–90 × 10–20 cm and glabrous. Inflorescences on separate shoots arise from rhizomes; spike is 16–25 × 8–10 cm; fertile bracts are pale green; coma bracts are purple, and apical ones are much narrower; each flower is surrounded by a membranous pink bracteoles which are 2.5 cm long. Flower is short, broad and barely exerted. Calyx is white green, 1.4 cm, pubescent and apex 3-dentate. Corolla tube is 3.5 cm, and lobes are pink, ovate and 1.7 × 1.5 cm. Labellum is yellowish with deeply coloured, median band, suborbicular and 2 × 2 cm. Staminodes are large, broad, erect, connate with base of stamens yellowish tinged with purple, oblong and 1.7 × 1 cm. Filament is short and erect with thick anther of 4 mm and base with spurs of 3

mm. Ovary is pubescent and white. Style filiform is white, and stigma is 4-lobed.



Plate 1 Java turmeric old plant habit



Plate 2 Java turmeric foliage



Plate 3 Harvested Java turmeric rhizomes



Plate 4 Close-up Java turmeric rhizome



Plate 5 Java turmeric rhizome—bright orange-yellow flesh

Nutritive/Medicinal Properties

Rhizome/Root Phytochemicals

The main rhizome constituents of *Curcuma* species including *C. xanthorrhiza* comprised curcuminoids and bisabolane-type sesquiterpenes (Itokawa et al. 2008). From the rhizomes, the following compounds were isolated: four bisabolane sesquiterpenoids, α -curcumene, ar-turmerone, β -atlantone and xanthorrhizol (Itokawa et al. 1985); five diarylheptanoids including two new compounds isolated and determined to be octahydrocurcumin ((3*S*,5*S*)-1,7-bis(4-hydroxy-3-methoxyphenyl)-heptane-3,5-diol) (Ia) and (1*ξ*)-1-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)-6-heptene-3,5-dione (II); and three known diarylheptanoids, dihydrocurcumin [1,7-bis(4-hydroxy-3-methoxyphenyl)-1-heptene-3,5-dione]; hexahydrocurcumin [1,7-bis(4-hydroxy-3-methoxyphenyl)-1-heptene-3,5-dione] and curcumin [1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione] (Uehara et al. 1987); three new bisabolane sesquiterpenoids, bisacurone, bisacumol and bisacurol, and one known compound, curlone (Uehara et al. 1989); four bisabolane sesquiterpenoids, named bisacurone epoxide and bisacurones A–C, isolated from chloroform-soluble fractions (Uehara et al. 1990); nine sesquiterpenoids, α -curcumene, ar-turmerone, xanthorrhizol, germacrone, β -curcumene, β -sesquiphellandrene, curzerenone, α -turmerone and β -turmerone; three curcuminoids, curcumin, mono-demethoxycurcumin and bisdemethoxycurcumin; and one monoterpenoid, camphor (Uehara et al. 1992); a curcumin analogue 1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-(1*E*,6*E*)-1,6-heptadiene-3,4-dione (Masuda et al. 1992); three non-phenolic linear 1,7-diarylheptanoid *trans-trans*-1,7-diphenyl-1,3-heptadien-4-one (alnustone), *trans*-1,7-diprienyl-1-hepten-5-ol and *trans,trans*-1,7-diphenyl-1,3-heptadien-5-ol together with germacrone, curzerenone and cinnamaldehyde (Claeson et al. 1993, 1996); two phenolic diarylheptanoids, 5-hydroxy-7-(4-hydroxyphenyl)-1-phenyl(1*E*)-1-heptene and 7-(3,4-dihydroxyphenyl)-5-hydroxy-1-phenyl(1*E*)-1-heptene (Suksamrarn et al. 1994); curcuminoids bisdemethoxycurcumin, demethoxycurcumin and curcumin (Ruslay et al. 2007); and curcuminoids (5 %) comprising curcumin (2.3 %),

bisdemethoxycurcumin (0.8 %) and demethoxycurcumin (1.9 %) (Jantan et al. 2012). Crude polysaccharide (CPE) extract from the rhizome of *C. xanthorrhiza* contained arabinose (18.69 %), galactose (14.0 %), glucose (50.67 %), mannose (12.97 %), rhamnose (2.73 %) and xylose (0.94 %) (Kim et al. 2007). (–)-Xanthorrhizol isolated from *Curcuma xanthorrhiza* rhizomes was transformed to several optically active bisabolane-type sesquiterpenoids: 10*R*-10,11-dihydro-10,11-dihydroxyxanthorrhizol; 10*S*-10,11-dihydro-10,11-dihydroxyxanthorrhizol; (–)-curcuquinone; (–)-curcuhydroquinone; helibisabonol A; and allylic alcohol (Sirat et al. 2007). Studies in Malaysia reported that the hexane extract of *Curcuma xanthorrhiza* afforded three pure compounds, which were identified as α -curcumene, germacrone and zederone, while dichloromethane extract gave yellow powder product, which was characterised as curcumin (5) together with colourless oil xanthorrhizol (Abd Rashid 2004). The presence of xanthorrhizol and absence of bisdemethoxycurcumin were species specific, distinguishing *Curcuma xanthorrhiza* (Javanese turmeric) from *Curcuma longa* (turmeric) (Wichtl 2002; Lechtenberg et al. 2004). Camphor, zingiberene, γ -elemene, trans- β -farnesene, ar-curcumene, benzofuran, α -cedrene, β -elemenone and xanthorrhizol were detected in *C. xanthorrhiza* rhizome (Ab Halim et al. 2012). Two new bisabolane sesquiterpenoids, (7*R*,10*R*)-10,11-dihydro-10,11-dihydroxyxanthorrhizol 3-*O*- β -D-glucopyranoside and (–)-curcuhydroquinone 2,5-di-*O*- β -D-glucopyranoside, along with five known ones, 13-hydroxyxanthorrhizol; 12,13-epoxyxanthorrhizol; xanthorrhizol; β -curcumene; and β -bisabolol, were isolated from the rhizomes of *Curcuma xanthorrhiza* Park et al. 2014).

C. xanthorrhiza rhizome oil was characterised by two major components ar-curcumene (41.4 %) and xanthorrhizol (21.5 %) (Zwaving and Bos 1992). *C. xanthorrhiza* rhizome oil comprised mainly sesquiterpenoids of which xanthorrhizol was the major component (Jantan et al. 1999). Jarikasem et al. (2005) reported that *C. xanthorrhiza* yielded 0.19 % (fresh weight basis) of essential oil; 25 constituents accounting for 78.56 % of total oil were identified and high amounts of 1,8-cineole (37.58 %), curzerenone (13.70 %) and *p*-cymene-8-ol

4.26 % were found. Other components were β -pinene 0.15 %, α -pinene 0.78 %, camphene 0.17 %, myrcene 0.63 %, limonene 1.45 %, β -ocimene 0.10 %, *p*-cymene 2.33 %, terpinolene 3.11 %, α -*p*-dimethyl styrene 0.72 %, camphor 1.39 %, 2-nonanol 0.70 %, α -elemene 0.13 %, β -caryophyllene 0.36 %, terpene-4-ol 0.84 %, isoborneol 0.44 %, α -terpineol 0.38 %, α -terpineol 2.20 %, borneol 0.76 %, caryophyllene oxide 1.03 %, humulene oxide 2.64 % and germacrone 0.25 %.

Essential oil extracted from the rhizome was reported to contain the derivatives of xanthorrhizol, camphene and curcumene, monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpene, hydrocarbons and other minor compounds (Mary et al. 2012). Mikusanti (2012) reported the essential oil of *C. xanthorrhiza* rhizome to contain camphor 4.64 %, zingiberene 2.26 %, germacrone 2.23 %, β -farnesene 3.64 %, α -curcumene 25.99 %, furanodiene 5.21 %, α -cedrene 32.71 %, dehydroandrostenedione 3.02 %, germacrone 1.37 % and α -chamigrene 14.22 %. The rhizome oil of *C. xanthorrhiza* was characterised by the presence of a high concentration of bisabolene-type sesquiterpenes and their oxygenated derivatives which accounted for more than 92 % of the oil (Jantan et al. 2012). The most abundant component was the sesquiterpene phenol, xanthorrhizol (31.9 %). The other major compounds present in the oil were β -curcumene (17.1 %), ar-curcumene (13.2 %), citronellyl pentanoate (5.7 %), camphor (5.4 %) and β -bisabolol (3.5 %). Other minor components included γ -curcumene (2.6 %), (*Z*)- γ -bisabolene (2.6 %), (*E*)- β -farnesene (1.2 %), (*Z*)-isoeugenyl acetate (1.2 %), (*E*)-citronellyl tiglate (0.9 %), 4-hydroxy-3-methoxycinnamaldehyde (0.9 %), *cis*-cadin-4-en-7-ol (0.8 %), α -eudesmol (0.8 %), ar-curcumen-15-al (0.8 %), camphene (0.7 %), (*E*)-amyl cinnamic alcohol (0.7 %), α -*cis*-bergamotene (0.6 %), β -bisabolene (0.6 %), caryophyllene oxide (0.5 %), cubenol (0.5 %), γ -elemene (0.4 %), 1,10-di-*epi*-cubenol (0.4 %), β -sesquiphellandrene (0.4 %), 1,10-decanediol (0.4 %), α -pinene (0.3 %), thujopsan-2- α -ol (0.3 %), *cis*-dehydro- β -terpineol (0.3 %), α -terpineol (0.3 %), 1-phenyl-hepta-1,3,5-triene (0.3 %), chamazulene (0.3 %), terpinene-4-ol (0.2 %), α -bisabolol oxide A (0.2 %), (*Z*)-isoeugenol (0.2 %),

sesquithuriferol (0.2 %), (Z)- β -farnesene (0.2 %), butyl dodecanoate (0.2 %), β -pinene (0.1 %), *cis*-pinane (0.1 %), myrcene (0.1 %), α -terpinene (0.1 %), (*E*, *Z*)-farnesol (0.1 %), 1,8-cineole (0.1 %), (Z)- β -ocimene (0.1 %), ethyl-4*E*-octenoate (0.1 %), dihydro citronellol acetate (0.1 %), α -cubebene (0.1 %), methyl perillate (0.1 %), (Z)- β -damascenone (0.1 %), methyl undecanoate (0.1 %), β -humulene (0.1 %), *n*-decanol (trace), geranyl acetate (trace), α -thujene (trace), α -phellandrene (trace), γ -terpinene (trace), 6,7-epoxymyrcene (trace) and (*E*)-ethyl cinnamate (trace).

Rohaeti et al. (2014) developed an analytical method to differentiate turmeric (*Curcuma longa*), java turmeric (*Curcuma xanthorrhiza*) and cassumunar ginger (*Zingiber cassumunar*), widely used in Indonesian medicine (jamu) by using Fourier transform infrared spectroscopy (FTIR) combined with some chemometric methods. Salea et al. (2014) optimised oil and xanthorrhizol extraction from *Curcuma xanthorrhiza* rhizome by using supercritical carbon dioxide extraction. The highest oil yield (8.0 %) was achieved at factor combination of 15 MPa, 50 °C, 20 g/min and 180 min, whereas the highest xanthorrhizol content (128.3 mg/g oil) in *Curcuma xanthorrhiza* oil was achieved at a factor combination of 25 MPa, 50 °C, 15 g/min and 60 min. Soxhlet extraction with *n*-hexane and percolation with ethanol gave oil yield of 5.88 % and 11.73 % and xanthorrhizol content of 42.6 mg/g oil and 75.5 mg/g oil, respectively.

Curcuma xanthorrhiza had been reported in scientific research to possess a variety of biological activities, including hepatoprotective, anti-inflammatory effects, anticarcinogenic effects, wound healing effects, anti-skin ageing, immunostimulating, antiplatelet, antimicrobial, antifungal, anti-*Malassezia*, antibabesial, nephroprotective, hypotriglyceridaemic and serum cholesterol-lowering effects. Itokawa et al. (2008) in their review of studies conducted between 1976 and mid-2008 reported that curcuminoids had anti-inflammatory, antioxidant, anti-HIV, chemopreventive and anti-prostate cancer activities.

Antioxidant Activity

The antioxidant activity of *C. xanthorrhiza* ginger was found to be greater than its curcuminoids curcumin, demethoxycurcumin and bisdemethoxycurcumin as assessed by the isothiocyanate and thiobarbituric acid assays (Jitoe et al. 1992). A curcumin analogue 1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-(1E,6E)-1,6-heptadiene-3,4-dione isolated from the rhizomes showed potent antioxidant activity against autoxidation of linoleic acid in a water–alcohol system (Masuda et al. 1992). Seven Zingiberaceous rhizomes including *C. xanthorrhiza* were found to possess inhibitory activity towards Epstein–Barr virus early antigen (EBV-EA) activation, induced by 12-O-tetradecanoylphorbol-13-acetate (TPA) (Vimala et al. 1999). The rhizome extracts that exhibited EBV activation inhibitory activity had no cytotoxicity effect in Raji cells.

Studies showed that *Curcuma xanthorrhiza* ethanol extracts exhibited high antioxidant activities compared to aqueous extracts (Qader et al. 2011). The results recorded a strong correlation between antioxidant activity and the total phenol contents. Additionally the plant extract showed non-toxic effects against a normal human lung fibroblast cell line (Hs888Lu). The rhizome was reported to have antioxidant index 0.69 as evaluated by b-carotene bleaching method and to contain 7.69 mg% vitamin C, 0.0085 mg% vitamin E, 1.28 mg% total carotenes, 0.65 mg% total xanthophylls, 14.4 mg% tannins and 112 mg/% phenolics (Chanwitheesuk et al. 2005). Leaves of *Kaempferia galanga* had total phenolic content (TPC) of 503 mg GAE/100 g and ascorbic acid equivalent antioxidant capacity (AEAC) of 287 mg AA/100 g and rhizome TPC of 57,250 mg GAE/100 g and AEAC of 134 mg AA/100 g (Chan et al. 2008).

The methanol extracts and rhizome oils of *C. xanthorrhiza* and *C. domestica* showed strong inhibitory activity on copper-mediated oxidation of human low-density lipoprotein (Jantan et al. 2012). Curcumin, demethoxycurcumin and bisdemethoxycurcumin, isolated from the methanol extracts of both plants, exhibited stronger activity than probucol (IC₅₀ value 0.57 µmol/L) as reference, with IC₅₀ values ranging from 0.15 to 0.33 µmol/L. Xanthorrhizol, the most abundant

component (31.9 %) of the oil of *C. xanthorrhiza*, showed relatively strong activity with an IC₅₀ value of 1.93 µmol/L. The high levels of curcuminoids in the methanol extracts and xanthorrhizol, ar-turmerone and zerumbone in the oils, and in combination with the minor components, were responsible for the high low-density lipoprotein antioxidant activity. *Curcuma longa* rhizome methanol extract was found to have a higher activity of FRAP with (231.7 mg/TE/g dw), while activity of *C. xanthorrhiza* extract was (100.4 mg/TE/g dw) compared to ascorbic acid activity (284.2 mg/TE/g dw) (Alafiatayo et al. 2014). *C. longa* also had higher contents of phenolic acid (42.7 mg GA/g dw) and polyphenols (39.4 mg GA/g dw).

Anticancer Activity

C. xanthorrhiza exhibited antitumour promoter activity using the short-term assay of inhibition of 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced Epstein–Barr virus early antigen (EBV-EA) in Raji cells and was not cytotoxic to Raji cells (Vimala et al. 1999). A methanol extract of *C. xanthorrhiza* was reported to inhibit significantly 7,12-dimethylbenz[a]anthracene (DMBA)-induced bacterial mutagenesis of *Salmonella typhimurium* TA98 and TA100 in the presence of S9 and the mutagenesis induced by H₂O₂ and tert-butyl hydroperoxide in *S. typhimurium* TA102, respectively (Park et al. 2008). In addition, TPA-induced mouse ear oedema was markedly inhibited by pretreatment with *C. xanthorrhiza* extract. The extract dose-dependently reduced ODC (ornithine decarboxylase) expression in mouse skin with TPA-induced acute inflammation. Furthermore, repeated treatment with 0.1 % *C. xanthorrhiza* extract reduced the average number of tumours per mouse and the percentage of tumour-bearing mice in a multistage mouse skin carcinogenesis induced by DMBA and TPA. These results demonstrated that the methanol extract of *C. xanthorrhiza* possessed cancer chemopreventive potential.

Four bisabolane sesquiterpenoids, α-curcumene, ar-turmerone, β-atlantone and xanthorrhizol, isolated from the rhizomes exhibited antitumour activity against sarcoma 180

ascites in mice (Itokawa et al. 1985). The antitumour effectiveness was rated (+ + +) for α -curcumene, (+ +) for ar-turmerone and (+ +) for xanthorrhizol at 50 mg/kg in the total packed cell volume method.

Xanthorrhizol significantly inhibited the formation of tumour nodules in mouse lung tissue and the intra-abdominal tumour mass formation (Choi et al. 2005). The antimetastatic activity of xanthorrhizol could be highly linked to the metastasis-related multiplex signal pathway including cyclooxygenase-2 (COX-2), matrix metalloproteinase-9 (MMP-9) and phosphorylated extracellular signal-regulated kinase (ERK). Ismail et al. (2005) showed that xanthorrhizol inhibited the proliferation of the cervical cancer cell line HeLa with an EC₅₀ value of 6.16 μ g/ml. Xanthorrhizol significantly increased apoptosis in HeLa cells by upregulation of tumour suppressor protein p53 and the pro-apoptotic protein Bax. Xanthorrhizol, however, did not affect the expression of the anti-apoptotic protein Bcl-2 and the viral oncoprotein E6. Cheah et al. (2006) found that xanthorrhizol inhibited the proliferation of the human breast cancer cell line, MCF-7, with an EC₅₀ value of 1.71 μ g/ml. Its antiproliferative effects on MCF-7 cells were by inducing apoptosis through the modulation of bcl-2, p53 and PARP-1 protein levels. Xanthorrhizol was found to exert antiproliferative effects on HepG2 cells by inducing apoptosis via the mitochondrial pathway (Handayani et al. 2007). The xanthorrhizol-treated HepG2 cells showed typical apoptotic morphology such as DNA fragmentation, cell shrinkage and elongated lamellipodia. The apoptosis mediated by xanthorrhizol in the HepG2 cells was associated with the activation of tumour suppressor p53 and downregulation of anti-apoptotic Bcl-2 protein expression, but not Bax.

In another study, topical application of xanthorrhizol before TPA treatment significantly inhibited TPA-induced mouse ear oedema and TPA-induced tumour promotion in DMBA-initiated ICR mouse skin (Chung et al. 2007). The topical application of xanthorrhizol following the induction of papillomas with TPA-induced hyperplasia and dysplasia also reduced tumour multiplicity and incidence in DMBA-initiated

mouse skin. The pretreatment with xanthorrhizol inhibited the expression of ODC (ornithine decarboxylase), inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) proteins and nuclear factor-kappaB (NF-kappaB) activation in both mouse skin. When mouse skin was treated after TPA-induced production of papillomas, xanthorrhizol remarkably suppressed the expression of ODC, iNOS and COX-2 and inhibited the activation of NF-kappaB. Further, xanthorrhizol was found to suppress the activation of extracellular signal-regulated protein kinase, p38, c-Jun-N-terminal kinase and Akt in mice after topical application for 6 weeks following the induction of papillomas. Taken together, the study demonstrated that xanthorrhizol delayed and inhibited tumour formation and also reversed the carcinogenic process at premalignant stages by reducing the protein levels of ODC, iNOS and COX-2 regulated by the NF-kappaB, mitogen-activated protein kinases and/or Akt.

Xanthorrhizol dose-dependently exerted antiproliferative effects against HCT116 human colon cancer cells (Kang et al. 2009). Xanthorrhizol also arrested cell-cycle progression in the G0/G1 and G2/M phase and induced the increase of sub-G1 peaks. Cell-cycle arrest was highly correlated with the downregulation of cyclin A, cyclin B1 and cyclin D1; cyclin-dependent kinase 1 (CDK1), CDK2 and CDK4; proliferating cell nuclear antigen; and inductions of p21 and p27, cyclin-dependent kinase inhibitors. The apoptosis by xanthorrhizol was markedly evidenced by induction of DNA fragmentation, release of cytochrome c, activation of caspases and cleavage of poly-(ADP-ribose) polymerase. Further, xanthorrhizol increased the expression and promoter activity of pro-apoptotic non-steroidal anti-inflammatory drug-activated gene-1 (NAG-1). In subsequent studies, it was found that apoptosis in xanthorrhizol-treated HepG2 cells was accompanied by truncation of BID, reduction of both anti-apoptotic Bcl-2 and Bcl-X(L) expression, cleavage of PARP and DFF45/ICAD proteins and DNA fragmentation (Tee et al. 2012). Taken together, the results suggested xanthorrhizol as a potent antiproliferative agent on HepG2 human hepatoma cells by inducing apoptosis via Bcl-2 family members.

Kim et al. (2013) recently reported that xanthorrhizol decreased cell viability, induced apoptosis and decreased the level of full-length PARP in SCC-15 oral squamous cell carcinoma (OSCC) cells. Xanthorrhizol treatment elevated intracellular Ca^{2+} and ROS levels in SCC-15 cells. Xanthorrhizol suppressed the number of tumours in buccal pouches and increased the survival rate in hamsters treated with DMBA. They found that xanthorrhizol may induce caspase-independent apoptosis through ROS-mediated p38 MAPK and JNK activation in SCC-15 OSCC cells and prevent chemical-induced oral carcinogenesis.

Anti-inflammatory Activity

The methanol rhizome extract (p.o.) showed an anti-inflammatory effect in carrageenan-induced oedema in rats (Ozaki 1990). The anti-inflammatory effects were also found in the successive ether-soluble fraction, the n-hexane-soluble fraction, fr. II, V and IX. The studies suggested that the anti-inflammatory action of *Curcuma xanthorrhiza* was the result of the germacrone that it contained. Three non-phenolic diarylheptanoids, identified mainly by high-field ^1H -NMR as *trans-trans*-1,7-diphenyl-1,3-heptadien-4-one (alnustone), *trans*-1,7-diprienyl-1-hepten-5-ol and *trans,trans*-1,7-diphenyl-1,3-heptadien-5-ol, exerted significant anti-inflammatory activity in the assay of carrageenan-induced hind paw oedema in rats (Claeson et al. 1993). The naturally occurring compound 1E,3E,1,7-diphenylheptadien-5-one isolated from *C. xanthorrhiza* rhizome exerted the most potent anti-inflammatory activity, with an ID_{50} value of similar magnitude to that of the reference drug oxyphenbutazone (67 vs. 46 $\mu\text{g}/\text{ear}$, respectively) in the murine model of ethyl phenylpropiolate-induced ear oedema (Claeson et al. 1996). *C. xanthorrhiza* extract (CXE) and xanthorrhizol (XAN) significantly inhibited production of inflammatory cytokines, such as tumour necrosis factor- α (TNF- α), interleukin-6 (IL-6), interleukin-1 β (IL-1 β) and C-reactive protein (CRP) in adipose tissue (27.8–82.7 %), liver (43.9–84.7 %) and muscle (65.2–92.5 %) (Kim et al. 2014).

Hepatoprotective Activity

C. xanthorrhiza was found to reduce significantly the acute elevation of serum transaminase levels induced by the two kinds of hepatotoxins and alleviated the degree of liver damage at 24 h after the intraperitoneal administration of two hepatotoxins (Lin et al. 1995). The study concluded that *C. xanthorrhiza* can protect the liver from various hepatotoxins and could be useful in the treatment of liver injuries and to have promise as a kind of broad spectrum hepatoprotective agent. Pretreatment of the standardised *C. xanthorrhiza* ethanolic extract (500 mg/kg) protected rats against ethanol-induced liver toxicity in rats (Devaraj et al. 2010b). The extract reduced fatty liver symptoms and significantly inhibited the increase of respective serum enzyme levels. *Curcuma xanthorrhiza* (CX) hexane fraction ameliorated carbon tetrachloride-induced hepatic damage in rats as evidenced by significant improvement in biochemical liver function, antioxidative liver enzymes and lipid peroxidation activity (Devaraj et al. 2014). Good recovery was observed in the treated hepatic tissues histologically. The results concluded that CX hexane fraction possessed prominent hepatoprotective activities which might be due to its in-vitro antioxidant activity.

Gastroprotective Activity

Oral administration of *Curcuma xanthorrhiza* leaf extract exhibited significant gastroprotective effect against ethanol-induced gastric ulcers in rats as evidenced by the significant reduction in ulcer areas (Rahim et al. 2014). Histology observation showed less oedema and leukocyte infiltration as compared with the ulcer control which exhibited severe gastric mucosa injury. Further, the leaf extract elevated the mucus weight, level of prostaglandin E2 and superoxide dismutase. The extract also reduced malondialdehyde amount significantly. Acute toxicity test did not show any sign of toxicity of the leaf extract (2 and 5 g/kg).

Neuroprotective Activity

Xanthorrhizol was found to have potent neuroprotective effects on glutamate-induced neurotoxicity and reactive oxygen species (ROS) generation in the murine hippocampal HT22 cell line (Lim et al. 2005). Xanthorrhizol inhibited H₂O₂-induced lipid peroxidation in rat brain homogenates. It reduced the expression of cyclooxygenase-2 and the inducible nitric oxide synthase, which consequently resulted in the reduction of nitric oxide. The production of proinflammatory cytokines, such as interleukin-6 and tumour necrosis factor, in activated microglial cells, was reduced by xanthorrhizol. The results suggested that xanthorrhizol could be an effective candidate for the treatment of Alzheimer's disease and other neurological disease-related ROS and inflammation.

Nephroprotective Activity

Studies showed that a single dose of cisplatin (45 mg/kg, i.p.) significantly elevated the levels of blood urea nitrogen, serum creatinine and the kidney-to-body weight ratio, but the pretreatment of xanthorrhizol (200 mg/kg/day, per os) for 4 days significantly attenuated the cisplatin-induced nephrotoxicity (Kim et al. 2005). The preventive effect of xanthorrhizol was more efficacious than that of curcumin at similar dose (200 mg/kg).

Hypolipidemic/Hypotriglyceridaemic Activity

Two phenolic diarylheptanoids, 5-hydroxy-7-(4-hydroxyphenyl)-1-phenyl(1*E*)-1-heptene and 7-(3,4-dihydroxyphenyl)-5-hydroxy-1-phenyl-(1*E*)-1-heptene, isolated from the rhizome exhibited significant hypolipidemic action by inhibiting hepatic triglyceride secretion (Suksamrarn et al. 1994). Wientarsih et al. (2002) reported that *C. xanthorrhiza* did not influence feed, protein and fat consumption and protein excretion but significantly increased fat excretion (cholesterol concentration was decreased by 46.6, 56.4 and 63.2 % and HDL (high-density lipoprotein) concentration was decreased by 9.9, 14.5 and 21.9 % at 2, 3 and 4 g/kg curcuma, respectively). *Curcuma xanthorrhiza*

significantly decreased LDL concentration and significantly decreased triglyceride concentration by 20.4, 28.5 and 29.5 % at 2, 3 and 4 g kg⁻¹, respectively. HMG-CoA reductase inhibitor was significantly increased by *C. xanthorrhiza*. Glucose was significantly reduced by 6.2, 7.6 and 18.0 % at 2, 3 and 4 g/kg *C. xanthorrhiza*, respectively. Lipid peroxidation was prevented at 3 and 4 g/kg *C. xanthorrhiza*. The enhanced fat excretion could have been mediated through an acceleration of lipid metabolism from extra-hepatic tissues to the liver, which would increase the excretion of cholesterol via the bile and into the faeces. The results suggested *C. xanthorrhiza* to have potential as a phytotherapeutic agent under atherosclerosis and cardiovascular disease conditions.

In rats administered with a cholesterol-free diet, *C. xanthorrhiza* decreased the concentrations of serum triglycerides and phospholipids, and liver cholesterol, and increased serum HDL-cholesterol and apolipoprotein A-I (apo A-I) (Yasni et al. 1993a). The activity of liver fatty acid synthase, but not glycerophosphate dehydrogenase, was decreased by *C. xanthorrhiza*. In rats on a high-cholesterol diet, *C. xanthorrhiza* did not suppress the elevation of serum cholesterol, although it did decrease liver cholesterol. Curcuminoids prepared from *C. xanthorrhiza* had no significant effects on the serum and liver lipids. These studies, therefore, indicated that *C. xanthorrhiza* contains an active principle(s) other than curcuminoids which could modify the metabolism of lipids and lipoproteins.

Addition of *C. xanthorrhiza* essential oil (0.02 %) to a purified diet in rats resulted in a lower hepatic triglyceride concentration without influencing the serum triglyceride, whereas addition of the hexane-soluble fraction (0.5 %) resulted in a lower concentration of serum as well as liver triglycerides (Yasni et al. 1994). Rats fed with the essential oil and hexane-soluble fraction had lower hepatic fatty acid synthase activity. The fraction containing α -curcumene, prepared from the hexane-soluble fraction, suppressed the synthesis of fatty acids from [¹⁴C] acetate in primary-cultured rat hepatocytes. Thus, α -curcumene was found to be one of the

active principles exerting triglyceride-lowering activity in *C. xanthorrhiza*.

Treatment with xanthorrhizol XAN (10 or 25 mg/kg/day) or *C. xanthorrhiza* extract CXE (50 or 100 mg/kg/day) significantly decreased fasting and postprandial blood glucose levels in high-fat diet-induced obese mice (Kim et al. 2014). Both treatments also lowered insulin, glucose, free fatty acid and triglyceride levels in the serum. Epididymal fat pad and adipocyte size were decreased by high doses of XAN (26.6 % and 20.1 %) and CXE (25.8 % and 22.5 %), respectively. XAN and CXE treatment also suppressed the development of fatty liver by decreasing liver fat accumulation.

Antiplatelet Activity

1-Methoxy-2-methyl-5-(1',5'-dimethylhex-4'-enyl)-benzene, synthesised by methylation of xanthorrhizol which was obtained from *C. xanthorrhiza*, showed an IC₅₀ value of 40.9 µM in platelet-activating factor (PAF) antagonistic activities (Jantan et al. 2004). The results indicated that the compound was a relatively strong PAF receptor binding inhibitor.

Antimicrobial Activity

Xanthorrhizol (1,3,5,10-bisabolatetraen-3-ol), isolated from *Curcuma xanthorrhiza* rhizome, possessed remarkable anticariogenic activity against *Streptococcus mutans* (Hwang et al. 2000a) and oral pathogens (Hwang et al. 2000b). MIC of xanthorrhizol against *S. mutans* was determined to be 2 µg/ml, which was much lower than other natural anticariogenic agents such as 16 µg/ml of sanguinarine, 125 µg/ml of tea polyphenol, 125 µg/ml of carvacrol, 250 µg/ml of isoeugenol, 500 µg/ml of eucalyptol and 500 µg/ml of thymol. 5-µg/ml treatment of xanthorrhizol killed completely *S. mutans* in a minute.

All six *Candida* species showed susceptibility to xanthorrhizol in the MIC (minimum inhibitory concentration) range of 1.0–15.0 mg/L for *Candida albicans*, 1.0–10 mg/L for *Candida glabrata*, 2.0–8.0 mg/L for *Candida*

guilliermondii, 2.5–7.5 mg/L for *Candida krusei*, 2.5–25 mg/L for *Candida parapsilosis* and 2.0–8.0 mg/L for *Candida tropicalis* (Rukayadi et al. 2006). Time-kill curves demonstrated that xanthorrhizol was able to kill the *Candida* strains with MFCs (minimum fungicidal concentrations) of 20 mg/mL, 15 mg/mL, 12.5 mg/mL, 10 mg/L, 30 mg/mL and 10 mg/L for *C. albicans*, *C. glabrata*, *C. guilliermondii*, *C. krusei*, *C. parapsilosis* and *C. tropicalis*, respectively. The results affirmed the potent anticandidal activity of xanthorrhizol and support the use of *C. xanthorrhiza* for the treatment of candidiasis. *Curcuma xanthorrhiza* rhizome ethanol extract inhibited *Staphylococcus aureus* and *Bacillus cereus* and ethyl acetate extract inhibited *Escherichia coli* in-vitro (Husein et al. 2009). The extract targeted the bacterial cell wall, bacterial spore, protoplast and spheroplast. Rukayadi et al. (2009) also found that xanthorrhizol in combination with ketoconazole or amphotericin B exhibited the synergistic anticandidal effects against all species of *Candida* tested. In combination with xanthorrhizol, the concentration of ketoconazole or amphotericin B for inhibiting the growth of the tested *Candida* species could be reduced by $\geq 50\%$. At 1/2 MIC dose of xanthorrhizol in combination with 1/2 MIC dose of ketoconazole or 1/2 MIC dose of amphotericin B, growth of all *Candida* species tested was inhibited and reduced viable cells by several logs within 4 h. Xanthorrhizol displayed potent activity against *Candida albicans* biofilms in-vitro and therefore might have potential therapeutic implication for biofilm-associated candidal infections (Rukayadi and Hwang 2013). Sessile minimum inhibitory concentrations (SMICs) determined at 50 % and 80 % reduction were against 18 *C. albicans* biofilms at 4–16 $\mu\text{g/mL}$ and 8–32 $\mu\text{g/mL}$, respectively. The results demonstrated that the activity of xanthorrhizol in reducing *C. albicans* biofilms OD_{490} was dependent on the concentration and the phase of growth of biofilm.

Xanthorrhizol showed promise as an antibacterial agent for inhibiting and removing *Streptococcus mutans* biofilms in-vitro (Rukayadi and Hwang 2006a, b). Studies demonstrated that coating of a polystyrene microtiter plate with 5 $\mu\text{g/mL}$ of

xanthorrhizol resulted in significant (up to 60 %) reduction of adherent bacterial cells compared to that of cells in uncoated wells. The result suggested that xanthorrhizol displayed potent activity in preventing *Streptococcus mutans* biofilm formation. A concentration of 5 µmol/L of xanthorrhizol completely inhibited biofilm formation by *S. mutans* at adherent phases of growth, whereas 50 µmol/L of xanthorrhizol removed 76 % of biofilm at plateau accumulated phase when exposed to *S. mutans* biofilm for 60 min. Kim et al. (2008) showed that *Streptococcus mutans* biofilm on glass slides treated with *Curcuma xanthorrhiza* extract had significantly fewer colony forming units (CFU, 57.6 and 97.3 %, respectively) than those exposed to 1 % DMSO, the negative control group. Further the biofilms treated with the extract maintained a neutral pH for 4 h, indicating that the extract inhibited acid production. Scanning electron microscopy showed morphological changes in the cell wall and membrane of the extract-treated biofilms, an uneven surface and a deformation in contour. Overall, the results indicated that *Curcuma xanthorrhiza* possessed strong bactericidal activity and inhibitory effects on acidogenesis and altered the microstructure of *S. mutans* biofilm and may have potential in anti-*S. mutans* therapy for the prevention of dental caries.

Xanthorrhizol also exhibited potential as an anti-*Malassezia* agent for inhibiting the growth of *Malassezia furfur* and *Malassezia pachydermatis* in-vitro (Rukayadi and Hwang 2007a). The MIC values of xanthorrhizol against *M. furfur* and *M. pachydermatis* were 1 · 25 and 0 · 25 µg/ml, respectively. The MFC of xanthorrhizol was 5 µg/ml for *M. furfur* and 2 · 5 µg/ml for *M. pachydermatis*. Time-kill curves demonstrated that treatment with 25 µg/ml of xanthorrhizol for 5 h was able to kill 100 % of *M. furfur*, while 20 µg/ml of xanthorrhizol for 15 min killed *M. pachydermatis* completely. *Malassezia* causes skin infection in pet animals and humans. The study demonstrated that xanthorrhizol may be a useful alternative for treating *Malassezia*-associated diseases.

Xanthorrhizol was found to be active against opportunistic filamentous fungal species tested, namely, *Aspergillus flavus*, *Aspergillus fumigatus*, *Aspergillus niger*, *Fusarium*

oxysporum, *Rhizopus oryzae* and *Trichophyton mentagrophytes*: the MICs being 2.0, 2.0, 2.0, 4.0, 1.0 and 1.0 µg/mL, while the MFCs were 4.0, 4.0, 4.0, 8.0, 2.0 and 2.0 microg/mL, respectively (Rukayadi and Hwang 2007b). The susceptibility of six species of filamentous fungi to xanthorrhizol was comparable to that of the commercial antifungal amphotericin B. Xanthorrhizol also exhibited activity to inhibit the conidial germination of all tested species. The results strongly suggested that xanthorrhizol could be developed as a natural antifungal agent.

Another study reported that xanthorrhizol exhibited antibacterial activity against food-borne pathogens (Lee et al. 2008). MICs and MBCs of xanthorrhizol against *Bacillus cereus*, *Clostridium perfringens*, *Listeria monocytogenes*, *Staphylococcus aureus*, *Salmonella typhimurium* and *Vibrio parahaemolyticus* were 8, 16, 8, 8, 16 and 8 µg/ml and 16, 32, 16, 16, 16 and 16 µg/ml, respectively. The bactericidal study, as determined by the viable cell count method, revealed that xanthorrhizol treatment at 4 x MIC reduced viable cells by at least 6 to 8 log for all six food-borne pathogens in 4 h. Xanthorrhizol maintained its antibacterial activity after thermal treatments (121⁰C, 15 min) under various pH ranges (pH 3.0, 7.0 and 11.0). These results strongly suggested that xanthorrhizol, conferring strong antibacterial activity with thermal and pH stability, could be effectively used as a natural preservative to prevent the growth of food-borne pathogens. The ethanol 70 % extract of *Curcuma xanthorrhiza* inhibited the growth of Gram-positive bacteria *Staphylococcus aureus* and *Streptococcus mutans* at a concentration of 1.0–5.0 % (w/v), while *Bacillus cereus* at a concentration of 2.0–50 % (w/v) (Mangunwardoyo et al. 2012). The minimum inhibitory concentration (MIC) of ethanol 70 % extract towards *S. aureus* and *S. mutans* was 0.1 % (w/v), and against *B. cereus* was 2.0 % (w/v).

The antimicrobial activity of *Curcuma xanthorrhiza* rhizome oil showed significant inhibitory activity against the human pathogenic bacteria, and no activity was observed against the fungi *Aspergillus niger* and *Fusarium oxysporum* (Mary et al. 2012).

Antibabesial Activity

Babesia is a protozoan parasite of the blood that causes a haemolytic disease known as babesiosis. Antibabesial activities of (12R)-12,13-dihydro-12,13-dihydroxyxanthorrhizol and (12S)-12,13-dihydro-12,13-dihydroxyxanthorrhizol, isolated from *Curcuma xanthorrhiza*, were compared with Ganaseg, a commercial drug (Matsuura et al. 2007). The IC₅₀ values of Ganaseg, (12R)- and (12S)-12,13-dihydro-12,13-dihydroxyxanthorrhizols were 0.6 µg/mL, 8.3 µg/mL and 11.6 µg mL, respectively. The curcuminoid, 3'-demethoxycyclocurcumin (1), isolated from *Curcuma xanthorrhiza*, exhibited antibabesial activity with IC₅₀ value of 16.6 µg/ml (Yamada et al. 2009).

Hypothermic Activity

Oral administration of the methanol extract of *C. xanthorrhiza* to mice resulted in a hypothermic effect in terms of rectal temperature. (Yamazaki et al. 1988a). Germacrone was identified as the active hypothermic principle in the extract (Yamazaki et al. 1988b).

Antinociceptive/Sleep Prolongation Activity

Oral administration of the methanol extract of *C. xanthorrhiza* to mice resulted in a prolonging effect on pentobarbital-induced sleeping time and a suppressive effect on acetic acid-induced writhing (Yamazaki et al. 1988b). Xanthorrhizol was identified as the active principle in prolonging effect on pentobarbital-induced sleeping time. The effect of xanthorrhizol was demonstrated to interact with cytochrome P-450 to inhibit metabolism of pentobarbital. Another constituent of the extract, germacrone, beside exerting a hypothermic effect was also involved in prolonging effect on pentobarbital-induced sleeping time, suppression of spontaneous activity, suppression of acetic acid-induced writhing and inhibition of stress-induced ulcers (Yamazaki et al. 1988b).

The methanol rhizome extract (p.o.) showed an analgesic activity in acetic acid-induced vascular permeability as well as the writhing symptom in mice (Ozaki 1990). The analgesic effect was also found in the successive ether-soluble fraction, the n-hexane-soluble fraction, fr. II, V and IX. Standardised *Curcuma xanthorrhiza* ethanolic extract did not show significant analgesic effect in the hot-plate and tail-flick tests (Devaraj et al. 2010a). However, in the formalin-induced pain test, the ethanolic extract significantly suppressed the paw licking time of rats in both early and late phases at doses 200 and 400 mg/kg of the extract, respectively. In the acute oral toxicity study, the ethanolic extract did not show any toxic effects in mice at 5 g/kg. The results suggested that the standardised *C. xanthorrhiza* ethanolic extract showed peripheral and central antinociceptive activity associated with neurogenic pain as well as a relative absence of toxic effects.

Analgesic Activity

Oral administration of the crude *Curcuma xanthorrhiza* rhizome extract at doses of 150 and 300 mg/kg body weight exhibited 33.2 and 50.5 % inhibition of acetic acid-induced writhing in mice, respectively (Mahmood et al. 2004).

Immunomodulatory Activity

Curcuma xanthorrhiza extract was found to increase the blastogenesis to the following mitogens (phytohaemagglutinin, concanavalin A and pokeweed) (Yasni et al. 1993b). *C. xanthorrhiza* increased the proportion of the splenic T cells, but exerted a variable effect on B-cell and T-cell subsets, i.e. elevations of B cells at 3 weeks and of Th cells at 4 weeks without any elevation of Ts cells. The effect of *C. xanthorrhiza* on a proportion of macrophages from the spleen and peripheral blood was not consistent. The results suggested that *C. xanthorrhiza* contained some principle(s) activating T- and B-cell-mediated immune functions.

Crude polysaccharide extract (CPE), isolated from the rhizome, was found to significantly increased the phagocytosis of macrophages and the release of NO (nitric oxide), H₂O₂,

TNF- α (tumour necrosis factor- α) and PGE₂ (prostaglandin E₂) in a dose-dependent manner and showed a similar activity to lipopolysaccharide (LPS) (Kim et al. 2007). CPE modulated iNOS and COX-2 expression. It was found that CPE stimulated the immune functions of macrophages, mediated in part by specific activation of NF- κ B (nuclear factor-kappa B).

The extracts of *Curcuma domestica*, *Phyllanthus amarus* and *C. xanthorrhiza* were found to generate the strongest oxidative burst of isolated human polymorphonuclear leukocytes with luminol-based chemiluminescence, with IC₅₀ values ranging from 0.5 to 0.7 μ g/ml (Jantan et al. 2011). For macrophage cells, the extracts which showed strong suppressive activity for luminol-based chemiluminescence were *C. xanthorrhiza* and *Garcinia mangostana*. Recent studies by Miksusanti (2012) reported that *C. xanthorrhiza* essential oil stimulated the proliferation of human lymphocytes in-vitro. The oil showed mitogenic activity similar to LPS and higher than ConA. Increases in the essential oil concentration in serial sample caused increasing in lymphocyte activation.

Anti-Skin Ageing Activity

Skin damage resulting from UV-induced generation of reactive oxygen species had been reported to be associated with upregulation of matrix metalloproteinases (MMPs), key regulators of the skin photoaging process and decreased collagen synthesis (Oh et al. 2009). Xanthorrhizol from *C. xanthorrhiza* (0.001–0.1 μ M) and *C. xanthorrhiza* extract (0.01–0.5 μ g/mL) induced a significant, dose-dependent decrease in the expression of MMP-1 protein and increased the expression of type 1 procollagen. At a concentration of 0.1 μ M, xanthorrhizol nearly completely abrogated MMP-1 expression. The MMP-1-suppressing and type 1 procollagen-inducing effects of xanthorrhizol treatment were greater than those of epigallocatechin-3-O-gallate (EGCG), a known natural anti-ageing agent. These results suggested that xanthorrhizol could be a potential candidate for the prevention and treatment of skin ageing. Two bisabolene

sesquiterpenoids, 13-hydroxyxanthorrhizol from *C. xanthorrhiza* rhizomes and (–)-curcuhydroquinone 2,5-di-*O*- β -D-glucopyranoside, decreased MMP-1 expression in UVB-treated human keratinocytes by *ca.* 8.9- and 7.6-fold at the mRNA level and by *ca.* 9.2- and 6.6-fold at the protein level, respectively (Park et al. 2014). The results indicated that the isolated compounds may have anti-ageing effects through inhibition of MMP-1 expression in skin cells.

Cholagogic Activity

C. xanthorrhiza rhizome essential oil showed slightly higher cholagogic activity than turmeric rhizome essential oil (Ozaki and Laing 1988). Oral administration of the essential oils caused a persistent increase of bile secretion in rats. The active principle of the essential oil of *C. xanthorrhiza* was shown to be d-camphor. The essential oil and d-camphor both caused a long-lasting increase of bile secretion involving increases both in the amount of total bile acids and in the solid matter weight in the excreted bile.

Oestrogenic Activity

Studies showed that xanthorrhizol, from *C. xanthorrhiza* rhizome, significantly increased Gal-4/ER luciferase activity in a dose-dependent manner and induced the endogenous ER–oestrogen response element (ERE) interaction in MCF-7 cells (Anggakusuma et al. 2009). Xanthorrhizol also significantly enhanced the expression of the pS2 gene in MCF-7 cells. In contrast, treatment using ICI 182780, an oestrogen receptor antagonist, suppressed all activities induced by xanthorrhizol, indicating that oestrogen receptor-dependent activities were involved. These results suggest that xanthorrhizol possessed oestrogenic activity and its oestrogenic effects were mediated by oestrogen-induced gene expression.

Diuretic Activity

Oral doses of *Curcuma xanthorrhiza* rhizome extract produced a maximum of 1.24 and 1.45 diuretic activity after 2 and 1 h of

the study in mice, respectively (Mahmood et al. 2004). The diuretic effect of the extract started after 1 h at doses of 150 and 300 mg/kg body weight of mice. It was observed that the diuretic activity increased with increasing the concentration of the test sample.

Antiviral Activity

Ethanol rhizome extract at doses of 100, 250 and 500 ppm exhibited antiviral activity against simian retrovirus serotype-2 (SRV-2) (Karyawati 2011). SRV-2 causes simian immune deficiency syndrome (SAIDS) in various macaque species.

Drug Delivery

Ambasari et al. (2012) showed that the best composition for producing curcuminoids—solid lipid nanoparticles (SLN) from *C. xanthorrhiza*—was palmitic acid, curcuminoids and surfactants with weight ratio 1:0.5:1.5 with entrapment efficiency of 72.98 %. The particle size was 285.5 nm.

Toxicity Studies

The ethanolic extract of *Curcuma xanthorrhiza* displayed no toxicity against brine shrimps with lethal concentration (LC₅₀) values of more than 1.0 mg/ml confirming that the extract was not toxic and bioactive (Devaraj et al. 2013). Oral administration of standardised ethanolic extract of *Curcuma xanthorrhiza* at the doses 300, 2000 and 5000 mg/kg resulted in no mortalities or evidence of adverse effects, indicating that *Curcuma xanthorrhiza* was non-toxic. This was further confirmed by the normal behavioural pattern, clinical signs of animals and histopathology analysis of the vital organs. The experimental results suggested that the standardised *Curcuma xanthorrhiza* ethanolic extract was non-toxic with a high margin of safety.

Traditional Medicinal Uses

The rhizomes of *Curcuma xanthorrhiza* are used in Indonesian folk medicine as cholagogues, aromatic stomachics, analgesics, a rheumatic remedy etc. (Burkill 1966; Ozaki 1990). Rhizomes of Java turmeric have been traditionally used for medicinal purposes in Malaysia, Singapore and Indonesia (Burkill 1966). It is administered for indigestion and rheumatism, as a tonic after childbirth and as an emmenagogue in amenorrhoea. The rhizome is used in Indonesian traditional medicine for various therapeutic purposes such as antihypertensive, antirheumatic, antioxidant, anti-inflammatory, etc. (Lim et al. 2005). The rhizomes are used as a tonic in many jamus in Indonesia. It is the most popular Indonesian herbal for hepatitis remedy and other liver disorders. It is deemed a broad spectrum hepatoprotective agent useful in the treatment of liver injuries and can protect the liver from various hepatotoxins, encourage bile discharge (cholagogue) and prevent the formation of gallstones and stomachic to treat various abdominal complaints and normalise digestion. A decoction of the rhizome is used for fever and constipation and taken by women as a galactagogue (increases breast milk production) and to reduce uterine inflammation after childbirth. Recently, temulawak has been used in supplement beverages to increase appetite (as natural appetiser) and to reinvigorate stamina. Temulawak was also reported to prevent avian flu. In Thailand it is used for the topical treatment of acne and skin inflammations. In Thailand, the rhizome is used to relieve stomach ache (Chanwitheesuk et al. 2005). The rhizome is used in dyspeptic complaints and as stomachic and carminative (van Wyk and Wink 2004). Turmeric (*Curcuma longa*), java turmeric (*Curcuma xanthorrhiza*) and cassumunar ginger (*Zingiber cassumunar*) are widely used in traditional Indonesian medicines (jamu) (Rohaeti et al. 2014).

Other Uses

C. xanthorrhiza also has insecticidal property. Xanthorrhizol from *C. xanthorrhiza* showed pronounced toxicity against neonate larvae of *Spodoptera littoralis* in a contact residue bioassay (Pandji et al. 1993). The LD₅₀ of xanthorrhizol

following topical application was found to vary between 6.92 and 8.13 $\mu\text{mol/kg}$ fresh weight irrespective of the larval stages studied. In a time course experiment, significant mortality of the larvae following topical contact with xanthorrhizol was observed as early as one hour following treatment, whereas all of the moribund larvae died within the first 6 h of observation. None of the compounds studied, however, including xanthorrhizol caused significant mortality of neonate larvae of *S. littoralis* when incorporated into artificial diet, suggesting inactivation of the compounds in the larval gut.

Comments

C. xanthorrhiza is normally propagated by division of the rhizomes.

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Curcuma zedoaria

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Scientific Name

Curcuma zedoaria (Christmann) Roscoe

Synonyms

Amomum latifolium Lam., *Amomum latifolium* Salisb., *Amomum zedoaria* Christmann, *Amomum zerumbet* J. König nom. illeg., *Costus luteus* Blanco, *Costus nigricans* Blanco, *Curcuma malabarica* Velay., Amalraj & Mural., *Curcuma officinalis* Salisb., *Curcuma pallida* Lour., *Curcuma raktakanta* Mangaly & M. Sabu, *Curcuma speciosa* Link (illeg.), *Curcuma zerumbet* (Berg.) Roxb., *Erndlia zerumbet* Giseke, *Roscoea lutea* (Blanco) Hassk. (illeg.), *Roscoea nigrociliata* Hassk.

Family

Zingiberaceae

Common/English Names

Cochin Turmeric, Hidden Lily Ginger, Indian Arrowroot, Kua, Long Zedoary, Round Zedoary, Setwall, White Turmeric, Wild Turmeric, Yellow Zedoary, Zedoary, Zedoary Turmeric

Vernacular Names

Arabic: Auruqul-Kafur, Gadwâr, Jadwar, Satwâl, Zadwâr, Zurambad, Zuranbad

Bangladesh: Shoti

Brazil: Zedoaria

Burmese: Thanuwen

Cambodia: Pratielpreah Angkaol

Chinese: E Zhu, E Shu, Yu Jin (Mandarin), Ngho South, Wat Gam (Cantonese)

Croatian: Zedoár, Kurkumovnik Zedoárový, Zedoárie, Zedoárové Koření

Czech: Zázvor Širokolistý

Danish: Zedoar

Dutch: Kurkuma Sort, Maagwortel, Paradijszaadsoort Of Var, Zedoar, Zedoarwortel, Zedoarwortelstok

Estonian: Tsitverijuur

French: Gingembre Bâtard, Zédoaire, Curcuma Zédoaire, Rhizome de Zédoaire

German: Giftheil, Weisse Curcuma, Zedoarwurzel, Zitwer, Zittwer Kurkume

Hungarian: Citvár, Citvor, Fehér Kurkuma, Kesernyész Gyömbér, Termesztett Gyömbér, Zeodária, Zedoária-gyökér

India: Katuri (Assamese), Aam Aadaa, Sutha, Yaipal (Bengali), Shatkachuro (Gujarati), Amb Halad, Gandamasti, Gandhmul, Jangli Haldi, Kachur, Kachura, Kakhur, Kalihaladi (Hindi), Ambe Haldi, Kaadu Arisina, Kachora, Kochora (Kannada), Adavi-Kachhola, Kaccolam, Kach-Cholam, Kach-Churi-Kizhanna, Kachcholam, Kachchurikizhanna, Kua, Pula-Kizhanna, Pulakizhanna, Pulan-Kizhanna (Malayalam), Meitei Yaingang (Manipuri), Kachar, Kachari, Kachora, Kachur, Kuv, Kuw, Narakachora (Marathi), Kedar (Oriya),

Dravida, Durlabha, Gandhamula, Gandhamulaka,
Gandhasara, Jatala, Kaccura, Kachhuraha, Kachura,
Kacoraka, Kalpaka, Karchur, Karchura, Karcura,
Karcurah, Karshya, Krachura, Mukhya, Nirvisha, Sathi,
Sati, Shathi, Shati, Vanaharidra, Vedhya (Sanskrit),
Amalanica, Amlavarittira, Castoorie Munjel,
Cunaittavakkilanku, Cunaittavam, Cuntiran, Cutatali,
Kaccolakkilanku, Kaccolam, Kaccoram, Kantapalaci,
Karccuram, Karppurakiccili, Karppurakkiccilikkilanku,
Karpurakam, Kastori-Manjal, Katturimancal,
Kicchilikizhangu, Kiccili, Kiccili-K-Kilanku, Kiccilik
Kilanku, Kiccilik-Kilanku, Kiccilikkilanku, Kicciliver,
Kich-Chilik-Kizhangu, Kichchilik-Kishangu,
Kichchilikkizhangu, Kichili Kilangu, Kichilic-Kizhanga,
Kichilikilhangu, Kirandi Dakaram, Korankimulam,
Kotukam, Kurpakatikkilanku, Kurupakatitam, Kuva,
Mancatpula, Nattukkiecilikkilanku, Niruvisam, Nirvisam,
Nirvisham, Perunkurumpai, Pirutupala, Poolan Kilangu,
Pula, Pulai, Pulakkilanku, Pulamulam, Pulan-Kizhanga,
Pulan-Kizhangu, Pulankilanku, Pulankilhangu, Pulavin
Kilanku, Talaivalipokki, Veppatti (Tamil), Adavipasuvu,
Kachoeramu, Kachoram, Kasthooripasupu, Kich-Chili-
Gaddalu, Kichchiligaddalu, Kichhiligaddalu, Kichili-
Gaddalu (Telugu), Biring, Tripuri, Rupini, Jadwar,
Kachura, Kharal Ki Hui, Zadwar Saida, Zarambad (Urdu)

Indonesia: Kunyit Putih, Temu Putih, Koneng Tegal,
Temu Kuning, Koneng Bodas, Kunir Putih

Italian: Radice Di curcuma, Zedoaria, Zedoaria Lunga

Japanese: Gajutsu

Korean: Achul, Pongchul, Kajyuchu, Keokyumeo Jedo,
Kokyumo Jedo

Laotian: Khi Min Khay, Khminz Hunz

Malaysia: Kunchur, Temu Kuning, Temmu Lawak, Temu
Putih

Nepal: Kacur, Van Haledo (Nepalese), Halu Bun, Kachur
(Nepalbhase)

Persian: Kazhur, Uruk-El-Kafur, Urukelkafur, Zhuranbad

Philippines: Tamahilan (Bikol), Koniko (Bontok), Alimpuyas, Alimpuying (Cebu Bisaya), Unig (Ifugao), Konik, Langkuas (Iloko), Tamo (Pampangan), Lampoyang (Panay Bisaya), Ganda (Sambali), Bolon, Barak, Luya-Luyahan, Tamahiba, Tamo, Tamokansi (Tagalog)

Polish: Kurkuma Plamista

Portuguese: Zedoária, Zedoeira

Russian: Zedoari

Slovak: Zedoár

Slovenian: Isiot

Spanish: Cedoaria, Cetoal

Swedish: Zittverrot

Thai: Haeo Dam Khamin-Khun, Khamin Hua Khuen, Khamin Khao, Khamin Khun, Khamin-Oi

Tibetan: Ka Tsu Ra

Turkish: Çevdar, Gulpa Hamar

Ukrainian: Kurkuma Zedoarskaya

Vietnam: M'Gang M' Lung (Ba Na), Bông Truật, Sung Meng (Dao), Nghệ Đen; Nga Truật; Ngải Tím; Bông Nga Truật; Tam Nại (Tay)

Yiddish: Tsitver-kurkume

Origin/Distribution

The species is indigenous to eastern Himalaya to Assam (Govaert 2014). Sirirugsa (1998) regarded it to be probably native to northeast India and Southeast Asia. It can be found wild in the mountainous areas of Vietnam (NIMM 1999). It has been introduced elsewhere and is cultivated in the south, Southeast Asia throughout Malaysia, South China, Taiwan, Japan, Madagascar and Brazil.

Agroecology

In its native range, it grows wild in the lowlands up to 1500 altitude. The species is highly hygrophilous; grows in full sun or light shade in dense plantings along streams, forest margin valleys, grass wasteland, stony localities and open waste places in and near towns; and is cultivated (Backer and Bakhuizen van den Brink 1968; NIMM 1999).

Edible Plant Parts and Uses

Zedoary root, heart of shoots, leaves and inflorescence are edible (Burkill 1966; Tanaka 1976; Morton 1976; Ochse and Bakhuizen van den Brink 1980; Facciola 1990; Sirirugsa 1998). In India, zedoary root is used fresh or in achar (pickles). *C. zedoaria* is used in a popular local dish called 'Berma bwtwi'—a soupy dish of dry fish, with cut pieces of zedoary root, green chilli, onion, turmeric powder and salt by the Tripura community in India (Deb et al. 2013). In Manipur, northeast India, the whole inflorescence head with flowers is used as vegetable. In Indonesia the rhizome is ground to a powder and added to curry pastes. The heart of young shoots is used raw or cooked in lalab (Ochse and Bakhuizen van den Brink 1980).

In Thailand, the young rhizome is used raw and cut in thin strips or slices and used in certain Thai salads or consumed together with other herbs and vegetables with certain types of nam phrik (Thai chilli pastes) or used in the preparation of curry pastes with coconut milk. The young rhizome is eaten as vegetable soup and leaves are used for flavouring fish and other food in Thailand (Sirirugsa 1998). Dried rhizomes have been reported to be used as bitters and ginger ale flavouring in beverages (Facciola 1990; Winter 2009). *Curcuma longa* and *Curcuma zedoaria* rhizomes, which are already used in industry to obtain food colouring and pharmaceutical products, have commercial potential as starch raw materials for the food industry (Burkill 1966; Leonel et al. 2003). The rhizomes are a source of shoti starch, used as a food for babies and

convalescents, recovering from chronic stomatitis (Khare 2004). It is cooling and demulcent.

Botany

Curcuma zedoaria is a perennial erect herb about 1–1.5 m with upright pseudostem (Plates 1 and 2) and subterranean, branched robust, conical, fleshy rhizome, which is greyish brown to brown outside and pale yellowish white inside; some roots develop several small, swollen, rounded to ellipsoidal tuber-like roots called t-roots (Plates 3 and 4). Its leaf sheaths are 35–60 cm long; leaf blades are oblong to oblong lanceolate, 25–75 by 8–20 cm, glabrous and green often with purple midvein on upper surface (Plates 1 and 2).

Inflorescence is cylindrical and 10–20 cm long by 8–15 cm wide on 15–20 cm scape arising separate from the rhizome before the leaves. On the rhizome node closest to the flower spike, a vegetative shoot always develops. No additional floral buds sprout, but more vegetative shoots develop. Flower spike with flower bracts imbricates and is oval-lanceolate greenish and pink at the tips; coma bracts are purple or dark pink and showy, each containing several yellow flowers, the lower flowers opening first (Plate 2). The calyx is small and bifid. The corolla tube is about 2 cm long and yellowish white and sometimes tinged with purple, and the labellum is yellowish white with dark-yellow median streak and is bilobed.

Staminodes are longitudinally folded, anther has long spurs, and the ovary is villous. Capsule is ovoid, triangular and dehiscent irregularly. Seeds are oblong, and lanceolate is white.



Plate 1 Zedoary ginger plant habit



Plate 2 Young leaf and inflorescence



Plate 3 Rhizome cut from the plant base



Plate 4 Pile of harvested rhizomes

Nutritive/Medicinal Properties

Rhizome/Root Phytochemicals

The rhizome was found to contain 83.22 % moisture content, 6.64 % total ash, 0.64 % acid-insoluble ash, 15.53 % alcohol-soluble extractives, 18.96 % water-soluble extractives, 12.51 % sugar, 15.70 % starch and 2.8 % total volatile oil (Srivastava et al. 2011). The weight (dry) and nutrient content of the primary rhizome, first-order branches and swollen tuber-like roots were reported, respectively, as follows: dry weight 88 g, 87.7 g and 87.8 g; carbohydrates 54.5 %, 64.9 % and 74.5 %; protein 22.7 %, 9.3 % and 4.0 %; fat 3.7 %, 7.5 % and 3.0 %; and ash 6.8 %, 6.2 % and 6.5 % (Maciel and Criley 2003). *Curcuma longa* and *Curcuma zedoaria* rhizomes showed low dry matter and high starch contents; the amylose contents of the starches (22 % *C. longa* and 21 % *C. zedoaria*) were similar to potato starch and had flat triangular shape, and the size was 20–30 μm for two starches (Leonel et al. 2003). The results of microscopic analysis showed. The final viscosity of *C. longa* was high (740 RVU) and the pasting temperature was 81 °C, and in *C. zedoaria* the final viscosity was 427 RVU and the pasting temperature was 78 C. The starch from *C. malabarica* tubers was white in colour, while

that from *C. zedoaria* starch was slightly yellowish due to the presence of the yellow pigment curcumin (Jyothi et al. 2003). The granule size and shape, amylose content and solubility did not show noticeable difference between starches from the two species. Both starches possessed 'B'-type x-ray diffraction pattern. *C. zedoaria* starch showed a lower peak viscosity and swelling volume than *C. malabarica* starch. The complete removal of curcumin from *C. zedoaria* starch by alcohol extraction resulted in an increase in the swelling and viscosity values. The breakdown in viscosity was quite low for both the starches, and setback was higher when compared to cassava and sweet potato starches. Differential scanning calorimetry (DSC) data showed that the onset of gelatinisation was earlier for *C. malabarica* starch. The enthalpy of gelatinization was almost the same for both the starches. The phosphorus content of *Curcuma* starch was quite high and similar to that of potato starch. The *Curcuma* starch was found to be easily digestible like arrowroot starch as seen from the in-vitro α -amylase digestibility patterns.

From the rhizome, the following compounds were isolated: sesquiterpenoid curcumol (Hikino et al. 1965, 1966a); sesquiterpenoid diketone curdione (germacr-1(10)-ene-5,8-dione) (Hikino et al. 1966b, c); sesquiterpenoid keto-dioxide zederone (Hikino et al. 1966d, g; Hikino et al. 1971 b); sesquiterpenic ketol curcolone (Hikino et al. 1967, 1968e); a furan-containing sesquiterpenoid named pyrocurzerenone (Hikino et al. 1968a); sesquiterpenes furanodiene and curzerene (Hikino et al. 1968b); sesquiterpene curcumenol (Hikino et al. 1968d); a sesquiterpenic keto-alcohol procurcumenol (Hikino et al. 1968f); curzerenone, epicurzerenone and isofuranogermacrene (curzerene) (Hikino et al. 1968c); sesquiterpene zedoarone (Fukushima et al. 1968); a sesquiterpenic hemiketal named isocurcumenol (Hikino et al. 1969a); sesquiterpenoids furanodienone and isofuranodienone (Hikino et al. 1969b); curzerenone, dihydro-curzerenone, tetrahydro-curzerenone, perbenzoic acid oxidation product of curzerenone and two epimeric isomers of eleman-6-one from catalytic hydrogenation of curzerenone (Fukushima et al. 1970); two furan-containing

sesquiterpenoids, furanodiene and isofuranogermacrene (curzerene) (Hikino et al. 1970a, b); sesquiterpenoid curmadiol (Hikino et al. 1971a); a sesquiterpenic dione dehydrocurdione (Hikino et al. 1972); sesquiterpenoids furanodienone, isofuranodienone, curzerenone, epicurzerenone and pyrocurzerenone (Hikino et al. 1975); ethyl *p*-methoxycinnamate (Gupta et al. 1976); 3",4"-*O*-diacetylafzelin, zerumbone, zerumbone epoxide, diferuloylmethane, feruloyl-*p*-coumaroylmethane and di-*p*-coumaroylmethane (Matthes et al. 1980); furanogermenone (Shibuya et al. 1982); (4*S*, 5*S*)-(+)-germacrone-4,5-epoxide, a biogenetically key compound for biosynthesis of various germacrene sesquiterpenoids in zedoary (Yoshihara et al. 1984); a guaiane, zedoarondiol (Kouno and Kawano 1985); a cyclopropanosesquiterpene curcumenone and two new spironolactones, curcumanolide A and curcumanolide B, and known related sesquiterpenes (Shiobara et al. 1985a); dehydrocurdione, from the rhizome, which was converted to curcumenol, isocurcumenol or new spironolactones in a highly selective manner (Shiobara et al. 1985b); three sesquiterpenoids, zedoarol (a furanoguaiane), 13-hydroxygermacrone (a germacrene) and curzeone (a furanocadinane) (Shiobara et al. 1986); sesquiterpenes, germacrene, curzerenone and germacrene epoxide (Shin et al. 1989); antifungal principle, methyl-*p*-methoxycinnamate (Joshi et al. 1989); a furan sesquiterpene (Zhao et al. 1991); curcuminoids, namely, curcumin, demethoxycurcumin and bisdemethoxycurcumin, and 3,7-dimethylindan-5-carboxylic acid, curcolonol and guaidiol from the ethanol extract (Syu et al. 1998); sesquiterpenoids *ar*-turmerone and β -turmerone (Hong et al. 2001); carabran-type sesquiterpenes curcumenolactones A, B and C, curcumenone, 4*S*-dihydrocurcumenone and curcarabranols A and B; germacrane-type sesquiterpenes furanodiene, iso-furanodiene, zedrone, germacrene, 13-hydroxygermacrone, glechomanolide, (+)-germacrone-4,5-epoxide, curdione, neocuproine and dehydrocurdione; guaiane-type sesquiterpenes 4-epicurcumenol, neocurcumenol, gajutsulactones A and B, zedoarolides A and B, curcumenol, isocurcumenol, procurcumenol, isoprocurcumenol,

alismoxide, 7 α -11 α -epoxy-5 β -hydroxy-9-guaiaen-8-one, aerugidiol, zedoarondiol, isozedoarondiol and zedoalactone B; bisaborane-type sesquiterpenes (+)-*ar*-turmerone, bisacumol and bisacurone; eudesmane-type sesquiterpenes β -eudesmol, β -dictyopterol and zedoarofuran; elemene-type sesquiterpene curzerenone; xanthane-type sesquiterpene curcumadione and diarylheptanoids curcumin, bis(4-hydroxycinnamoyl)methane and *N*^G-monomethyl-L-arginine (L-NMMA) (Matuda et al. 2001a, b, c, d); 1,7-bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one, procucumenol and epiprocurcumenol (Jang et al. 2004); four curcuminoids (curcumin, dihydrocurcumin, tetrahydrodemethoxycurcumin and tetrahydrobisdemethoxycurcumin) isolated together with two bisabolane-type sesquiterpenes (Matsuda et al. 2004); curcumol, germacrone and curdione (Yang et al. 2005); antibabesial zedoalactones A, B and C (Kasahara et al. 2005); furanodiene and furanodienone, along with new sesquiterpene compound **3** and known eight sesquiterpenes, zederone, curzerenone, curzeone, germacrone, 13-hydroxygermacrone, dehydrocurdione, curcumenone and zedoaronediol (Makabe et al. 2006); curdione (Oh et al. 2007); a mannose-binding lectin with molecular mass of 13 kDa (Tiphthara et al. 2007); a sesquiterpenoid curcuzederone and flavonoid naringenin (Eun et al. 2010); and curcumenol with the systemic name 9-isopropylidene-2,6-dimethyl-11-oxatricyclo[6.2.1.0^{1,5}]undec-6-en-8-ol (Hamdi et al. 2010). A heteroglycan (Nandan et al. 2011), isocurcumenol (25.24 %), methyl sterolate (24.94 %), 4,5,6,6A-tetrahydro-2[1H]-pentalenone (14.49 %), isolongifolene (9.31 %), isovelleral (5.92 %) and elemene (3.75 %) were the major compounds in the petroleum ether fraction; other compounds included dihydro neoclovene (3.48 %), eremanthron (2.89 %), eucalyptol (2.04 %), germacrone (1.87 %), camphor (1.58 %), 9-octadecynoic acid methyl ester (1.36 %), octahydroanthracene (1.25 %), β -selinene (1.03 %) and azulene (0.87 %) (Lakshmi et al. 2011). A sesquiterpenoid curcuzedoalide, a diterpene curminol D and indole derivative indole-3-carbaldehyde (Park et al. 2012); curzerenone, neocurdione, curdione, alismol and zederone, and a mixture of sterols, namely, campesterol, stigmasterol and β -sitosterol

were isolated from the hexane fraction (Syarifah Nur et al. 2013).

The major sesquiterpenoid of essential oil of *Zedoariae* rhizoma from China was furanogermenone; others were dehydrocurdione, germacrone, curcumenol, furanodiene, furanodienone + curserenone and zederone (Shibuya et al. 1986). The major sesquiterpenoid of essential oil of *Zedoariae* rhizoma from Taiwan was curcumenol, followed by furanodienone + curserenone, dehydrocurdione, germacrone, furanodiene and furanodiene. The major sesquiterpenoid of essential oil of *Zedoariae* rhizoma from Yakushima, Japan, was dehydrocurdione, followed by furanodienone + curserenone, (4*S*,5*S*)-(+)-germacrone-4,5-epoxide, furanogermenone, curcumenol, zederone, germacrone and furanodiene. Malek et al. (2004) reported the main volatile constituents of the essential oil as follows: furanogermenone (45.23 %), curserenone (8.65 %), germacrone (5.47 %), furanodiene (4.01 %), δ -guaiene (3.53 %), β -elemene (2.89 %) and β -selinene (2.82 %).

Ethanollic extracts of *C. zedoaria* rhizomes collected from various parts of Thailand contained curcumin, demethoxycurcumin and bisdemethoxycurcumin in the range of 1.46–5.73 %w/w (average 2.73 %w/w), 3.15–10.98 %w/w (average 7.37 %w/w) and 0.49–2.99 %w/w (average 1.40 %w/w), respectively (Paramapojn and Gritsanapan 2007, 2009). The highest average total curcuminoid content in the extracts was found to be 16.83 %w/w, while the lowest content was 6.09 %w/w. The hexane and dichloromethane fractions of *C. zedoaria* rhizomes afforded 19 compounds, namely, labda-8(17),12 diene-15,16-dial (1), dehydrocurdione (2), curcumenone (3), comosone II (4), curcumenol (5), procurcumenol (6), germacrone (7), zerumbone epoxide (8), zederone (9), 9-isopropylidene-2,6-dimethyl-11-oxatricyclo[6.2.1.0(1,5)]undec-6-en-8-ol (10), furanodiene (11), germacrone-4,5-epoxide (12), calcaratarin A (13), isoprocurcumenol (14), germacrone-1,10-epoxide (15), zerumin A (16), curcumanolide A (17), curcuzedoalide (18) and gweicurculactone (19) (Ahmed Hamdi et al. 2014).

Curcuma zedoaria rhizome volatile oil was found to contain 1,8-cineole (18.5 %), *o*- and *p*-cymene (18.42 %) and α -phellandrene (14.93 %) as major constituents followed by terpinolene (4.11 %), α -pinene (3.28 %), β -turmerone isomers (3.1 %), β -pinene (2.93 %), β -phellandrene (2.0 %), *p*-cymene-8-ol (1.84 %), linalool (1.8 %), myrcene (1.62 %), *ar*-turmerone (1.60 %) and δ -3-carene (1.18 %) (Singh et al. 2003). Other minor components <1 % included camphene, sabinene, 6-methyl-5-hepten-2-one, octanal, α -terpinene, β -phellandrene, (*Z*)- β -ocimene, (*E*)- β -ocimene, γ -terpinene, *cis*-sabinene hydrate, *cis*-linalool oxide, citronellol, terpinen-4-ol, nerol and β -caryophyllene. Thirty-six compounds were identified in the rhizome essential oil, including 17 terpenes, 13 alcohols and 6 ketones (Mau et al. 2003). The yields of fractions II and III were 83.66 and 10.71 %, respectively. Epicurzerenone and curzerene were found in the first and second highest amounts (24.1 and 10.4 %). The essential oil was found to contain a high content of epicurzerenone (46.6 %), curdione (13.7 %) and 5-isopropylidene-3,8-dimethyl-1(5H)-azulenone (9.15 %) (Lai et al. 2004). Some other minor components were 1,8-cineole (1.36 %), camphor (1.46 %), β -elemene (1.90 %), α -terpineol (1.45 %), α -curcumene (0.70 %), curcumol (1.89 %), isocurcumenol (1.84 %), α -pinene, β -pinene, epicurcumenone, curdione and several unknowns. The essential oil of *C. zedoaria* from northeast India was found to contain 37 constituents about 87.7 % of the total oil (Purkayastha et al. 2006). Curzerenone (22.3 %) was the major component, followed by 1,8-cineole (15.9 %) and germacrone (9.0 %). The presence of β -turmerone (19.88 %), 1,8-cineole (8.93 %), 7-zingiberene (7.84 %), β -sesquiphellandrene (6.75 %), β -selinene (6.27 %), γ -curcumene (5.57 %), β -bisabolene (3.69 %), *ar*-turmerone (2.27 %), α -turmerone (2.17 %) and α -elemene (1.85 %) were found as constituents in *Curcuma zedoaria* rhizome volatile oil (Champakaew et al. 2007). 8,9-Dehydro-9-formyl-cycloisolongifolene, 6-ethenyl-4,5,6,7-tetrahydro-3,6-dimethyl-5-isopropenyl-*trans*-benzofuran, eucalyptol and γ -elemene were found in zedoary essential oil (Chen et al. 2013).

A total of 60 components were identified in the rhizome essential oil (Singh et al. 2013). The major components were

curzerenone (31.6 %), germacrone (10.8 %) and camphor (10.3 %). Other components were α -pinene, camphene, β -pinene, myrcene, *p*-cymene, 1,8-cineole, 2-nonanone, linalool, α -nonanol, *trans*-pinocarveol, β -terpineol, *isoborneol*, borneol, 4-terpineol, *p*-cymen-8-ol, α -terpineol, myrtenol, verbenone, carvone, *isobornyl* acetate, 1,2,4-trimethoxyethyl-benzene, 2-undecanone, 2-undecanol, δ -elemene, β -elemene, β -bourbonene, (*E*)- β -caryophyllene, α -santalene, γ -elemene, *trans*- α -bergamotene, aromadrene, α -humulene, β -chamigrene, germacrene D, β -selinene, α -agarofuran, germacrene B, caryophyllene, furanodienone, T-cadinol, α -cadinol, *ar*-turmerone, γ -(*E*)atlantone, curdione, curcumenol and α -(*E*)atlantone. In the ethanol oleoresin, a total of 26 components were found with curzerenone (30.5 %), germacrone (7.0 %), camphor (5.5 %) and curcumenol. The major constituents, furonodienone and furanodiene, were also found in minor amounts. Twenty-five compounds were found in the isopropanol oleoresin and 40 components in the ethyl acetate oleoresins with curzerenone, germacrone, camphor and curcumenol as major components in both oleoresins.

Yoshihara et al. (1986) found that acidic treatment of (4*S*, 5*S*)-(+)-germacrone-4,5-epoxide (2), a biogenetic intermediate found in the zedoary essential oil, furnished three guaiane sesquiterpenoids: GU-1 (procurcumenol), GU-2 and GU-3, while alkaline treatment of 2 provided an eudesmane sesquiterpenoid EU-1 as respective major reaction products. Procurcumenol and GU-2 were found in minor quantities in *C. zedoaria* rhizomes from Yakushima, Japan. The sesquiterpene, germacrone, was converted through, the key intermediate, (4*R*,5*R*)-germacrone-4,5-epoxide, into guaiane-type sesquiterpenes by suspension-cultured cells of *Curcuma zedoaria* (Sakui et al. 1992). A eudesmane-type product was also isolated. Other intermediate products included (1*S*, 10*S*)-germacrone-1,10-epoxide, curcumenone and dihydrocurcumenone. Wang et al. (2004) found that addition of precursors of calcium pantothenate, ammonium acetate and potassium acetate during the middle period of *C. zedoaria* cell suspension culture in MS medium enhanced the volatile oil content, respectively, and ammonium acetate was most effective among them. The highest yield of volatile oil

obtained was 3.11 % and 8.27 g/L, respectively, which was 1.25 and 1.2 times of the control group. After 14 days of cell culture in a 5-L bioreactor, the optimal yield of zedoary essential oil (1.78 %) was obtained when using petroleum ether at 40 °C in 6 h of extraction, and the best curcumin yield (9.69 %) was obtained at 60 °C in 6 h via extraction with 90 % ethanol (Loc et al. 2008). The activities of antioxidant enzymes from zedoary cells were also assessed. The specific activities of antioxidation enzymes peroxidase, superoxide dismutase and catalase reached maximum values of 0.63 U/mg of protein, 16.60 U/mg of protein and 19.59 U/mg of protein after 14 days of culture, respectively.

Total arsenic contents (dry weight basis) in six edible Zingiberaceous rhizomes, namely, *Alpinia galanga* (Khaa), *Boesenbergia rotunda* (Kra chaai), *Curcuma longa* (Khamin chan), *Curcuma zedoaria* (Khamin oi), *Zingiber cassumunar* (Plai) and *Zingiber officinale* (ginger), were found to be 92.4, 103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively (Ubonnuch et al. 2013). Total inorganic arsenic was 92.4, 103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively. All investigated amounts of total and inorganic arsenic were much lower than limits recommended by Thai Food and Drug Administration.

Other Plant Part Phytochemicals

Young shoots of *C. zedoaria* were found to contain (+)-germacrone-4,5-epoxide, a key intermediate in the biogenesis of germacrone-type sesquiterpenoids (Shiobara et al. 1985a).

Twenty-three compounds were identified in *C. zedoaria* leaf essential oil, accounting for 75 % of the oil and comprised mainly of mono- and sesquiterpenoids, monoterpene hydrocarbons (2.3 %), oxygenated monoterpenes (26 %), sesquiterpene hydrocarbons (38 %) and oxygenated sesquiterpenes (13.5 %) (Garg et al. 2005). The major constituents were α -terpinyl acetate (8.4 %), isoborneol (7 %), dehydrocurdione (9 %) and selina-4(15),7(11)-dien-8-one (9.4 %).

Numerous studies conducted reported that the rhizomes displayed antimicrobial, antifungal, antiallergic, antitumoural, analgesic, antiinflammatory, antioxidant, hepatoprotective, cytotoxic, vasorelaxant and lipopolysaccharide inhibition and NO production inhibitory activities and other pharmacological activities. These are elaborated below.

Antioxidant Activity

The methanol extract of fresh and dry rhizomes exhibited strong DPPH radical scavenging activity that was significantly higher compared to the trolox standard (Sumathi et al. 2013). *C. zedoaria* essential oil at 20 mg/mL was moderate to good in antioxidant activities by three different methods, good in reducing power and excellent in scavenging effect on 1,1-diphenyl-2-picrylhydrazyl radical but low in chelating effect on ferrous ion (Mau et al. 2003). However, after fractionation, with regard to all antioxidant properties assayed, fraction IV showed consistently better effects than the essential oil did. The compound in fraction IV responsible for better antioxidant properties might be 5-isopropylidene-3,8-dimethyl-1(5H)-azulenone. Chen et al. (2008) reported crude rhizome extraction yield of 92.5 mg/g and total phenol contents of 33.4 mg/g, antioxidant capacity of the methanol rhizome extract of 76 %, DPPH-free radical scavenging activity of 65.4 % and reducing power (absorbance 700 nm) of 0.9 absorbance. Values of EC₅₀ of all *C. zedoaria* extracts from 10 locations in Thailand for 1,1-diphenyl-2-picrylhydrazyl (DPPH)-free radical scavenging activity were found in the range of 18.29–40.33 µg/ml (average 25.71 µg/ml) (Paramapojn and Gritsanapan 2009). Free radical scavenging activity of the separated pure curcuminoid compounds was found in descending order of curcumin > demethoxycurcumin > bisdemethoxycurcumin. The amount of major antioxidants β-carotene (2.31, 2.24 mg/g), ascorbic acid (2.17, 2.15 mg/g) and total polyphenols (37.07, 32.49 mg/g) present, respectively, in both the methanolic and aqueous extracts of *C. zedoaria* rhizomes was similar (Peng et al. 2010). Consequently, both of the extracts showed similar antioxidant effects. The inhibition effect on lipid peroxidation was similar

with both extracts. In contrast, the content of cucuminoids (curcumin, desmethoxycurcumin, bisdesmethoxycurcumin) (44.3-mg/g extract) in the methanol extract was higher than the curcuminoids (curcumin, desmethoxycurcumin) in the aqueous extract (0.09-mg/g extract).

Chloroform-soluble fraction of *C. zedoaria* exhibited highest percent inhibition of DPPH radical, i.e. 67.97 % at concentration of 250 µg/ml as compared to other fractions (Abbasi 2011). IC₅₀ value of chloroform fraction was found to be 117.08 relative to butylated hydroxytoluene (BHT), with IC₅₀ of 12.54 µg/ml. It also showed highest value of total antioxidant activity, i.e. 1.358 as well as the highest FRAP value (291.25 TE µM/mL), highest amount of total phenolic compounds (155.27 GAE µg/g) and highest percentage of inhibition of lipid peroxidation (42.24 %) as compared to other studied fractions. Ethyl acetate soluble fraction showed moderate to good antioxidant activity. The n-hexane-soluble fraction, n-butanol soluble fraction and remaining aqueous fraction showed no activity.

Hydroethanolic extract of *Curcuma zedoaria* rhizome was found to have antioxidant activity in-vitro (Srividya et al. 2012). IC₅₀ value of DPPH scavenging activity was 930 µg/ml, >1000 µg/ml for nitric oxide method; concentration required for reducing power was found to be 2.525 µg/ml; and total antioxidant capacity was found to be 230.2 mM equivalent of ascorbic acid. Total phenol content was found to be 34.45 mg/g equivalent of gallic acid, and total flavonol content was found to be 45.56 mg/g equivalent of quercetin. In terms of lipid peroxide inhibition, the relative efficacy of *C. zedoaria* essential oil and oleoresins compared with antioxidant standards was BHT (butylated hydroxyl toluene) > essential oil > PG (propyl gallate) > isopropanol oleoresin > ethyl acetate oleoresin > butylated hydroxyl anisole (BHA) > ethanol oleoresin > control (Singh et al. 2013). In DPPH scavenging efficacy (based on IC₅₀), the rankings were ethyl acetate oleoresin < isopropanol oleoresin < essential oil < ethanol oleoresin < BHA + BHT < PG. In linoleic acid peroxidation inhibition, the ranking was PG = essential oil >

BHt > isopropanol oleoresin > ethyl acetate oleoresin > ethanol oleoresin > BHA > control. In Fe²⁺ chelating activity, the ranking was PG > ethyl acetate oleoresin > isopropanol oleoresin > essential oil > BHT > ethanol oleoresin > BHA > control. In thiobarbituric acid assay, the ranking was essential oil > isopropanol oleoresin, ethyl acetate, ethanol higher than BHA and BHT.

Anticancer Activity

In-Vitro Studies

Curcuminoids, namely, curcumin, demethoxycurcumin and bisdemethoxycurcumin, from rhizome extracts were demonstrated to be cytotoxic against human ovarian cancer OVCAR-3 cells with CD₅₀ values of 4.4, 3.8 and 3.1 µg/mL, respectively (Syu et al. 1998). Among the fractions from *C. zedoaria* hexane extract, final fraction H2-3-1 and H2-3-3 showed cytotoxic effect on SiHa and HepG2 cell lines (Kim et al. 2003). Apoptosis and DNA fragmentation were observed in SiHa cell line after 24 h upon treatment with the final fractions H2-3-1 and H2-3-3. Furthermore, the fractions were shown to be able to induce cell death in [3H]thymidine incorporation test. The two fractions, H2-3-1 and H2-3-3, were determined as (–)-α-curcumene and β-turmerone. *Curcuma zedoaria* strongly inhibited cell growth of four human hepatoma cell lines: HuH-7 (p53 mutant), PLC/PRF/5 (p53 mutant), HepG2 (p53 wild type) and Hep3B (p53 null) (Song et al. 2004). *C. zedoaria* essential oil efficiently inhibited the proliferation of human promyelocytic leukaemia HL-60 cells via apoptosis (Lai et al. 2004). In Ames genotoxicity test, CZ-1-III did not show any transformation of revertant with or without S-9 metabolic activating system, indicating the lack of mutagenic effect of the compound. In-vitro studies showed that *C. zedoaria* rhizome potently inhibited human hepatic myofibroblast cell (hMF) growth (IC₅₀ = 8.5 µg/ml), in a pertussis toxin-insensitive manner (Kim et al. 2005). Its potent antiproliferative and antifibrogenic effects towards hMF were probably mediated via an intracellular mechanism, through early COX-2-dependent release of prostaglandin E2 and

cAMP and delayed COX-2 induction. The results suggested that *C. zedoaria* rhizome may have therapeutic potential in chronic liver disease. *Curcuma caesia*, *Curcuma zedoaria* and *Curcuma aeruginosa* extracts inhibited lipid peroxidation activity by 40 % at 250 µg/ml and inhibited cyclooxygenase COX-1 and COX-2 enzymes between the ranges of 3–56 and 5–30 %, respectively (Liu et al. 2013).

Curcuma zedoaria essential oil exhibited anti-angiogenic activity in-vitro (aortic ring and chick embryo chorioallantoic membrane) and in-vivo, resulting in suppressing melanoma growth and lung metastasis in mice (Chen et al. 2011). The anti-angiogenic activity was associated with down-regulating matrix metalloproteinases MMP-2 and MMP-9 expression in serum. Crude ethanol rhizome extracts of *Z. zerumbet* and *C. zedoaria* showed cytotoxicity against brine shrimp nauplii with LC₅₀ of 1.24 µg/mL and 33.593 µg/mL after 24 h of exposure, respectively (Hossain et al. 2012). The results indicated both rhizomes could be used as a source of cytotoxic agent. Of the compounds isolated from the hexane fraction of *C. zedoaria* rhizome, curzerenone and alismol significantly inhibited cell proliferation in human cancer cell lines MCF-7, Ca Ski and HCT-116 in a dose-dependent manner (Syarifah Nur et al. 2013). Both compounds induce apoptosis through the activation of caspase-3 signalling pathway. Cell viability of human ovarian cancer SiHa cells was inhibited >73 % after 48-h incubation upon treatment with α-curcumene, from *C. zedoaria* (Shin and Lee 2013). The apoptotic effect of α-curcumene on SiHa cells involved caspase-3 activation through the release of mitochondrial cytochrome c.

Human breast cancer MDA-MB-231 cells were inhibited by petroleum ether extracts of *Curcuma zedoaria* in a time- and dose-dependent manner, producing significant G0/G1 cell cycle arrest in-vitro (Gao et al. 2014). The level of expression of proteins E-cadherin and E-cadherin mRNA was significantly increased, while proteins SDF-1, CCR7 and CXCR4 mRNA were decreased after being incubated with the extract at the concentrations of 300 µg/mL than control. Of the compounds isolated from the rhizome, curcumenone and curcumenol displayed strong antiproliferative activity (IC₅₀ =

8.3 and 9.3 µg/mL, respectively) and were found to induce apoptotic cell death on MCF-7 cells (Ahmed Hamdi et al. 2014). In-vitro studies showed that β-elemene extracted from *C. zedoaria* reversed the drug resistance of lung cancer A549/DDP cells via the mitochondrial apoptosis pathway (Yao et al. 2014). Consistent with a role in activating apoptosis, β-elemene decreased mitochondrial membrane potential, increased intracellular reactive oxygen species concentration and decreased the cytoplasmic glutathione levels in a time- and dose-dependent manner, triggering the release of cytochrome c into the cytoplasm and the modulation of apoptosis-related genes. The extracts of six out of thirty Thai ethnomedicinal plants, *Curcuma longa*, *C. zedoaria*, *Derris scandens*, *Grangea maderaspatana*, *Stephania pierrei* and *S. suberosa*, were found to have anticancer potential as they exhibited topoisomerase II poison activity against yeast cells (Sangmalee et al. 2012).

Curcuma zedoaria essential oil (zedoary) exhibited cytotoxic effects on non-small-cell lung carcinoma (NSCLC) cells and caused cell apoptosis (Chen et al. 2013). Zedoary essential oil increased the sub-G1 population and the level of annexin-V binding and induced cleavage and activation of caspase-3, caspase-8 and caspase-9 and poly(ADP ribose) polymerase. Zedoary essential oil led to the release of AIF, endonuclease G and cytochrome c into the cytosol and increased levels of p53 in H1299 cells. Zedoary essential oil slightly inhibited the phosphorylation of ERK1/2 and enhanced the phosphorylation of JNK1/2 and p38 and also inhibited AKT/NF-κB signalling pathways in H1299 cells. Intraperitoneal administration of zedoary essential oil significantly suppressed the growth of H1299 cells in-vivo.

The chloroform fraction of *Curcuma zedoaria* inhibited leiomyomal cell proliferation significantly compared to myometrial cell proliferation by inhibiting transforming growth factor-β receptor 2 in leiomyomal tissue (Bajracharya et al. 2009). The plant extract may be developed as an alternative remedy to leiomyoma with minimal side effects compared to the current treatments.

In-Vivo Studies

Intraperitoneal administration of *C. zedoaria* polysaccharides at the dose of 10 mg/kg/day for ten consecutive days to the male ICR mice implanted with sarcoma 180 tumour cells exerted 88 % inhibition of tumour development (Moon et al. 1985). *C. zedoaria* polysaccharide fraction, CZ-1-III, at a dose of 6.25 mg/kg/day showed 50 % inhibition in solid tumour (sarcoma 180) growth (Kim et al. 2000). When mice were injected with fractions, CZ-1 and CZ-1-III, at doses of 100.0 mg/kg, 91.6 and 97.1 % of tumour growth were inhibited, respectively, indicating that the cytotoxic effect of the polysaccharide on sarcoma 180 cells increases upon increasing the amount of polysaccharide administered. In the micronucleus and chromosomal aberration assays for clastogenic effect, performed using Chinese hamster lung fibroblast cells, neither micronucleus formation nor chromosomal aberration was induced regardless of the presence of S-9 metabolic activating system for up to 259.0 µg/ml concentration of CZ-1-III. Inhibition of CZ-1-III on micronucleus formation induced by mitomycin C was exhibited in a dose-dependent manner, maximally up to 52.0 %. The results strongly suggested that CZ-1-III, the polysaccharide fraction from *C. zedoaria*, decreased tumour size of mouse and prevented chromosomal mutation.

Seo et al. (2005) reported that intake of *C. zedoaria* water extract at doses of 250 and 500 mg/kg for 6 weeks from 2 weeks before B16 melanoma tumour inoculation significantly reduced the number of metastatic surface nodules in the lung, resulting in an extended life span of mice. The intake of the extract for 6 weeks increased nitric oxide (NO) production by macrophages following stimulation with lipopolysaccharide in a dose-dependent manner. The elevated NO was found to serve as a cytotoxic mediator against B16 melanoma cells in coculture with macrophages. The extract was found to possess anti-migratory effects on B16 melanoma cells and that the macrophage function-modulating activity by the extract appeared to underlie its antimetastatic activity, which led to a decrease in the number of lung metastatic surface nodules and the extension of life span. Isocurcumenol was found as the

active compound from the rhizome in inhibiting the proliferation of Dalton's lymphoma ascite (DLA) cancer, nasopharyngeal carcinoma (KB) and leukemic (K562) and lung cancer A549 cells without inducing significant toxicity to the normal cells (Lakshmi et al. 2011). Fluorescent staining exhibited the morphological features of apoptosis in the compound-treated cancer cells. In-vivo tumour reduction studies revealed that a dose of 35.7 mg/kg body weight significantly reduced the ascitic tumour in DLA-challenged mice and increased the lifespan with respect to untreated control mice. Results highlighted the antitumour potential of isocurcumenol isolated from *Curcuma zedoaria* with potential to be developed as a good antitumour agent.

Antimutagenic Activity

Peng et al. (2010) found that the methanolic and aqueous extracts of *C. zedoaria* rhizomes showed no mutagenicity when tested with *Salmonella typhimurium* TA97, TA98, TA100 and TA102 strains either with or without the S9 mix. Moreover, the two extracts, particularly methanolic, presented a greater antimutagenicity than the aqueous did either in 2-amino-3-methylimidazo(4,5-f)quinoline (IQ) or 4-nitroquinoline-N-oxide(4-NQO) mutagens.

Antiallergic Activity

The 80 % aqueous acetone *C. zedoaria* rhizome extract inhibited release of β -hexosaminidase, as a marker of antigen-IgE-mediated degranulation, in RBL-2H3 cells and passive cutaneous anaphylaxis reaction in mice (Matsuda et al. 2004). From the active fraction, curcumin showed the highest activity against β -hexosaminidase release with IC_{50} of 5.3 μ M, followed by bisdemethoxycurcumin (IC_{50} = 11 μ M). Further, effects of curcumin and bisdemethoxycurcumin on calcium ionophore (A23187 and ionomycin)-induced degranulation and antigen-induced release of TNF- α and IL-4 were determined.

Antiinflammatory Activity

Oral administration of dehydrocurdione (40–200 mg/kg) from *C. zedoaria* mitigated the writhing reflex induced by acetic acid and the fever elicited by baker's yeast in Sprague Dawley rats (Yoshioka et al. 1998). A higher dose (200 mg/kg) of dehydrocurdione was required to inhibit the carrageenan-induced paw oedema. Oral administration of dehydrocurdione at 120 mg/kg/day for 12 days significantly reduced chronic adjuvant arthritis. Unlike indomethacin (IC_{50} 0.1 μ M), dehydrocurdione showed minimal cyclooxygenase inhibition. However, dehydrocurdione (100 μ M–5 mM) significantly reduced free radical formation from hydrogen peroxide and ferrous iron. In addition to the well-known effect of zedoary as a stomachic, dehydrocurdione, the major component of *Curcuma zedoaria*, exhibited antiinflammatory potency related to its antioxidant effect. *Curcuma zedoaria* was found from several Korean herbal plant extracts that showed potent inhibition of COX-2 activity (>80 % inhibition at the test concentration of 10 μ g/ml) and iNOS activity (>70 % inhibition at the test concentration of 10 μ g/ml) in lipopolysaccharide (LPS)-induced mouse macrophages RAW264.7 cells (Hong et al. 2002a). In another study, β -turmerone and *ar*-turmerone, sesquiterpenoids isolated from the rhizome, inhibited lipopolysaccharide (LPS)-induced prostaglandin E₂ production in cultured mouse macrophage cell RAW 264.7 in a dose-dependent manner (IC_{50} = 7.3 μ M for β -turmerone; IC_{50} = 24.0 μ M for *ar*-turmerone). Further, these compounds exhibited inhibitory effects on LPS-induced nitric oxide production in the cell system (Hong et al. 2002b). Sesquiterpenoids β -turmerone and *ar*-turmerone isolated from *Curcuma zedoaria* rhizome showed potent inhibitory activity of COX-2 (β -turmerone, IC_{50} = 1.6 mg/mL; *ar*-turmerone, IC_{50} = 5.2 mg/mL) and iNOS (β -turmerone, IC_{50} = 4.6 mg/mL; *ar*-turmerone, IC_{50} = 3.2 mg/mL) (Lee et al. 2002).

Sixteen sesquiterpenes: gajutsulactones A (IC_{50} 93 μ M) and B (84 μ M), curcumenone (82 μ M), furanodiene (75 μ M), isofuranodienone (68 μ M), 13-hydroxygermacrone (98 μ M), glechomanolide (42 μ M), neocurdione (98 μ M), curcumenol

(55 μ M), isocurcumenol (57 μ M), procurcumenol (56 μ M), (+)-*ar*-turmerone (92 μ M), bisacumol (76 μ M), bisacurone (86 μ M), b-eudesmol (44 μ M), b-dictyopterol (96 μ M) and two diarylheptanoids, curcumin (13 μ M) and [bis(4-hydroxycinnamoyl)methane (87 μ M) isolated from the rhizome, inhibited nitric oxide production in lipopolysaccharide-activated mouse peritoneal macrophages substantiating the traditional effects of this herbal medicine for the treatment of 'Oketsu' syndrome caused by blood stagnation with inflammation (Matsuda et al. 2001c;d). In another study, 1,7-bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one (1), procurcumenol (2) and epiprocurcumenol isolated from the rhizome inhibited the production of tumour necrosis factor- α (TNF- α) by lipopolysaccharide (LPS)-activated macrophages from the results of bioassay (IC₅₀ values of 1 and 2 were 12.3 and 310.5 μ M, respectively) (Jang et al. 2001) and inhibited nitric oxide synthesis in lipopolysaccharide (LPS)-activated macrophages with IC₅₀ values of 8, 75 and 77 μ M, respectively (Jang et al. 2004). Compound 1 was the most active suppressing the expression of iNOS in a dose-dependent manner. Makabe et al. (2006) found that furanodiene and furanodienone isolated from the rhizome suppressed 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation of mouse ears by 75 % and 53 %, respectively, at a dose of 1.0 μ mol. Their activities are comparable to that of indomethacin, the normally used antiinflammatory agent. Curdione from *Curcuma zedoaria* rhizome inhibited the production of prostaglandin E₂ in lipopolysaccharide (LPS)-stimulated mouse macrophage RAW 264.7 cells in a concentration-dependent manner (IC₅₀ = 1.1 μ M) (Oh et al. 2007). Mechanistic studies suggested that the suppression of cyclooxygenase-2 (COX-2) mRNA expression was, at least in part, involved in the antiinflammatory activity of curdione. Zerumbone and zerumbone 2,3-epoxide isolated from *C. zedoaria* rhizome inhibited NF- κ B activation and NO production in LPS (lipopolysaccharide)-stimulated RAW 264.7 cells (Giang et al. 2009). The IC₅₀ of these compounds were 1.97 μ M and 30.11 μ M in the NF- κ B

activation assay and 3.58 μM and 34.7 μM in the nitric oxide production assay, respectively.

Freund's Complete Adjuvant (FCA)-induced arthritic rats showed significant decrease in ambulation and rearing and increase in latency time to explore and grooming, urination and defecation; in contrast arthritic rats treated with ether and chloroform *C. zedoaria* root extract but not the methanol root extract showed significant recovery in all behavioural aspects (Kaushik and Jalalpure 2011a). On the basis of radiography examination, control arthritic and methanol root-treated arthritic rats showed highest swelling compared with normal non-arthritic rats; however, all ether and chloroform root-treated groups showed significant reduced swelling. Ethanol extract of *C. zedoaria* rhizome at 200 and 400 mg/kg showed good antiinflammatory effect against carrageen and histamine-induced paw oedema in rats; the aqueous extract exhibited no activity (Kaushik and Jalalpure 2011b). *Curcuma zedoaria* rhizome extract significantly inhibited carrageenan-induced inflammatory response in rats in a dose-related manner (Ullah et al. 2014). In in-vitro antiinflammatory test, the extract significantly inhibited protein denaturation of 77.15, 64.43, 53.04, 36.78 and 23.70 % for doses of 500, 400, 300, 200 and 100 $\mu\text{g/mL}$, respectively.

Immunomodulating Activity

Polysaccharide fractions CZ-I and CZ-III, from *C. zedoaria* rhizomes, exhibited a strong, dose-dependent lysosomal enzyme activity in macrophages and RAW 264.7 cells (Kim et al. 2001). Phagocytic activity increased as a similar pattern in both the Gram-negative and Gram-positive bacteria, time-dependently. CZ-I-III was found to augment the oxygen burst response but had an even higher activity in-vivo than in-vitro. Also a significant increase of H_2O_2 , NO and $\text{TNF-}\alpha$ production was observed. However, the production of $\text{TNF-}\alpha$ at the concentration of 1000 $\mu\text{g/mL}$ decreased. The data suggested that *C. zedoaria* had macrophage-stimulating activity and the potential of being used as a biological response modifier. The intraperitoneal administration of

Curcuma zedoaria crude extract to C57Bl/6 J mice injected with B16F10 murine melanoma cells elicited a significant increase in total white and red blood cell counts, a decrease in peritoneal cell number and tumour volume reduction, whereas the oral administration revealed a noteworthy augmentation only in total leukocyte count (Carvalho et al. 2010).

Antimicrobial Activity

Ethyl *p*-methoxycinnamate, isolated from the rhizome, inhibited the growth of *Trichophyton rubrum*, *Aspergillus niger*, *Saccharomyces cerevisiae* and *Epidermophyton floccosum* at a concentration less than 10 µg/ml; *Aspergillus fumigatus*, *Penicillium purpurogenum*, *Trignoposis variabilis*, *Microsporum gypseum*, *Sclerotium rolfsii*, *Geotrichum candiade*, *Fusarium oxysporum* and *Helminthosporium oryzae* at a concentration less than 25 µg/ml; and *Candida krusei* and *Trichophyton mentagrophytes* at a concentration less than 50 µg/ml (Gupta et al. 1976). The spores of *Trichophyton rubrum* lost viability or ability to germinate when exposed to the ethanolic rhizome extract (30 µg/ml) for 2 h. Extracts from several Zingiberaceous species, especially *Alpinia galanga*, *Curcuma zedoaria* and *Zingiber purpureum*, were found to have pronounced inhibitory activities in-vitro against a wide variety of human pathogenic fungi, including strains resistant to the common antifungals amphotericin B and ketoconazole such as *Cryptococcus neoformans*, *Saccharomyces cerevisiae*, *Candida albicans*, *Wangiella dermatitidis*, *Alternaria alternata*, *Aspergillus fumigatus*, *Fusarium oxysporum*, *Microsporum gypseum*, *Rhizopus sp.*, *Trichophyton mentagrophytes* and *Pseudallescheria boydii* (Ficker et al. 2003).

Vibrio parahaemolyticus was the most sensitive pathogen to *C. zedoaria* essential oil, followed by *Staphylococcus aureus*, *Bacillus cereus*, *Salmonella typhimurium* and *Pseudomonas aeruginosa*, while the most resistant strain appeared to be *Escherichia coli* (Lai et al. 2004). Petroleum ether, hexane, chloroform, acetone and ethanol extracts of *C. zedoaria* tubers exhibited antibacterial as well as antifungal activity in-vitro against five bacterial and two fungal strains,

respectively, with MIC values of 0.01–0.15 mg/ml (Wilson et al. 2005). The results of a linear regression method showed that the antimicrobial efficacy of *Curcuma zedoaria* extract against *Streptococcus mutans*, *Enterococcus faecalis*, *Staphylococcus aureus* and *Candida albicans* was similar to that of commercial products, and its incorporation into a mouth rinse could be an alternative for improving the antimicrobial efficacy of the oral product (Bugno et al. 2007). The rhizome methanol extract was inhibitory in-vitro to growth of *Escherichia coli*, *Salmonella enterica* and *Staphylococcus aureus*, all with MIC of 0.05 mg/ml (Chen et al. 2008). *Curcuma zedoaria* methanol extract showed significant activity against some tested Gram-negative bacteria *Salmonella typhi*, *Salmonella paratyphi A*, *Salmonella paratyphi B*, *Escherichia coli*, *Shigella boydii*, *Shigella dysenteriae* and *Shigella sonnei* (Shahriar 2010). The ethyl acetate extract exhibited moderate activity while the n-hexane showed little activity.

Das and Rahman (2012) reported that the methanol and petroleum ether extracts of the rhizome and leaf (400 µg/disc) exhibited mild activity (11–14-mm inhibition zone) against Gram-positive bacteria *Bacillus cereus*, *B. megaterium*, *B. subtilis*, *Staphylococcus aureus* and *Sarcina lutea*; Gram-negative bacteria *Salmonella paratyphi*, *Salmonella typhi*, *Vibrio mimicus*, *V. parahaemolyticus*, *Escherichia coli*, *Shigella dysenteriae*, *Shigella boydii* and *Pseudomonas aeruginosa*; and fungi *Saccharomyces cerevisiae*, *Candida albicans* and *Aspergillus niger* compared to the weaker activity of the stem extracts (7-mm inhibition zone) and the potent activity of the standard antibiotic kanamycin (37–38 mm inhibition zone) against the tested microorganisms. The most effective antimicrobial activity against four Gram-positive strains (*Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Streptococcus pneumoniae*) and six Gram-negative strains (*Escherichia coli*, *Proteus vulgaris*, *Proteus mirabilis*, *Salmonella typhi para A*, *Salmonella typhi para B* and *Shigella dysenteriae*) was found to be plant extracts of *Punica granatum* followed by *Curcuma zedoaria*, *Grewia asiatica*, *Carissa carandas* and *Curcuma caesia* (Israr et al. 2012). The hydroalcoholic extract of

Curcuma zedoaria exhibited antifungal activity against yeasts of the genus *Candida* isolated from the oral cavity of patients infected with the human immunodeficiency virus (Shinobu-Mesquita et al. 2011). A total of 53 yeasts were identified, 49 of them *Candida albicans*, two *Candida tropicalis* and two *Candida glabrata*. These yeasts were inhibited by low concentrations of the extract of *C. zedoaria* (between 1.95 and 15.63 µg/mL). In addition, 7.82 µg/mL inhibited 90 % of the yeasts. The results suggested that *Curcuma zedoaria* in topical pharmaceutical forms may have practical application for the treatment of oropharyngeal candidosis or candidiasis. The petroleum ether, chloroform and methanol extracts of *C. zedoaria* exhibited antibacterial activity against two Gram-negative strains (*Escherichia coli* and *Pseudomonas aeruginosa*) and two Gram-positive strains (*Bacillus cereus* and *Staphylococcus aureus*) using the agar well diffusion method (Banisalam et al. 2013).

Analgesic/Antinociceptive Activity

The hydroalcoholic extract of *C. zedoaria* rhizome; fractions, especially dichloromethane; and its active compound, curcumenol, exhibited potent and dose-related analgesic activity when evaluated in several models of pain in mice, including writhing, formalin and capsaicin (Navarro et al. 2002). Curcumenol presented promising analgesic effects, being several times more potent than different reference drugs evaluated in the same experimental models. The calculated ID₅₀ values (µmol/kg, i.p) were 22 and 12 when evaluated in writhing and capsaicin tests, respectively, and 29 µmol/kg in relation to the second phase of the formalin model. The lack of effect in the hot-plate test suggested that curcumenol acted by a mechanism which did not involve the participation of the opioid system. The chloroform and methanol extracts of *C. zedoaria* rhizomes showed significant analgesic activity on Swiss albino mice (Ali et al. 2004). Oral administration of the crude extracts at a dose of 400 mg/kg body weight exhibited 29.5 and 38.0 % inhibition of acetic acid-induced writhing in mice, respectively, while the hexane extract showed weak analgesic activity.

C. zedoaria exhibited about three times more terpenoids (curcumenol (1) and dehydrocurdione (2)) in the mother rhizome in autumn than in other parts and seasons studied (Pamplona et al. 2006). Dichloromethane extracts obtained from *C. zedoaria* mother rhizome collected in autumn and winter at doses of 10 mg/kg body weight, administered intraperitoneally to mice, caused considerable antinociceptive activity inhibiting 91.1 and 93.4 % of the acetic acid-induced abdominal constrictions, respectively, whereas compounds 1 and 2 caused inhibitions of 64.0 and 46.0 %, respectively (Pamplona et al. 2006). The results confirm that both compounds contributed to explain the antinociceptive effect of the plant but suggested that other compounds were also acting as analgesics. *Curcuma zedoaria* leaf methanol extract attenuated the abdominal constrictions induced by intraperitoneal injection of acetic acid in mice, indicating its antinociceptive potential (Shoha et al. 2011). The methanol rhizome extract exhibited mild analgesic activity (66.67 % writhing inhibition) in the acetic acid-induced writhing assay (Das and Rahman 2012). The petroleum ether extracts of the rhizomes, leaves and stem exhibited moderate analgesic activity with writhing inhibition of 70.24 %, 75 % and 71.43 %, respectively, while the petroleum ether extract of the leaves showed significant analgesic (writhing inhibition 91.67 %).

In the hot-plate method, *Curcuma zedoaria* rhizome extract increased the reaction time of heat sensation significantly to 61.99 % and 78.22 % at the doses of 250 and 500 mg/kg b/w, respectively (Ullah et al. 2014). In acetic acid-induced writhing test, the percent inhibition of writhing response by the extract was 48.28 % and 54.02 % at 250 and 500 mg/kg doses, respectively. The extract also significantly inhibited the licking response in both the early phase (64.49 %) and the late phase (62.37 %) in formalin-induced writhing test.

Vasorelaxant/Vasodilatory/Spasmolytic Activity

The aqueous acetone extract of *Curcuma zedoaria* rhizome exhibited inhibitory effects on contractions induced by high concentrations of potassium cation (K^+) in isolated rat aortic strips (Matsuda et al. 2001a). Several isolated active sesquiterpenes and diarylheptanoids (e.g. germacrone, glechomanolide, isocurcumenol, β -eudesmol and β -dictyopterol) showed potent inhibitory effects on contractions induced by high concentrations of K^+ in isolated rat aortic strips (inhibition >80 % at 100 μ M), while they did not inhibit norepinephrine-induced contractions. Thus, the vasorelaxant activities of these sesquiterpenes were presumed to be dependent on their calcium channel-blocking activity.

Methanol extracts of five *Curcuma* drugs derived from *Curcuma longa*, *C. kwangsiensis*, *C. phaeocaulis*, *C. wenyujin* and *C. zedoaria* exhibited intense effects on relaxation in rings precontracted by prostaglandin F(2 α) (PGF(2 α)) despite pretreatment with and without N(G)-nitro-L-arginine methyl ester (L-NAME) as an inhibitor of NO synthesis (Sasaki et al. 2003). The maximal activities were approximately 80 % at 10^{-3} g/ml. From these methanol extracts, curcumin and eight sesquiterpenes, three bisabolene-type sesquiterpenes (α -turmerone, β -turmerone and *ar*-turmerone), two furanogermacrane-type sesquiterpenes (furanodiene and furanodienone) and three germacrane-type sesquiterpenes (curdione, germacrone and dehydrocurdione), were isolated. All these compounds showed NO (nitric oxide)-independent relaxation effects with almost the same intensities. Polysaccharides, the main constituents of methanol-insoluble compounds of water extracts, in contrast, showed contraction effects; only polysaccharides in *C. zedoaria* showed NO-dependent relaxation as well as contraction. All water extracts showed relaxation effects as sum of the methanol-soluble compound-induced relaxation and polysaccharide-induced contraction. Therefore, all *Curcuma* drugs tested in the study could be effective for vasodilation. Moreover, the drug derived from *C. zedoaria* exhibited potential to cure Oketsu with its various acting points.

Water-soluble fraction of *Curcuma zedoaria* exerted nonspecific inhibition on the contractile responses of the isolated rat duodenum and ileum to acetylcholine, histamine and potassium ion and caused the inhibition of the spontaneous movements and the relaxation of the isolated rat duodenum and ileum (Maede et al. 1984).

Hepatoprotective Activity

The sesquiterpenoid furanogermenone was isolated from *C. zedoaria* rhizome as the antihepatotoxic principle against CCl₄-induced liver lesion in mice (Yamahara et al. 1982a, b). It prevented the prolongation of sleeping time in mice caused by CCl₄ and suppressed the increase in serum glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT) and lactate dehydrogenase levels but had no significant effect against other hepatotoxins D-galactosamine, ethionine, thioacetamide, phalloidin and α -amanitin. Alcoholic extract of *C. zedoaria* roots administered at a dose of 300 mg/kg exhibited hepatoprotective activity against CCl₄-induced liver damage in animal studies (Rana and Avadhoot 1992). The extract was found effective in preventing damage which was evident by morphological, biochemical and functional parameters.

Principal sesquiterpenes, furanodiene, germacrone, curdione, neocurdione, curcumenol, isocurcumenol, aerugidiol, zedoarondiol and curcumenone and curcumin, isolated from the rhizome, were found to show potent protective effect on D-galactosamine (D-GalN)/lipopolysaccharide (LPS)-induced acute liver injury in mice (Matsuda et al. 1998). Plausible action mechanisms for their hepatoprotective activity were clarified on the basis of the inhibitory effect on D-GalN-induced cytotoxicity in primary-cultured rat hepatocytes, LPS-induced NO production in cultured mouse peritoneal macrophages and D-GalN/tumour necrosis factor- α (TNF- α)-induced liver injury in mice. They also reported that curcumenone, a principal carabran-type sesquiterpene from *C. zedoaria* rhizome, exhibited potent protective effect on D-galactosamine/lipopolysaccharide-

induced acute liver injury in mice (Matsuda et al. 2001b). Additionally, curcumenolactones A and B and the other constituents showed protective effect on D-galactosamine-induced cytotoxicity in primary-cultured rat hepatocytes. Morikawa et al. (2002) found that the 80 % aqueous acetone extract of *Zedoariae rhizoma* was found to show a protective effect against D-galactosamine (D-GalN)/lipopolysaccharide-induced acute liver injury in mice. Eleven isolated sesquiterpenes (furanodiene, curdione, neocuproine, dehydrocurdione, germacrone, 13-hydroxygermacrone, curcumenol, isocurcumenol, aerugidiol, zedoarondiol and curcumenone) and a diarylheptanoid (curcumin) were found to inhibit the increase in serum aspartate aminotransaminase and alanine aminotransaminase at a dose of 50 mg/kg p.o. in agreement with the previous in-vitro studies, except for dehydrocurdione, aerugidiol and zedoarondiol. Curdione, neocurdione, curcumenol and isocurcumenol, in particular, potentially inhibited the increase at a dose of 12.5 mg/kg p.o. In addition, the eight sesquiterpenes, furanodiene, curdione, neocurdione, dehydrocurdione, germacrone, 13-hydroxygermacrone, curcumenol and curcumenone, also showed a protective effect against D-GalN/tumour necrosis factor- α -induced liver injury in mice at a dose of 50 mg/kg p.o. Studies showed that intraperitoneal administration of β -elemene could reduce the collagen disposition in liver and inhibit the progression of CCl₄-induced liver fibrosis in rats (Zhu et al. 2009). In addition, the levels of plasma ANG II and the expression of hepatic AT₁R in rats with liver fibrosis were also suppressed by β -elemene. It was concluded that the ANG II-AT₁ receptor pathway plays an important role in the development of hepatic fibrosis and β -elemene could down-regulate the levels of plasma ANG II and the expression of hepatic AT₁R in rats with liver fibrosis.

Antihyperlipidemic/Antihypercholesterolem ic Activities

Among 100 traditional Chinese herbs tested, only two herbs, *Curcuma zedoaria* and *Poncirus trifoliata*, showed significant

inhibition on 3-hydroxy-3-methylglutaryl-coenzyme A reductase in Vero cells (Liu et al. 2002). 3-Hydroxy-3-methylglutaryl-coenzyme A (HMG Co-A) reductase inhibitor with its lipid lowering property had been shown to decrease coronary events and mortality. Thus, these traditional medicinal herbs with effective HMG Co-A reductase inhibitory activity might be developed into new hypocholesterolemic agents. Hydroethanolic extract of *Curcuma zedoaria* rhizome was found to have antihyperlipidemic activity (Srividya et al. 2012). The extract was effective in reducing total cholesterol levels by 17.1 % and 19.65% after 12 days of pretreatment in adult male rats at a dose of 200 and 400 mg/kg b/w, respectively. No significant changes were seen on LDL, VLDL and HDL cholesterol levels.

Antihyperglycaemic Activity

Curcuma zedoaria leaf methanol extract showed dose-dependent and statistically significant antihyperglycaemic activity following glucose loading in mice (Shoha et al. 2011). Methanolic extract of *C. zedoaria* rhizomes, when orally administered to glucose-loaded mice, significantly and dose-dependently reduced concentrations of serum glucose (Rahmatullah et al. 2012). At extract doses of 50, 100, 200 and 400 mg/kg body weight, serum glucose concentrations were reduced by, respectively, 36.9, 39.4, 41.1 and 55.1 %. In comparison, a standard antihyperglycaemic drug, glibenclamide, reduced serum glucose concentration by 63.9 % at a dose of 10-mg/kg body weight.

Alcohol Drunkenness Protective Activity

The 30 % ethanol extract (1000 mg/kg) of *C. zedoaria* rhizome prevented drunkenness 60 and 120 min after 40 % alcohol administration while the n-hexane-soluble fraction (300 mg/kg) and an isolated compound curcumenone (3, 10 or 30 mg/kg) prevented drunkenness at 30, 60 or 120 min (Kimura et al. 2013). The extract, n-hexane-soluble fraction and curcumenone reduced the elevation in blood alcohol

concentrations 30 and 60 min after 40 % alcohol administration. Curcumenone (10 and 30 mg/kg) enhanced liver alcohol dehydrogenase activity 30 and 60 min after 40 % alcohol administration.

Hypotensive Activity

Curcuma herbs were found to have hypotensive and protective effect on the endothelium in spontaneously hypertensive rats; *Curcuma zedoaria* (CZ) was found to be more effective than *C. longa* (Goto et al. 2005). Systolic blood pressure of the 3 %CZ and captopril groups decreased significantly as compared to the control group. Acetylcholine-induced endothelium-dependent relaxations of the 3 %CZ and captopril groups were significantly increased to a greater degree than the control group. Its mechanism was thought to be related to a radical scavenging effect and improvement of hemorheology.

CNS Depressant Activity

The methanolic extract of *Curcuma zedoaria* rhizome exhibited a significant prolongation of hexobarbital-induced hypnosis (Shin et al. 1989). A single treatment (100–200 mg/kg, i.p.) of germacrone, curzerenone and germacrone epoxide, isolated from *C. zedoaria* rhizome, showed not only a significant prolongation of hexobarbital-induced sleeping time but also a significant inhibition of aminopyrine N-demethylase activity in mice and further exhibited a typical type I binding spectra with oxidised rat hepatic cytochrome P-450 induced by phenobarbital. The results suggested that the sesquiterpenes possessed CNS depressant property.

Antityrosinase Activity

Combination of *Curcuma zedoaria* and *Aloe vera* extracts (1:1 ratio) inhibited melanin synthesis in murine melanoma cells (Krishnamoorthy et al. 2009). Extract combinations at a concentration of 1–5 μ l showed 50–150 % reduction in melanogenesis without altering the cell proliferation.

Tyrosinase activity was very low in extract-treated cells when compared to control.

Bile Secretion Stimulatory Activity

Oral administration of *Curcuma zedoaria* powder (C.Z.) significantly inhibited the intestinal transit of charcoal in mice, significantly increased the bile secretion in rats and slightly inhibited the stomach secretion in rats (Maede et al. 1984). The effect of C.Z. on the bile secretion lasted longer than that of dehydrocholate.

Antivenom Activity

Curcuma zedoaria aqueous extract showed clear inhibitory activity effects on the binding of anti-cobra (*Naja siamensis*) venom antibody to antigen, cobra venom, in the modified enzyme-linked immunosorbent assay (ELISA) (Daduang et al. 2005). The extract attenuated toxin activity by extending contraction time of diaphragm muscle after envenomation and had a potency to protect cellular proteins from venom degradative enzymes.

Uterine Myoelectric Activity

Decoction of *C. zedoaria* significantly and dose-dependently increased the spike area, the duration and the number of bursts of action potentials of the uterine smooth muscle in virgin rats (Xu et al. 2001). Atropine and phentolamine decreased the exciting effect of *C. zedoaria*, whereas verapamil, diphenhydramine and indomethacin had no effect on the excitation activity, suggesting that the mechanism may be associated with M-receptor and α -receptor.

Antipyretic Activity

Studies showed that the ethanol extract of *Curcuma zedoaria* rhizome significantly reduced yeast-induced elevated body temperature in rats in a dose-dependent manner and the antipyretic effect at a dose of 750 mg/kg was comparable to

that of the standard antipyretic drug paracetamol (10 mg/kg) (Azam et al. 2014).

Hemagglutinating Activity

A mannose-binding lectin isolated from rhizomes exhibited hemagglutinating activity towards rabbit erythrocytes, which could be inhibited by mannose only (Tipthara et al. 2007).

Reproductive Toxicity

Curcuma zedoaria, a traditional Chinese herb, was used widely but absolutely prohibited for pregnant women (Chen et al. 2011). They hypothesised that some components from it could inhibit angiogenesis and then damaged the supply of oxygen and nutrition to the embryo, which finally led to gestation failure. Studies in rat embryo cultures and pregnant rats by Zhou et al. (2013) found that *Curcuma zedoaria* essential oil (100 mg/kg or 200 mg/kg) could induce embryotoxicity ex-vivo and reproductive toxicity in-vivo. Its reproductive toxicity was related with inhibition of vascular endothelial growth factor (VEGF)-mediated placental angiogenesis. Sesquiterpenoids in essential oil were the main embryotoxic compounds.

Cytochrome Inhibitory Activity

C. longa and *C. zedoaria* methanol extracts significantly decreased the activity of cytochrome CYP3A4 by about 85–98 % in 1 α ,25-dihydroxyvitamin D3-treated Caco-2 cells (Hou et al. 2007). The 50 % inhibitory concentrations of *C. longa* and *C. zedoaria* extracts were 0.019 and 0.014 mg/ml, respectively. They caused a 60–70 % decrease in CYP3A4 protein. Curcumin treatment caused a 30–40 % decrease in CYP3A4 catalytic activity and a 38 % decrease in CYP3A4 protein expression. Moreover, it was found that both *Curcuma* extracts and curcumin treatment had no influence on CYP3A4 mRNA expression. Their results suggested that administration of *Curcuma* drugs might inhibit the catalytic activity of

intestinal CYP3A4. However, curcumin was not the major compound responsible for this inhibitory effect.

Insecticidal Activity

Curcuma zedoaria (zedoary oil) exerted significant larvicidal activity against the two mosquito species *Anopheles dirus*, the major malaria vector in Thailand, and *Aedes aegypti*, the main vector of dengue and dengue hemorrhagic fever, after 24-h exposure; *A. dirus* larvae showed the highest susceptibility to zedoary oil (Pitasawat et al. 2007). All five essential oils including zedoary exerted a promising adulticidal efficacy against both laboratory and natural field strains of *A. aegypti* (Chaiyasit et al. 2006). Efficacy ranking was caraway followed by zedoary, celery, long pepper and Chinese star anise, with an LC₅₀ in the laboratory strain of 5.44-, 5.94, 5.96, 6.21 and 8.52 µg/mg female, respectively, and 5.54, 6.02, 6.14, 6.35 and 8.83 µg/mg female, respectively, in the field strain. Zedoary oil exhibited pronounced potential against the fourth instar larvae of *A. aegypti* with an LC₅₀ and LC₉₉ of 33.45 and 83.39 ppm, respectively (Champakaew et al. 2007). Application of zedoary oil at a dosage yielding ten times that of LC₉₉ offered complete larval mortality (100 % mortality) for a period of 3 days, and the larval mortality subsequently decreased to lower than 50 % after application for more than 5 days. Zedoary oil-impregnated sand granules provided remarkably longer activity, with a larval mortality of 100 % for a period of 9 days; and mortality below 50 % was obtained in week 3 of application. The efficacy in killing *A. aegypti* larvae and good biological stability of zedoary oil-impregnated sand granules indicated the product to be a promising alternative to essential oil in the development of new botanical natural larvicide for use in mosquito control programmes.

Results of studies indicated the potential of essential oils extracted from *Boesenbergia rotunda*, *Zingiber zerumbet*, *Litsea petiolata*, *Curcuma zedoaria* and *Zingiber cassumunar* with good repellency against *Aedes aegypti* and *Culex quinquefasciatus* and high biting deterrence for deterred biting (Phukerd and Soonwera 2014).

Antiprotozoal/Antiamoebic Activity

Curcuma zedoaria rhizome extract was found to have appreciable antibabesial activity against the protozoan *Babesia gibsoni*, with IC₅₀ value of 41.7 µg/ml without acute toxicity in mice at the intraperitoneal dose of 0.7 g/kg of body weight (Subeki et al. 2004). Antibabesial (*Babesia gibsoni*) zedoalactones A, B and C were isolated from *Curcuma zedoaria* (Kasahara et al. 2005). The IC₅₀ value of the standard diminazene aceturate was 0.6 µg/mL, while those of zedoalactones A, B and C were 16.5, 1.6 and 4.2 µg/mL, respectively.

Alcoholic extract of *Curcuma zedoaria* root exhibited antiamoebic activity in-vitro against *Entamoeba histolytica* strain NIH: 200 (Ansari and Ahmad 1991).

Anti-halitosis Activity

Studies showed that chlorhexidine gluconate lowered volatile sulphur compound (VSC—gases responsible for halitosis (bad breath)) production immediately and that this effect lasted up to 3 h, while *Curcuma zedoaria* and *Camellia sinensis* had immediate inhibitory effects but no residual inhibitory effects on VSC (Farina et al. 2012). It was concluded that both plant extracts, prepared as infusions and used as mouthwashes, did not have a residual neutralising effect on VSC.

Antiulcerogenic Activity

Oral and subcutaneous administrations of *C. zedoaria* extracts significantly inhibited stress ulcer formation in restrained and water-immersed mice (Watanabe et al. 1986). A n-hexane-soluble fraction (YK-3) was more effective than a methanol-soluble fraction (YK-2) of the original methanol extract (YK-1). Among the isolated compounds from subfractions YK-4 (curzerenone, furanodienone, furanogermenone), YK-5 (dehydrocurdione), YK-6 (curcumenol, (4*S*,5*S*)-(+)-germacrone 4,5-epoxide, zederone) of YK-3, furanogermenone and (4*S*,5*S*)-(+)-germacrone-4,5-epoxide exhibited potent preventive effect against stress ulceration.

Moreover, oral administration of YK-3, YK-4 and YK-8 significantly inhibited formation of both HCl-induced and indomethacin-induced gastric ulcers. In pyloric-ligated albino rats, administration of *C. zedoaria* root powder (200 mg/kg) reduced the gastric pH, free acid, total acid and ulcer index significantly, and the results were comparable to that of standard drug omeprazole (30 mg/kg i.p.) (Gupta et al. 2003).

Toxicity/Toxicological Studies

The high-protein flour prepared from rhizomes of shoti (*Curcuma zedoaria*) was found to be highly toxic to 5-week-old rats and caused 100 % mortality within 6 days when given at 320-g/kg diet (Latif et al. 1979). Fresh rhizomes minced and dried and the resulting meal given to weanling rats at 400-g/kg diet caused all the animals to lose weight rapidly, and two of the five rats died within 4 days. This same shoti meal when given to 1-day-old chicks at 100 and 200 g/kg diet caused no chick mortality, and all chick survived the test period (20 days), but body weight, food intake and efficiency of food conversion decreased with increase in the level of shoti meal in the diet.

Studies found that the zedoary fluid extract presented low cytotoxicity on fibroblast of human lineage LMF derived from oral mucosa and probably could be used for antiseptic purposes in oral hygiene products (Fernandes et al. 2012).

Zedoary Delivery Studies

Formulation of zedoary turmeric oil in the form of self-emulsifying microspheres improved the bioavailability of the water-insoluble oily drug in rabbits over conventional self-emulsifying system (SES) formulation (You et al. 2005). The microsphere bioavailability (F) to the conventional SES for oral administration was 157.7 %.

Following oral administration of a self-nanoemulsifying drug delivery system (SNEDDS) for zedoary turmeric oil (ZTO) in rats, both AUC and C_{max} of germacrone (GM), a representative bioactive marker of zedoary turmeric oil,

increased by 1.7-fold and 2.5-fold, respectively, compared with the unformulated zedoary turmeric oil (Zhao et al. 2010).

Traditional Medicinal Uses

Curcuma zedoaria rhizome has been reported to be carminative, stimulant, stomachic, expectorant, demulcent and rubefacient and used in flatulence and dyspepsia (Khare 2004). Fresh root is used for checking leucorrhoeal discharge and also for blood purification. Zedoary's effect on digestive organs is similar to ginger but milder. Along with other therapeutic applications, the Ayurvedic Pharmacopoeia of India indicated the use of the rhizome in goitre.

Curcuma zedoaria is used in India system of medicine since time immemorial (Srivastava et al. 2011). The rhizome is aromatic, pungent, bitter and useful in flatulent colic and debility of the digestive organs and also used as an ingredient in bitter tincture of zedoary and antiperiodic pills. A paste of rhizome is useful externally for cuts, wounds, itching and in sprains. In India the rhizome is used for poulticing. In Ceylon the rhizome is used as a tonic and carminative and that the Arabs consider it to be a tonic and aphrodisiac. Various parts of *Curcuma zedoaria* are used in Ayurveda and other folk and tribal system of medicines for the treatment of different ailments such as diarrhoea, cancer, flatulence and dyspepsia (Lobo et al. 2009). *C. zedoaria* is a constituent of a wide variety of Ayurvedic preparations like Dasamularishtam, Valiya, Rasnadi Kashayam and so forth (Lakshmi et al. 2011). *C. zedoaria* is the chief ingredient in several Unani preparations used to treat peptic ulcer (Gupta 2003). Its roots have traditionally been used by Unani system of medicine as a remedy against intestinal infections including amoebiasis (Ansari and Ahmad 1991). The rhizome is used for curing stomach diseases, toothache, blood stagnation, leucoderma, tuberculosis and enlargement of spleen and for promoting menstruation in traditional medicine in Asia (Saikia and Nath 2003). Traditionally, *C. zedoaria* root has been used as antiinflammatory and antiarthritic drug (Kaushik and Jalapure 2011a, b). *C. zedoaria* is used as an ingredient in some strengthening conserves taken by women to remove weakness

after childbirth in Bombay (Burkill 1966). In Java the rhizome is chewed, or its decoction given, as a strengthening medicine after childbirth as is done in India. Zedoary decoction is used as tonic and for indigestion in Peninsular Malaysia.

In Bulacan Province, Philippines, the fresh rhizomes are burned and the ash is applied externally to wounds, ulcers and sprains (Stuart 2014). The Filipinos also use the juice of the fresh rhizome as an effective remedy in certain form of dermatitis (pañó blanco). The rhizome is also used as a topical and is applied on the stomach as stomachic. *C. zedoaria* rhizome has many traditional medicinal uses in Vietnam: as stomachic in treating abdominal pains, dyspepsia, flatulence, menstrual haematometra, amenorrhoea, menorrhagia and dysmenorrhoea, often in combination with other herbs (NIMM 1999). It is also prescribed for infantile diarrhoea, gastralgia, constipation and eructation.

The *Curcuma zedoaria* rhizome (Ezhu) is extensively used in traditional Chinese medicine to treat various ovarian and cervical cancers (Zhao et al. 1991). *Curcuma zedoaria* rhizome has been used traditionally to treat gastrointestinal diseases as an aromatic stomachic drug, and this is currently used to treat alcohol-induced loss of appetite and nausea in Japan (Kimura et al. 2013). Rhizomes are used in relief of stomach ache and as a carminative in Thailand (Srirugsa 1998).

Other Uses

Among *Curcuma* species, the beautiful inflorescence and luxurious foliage of *C. zedoaria* (a traditional source of zedoary spice, tonic and perfume) has potential in floriculture (Maciel and Criley 2003). The rhizomes represent one of the most important sources of native perfumery in India.

The rhizome oil was found to have insecticidal and antifungal properties. Via topical applications, *Alpinia conchigera*, *Zingiber zerumbet* and *Curcuma zedoaria* rhizome oils exhibited similar toxicity against *Sitophilus zeamais* (LD₅₀ 18–24 µg oil/mg insect) (Suthisut et al. 2011).

Tribolium castaneum had similar sensitivity to all three oils (35–58 µg/mg), and it was less sensitive than *S. zeamais*. In antifeedant tests, the three extracted oils were able to decrease the consumption of flour discs, especially *Z. zerumbet* oils. *Curcuma zedoaria* rhizome volatile oil was found to be highly insecticidal against *Odontotermes obesus* Rhamb. (white termite), and the minimum dose for 100 % mortality was recorded as 2 µL per Petri plate for 24-h exposure duration (Singh et al. 2003). *Curcuma zedoaria* rhizome volatile oil showed complete mycelial inhibition of *Colletotrichum falcatum* at 4 µL per Petri plate of the oil and was ineffective in controlling the mycelial growth of *Aspergillus terreus*, *Fusarium graminearum*, *F. solani* and *Curvularia pallescens* (Singh et al. 2003). *Curcuma zedoaria* rhizome oil showed complete mycelial inhibition of *Colletotrichum falcatum* at 2000-ppm concentration (Singh et al. 2002).

Nurdin et al. (2013) found that administration of cumin (*Cuminum cyminum*), white turmeric (*Curcuma zedoaria*) and mango turmeric (*Curcuma mangga*) to lactating Fries Holland dairy cows reduced levels of heavy metal lead (Pb) in cow's milk produced, with a consecutive decrease of 98.36, 99.33 and 99.37 % and the very real effect on elevated levels of Pb in faeces by 68.01, 64.52 and 80.54 %. Mango turmeric was the best treatment of three treatments in decreasing lead level in milk.

Comments

Refer also to notes on *Alpinia*, *Curcuma* and *Zingiber* species in this volume and *Zingiber zerumbet* in Edible Medicinal and Non-Medicinal Plants (Volume 8, Flowers) (Lim 2014).

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Kaempferia galanga

T. K. Lim¹ 

(1) Canberra, Australia

Scientific Name

***Kaempferia galanga* L.**

Synonyms

Alpinia sessilis J.Koenig, *Kaempferia procumbens* Noronha, *Kaempferia humilis* Salisb., *Kaempferia plantaginifolia* Salisb., *Kaempferia latifolia* Donn ex Hornem., *Kaempferia marginata* Carey ex Roscoe, *Kaempferia rotunda* Blanco (nom. illeg.), *Kaempferia galanga* var. *latifolia* (Donn ex Hornem.) Donn, *Kaempferia galanga* var. *galanga*

Family

Zingiberaceae

Common/English Names

Aromatic Ginger, Blackthorn, East Indies Galangal, Galangal, Galangal Resurrection Lily, Kentjur, Lesser Galangal, Lesser Galangale, Marba, Resurrection Ginger, Resurrection Lily, Sand Ginge

Vernacular Names

Burmese: Kun-Sa-Gamon

Chinese: Sā Gēung, Sāan Nòih, Sān Nài, Shā Jiāng, Shān Nài

Danish: Lille Galanga

Dutch: Kentjoer

French: Kaempferide, Faux Galanga, Faux Galingale, Galanga Camphré

German: Kleiner Galgant, Gewürzlilie, Sandingwer

Greek: Kineszike Piperoriza

India: Chandumula, Ekangi (Bengali), Abhuyicampa, Candramula, Chandramula, Sidhoul (Hindi), Kachchura, Kachhoora, Kacora (Kannada), Chengazhinirkizhangu, Kacchulam, Kaccolam, Kaccoram, Kaccuri, Kachhulam, Katjulam, Katsjula-Kekengu (Malayalam), Kachri, Kapur-Kacheri, Kapurkachri (Marathi), Bhucampaka, Candrani, Chandramulika, Chundramoolika, Corakah, Karcurah, Sadi, Sathi, Sati, Sugandhamula, Sugandhavacha (Sanskrit), Kaccolam, Kaccoli K-Kilanku, Kachhola Kilangu, Kacholum, Kachulakalanga, Katcolam, Katsjula Kelengu, Pulankilanku (Tamil), Candramula, Chandramoola, Kachoram, Sime-Kich-Chilik (Telugu)

Indonesia: Ceuko (Aceh), Asauli, Sauleh, Soul, Umpa (Ambon), Cekuh (Bali), Kěnchur, Chěkur, Chěngkur (Java), Kencor (Madura), Kencur, Sukung (Minahasa), Bataka (North Sulawesi), Cekir (Sumba), Cikur (Sunda), Chikur (Sunda Islands), Bataka (Ternate, Tidore)

Japanese: Ban-Ukon, Kenchoru

Khmer: Khhiey

Korean: Sannae

Laos: Van Hom

Malaysia: Cekur, Cekur Jawa, Cengkur, Kencur, Kuncur (Malay), San Kiong (Cantonese)

Philippines: Kisol, Kosol (Bisaya), Doso, Doto (Bontok), Kisol (Bukidon), Disol (Iloko), Gisol, Kusol (Pampangan), Dosol (Sambali), Duso, Dusol, Dusog, Gisol, Gisol Na Bilog (Tagalog)

Polish: Kentior

Russian: Maraba

Sri Lanka: Ingurupiyali, Ingrupiyali (Sinhala)

Thai: Proh, Proh hom, Hom pro, Waan hom, Waan teen din, Wan phaen din yen, Waan nonlap, Waan haao non, Ueang din

Vietnam: Cẩm Địa La, Địa Liên, Sa Khương, Ngải Máu, Sơn Nại, Tam Nại

Origin/Distribution

The plant is native to India and widely cultivated in India and SE Asia (Mainland SE Asia, Java, Philippines, New Guinea).

Agroecology

The species occurs in tropical ecological areas having mean annual temperature range of 17–30 °C and a relative humidity above 75 % and rainfall averaging 2000 mm a year. It thrives best in partial shade in open forests, forest margins and bamboo forest up to altitude of 1000 m. It prefers sandy or loamy soils which are free draining and friable with pH from 5.5 to 6.5 and is also drought tolerant.

Edible Plant Parts and Uses

Kaempferia galanga has been widely used as a spice, food flavouring and folk medicine (Sirisangtragul et al. 2011). Leaves of *Kaempferia galanga* and *C. longa* are ingredients of curries (Chan et al. 2008). Leaves of *K. galanga* and *K. rotunda* are eaten fresh or cooked as vegetables and used as cosmetic powder and as food flavouring agents (Ibrahim 1999).

Leaves and rhizomes are eaten as vegetable (lalab, sepan, urab or sayur tumis) or are utilised as spice for all kind of dishes (especially for flavouring rice) (Ochse and Bakhuizen van den Brink 1980). The rhizomes are used in the preparation of a beverage called 'beras kencur'. The rhizomes are chewed together with betel nuts and betel pepper leaf (Burkill 1966). An essential oil, extracted from the rhizomes by distillation, is utilised in perfumery, for flavouring curry and for medicinal purposes.

Botany

Kaempferia galanga is a perennial low and stemless, rhizomatous, perennial herb (Plates 1, 2, 3 and 4). Rhizomes are pale yellow to yellowish green inside, cylindric, tuberous, fibrous and aromatic (Plates 2, 3, 4 and 5). Leaves are usually 2-3-5, spreading low and horizontally on ground (Plates 1, 2, 3 and 4); leaf sheath is 2–3 cm long; leaf blade is green, broadly ovate to sub-orbicular, 7–20 × 3–17 cm are glabrous on both surfaces or villous abaxially; apex is acute; the base attenuates into the petiole. Inflorescences are terminal emerging from between the leaves, enclosed by imbricate leaf sheaths and sessile and have few to many flowers; bracts are lanceolate and 2.5 cm long. Calyx is equalling bract. Corolla tube is 2–2.5 cm long; lobes are white; lip is bilobed with lilac or purple spots. Lateral staminodes are obovate-cuneate and 1.2 cm long. Labellum is 2.5 × 2 cm; apex is 2-cleft; lobes are white with purple markings at base. Anther is sessile; connective appendage is deeply bilobed and strongly reflexed.



Plate 1 Lesser galangal plant habit



Plate 2 Lesser galangal with variegated foliage



Plate 3 Lesser galangal whole plant sold in the market



Plate 4 Lesser galangal plant with attached rhizomes

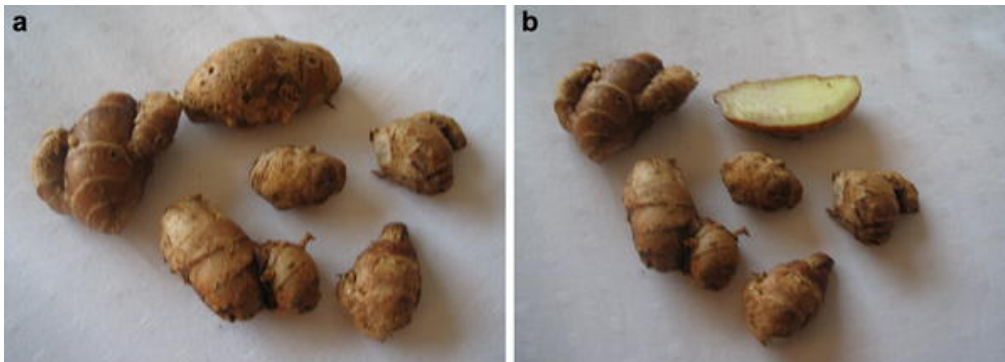


Plate 5 (a, b) Lesser galangal rhizomes whole and cut

Nutritive/Medicinal Properties

Leaf Nutrients/Phytochemicals

Proximate nutrient composition (g% fresh weight) of the leaves was reported by Yeoh and Wong (1993) as follows: moisture 94.4 g%, energy 118 kJ, protein 1 g%, starch 0.5 g%, soluble sugars 0.3 g%, lipid 2.3 g%, dietary fibre 1.3 g%, ash 1.4 g%, aspartic acid 10.8 g%, threonine 4.9 g%, serine 5.5 g%, glutamic acid 13.6 g%, proline 5.5 g%, glycine 9.0 g%,

alanine 5.6 g%, valine 4.9 g%, methionine 2.1 g%, isoleucine 3.4 g%, leucine 9.0 g%, tyrosine 4.3 g%, phenylalanine 5.9 g%, histidine 2.2 g%, lysine 7.0 g%, tryptophan 2.0 g%, arginine 4.1 g% and minerals (mg/100 g): Ca 109 mg, Mg 58 mg, Fe 57 mg, K 201 mg and Cu 0.6 mg.

Two active aromatic compounds ethyl *trans-p*-methoxycinnamate and ethyl cinnamate were isolated from the plant (Huang et al. 2008). Essential oil of in-vitro whole plants possessed higher percentage of ethyl p-methoxycinnamate (51.2 %) when compared to rhizome oil (Rao et al. 2009). Other major compounds present were 1,8-cineole, α -gurjunene, γ -cadinene and β -sinensal.

Linoleoyl chloride was detected as the main component (21.42 %) of *K. galanga* leaf oil followed by caryophyllene oxide 11.75 %, cubenol 9.66 %, caryophyllene 5.60 %, 2-propenoic acid 3-(4-methoxyphenyl)-ethyl ester 5.56 %, isodene 4.91 %, ethyl cinnamate 3.66 %, borneol 2.86 %, δ -cadinene 2.23 %, δ -selinene 2.03 %, ylangene 1.98 %, α -bulnesene 1.38 %, seychellene 1.19 %, α -caryophyllene 1.11 %, pentadecane 1.10 % and (*E*)-6-hexadecen-4-yne 1.09 % (Bhuiyan et al. 2008). The remaining constituents (<1 %) were camphor; *m*-cymene; α -pinene; camphene; α -phellandrene; β -pinene; β -myrcene; cyclooctanol; β -phellandrene; 3-carene; limonene; eucalyptol; *Z*-ocimene; γ -terpinene; 1-undecanol; 2-carene; fenchone; linalool; nonanal; α -campholenal; *trans*-pinocarveol; (+)-isomenthone; umbellulone; menthyl acetate; 4-terpineol; tridecanedial; myrtenal; 1-isobutyl-1-methylsiletane; decanal; methyl cyclobutyl(methyl)phosphinate; isothujol; *Z,E*-2,13-octadecadien-1-ol; bornyl formate; isoamyl caproate; thujone; 2-dodecenal; 2,6-octadienal, 3,7-dimethyl-; bornyl acetate; neomenthol; carveol; carveol acetate; terpinyl acetate; α -cubebene; 2-undecenal; α -bourbonene; β -elemene; δ -selinene; guaiane; 1,6,10-dodecatriene, 7,11-dimethyl-3-methylene-, (*E*); 9,12,15-octadecatrien-1-ol, (*Z,Z,Z*)-; α -muurolene; germacrene D; thujopsene-I3; valencene; γ -selinene; thiepino[3,2-*e*]isobenzofuran-1,3-dione, 3a,10b-dihydro-3a,10b-dimethyl; α -selinene; ethanone, 1-(1,3a,4,5,6,7-hexahydro-4-hydroxy-3,8-dimethyl-5-azulenyl)-; guaiane; α -calacorene; δ -

cadinol; γ -elemene; dihomog- γ -linolenic acid; (-)-globulol;
 cyclohexanepropanal,2,2-dimethyl-6-methylene-; 12-
 oxabicyclo[9.1.0]dodeca-3,7-diene,1,5,5,8-tetramethyl-, [1R-
 (1R,3E,7E,11R)]-; alloaromadendrene oxide-(1); β -humulene;
 2,3,3a,4,5,6,7,7a-octahydro-1H-cyclopenta[a]pentalen-7-ol; τ -
 cadinol; nitrofurate; cycloisolongifolene, 8,9-dehydro-;
 hydrocotarnine; acetic acid N'-(3,4-dichloro-phenyl)-
 hydrazide; oleyl alcohol; 1-nonadecene; megastigma-
 4,6(Z),8(Z)-triene; khusilol; 2,4a,8,8-
 tetramethyldecahydrocyclopropa[d]naphthalene; 2-
 pentadecanone, 6,10,14-trimethyl-; octadecanoic acid, ethyl
 ester; methyl (Z)-5,11,14,17-eicosatetraenoate; 14-methyl-8-
 hexadecyn-1-ol; farnesol; methyl palmitate; biformene; ethyl
 palmitate; 7-hexadecenal, (Z)-; phytol; *cis*-vitamin A
 aldehyde; linoleic acid ethyl ester; 3-tetradecanynoic acid; and
 β -iraldeine (0.10 %).

Rhizome Nutrient/Phytochemicals

Nutritive composition of *K. galanga* rhizomes was determined
 as follows: energy 350.9 cal/100 g, moisture 11 %, crude
 protein 7.88 %, carbohydrate 76 %, crude fat 1.7 %, crude
 fibre 9 %, ash 3.42 %, K 1375 ppm, Ca 508.2 ppm, Na 71.50
 ppm, Mg 313.4 ppm, Fe 18.90 ppm, Mn 79.9 ppm, Zn 14.52
 ppm, Cu 0.251 ppm, Ni 0.251 ppm and Cr 0.761 ppm
 (Indrayan et al. 2009). The rhizomes of aromatic ginger have
 been reported to contain 3-carene-5-one (Kiuchi et al. 1987);
 ethyl *p*-methoxycinnamate with the structure ethyl (*E*)-3-(4-
 methoxyphenyl)propenoate; C₁₂H₁₄O₃ (Luger et al. 1996); and
 two sulfonated diarylheptanoid epimers, namely,
 kaempulfonic acids A and B (Wang et al. 2013).

K. galanga rhizome was found to have secretory sacs
 containing volatile oil, oleoresin and starch grains which were
 also found in the parenchyma cells (Tunsaringkarn et al.
 2007). The mean contents of foreign matter, total ash, acid-
 insoluble ash, ethanol-soluble extractive, water-soluble
 extractive, loss on drying, moisture and volatile oil were 0.06,
 7.03, 3.75, 2.39, 16.05, 10.39, 9.62 and 0.72 % of dry weight,
 respectively. Major compounds detected in *K. galanga*

rhizome volatile oil were ethyl cinnamate (39.97 %), pentadecane (20.85 %), ethyl-*p*-methoxycinnamate (18.35 %), 1,8-cineol (5.32 %), borneol (3.22 %) and α -terpinene (1.77 %). Other minor components (<1 %) were α -pinene; camphene; *o*-cymene; *m*-cymene; d-limonene; *trans*-2-carene-4-ol; *p*-mentha-1,5-dien-8-ol; 4-terpineol; 4-terpineol; *p*-cymen-8-ol; α -terpineol; eucarvone; verbenone; tetradecane; α -gurjunene; τ -cadinene; δ -cadinene; 2-propenoic acid, 3-(4-methoxyphenyl)-, ethyl ester; 8-heptadecene; (Z)6,(Z)9-pentadecadien-1-ol; and heptadecane.

K. galanga rhizome was found to contain cineol, borneol, 3-carene, camphene, kaempferol, kaempferide, cinnamaldehyde, *p*-methoxycinnamic acid, ethyl cinnamate and ethyl-*p*-methoxycinnamate (Nakao and Shibuya 1924).

The following compounds were identified in the rhizome oil: ethyl cinnamate, ethyl *p*-methoxycinnamate, camphene, *l*- Δ^3 -carene, *p*-methoxystyrene, borneol and *n*-pentadecane (Panicker et al. 1926). *Kaempferia galanga* rhizome oil contained 54 components, of which the major constituents were ethyl *trans*-*p*-methoxycinnamate (51.6 %), ethyl cinnamate (16.5 %), pentadecane (9.0 %), 1,8-cineole (5.7 %), γ -car-3-ene (3.3 %) and borneol (2.7 %) (Wong et al. 1992). Terpenoid constituents amounted to 16.4 %. Sudibyo (2000) reported the main components of *K. galanga* rhizome oil to be β -phyllandrene, α -terpineol, ethyl cinnamate and dihydro- β -sesquiphyllandrene. Tewtrakul et al. (2005) reported the major chemical constituents identified in the volatile oil of *K. galanga* rhizome as follows: ethyl-*p*-methoxycinnamate (31.77 %), methyl cinnamate (23.23 %), carvone (11.13 %), eucalyptol (9.59 %) and pentadecane (6.41 %). The other identified components were α -pinene (1.28 %), camphene (2.47 %), benzene (1.33 %) and borneol (2.87 %). The most abundant compounds present in the rhizome oil were two esters, viz. ethyl *p*-methoxycinnamate (46.8 %) and ethyl cinnamate (24.8 %), and a hydrocarbon *n*-pentadecane (5.8 %) (Rao et al. 2009). The rhizome also contained kaempferol (Guo et al. 2012).

Bhuiyan et al. (2008) found that the rhizome oil contained 2-propenoic acid, 3-(4-methoxyphenyl), ethyl ester (63.36 %),

ethyl cinnamate (6.31 %), 4-cyclooctene-1-methanol (4.61 %), caryophyllene oxide (4.37 %), limonene (3.22 %), borneol (2.46 %), cubenol (1.67 %) and nerolidol acetate (1.05 %) as the main components. The remaining constituents (<1 %) included the following: α -muurolene; α -terpinene; 12-oxabicyclo(9.1.0)dodeca,3,7-diene,1,5,5,8-tetramethyl; 13-tetradec-11yl-1-ol; 1-undecene; 2-cyclohexen-1-one, 2-methyl-5-(1-methylethenyl); 3-octen-1-ol (2); 4,4,8-trimethyltricyclo[6.3.1.0.(1.5)]dodecane-2,7,-diol; 4-terpineol; 5-nonanol-5-methyl; 6-octenal,3,7-dimethyl; allyl-3-methoxybenzoate; aromadendrene oxide; β -cedren-9-L-ol; β -elemene; 4-methoxybenzoic acid; β -linalool; borneol; bornyl acetate; bornyl formate; β -pinene; cadinene; calamine; camphene; carotol; carvacrol; carveol; carvyl acetate; cholestan-3-ol, 2-methylelene (3B,5a); *cis*-2-pinanol; *cis*-L-copaene-8-ol; *cis*-sabinene hydrate; cycloisolongifolene, 9,10-dehydro; cyclopentanol, 1-(methylenecyclopropyl); *E*-ocimene; dihydrocarveol; eucalyptol; eucarvone; geranyl methyl ether; guaiacol; hydrindane; isolongifolene, 7,10-dehydro; isopulegol; isopulegol acetate; jasmine; α -bisabolol; α -calacorene; ledol; linalyl isovalerate; longipinocarvone; α -phellandrene; α -pinene; α -pinocarveol; α -selinene; *m*-cymene, 5-tert butyl; megastigmatrienone; methyl chavicol; methyl cinnamate; *m*-methoxymandelic acid; murolan-3,9(11)-diene-10-peroxy; nerolidol acetate; *o*-cymene; γ -cymen-8-ol; γ -anisaldehyde; pentadecane; phytol; γ -methoxyhydrocinnamic acid; tetracyclo[6,3,2,0(2.5),0(1,8)]-tridecan-9-ol,4,4,-dimethyl; thujone; thymol; thymoquinone; ylangene; *Z*-ocimene; β -elemene; and γ -muurolene.

A total of 58 and 56 compounds were identified in the rhizome essential oil of 'Kasthuri' (yield 1.88 %) and 'Rajani' (1.76 %) varieties of *K. galanga*, respectively (Indrayan et al. 2007). Thirteen compounds were identified in the rhizome oil of 'Kasthuri' but were not present in the rhizome oil of 'Rajani', and another 11 compounds identified in 'Rajani' oil were not present in 'Kasthuri' oil. Forty-five compounds were common to both oils. Acid values of 2.10 and 2.52, saponification values of 92.2 and 102.3 and iodine values of 98.8 and 108.4 were determined for 'Kasthuri' and 'Rajani' oils, respectively. Comparative chemical composition of

‘Kasthuri’ and ‘Rajani’ oils were, respectively, as follows: 2-heptanol (-, 0.02 %), styrene (0.01, -%), α -thujunene (0.07, 0.05 %), tricylene (0.11, 0.08 %), α -pinene (0.97, 0.73 %), camphene (1.98, 1.67 %), α -phellandrene (0.17, 0.12 %), β -myrcene (0.17, 0.12 %), β -pinene (0.39, 0.38 %), δ -carene (7.86, 5.58 %), *p*-cymene (0.06, 0.03 %), *m*-cymene (1.05, 0.71 %), D-limonene (0.9, 0.71 %), 1,8-cineole (8.07, 13.57 %), *Z*-3-octen-1-ol (0.05, -%), 1-octanol (0.31, 0.17 %), artemisia alcohol (-, 0.04 %), *trans*-isomyrcenol (0.47, 0.43 %), β -linalool (0.06, 0.14 %), (S)-*cis*-verbenol (0.08, 0.04 %), *cis*-limonene oxide (-, 0.02 %), 2-(2-methyl-1-propenyl)-1,5-cyclohexadiene (0.28, 0.10 %), propan-2-ol (0.16, 0.08 %), unidentified (0.38, 0.21 %), camphor (0.11, 4.25 %), α -phellandren-8-ol (0.92, 0.34 %), *trans*-dihydro- α -terpineol (0.28, -%), isoborneol (-, 2.11 %), terpinene-4-ol (0.95, -%), borneol (3.36, 2.57 %), *p*-cymen-8-ol (0.71, 0.60 %), α -terpineol (0.35, 0.45 %), eucarvone (1.35, 0.69 %), carvone (-, 0.06 %), perillaaldehyde (0.42, 0.17 %), *p*-anisaldehyde (0.11, 0.10 %), thymol (0.12, 0.11 %), bornyl acetate (0.20, 0.12 %), α -terpinyl acetate (0.05, 0.03 %), ethyl-*cis*-cinnamate (0.08, 0.04 %), carvone oxide (0.10, 0.49 %), β -elemene (0.10, 0.49 %), α -gurjunene (0.12, 0.10 %), β -caryophyllene (-, 0.27 %), δ -selinene (-, 0.09 %), ethyl *trans*-cinnamate (18.83, 13.14 %), germacrene D (0.07, 0.21 %), *n*-pentadecane (3.22, 2.41 %), eremophilene (-, 0.34 %), germacrene A (-, 0.10 %), δ -cadinene (0.58, 0.50 %), unidentified (0.57, 0.29 %), caryophyllene oxide (0.18, 0.13 %), (-)-spathulenol (0.19, 0.13 %), germacrene D-4-ol (-, 7.97 %), dendrolasin (0.49, -%), cedrol (0.27, -%), 1-hexadecene (0.25, -%), hexylbenzoate (0.52, 0.45 %), davanone (0.77, 0.60 %), ledol (0.42 %, 0.18 %), (-)-globulol (0.26, 0.34 %), α -bisabolol (0.12, -%), juniper camphor (-, 0.33 %), heptadecane (0.27, -%), ethyl-*trans*-*p*-methoxycinnamate (39.09, 35.09 %), pentadecanol (0.12, -%), hexadecanol (0.12, -%), unidentified (0.12, -%), kaur-16-ene (0.27, -%) and 17-(acetyloxy)-kauran-18-al (0.22, -%). The rhizome oil of *K. galanga* consisted mainly of ethyl-*p*-methoxycinnamate (58.47 %), isobutyl β -2-furylacrylate (30.90 %) and hexyl formate (4.78 %). The other minor compounds isolated in concentrations of <1 % were monoterpenes, camphene, terpinolene, 2-

cyclohexylcyclohexane, γ -cadinene and citral-2; oxygenated monoterpene derivatives, borneol, camphene hydrate, allyl salicylate, isoeugenol, acetyl eugenol and *n*-hexyl angelate; oxygenated sesquiterpene geranyl-*n*-heptanoate; and miscellaneous compounds, isoamyl hexanoate, *n*-hexanal, diallyl sulphide, 2-ethoxythiazole, 2-ethyl-4-methylthiazole, isobutyl disulfate, 2-cyclohexyethyl acetate, 6-methylcoumarin, cinnamyl isobutyrate and cyclohexenyl cyclohexanone (Sukari et al. 2008).

Forty-two components were identified in microwave-assisted hydrodistillation (MHD) rhizome oil and forty-five components in traditional hydrodistillation rhizome oil (Wang et al. 2009). Among the identified volatile compounds from *K. galanga*, the main components from both oils were found to be similar, but their contents were significantly different including isoamyl *p*-methoxycinnamate (42.8 %, 27.5 %), *n*-pentadecane (21.6 %, 32.8 %), ethyl cinnamate (16.1 %, 17.1 %), cyperene (2.0 %, 3.4 %) and *p*-methoxystyrene (1.6 %, 2.6 %) in MHD oil and HD oil, respectively. The major compound of rhizome oil identified from conventionally propagated (CP) and in-vitro propagated (IVP) *K. galanga* rhizomes was ethyl *p*-methoxy cinnamate, 82.01 % and 71.77 %, respectively, and other compounds were ethyl cinnamate 9.69, 18.14 %; 3-carene 3.41, 2.05 %; eucalyptol 1.60, 2.70 %; borneol 0.62, 1.69 %; and pentadecane 0.57, 1.46 %, respectively (Sahoo et al. 2014). Twenty-eight components were identified in *Kaempferia galanga* rhizomes essential oil, and the major compounds were ethyl-*p*-methoxycinnamate (38.6 %), ethyl cinnamate (23.2 %), 1,8-cineole (11.5 %), *trans*-cinnamaldehyde (5.3 %) and borneol (5.2 %) (Liu et al. 2014).

Numerous studies had reported that *K. galanga* extracts possessed anti-inflammatory, analgesic, nematocidal, mosquito repellent, larvicidal, vasorelaxant, sedative, antineoplastic, antimicrobial, antioxidant, anti-allergic and wound healing properties (Umar et al. 2011; Singh et al. 2013). Ethyl-*p*-methoxycinnamate and ethyl cinnamate were found to be the most vital constituents responsible for most of these pharmacological properties.

Antioxidant Activity

Leaves of *Kaempferia galanga* had very low phenolic content (TPC) of 146-mg GAE/100 g and ascorbic acid equivalent antioxidant capacity (AEAC) of 77-mg AA/100 g and rhizome TPC of 57-mg GAE/100 g and AEAC of 17-mg AA/100 g (Chan et al. 2008). The rhizome was reported to have antioxidant index of 3.15 as evaluated by β -carotene bleaching method and to contain 5.37 mg% vitamin C, 0.0035 mg% vitamin E, 1.91 mg% total carotenes, 1.59 mg% total xanthophylls, 4.48 mg% tannins and 26.4 mg/% phenolics (Chanwitheesuk et al. 2005).

The antioxidant activities of *K. galanga* rhizome oil from in-vitro-propagated (IVP) plants were better than that of conventionally propagated (CP) oil samples (Sahoo et al. 2014). For DPPH scavenging activity, the IC₅₀ values were 26 μ g/ml for CP and 19.5 μ g/ml for IVP, and H₂O₂ scavenging activity IC₅₀ values were 29 μ g/ml for CP and 24.5 μ g/ml for IVP.

Anticancer Activity

The methanol rhizome extract was found to be highly cytotoxic to HeLa cells (Kosuge et al. 1985). Ethyl *p*-methoxy-*trans*-cinnamate was found to be the cytotoxic principle in the extract. *Kaempferia galanga* rhizome exhibited antitumour promoter activity using the short-term assay of inhibition of 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced Epstein–Barr virus early antigen (EBV-EA) in Raji cells (Vimala et al. 1999). Another study showed that both *cis*- and *trans*-ethyl-*p*-methoxycinnamate isolated from *Kaempferia galanga* exhibited inhibitory effect in-vitro in Epstein–Barr virus assay, ear oedema test, ornithine decarboxylase (ODC) activity and two-stage carcinogenesis test (Xue and Chen 2002). It also elicited inhibitory effects in TPA tests or croton oil-induced ear oedema and ODC activity in specimen of mouse epidermis and extent of papilloma, indicating a relatively strong anticarcinogenic potential of ethyl-*p*-methoxycinnamate in *Kaempferia galanga*.

Treatment of human lung cancer cell line A549 cells with kaempferol resulted in a dose- and time-dependent reduction in cell viability and DNA synthesis with the rate of apoptosis equivalent to 0.9, 5.2, 16.8, 25.4 and 37.8 % on treatment with 0, 17.5, 35.0, 52.5 and 70.0 μ M kaempferol, respectively (Nguyen et al. 2003). The results suggested that inactivation of Akt-1 and alteration of Bcl-2 family of proteins were not sufficient for kaempferol to induce apoptosis, and activation of MEK–MAPK was a requirement for kaempferol-induced cell death mechanism in A549 cells. Bestwick et al. (2007) found that kaempferol inhibited HL-60 promyelocytic leukaemia cell as a result of a heterogeneous response, dominated by cell cycle alternations, and involved a limited cytotoxicity resulting from a membrane damage centred as well as an apoptotic process. Yoshida et al. (2008) showed that the combined treatment with kaempferol and TRAIL (TNF-related apoptosis inducing ligand) drastically induced apoptosis in human colon cancer SW480 cells, compared to single treatments. Kaempferol markedly upregulated TRAIL receptors, DR5 and DR4. The cotreatment induced no apoptosis in normal human peripheral blood mononuclear cells and little apoptosis in normal human hepatocytes. *K. galanga* crude ethanol extract was of seven Thai medicinal plants found to have promising cytotoxic activity against human cholangiocarcinoma CL-6 cell line with survival of less than 50 % at the concentration of 50 μ g/ml (Mahavorasirikul et al. 2010). One recipe containing *Atractylodes lancea*, *Kaempferia galanga*, *Zingiber officinal*, *Piper chaba*, *Mesua ferrea* and Pra-Sa-Prao-Yhai recipe showed potent cytotoxic activity with mean IC₅₀ values of 24.09, 37.36, 34.26, 40.74, 48.23 and 44.12 μ g/ml, respectively. *K. galanga* extract also possessed high activity against human laryngeal (Hep-2) cell.

In another study, ethyl *p*-methoxycinnamate from the rhizome was found to inhibit the proliferation of the human hepatocellular liver carcinoma HepG2 cell line in a dose-dependent manner and induced the significant increase of the sub-G0 cell population (Liu et al. 2010). Ethyl *p*-methoxycinnamate not only induced cells to enter into apoptosis but also affected the progress of the cell cycle. In 0.3

% benzo(a)pyrene-induced fibrosarcoma in mouse, administration of three thiourea derivatives, *N*-(methylphenyl)-*N'*-(*p*-methoxycinnamoyl)thiourea, *N*-(methoxyphenyl)-*N'*-(*p*-methoxycinnamoyl)thiourea and *N*-(*p*-chlorophenyl)-*N'*-(*p*-methoxycinnamoyl)thiourea, synthesised from ethyl *p*-methoxycinnamate isolated from *Kaempferia galanga*, inhibited fibrosarcoma growth via inhibition of COX-2 (Ekowati et al. 2012).

In the brine shrimp lethality bioassay, all extracts of the rhizome and leaf of *Kaempferia galanga* showed moderate cytotoxic activity when compared with the standard drug vincristine sulphate (Dash et al. 2014). The LC₅₀ value of the acetonic leaf extract was 4.78 µg/ml, while the LC₅₀ of vincristine sulphate was 0.52 µg/ml. Ethyl-*p*-methoxycinnamate isolated from *Kaempferia galanga* exhibited antiangiogenic activity (Umar et al. 2014). It considerably inhibited microvessel sprouting from the rat aorta. These mechanistic studies showed that ethyl-*p*-methoxycinnamate strongly inhibited the differentiation and migration of endothelial cells, which was further confirmed by the reduced level of vascular endothelial growth factor.

Antiangiogenic Activity

Both *n*-hexane and ethyl acetate fractions of the ethanol extract of the dried plant exhibited antiangiogenic activity, and two major active components (*trans*-ethyl *p*-methoxycinnamate and kaempferol) showed potent antiangiogenic effects on wild-type zebrafish (He et al. 2012). *Trans*-ethyl *p*-methoxycinnamate was found to dose-dependently inhibit vessel formation on both wild- and *Tg(fli1a:EGFP)y1*-type zebrafish embryos. In-vitro, it specifically inhibited the migration and tube formation of human umbilical vein endothelial cells. In-vivo, it could block basic fibroblast growth factor (bFGF)-induced vessel formation.

Antimicrobial Activity

The 95 % ethanol extract of *K. galanga* possessed antibacterial activity against *Staphylococcus aureus* and hot water extract of the plant against *Escherichia coli* (George and Pandalai 1949). *K. galanga* rhizome volatile oil was found to be inhibitory in-vitro to *Salmonella typhi*, *Shigella flexneri*, *Escherichia coli* and *Candida albicans* (Tewtrakul et al. 2005). The petroleum ether and methanol extracts of *K. galanga* rhizome exhibited antimicrobial activity against pathogenic, Gram-negative bacteria, i.e. *Escherichia coli*, *Salmonella* sp. and *Shigella* sp., and Gram-positive bacteria, i.e. *Bacillus* sp. and *Pseudomonas* sp., with minimum inhibitory concentration (MIC) of 2–16 µg/ml (Parvez et al. 2005). The acetone extract exerted no activity. *K. galanga* rhizome extract exhibited higher antibacterial activity in-vitro against *Staphylococcus aureus* than against *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* (Indrayan et al. 2009).

Ethyl *p*-methoxycinnamate from *Kaempferia galanga* was shown to inhibit *Mycobacterium tuberculosis* H37Ra, H37Rv, drug-susceptible and multidrug-resistant (MDR) clinical isolates with MIC values of 0.242–0.485 mM (Lakshmanan et al. 2011). No cross resistance was observed to any standard anti-TB drugs in the MDR strains. The essential oil of *K. galanga* rhizome showed selective toxicity against *Aspergillus fumigatus* with a MIC value of 0.63 µg/µl (Jantan et al. 2003). Ethyl-*p*-methoxycinnamate, isolated from the rhizome, inhibited in-vitro growth of *Mycobacterium tuberculosis* and *Candida albicans* (Yenjai et al. 2003). The ethanol, methanol, petroleum ether, chloroform and aqueous extracts of *Kaempferia galanga* rhizome exhibited significant antimicrobial activity in-vitro against ten human pathogenic bacteria, namely, *Staphylococcus aureus*, *Streptococcus faecalis*, *Bacillus cereus*, *Bacillus subtilis*, *Enterobacter aerogenes*, *Salmonella typhi*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Vibrio cholera*, and four fungal species, *Aspergillus niger*, *A. flavus*, *A. fumigatus* and *Candida albicans* using disc diffusion assay (Kochthressia et al. 2012). Highest inhibition zone was recorded for ethanolic extract against *Staphylococcus aureus*. The rhizome and leaf extracts of *Kaempferia galanga* (400 µg/disc) showed moderate antibacterial activity against both

Gram-positive bacteria *Staphylococcus aureus* and *Bacillus cereus* and Gram-negative bacteria *Escherichia coli*, *Pseudomonas aeruginosa* and *Shigella dysenteriae* as compared with the standard drug ciprofloxacin (5 µg/disc) (Dash et al. 2014).

Anti-inflammatory Activity

K. galanga aqueous leaf extract exhibited significant dose-dependent anti-inflammatory activity when assessed using the carrageenan-induced paw oedema test in mice (Sulaiman et al. 2008). Two doses, 600 mg/kg and 1200 mg/kg, of *K. galanga* alcoholic extract exhibited significant anti-inflammatory activity in carrageenan model and cotton pellet granuloma model in rats in comparison to control (Vittalrao et al. 2011). The chloroform rhizome extract exerted the highest inhibition (42.9 %) on carrageenan-induced rat paw oedema compared to control (Umar et al. 2012). On fractionation the chloroform fraction (1 g/kg) showed the highest inhibitory effect (51.9 %), on carrageenan-induced oedema. On further fraction, the hexane–chloroform subfraction was the most effective in inhibiting oedema (53.7 %), and ethyl-p-methoxycinnamate (EPMC) was isolated as the major active component. It dose-dependently inhibited carrageenan-induced oedema with an MIC of 100 mg/kg in an in-vitro study, and EPMC nonselectively inhibited the activities of cyclooxygenases 1 and 2, with IC₅₀ values of 1.12 µM and 0.83 µM, respectively. The results suggested that anti-inflammatory activity of *K. galanga* may be exerted by the inhibition of cyclooxygenases 1 and 2. Ethyl-p-methoxycinnamate isolated from *Kaempferia galanga* strongly inhibited granuloma tissue formation in rats (Umar et al. 2014). The inhibition of interleukin and tumour necrosis factor by ethyl-p-methoxycinnamate was significant in both in-vivo and in-vitro models; however, only a moderate inhibition of nitric oxide was observed in human macrophage cell line (U937). In the carrageenan-induced paw oedema test, at a dose of 400 mg/kg, the methanolic extract of *K. galanga* rhizome, chloroform and n-hexane fractions showed a significant inhibition of rat paw oedema with 55.08, 48.85 and

71.88 % inhibition after 2 h of the study period (Chowdhury et al. 2014).

Sedative/Antidepressant Activity

Inhalation of *Kaempferia galanga* hexane extract at the doses of 1.5 and 10 mg showed significant reduction of locomotor activity, indicating considerable sedative and relaxant effects (Huang et al. 2008). Two of its aromatic components ethyl *trans-p*-methoxycinnamate and ethyl cinnamate also proved to possess sedative effects at 0.0014 mg and 0.0012 mg, respectively.

Monoamine oxidase inhibitor contained in the rhizomes of *Kaempferia galanga* was isolated and identified as ethyl *p*-methoxy-*trans*-cinnamate (Noro et al. 1983). It exhibited competitive inhibition with respect to benzylamine.

Antinociceptive Activity

K. galanga aqueous leaf extract exhibited significant antinociceptive activity when assessed using the abdominal constriction, hot plate and formalin tests, with activity observed in all animal tests occurring in a dose-dependent manner (Sulaiman et al. 2008). In addition, the antinociceptive activity of *K. galanga* extract was significantly reversed when prechallenged with 10-mg/kg naloxone. In another study, two doses 600 mg/kg and 1200 mg/kg of *K. galanga* alcoholic extract exhibited significant analgesic activity in tail flick model and hot plate model in rats in comparison to control (Vittalrao et al. 2011). In separate studies, *K. galanga* rhizome extract at test doses of 50, 100 and 200 mg/kg, p.o., exhibited dose- and time-dependent antinociceptive activity in mice and rats using acetic acid-induced writhing, formalin, hot plate and tail flick tests (Ridtidid et al. 2008; Saewong et al. 2008). The extract administered at 200 mg/kg, p.o., had a stronger antinociceptive effect than aspirin (100 mg/kg, p.o.) but less than morphine (5 mg/kg, s.c.). Naloxone (2 mg/kg, i.p.) abolished the antinociceptive action of both morphine (5 mg/kg, s.c.) and the extract (200 mg/kg, p.o.) in a similar manner. The antinociceptive mechanisms appear to be both

peripherally and centrally mediated actions. In acetic acid-induced writhing test, the chloroform and n-hexane fractions of *K. galanga* rhizome methanol extract at a dose of 400 mg/kg showed a significant reduction in the number of writhes with 38.19 and 62.31 % writhing inhibition, respectively (Chowdhury et al. 2014). In the tail flick assay in rats, ethyl-p-methoxycinnamate isolated from *Kaempferia galanga* prolonged the tail flick time in rats by more than twofold compared with the control animals, indicating its analgesic effects (Umar et al. 2014).

Antihyperlipidemic Activity

The oral administration of both *A. galanga* and *K. galanga* extracts (20 mg/day) effectively lowered the serum and tissue levels of total cholesterol, triglycerides and phospholipids and significantly increased the serum levels of high-density lipoproteins (HDL) in high-cholesterol-fed white Wistar rats over a period of 4 weeks (Achuthan and Padikkala 1997). The results were indicative of these plants in various lipid disorders especially atherosclerosis. Studies showed that sniffing of *K. galanga* (kencur) essential oil, its fraction 2 containing δ -3-carene or its pure constituent 2-propenoic acid, 3-(4-methoxyphenyl)-ethyl ester (EPMC) for 5 weeks by rats fed with a high-fat diet had an impact on body weight and total cholesterol levels (Batubara et al. 2014). Fraction 2 which consisted of δ -3-carene had slimming effects, while kencur crude essential oil and EPMC decreased the cholesterol and triglyceride level in rats' blood.

Antihypertensive Activity

The chloroform extract of *K. galanga* exhibited vasorelaxant effects on the smooth muscles of the rat aorta (Mustafa et al. 1996). Ethyl cinnamate isolated from the rhizome exhibited vasorelaxant effect in the rat aorta (Othman et al. 2002). It inhibited the tonic contractions induced by high K^+ and phenylephrine in a concentration-dependent manner, with respective IC_{50} values of 0.30 mM and 0.38 mM. The relaxant effect against phenylephrine-induced contractions was greater

in the presence of endothelium. It was found that the inhibitory effects of ethyl cinnamate may involve inhibition of Ca^{2+} influx into vascular cells and release of nitric oxide (NO) and prostacyclin from the endothelial cells. *K. galanga* rhizome extract also exhibited potent brine shrimp lethality bioactivity with an ED_{50} value of 7.92 $\mu\text{g/ml}$ (Othman et al. 2006).

Intravenous administration of *K. galanga* extract induced a dose-related reduction of basal mean arterial pressure (MAP) (130 mmHg) in the anaesthetized rat, with maximal effects seen after 5–10 min of injection. Ethyl cinnamate was found to be the vasorelaxant active compound in the active fraction; ethyl *p*-methoxycinnamic acid was also isolated but did not exhibit any relaxant effect on the precontracted thoracic rat aorta.

Antihyperglycaemic Activity

In the oral glucose tolerance test in mice, the methanolic extract of *K. galanga* rhizome, chloroform and *n*-hexane fractions at 200-mg/kg body weight inhibited rise in blood glucose level (Chowdhury et al. 2014). After 30 min of glucose load, the methanolic extract and chloroform-soluble fraction remarkably reduced blood glucose level with 61.2 and 89.63 % reduction compared to control which were more prominent than that of glibenclamide (34.78 % reduction) compared to control. The percentage maximal inhibition of glucose load of *n*-hexane fraction vs. control was 133.33 % which was higher than that of standard.

Antiulcerogenic Activity

The methanolic extract of *K. galanga* rhizome showed antiulcer activity in the ethanol/HCl-induced, restraint water immersion stress-induced, pylorus ligation-induced and indomethacin-induced gastric lesion test models in rats (Wanajak 1999). It was speculated that the methanolic extract of *K. galanga* acted through a defensive mechanism to protect gastric ulceration or that *K. galanga* possessed a cytoprotective activity. The extract also caused an increase of gastric mucus, an endogenous defensive factor in response to

ethanol/HCl-induced gastric ulcers. The antiulcer activity mediated via anticholinergic activity was dismissed, since *K. galanga* showed cholinergic activity when tested in isolated guinea pig ileum. *Kaempferia galanga* rhizome extract inhibited the growth of *Helicobacter pylori* with MIC of 25 µg/ml (Bhamarapravati et al. 2003).

Wound Healing Activity

Studies showed that *K. galanga* significantly reduced the time required for epithelialisation and reversed the epithelialisation delaying effect of dexamethasone significantly (Shanbhag et al. 2006). Coadministration of *K. galanga* with dexamethasone had significantly increased the breaking strength of dexamethasone-treated group in the incision wound model. In the dead space wound model, the mean dry weight of granulation tissue in control group was 42.12 mg which was significantly increased to 49.75, 64.00 and 61.87 mg in groups treated with *K. galanga*, dexamethasone and dexamethasone + *K. galanga*, respectively. In excision wound model, the percentage of the wound contraction was significantly increased by *K. galanga* only on 16th day, and also it reversed the dexamethasone-suppressed wound contraction on the 16th day.

Antiallergic Activity

Kaempferia galanga rhizome water extract at 100 µg/ml elicited 75 % anti-allergic activity as determined by the percent inhibition of the release of β-hexosaminidase from rat basophilic leukaemia RBL-2H3 cells, whereas the ethanol extract elicited 54.5 % and the volatile oil 57.8 % at the same concentration (Tewtrakul and Subhadhirasakul 2007). The IC₅₀ values were 49.5, 78.6 and 80.5 µg/ml, respectively.

Osteogenic Activity

Kaempferol, a flavonol derived from the rhizome of *Kaempferia galanga*, had been reported as a well-known phytoestrogen possessing osteogenic effects (Guo et al. 2012).

Kaempferol stimulated osteogenic differentiation of cultured rat osteoblasts by activating transcriptional activity of pERE-Luc and inducing oestrogen receptor α (ER α)-phosphorylation. Kaempferol also promoted the mineralization process of osteoblasts.

Herbal–Drug Interaction Activity

Studies found that ethyl-*p*-methoxycinnamate (EPMC) at a concentration of 2.42 mM was relatively non-toxic to primary cultured hepatocytes; at this concentration it induced CYP1A1 and CYP1A2 mRNA expressions in the mouse hepatocytes (Sirisangtragul et al. 2011). However, EPMC at this concentration did not show significant induction of CYP2B9 and CYP3A11 mRNA expressions. In addition, EPMC could modulate the inductive expression of CYP1A1 mRNA by specific inducers B[a]A and β -NF. Oral administration of dichloromethane extract of *K. galanga* (100 mg/kg which is equivalent to 80-mg/kg EPMC) and EPMC (120 and 160 mg/kg) to mice for 28 consecutive days decreased hepatic microsomal P450 content (Sirisangtragul and Sripanidkulcha 2011). The CYP1A1 and CYP2B activities significantly increased, whereas CYP2E1 activity was significantly inhibited only at the highest concentration of EPMC (160 mg/kg). None of the treatments did affect CYP1A2 and CYP3A4 activity when compared to the control group. The results indicated that *K. galangal* and its active compound, EPMC, may participate in herbal–drug interaction and may also increase risk of toxicity and chemical carcinogenesis from drugs and compounds metabolised via CYP1A1, CYP2B and CYP2E1.

Skin Whitening/Antityrosinase Activity

Ko et al. (2014) found that ethyl *p*-methoxycinnamate from *K. galanga* significantly and dose-dependently decreased melanin synthesis in B16F10 murine melanoma cells stimulated with α -melanocyte-stimulating hormone (α -MSH). Further, ethyl *p*-methoxycinnamate decreased microphthalmia-associated transcription factor and tyrosinase levels in α -MSH-stimulated B16F10 cells. These results indicated that the pigment

inhibitory effect of ethyl *p*-methoxycinnamate resulted from downregulation of tyrosinase. Thus, ethyl *p*-methoxycinnamate isolated from *K. galanga* could be developed as a skin whitening agent to treat hyperpigmentary disorders.

Wound Healing Activity

In excision wound in Wistar rat, the percentage of the wound contraction was significantly increased only on the 16th day, and also it reversed the dexamethasone-suppressed wound contraction on the 16th day (Tara Shanbhag et al. 2006). *K. galanga* significantly reduced the time required for epithelialisation and reversed the epithelialisation delaying effect of dexamethasone significantly. Coadministration of *K. galanga* with dexamethasone had significantly increased the breaking strength of dexamethasone-treated group.

Insecticidal Activity

Ethanol extract of *Kaempferia galanga* caused marked larvicidal effects against 4th instar larvae of *Culex quinquefasciatus* after 24-h exposure with LC₅₀ values of 50.54 ppm (Pitasawat et al. 1998). The hexane fraction of *Kaempferia galanga* was found to exhibit the highest larvicidal effect against the fourth instar of *Culex quinquefasciatus* with the LC₅₀ of 42.33 ppm but did not show any promising adulticidal effect; instead it caused a knockdown effect which might be useful as a repellent (Choochote et al. 1999). In a laboratory study, the hexane fraction possessed repellency against *Aedes aegypti* (ED₅₀ value of 30.73 µg/cm²) and provided biting protection for 3 h. In a field study, it could protect against certain mosquitoes, i.e. *Armigeres subalbatus*, *Anopheles barbirostris*, *Anopheles aconitus*, *Mansonia uniformis*, *Culex quinquefasciatus*, *Culex gelidus*, *Culex tritaeniorhynchus* and *Aedes aegypti*. The hexane fraction did not cause dermal irritation when applied on human skin.

Ethyl *p*-methoxycinnamate, isolated from the rhizome, was the most toxic of the test compounds to larvae of *Culex pipiens pallens*, *Aedes aegypti* and *Ochlerotatus togoi* mosquito species (LC₅₀ 12.3–20.7 mg/L) but less toxic than either fenthion (0.0096–0.021 mg/L) or temephos (0.0039–0.0079 mg/L) (Ahn et al. 2008). Ethyl cinnamate and 3-carene were highly active against *C. pipiens pallens* larvae (24.1 and 21.6 mg/L) but less toxic to *A. aegypti* and *O. togoi* larvae (40 and 60 mg/L, respectively). The toxicity of these compounds to larvae from the Jinhae colony of *C. pipiens pallens* was almost the same as their toxicity to the laboratory-reared larvae, although the larvae from the colony exhibited low levels of resistance to fenthion (resistance ratio 9.1) and temephos (5.8).

K. galanga rhizome essential oil exhibited contact toxicity against the booklouse, *Liposcelis bostrychophila*, with an LC₅₀ value of 68.6 µg/cm² (Liu et al. 2014). Among its constituents, ethyl cinnamate (LC₅₀ = 21.4 µg/cm²) exhibited stronger contact toxicity than ethyl *p*-methoxycinnamate and *trans*-cinnamaldehyde (LC₅₀ = 44.6 and 43.4 µg/cm², respectively), while 1,8-cineole showed weak acute toxicity. The essential oil also possessed fumigant toxicity against the booklouse with a LC₅₀ value of 1.5 mg/L air. 1,8-Cineole and *trans*-cinnamaldehyde (LC₅₀ = 1.1 and 1.3 mg/L, respectively) possessed stronger fumigant toxicity against the booklouse than ethyl cinnamate and ethyl *p*-methoxycinnamate (LC₅₀ = 10.2 and 10.2 mg/L air, respectively). *trans*-Cinnamaldehyde was strongly repellent to booklice, whereas ethyl cinnamate and ethyl *p*-methoxycinnamate were weakly repellent and 1,8-cineole did not repel booklice. The results indicated that the essential oil and its constituent compounds had potential for development into natural insecticides or fumigants and repellents for control of insects in stored grains.

Anthelmintic Activity

Hot water extract of *K. galanga* rhizome showed moderately strong larvicidal activity against the second stage of dog roundworm *Toxocara canis*, a common parasite in visceral

larva migrans. Larvicidal principles obtained from the methanol rhizome extract were identified as ethyl cinnamate, ethyl-*p*-methoxycinnamate and *p*-methoxycinnamic acid (Kiuchi et al. 1988). Among five free acids tested, cinnamic acid and *p*-methoxycinnamic acids showed the strongest activity. Larvicidal activities of alkyl (methyl-butyl) esters of cinnamic acid and *p*-methoxycinnamic acids were weaker than those of free acids, but *p*-hydroxycinnamic acid, *p*-acetoxycinnamic acid and alkyl esters especially propyl and butyl esters were more active than the corresponding free acids.

Amoebicidal Activity

K. galanga also exhibited amoebicidal activity against three species of *Acanthamoeba*: *A. culbertsoni*, *A. castellanii* and *A. polyphaga*, the causative agents of granulomatous amoebic encephalitis and amoebic keratitis (Chu et al. 1998). The plant induced encystment of all three species of *Acanthamoeba* and was not lytic for normal macrophage cultures.

Toxicity Studies

The ethanolic rhizome extract, when tested by the Hippocratic screening test in rabbits, demonstrated signs that indicated CNS depression such as a decrease in motor activity and respiratory rate and a loss of screen grip and analgesia (Kanjapothi et al. 2004). In the acute toxicity test, oral administration of 5 g/kg of *Kaempferia galanga* produced neither mortality nor significant differences in the body and organ weights between controls and treated animals. Moreover, both gross abnormalities and histopathological changes were not comparatively detectable between all controls and treated animals of both sexes. Similar results were observed in subacute toxicity studies, when varying doses of 25, 50 or 100 mg/kg of ethanolic *Kaempferia galanga* extract were administered orally per day for a period of 28 days. Haematological analysis showed no differences in any of the parameters examined (WBC count, platelet, haematocrit and haemoglobin estimation) in either the control or treated

groups of both sexes. However, the differential leukocyte counts showed a slight but significant decrease of lymphocyte count in the 50- and 100-mg/kg male rat groups. In the blood chemistry analysis, no significant change occurred in the blood chemistry parameters, including glucose, creatinine, blood urea nitrogen, aspartate transaminase, alanine transaminase, alkaline phosphatase, total protein and albumin of both sexes. Pathologically, neither gross abnormalities nor histopathological changes were observed. No sign of irritation was observed during the dermal irritation test of the hexane fraction of *Kaempferia galanga*.

Traditional Medicinal Uses

According to NIMM (1999), in Vietnam folkloric medicine, *K. galanga* is considered to be stomachic, and it stimulates stomach functions, promotes digestion, relieves pain and is employed for the therapy of dyspepsia, gastralgia, abdominal pain due to cold and diarrhoea. For external application, alcohol maceration of the plant is used as a liniment treatment for rheumatism, arthralgia and oedema. For cure of dental caries, powdered galanga is applied to carious patches on the teeth and used as antifebrile through inhalation of the vapour from a boiling decoction. Mixed with honey, it is effective against cough and chest pain. It also serves as material for gargle. It is one of the ingredients of the Vietnamese ‘Bach Dia Can’ tablets which comprise *K. galanga*, *Angelica dahurica* and *Pueraria thomsonii* and found to be effective in clinical therapy as analgesic and antipyretic agents.

In traditional Thai medicine, the stem is used for menstrual stimulation and in the treatment of dyspepsia; the leaves and flowers are used for the treatment of *Tinea versicolor* and eye diseases and seizures, respectively (Thamaree and Tankeyoon 1981; Sighabutra 1993; Ridditid et al. 2008). *Kaempferia galanga* rhizome has been widely used for the treatment of asthma, hypertension, rheumatism, indigestion, cold and headache and relief abdominal pain (Ridditid et al. 2008; Sirisangtragul and Sripanidkulcha 2011); fungal- and bacterial-derived skin diseases (Tungtrongjit 1978); urticaria and allergy (Tewtrakul and Subhadhirasakul 2007); and

aphthous ulcers (Mekseepralard et al. 2010). The rhizomes of *K. galanga* have been used in a decoction or powder for indigestion, cold, pectoral and abdominal pains, headache and toothache and as gargles. Its alcoholic maceration has also been applied as liniment for rheumatism (Kanjapothi et al. 2004); the rhizome extract is used as carminative and haemagogic and to relieve flatulence (Chanwitheesuk et al. 2005) and to relax smooth muscles of the small intestine (Saralamp et al. 1996).

In Malaysia, the plant juice is deemed expectorant and carminative and used in many medicaments especially in children's medicines (Burkill 1966). Leaves were used in lotions and poultices for various ailments—for sore throats, fevers, swellings, rheumatism and sore eyes. Ashes of leaves are applied to swollen breast, and juice spat on abdomen of infant. The root was used in cosmetics. In Borneo, chekur was used in preparation of yeast and in dyeing. *K. galanga* is used in traditional Malay medicine for the treatment of various disorders including hypertension, rheumatism and asthma (Zakaria and Mustafa 1994; Othman et al. 2002, 2006). In Malaysia and Indonesia, this plant is used to make a gargle, and the leaves and rhizomes are chewed to treat coughs or pounded and used in poultices or lotions applied to relieve many ailments; the juice of the rhizome is used as an expectorant and carminative and is often a part of children's medicine and tonics; the rhizome is also used to treat abdominal pain and as an embrocation or sudorific to treat swelling and muscular rheumatism (Othman et al. 2006). *K. galanga* leaves possessed antinociceptive and anti-inflammatory activities and thus supports the Malay's traditional uses of the plant for treatments of mouth ulcer, headache and sore throat (Sulaiman et al. 2008). The rhizome is applied locally to the forehead to relieve colds and nosebleeds. In Indonesia it is an important ingredient of jamu.

The most common indications for its use, besides hypertension, include rheumatism, asthma, headaches, cough and toothaches and as a poultice for applying to bruises and wounds (Perry and Metzger 1980). In the Philippines, the rhizome mixed with oil is an effective cicatrizant; Filipinos

use a decoction of the rhizomes as a tonic and for dyspepsia, headache and malarial chills. In the Visayas the rhizomes are given to women after childbirth (Stuart 2014). *K. galanga* is used in hair wash for its fragrance and to eliminate dandruff. The rhizome of both *Alpinia galanga* and *Kaempferia galanga* is widely used in the Ayurvedic system of medicine in the treatment of various inflammatory diseases, diabetes mellitus and obesity (Achuthan and Padikkala 1997). The rhizomes are considered stimulating, expectorant, carminative and diuretic (Indrayan et al. 2009).

In China, *K. galanga* is commonly used as food spice and medicine, traditionally employed to treat symptoms ranging from hypertension, pectoral and abdominal pains, headache, toothache, rheumatism, dyspepsia, coughs and inflammatory tumour (Huang et al. 2008). It also has also been used to help restlessness, stress, anxiety and depression. In Japan, *Kaempferia galanga* has been used as one of the main ingredients in a scent bag which is recognised as improving sleep or minimising stressful situations as it possessed a strong characteristic balsamic odour (Huang et al. 2008). Rhizomes have been used as aromatic stomachic and incense in Chinese medicine (Kiuchi et al. 1988).

Other Uses

K. galanga are also used as perfume in shampoos, powder and other cosmetic articles. In Borneo, it enters into the preparation of yeast and of dyes (Burkill 1966). *K. galanga* is used as an insecticide against clothe moth (NIMM 1999).

Methanol extracts of the plant have shown larvicidal activity against the second-stage larva of dog roundworm (*Toxocara canis*) (Kiuchi et al. 1988). Among 40 medicinal plant species, *K. galanga* showed the most potent nematocidal activity against the pine wood nematode *Bursaphelenchus xylophilus* (Choi et al. 2006). Two cinnamates, ethyl *trans*-cinnamate and ethyl *p*-methoxycinnamate, were found to be responsible for much of the activity. The nematocidal activity of ethyl *trans*-cinnamate and ethyl *p*-methoxycinnamate was 100 % at 60 µg/ml. Hong et al. (2011) found that ethyl

cinnamate (EC) and ethyl *p*-methoxycinnamate (EMC) exhibited nematocidal and hatching inhibitory activities against *Meloidogyne incognita*. In direct-contact mortality bioassays, EC (0.037 mg/ml) and EMC (0.041 mg/ml) were more toxic than carbofuran (0.092 mg/ml) but less toxic than fosthiazate (0.002 mg/m) towards second-stage juveniles based upon 48-h LC₅₀ values. EC and EMC treatments resulted in 100 % and 93 and 81 % inhibition of hatch at 125.0 and 62.5 µg/ml, respectively. In contact + fumigant mortality bioassays with second-stage juveniles, EC and EMC applied at 0.25 and 0.125 mg/g soil resulted in 81 and 80 % and 77 and 73 % mortality, respectively, while carbofuran and metam sodium treatments resulted in 86 and 96 % and 57 and 73 % mortality, respectively. Fosthiazate resulted in 92 % mortality at 0.063 mg/g soil. In vapour-phase mortality bioassays with second-stage juveniles, EC and EMC were more effective in a closed container than in an open one, indicating that mode of delivery was, in part, a result of vapour action.

Comments

The plant is usually propagated by using rhizome pieces or division of the rhizomes as regeneration from seeds is poor. Studies have shown successful and rapid propagation of tissue culture plantlets derived from leaves and rhizome tips and buds (Shirin et al. 2000; Rahman et al. 2005; Parida et al. 2010).

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Kaempferia rotunda

T. K. Lim¹ 

(1) Canberra, Australia

Scientific Name

Kaempferia rotunda L.

Synonyms

Kaempferia longa Jacq., *Kaempferia versicolor* Salisb.,
Zerumbet zeylanica Garsault (Inval.)

Family

Zingiberaceae

Common/English Names

Asian Crocus, Hainan Resurrection Lily, Himalayan Crocus,
Indian Crocus, Peacock Ginger, Resurrection Lily, Round-
rooted Galangal, Tropical Crocus

Vernacular Names

Bangladesh: Bhuichampa, Misri Dana

Chinese: Hai Nan San Qi, Sha Jiang

India: Bhuichampa (**Bengali**), Bhuichampa Bhuyicampa
(**Hindi**), Kallu Kove, Kalluloove, Kumada Gedde,

Kumudagadde, Nela Sampige, Nelasampige, Utpala
Hoovu (Kannada), Cennalinirkilannu,
Cennalinirkkilannu, Cennalinirkuva, Chenchineerkilang,
Chengzhineer, Malankoova, Malan-Kua (Malayalam),
Bhuichampa, Bhuichapa, Bhummy-Champo, Booichampa
(Marathi), Bhucampaka, Bhuchampaka, Bhumicampaka,
Bhumichampa, Bhumichampaka, Hallakah, Hallakam,
Utpala, Utpalam (Sanskrit), Karunkuvalai, Konda-
Kalava, Neerpichin, Nerpichan, Nerppicin, Pucanpakam,
Pumicampakam, Pumicanpakam (Tamil),
Bhoochampakamu, Bhucampakamu, Bhuchampakamu,
Kondakalava, Kondakaluva (Telugu)

Indonesia: Ardong, Kunir Putih, Kunci Pepet (Javanese),
Konjek Pote, Konce Pet, Konce Pote (Madurese), Kuncit
Putih, Temu Putih (Malay), Koneng Bodas, Koneng Putih
(Sundanese)

Malaysia: Ardong, Kunci Pepet, Kunir Putih, Temu Putih

Nepal: Bhui-Champha

Philippines: Gisol Na Bilóg (Tagalog)

Thailand: Ueang Din, Waan Hao Non, Waan Nonlap

Vietnam: Cầm Địa La, Ngải Máu, Tam Thất Nam

Origin/Distribution

It is indigenous to Indian subcontinent, through Southeast Asia to Southern China.

It is cultivated in China (Guangdong, Guangxi, Hainan, Yunnan), Taiwan, India, Indonesia, Malaysia, Myanmar, Sri Lanka, Vietnam and Thailand.

Agroecology

In its native range, it occurs under partial shade, in open lower montane forests, forest margins and bamboo forest and open grasslands from sea level to 1300 m elevation. It grows on all types of soil.

Edible Plant Parts and Uses

The small ovate tubers of the roots, rhizomes, shoots and leaves are eaten fresh or cooked as vegetables. All are used as flavouring spice in Southeast Asia. Young leave as eaten as ‘lalap’ or ‘sayor’.

Botany

Kaempferia rotunda is a small rhizomatous stemless herb to 65 cm high. Rhizomes are fleshy, short, robust subterranean bearing slender, cylindrical roots terminating in swollen, subglobose, ovate or spindle-shape, yellowish-white tubers which is 1.15 cm long and 1.2.5 cm thick (Plates 2a, b). Leaves 2-3-5 are erect, distichous, short-petiolate sheaths which are 7–25 cm long, with lamina which is oblong lanceolate to elliptical and 7–36 cm (usually 12–25 cm) long by 4-7-11 cm wide, acuminate, glabrous, puberulous below, variegated or patterned dark and pale green on either side of midvein on adaxial surface and red/maroon/purple abaxially (Plate 1). Inflorescence emerges on separate shoot from the rhizome before the leaves, with 4–6 flowers, fragrance, purple-brown bracts and 2-toothed bracteole apex. Calyx is 4–7 cm and splits on 1 side, with 3-toothed white or greenish apex, and is a corolla tube equalling calyx; lobes are spreading, white, linear and 5 cm. Lateral staminodes are erect, white and lanceolate, with acute apex. Labellum is violet, obcordate and apically 2 cleft to base; lobes are down-curved, 3.5×2 cm, with acute apex. Anther’s connective appendage is erect and bi-cleft. Ovary is 4–6 mm and hairy.



Plate 1 Variegated green leaves with purple underside

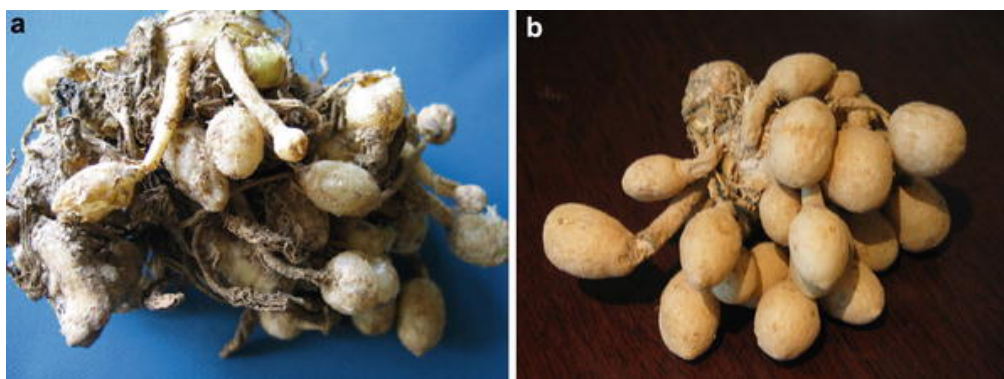


Plate 2 (a, b) Small rounded tubers

Nutritive/Medicinal Properties

The following compounds were isolated from the rhizomes: benzyl benzoate and the cyclohexane derivative and crotopoxide (Nugroho et al. 1996); three cyclohexane diepoxides, (–)-(1*R*,2*R*,4*R*,5*S*,6*R*,7*R*)-4-benzoyloxymethyl-3,8-dioxatricyclo[5.1.0.0^{2,4}] octane-5,6-diol 6-acetate; (+)-(1*R*,2*R*,4*R*,5*S*,6*R*,7*R*)-4-benzoyloxy-methyl-3,8-dioxatricyclo[5.1.0.0^{2,4}]octane-5,6-diol 5-acetate; and (–)-(1*R*,2*R*,4*R*,5*S*,6*R*,7*R*)-4-benzoyloxymethyl-3,8-dioxatricyclo[5.1.0.0^{2,4}] octane-5,6-diol 6-benzoate together with crotopoxide and (–)-zeylenol (Pancharoen et al. 1996); 3-deacetylcrotopoxide and 2-hydroxy-4,4',6'-trimethoxychalcone (Jantan et al. 2004); six polyoxygenated cyclohexane derivatives identified as (–)-6-acetylzeylenol (1), four acylated derivatives of 1-benzoyloxymethyl-1,6-epoxycyclohexan-2,3,4,5-tetrol (3–6), a Diels–Alder adduct of 3-benzoyl-1-

benzoyloxymethylcyclohexa-4,6-dien-2,3-diol (7), (–)-zeyleanol (2), a triacylated derivative of salicin (9) and the cyclohexane diepoxide and crotepoxide (8) (Stevenson et al. 2007); 3-deacetylcrotepoxide (Jantan et al. 2008); 1, 2'-hydroxy-4,4',6'-trimethoxy-chalcone and (+)-crotepoxide (Lotulung et al. 2008); [1*R*-(1 α ,2 α ,4 α ,5 β ,6 α ,7 α)]-4-benzoyloxymethyl-5,6-dihydroxy-3,8-dioxatricyclo-[5.1.0.0]octan-5-yl acetate (3-deacetyl-crotepoxide) (Sirat et al. 2010a); (*E*)-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (Sirat et al. 2010b); and three known flavanones, namely, 5-hydroxy-7-methoxyflavanone; 7-hydroxy-5-methoxyflavanone and 5,7-dihydroxyflavanone (Atun et al. 2013). A lectin (designated as KRL) was purified from *Kaempferia rotunda* rhizome (Kabir et al. 2011). It was determined to be a 29.0 kDa polypeptide and to be a divalent ion-dependent glycoprotein with 4 % neutral sugar. Aznam et al. (2012) isolated the following flavonoids from the hexane rhizome extract: 4'-hydroxy-8-methoxy-flavanone, 6-hydroxy-8-methoxy-flavanone and 4', 8-dihydroxy-flavanone.

Three new cyclohexane oxides and ten known compounds, comprising of cyclohexane oxides, esters, carboxylic acid, labdane diterpene and flavonoids, were isolated from *K. rotunda* rhizomes from Malaysia and Indonesia (Yau 2009). Two new compounds were identified as 2-(benzoyloxymethyl)phenyl (3-O-acetyl)- β -glucopyranoside and 3-debenzoylcrotepoxide A, together with seven known compounds: crotepoxide, 4-benzoyloxymethyl-3,8-dioxatricyclo[5.1.0.0^{2,4}]octane-5,6-diol 5-acetate, 1,6-desoxypipoxide, curcuminol C, 2'-hydroxy-4,4',6'-trimethoxychalcone and naringenin 4',7-dimethyl ether were isolated from the Malaysian species, while a new compound identified as 3-acetoxy-2-benzoyloxy-1-(benzoyloxymethyl)-cyclohexa-4,6-diene with the seven known compounds, namely, crotepoxide; 4-benzoyloxymethyl-3,8-dioxatricyclo[5.1.0.0^{2,4}]octane-5,6-diol 5-acetate; 1,6-desoxypipoxide; 6-acetylzeyleanol; *trans*-docosyl ferulate; benzyl benzoate and benzoic acid, were isolated from the Indonesian species. A new polyoxygenated cyclohexane compound, (–)-3-acetyl-4-benzoyl-1-benzoyloxymethyl-1,6-diepoxycyclohexan-2,3,4,5-tetra, together with 11 constituents

was isolated from *K. rotunda* methanol extract (Lallo et al. 2014).

Sereena et al. (2011) identified n-dodecane (33.1 %), stearaldehyde (37.9 %), hexadecane (6.32 %), dodecanoic acid (9.48 %) and kauren-ol (12.6 %) in the dried powdered rhizome petroleum ether extract. In the rhizome essential oil, 13 compounds were identified: bornyl acetate (30.12 %), benzyl benzoate (16.6 %), camphor (7.18 %), camphene (7.54 %), borneol (5.93 %), cineol (4.16 %), caryophyllene (3.05 %), linalool (2.6 %), *n*-tetradecane (2.18 %), α -pinene (1.35 %), aromadendrene (1.31 %), β -pinene 1.13 %) and caryophyllene oxide (0.94 %)

The most abundant volatile constituents of *K. rotunda* rhizomes extracted by GC and GC–MS (EI) analyses were benzyl benzoate (69.7 %, 20.2 %), *n*-pentadecane (22.9 %, 53.8 %) and camphene (1.0 %, 6.2 %) (Woerdenbag et al. 2004). *K. rotunda* rhizome yielded < 0.03 % oil (Sirat et al. 2005). Twenty-three compounds were found, among which were monoterpenes (19 %), sesquiterpenes (10.1 %), esters (39.2 %) and hydrocarbons (27.3 %). The major esters were bornyl acetate (24.9 %) and benzyl benzoate (15.3 %). Pentadecane (25.4 %) and camphor (12.1 %) were the major hydrocarbon and monoterpene, respectively. The rhizome was found to be deficient in sesquiterpenoids. Fifty-one volatile compounds were isolated and identified from *Kaempferia rotunda*, and the main compounds were α -pinene (6.83 %), camphene (13.00 %), β -pinene (18.97 %), camphor (5.80 %) and linalool oxide (5.11 %) (Xu et al. 2012).

Leaf Phytochemicals

Flavonoids, crotopoxide, chalcones, quercetin, protocathechuic acid, β -sitosterol, stigmasterol, syringic acid and some hydrocarbons were found in the methanol leaf extract (Imam et al. 2013).

Antioxidant Activity

The chloroform-soluble rhizome extract exhibited significant scavenging effect on the on 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radicals ($IC_{50} = 180 \mu\text{g/mL}$) (Lotulung et al. 2008). Two compounds of the chloroform-soluble extract were isolated and identified. Compound 1, 2'-hydroxy-4,4',6'-trimethoxy-chalcone was found as the active constituent ($IC_{50} = 142 \mu\text{g/mL}$). Compound 2, (+)-crotopoxide, was inactive ($IC_{50} = 1516 \mu\text{g/mL}$). *K. rotunda* methanol rhizome extract was found to have significant antioxidant activity (Mohanty et al. 2008). The quantification of malondialdehyde (MDA) and 4-hydroxyl-2-nonenal (4-HNE) could be directly correlated with the lipid peroxidation inhibition capacity of the extract.

Antiplatelet activity

Studies reported that 3-deacetylcrotopoxide and 2-hydroxy-4,4',6'-trimethoxychalcone from *K. rotunda* rhizome inhibited platelet-activating factor receptor binding of rabbit platelets with IC_{50} values of 45.6 and 57.4 μM , respectively (Jantan et al. 2004). They also showed that 3-deacetylcrotopoxide showed strong inhibition on human platelet aggregation induced by arachidonic acid with IC_{50} value $< 84 \mu\text{M}$ (Jantan et al. 2008).

Antihyperglycaemic Activity

The methanol rhizome extract caused dose-dependent significant lowering in serum glucose levels in mice, when administered at doses of 50, 100, 200 and 400 mg per kg body weight to glucose-loaded mice as compared to control animals (Sultana et al. 2012). Highest lowering of serum glucose (39.6 %) was observed at an extract dose of 400 mg. In comparison, a standard antihyperglycaemic drug, glibenclamide, when administered at a dose of 10 mg per kg body weight, lowered serum glucose.

Antinociceptive Activity

The methanol rhizome extract demonstrated dose-dependent significant antinociceptive activity when administered to mice

compared to control animals (Sultana et al. 2012). At a dose of 400 mg extract per kg body weight, the number of abdominal writhings was inhibited by 69.4 % as compared to 73.4 % inhibition obtained with a standard antinociceptive drug, aspirin, administered at a dose of 400 mg per kg body weight.

Antimutagenic Activity

The methanol rhizome extract and isolated flavanones, namely, 5-hydroxy-7-methoxyflavanone, 7-hydroxy-5-methoxyflavanone and 5,7-dihydroxyflavanone, showed significant antimutagenic effect compared to control group based on the number of micronucleated polychromatic cell erythrocytes (MNPCE) from male Balb/c mice (8–12 week) induced by cyclophosphamide (Atun et al. 2013).

Anticancer Activity

A lectin KRL from the rhizome exhibited antiproliferative activity against Ehrlich ascites carcinoma (EAC) cells with 51 % and 67 % inhibition in-vivo in mice administered with 1.25 mg/kg/day and 2.5 mg/kg/day of KRL, respectively, by injection for 5 days (Kabir et al. 2011; Kabir and Reza 2014). KRL lectin inhibited 6.2–50.5 % EAC cell growth at the range of 7.5–120 µg/ml protein concentration. The cell cycle arrests at G0/G1 phase of EAC cells. (–)-3-acetyl-4-benzoyl-1-benzoyloxymethyl-1,6-diepoxy cyclohexan-2,3,4,5-tetraol isolated from *K. rotunda* exhibited moderate cytotoxic activity against pancreatic (PSN-1) and breast (MDA-MB231) cancer cell lines but did not affect the normal TIG-3 cell line (Lallo et al. 2014).

Agglutination/Antimicrobial Activity

A lectin (designated as KRL), purified from rhizomes, was found to agglutinate different groups of human blood cells (Kabir et al. 2011). Methyl- α -D-mannopyranoside, D-mannose and methyl- α -D-glucopyranoside were the most potent inhibitors. KRL lost its activity markedly in the presence of denaturants and exhibited high agglutination activity from pH

6.0 to 8.2 and from temperature 30 to 60 ° C. The lectin showed toxicity against brine shrimp nauplii with the LC₅₀ value of 18 µg/ml and strong agglutination activity against seven pathogenic bacteria. KRL inhibited the growth of six bacteria partially and did not show antifungal activity. *K. rotunda* lectin (KRL) showed agglutination activity against *Escherichia coli* and *Staphylococcus aureus*, with partial inhibition of their growth (Kabir and Reza 2014).

Wound Healing Activity

Methanol and aqueous extracts of *K. rotunda* leaves exhibited significant wound healing activity in albino mice (Imam et al. 2013). In the incision wound model, a significant increase in skin breaking strength was observed in the extract-treated groups. In the excision of the wound of the animal model, both extracts affected the contraction rate significantly.

Antiviral Activity

K. rotunda rhizome hexane extract was found to have strong activity against H5N1 AI virus, and the methanol extract exerted lower antiviral activity (Aznam et al. 2012).

Anthelmintic Activity

The alcoholic rhizome extract exhibited significant anthelmintic activity at highest concentration of 100 mg/ml against *Pheretima posthuma* and *Ascaridia galli* (Agrawal et al. 2011).

Traditional Medicinal Uses

Kaempferia rotunda is used in folk medicines in Bangladesh for treatment of high blood sugar level and pain (Sultan et al. 2012). *Kaempferia rotunda*, known as kunci pepet or kunir putih in Indonesia, has been traditionally used in abdominal pain, wounds and diarrhoea colic disorder and as sputum laxative (Atun et al. 2013). Rhizomes and tubers are used in cosmetics, in perfumery and in various ‘jamu’ (traditional

Indonesian herbal medicine) preparations in Indonesia. In Java the rhizomes are used for stomach ailments and as a cooling medicine; the leaves are used for poulticing in India (Burkill 1966). In the Philippines rhizomes are used for gastric disorders and externally mixed with coconut oil as a cicatrizant (Stuart 2013). In India, rhizomes are used for treating mumps and for wounds and bruises (Chopra et al. 1986). An ointment of the powder is useful in healing wounds. The juice of the rhizomes is taken internally and acts as a resolvent of phlegm, of dropsical affections of the hands and feet and of effusions in joints. The rhizomes are used in local medicine by grinding (fresh or dried) and making a paste with water in Nepal. This paste is mixed with other herbs and applied to sprains and covered with a bandage.

Other Uses

Kaempferia rotunda is planted as an ornamental plant for its variegated foliage and flowers. Its rhizomes are used in perfumery and cosmetics for dyeing and as tranquiliser.

The rhizome also has insecticidal activity. The rhizomes are also used in preparations to prevent insect moths in the clothes. Extracts from rhizomes of *Kaempferia rotunda* rhizome extract when incorporated into artificial diets displayed significant insecticidal activity against neonate larvae of the pest insect, *Spodoptera littoralis*, in chronic feeding bioassay at a concentration of 2500 ppm (Nugroho et al. 1996). Its bioactive constituent, benzyl benzoate, exhibited insecticidal activity when applied topically (LC₅₀, 5.6 µg/cm), suggesting detoxification in the larval gut when applied orally. Another constituent crotepoxide was less active in the chronic feeding bioassay (LC₅₀, 1450 ppm) and was inactive in the residue–contact bioassay. The methanol extract of the rhizomes of *K. rotunda* and (–)-2-acetyl-4-benzoyl-1-benzoyloxymethyl-1,6-epoxycyclohexan-2,3,4,5-tetrol (2-acetylrotepoxide B; 6) exhibited antifeedant activity against larvae of *Spodoptera littoralis* (Stevenson et al. 2007). (–)-Zeylenol (2) also showed antifeedant activity, whereas (–)-6-acetylzeylenol (1) was inactive.

Comments

The plant is propagated by using fragments of the rhizomes.

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Zingiber montanum

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Scientific Name

Zingiber montanum (J. Koenig) Link ex A. Dietr

Synonyms

Amomum cassumunar (Roxb.) Donn, *Amomum montanum* J. Koenig, *Amomum xanthorrhiza* Roxb. ex Steud., *Cassumunar roxburghii* Colla, *Jaegera montana* (J. Koenig) Giseke, *Zingiber anthorrhiza* Horan., *Zingiber cassumunar* Roxb., *Zingiber cassumunar* var. *palamauense* Haines, *Zingiber cassumunar* var. *subglabrum* Thwaites, *Zingiber cliffordiae* Andrews, *Zingiber luridum* Salisb., *Zingiber montanum* (J. Koenig ex Retz.) Theilade, *Zingiber purpureum* Roscoe, *Zingiber purpureum* var. *palamauense* (Haines) K.K.Khanna, *Zingiber xanthorrhizon* Steud.

Family

Zingiberaceae

Common/English Names

Bengal Ginger, Bitter Ginger, Cassumunar Ginger, Thai Ginger

Vernacular Names

Bangladesh: Bon Ada

Burmese: Meik-Thalin

Chinese: Ye Jiang

Cuba: Jengibre Amargo

Dominican Republic: Jengibre Amargo, Jengibre Cimarron

French: Gingembre De Siam, Gingembre Marron

German: Blockzitwer, Gelber Zitwer, Zitwer

India: Bun-Ada, Moorada (Bengali), Bun-Ada, Jangliadrak (Hindu), Nisa, Malabri Halad (Kannada), Tekhaoyaikhu (Manipur), Nisa, Malabri Halad (Marathi), Vana-Ardraka (Sanskrit), Kattu Ingi (Tamil), Car-Puspoo (Telugu), Aardikaa, Adarakhi, Bana-Adarakhi, Kadshunti, Karallamu, Peju, Peyu, Shringaberikaa

Indonesia: Banglai, Bangle, Benge, Mungle (Acheh), Unin Makei (Ambon), Banggele (Bali), Bungle (Batak), Panini (Bugis), Bangle, Benge, Nunglai, Kunit Bolai (Javanese), Pandhiyang (Madura), Bale (Makassar), Kunik Bolai (Minang), Mugle, Benge, Bungle, Baglai, Baniai, Banglai, Bunglai,; Bangle, Kunit Bolai, Kunyit Bolai Mugle, Benge, Bungle, Baglai, Baniai, Banglai, Bunglai,; Bangle, Kunit Bolai, Kunyit Bolai (Sumatra), Pandhiyang, Panglai (Sundanese)

Japanese: Shikyoku

Malaysia: Bangle, Bolai, Boleh, Bonglai (Plate 2), Bonglaibulai, Bungelai, Kunyit Bolai, Kunyit Terus Putih, Lampoyang Kuning, Lia Betong, Tepus Merah (Iban)

Nepalese: Van Aduvaa

Puerto Rico: Jengibre Colorado

Spanish: Jengibre, Jengibre Amargo

Thai: Wan Fai, Wan Fi (Central) Plai (General), Phlai, Plai, Bpulai, Puloi, Pu Loei (Northern), Min Sa Lang (Shan Mae Hong Son)

Vietnamese: Gùng Tia

Origin/Distribution

Z. montanum is considered native to India and southeast Asia – Myanmar, Thailand, Malaysia and Indonesia. The species is considered native to Vietnam in Wiart (2012) but naturalised according to the Kew World Checklist (Govaerts 2014). In Borneo, it is listed as naturalised in the Kew World Checklist (Govaerts 2014), whereas USDA-ARS (2014) lists the species as native. The species has been widely cultivated across tropical Asia for food flavouring, often as a substitute for *Z. officinale*, and for a variety of medicinal uses (Wolff et al. 1999; Jiang et al. 2006; USDA-ARS 2014).

Agroecology

In its native range, the species occurs in humid, warm and shady forests from low to medium elevations. In Indonesia, *Z. montanum* is found up to 1300 m (Backer and Bakhuizen van den Brink 1968; Wolff et al. 1999; Acevedo-Rodríguez and Strong 2005). In India, it commonly grows well in wetland habitats and in moist and shady forest areas under physiologically stressed conditions (Chirangini and Sharma 2005). *Z. montanum* is a naturalised weed in moist second-growth forest in limestone hills, at altitudes around 200–250 m (Acevedo-Rodríguez and Strong 2005). The species thrives in shady conditions but will tolerate full sun with adequate water. It prefers well-drained, sandy lam or loamy clay soils, optimum temp 25–30 in 60–85 % relative humidity

Edible Plant Parts and Uses

Rhizomes are used for food flavouring in Thailand (Chanwitheesuk et al. 2005; Bua-in and Paisooksantivatana 2009; Ubonnuch et al. 2013). The rhizome has a strong

camphoraceous odour; warm, spicy, bitter taste and fleshy; bright yellow colour and is strongly scented and is used as a flavouring agent in many food preparations and as a substitute for true ginger (Chirangini and Sharma 2005). It is also used as a substitute for and an adulterant of *Zingiber officinale* in the global ginger spice trade (Jiang et al. 2006). Flowers and young shoots are eaten as side dish vegetables for appetisers (Triboun et al. 2005).

Botany

Zingiber montanum is a perennial, clumping herb; rhizomes are horizontal creeping, tuberous, cylindrical to ovoid, irregular, palmately and profusely branched, laterally compressed and strongly aromatic with yellow flesh colour (Plate 3). Psuedostem is cylindrical, erect, enveloped by leafy sheaths and reaching 1.2–1.8 m high. Leaves are alternate, distichous, simple, subsessile or shortly petiolate, lanceolate-oblong and 3.5–5.5 cm by 18–35 cm long (Plate 1). Leaf sheaths are oblong, with membranous margins; ligules are ovate and membranous. Inflorescence is radical; spikes are cylindrical, fusiform or cone like, borne on a peduncle spike (scape) arising from rhizome and 8–60 cm high with 5–7 cataphylls; bracts are divided into outer and inner, spirally arranged, very dense, persistent and red or purplish brown; the outer is broadly ovate to suborbicular and cucullate, while the inner is ovate and glabrous. Flowers are ebracteolate, bisexual, zygomorphic and epigynous; calyx is 1.2–1.5 cm, membranous, glabrous and white; corolla has 4 lateral lobes and is linear-lanceolate, yellowish-white and reddish lineolate on margins; labellum is white or pale yellow and suborbicular; apex is emarginate; central lobe is broadly rounded; stamen is 1 cm long and pale yellow; ovary is 3 loculed, inferior, 3–4 mm long and pubescent. Capsule is ovoid to subglobose and 1–1.5 cm diameter.



Plate 1 Broad lanceolate leaves



Plate 2 Plant label



Plate 3 Irregular and ovoid rhizome

Nutritive/Medicinal Properties

Rhizome Phytochemicals

Mineral composition in *Z. purpureum* rhizomes (g/100 g) was reported by Kasarkar and Kulkarni (2012) as N, 2.07 g; NO_3^- , 0.059 g; P, 0.59 g; K, 1.07 g; Ca, 0.40 g; S, 0.085 g; Na, 0.65 g; Zn, 0.062 g; Fe, 1.02 g; Cu, 0.18 g; Mo, 0.007 g; B, 0.178 g; Mg, 1.43 g; and Mn, 0.4 g.

The novel aromatic compounds *cis*-3-(2',4',5'-trimethoxyphenyl)-4-[(*E*)-2''',4''',5'''-trimethoxystyryl]cyclohex-1-ene; *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-3''',4'''-dimethoxystyryl]cyclohex-1-ene; a substance assigned the tentative structure *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-2''',4''',5'''-trimethoxystyryl]cyclohex-1-ene; (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-ol; (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-yl acetate; and 8-(3',4'-dimethoxyphenyl)-2-methoxynaphtho-1,4-quinone were isolated from *Zingiber cassumunar* rhizomes (Amatayakul et al. 1979). Thirteen aromatic compounds were isolated from *Z. cassumunar* rhizomes and elucidated as *cis*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene; *cis*-3-(2,4,5-trimethoxy-phenyl)-4-[(*E*)-2,4,5-

trimethoxystyryl]cyclohex-1-ene (alflabene); *cis*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-2,4,5-trimethoxystyryl]cyclohex-1-ene; (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-ol; 8-(3,4-dimethoxyphenyl)-2-methoxynaphtho-1,4-quinone; *cis*-4[(*E*)-3,4-dimethoxystyryl]-3-(2,4,5-trimethoxyphenyl)cyclohex-1-ene; *trans*-3-(3,4-dimethoxyphenyl)-4[(*E*)-3,4-dimethoxystyryl]-cyclohex-1-ene; *trans*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-2,4,5-trimethoxystyryl]cyclohex-1-ene; (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-yl palmitate; (*E*)-1-(3,4-dimethoxyphenyl)but-1-ene; (*E*)-1-(2,4,5-trimethoxyphenyl)but-1-ene; (*E*)-1-(3,4-dimethoxyphenyl)butadiene; and 2-methoxy-8(2,4,5-trimethoxyphenyl)-naphtho-1,4-quinone; together with vanillin, vanillic acid, veratric acid, terpinene-4-ol and curcumin (Kuroyanagi et al. 1980).

Cassumunaquinones 1 and 2 were isolated from the rhizome and their structures elucidated as 2-methoxy-8(3,4-dimethoxyphenyl)-1,4-naphthaquinone and 2-methoxy-8(2,4,5-trimethoxyphenyl)-1,4-naphthaquinone, respectively (Dinter et al. 1980b). Two cassumunar phenylbutadiene dimers of the 3-aryl-4-styrylcyclohexene series, identified as alflabene and cassumunene, together with one monomeric 4-phenylbut-3-ene identified as (2-(3,4-dimethoxystyryl)ethanol) were isolated from *Z. cassumunar* rhizomes (Dinter et al. 1980a). Five novel phenylbutanoids including (*E*)-4-(3',4'-dimethoxy)but-3-en-1-yl palmitate and 3,4-dimethoxybenzaldehyde 2,4,5-trimethoxybenzaldehyde were isolated from *Zingiber cassumunar* rhizomes (Tuntiwachwuttikul et al. 1981). Three compounds were isolated from the *n*-hexane-soluble fraction of *Z. cassumunar* rhizome and identified as (*E*)-1-(3,4-dimethoxyphenyl)but-1-ene, (*E*)-1-(3,4-dimethoxyphenyl)butadiene and zerumbone (Ozaki et al. 1991).

Zerumbone, a sesquiterpene, was isolated from the rhizome (Kishore and Dwivedi 1992; Al-Amin et al. 2012). The rhizomes were found to contain diferuloylmethane (curcumin), (*p*-hydroxycinnamoyl)-feruloylmethane and *p,p'*-dihydroxyldioinna-moyldethane (Jitoe et al. 1992); cassumunarin A, B and C (Jitoe et al. 1994); and cassumunins A, B and C (Matsuda et al. 1993; Matsuda and Jitoe 1994).

Two phenylbutenoid dimers, ($\pm$)-*trans*-3-(2,4,5-trimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]-cyclohexene and *cis*-1,2-bis[(*E*)-3,4-dimethoxy-styryl]cyclobutane, were isolated from the fresh rhizomes of *Zingiber cassumunar* along with the two known phenylbutenoid dimers (Jitoe et al. 1993). Four new phenylbutenoid monomers, (*E*)-4-(4-hydroxy-3-methoxyphenyl)but-3-en-1-yl acetate; (*E*)-4-(4-hydroxy-3-methoxyphenyl)but-2-en-1-ol; (*E*)-2-hydroxy-4-(3,4-dimethoxyphenyl)but-3-en-1-ol and (*E*)-2-methoxy-4-(3,4-dimethoxyphenyl)but-3-en-1-ol, were isolated from fresh rhizomes of *Zingiber cassumunar* along with the three known phenylbutenoid monomers (Matsuda and Jitoe 1995). Five anti-inflammatory components were isolated from the rhizome hexane extract and identified as (*E*)-4-(3',4'-dimethoxyphenyl)but-3-enyl acetate; *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-3'',4''-dimethoxystyryl]cyclohex-1-ene; *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-2'',4'',5''-trimethoxystyryl]cyclohex-1-ene; *cis*-3-(2',4',5'-trimethoxyphenyl)-4-[(*E*)-2'',4'',5''-trimethoxystyryl]cyclohex-1-ene and (*E*)-4-(3'-4'-dimethoxyphenyl)but-3-en-1-ol (Pongprayoon et al. 1997b).

A potential cytotoxic principle, curcumin, along with two inactive compounds, (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-ol and (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-yl acetate, were isolated from *Z. cassumunar* rhizome (Han et al. 2003). A new cytotoxic phenylbutenoid dimer, ($\pm$)-*trans*-3-(4-hydroxy-3-methoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene, was isolated from the rhizomes of *Zingiber cassumunar* along with the three known compounds, ($\pm$)-*trans*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene; 4-(3,4-dimethoxyphenyl)but-1,3-diene and 4-(2,4,5-trimethoxyphenyl)but-1,3-diene (Han et al. 2004). A new phenylbutenoid glycoside, (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-*O*- β -D-glucopyranoside; known phenylbutenoids, 4-(2,4,5-trimethoxyphenyl)-but-1,3-diene; 4-(3,4-dimethoxyphenyl)but-1,3-diene; (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-ol and (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-yl acetate; and two phenylbutenoid dimers,

(±)-*trans*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene and (±)-*trans*-3-(4-hydroxy-3-methoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene, were isolated from the chloroform extract of *Z. cassumunar* rhizomes (Han et al. 2005). Two phenylbutenoids, (*E*)-4-(3',4'-dimethoxyphenyl)but-3-enyl acetate and (*E*)-4-(3',4'-dimethoxyphenyl)but-1,3-diene, were isolated from *Zingiber cassumunar* rhizomes with the purity of 98.7 and 95.1 %, respectively, from 600 mg of the crude sample (Lu et al. 2005). From the n-hexane rhizome extract, 3-(3,4-dimethoxy-phenyl)-4-(3,4-dimethoxystyryl)cyclohexene was isolated (Fachriyah et al. 2007). Compared with classical elution, the elution–extrusion countercurrent chromatography approach exhibited strong separation efficiency of and great potential to be a high-throughput separation technique in the case of complex samples (Lu et al. 2008). It afforded the separation of four phenylbutenoids over 90 % pure and of a mixture of diastereoisomers (phenylbutenoid dimers) from the crude ethanol extract of *Zingiber cassumunar*. The compounds separated were (*E*)-4-(3,4-dimethoxyphenyl)-3-butene-1,2-diol (95 % purity), (*E*)-4-(3,4-dimethoxyphenyl)-but-3-en-1-ol (96,8 %), (*E*)-3-(3,4-dimethoxyphenyl)propenal (94.2 %), (*E*)-4-(3,4-dimethoxyphenyl)-but-3-en-1-yl acetate (91.5 %) and mixture (44.2/39.8 %) of 5 and 6, viz. (5) (±)-*trans*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene and (6) (±)-*cis*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene.

Eleven volatile compounds were identified in the head space of *Z. cassumunar*; they were sabinene (55.69 %), α-terpinene (9.03 %), γ-terpinene (8.99 %), β-pinene (7.36 %), 1*S*,1*R*- α-pinene (6.85 %), α-thujene (5.30 %), β-myrcene (1.84 %), β-phellandrene (1.73 %), terpinolene (1.38 %), *p*-cymene (1.21 %) and α-phellandrene (0.6 %) (Chatpaisum et al. 2009). From *Z. cassumunar* rhizome methanol extract, six new phenylbutanoids, phlains I–VI, were isolated together with 16 known constituents, namely, dimethoxybenzaldehyde (0.027 %), 2,4,5-trimethoxybenzaldehyde (0.010 %), (*E*)-1-(3,4-dimethoxyphenyl)buta-1,3-diene (2.17 %), (*E*)-1-(2,4,5-trimethoxyphenyl)buta-1,3-diene (0.20 %), (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-ol (0.75 %), (*E*)-4-(3,4-

dimethoxyphenyl)but-3-enyl acetate (0.58 %), (*E*)-1-(3,4-dimethoxyphenyl)but-1-ene (0.066 %), (*E*)-1-(2,4,5-trimethoxyphenyl)but-1-ene (0.035 %), ($\pm$)-*cis*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene (0.62 %), ($\pm$)-*cis*-3-(2,4,5-trimethoxyphenyl)-4-[(*E*)-2,4,5-trimethoxystyryl]cyclohex-1-ene (0.0049 %), cassumunaquinone 1 (0.0077 %), cassumunaquinone 2 (0.0083 %), curcumin (0.22 %), (–)- β -sesquiphellandrene (0.17 %), vanillic acid (0.071 %) and β -sitosterol (0.073 %) (Nakamura et al. 2009).

From the ethyl acetate-soluble fraction of *Z. cassumunar* rhizome, eight new phenylbutanoids, cassumunols A–H were isolated together with 30 known constituents, namely, phlains I, II, III, IV, V and VI, (*E*)-1-(3,4-dimethoxyphenyl)buta-1,3-dien; (*E*)-1-(2,4,5-trimethoxyphenyl)buta-1,3-dien; (*Z*)-1-(2,4,5-trimethoxyphenyl)buta-1,3-dien; (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-ol; (*E*)-4-(3,4-dimethoxyphenyl)but-3-enyl acetate; (*E*)-4-(3,4-dimethoxyphenyl)but-3-ene-1,2-diol; (*E*)-1-(3,4-dimethoxyphenyl)but-1-ene; (*E*)-1-(2,4,5-trimethoxyphenyl)but-1-ene; ($\pm$)-*cis*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene; ($\pm$)-*cis*-3-(2,4,5-trimethoxyphenyl)-4-[(*E*)-2,4,5-trimethoxystyryl]cyclohex-1-ene; ($\pm$)-*trans*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene; ($\pm$)-*trans*-3-(2,4,5-trimethoxyphenyl)-4-[(*E*)-2,4,5-trimethoxystyryl]cyclohex-1-ene; (*E*)-3-(3,4-dimethoxyphenyl)propenal; (*E*)-3-(2,4,5-trimethoxyphenyl)propenal; curcumin; cassumunaquinones 1 and 2; cassumunarins A and C; 3,4-dimethoxybenzaldehyde; 2,4,5-trimethoxybenzaldehyde; vanillic acid; (–)- β -sesquiphellandrene and β -sitosterol (Matsuda et al. 2011). (*E*)-4-(3,4-dimethoxyphenyl)butadiene (DMPBD) was found in the range of 0.90 to 1.61 (w/w) in *Z. cassumunar* rhizome extracts (Tangyuenyongwatana et al. 2012)

Plai oil was found to comprise of α -pinene, β -pinene, sabinene, myrcene, γ -terpinene, limonene, *p*-cymene, terpinene and terpine-4-ol (Casey et al. 1971). The essential oil of *Zingiber cassumunar* rhizome from Indonesia comprised mainly monoterpenes with sabinene and terpinen-4-ol as main

constituents (Taroeno et al. 1991). Sesquiterpenes accounted for a small part of the oil with sesquiphellandrene being the principal constituent. In addition to these terpenes, the oil contained a number of phenylbutanoids. The essential oil obtained by hydrodistillation contained about 25 % of these phenylbutanoids, whereas the oil obtained by extraction with light petroleum had about 46 %, with *trans*-1-(3,4-dimethoxyphenyl)but-1-ene, *trans*-1-(3,4-dimethoxyphenyl)butadiene and *trans*-4-(3,4-dimethoxyphenyl)but-3-ene-1-yl acetate as the main constituents. Other compounds thuy-4(10)-ène, *p*-cymène and *p*-menth-1-én-4-ol were also found.

The rhizome oil contained 32 components as follows: triquinacene, 1,4-*bis* (methoxy) (26.47 %), (*Z*)-ocimene (21.97 %), terpinen-4-ol (18.45 %), γ -terpinene (3.86 %), β -phellandrene (3.49 %), *cis*-sabinene hydrate (3.00 %), β -pinene (2.55 %), β -sesquiphellandrene (2.45 %), α -pinene (2.30 %), 4-terpinyl acetate (2.10 %), methyl eugenol (2.07 %), 2-allyl-1,4-dimethoxy-3-methyl benzene (1.74 %), β -myrcene (1.58 %) and terpinyl acetate (1.10 %) (Bhuiyan et al. 2008). Minor components <1 % included α -thujene; camphene; *m*-cymene; 2-carene; borneol; *trans*-piperitol; bornyl acetate; germacrene D; (*Z*) 1,6,10-dodecatrien, 7,11-dimethyl-3-methylene; γ -selinene; α -selinene; α -bergamotene; β -bisabolene; megastigmastrienone; lachnophyllum ester; δ -cadinene; juniper camphor and 2-propenoic acid, 3(4-methoxyphenyl) ethyl ester (Bhuiyan et al. 2008).

Zingiber cassumunar hydrodistilled rhizome oil containing terpinen-4-ol (50.5 %), (*E*)-1-(3,4-dimethoxyphenyl)buta-1,3-diene (19.1 %), (*E*)-1-(3,4-dimethoxyphenyl)but-1-ene (6.0 %) and β -sesquiphellandrene (5.9 %) as major constituents out of 21 compounds identified (Bordoloi et al. 1999). Constituents of plai rhizome essential oil extracted by hexane and hydrodistillation were determined to be, respectively, as follows: terpinene-4-ol (33.11–49.36; 21.85–29.56 %), sabinene (24.05–39.11; 36.71–53.50 %), γ -terpinene (6.68–7.74; 5.27–7.25 %), (*E*)-1-(3,4-dimethoxyphenyl)butadiene (DMPBD) (5.31–8.28; 0.95–16.16 %), α -thujene (0–0.7; 0.44–0.60 %), α -pinene (0.34–0.69; 1.15–2.0 %), β -pinene (1.36–

2.43; 2.25–3.78 %), β -myrcene (1.63–2.13; 1.83–2.65 %), α -terpinene (1.83–3.18; 2.04–3.39 %), *p*-cymene (0.77–1.66; 0.74–1.69 %), β -phellandrene (0.84–2.34; 0.74–1.69 %), (*Z*)-sabinene hydrate (0.61–1.25; 0 %), terpinolene (0.87–1.11; 0.84–1.09 %), (*E*)-sabinene hydrate (0.54–1.07; 0–0.49 %), (*Z*)-*p*-menth-2-en-1-ol (0.54–0.62; 0–0.41 %), α -terpineol (0–0.76; 0–0.29 %), myrtenol (0–0.27; 0–0 %), β -terpinyl acetate (0.21–0.46; 0–0.29 %), β -sesquiphellandrene (0.27–0.53; 0.83–1.03 %), 4-(2,4,5-trimethoxyphenyl)but-1,3-diene (0.28–0.34; 0–0.21 %) and two unknowns (Sukkata et al. 2009).

Fifteen compounds were found in the fresh rhizome essential oil collected from 6 different regions in Thailand: sabinene (38.20–47.54 %), terpinene-4-ol (11.50–24.36 %), (*E*)-1(3, 4-dimethylphenyl) butadiene (DMPD) (1.24–27.54 %), sabinene hydrate (2.70–5.81 %) were the major compounds, followed by terpinyl acetate (1.62–2.693 %), terpinolene (0.41–1.89 %), α -thujene (tr-0.89 %), α -pinene (0.78–1.37 %), β -myrcene (1.76–2.46 %), α -terpinene (1.31–1.70 %), *p*-cymene (1.32–2.88 %), β -phellandrene (tr-1.36 %), γ -terpinene (0.85–1.55 %), β -sesquiphellandrene (1.03–1.48 %) and unknown (1.12–2.18 %) (Bua-in and Paisooksantivatana 2009). Samples collected from western Thailand contained the highest amount of essential oil (11.07 mL/kg), the accession from Kanchanaburi province gave the highest volume (21 mL/kg), whereas those from eastern Thailand contained the lowest volume (4.95 mL/kg).

Studies showed that the yield of oil obtained from Kaco, Chiang Mai and Prachuap Khiri Khan provinces in Thailand by hexane extraction was 0.983 %, 0.900 % and 0.857 % (w/w), respectively, while by hydrodistillation the yield was 1.137 %, 1.262 % and 1.373 % (w/w), respectively (Sukkata et al. 2009). The results showed that essential oils in the plai rhizomes isolated by hexane extraction and by hydro distillation were rather similar in their major composition, but different in minor components. The plai oil obtained by hexane extraction contained mainly of sabinene (24.05–39.11 %), γ -terpinene (6.68–7.74 %), terpinen-4-ol (33.11–49.36 %) and (*E*)-1-(3,4-dimethoxyphenyl) butadiene (DMPBD) (5.31–8.28 %), whereas that obtained by hydrodistillation contained sabinene (36.71–53.50 %), γ -terpinene (5.27–7.25 %),

terpinen-4-ol (21.85–29.96 %) and DMPBD (0.95–16.16 %). Minor components included α -thujene, α -pinene, β -pinene, β -myrcene, α -terpinene, *p*-cymene, β -phellandrene, (*Z*)-sabinene hydrate (only in hexane extracts), terpinolene, (*E*)-sabinene hydrate, (*Z*)-*p*-menth-2-en-1-ol, α -terpineol, myrtenol (only in Prachuap Khiri Khan hexane extract), β -terpinyl acetate, β -sesquiphellandrene, 2 unknowns and 4(2,4,5-trimethoxyphenyl)but-1-3-diene.

Fourteen compounds were identified in *Z. cassumunar* rhizome essential oil: terpinen-4-ol (67.06 %), γ -terpinene (13.26 %), α -terpinolene (3.04 %), neo-allo-ocimene (2.52 %), *p*-cymenol-8-ol (2.36 %), γ -terpinene (1.76 %), caryophyllene oxide (1.19 %), *cis*-piperitol (1.03 %), allo-ocimene (0.68 %), dill ether (0.59 %), *cis*-sabinene hydrate (0.54 %), *trans*-linalool oxide (0.47 %), α -terpinene (0.4 %) and δ -elemene (0.31 %) (Okonogi and Chaiyana 2012). Marliani (2012) identified the following major compounds in *Z. cassumunar* rhizome essential oil: 4-terpineol (42.5 %), β -pinene (23.41 %), γ -terpinene (6.28 %) and β -sesquiphellandrene (5.92 %). Other minor components found included α -pinene, β -myrcene, α -terpinene, sabinene, *cis*-sabinene hydrate, α -terpinolene, *trans*-sabinene hydrate, thujil alcohol, linalyl acetate, linalool, α -terpineol, α -terpineol acetate and zingiberene.

Fifteen components were found in *Z. cassumunar* rhizome essential oil which consisted of sesquiterpenes (98.78 %) with and small amount of monoterpenes (1.22 %) (Tg Kamzeri et al. 2012). The major compounds were 2,6,9,9-tetramethyl-2,6,10-cycloundecatrien-1-one (60.77 %), α -caryophyllene (23.92 %) and caryophyllene oxide (6.44 %). The minor compounds were 1,5,5,8-tetramethyl-12-oxabicyclo[9.1.0]doceca-3,7-diene (3.32 %), caryophyllene (2.03 %), γ -gurjunen epoxide-(1) (1.54 %), 4,6,6-trimethyl-2-(3-methylbuta-1,3-dienyl)-3-oxatricyclo[5.1.0.0(2,4)]octane (0.76 %), 1-oxaspiro[2.5]ocatane, 5,5-dimethyl-4-(3-methyl-1,3-butadienyl) (0.52 %), 1-isopropyl-4-methylbicyclo[3.1.0]hex-2-ene (0.12 %), 3-carene (0.05 %), *o*-cymene (0.30 %), β -myrcene (0.11 %), D-limonene (0.06 %), eucalyptol (0.04 %) and γ -terpinene (0.02 %).

Among the 10 *Zingiber* species, *Z. montanum* rhizome extract showed the highest total curcuminoid content (2.633%w/w) and yielded the highest amount of essential oil (0.89 % v/w) and terpinen-4-ol content (14.5 %) (Kantayos and Paisooksantivatana 2012). Light intensity of 50 % or 25 % increased the biomass of cassumunar ginger but decreased the volatile oil content (Manochai et al. 2010). Plants grown under full sun gave maximum rhizome oil yield (15.34 ml/kg). A 120-day water deficit resulted in high volatile oil content and increased sabinene content. The quantity of volatile oil in the cassumunar ginger exposed to a 120-day water deficit was almost twice that of both the control and the sample exposed to a 30-day deficit. The highest terpinen-4-ol content was obtained after a 60-day water deficit, and (*E*)-1-(3',4'-dimethoxyphenyl) butadiene content tended to decrease with prolonged water deficiency. Fifteen compounds were identified in cassumunar ginger volatile oil α thujene, α -pinene, sabinene, β -myrcene, α -terpinene, p-cymene, β -phellandrene, γ -terpinene, sabinene hydrate, terpinolene, terpinen-4-ol, α -terpinene, terpinyl acetate, β -sesquiphellandrene and (*E*)-1-(3,4-dimethoxyphenyl)-butadiene (DMPBD).

Panichayupakaranant and Lateh (2013) reported *Z. cassumunar* to contain the following chemical compounds: phenylbutanoid monomers, namely, (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-ol (compound D); (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-yl-acetate (compound D acetate); 4-(3,4-dimethoxyphenyl)but-1,3-diene (DMPBD); 4-(2,4,5-trimethoxyphenyl)but-1,3-diene; (*E*)-1-(3,4-dimethoxyphenyl)but-1-ene; (*E*)-3-hydroxy-1-(3,4-dimethoxyphenyl)but-1-ene; (*E*)-4-(4-hydroxy-3-methoxyphenyl)but-2-en-1-ol; (*E*)-4-(4-hydroxy-3-methoxyphenyl)but-3-en-1-yl acetate; (*E*)-2-hydroxy-4-(3,4-dimethoxyphenyl)but-3-en-1-ol; (*E*)-2-methoxy-4-(3,4-dimethoxyphenyl)but-3-en-1-ol and (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-O- β -D-glucopyranoside; phenylbutanoid dimers (cyclohexane derivatives), namely, *trans*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene; *trans*-3-(4-hydroxy-3-methoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene; *trans*-3-(2,4,5-

trimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohexene; *cis*-3-(2',4',5'-trimethoxyphenyl)-4-((*E*)-2''',4''',5'''-trimethoxystyryl)cyclohex-1-ene (compound C); *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-3''',4'''-dimethoxystyryl]cyclohex-1-ene; *cis*-3-(3',4'-dimethoxyphenyl)-4-(*E*)-2''',4''',5'''-trimethoxystyryl)cyclohex-1-ene and *cis*-1,2-bis[(*E*)-3,4-dimethoxystyryl]cyclobutane; aryl phenylbutanoids (naphthoquinone derivatives), namely, 2-methoxy-8-(3',4'-dimethoxyphenyl)-1,4-naphthoquinone and 2-methoxy-8-(2',4',5'-dimethoxyphenyl)-1,4-naphthoquinone; curcuminoids, namely, curcumin, cassumunin A, cassumunin B, cassumunin, cassumunarin A, cassumunarin B and cassumunarin C; monoterpenoids, namely, terpinen-4-ol, sabinene, β -pinene, α -pinene, (*Z*)-ocimene, δ -3-carene, γ -terpinene, α -terpinene, α -terpineol, *p*-cymene, terpinolene, myrcene, α -thujene, α -phellandrene, β -phellandrene, linalool, *cis*-linalool oxide, isopulegol, citronellal and *cis*-piperitol; and sesquiterpenoids, namely, 2,6,9,9-tetramethyl-2,6,10-cycloundecatriene-1-one, α -caryophyllene, β -caryophyllene, zerumbone, β -sesquiphellandrene, β -bisabolene, δ -elemene, γ -elemene, α -zingiberene, α -humulene, (*Z*)-nerolidol, (*E*)-nerolidol, γ -cadinene, juniper camphor, germacrene D, γ -selinene, α -selinene and α -bergamotene.

Total arsenic contents (dry weight basis) in six edible Zingiberaceous rhizomes, namely, *Alpinia galanga* (Khaa), *Boesenbergia rotunda* (Kra-chaai), *Curcuma longa* (Khamin-chan), *Curcuma zedoaria* (Khamin-oi), *Zingiber cassumunar* (plai) and *Zingiber officinale* (ginger) were found to be 92.4, 103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively (Ubonnuch et al. 2013). Total inorganic arsenic contents were 92.4, 103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively. All investigated amounts of total and inorganic arsenic were much lower than limits recommended by Thai Food and Drug Administration.

Two bioactive phenylbutanoids of *Z. cassumunar*, (*E*)-4-(2',4',5'-trimethoxyphenyl)but-1,3-diene and (*E*)-4-(2',4',5'-trimethoxyphenyl)but-1-ene were synthesised (Sinha et al. 2005). Tuntiwachwuttikul et al. (1980) synthesised the following aromatic compounds from *Z. cassumunar*, *cis*-3-

(2',4',5'-trimethoxyphenyl)-4-[(*E*)-2''',4''',5'''-trimethoxystyryl]cyclohex-1-ene; *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-3''',4'''-dimethoxystyryl]cyclohex-1-ene; *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-2''',4''',5'''-trimethoxystyryl]cyclohex-1-ene; (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-ol and (*E*)-4-(3',4'-dimethoxyphenyl)but-3-enyl acetate. Several phenylbutenoid derivatives were isolated from bangle (*Z. cassumunar*) rhizome: [(*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-ol], [(*E*)-4-(2',4',5'-trimethoxyphenyl)but-3-en-1-ol] and [(*E*)-4-(3',4',1-trimethoxyphenyl)but-3-en-1-ol] (Chairul and Chairul 2009; Elya et al. 2009). Phenylbutenoid dimers *trans*-3-(3'4'-dimethoxyphenyl)-4-[(*E*)-3'',4''-dimethoxystyryl]cyclohex-1-ene and *cis*-3-(3'4'-dimethoxyphenyl)-4-[(*E*)-3'',4''-dimethoxystyryl]cyclohex-1-ene were isolated from *Zingiber purpureum* (Matsui et al. 2012).

Leaf Phytochemicals

Mineral composition in *Z. purpureum* leaves (g/100 g) was reported by Kasarkar and Kulkarni (2012) as N, 2.18 g; NO³⁻, 0.071 g; P, 0.53 g; K, 1.01 g; Ca, 0.70 g; S, 0.10 g; Na, 0.4 g; Zn, 0.64 g; Fe, 4.02 g; Cu, 1.57 g; Mo, 0.0063 g; B, 0.476 g; Mg, 1.85 g; and Mn, 0.30 g.

In *Zingiber cassumunar* hydrodistilled leaf oil, 39 components were identified, and the main compounds were found to be l(10), 4-furanodien-6-one (27.3 %), curzerenone (25.7 %) and β -sesquiphellandrene (5.7 %) (Bordoloi et al. 1999). Sixty-four components were found in the leaf essential oil: sabinene (14.99 %), β -pinene (14.32 %), caryophyllene oxide (13.85 %), caryophyllene (9.47 %), γ -pinene (6.31 %), methyl *p*-methoxycinnamate (5.02 %), triquinacene, 1,4, bis(methoxy) (3.79 %), camphene (3.56 %), borneol (2.96 %), crypton 2.47 %, β -myrcene (1.46 %), apiol (1.40 %), (*Z*) 1.6.10-dodecatriene, 7,11-dimethyl-3 methylene (1.24 %), (*E*)-ocimene (1.21 %), β -sesquiphellandrene (1.21 %) and β -phellandrene (1.04 %) (Bhuiyan et al. 2008). Other minor components <1 % included (-)-spathulenol; 3,4,5-trimethoxybenzylchloride; 3-cyclobexen-1-one; 3(hydro-

xymethyl)-6-(1-methylethyl), 3-cyclohexene-1-methanol; terpinene-4-ol; *trans*-5-caranol; 5-nonol, -methyl; 7-hexadecenal; 7-oxabicyclo (2.2.1) hept-5-en-2-one; aromadendrene oxide; β -bisabolene; β -elemene; benzene-1-methyl, 4-4(1-methylethyl); *Z*- α -*trans*-bergamotol; β -linalool; β -myrcene; borneol acetate; cedrene; chamigrene; cholestan-3-ol, 2methylene-(3 β ; 5L); *cis*-bicyclo (4.4.0) decan-1-ol-3-one; cubenol; cuminal; cuminol; 3-ethenyl cyclohexanone; 5-methyl-3-(1-methylethenyl) cyclohexene; damascone; *epi*-13-manool; isogeraniol; isolimonene; juniper camphor; γ -caryophyllene; γ -methylfuran; longo pinocarvone; methylvanillin; myrtanal; ocimene; pentadecyne; phellandral; pinocarvone; pseudo limonene; τ -muurol; tetra[6.3.2.0(25),0(1,8)] tridecan-9-ol,4,4-dimethyl; *trans*-nerolidol; *trans*-pinocarveol and triquinacene, 1,4,7-tris (methoxy).

Antioxidant Activity

The antioxidant activity of *Zingiber cassumunar* ginger was found to be greater than its curcuminoids curcumin, demethoxycurcumin and bisdemethoxycurcumin as assessed by the isothiocyanate and thiobarbituric acid assays (Jitoe et al. 1992). Three curcuminoids, diferuloylmethane, (*p*-hydroxycinnamoyl)-feruloylmethane and *p,p'*-dihydroxyldioinna-moyldethane, were obtained after purification. The most active antioxidant fraction from the organic extract of *Z. cassumunar* rhizomes was found to contain three potent antioxidants, cassumunarin A, B and C, which were found to represent a new type of complex curcumin (Jitoe et al. 1994). The antioxidant activity of cassumunins A, B and C was stronger than that of curcumin as determined by inhibitory activity of autooxidation of linoleic acid in a buffer–ethanol system (Masuda and Jitoe 1994; Matsuda et al. 1995). Pretreatment of rat thymocytes with cassumunin A and cassumunin B, from *Z. cassumunar*, at concentrations ranging from 100 nM to 3 μ M dose dependently prevented the hydrogen peroxide (H₂O₂)-induced decrease in cell viability (Nagano et al. 1997). Respective potencies of cassumunins A and B in protecting the cells

suffering from H₂O₂-induced oxidative stress were greater than that of curcumin. Fresh rhizome samples collected from six different sources in Thailand showed significantly different DPPH scavenging activities (Buain and Paisooksantivatana 2009). The antioxidant activities of the rhizome extract obtained from the north showed the highest activity (80.88 %), followed by those from the east (76.47 %), the south (72.51 %), the northeast (67.38 %), the west (66.66 %) and the central region (57.63 %).

Zingiber montanum rhizome exhibited strong antioxidant potential as assessed by sulphur (thiyl) free radical (GS.) reactivities using curcumin as reference indicator (Chirangini et al. 2004). The rhizome was reported to have antioxidant index 10.9 as evaluated by β -carotene bleaching method and to contain 5.87 mg% vitamin C, 0.0065 mg% vitamin E, 1.27 mg% total carotenes, 0.54 mg% total xanthophylls, 1.18 mg% tannins and 83.9 mg/% phenolics (Chanwitheesuk et al. 2005). Using chemical assays like diphenylpicrylhydrazyl (DPPH), superoxide (O₂⁻) and hydroxyl (OH[·]) free radical scavenging methods, methanol extract of the rhizome was found to possess significant antioxidant potential (Sharma et al. 2007). Increased percent of DPPH decolouration from 50 to 500 μ g/ml indicated concentration-dependent scavenging activity of DPPH radicals by the crude extract of this species. Even at a low concentration of 1 μ g/ml, the rhizome extract showed strong (similar to 75 %) OH scavenging activity. Similarly, the crude extract showed a concentration-dependent inhibition of O-2 radical production where a concentration of 50 μ g/ml almost showed 100 % inhibition.

The antioxidant activities of cassumunar ginger were 52.98 %, 41.75 % and 42.93 % in plants grown at 100 %, 50 % and 25 % sunlight, respectively (Manochai et al. 2010). Light intensity of 50 % or 25 % increased the biomass of cassumunar ginger but decreased the volatile oil content; antioxidant activity was not significantly affected. A 120-day water deficit resulted in high volatile oil content and increased sabinene content, but DPPH scavenging activity was not affected. *Z. montanum* rhizome extract had a total phenolic content of 6.53 mg GAE/g DW and exhibited antioxidant

activity and in the DPPH assay with IC₅₀ of 4.71 mg/ml IC₅₀ and in the ABTS assay with IC₅₀ of 13.91 mg/ml (Kantayos and Paisooksantivatana 2012).

Anticancer Activity

Z. montanum rhizome extract at low concentration exhibited high cytotoxic properties as revealed by MTT assay using NIH 3 T3 mouse fibroblast cell line (Sharma et al. 2007). Curcumin from *Z. cassumunar* rhizome showed significant cytotoxicity against several human cancer cell lines, Col2 human colon cancer (IC₅₀ of 2.30 µg/ml), lung carcinoma A549 (IC₅₀ 12.30 µg/ml) and SNU638 stomach cancer (IC₅₀ 18.80 µg/ml) (Han et al. 2003). The phenylbutenoid dimer (±)-*trans*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene (PSC), isolated from *Zingiber cassumunar*, arrested cell cycle progression of lung carcinoma A549 at the G₀/G₁ phase in a concentration- and time-dependent manner (Lee et al. 2007). The results suggested that one of the antiproliferative mechanisms of PSC was to suppress cell cycle progression by increasing p21 expression and downregulating cyclins and cyclin-dependent kinases. Of five phenylbutenoid derivatives from *Z. cassumunar* rhizomes, compound (1) (±)-*trans*-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene exhibited highly potent P-glycoprotein inhibitory activity, decreasing the IC₅₀ value of daunomycin (DNM) to 4.31 µM in multidrug-resistant (MDR) human breast cancer cell line, MCF-7/ADR (DNM IC₅₀ = 37.1 µM) (Chung et al. 2009). In the positive control, verapamil decreased the IC₅₀ value of DNM to 6.94 µM. Three phenylbutenoid monomers also resulted in a significant decrease in the IC₅₀ values of DNM compared with the control. Compound (1) markedly enhanced [(3)H]-DNM accumulation and significantly reduced [(3)H]-DNM efflux compared with the control, and this effect was more potent than that of verapamil, a well-known P-glycoprotein inhibitor. The results suggested that compound 1 of *Z. cassumunar* could be developed as a potent chemosensitising agent that reverses P-gp-mediated MDR in human cancer chemotherapy. The methanolic extract and its ethyl

acetate-soluble fraction from the rhizomes of *Zingiber cassumunar* inhibited invasion of human fibrosarcoma HT 1080 cells (Matsuda et al. 2011). Among the constituents, phlains I and III, (*E*)-1-(3,4-dimethoxyphenyl)buta-1,3-diene, (*E*)-1-(2,4,5-trimethoxyphenyl)buta-1,3-diene and (–)- β -sesquiphellandrene showed anti-invasion effects. Interestingly, (*E*)-1-(2,4,5-trimethoxyphenyl)buta-1,3-diene [inhibition 46.8 % at 30 μ M] significantly inhibited the invasion, and only a weak cytotoxic effect was observed. The phenylbutenoid dimer, *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-3''',4'''-dimethoxystyryl]cyclohex-1-ene (ZC-B11), isolated from *Zingiber cassumunar* rhizome exhibited cytotoxic activity on various cancer cell lines (Anasamy et al. 2013). ZC-B11 was found to exert the most potent antiproliferative effect towards T-acute lymphoblastic leukaemia CEMss cells with IC₅₀ value of 7.11 μ g/mL followed by HepG2, MCF-7, MDA-MB-231 and HeLa cells with IC₅₀ values of 17.65 μ g/mL, 21.28 μ g/mL, 32.38 μ g/mL and >50 μ g/mL, respectively, after 72 h incubation. It was found that ZC-B11 exhibited apoptogenic properties in T-acute lymphoblastic leukaemia cells via induction of p53-independent mitochondrial signalling pathway. The compound exhibited no cytotoxic effects towards normal human blood mononuclear cells. Terpinen-4-ol from plai rhizome was found to induce human leukaemic MOLT-4 cell apoptosis via both intrinsic pathway involving the loss of mitochondrial transmembrane potential (MTP) and release of cytochrome c into the cytosol and extrinsic pathway by caspase-8 activation resulting in the cleavage of cytosolic Bid (Khaw-on and Banjerdpongchai 2012).

Antiviral Activity

Seven Zingiberaceous rhizomes including *Z. cassumunar* were found to possess inhibitory activity towards Epstein–Barr virus early antigen (EBV-EA) activation, induced by 12-*O*-tetradecanoyl phorbol-13-acetate (TPA) (Vimala et al. 1999). The rhizome extracts that exhibited EBV activation inhibitory activity had no cytotoxicity effect in Raji cells. *Zingiber montanum* was one of the four herbs that could reduce >50 % of infectivity of highly pathogenic avian influenza virus

(H5N1) in a cell-based assay (Klaywong et al. 2014). It was able to inhibit association between nonstructural protein 1 RNA binding domain (RBD) and double-stranded (ds) RNA in electrophoresis mobility shift assay.

Antimicrobial Activity

Extracts from several Zingiberaceous species, especially *Alpinia galanga*, *Curcuma zedoaria* and *Zingiber purpureum*, were found to have pronounced inhibitory activities in-vitro against a wide variety of human pathogenic fungi, including strains resistant to the common antifungals amphotericin B and ketoconazole such as *Cryptococcus neoformans*, *Saccharomyces cerevisiae*, *Candida albicans*, *Wangiella dermatitidis*, *Alternaria alternata*, *Aspergillus fumigatus*, *Fusarium oxysporum*, *Microsporum gypseum*, *Rhizopus sp.*, *Trichophyton mentagrophytes* and *Pseudallescheria boydii* (Ficker et al. 2003). Terpinen-4-ol and sabinene, from *Z. cassumunar* extract, exhibited antimicrobial activity in-vitro (Giwanon et al. 2000). Terpinen-4-ol was active against nice bacterial species with MUC of 2–5 mg/ml, while sabinene was not active against *Escherichia coli*, *Salmonella typhimurium*, *Bacteroides fragilis* and *Peptococcus sp.* The ethno rhizome extract inhibited growth of *E. coli* with MIC (minimum inhibitory concentration) of 12.5 % and MBC (minimum bactericidal concentration) of 25 % (Raharjoyo and Gunardi 2009).

Z. cassumunar essential oil exhibited high activity against the yeasts *Saccharomyces cerevisiae*, *Cryptococcus neoformans*, *Candida albicans*, *Candida tropicalis* and *Torulopsis glabrata* with inhibition zones of 11.7–15.7 mm (Jantan et al. 2003). *Zingiber cassumunar* essential oil exhibited antimicrobial activity against a wide range of Gram-positive and Gram-negative bacteria, dermatophytes and yeasts (Pithayanukul, et al. 2007). Dermatophytes were found to be the most susceptible microorganisms followed by yeasts, whereas bacteria were the least susceptible. The minimum bactericidal concentration (MBC) ranged from 0.62 to 2.5 vol % for plai oil and from 52 to 79 mg/mL for the 5 wt % plai oil gel, whereas the minimum fungicidal concentration (MFC)

ranged from 0.31 to 1.25 vol % for plai oil and from 13.8 to 39.5 mg/mL for the 5 % plai oil gel. The crude ethanolic extract of *Z. cassumunar* rhizome inhibited only *Corynebacterium* sp. (Prakatthagomol et al. 2012). The essential oil of *Z. cassumunar* rhizome inhibited *Escherichia coli* and *Pasteurella multocida*, whereas its crude extract did not. The antibacterial action of the oil appeared to be a bactericidal effect. *Z. cassumunar* rhizome essential oil inhibited *Staphylococcus aureus* dan *E. coli* with MBC of 3.125 % (Marliani 2012).

Anti-inflammatory Activity

The methanol extract of *Z. cassumunar* rhizome (p.o.) which exhibited anti-inflammatory activity in the carrageenin-induced oedema in rats was found to be associated with its active constituent (*E*)-1-(3,4-dimethoxyphenyl)but-1-ene (Ozaki et al. 1991). The anti-inflammatory activity of cassumunins A, B and C was stronger than that of curcumin as measured by inhibition of oedema formation on mouse ear induced by 12-*O*-tetradecanoylphorbol-13-acetate (Matsuda et al. 1993; Matsuda and Jitoe 1994; Matsuda et al. 1995).

Two phenylbutenoid dimmers from *Z. cassumunar* rhizomes, (±)-trans-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene and (±)-trans-3-(4-hydroxy-3-methoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene exhibited considerable cyclooxygenase-2 (COX-2) inhibitory activity with IC₅₀ values of 2.71 and 3.64 μM as measured by prostaglandin E2 production in lipopolysaccharide-stimulated mouse macrophage RAW 264.7 cells (Han et al. 2005). Two phenylbutenoid monomers, 4-(2,4,5-trimethoxyphenyl)-but-1,3-diene and 4-(3,4-dimethoxyphenyl)but-1,3-diene, showed moderate activity (IC₅₀ 14.97, 20.68 μM, respectively). The other three phenylbutenoids, (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-ol, (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-yl acetate and (*E*)-4-(3,4-dimethoxy-phenyl)but-3-en-1-*O*-β-D-glucopyranoside (7), were found to be inactive. The essential oil of the rhizome of *Zingiber cassumunar* exhibited a topical anti-inflammatory effect, when tested using the model of

carrageenan-induced hind paw oedema in rats ($ID_{50} = 22$ mg oil/paw) (Pongprayoon et al. 1997a). Of the five major components of the oil (*E*)-1-(3,4-dimethoxyphenyl)butadiene (DMPBD), terpinen-4-ol and α -terpinene significantly inhibited oedema formation, whereas sabinene and γ -terpinene were inactive up to 6 mg/paw. The most active compound, DMPBD, was found to be an anti-inflammatory agent twice as potent as the reference drug diclofenac ($ID_{50} = 3$ vs. 6 mg/paw, respectively). A hexane extract of *Zingiber cassumunar* rhizome exhibited topical anti-inflammatory activity, when tested in the model of 12-O-tetradecanoylphorbol-13-acetate-induced ear oedema in rats ($ID_{50} = 854$ μ g/ear) (Pongprayoon et al. 1997b). Five active components were isolated from the extract and identified as (*E*)-4-(3',4'-dimethoxyphenyl)but-3-enyl acetate; *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-3''',4'''-dimethoxystyryl]cyclohex-1-ene; *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-2''',4''',5'''-trimethoxystyryl]cyclohex-1-ene; *cis*-3-(2',4',5'-trimethoxyphenyl)-4-[(*E*)-2''',4''',5'''-trimethoxystyryl]cyclohex-1-ene; and (*E*)-4-(3'-4'-dimethoxyphenyl)but-3-en-1-ol. Compounds 1–5 exerted potent topical anti-inflammatory activities with ID_{50} values of 62, 21, 20, 2 and 47 μ g/ear, respectively. The ID_{50} of the reference drug diclofenac was determined to be 61 μ g/ear. Compound D, (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-2-ol, from the hexane extract of *Z. cassumunar* rhizome, exerted marked inhibition on carrageenin-induced rat paw oedema as well as on the exudate formation, leukocyte accumulation and prostaglandin biosynthesis in carrageenin-induced rat pleurisy (Panthong et al. 1990, 1997). Compound D possessed only slight inhibition on both primary and secondary lesions of adjuvant-induced arthritis and had no effect on cotton pellet-induced granuloma.

(*E*)-1-(3,4-dimethoxyphenyl) butadiene (DMPBD), isolated from *Z. cassumunar*, dose dependently inhibited the rat ear oedema induced by ethyl phenylpropionate (EPP), arachidonic acid (AA) and 12-O-tetradecanoylphorbol 13-acetate (TPA), and it was more potent than any other standard drugs being used (Jeenapongsa et al. 2003). In EPP-induced

oedema, IC_{50} of DMPBD and oxyphenbutazone were 21 and 136 nmol per ear, respectively. The IC_{50} of DMPBD and phenidone were 60 and 2520 nmol per ear, respectively, in AA-induced oedema, whereas DMPBD was 11 times more potent than diclofenac in TPA-induced oedema (IC_{50} = 660 and 7200 pmol per ear, respectively). DMPBD and diclofenac inhibited the rat paw oedema induced by carrageenan but not by platelet activating factor (PAF). In in-vitro study DMPBD, aspirin and phenidone inhibited collagen-induced platelet aggregation with IC_{50} of 0.35, 0.43 and 0.03 mM, respectively. Whereas IC_{50} of these agents in ADP, AA and PAF inductions were 4.85, 3.98 and 1.30 mM; 0.94, 0.13 and 0.04 mM; and 1.14, 6.96 and 2.40 mM, respectively. These results indicated that DMPBD possessed potent anti-inflammatory activity through the inhibition of cyclooxygenase and lipoxygenase pathway and seems to have more prominent effects on the lipoxygenase pathway.

Z. cassumunar extract, at 25 and 50 $\mu\text{g/mL}$, with or without 10 μM of retinoic acid, significantly decreased hyaluronan levels in cultured human oral fibroblasts (Ong-Chai et al. 2009). Consistent with decreased hyaluronan levels, mRNA expression of hyaluronan synthase-2, but not hyaluronan synthase -1 or hyaluronan synthase -3, was selectively downregulated by the extract. Collectively, the data indicated that the ethanol extract of *Z. cassumunar* inhibited hyaluronan synthesis in human oral fibroblasts, which may be involved in chronic inflammatory disorders, particularly in the oral cavity. The methanolic extract of *Zingiber cassumunar* rhizomes showed nitric oxide (NO) production inhibitory effects induced by lipopolysaccharide (LPS) in mouse peritoneal macrophages (Nakamura et al. 2009). Among its constituents, phlavin III (IC_{50} = 24 μM), (*E*)-1-(3,4-dimethoxyphenyl)buta-1,3-diene (69 μM), (*E*)-1-(2,4,5-trimethoxyphenyl)buta-1,3-diene (83 μM) and cassumunaquinone 1 (47 μM) displayed inhibitory effects. Active compounds, terpinene-4-ol and (*E*)-1-(3,4-dimethoxyphenyl) butadiene (DMPBD), displaying anti-inflammatory activity, were successfully extracted from

Zingiber cassumunar rhizome by pressurised liquid extraction (PLE) using methanol or ethanol and by superheated water extraction (Chienthavorn et al. 2011).

Plai oil extracted from *Zingiber cassumunar* rhizome which contained (*E*)-1-(3,4-dimethoxyphenyl) butadiene (DMPBD) as active ingredient had been proven to exert anti-inflammatory effect (Nakrong and Bunrathep 2013). Eighteen formulas of plai emulgel were formulated by various type and concentrations of gel-forming agents (1–2 % w/w), such as carbopol 121, carbopol 934, carbopol 940, hydroxypropyl cellulose (HPC), hydroxypropylmethyl cellulose (HPMC) and methyl cellulose (MC), combined with similar amount of plai oil (5 % w/w), propylene glycol (20 % w/w), EDTA (0.2 % w/w) and paraben concentrate (0.2 % w/w). The best formula showing outstanding results was number 4 containing 1 % carbopol 934 as gel-forming agent along with 5 % plai oil, 20 % propylene glycol, 0.2 % EDTA and 0.2 % paraben concentrate. After 180 days, the content of the marker (DMPBD) in this formula, kept at 15 °C, was still more than 95 %.

The anti-inflammatory activity of phenylbutanoid-enriched (48.3 %) *Z. cassumunar* extracts via inhibition of nitric oxide production by murine macrophage-like RAW264.7 cells was stronger than those of the four individual phenylbutanoids, (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-ol (I), (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-yl acetate (II), (*E*)-1-(3,4-dimethoxyphenyl)butadiene (III) and (*E*)-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene (IV), the crude hexane extract and *Z. cassumunar* essential oil (Kaewchoothong et al. 2012). Studies found that *Zingiber cassumunar* (Phlai) and some of its constituents could reduce inflammation by reducing cyclooxygenase COX-2 and PGE2 production in human dental pulp cells stimulated by with lipopolysaccharide (LPS) (Aupaphong et al. 2013). These phlai constituents *cis*-3-(3',4'-dimethoxyphenyl)-4-[(*E*)-3''',4'''-dimethoxystyryl]cyclohex-1-ene (compound B), *cis*-3-(2',4',5'-trimethoxyphenyl)-4-[(*E*)-2''',4''',5'''-trimethoxystyryl]cyclohex-1-ene (compound C) and (*E*)-1-(3',4'-dimethoxyphenyl)but-1,3-diene (DMPBD) could reduce

PGE2 level and COX-2 expression. *Cis*-3-(3',4'-dimethoxyphenyl)-4-

[(*E*)-2''',4''',5'''-trimethoxystyryl]cyclohex-1-ene (compound C) reduced PGE2 levels but had less effect on COX-2. All constituents showed no significant change on COX-1.

Of six Zingiberaceous plants, ethanolic rhizome extract of *Kaempferia parviflora* exhibited the most potent anti-allergic effect against antigen-induced β -hexosaminidase release as a marker of degranulation in RBL-2H3 cells, with an IC_{50} value of 10.9 μ g/ml, followed by *Zingiber cassumunar* (EtOH, IC_{50} = 12.9 μ g/ml) and *Curcuma mangga* (water, IC_{50} = 36.1 μ g/ml) (Tewtrakul and Subhadhirasakul 2007). The volatile oils of these six plants were apparently inactive (IC_{50} > 100 μ g/ml). Crude phlai extracts (0.25–2.0 mg/ml) and its constituent (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-ol (compound D) (0.5–4.0 mg/ml) inhibited pro-MMP (matrix metalloproteinase)-9 cleavage by house dust mite (Poachanukoon et al. 2015). Additionally, crude phlai extracts (100 μ g/ml) and compound D, at concentrations of 50 and 100 μ g/ml, attenuated the phorbol 12-myristate 13-acetate (PMA)-induced MMP-9 gene and expression in airway epithelial cells (NCI-H292).

The active compound of *Z. cassumunar*, (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-ol (compound D), at the concentration of 10–100 μ M significantly decreased the mRNA expressions of matrix metalloproteinases MMP-1, -2, -3 and -13 in which was induced by interleukin IL-1 β in human synovial fibroblast cell line, SW982 (Chaiwongsa et al. 2013). An increase in the mRNA expression of IL-1 β and ICE was also suppressed by compound D. The results suggested that the potent activities of this compound may be involved in the reduction of IL-1 β protein synthesis in both pro-form and active form which played an important role in upregulation of MMPs. The results revealed that the chondroprotective activity of *Z. cassumunar* in the transcriptional level by suppressing cytokine-induced catabolic genes caused cartilage erosion in rheumatoid arthritis. A double-blind, randomised,

controlled trial of the combination of 4 % ginger (*Z. officinale*) and plai (*Z. cassumunar*) extract in a gel (Plygersic gel) comparing with 1 % diclofenac in 50 patients with osteoarthritis knees found that both treatments could significantly improve knee joint pain, symptoms, daily activities, sports activities and quality of life measured by KOOS following 6 weeks of treatment (Niempoog et al. 2012). Plygersic gel and 1 % diclofenac relieved joint pain, improved problematic symptoms and improved the quality of life in osteoarthritis knee patients during a 6-week treatment regimen. Results of in-vitro studies indicated that *Z. cassumunar* extracts inhibited cyclooxygenase-2 and matrix metalloproteinases MMP-2 production by lipopolysaccharide-activated human gingival fibroblasts by blocking proinflammatory signalling pathway involving ERK1/2, JNK and p38 (Koontongkaew et al. 2013). Ninomiya et al. (2013) found that oral treatment with 50 µL of 40 mg/mL terpinen-4-ol 3 h after the *Candida albicans* oral infection clearly suppressed the increase of the inflammatory symptoms such as pain in the tongue, oedema or tissue damage. In-vitro analysis of the effects of terpinen-4-ol on cytokine secretion of macrophages indicated that 800 µg/mL of this substance significantly inhibited the cytokine production of the macrophages cultured in the presence of heat-killed *C. albicans* cells.

In-vitro studies using the Caco-2 cell monolayer model found that compounds (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-yl linoleate, (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-yl oleate (2) and (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-yl palmitate originated from Prasaplai preparation (a Thai herbal formula of *Z. cassumunar* and *Nigella sativa*) may be transported through a facilitated mechanism and may serve as anti-inflammatory prodrugs to increase the compound D (*E*)-4-(3,4-dimethoxyphenyl)but-3-en-1-ol (a bioactive ingredient of *Z. cassumunar*) level in the blood (Tangyuenyongwatana et al. 2009).

Clinical Studies

In a double-blinded randomised controlled study of patients with ankle sprain, treatment with a topical cream Phygesal containing 14 % phlai rhizome oil for 7 days was found to be efficacious in reducing pain and severity of swelling (Laupattarakasem et al. 1993). Patients were taking less analgesics (paracetamol) during the first two days. The treated ankles could dorsiflex more than the placebo group, but magnitude of plantar flexion was not different between both groups. In another randomised double-blinded, placebo controlled clinical trial conducted in 60 healthy volunteers with mild to moderate acne vulgaris, the group treated with plai gel had higher reduction in non-inflammatory and inflammatory acne lesions at 2 and 4 weeks as compared to the placebo (Limwattananon et al. 2008). Plai gel was safe. Adverse events were not found in the study. The compliance to use plai gel was greater than 90 %.

Antiasthmatic Activity

In an acute asthmatic attack study of asthmatic children (9–13 years old), oral administration of plai (260 mg) was found to improve pulmonary function parameters such as VC (vital capacity), FEV₁ (forced expiratory volume in one second) and PEF_R (peak expiratory flow rate) after 2 h, while pulse and blood pressure were not changed (Tuchinda et al. 1984). In a long-term asthma treatment of children (9–14 years old), 3 months oral administration of plai (130 mg) revealed significant reduction of medication scores and improvement of VC and morning PEF_R during treatment with plai, while FEV₁ and evening PEF_R were not changed. Neither side effect nor toxic effect was found after plai treatment in both parts of study. In an open study on 22 individuals (8 men and 16 women, aged 19–44 with mean age 44.1 years) with moderate bronchial asthma, twice daily oral administration of *Z. cassumunar* (500 mg for body weight ≤55 kg, 1001 mg for body weight >55 kg) for 16 weeks gave significant protection against asthmatic attacks in 19 out of 22 cases (86.4 %) (Youngchaiyud et al. 1985). Statistically, significant reduction in asthmatic symptoms and the reduction in the use of bronchodilators and steroids were noted between 1–3 and 2–4

months after treatment, respectively. Statistically, significant improvement in peak expiratory flow rate and FEV₁ was also noted in the second month of treatment. Slightly increased frequency in bowel movement was noted in 5 patients, and one patient complained of mild headache.

Analgesic Activity

The methanol extract of *Z. cassumunar* rhizome (p.o.) exhibited analgesic activity in acetic acid-induced vascular permeability, and writhing test in mice found to be associated with its active constituent (*E*)-1-(3,4-dimethoxyphenyl)but-1-ene (Ozaki et al. 1991). Compound D, (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-2-ol, from the hexane extract of *Z. cassumunar* rhizome, elicited analgesic activity when tested on acetic acid-induced writhing response in mice but had weak inhibitory activity on tail flick responding to radiant heat (Panthong et al. 1997). Suksaeree et al. (2014b) successfully prepared plai patches from different polymer blends (chitosan/hydroxypropylmethyl cellulose blends and chitosan/polyvinyl alcohol blends) with suitable physicochemical properties for use in topical applications for pain and inflammation relief. The content of (*E*)-4-(3', 4'-dimethoxyphenyl)-but-3-en-1-ol content was 5.33 mg and 8.75 mg in 2 cm × 2 cm for chitosan/hydroxypropylmethyl cellulose/glycerine plai patches and chitosan/polyvinyl alcohol/glycerine plai patches, respectively (Suksaeree et al. 2014a)

Anaesthetic Activity

Plai juice was found to have local anaesthetic effects (Anantasanta and Asayakun 1975). It reduced pain, and at a concentration of 300 mg/ml, it reduced conductivity in the sciatic nerve of the toad (84.46 %), while the drug lidocaine at a concentration of 0.2 mg/ml reduced conductivity by 93.09 %.

Central Nervous System Activity

Studies by Okonogi and Chaiyana (2012) found that *Z. cassumunar* oil possesses inhibitory activity against not only acetylcholinesterase (AChE) but also butyrylcholinesterase (BChE). Formulation of cassumunar oil as microemulsion revealed that alkyl chain length and number of hydroxyl groups of cosurfactant exhibited a remarkable effect on the pseudoternary phase diagram. The suitable *Z. cassumunar* oil microemulsion was composed of Triton X-114 in combination with propylene glycol. The anti-cholinesterase activity of this microemulsion was much higher than that of native *Z. cassumunar* oil. It exhibited twenty times and twenty five times higher inhibitory activity against AChE and BChE, respectively.

Phenylbutenoid dimers *trans*-3-(3'4'-dimethoxyphenyl)-4-[(*E*)-3'',4''-dimethoxystyryl]cyclohex-1-ene (Comp.1) and *cis*-3-(3'4'-dimethoxyphenyl)-4-[(*E*)-3'',4''-dimethoxystyryl]cyclohex-1-ene (Comp.2), isolated from *Zingiber purpureum*, significantly induced neurite sprouting in PC12 cells and significantly increased neurite length and number of neurites in primary cultured rat cortical neurons (Matsui et al. 2012). In-vivo chronic treatment with fluoxetine or both compounds significantly increased the number of BrdU/NeuN double-labelled cells in dentate gyrus of olfactory bulbectomized (OBX) mice. The results indicated that both compounds had neurotrophic effects and the potential for disease modification in depression and dementia.

Phenylbutenoid dimers *trans*-3-(3'4'-dimethoxyphenyl)-4-[(*E*)-3'',4''-dimethoxystyryl]cyclohex-1-ene (compound 1) and *cis*-3-(3'4'-dimethoxyphenyl)-4-[(*E*)-3'',4''-dimethoxystyryl]cyclohex-1-ene (compound 2), isolated from *Zingiber purpureum*, significantly induced neurite sprouting in PC12 cells and significantly increased neurite length and number of neurites in primary cultured rat cortical neurons (Matsui et al. 2012). In-vivo chronic treatment with both compounds or fluoxetine significantly increased the number of BrdU/NeuN double-labelled cells in dentate gyrus of olfactory bulbectomized (OBX) mice. The results indicated that both compounds had neurotrophic effects, and the potential for disease modification in depression and dementia.

Immunomodulatory Activity

Of several phenylbutenoid derivative isolated from *Z. cassumunar*, [(*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-ol] compound had the highest immunostimulant activity (99.0 %) compared to compound [(*E*)-4-(2',4',5'-trimethoxyphenyl)but-3-en-1-ol] (93.7 %) and [(*E*)-4-(3',4',1-trimethoxyphenyl)but-3-en-1-ol] (80.0 %) (Chairul and Chairul 2009). The ethyl acetate fraction of *Z. cassumunar* rhizome methanol extract showed the greatest immunostimulant activity, produced by three phenylbutanoids (Elya et al. 2009). One of them was a potent immunostimulant [(*E*)-4-(3',4'-dimethoxyphenyl) but-3-en-1-ol]; the other two compounds [(*E*)-4-(2',4', 5'-trimethoxyphenyl)-3-en-1-ol and (*E*)-4-(3',4'-dimethoxyphenyl)-3-en-1-methoxy-1-ol] were less effective.

Antipyretic Activity

Compound D, (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-2-ol, from the hexane extract of *Z. cassumunar* rhizome, possessed marked antipyretic effect when tested on yeast-induced hyperthermia in rats (Panthong et al. 1997).

Antihyperlipidaemic/Antiobesity Activity

Of the three traditional herbal slimming agents, the ethanol rhizome extract of *Z. cassumunar*, at 100 ppm, exhibited the highest inhibition effect on the activity of pancreatic lipase (29.17 %) (Iswantini et al. 2011). The inhibitory effect was higher than 100 ppm of Xenical[®]/orlistat as the positive control, with the inhibition rate of 17.53 %.

Gastroprotective Activity

The methanol extract of *Zingiber montanum* rhizome showed 61.97 % and 83.10 % inhibition of the 1 N HCl-induced gastric lesions at doses of 200 mg/kg and 400 mg/kg, respectively, in mice (Al-Amin et al. 2012). Its active constituent, zerumbone, showed potent cytoprotective effect against necrotising agent (HCl) and non-steroidal anti-

inflammatory drug (indomethacin)-induced gastric ulceration in mice. It also exhibited moderate cytoprotective effect against noxious agent (ethanol)-induced gastric lesions.

Cytochrome P450 3A4 Inhibition Activity

Methanol extract of *Z. cassumunar* rhizome at 0.5 mg/ml exhibited more than 30 % increase of cytochrome CYP3A4 inhibition via erythromycin N-demethylation and dextromethorphan O-demethylation activities in human liver microsomes (Subehan et al. 2006).

Angiotensin I-Converting Enzyme Inhibitory

Of 15 Zingiberaceous plant rhizome, pepsin hydrolysates from *Zingiber cassumunar* revealed the highest angiotensin I-converting enzyme inhibitory activity (IC₅₀ of 0.38 mg/mL) and was enriched to a single active hexapeptide by RP-HPLC with a strong angiotensin I-converting enzyme inhibitory activity (IC₅₀ of 0.011 2 mg/mL) and acted as a competitive inhibitor of angiotensin I-converting enzyme (K(i) of 1.25×10^{-6} mg protein/mL) (Yodjun et al. 2012).

Uterine Relaxant Activity

(*E*)-4-(3',4'-Dimethoxyphenyl)-but-3-en-1-ol, compound D, from *Zingiber cassumunar* rhizome hexane extract, exhibited a dose-related uterine relaxant effect when tested in the rat uterus (non-pregnant) Kanjanapothi et al. 1987). The uterine response of pregnant rats varied with the stage of pregnancy, and the uterus of the post-implantation period was found to be the most sensitive. The study found that compound D did not act via β -adrenergic receptor stimulation, but might share with papaverine a similar mechanism of action.

Radioprotective Activity

Zingiber montanum ethanol extract protected bone marrow cells in rats from γ -radiation-induced chromosomal (breaks,

fragments, gaps, rings, endoreduplications and dicentric chromosomes) (Thokchom et al. 2012). Intraperitoneal administration of the extract at a dose of 0.5 g/kg considerably reduced the frequency of the aberrations stated above in irradiated animals with DMF (dose modification factor) value of 1.36 at 1–5 Gy dose range of γ -radiation. The incidence of micronucleated polychromatic erythrocytes and micronucleated normochromatic erythrocytes due to the radiation exposure was considerably reduced in extract-treated rats with DMFs 1.34 and 1.17, respectively, as compared to that of the extract-untreated groups. *Z. cassumunar* rhizome extracts with 60 % ethanol were found to protect plasmid pBR322 DNA exposed to varying doses of γ -radiation to a very significant extent (Sharma and Thokchom 2011). Various types of chromosomal abnormalities induced in rat bone marrow cells by γ -radiation could be effectively protected in animals fed with *Z. montanum* rhizome extract through oral or intraperitoneal administration.

Chondroprotective Activity

Two compounds, *cis*-3-(2',4',5'-trimethoxyphenyl)-4-{{(*E*)-2''',4''',5'''-trimethoxystyryl}cyclohex-1-ene and (*E*)-4-(3',4'-dimethoxyphenyl)but-3-en-1-ol, isolated from the hexane fraction exhibited chondroprotective potential against cytokine-induced cartilage degradation in explant culture (Chaiwongsa et al. 2012). At concentrations of 10 and 100 μ M, both compounds significantly inhibited the IL-1 β -induced cartilage degeneration by conserving the content of the cartilage matrix biomolecules such as collagen and uronic acid (UA) within the cartilage explants and also resulted in the decline of releasing sulphated glycosaminoglycans and hyaluronic acid (HA) into the culture media. The increase in activities of matrix metalloproteinase-2 (MMP-2) and MMP-13 caused by IL-1 β was significantly diminished by both compounds.

Pediculicidal Activity

All tested herbal shampoo was found to be more effective in-vitro than commercial malathion shampoo with 100 % mortality at 60 s, and LT₅₀ values ranged from 11.30 to 31.97 s against human head lice *Pediculus humanus capitis* compared to malathion shampoo with LT₅₀ values ranging from 12.39 to 13.67 s (Watcharawit and Soonwera 2013). LT50 values indicated the order of pediculicidal activity in the herbal shampoos as *Z. cassumunar* shampoo > *Piper betle* shampoo > *Zanthoxylum limonella* shampoo > *Averrhoa bilimbi* shampoo > *Piper ribesioides* shampoo > *Myristica fragran* shampoo > *Tacca chantrieri* shampoo > *Plectranthus amboinicus* shampoo. Phlai at 10 % (v/v) showed the highest efficacy against adult brown dog ticks (*Rhipicephalus sanguineus*), followed by phlai at 5 % (Phnosena et al. 2006).

Insecticidal Activity

The larvicidal activity of the dichloromethane extract of *Zingiber purpureum* rhizome against the second instar of *Aedes aegypti* was shown to be due to 4-(3',4'-dimethoxyphenyl)buta-1,3-diene (Bandara et al. 2005). The diene also showed ovicidal activity against the bruchid *Callosobruchus maculatus* (F.) (Coleoptera:Bruchidae). Most of the eggs laid by bruchids on treated cowpea seeds were transparent, and very few of them contained developing embryos. Coated granules showed activity similar to that of the crude extract but were found to lose activity rapidly. Impregnated granules were found to be less active than the crude extract.

Zingiber cassumunar and sweet basil (*Ocimum basilicum*) plant oils were found to be effective as repellents and feeding deterrents against *Anopheles minimus* (205 min protection time and a biting rate of 0.9 %), *Culex quinquefasciatus* s (165 min protection time and 0.9 % biting rate) and *Aedes aegypti* (90 min protection time and 0.8 % biting rate) (Phasomkusolsil and Soonwera 2010).

Undiluted oils of *Zingiber cassumunar* (plai) exhibited 100 % repellency against host-seeking chiggers (larvae) of *Leptotrombidium imphalum*, a vector of scrub typhus, a

rickettsial disease, endemic in many areas of Asia (Eamsobhana et al. 2009).

Spermicidal Activity

Fractions 3 and 4 extracted from *Z. cassumunar* rhizome and its constituent from fraction 4, terpinen-4-ol, displayed in-vitro spermicidal activity on ox sperms with ED₁₀₀ concentrations of 0.05, 0.025 and 0.015, respectively, equivalent to that of 0.025 % of nonyl phenoxy polyethoxy ethanol (Wasuwat et al. 1986).

Antityrosinase Activity

From the rhizome, Saeio et al. (2011) obtained an essential oil yield of 0.477%w/w and showed that the oil exhibited antioxidant activity and also antityrosinase activity using mushroom tyrosinase.

Laxative Activity

Rhizome extract was found to have a laxative effect in rats (Nuratmi et al. 2005). Frequency of defecation, faeces (dry or weight) and water expelled increased dose dependently when used at a dosage of 40, 120 and 400 mg/g bw.

Anthelminthic Activity

Z. cassumunar hexane extract exhibited anthelminthic activity in-vitro against *Ascaris suum* in a dose-dependent manner (Soleha and Purba 2006). The dosage of 189.3 mg/100 ml caused 27.77 % worm mortality equal to 250 mg/100 ml pyrantel pamoate as positive control. The infusion of purple ginger had strongest activity as anthelmentics rather than in alcohol and n-hexane extract forms. Compared to the published activities of the other herbs, i.e. *Artemisia cina*, *Carica papaya*, *Momordica charantia*, *Punica granatum* and *Vitex trifolia*, the purple ginger had the strongest activity against *Ascaris* worm. Infusion and extract of *Z. cassumunar* exhibited anthelminthic activity against *Haemonchus*

contortus in-vitro (Beriajaya et al. 1998). The extract showed better effect compared to the infusion at a concentration of 0.5 and 2.5 %, respectively.

Pharmacokinetic Studies

Maximum plasma level of 0.75 µg/ml was observed at 1.04 h after oral administration of plai preparation prepared from *Z. cassumunar* rhizome ethanolic extract to rats (Koysooko et al. 1988). Elimination half-life in monkeys (2.31 h) was found to be not statistically different from rats (2.00 h). Prolonged half-life after multiple dosing was observed in monkeys. An accumulation ratio of 3.13 was found after long-term drug administration. After oral administration of 25 mg compound B from plai to male Wistar rats, mean max concentration in the plasma was 192 mg/ml at 1.12 h, the mean absorption rate of compound B was 0.035 min and mean elimination rate constant was 0.38 h (Pongsakorn et al. 1988). Following topical application of *Z. cassumunar* rhizome oil, terpinen-4-ol rapidly was distributed into the dermis and demonstrated linear pharmacokinetics with no changes in the dose-normalised area under the concentration-time curves across the investigated dosage range (Chooluck et al. 2012). The mean percentages of free terpinen-4-ol distributed in the dermis per amount of administered were 0.39 %, 0.41 % and 0.30 % for 2, 4 and 8 mg/cm² doses, respectively.

Toxicity Studies

Panyathanya et al. (1989) found that the therapeutic dose of plai (10–20 mg/kg body weight/day) showed neither acute nor chronic toxicity in rats. The LD 50 (lethal dose 50) of the alcohol and hexane extract was 20 g/kg bw and 80 g/kg bw, respectively, in the acute toxicity test. In the chronic test, no significant abnormal urinary, haematological and biochemical findings nor definite pathological changes were found.

Toxicity studies of the mask product derived from the ethanolic extracts of *Zingiber montanum* rhizome and *Morus alba* leaves did not produced skin sensitisation in guinea pigs but caused mild skin irritation in rabbits (Reungpatthanaphong

2011). The dermal LD₅₀ of the mask product in Wistar rats was more than 2000 mg/kg body weight.

Traditional Medicinal Uses

Zingiber cassumunar is widely used in folklore remedies as a single plant or as component of herbal recipes in Thailand and many Asian countries for the treatment of conditions, such as inflammation, sprains and strains; rheumatism, muscular pain, wounds and asthma; cough and respiratory problems; and as a mosquito repellent, a carminative, a mild laxative and an antidysenteric agent (Burkill 1966; Pithayanukul et al. 2007; Sukatta et al. 2009; Panichayupakaranant and Lateh 2013). Rootstock is regarded to be restorative and carminative and to relieve flatulence (Chanwitheesuk et al. 2005). The rhizomes are used for food flavouring and are used medicinally in tropical Asia, primarily as a carminative and stimulant for the stomach and against diarrhoea and colic (Bua-in and Paisooksantivatana 2009). In Thai traditional medicine, the rhizomes are consumed to relieve asthma and muscle and joint pain. The rhizome of *Zingiber cassumunar* and the seed of *Nigella sativa* are two ingredients in Thai traditional medicine to relieve dysmenorrhoea and adjust the menstrual cycle (Tangyuenyongwatana et al. 2009). Chamratpan and Homchuen (2005) reported that the natives of upper northeastern of Thailand use cassumunar ginger to cure paralysis symptoms and sprains and as massage cream. *Zingiber cassumunar* has been used for pain relief in arthritis including osteoarthritis and rheumatoid arthritis (Chaiwangsa et al. 2012). Various lotions and decoctions are applied to swellings, rheumatism, bruise, numb feet and other painful parts (Sirirugsa (1998). In Thailand, the species is the prime ingredient in massage oil to relieve muscle pain, and the rhizomes are taken against asthma, while in Laos, it is applied against abscesses, fever, colic, diarrhoea and other intestinal disorders, a depurative, as well as a poison antidote (Wolff et al. 1999; Anasamy et al. 2013).

In Indonesia, *Zingiber cassumunar* rhizome has been used in traditional medicine as blood purifier, vermifuge, laxative,

expectorant, carminative, body warming (Fachriyah et al. 2007) and slimming agents in jamu (Iswantini et al. 2011). It is also used in Indonesian traditional medicine as a vermifuge and an analeptic for the uterus and to relieve pain, colic, diarrhoea and rheumatism (Ozaki *et al.* 1991); the rhizome is used in decoction for constipation, flatulence or colic and as a vermifuge (Burkill 1966). In Sarawak, bongelai is used externally for fever and as post-partum medication in childbirth. Bongelai is pounded alone or with *Gendarussa* into a poultice for swelling and rubbed on the body after childbirth. Boiled with ginger and *Acorus*, the decoction is used hot for bathing during fevers. Bongelai is prescribed in applications for numb feet, gonorrhoea and pains in various places and as a cosmetic (Burkill 1966). The leaves boiled with pepper and the decoction drunk for stomachache. In India, the rhizome is used as an antidote to snakebite and stimulant, is carminative, is given in diarrhoea and colic and is used to treat fever and intestinal disorders (Prakash and Mehrotra 1996). Traditional medical practitioners use rhizomes in the treatment of piles and cough in Manipur (Chirangini and Sharma 2005). *Zingiber montanum* rhizome has been extensively used as a folk medicine to ameliorate peptic ulcer at northern part of Bangladesh (Al Amin et al. 2012).

Cassumunar ginger oil cream for medical purpose is available under trade name Plygesal in Thailand (Suntornanasat et al. 1990). This cream has been developed to relieve muscular pain, bruises, sprains and swelling. Nowadays, they are sold in drugstores as anti-inflammatory drug which has various forms such as cream, gel, balm and oil. Plaitanoids, an extract from cassumunar ginger rhizomes, containing arylbutanoids (e.g. DPMD) and essential oil, have been developed and used as a raw material for more than 30 products such as toothpaste, shampoo, skinwhitening, massage oils and essential oils for spas (Wanauppathamkul 2003). For example, twin lotus has added cassumunar ginger extract to its toothpaste, while aesthetic clinic uses it as a major component in soaps, shampoos and lotions. Recently, it has been used as skinwhitening and anti-ageing agent. Plai has long been regarded by Thai massage therapists as one of those oils necessary to have in their kit to combat joint and muscle

problems. Furthermore, it is well known that plai essential oils have been shown to cure acne, bruises, burnt skin, skin inflammation, muscle pain, insect bite and asthmatic symptoms. They are even proven to relieve cough and respiratory symptoms as well.

Other Uses

Additionally, *Z. montanum* has been shown to exhibit pesticidal and fungicidal activity. *Zingiber cassumunar* rhizome extract exhibited strong fungitoxic action against *Rhizoctonia solani*, the damping-off pathogen (Kishore and Dwivedi 1992). Its antifungal principle was identified to be zerumbone—a sesquiterpene. Its minimum effective dose against *R. solani* was 1000 ppm, much lower than some commercial fungicides. Zerumbone had fungistatic activity and a narrow fungitoxic spectrum and was not phytotoxic. Moreover, when used as a seed treatment, zerumbone could control damping-off disease of *Phaseolus aureus* caused by *Rhizoctonia solani* by 85.7 %.

The methanol extract of *Z. cassumunar* was found to be lethal to *Spodoptera litura*, and the bioactive component was found to be a mixture containing β -pinene and sabinene as major constituents (Rukachaisirikul et al. 1983). Extracts from *Zingiber cassumunar* rhizomes when incorporated into artificial diets displayed significant insecticidal activity against neonate larvae of the insect pest *Spodoptera littoralis* in chronic feeding bioassays at concentrations of 2500 ppm and 1250 ppm, respectively (Nugroho et al. 1996). Bioassay-guided isolation afforded two phenylbutanoids from *Z. cassumunar* rhizomes which had LC_{50} values against neonate larvae of 121 and 127 ppm, respectively, in the chronic feeding bioassay. Both compounds were also active in the residue-contact bioassay (LC_{50} values of 0.5 and 3.6 $\mu\text{g}/\text{cm}^2$, respectively).

Bongelai roots are used for amulets attached to necklaces for babies and children by the native Sakai in Peninsular Malaysia for occult purposes (Burkill 1966). The Malays chew the rhizome and spit it over the abdomen of an infant.

Comments

Z. montanum can be propagated by seeds and rhizome division (Acevedo-Rodríguez and Strong 2005). It is listed as ‘moderately invasive’ in northeastern Bangladesh, based on a 2010 forest undergrowth vegetation survey undertaken in a protected national park (Rahman et al. 2010). It is deemed a naturalised weed and cultivation escape in Puerto Rico and the Greater Antilles (Acevedo-Rodríguez and Strong 2005)

Refer to notes on *Zingiber spectabile* in this volume and *Zinger zerumbet* in Edible Medicinal and Non-medical Plant Volume 8 Flowers (Lim 2014).

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Zingiber officinale

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Scientific Name

***Zingiber officinale* Roscoe**

Synonyms

Amomum angustifolium Salisb. (Illeg.), *Amomum zingiber* L., *Amomum zinziba* Hill, *Curcuma longifolia* Wall, *Zingiber aromaticum* Noronha (Inval.), *Zingiber cholmondeleyi* (F.M.Bailey) K. Schum., *Zingiber majus* Rumph., *Zingiber missionis* Wall., *Zingiber officinale* var. *cholmondeleyi* F.M. Bailey, *Zingiber officinale* f. *macrorhizonum* (Makino) M. Hiroe, *Zingiber officinale* var. *macrorhizonum* Makino, *Zingiber officinale* f. *rubens* (Makino) M. Hiroe, *Zingiber officinale* var. *rubens* Makino, *Zingiber officinale* var. *rubrum* Theilade, *Zingiber officinale* var. *sichuanense* (Z.Y. Zhu, S.L. Zhang & S.X. Chen) Z.Y. Zhu, S.L. Zhang & S.X. Chen, *Zingiber sichuanense* Z.Y. Zhu, S.L. Zhang & S.X. Chen, *Zingiber zingiber* (L.) H. Karst.

Family

Zingiberaceae

Common/English Names

Ginger, Canton Ginger, Common Ginger, Culinary Ginger, Green Ginger, Jamaican Ginger, Stem Ginger, True Ginger

Vernacular Names

Albanian: Xhenxhefil

Angolan: Ndjibidi (Kimundu), Gengibre, Gengibre-das-boticas (Portuguese)

Arabic: Sanjzabile Ratal, Sanjzabile Yabis, Skengbir, Zanjabil

Armenian: Gojabghbegh, Kočapğpeğ, Kochapghpegh

Benin: Dote (Fon), Dote (Gèn), Dote(Goun), Atale, Ata Ile (Yoruba)

Bosnian: Crni Ingver, Đumbir, Gingibar, Ingver, Isiot, Isnot, Mrki ingver, Pravi Ingver, Vruća Trava, Zinđefil

Brazilian: Gengibre

Bulgarian: Dzhindzhifil

Burmese: Gyin, Gyin Sein, Ginsin-Khaiv, Khyenseing

Chinese: Geung (Cantonese), Gan Jiang, Gān Jiāng, Jaing, Lao Jiang, Sheng Jiang, Shēng Jiāng, Zi Jiang

Croatian: Cencer, Crni Ingver, Đindibar, Đumber, Đumbir, Gingibar, Indiber, Ingver, Isiot, Isjet, Mrki Ingver, Pravi Ingver, Vruća Trava, Zenzer

Czech: Dumbir, Zázvor, Zázvor Pravý, Zázvorník Lékařský

Danish: Ægte Ingefær, Alzangabeel Ingefær, Ingefær

Democratic Republic of Congo: Tangawisi, Tangawusa (Kikongo), Tangawisi (Kiyansi), Tangawiwi, Tangawisi (Lingala)

Dutch: Gember, Amoom

Egyptian: Zangabîl

Esperanto: Zingibro

Estonian: Harilik Ingver

Ethiopian: Hargisa (Afaan Oromoo), Jinjible, Zinjible (Amharic), Jinjibila (Oromoo), Zingibil (Amarinya), Jaanjiibeello (Gedeoffa), Dendabil (Tigrinya), Zingibil (Shinasha), Zingibil (Shenko)

Ewe: Agumetakui, Nkrawusa, Nkrama, Nkrabo

Fante: Akakadur, Tsintsimir, Tsintsimin

Fiji: Cagolaya Ni Vavalagi, Dani Dani, Drove, Layalaya, Adi

Finnish: Inkivääri

French: Amome, Gingembre, Gingembre Commun, Gingembre Officinal, Gingembre traditionnel, L'Amome des Indes

Gabon: Ndongo Ya Tsina

German: Ingwer-Gewürz, Gemeiner Ingber, Ingwer

Ghana: Akakaduro (Asante-Twi)

Greek: Tzintzer, Piperoriza, Ziggiveris

Hausa: Afu, Chitta

Hawaiian: 'Awapuhi Pake

Hebrew: Zangvil

Hmong: Kai

Hungarian: Álgömbér, Fűszergyömbér, Gyömbér, Közönséges gyömbér

Icelandic: Engifer

Indian: Aadaa, Ada (Assamese), Aadaa, Adrak, sont (Bengali), Aadu, Ada, Adarak, Adrak, Adrakh, Adruka, Sindhi, Sonth, Soonth (Hindi), Aardraka, Alla, Ardraka, Hasi Shunti, Hasishunthi, Hasisunthi, Khaara Genasu, Pali, Shunthi, Shunti, Sonte, Sonti, Sundi, Sunthi, Sunti, Vanasunthi (Kannada), Sho-ont (Kashimiri), Ardrakam, Cincatakam, Cinciver, Cukku, Inchi, Inci, Injee, Inschi, Inschikua, Ischi, Sryngiveram, Tikshnottham (Malayalam), Aale, Āle, Alem, Alen, Sunte, Sunth (Marathi), Ada (Oriya), Allam, Artrakam, Arttarakam,

Arukkan, Atakam, Attirakam, Caupannam, Cauvarnam, Chukku, Conti, Cukku, Cunti, Ilakkottai, Inci, Inji, Katu Pattiram, Moruhalasatam, Nakaram, Navacuru, Shukku, Sukku, Ularnta Inci, Upakullam, Verkkompu, Vicvapesajam, Vitamutiya Amirtan (Tamil), Aardrakamu, Allam, Allamu, Allamu Chettu, Allumu, Ardrakamu, Mahaushadamu, Mahaushadhamu, Shunthi, Sonthi, Sonti, Sringabaeramu, Sryngaberamu, Sonthi, Sunthi (Telugu), Ab Adrak Taza, Abe-e-adrak, Adi, Adrak, Adraka, Adrak Bayraisha, Murraba-i-zanjibil, Sonth, Sonth Nim Kofta, Tirkuta, Zanjabil, Zanjibil, Zanjibil Nim Kofta, Zanjibil Saida, Zanjibil Sayida, Zanjilbil, Zinjibil, Zufa-i-khushk (Urdu)

Indonesian: Jahya, Lahya (Balinese), Alia, Halia, Jae (Malay) Jae, Jahe (Javanese), Jhai (Madurese) Jahe, Jahe badakjahe berem (Sundanese)

Italian: Zenzero, Zenzevero, Pepe Zenzero

Japanese: Jinjaa, Kintoki, Shooga, Shouga, Zenzero Officinale

Kampuchean: Khnehey, Khnhei, Khnhei Phlung

Kenyan: Tanguas, Tangawizi (Luo), Etangausi (Suba)

Korean: Saeng Gang

Laotian: Khing

Libyan: Schéngibil, Éngibil

Madagascar: Sakaintany

Malaysian: Attuja, Halia, Haliya, Halia Bara, Halia Cina, Haliya Udang, Halia Nasi, Halia Padi, Jahi, Sonth

Mexican: Anchoas (Spanish)

Morocco: Skînzhbîr, Skinjibir, Zanjabil

Nepalese: Aduvaa, Aduva, Agnimanth, Sutho

Nigerian: Sarkin Zabur (Bauchi State), Jinja (Efik), Chittar Aho, Kakzawa (Huasa), Ginger, Jinja (Ibibio), Jinja (igbo), Atale, Ginija (Ogun State), Aje, Ata-ile (Ondo), Atale, Ata-ile, Orin (Yoruba)

Norwegian: Ingefær

Nzema: Sinziminli

Papiamento: Ehember

Papua New Guinea: Li (Madang Province), Asuvate, Kireli, Kovulu, Komga, Laki (Morobe Province), Lei (Kasiriru Island, Admiralty Islands)

Persian: Jamveel, Zanzabil, Sanjzabile Khushk, Sanjzabile Tar

Philippines: Luy-a (Bisaya), Laya (Bontok), Laya (Ibanag), Laiya (Ifugao), Baseng, Laya (Iloko), Laya (Itogon), Laial (sambali), Fute Giya, Giya, Kasumba Giya, Laya, Loya Agarisen, Luya (Tagalog)

Polish: Imbir Lekarski, Jembier

Portuguese: Gengibre, Gengibre Amarelo, Gengibre Das Boticas Jengibre, Ingever, Kion

Republic of Guinea: Nyamaku (Manika), Sakan (Pular), Nyökhömindyi (Soso)

Russian: Imbir', Imbir' Lekarstvennyi

Samoan: Fiu

Senegal: Niamahu (Bambara), Citaraho, Sakanjabir (Hausa), Gingembre (local French), Dinjar, Dinjer, Jinjër (Wolof)

Serbian: Činčibar, Crni ingver, Đumbir, Džumbir, Gingibar, Imbor, Ingver, Isiot, Mrki Ingver, Pravi Ingver, Vruća Trava, Zendžefil, Žumbir

Sierra Leone: Kijre (Kpaa Mende), Ginga (Krio), Kijei (Mende), Ta San (Temne)

Slovakian: Ďumbier, Ďumbier lekársky, Zázvor Ingver

Slovenian: Imber

South African: Ginja (isiXhosa), Ijinja (Xhosa)

Spanish: Jengibre, Jengibre Oficial

Sri Lankan: Inguru (Sinhala)

Swedish: Ingefär, Ingefära

Tahitian: Re'a Tinito

Tanzania: Tangawizi (Luguru)

Thai: Khing; Khing Daeng, Khing Klaeng, Khing Phueak (Chiang Mai), Sa e (Karen).

Tiβn: Gamug, Sga Smug, Sman-Sga

Turkish: Zencebil, Zencefil, Zentzephil

Uganda: Ntangahuzi (Runyaruguru), Ntangahuzi (Runyankore), Tangawuzi (Rutooro), Ntangawizi (Swahili)

Ukranian: Imbir Sadovij

Vietnamese: Cây Gừng, Gừng, Sinh khương

Welsh: Sinsir

Origin/Distribution

The species is reported to be indigenous in Southeast Asia (Ravindran and Babu 2005) and is distributed from India to South Central China (Govaert 2014). It is widely cultivated in the tropics and subtropics in Asia, Africa and the Caribbean.

Agroecology

In tropical Asia, ginger is found in warm, humid monsoon forests. It requires a frost-free climate and 1500 mm of rain annually or supplementary irrigation. It thrives best on well-drained, loamy or alluvial fertile soils and likes the addition of well-rotted manure or compost. It is intolerant of waterlogging. Light shade is required.

Edible Plant Parts and Uses

Ginger is a popular spice used as a flavouring agent in food, beverage and confectionary products such as marmalade, pickles, chutneys, ginger beer, ginger ale, ginger wine, ginger tea, crystallised gingers, preserves, candies, sweets, liquors,

biscuits, cakes, ginger bread and other bakery products (Wang et al. 2011; Wikipedia 2014). Ginger—fresh, dried, powdered, juiced, essence or as paste—is an important ingredient in many Asian cuisine: seafood, meat and vegetarian dishes, curries, soups, sauces, chilli sauces, salads and noodles.

In Japan, ginger is pickled to make beni shoga and gari or grated and used raw on tofu or noodles. It is also made into a candy called ‘shoga no sato zuke’. In the traditional Korean kimchi, ginger is either finely minced or just juiced before the fermentation process. In Burma ginger is consumed in a salad dish called ‘gyin-thot’, which consists of shredded ginger preserved in oil and a variety of nuts and seeds. In the Philippines, ginger is brewed into the native beverage tahu or salabat. In Corfu island, Greece, a traditional drink called *τσιτσιμπύρα* (‘tsitsibira’), a type of ginger beer, is made. In the Caribbean, ginger is a popular spice for cooking and is utilised in drinks such as ‘sorrel’, a seasonal drink made during the Christmas season. Jamaicans make ginger beer as a carbonated beverage and also fresh in their homes. Ginger tea and the famous regional specialty Jamaican ginger cake are often made from fresh ginger, as well as sweet foods such as ginger ale, gingerbread, ginger snaps, ‘parkin’, ginger biscuits and ‘speculaas’. A ginger-flavoured liqueur called ‘Canton’ is produced in Jarnac, France. Ginger wine is a ginger-flavoured wine produced in the UK. Ginger is also added to tea and coffee. In Nigeria the use of ginger as medicine is vast; it is also used for spicing almost all kinds of food including tea, and it is one of the major ingredients of ‘zobo’, a local drink in Nigeria (Isaac et al. 2014).

In Indonesia, young, fresh ginger is eaten raw as ‘lalab’ and used for ‘sayur’ and for pickles called ‘achar’, while the old rhizomes are used as a manisan (‘sweetmeat’) (Ochse and van den Brink 1980). Sambal jahe is a paste of grated ginger and vinegar eaten with roasted meat and rice. A delicacy called ‘bintang jahe’ is a kind of dodol made of steamed potato, sago meal and ginger and sugar. ‘Tengteng jahe’ is a firm delicacy made from ginger and palm sugar. A savoury jelly can be obtained from a decoction of young rhizome. A popular warming drink made of ginger and sugar called

‘wedang jahe’ (Javanese), ‘bandrek’ (Sundanese, Malay) and ‘sorbat’ (Malay) or ‘bidang jahe’ (Madurese) is frequently drunk by the locals. In Vietnam, the fresh leaves, finely chopped, can also be added to shrimp and yam soup (‘canh khoai mỡ’) as a top garnish and spice to add a much subtler flavour of ginger than the chopped root.

Botany

A herbaceous perennial with slender, erect leafy shoot, 0.6 cm diameter and growing 50–100 cm high (Plates 1 and 2).

Rhizomes subterranean, irregularly branched, thickened and fleshy, light brown externally and pale yellow inside, strongly aromatic (Plates 3, 4, 5, and 6). Some cultivars are pinkish to reddish externally. Leaves distichous, lanceolate to linear–lanceolate (Plates 1 and 2), 15–25 cm long and about 2 cm wide, sessile, glabrescent, ligule weakly bilobed, membranous. Scape arising from rhizome, erect 15–25 cm high, covered with imbricate bracts. Inflorescence radical, ellipsoid to ovoid, 5 cm long with pale green, ovate, cuspidate floral bracts, 2.5 cm long with mucronate tips. Flowers from axil of bracts, calyx < or 1 cm, corolla greenish yellow, tube 2 cm long, lip (mid-lobe) oblong–obovate, dull purplish mottled with cream blotches, stamens dark purple, anther 9 mm, connective appendage 7 mm. Fruit a red capsule.



Plate 1 Ginger plant habit



Plate 2 Young ginger plants



Plate 3 Harvested ginger pinkish red ginger rhizomes with pseudostem attached



Plate 4 Harvested young ginger white rhizomes with pseudostem attached



Plate 5 Old ginger rhizomes



Plate 6 Close-up of ginger rhizome

Nutritive/Medicinal Properties

Proximate nutrient composition (per 100 g edible portion) of raw ginger root was reported by USDA-ARS (2014) as follows: water 78.89 g, energy 80 kcal (333 kJ), protein 1.82 g, total lipid 0.75 g, ash 0.77 g, carbohydrate 17.77 g, total dietary fibre 2 g, total sugars 1.70 g, Ca 16 mg, Fe 0.60 mg, Mg 43 mg, P 34 mg, K 415 mg, Na 13 mg, Zn 0.34 mg, Cu 0.226 mg, Mn 0.229 mg, Se 0.7 µg, vitamin C 5.0 mg, thiamine 0.025 mg, riboflavin 0.034 mg, niacin 0.750 mg, pantothenic acid 0.203 mg, vitamin B6 0.160 mg, total folate 11 µg, total choline 28.8 mg, vitamin E (α -tocopherol) 0.26 mg, vitamin K (phylloquinone) 0.1 µg, total saturated fatty acids 0.203 g, 8:0 0.007 g, 12:0 0.039 g, 14:0 0.018 g, 16:0 0.120 g, 18:0 0.017 g, total monounsaturated fatty acids 0.154 g, 16:1 undifferentiated 0.021 g, 18:1 undifferentiated 0.119 g, 20:1 0.007 g, total polyunsaturated fatty acids 0.154 g, 18:2 undifferentiated 0.120 g, 18:3 undifferentiated 0.034 g, phytosterols 15 mg, tryptophan 0.012 g, threonine 0.036 g, isoleucine 0.051 g, leucine 0.074 g, lysine 0.057 g, methionine 0.013 g, cystine 0.008 g, phenylalanine 0.045 g, tyrosine 0.020 g, valine 0.073 g, arginine 0.043 g, histidine 0.030 g, alanine 0.031 g, aspartic acid 0.208 g, glutamic acid 0.162 g, glycine 0.043 g, proline 0.041 g and serine 0.045 g. The following free amino acids were isolated from ginger rhizome: glutamic acid, aspartic acid, asparagine, serine, glycine, threonine, alanine,

glutamine, arginine, γ -aminobutyric acid, valine and phenylalanine, and from the neutral amino acid fraction, L-pipecolic acid (2-piperidinecarboxylic acid) was isolated (Murakami et al. 1965).

Isolated ginger and turmeric starches had purity of approximately 85 and 77 %, respectively (Braga et al. 2006). The turmeric starch (B-type) demonstrated more resistance under the pressure than ginger starch (C-type), in spite of its lower amylopectin content (52 %) as compared to ginger starch (66 %). The chemi-physico composition of ginger starch before SFE (supercritical fluid extraction) and after SFE were starch purity (85, 84 %), total protein (0.53, 0.56 %), ash (0.91, 0.16 %), reducing sugars (tr, tr), moisture (8.2, 9.7 %), onset temperature (69.3, 66.3 °C), peak temperature (83.24, 82.6 °C), conclusion temperature (99, 96 °C), enthalpy of gelatinisation (20, 19 J/g), pasting temperature (86.6, 86.5 °C), peak time (5.9, 6.0 min), viscosity peak (2650, 2769 cP), breakdown (148, 172 cP), final viscosity (4175, 4060 cP) setback (1673, 1463 cP), amylose (34, 34 %), amylopectin (66, 66 %), swelling factor (4.45, 4.41) and turbidity (ABS absorbance) (2.20, 2.25).

Ginger (from Cochin) was analysed by Thresh (1879a, b, 1880, 1881, 1882). Ginger oleoresin, extracted by ether, contained volatile oil (1.35 %), inert neutral resin (0.95 %), inert acid resins, resins a and b (0.865 %), fat (wax, 1.205 %) and the pungent, active principle, 'gingerol' (0.6–1.4 %), a viscid, odourless liquid of neutral reaction, non-glucosidal and soluble in diluted and strong alcohol, benzol, volatile oils, carbon disulphide, caustic potash and ammonia and glacial acetic acid; it is very slightly soluble in petroleum ether. The ether-insoluble part of ginger contained mucilage, starch (13–18 %), a trace of alkaloid, metarabin 8.12 %, paraben 14.4 %, oxalic acid 0.427 %, cellulose 3.75 %, albuminoids 5.57 %, vasculose 14.46 %, moisture 13.53 % and left, upon incineration, 3.5–5 % ash.

Ginger oleoresin, a reddish brown to dark brown product, was obtained by extraction of dry ginger with pure solvent and subsequent careful removal of the solvent by distillation. It comprised a mixture of essential oil (oil of ginger) and the

non-volatile ether extract consisting of pungent principle and some resinous materials (BIS 1984). Gingerol, the pungent principle, was isolated from ginger and synthesised, and its structure was elucidated (Lapworth et al. 1917). A new pungent principle, shogaol, was isolated from ginger (Nomura 1918). Lewis et al. (1972) investigated the standardisation of ginger oleoresins and found ethylene dichloride to be most efficacious of four solvents: acetone, alcohol, hexane and ethylene dichloride. Ginger oleoresin was reported to contain 20–30 % volatile oil, 10 % fixed and non-volatile oil and 5–50 % pungent resinous components of the gingerols. Yields of oleoresins were reported to be affected by cultivar, harvesting age, choice of solvents and methods of extraction; some cultivars afforded oleoresin yield as high as 20 %. Mathew et al. (1973) reported the following volatile oil and oleoresin profile of different ginger varieties: cv Cochin comprising 2.2 % volatile oil (v/w) and non-volatile oil 4.25 % with lemon-like odour and flavour; cv Sierra Leone comprising 1.6 % volatile oil and 7.2 % non-volatile oil with pungent and slightly camphoraceous flavour; cv Jamaican comprising 1 % volatile oil and 4.4 % non-volatile oil with delicate aroma and flavour; and cv Nigerian with 2.5 volatile oil and 6.5 % non-volatile oil with very pungent and camphoraceous flavour. The principal compounds responsible for ginger pungency had been identified as gingerols and shogaols, a group of phenolic alkanones whose structures had been elucidated both by isolation and synthesis (Connell 1969a, b; Connell and Sutherland 1969). Ginger oleoresins were found to contain gingerols, shogaols, essential oils and other non-volatile compounds such as carbohydrates and fatty acids (Connell 1970b). Five sesquiterpenes, *ar*-curcumene, α , α -zingiberene, (–)- β -sesquiphellandrene and *trans*- β -farnesene, were found in the essential oil. Under gas chromatographic conditions, gingerols were decomposed into zingerone, aldehydes and shogaols (Connell 1969b). Hexanal and minor amounts of the other aldehydes and zingerone were also formed on treatment with hot alkali of an extract of gingerols (Connell 1970b). According to Connell (1970a), ginger pungency was due to related keto-alcohols together with zingerone. Fresh ginger rhizome contained only the pungent component gingerol, but

during processing, drying the compound caused loss of water and part of it was converted to shogaol which was less pungent. During extraction further degradation occurred leading to formation of paradol and zingerone. Gingerols, shogaols, paradols and related compounds were found in ginger; compounds containing a β -hydroxy ketone grouping, e.g. the gingerols, were decomposed to aliphatic aldehydes and zingerone under the conditions of gas chromatography (Connell and McLachlan 1972). Connell (1969a) and Connell and Sutherland (1969) reported that in ginger oleoresin, the ratio of compounds gingerol/shogaol/zingerone was 60:30:10, and the ratio for (6)-, (8)- and (10)-gingerols was 56:13:31, respectively. The structure of [6]-paradol was confirmed by synthesis from [6]-gingerol (Connell 1970a). Dried ginger rhizomes afforded a complex mixture of substances including a series of S-(+)-gingerols (i.e. 1-(4'-hydroxy-3'-methoxyphenyl)-5-hydroxyalkan-3-ones) with 10, 12 and 14 carbon atom side chains, essential oil, palmitic and other fatty acids and other unidentified substances (Connell and Sutherland 1969). Shogaol and zingerone were absent but are formed by the action of alkalis or heat on gingerol or the oleoresin. The gingerol with the 11-carbon side chain, claimed by Lapworth et al. (1917) as the principal pungent substance in ginger, was also absent. The pungent compounds of ginger had earlier been shown to be homologous gingerols, the dehydration product shogaols and the degradation product zingerone (Narasimhan and Govindarajan 1978). The changes in these compounds were found to affect quality with reduction in pungency and formation of off-flavour. Careful threshold tests for pungency of different oleoresins and purified pungent isolates, gingerols and shogaols established that shogaols were twice as pungent as gingerols.

The total arsenic contents (dry weight basis) in six edible Zingiberaceous rhizomes, namely, *Alpinia galanga* (Khaa), *Boesenbergia rotunda* (Kra-chaai), *Curcuma longa* (Khaminchan), *Curcuma zedoaria* (Khamin-oi), *Zingiber cassumunar* (plai) and *Zingiber officinale* (Ginger), were found to be 92.4, 103.5, 61.7, 89.8, 106.7 and 69.3 ng/g, respectively (Ubonnuch et al. 2013). All investigated amounts of total and inorganic arsenic were much lower than the limits

recommended by Thai Food and Drug Administration. Ginger rhizomes collected from different locations of north western Himalayas were found to contain the volatile toxic heavy metals arsenic (As) and mercury (Hg) which varied from not detectable to 0.13 µg/g and 0.01–0.42 µg/g, respectively (Gupta et al. 2010). The non-volatile metals lead (Pb) and cadmium (Cd) ranged from 0.06–0.64 µg/g to 0.002–0.03 µg/g, respectively. The results illustrated the findings that soil was the major but not the only source of metal accumulation in the plants. In another more recent study, of 46 ginger germplasms, collected from the north western Himalayan India, they quantified 18 elements in the acid digested rhizomes as follows: K > Mg > Fe > Ca > Na > Mn > Zn > Ba > Cu > Cr > Ni > Pb > Co > Se > As > Be > Cd (Pandotra et al. 2015). The toxic element Hg was not detected in any of the investigated samples. The study suggested raw ginger to be a good source of beneficial elements/minerals like Mg, Ca, Mn, Fe, Cu and Zn.

Curcumin, demethoxycurcumin and 6-dehydrogingerdione were identified as the main common compounds contributing to the yellow colour, and their average amounts were 2.2, 1.6 and 20.0 mg/100 g fresh weight, respectively, in 62 kinds of ginger rhizomes originating from different cultivars or different cultivation locations in Japan (Yoko and Aya 2014). Curcumin and demethoxycurcumin were contained in cv. *Kintoki* samples at higher levels. However, their variation suggested that the yellow pigment of ginger rhizome was more dependent on the cultivation conditions and less on the cultivar. Also, it was found that yellow pigments were synthesised during rhizome maturation. The proximate analysis of both Guangdong-ginger (GG) and Chu-ginger (CG) rhizomes had similar profiles (Yeh et al. 2014). The total contents of organic acids were 37.33 and 91.06 mg/g dry weight for GG and CG, respectively, with oxalic and tartaric acids being two major acids. Gingerols and shogaol in both gingers were similar, but curcumin content was higher in GG. The essential oils exhibited similar volatile profiles, and 60 and 65 compounds were identified for GG and CG, respectively. Among the essential oil major components were

camphene, sabinene, α -curcumene, zingiberene, α -farnesene, β -sesquiphellandrene, neral and geranial.

Two pungent compounds, hexahydrocurcumin and dihydrogingerol, were isolated from polar ethyl acetate fraction of ginger acetone extract, and two additional pungent principles were isolated from crude gingerol fraction (Murata et al. 1972). The following volatile compounds were identified from ginger rhizome: *n*-heptane, *n*-octane, *n*-nonane, acetaldehyde, propionaldehyde, *n*-butyraldehyde, isovaleraldehyde, acetone, *n*-propanol, *n*-nonanol, diethyl sulphide, ethyl isopropyl sulphide, methyl allyl sulphide, methyl and ethyl acetates, α -pinene, camphene, β -pinene, sabinene, myrcene, limonene, β -phellandrene and 1,8-cineole (Kami et al. 1972). Zingerone, gingerol [4]-gingerol, [6]-gingerol, [6]-methylgingerdiol, [6]-gingerdiacetate, [6]-methyl gingerdiacetate, methylgingerol, [6]-gingerdiol, [8]-gingerdiol, [10]-gingerdiol and [6]-shogaol were identified in ginger extract (Masada et al. 1974). Two sesquiterpene alcohols (*cis*- β -sesquiphellandrol and *trans*- β -sesquiphellandrol) were isolated from ginger oil (Bednarczyk et al. 1975). They were shown to be stereoisomers of 5-(1,5-dimethyl-4-hexenyl)-2-methylene-3-cyclohexenol. Two diterpenes, galanolactone and (*E*)-8 β ,17-epoxylabd-12-ene-15,16-dial, were isolated as the main compounds together with known pungent compounds, [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol from the rhizome of ordinary small-type Japanese ginger generally called 'Kintoki' (Kano et al. 1990).

Gingerdiones, postulated intermediates in the biosynthesis of the gingerols, were identified together with desmethylhexahydrocurcumin and the shogaol analogues of the hexahydrocurcumins from ginger (Harvey 1981). In addition to [6]-gingerol, four new constituents—[6]-dehydrogingerdione, [10]-dehydrogingerdione, [6]-gingerdione and [10]-gingerdione—were isolated as potent inhibitors of prostaglandin (PG) biosynthesis from ginger roots (Kiuchi et al. 1982). Two homologous series of gingerol compounds were identified in ginger extracted by liquid carbon dioxide: 6-, 8-, 10-, 12-, 14-gingerols and methyl-6-, methyl-8-, methyl-10-, methyl-12-gingerols (Chen et al.

1986b). 6-gingerol (11.88 %) is the most abundant pungent compound, followed by 10- gingerol (2.38 %) and 8-gingerol (1.67 %), and traces of 6-shogaol were also identified in the liquid carbon dioxide extract (Chen et al. 1986a). Isomeric shogaols were derived by thermal dehydration of isolated gingerols of ginger (Chen et al. 1986c). Two homologous series of isomeric shogaol compounds, *cis*- and *trans*-6-shogaol, 8-shogaol, 10-shogaol, 12-shogaol and *syn*- and *anti*-methyl-6-shogaol, methyl-8-shogaol, methyl-10-shogaol, were identified. Thermal degradation of 6-, 8-, 10-, 12-, 14-gingerols and methyl-6, methyl-8, methyl-10, methyl-12 gingerols produced aldehydes (C₆, C₈, C₁₀, C₁₂ and C₁₄) and ketones (2-heptanone, 2-nonanone, 2-undecanone and 2-tridecanone) (Chen and Ho 1987). Also hexanal, octanal, decanal, 2-heptanone, 2-nonanone and 2-undecanone had been found in steam-distilled volatiles of ginger.

Yoshikawa et al. (1993) found that Japanese *Zingiberis Rhizoma* and fresh ginger root contained 6-gingerol (1), 6-dehydrogingerdione (6) and galanolactone (7) as major constituents, whereas 7 was not detected in imported *Zingiberis Rhizoma* and 6 was detected in Vietnamese *Zingiberis Rhizoma*. Additionally, the contents of 1 and 7 in fresh ginger root decreased remarkably during the processing procedure for *Zingiberis Rhizoma*. Free and glycosidically bound aroma compounds were isolated from the juice of ginger rhizomes (Wu et al. 1990b). Glycosidically bound aliphatic alcohols, monoterpene alcohols, acids and aldehydes were isolated from ginger for the first time. α -zingiberene, β -sesquiphellandrene, β -bisabolene, *ar*-curcumene, [6]-shogaol, [8]-shogaol, [6]-paradol, [6]-gingerdione, [6]-gingerol, [8]-gingerol, [10]-gingerol, [6]-gingerdiol, (3*S*,5*S*)-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane-3,5-diol and (3*S*,5*S*)-dihydroxy 1-(4'-hydroxy-3',5'-dimethoxyphenyl)-7-(4''-hydroxy-3''-methoxyphenyl)heptane were isolated from the rhizome (Yamahara et al. 1992). At 1000 μ mol/L, [6]-shogaol and [8]-shogaol were conspicuously pungent and [6]-paradol, [6]-gingerdione, [6]-gingerol and [6]-gingerdiol and (3*S*,5*S*)-dihydroxy 1-(4'-hydroxy-3',5'-dimethoxyphenyl)-7-(4''-hydroxy-3''-methoxyphenyl)heptane were evidently pungent. Also

(*E*)-2-alkenals, 2-octyl acetate, 2-(2',3'-epoxy-3'-methylbutyl)-3-methylfuran, (*E*)-3-7,-dimethyl-3,6-octadienal and (*Z*)-3-7,-dimethyl-3,6-octadienal were newly identified. The major pungent compounds in ginger were identified as [6]-gingerol, [8]-gingerol, [10]-gingerol, [6]-shogaol, [8]-shogaol, [10]-shogaol and [6]-gingerdiol (He et al. 1998). Another eight minor compounds were tentatively identified as gingerol analogues. Five new diarylheptanoids were isolated from ginger rhizomes; they were oxygenated at C-1, C-3 and C-5 on the heptane chain and cyclised between C-1 and C-5 through oxygen (Kikuzaki and Nakatani 1996). Five sulphonated compounds, namely, 4-gingesulphonic acid and shogasulphonic acids A [5-sulfonyl-1,7-bis(4-hydroxy-3-methoxyphenyl)-heptan-3-one], B [5-sulfonyl-1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)-heptan-3-one], C [5-sulfonyl-1,7-bis(3,4-dihydroxyphenyl)-heptan-3-one] and D [5-sulfonyl-1,7-bis(4,5-dihydroxy-3-methoxyphenyl)-heptan-3-one], 4-gingesulphonic acid were isolated together with seven known compounds: [6]-gingerol, [8]-gingerol, [10]-gingerol, [6]-shogaol, [6]-paradol, [6]-ginger acetate and [6]-gingesulphonic acid from ginger rhizome (Hori et al. 2003).

The following compounds were isolated from *Z. officinale* rhizomes: four diarylheptenones: 1,7-bis(4-hydroxy-3-methoxyphenyl)hept-4-en-3-one (gingerenone A), 7-(3,5-dimethoxy-4-hydroxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)hept-4-en-3-one (gingerenone B), 1-(3,5-dimethoxy-4-hydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)hept-4-en-3-one (isogingerenone B) and 1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)hept-4-en-3-one (gingerenone C) (Endo et al. 1990); six diarylheptanoids: 5-hydroxy-7-(4-hydroxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)-3-heptanone; 3,5-diacetoxy-7-(3,4-dihydroxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)heptane; 5-hydroxy-7-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-3-heptanone; 5-hydroxy-7-(4-hydroxy-3,5-dimethoxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)-3-heptanone; (3*R*,5*S*)-3,5-dihydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane and (3*S*,5*S*)-3,5-diacetoxy-1,7-bis(3,4-dihydroxyphenyl)heptane together with two known

diarylheptanoids (Kikuzaki et al. 1991a); two diarylheptanoids: meso-3,5-diacetoxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane and 3,5-diacetoxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane together with dehydroxytetrahydrocurcumin (gingerenone A) [1,7-bis(4-hydroxy-3-methoxyphenyl)hepten-3-one] and hexahydrocurcumin [5-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptan-3-one] (Kikuzaki et al. 1991b); [6]-gingerdiol and four analogues: (3*R*,5*S*)-5-acetoxy-3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)decane; (3*R*,5*S*)-3-acetoxy-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)decane; (3*R*,5*S*)-3,5-diacetoxy-1-(4-hydroxy-3-methoxyphenyl)decane; and (3*R*,5*S*)-3,5-diacetoxy-1-(3,4-dimethoxyphenyl)decane (Kikuzaki et al. 1992); 6-gingesulphonic acid and three new monoacyldigalactosylglycerols: gingerglycolipids A, B and C (Yoshikawa et al. 1992); three dehydroshogaols [6]-dehydroshogaol, [8]-dehydroshogaol and [10]-dehydroshogaol (Wu et al. 1998); 1-dehydrogingerdione (Charles et al. 2000); and a cyclic diarylhaptanoid 1,5-epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(3,4-dihydroxy-5-methoxyphenyl)heptanes (He et al. 2001). Seven new diarylheptanoids—(3*S*,5*S*)-3,5-diacetoxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane; (3*R*,5*S*)-3-acetoxy-5-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane; (3*R*,5*S*)-3,5-dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane; (5*S*)-5-acetoxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptan-3-one; 5-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptan-3-one; 5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxy-5-methoxyphenyl)heptan-3-one and 1,5-epoxy-3-hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane—were isolated from ginger rhizomes along with 25 known compounds, i.e. 8 diarylheptanoids, 14 gingerol analogues, a diterpene and 2 steroids (Ma et al. 2004). A total of 31 gingerol-related compounds were identified from the methanolic crude extracts of fresh ginger rhizome including the gingerols, methylgingerols, gingerol acetates, shogaols, paradols, gingerdiols and mono- and diacetyl gingerdiols, and dehydrogingerdiones were isolated from the methanol rhizome extract: [4]-gingerol, [6]-gingerol, [8]-

gingerol, [10]-gingerol, [12]-gingerol, methyl [6]-gingerol, methyl [8]-gingerol, methyl [10]-gingerol, [6]-shogaol, [8]-shogaol, [10]-shogaol, [12]-shogaol, 1-dehydro-[6]-gingerdione, 1-dehydro-[8]-gingerdione, 1-dehydro-[10]-gingerdione, 1-dehydro-[12]-gingerdione, acetoxy-[6]-gingerol, acetoxy-[8]-gingerol, acetoxy-[10]-gingerol, methyl acetoxy-[6]-gingerol, 3- or 5-acetoxy-[6]-gingerdiol, methyl 3- or 5-acetoxy-[6]-gingerdiol, [6]-paradol, diacetoxy-[4]-gingerdiol, diacetoxy-[6]-gingerdiol, diacetoxy-[8]-gingerdiol, diacetoxy-[10]-gingerdiol, methyl diacetoxy-[4]-gingerdiol, methyl diacetoxy-[6]-gingerdiol, methyl diacetoxy-[8]-gingerdiol and methyl diacetoxy-[10]-gingerdiol (Jiang et al. 2005). Diarylheptanoids, namely, 5-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-3-heptanone; 5-hydroxy-1-(4-dihydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)-3-heptanone; 3,5-dihydroxy-1,7-bis(4-hydroxy-3,5-dimethoxyphenyl)heptane; 5-dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane; 3-acetoxy-5-hydroxy-1,7-bis(3,4-dihydroxy-5-methoxyphenyl)-heptane; 3-acetoxy-5-hydroxy-1,7-bis(3,4-dihydroxyphenyl)heptane; 3,5-dihydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane; 5-hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-3-heptanone; 5-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)-3-heptanone; 3-acetoxy-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxy-5-methoxyphenyl)heptane; 3,5-diacetoxy-1,7-bis(3,4-hydroxy-5-methoxyphenyl)heptane; 3,5-diacetoxy-1-(3,4-dihydroxyphenyl)-7-(3,4-dihydroxy-5-methoxyphenyl)heptane; 3,5-diacetoxy-1,7-bis(3,4-dihydroxyphenyl)heptane; 3-acetoxy-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxy-3,5-dimethoxyphenyl)heptane; 3-acetoxy-5-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane; 3,5-diacetoxy-7-(3,4-dihydroxy-5-methoxyphenyl)-1-(4-hydroxy-3,5-dimethoxyphenyl)heptane; 5-diacetoxy-7-(4-hydroxyphenyl)-1-(3,4-dihydroxyphenyl)heptane; 3,5-diacetoxy-7-(4-hydroxy-3-methoxyphenyl)-1-(3,4-dihydroxy-5-methoxyphenyl)heptane; 5-diacetoxy-7-(3,4-dihydroxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)heptane;

3,5-diacetoxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane; 5-diacetoxy-7-(4-hydroxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)heptane; 5-diacetoxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane; and dihydrocurcumin, were isolated from the rhizome (Jiang et al. 2007). A cyclic diarylheptanoid, 1,5-epoxy-3-hydroxy-1-(3-methoxy-4,5-dihydroxyphenyl)-7-(4-hydroxyphenyl)-heptane, and a new monoterpene, 10-*O*- β -D-glucopyranosyl-hydroxycineole, were isolated from the rhizome (Zhao et al. 2007). Three diarylheptanoids, 5-[4-hydroxy-6-(4-hydroxyphenethyl)tetrahydro-2H-pyran-2-yl]-3-methoxybenzene-1,2-diol; sodium(*E*)-7-hydroxy-1,7-bis(4-hydroxyphenyl)hept-5-ene-3*S*-sulfonate and sodium(*E*)-7-hydroxy-1,7-bis(4-hydroxyphenyl)hept-5-ene-3*R*-sulfonate; and a monoterpenoid hydroxycineole-10-*O*- β -D-glucopyranoside and known compounds—5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)heptan-3-one; 5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4,5-dihydroxy-3-methoxyphenyl)heptan-3-one; 5-hydroxy-1-(4,5-dihydroxy-3-methoxyphenyl)-7-(4-dihydroxy-3-methoxyphenyl)heptan-3-one and 1,5-epoxy-3-hydroxy-1-(4,5-dihydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)heptane—were isolated from ginger rhizomes (Tao et al. 2008). Three new diarylheptanoids, i.e. sodium(5*S*,2*E*)-1,7-bis(4-hydroxyphenyl)-1-hydroxy-2-hepten-5-sulfonate; sodium(5*R*,2*E*)-1,7-bis(4-hydroxyphenyl)-1-hydroxy-2-hepten-5-sulfonate and 3,5-diacetoxy-1-(3-methoxy-4,5-dihydroxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane, were isolated from ginger rhizomes (Zhou et al. 2007). Twenty-seven gingerol-related compounds were identified in the methanolic crude extracts of ginger rhizome: [4]-gingerol, [6]-gingerol, [6]-gingerdiol, methyl-[6]-gingerol, methyl-[8]-gingerol, acetoxy-[6]-gingerdiol, acetoxy-[4]-gingerol, nor-[8]-gingerdione, [6]-shogaol, [8]-gingerol, acetoxy-[8]methylgingerdiol, nor-[12]-paradol, [8]-dehydrogingerdione, methyl-[8]-gingerol, acetoxy-[8]-gingerol, [10]-gingerol, [10]-gingerdione, methyl-[10]-gingerol, methyl acetoxy-[8]-gingerol, [10]-shogaol, methyl-[8]-paradol, [12]-paradol, methyl-[10]-shogaol, [12]-shogaol,

[14]-dehydrogingerdione and methyl-[12]-gingerol (Ahui et al. 2013).

Ginger ether extract afforded one new compound, *O*-methyldehydrogingerol, with the structure 1-(4'-hydroxy-3'-methoxyphenyl)-5-methoxy-1-decen-3-one along with twenty-eight known compounds, including 1-dehydro-[6]-dehydrogingerol, *ar*-curcumen-15-al, 3-(4-hydroxy-3-methoxyphenyl)propionic acid methyl ester, curcumin, 1 β -hydroxybisabola-2,10-dien-4-one, [6]-dehydrogingerdione, [11]-isodehydrogingerdione, [6]-dehydroshogaol, [8]-dehydroshogaol, [10]-dehydroshogaol, [6]-gingerdione, [6]-gingerol, [8]-gingerol, [10]-gingerol, [4]-shogaol, [6]-shogaol, [8]-shogaol, vanillin, dihydrocurcumin, methyl-[6]-gingerol, *ar*-curcumene, vanillic acid, hexahydrocurcumin, [6]-gingerdiol, 2,5-dihydroxybisabola-3,10-diene, glyceryl-1-hexadecanoate, gingerenone A and cryptomeridiol (Liao et al. 2012). Twenty-two components were characterised in the steamed ginger: 5-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)-3-heptanone; 3-acetoxy-5-hydroxy-1,7-bis(3,4-dihydroxyphenyl)heptane; 3,5-dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane; 3,5-dihydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptane; 3-acetoxy-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)heptane; 5-hydroxyl,7-bis(4-hydroxy-3-methoxyphenyl)-3-heptanone; 4-gingerol; 3-acetoxy-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxy-5-methoxyphenyl)heptane; 3-acetoxy-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxy-3,5-dimethoxyphenyl)heptane; 3,5-diacetoxy-7-(4-dihydroxy-3-methoxyphenyl)-1-(3,4-dihydroxy-5-methoxyphenyl)heptane; 6-gingerdiol; 6-gingerol; 3,5-diacetoxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane; methyl 6-gingerol; 3- or 5-acetoxy-g-gingerdiol; 8-gingerol; 6-shogaol; diacetoxy-6-gingerdiol; 1-dehydro-6-gingerdione; 10-gingerol; methyl diacetoxy-6-gingerdiol and 8-shogaol (Chen et al. 2012).

Two novel glucosides of 6-gingerdiol were isolated from fresh ginger and their structures were determined as 1-(4-*O*- β -

D-glucopyranosyl-3-methoxyphenyl)-3,5-dihydroxydecane and 5-*O*- β -D-glucopyranosyl-3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)decane (Sekiwa et al. 2000). Both glucosides were found to be the precursors or intermediates of 6-gingerdiol. One new diarylheptanoid, namely, (4*E*,6*E*)-7-(3,4-dihydroxy-5-methoxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)hepta-4,6-dien-3-one, was isolated from ginger rhizomes, along with ten known ones: tetrahydrocurcumin; curcumin; 5-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptan-3-one; gingerenone A; 7-(3,4-dihydroxyphenyl)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)heptan-3-one; (*E*)-1,7-bis(4-hydroxy-3-methoxyphenyl)hept-1-ene-3,5-dione; (*E*)-7-(4-hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)-hept-1-ene-3,5-dione; shogasulphonic acid A; 1,5-epoxy-3-hydroxy-1-(3,4-dihydroxy-5-methoxyphenyl)-7-(4-hydroxy-3-methoxyphenyl)heptane and (3*S*,5*S*)-3,5-diacetoxy-1,7-bis(3,4-dihydroxyphenyl)heptane (Li et al. 2012b).

Compound identified fractions from the dichloromethane extracts of organically grown samples of fresh Chinese white and Japanese yellow varieties of ginger included paradols, dihydroparadols, gingerols, acetyl derivatives of gingerols, shogaols, 3-dihydroshogaols, gingerdiols, mono- and diacetyl derivatives of gingerdiols, 1-dehydrogingerdiones, diarylheptanoids and methyl ether derivatives of some of these compounds (Jolad et al. 2004). The compounds identified were [6]-paradol, [7]-paradol, [8]-paradol, [9]-paradol, [10]-paradol, [11]-paradol [13]-paradol and methyl [6]-paradol; [4]-gingerol, [6]-gingerol, [7]-gingerol, [8]-gingerol, [10]-gingerol, methyl [4]-gingerol and methyl [6]-gingerol; [4]-, [6]-, [8]-, [10]-, [12]-shogaols, methyl [6]-shogaol and methyl [8]-shogaol; acetoxy-[4]-gingerol, acetoxy-[4]-gingerol, acetoxy-[6]-gingerol, acetoxy-[8]-gingerol, acetoxy-[10]-gingerol and methyl acetoxy-[6]-gingerol; 1-dehydro-[3]-gingerdione, 1-dehydro-[6]-gingerdione, 1-dehydro-[8]-gingerdione and 1-dehydro-[10]-gingerdione; [4]-gingerdiol, [6]-gingerdiol, [8]-gingerdiol and [10]-gingerdiol; 5-acetoxy-[4]-gingerdiol, 5-acetoxy-[6]-gingerdiol, 5-acetoxy-[7]-gingerdiol, methyl 5-acetoxy-[4]-gingerdiol and methyl 5-acetoxy-[6]-gingerdiol; diacetoxy-[4]-gingerdiol, diacetoxy-

[6]-gingerdiol, methyl diacetoxy-[4]-gingerdiol, methyl diacetoxy-[6]-gingerdiol and methyl diacetoxy-[10]-gingerdiol; 3-dihydro-[6]-demethoxyshogaol; 5-methoxy-[6]-gingerol; 1,7-bis-(4'-hydroxy-3'-methoxyphenyl)-4-heptene-3-one; 1,7-bis-(4'-hydroxy-3'-methoxyphenyl)-3,5-heptadione; 1-dehydro-3-dihydro-[10]-gingerdione; 6-dihydroparadol; acetoxy-6-dihydroparadol; 1-(4'-hydroxy-3'-methoxyphenyl)-7-octen-3-one, 1-(4'-hydroxy-3'-methoxyphenyl)-7-decen-3-one and 1-(4'-hydroxy-3'-methoxyphenyl)-7-dodecen-3-one; and [4]-isogingerol. Thermal degradation products of gingerols included 4-(4-hydroxyphenyl)-2-butanone, 4-hydroxy-3-methoxybenzenepropanal, 3,4-dimethoxybenzenepropanal, zingerone, zingerone methyl ether, gingerol and zingerol 2-methyl ether. The major constituent in the two varieties was [6]-gingerol, a chemical marker for *Z. officinale*. White ginger and yellow ginger contained 27.56, 33.96 % [6]-gingerol; 3.20, 4.64 [8]-gingerol; 5.38, 7.91 % [10]-gingerol; and 0.36, 0.35 % [6]-shogaol. 115 compounds were identified from the methylene chloride extract of commercially processed dry ginger, 88 with retention times (R(t)) >21 min and 27 with < 21 min (Jolad et al. 2005). Of those 88 compounds, 45 were previously reported by Jolad et al. (2004) from fresh ginger, 12 were cited elsewhere in the literature and the rest (31) were new: methyl [8]-paradol; methyl [6]-isogingerol; methyl [4]-shogaol; [6]-isoshogaol; 6-hydroxy-[8]-shogaol; 6-hydroxy-[10]-shogaol; 6-dehydro-[6]-gingerol; 5-methoxy-[4]-gingerol; 5-methoxy-[8]-gingerol; 5-methoxy-[10]-gingerol; 3-acetoxy-[4]-gingerdiol; 5-acetoxy-[6]-gingerdiol (stereoisomer); diacetoxy-[8]-gingerdiol; methyl diacetoxy-[8]-gingerdiol; 6-(4'-hydroxy-3'-methoxyphenyl)-2-nonyl-2-hydroxytetrahydropyran; 3-acetoxydihydro-[6]-paradol methyl ether; 1-(4'-hydroxy-3'-methoxyphenyl)-2-nonadecen-1-one and its methyl ether derivative; 1,7-bis-(4'-hydroxy-3'-methoxyphenyl)-5-methoxyheptan-3-one; 1,7-bis-(4'-hydroxy-3'-methoxyphenyl)-3-hydroxy-5-acetoxyheptane; acetoxy-3-dihydrodemethoxy-[6]-shogaol; 5-acetoxy-3-deoxy-[6]-gingerol; 1-hydroxy-[6]-paradol; (2*E*)-geranial acetals of [4]- and [6]-gingerdiols; (2*Z*)-neral acetal of [6]-gingerdiol; acetaldehyde acetal of [6]-gingerdiol; 1-(4-hydroxy-3-

methoxyphenyl)-2,4-dehydro-6-decanone and the cyclic methyl orthoesters of [6]- and [10]-gingerdiols (Jolad et al. 2005). Of the 27 R(t) <21 min compounds, 5 were from fresh ginger, 20 others were found elsewhere in the literature and two were new: 5-(4'-hydroxy-3'-methoxyphenyl)-pent-2-en-1-al and 5-(4'-hydroxy-3'-methoxyphenyl)-3-hydroxy-1-pentanal. Most of the short R(t) compounds were probably formed by thermal degradation during GC (which mimics cooking) and/or commercial drying. The concentrations of gingerols, the major constituents of fresh ginger, were reduced slightly in dry ginger, while the concentrations of shogaols, the major gingerol dehydration products, increased.

Among 22 compounds isolated from fresh ginger rhizomes, the following compounds were considered to have high flavour dilution factors: linalool, geraniol, geranial, neral, isoborneol, borneol, 1,8-cineole, 2-pinen-5-ol, geranyl acetate, (*E*)-2-octenal, (*E*)-2-decenal and (*E*)-2-dodecenal (Nishimura 1995). In addition (*E*)-2-alkenals, 2-octyl acetate, 2-pinen-5-ol, 2-(2',3'-epoxy-3'-methylbutyl)-3-methylfuran and (*E*)- and (*Z*)-3,7-dimethyl-3,6-octadienal were newly identified compounds in ginger. Nishimura (2001) considered that monoterpenoids, linalool, 4-terpineol, isoborneol and borneol, as well as geranial and neral, might contribute to the characteristic odour of the Japanese fresh ginger. The following odour components were reported: *R*-(-) linalool (66 %) floral, *S*-(+) linalool (34 %) black tea-like, weaker floral note; *R*-(-) 4-terpineol (71 %), musty, *S*-(-) 4-terpineol (29 %) musty, dusty; (1*R*,2*R*,4*R*)-(-) isoborneol, (1*S*,2*S*,4*S*)-(+)-isoborneol (100 %) camphoraceous, India ink-like; (1*S*,2*R*,4*S*)-(-) borneol (8 %) camphoraceous, India ink-like; and (1*R*,2*S*,4*R*)-(+)-borneol (92 %) camphoraceous, India ink-like, fatty, putrid.

Composition of ginger oleoresin by ethanol extract, CO₂ extraction, ethyl acetate extract of young rhizomes, mature rhizomes and steamed rhizomes were, respectively, determined as follows: zingiberene (11.8, 27.1, 28.8, 26.2, 30.4 %), *ar*-curcumene (4.2, 15.1, 3.4, 6.0, 9.7 %), β -bisabolene (7.1, 11.8, 11.7, 10.8, 20.2 %), farnesene (0.4, 3.1, 0.3, 1.3, 3.3 %), β -sesquiphellandrene (8.0, 14.0, 10.8, 10.3,

14.8 %), citral (1, 0, 0.6, 5.1, 0 %), geraniol (0, 0, 2.8, 0, 1 %), geranyl acetate (1, 1–8.9, 0.2, 1.5 %), 1,8-cineole (0, 1.8, 2.3, 3.1, 0.2 %), camphene (0, 2.1, 0.2, 5.3, 1.1 %), sabinene (0, 2.3, 0.6, 4.8, 1.1 %) [6]-gingerol (19.4, 1.6, 3.6, 2.9, 1.0 %) and [6]-shogaol (14.0, 0.6, 0, 0, 6.5 %) (Takahashi et al. 2011).

Shogaols and paradols were found to be even more pungent than gingerols and were virtually absent in fresh ginger and were derived from gingerols during thermal processing or long-term storage (Zhang et al. 1994). Shogaols were gingerol analogues with a 4,5 double bond resulting from the elimination of the 5-hydroxy group. Paradols were formed by hydrogenation of the corresponding shogaol. [6]-gingerol (5-hydroxy-1-(4'-hydroxy-3'-methoxyphenyl)-3-decanone) was the most abundant constituent in fresh ginger but was found to decrease during thermal processing and postharvest storage. The main components of the steam-distilled ginger oil (total 46) were monoterpenes and sesquiterpenes; the pungent components of ginger were not found (Yu et al. 1997). Besides sesquiterpenes, the other two oils contained mainly the pungent components; the total content was 18.61 % in the cold-pressed ginger oil (total of 50 components) and 23.09 % in the supercritical CO₂-extracted ginger oil (total of 60 components), respectively. These two oils preserved the typical spicy odour and pungency of ginger. The total pungency principle oleoresin extracted for fresh ginger–solar dried– solar dried/steam-distilled ginger rhizomes was in the ratio [20:1:2] with respect to the [6]-gingerol content (Balladin et al. 1998). Histological analysis revealed that the oleoresin (pungent principles—gingerols and shogaols) was not observable in cell sections of the fresh ginger rhizomes (Balladin et al. 1999). However, the number of the oleoresin organelles increased in the order of solar dried and solar dried/steam-distilled ginger rhizomes, the latter having a high oleoresin extraction yield with acetone of 8.0 g per 100 g ginger rhizome (dry wt). The major substances present in the ginger oleoresins extracted with CO₂ and co-solvents (ethanol and isopropyl alcohol) were α -zingiberene, gingerols and shogaols; the amounts of these compounds were significantly affected by temperature, pressure and solvent (Zancan et al.

2002). Nonetheless, the antioxidant activity of the ginger extracts remained constant at $\approx 80\%$ and decreased to $\approx 60\%$ in the absence of gingerols and shogaols.

The yield of oleoresins from two Nigerian ginger varieties ranged within 86–140g/kg with UG14 giving the highest yield and UG26 the lowest (Meadows et al. 2006). In terms of pungency the range was within 60,000–120,000 Scoville heat units. In terms of the yield of 6-gingerol, the range was within 133–216g/kg of oleoresin. Ginger could be harvested from 4 months maturity after planting for a good yield of oleoresin and 6-gingerol. Ginger oleoresin was found to contain 24 pungent compounds and 50 volatile compounds (Zhan et al. 2008). The volatile compounds were mainly α -zingiberene (22.29 %), β -sesquiphellandrene (8.58 %), α -farnesene (3.93 %), β -bisabolene (3.87 %) and α -curcumene (2.63 %). The pungent compounds of ginger were mainly 6-gingerol (9.38 %), 6-shogaol (7.59 %) and zingerone (9.24 %) produced by the thermal degradation of gingerols or shogaols. The mass spectral fragmentation patterns for the three new compounds (6-isogingerol, (Z)-10-isoshogaol, (E)-10-isoshogaol) were interpreted. Jamaican ginger cultivars showed total pungencies as high as 1.59 %, due to the cumulative effects of 6-, 8-, 10-gingerols and 6-shogaol (Salmon et al. 2012). It was found that the two blue varieties, Bulbous Blue and Frog Blue, were the more astringent types, followed by Yellow Tambrick. Hawaiian ginger was found to have approximately two-thirds pungency of Bulbous Blue ginger. Essential oil yields of the cultivars varied in the same way as the pungencies, with Bulbous Blue ginger showing the highest yield at 1.291 %, while Hawaiian ginger showed 45 % less average oil content. Gingers from other sources have been noted as having higher yields ranging up to 2.5 % for Australian and Nigerian ginger. More than 30 oleoresin components were detected from supercritical CO₂ extraction of ginger oleoresin; α -curcumene (3.69 %), zingiberene (17.11 %), α -farnesene (2.28 %), β -bisabolene (5.12 %) and β -sesquiphellandrene (7.77 %) were found, and the pungent compounds were mainly gingerol (7.70 %) and zingerone (30.36 %) produced by the thermal degradation of gingerols in the analysis (Li et al. 2012c).

Supercritical carbon dioxide (SC CO₂) purified ginger extract was found to contain 75.92 % [6]-gingerol, 1.25 % [6]-shogaol, 4.54 % [4]-gingerol, 13.15 % [10]-gingerol and 0.37 % 6-gingerdiol (Sonale and Kadimi 2014). Small quantities of [4]-gingerdiol, [10]-gingerdiol and [6]-gingerdiacetate were also found in the ginger extract. Paradol analogues were not detected in their study. (+)(S)[6]-gingerol, (+)(S)[8]-gingerol and (+)(S)[10]-gingerol active principle of ginger were synthesised from optically active epoxide 7 obtained from β -keto sulfoxide 5 (Solladie and Ziani-Cherif 1993).

The gingerols, including [6]-, [8]- and [10]-gingerols, a series of chemical homologues differentiated by the length of their unbranched alkyl chains, were identified as major active components in fresh ginger rhizome (Jiang et al. 2006a). In the metabolic profiling analysis, *Z. officinale* samples derived from different origins showed no qualitative differences in major volatile compounds, although they did show some significant quantitative differences in non-volatile composition, particularly regarding the content of [6]-, [8]- and [10]-gingerols, the most active anti-inflammatory components in this species (Jiang et al. 2006b). The following compounds were found at concentration levels > 5 % across the ginger samples from different origins: camphene; 3-methylene-6-(1-methylethyl)-cyclohexene; (*E*)- α -citral; 2-methyl-6-*p*-tolyl-2-heptene; cedr-8-ene; α -marnesene (1,3,6,10-dodecatetraene, 3,7,11-trimethyl-); α -sesquiphellandrene and [6]-gingerol. Compounds found at 0.5–5 % concentrations included 1*R*- α -pinene, α -pinene, α -linalool, (1*S*,2*R*,4*S*)-(-)borneol, (*Z*)- α -citral, α -cubebene or copaene, germacrene D, eudesma-4(14), 11-diene, [6]-shogaol, [7]-paradol, [8]-gingerol, [10]-shogaol and [11]-paradol. Compounds < 0.5 % included 1,7,7-trimethyl-tricyclo[2.2.1.0(2,6)]heptane; (-)3,7-dimethyl-1,6-octadiene; 4(10)-thujene; 2(10)-pinene; 2-methyl-5-(1-methylethyl)-1,3-cyclohexadiene; cymene; cineol; *p*-mentha-1,4(8)-diene, (-)-alcanfor; citronellal; *p*-menth-1-en-8-ol; 2-undecanone; (+)cyclosativene; zingiberene; α -farnesene (1,6,10-dodecatriene, 7,11-dimethyl-3-methylene); cadinene; (+)-epi-bicyclosesquiphellandrene; panasinsen; [6]-paradol; acetoxy-

[6]-gingerol; [8]-shogaol; diacetoxy-[6]-gingerdiol and [9]-paradol.

Fourteen compounds, [4]-gingerol, [6]-gingerol, [8]-gingerol, [10]-gingerol, [6]-paradol, [4]-shogaol, [6]-shogaol, 1-dehydro-[10]-gingerdione, [10]-gingerdione, hexahydrocurcumin, tetrahydrocurcumin, gingerenone A, 1,7-bis-(4'-hydroxy-3'-methoxyphenyl)-5-methoxyheptan-3-one and methoxy-[10]-gingerol, were isolated from ginger (Koh et al. 2009). A phenylpropanoid ester mixture, (*E*)-geranylferulic acid (1a) and (*Z*)-geranylferulic acid (1b), along with 13 known compounds: [6]-gingerol, [8]-gingerol, [10]-gingerdione, 1-dehydro-[6]-gingerdione, 1-dehydro-[8]-gingerdione, [6]-paradol, [8]-paradol, [6]-gingerol diacetate, 6-hydroxy-[6]-shogaol, galanolactone, *trans*- β -sesquiphell-androl, *trans*-sesquipiperitol and 4 α ,5 β -dihydroxybisabola-2,10-diene—were isolated from ethanol ginger extract (Hong and Oh 2012). Phenylalkanooids, (*E*)-3-hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-tetradecan-6-en-5-one, and 13 known compounds comprising eight phenylalkanooids ([4]-shogaol; [6]-shogaol; [6]-gingerol, [6]-dehydrogingerdione; 3*R*,5*S*-[6]-gingerdiol; 3*S*,5*S*-[6]-gingerdiol; 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-hexan-5-one and 3-hydroxy-1-(3,5-dimethoxy-4-hydroxyphenyl)-hexan-5-one) including two benzenoids (vanillin and ferulic acid) and three diarylheptanoids (gingerenone A, hexahydrocurcumin and 1,7-bis(4-hydroxy-3-methoxyphenyl)heptan-3-one) were isolated from ginger rhizome (Li et al. 2013a). Two novel gingerdione dimers, bisgingerdiones A and B; two new gingerol derivatives, (5*R*)-5-acetoxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptan-3-one and methyl (*Z*)-neral acetal-[6]-gingerdiol; and 38 known compounds (27 gingerol derivatives, five steroids and six monoterpenoids) were isolated from Tongling white Ginger rhizomes collected from Tongling, China (Feng et al. 2011).

The bioactive components of ginger rhizomes were characterised by spectroscopic analysis as zingerone and dehydrozingerone [4-(4'-hydroxy-3'-methoxyphenyl)-(*E*)-3-buten-2-one] (Kuo et al. 2005). A series of substituted dehydrozingerones [(*E*)-4-phenyl-3-buten-2-ones] were

prepared in appreciable yields by the reaction of appropriate benzaldehydes with acetone, and the products were evaluated in terms of variation in the dehydrozingerone structure. The synthetic dehydrozingerone analogues were 4-(3'-hydroxy-4'-methoxyphenyl)-(E)-3-buten-2-one; 4-(4'-hydroxy-2'-methoxyphenyl)-(E)-3-buten-2-one; 4-(2'-hydroxy-3'-methoxyphenyl)-(E)-3-buten-2-one; 4-(2'-hydroxy-4'-methoxyphenyl)-(E)-3-buten-2-one; 4-(2'-hydroxy-5'-methoxyphenyl)-(E)-3-buten-2-one; 4-(2'-hydroxy-6'-methoxyphenyl)-(E)-3-buten-2-one; 4-(2'-hydroxyphenyl)-(E)-3-buten-2-one; 4-(3'-hydroxyphenyl)-(E)-3-buten-2-one; 4-(4'-hydroxyphenyl)-(E)-3-buten-2-one; 4-(2'-methoxyphenyl)-(E)-3-buten-2-one; 4-(3'-methoxyphenyl)-(E)-3-buten-2-one; 4-(4'-methoxyphenyl)-(E)-3-buten-2-one; 4-phenyl-(E)-3-buten-2-one; 4-(3'; 4'-methylenedioxyphenyl)-(E)-3-buten-2-one; 4-(4'-hydroxy-3'; 5'-dimethoxyphenyl)-(E)-3-buten-2-one; 4-(3'-hydroxy-2'-isopropoxyphenyl)-(E)-3-buten-2-one; 4-(2'-hydroxy-4'-isopropoxyphenyl)-(E)-3-buten-2-one; 4-(5'-hydroxy-2'-isopropoxyphenyl)-(E)-3-buten-2-one; 4-(3'-hydroxy-4' isopropoxyphenyl)-(E)-3-buten-2-one; 4-(2'; 3'-diisopropoxyphenyl)-(E)-3-buten-2-one; 4-(2',4'-diisopropoxyphenyl)-(E)-3-buten-2-one; 4-(2',5'-diisopropoxyphenyl)-(E)-3-buten-2-one; 4-(3',4'-diisopropoxyphenyl)-(E)-3-buten-2-one; 4-(2'; 3'-dihydroxyphenyl)-(E)-3-buten-2-one; 4-(2'; 4'-dihydroxyphenyl)-(E)-3-buten-2-one; 4-(2'; 5'-dihydroxyphenyl)-(E)-3-buten-2-one; and 4-(3',4'-dihydroxyphenyl)-(E)-3-buten-2-one.

Chemical compounds identified in ginger oleoresin obtained with ethanol (6 h), isopropanol (6 h) and liquid carbon dioxide CO₂-E1 were reported, respectively, by Nobrega et al. (1997) as follows: 2-heptanol (0; 0; 0.4 %), α -pinene (1.11; 1.14; 0.85 %), camphene (2.97; 4.02; 2.78 %), β -myrcene (1.26; 2.10; 3.12 %), β -pinene (4.72; 4.99; 22.63 %), m-diethylbenzene (0; 0; 1.38 %), O-diethylbenzene (0; 0; 0.75 %), citronellal (0; 0; 1.23 %), neral (1.13; 1.97; 3 %), nonanal (0; 0.97; 0 %), geranial (2.54; 5.16; 2.17 %), 2-undecanone (0; 0; 0.87 %), *ar*-curcumene (3.05; 2.99; 4.19 %), α -zingiberene (37.53; 35.10; 31.18 %), farnesene (18.74; 14.43; 12.47 %), β -

sesquiphellandrene (12.86; 11.25; 8.83 %), 6-gingerol (3.82; 1.29; 0) and unknown (9.31; 18.88; 3.36 %). Chemicals obtained with ethanol (2 h) and isopropanol (2 h) included *p*-cymene (3.19; 4.52 %), methyl 11-octadecenoate (12.71; 5.98 %), methyl linolelaidate (18.93; 6.62 %), methyl 4,6,10,14-tetramethyl pentadecanoate (4.01; 4.99 %) and methyl 14-methyl pentadecanoate (24.3; 15.20 %).

Ginger harvested at 8 months from Bourbon, Portland, had the highest oleoresin yield (8.46 %) (Bailey-Shaw et al. 2008). [6]-Gingerol was found to be the most abundant pungent bioactive principle in all the oleoresin samples investigated, with the 9 months sample from Bourbon, Portland containing the highest level (28.94 %). The content of [6]-gingerols was also found to be consistently high (7–9 months) in oleoresin samples from Johnson Mountain, St. Thomas (15.12–16.02 %). The results suggest that Bourbon in Portland may be the most ideal location for cultivating ginger for high yields and quality; however, Johnson Mountain in St. Thomas could prove to be the least restrictive location, allowing for harvesting of good quality material throughout the maturity period (7–9 months). Major volatile constituents of the essential oil from 17 northeast Indian ginger cultivars were camphene (8.49 %), neral (4.95 %), geranial (12.36 %), zingiberene (20.98 %) and β -sesquiphellandrene (7.96 %) (Kiran et al. 2013). Assam Fibreless cultivar showed the highest yield of essential oil (4.17 %) and higher monoterpene hydrocarbon content (38.65 %) than sesquiterpene hydrocarbon (25.38 %). Among all these cultivars, Assam Tinsukia had the highest citral content (23.66 %) and Meghalaya mahima had the highest zingiberene content (29.89 %). Except Mizoram Thinglaidum, Mizoram Thingria, Nagaland Nadia and Tripura I ginger cultivars, the remaining six northeast Indian cultivars showed an increase in the citral content during maturity. At 6-month maturity, a higher undecanone level was found in Nagaland Nadia (7.36 %), Tripura I (6.23 %) and Tripura III (9.17 %) cultivars. The Nagaland Nadia cultivar showed higher *ar*-curcumene (9.57 %) content than zingiberene (5.84 %), which was unique among all cultivars. Ginger harvested at 9-month maturity from the Tripura II cultivar had the highest citral content

(22.03 %), and the Meghalaya mahima cultivar had the highest zingiberene content (29.89 %). The oleoresin content was found to decrease with maturity in all cultivars, except Assam Fibreless and Manipur I. Moreover, the highest oleoresin (11.43 and 9.42 %) and [6]-gingerol (1.67 and 1.67 g) contents were observed for Tripura II and Nagaland Nadia, respectively.

Radiation treatment (10 kGy) reduced the decrease of the oleoresin content of ginger during the storage period by 14 % in ungrounded samples and 11 % in ground samples (Onyenekwe 2000). There was a dose-dependent decrease in the 6-gingerol content of the ground ginger, decreasing by 65.6, 67.4 and 70.4 % for the 0, 5 and 10 kGy irradiated samples, respectively, while the corresponding values for the ungrounded ginger samples were 37.8, 40.0 and 44.3 % at the end of the storage period. γ -irradiation at a dose of 60 Gy did not bring about any detectable qualitative and quantitative changes in the aroma constituents (Variyar et al. 1997). A decrease in gingerol content was observed in the γ -irradiated rhizome samples stored for 2 months at ambient temperatures (28–30°C) in perforated low-density polyethylene bag (Variyar et al. 2007). This decrease was approximately 21 %, 22 % and 10 % in irradiated ginger stored at 0, 1 and 2 months, respectively, compared with their corresponding non-irradiated controls. γ -irradiation at a dose of 60 Gy was found to prevent sprouting and extend the shelf life of fresh ginger under ambient conditions without affecting its flavouring principles.

6-Gingerol, 6-shogaol, 8-gingerol and 10-gingerol were extracted from a wide variety of ginger-containing dietary supplements, spices, teas, mints and beverages (Schwertner and Rios 2007). The recoveries of 6-, 8- and 10-gingerol and 6-shogaol from the ginger dietary supplements and ginger-containing products were 94.7, 93.6, 94.9 and 97.1 %, respectively. The gingerol composition of various ginger-containing spices, teas and beverages also was found to vary widely. The variations (CV's) in the 6-gingerol, 6-shogaol, 8-gingerol and 10-gingerol concentrations of nine different ginger root dietary supplements were 115.2, 45.7, 72.3 and 141.7 %, respectively. Using high-speed counter-current

chromatography with stepwise elution, Wang et al. (2011) obtained 132 mg of 6-gingerol, 31 mg of 8-gingerol and 61 mg of 10-gingerol from 360 mg of pre-purified ginger extract sample. The purity of each compound was over 98 %. Schwertner et al. (2006) found that the amounts of 6-gingerol, 6-shogaol, 8-gingerol and 10-gingerol in the ginger root dietary supplements varied widely both on a milligram per gram basis and on a milligram per capsule basis. The 6-gingerol concentration of the ginger powder dietary supplements ranged from 0.0 to 9.43 mg/g (mean 2.56 mg/g), 6-shogaol ranged from 0.16 to 2.18 mg/g (1.27), 8-gingerol ranged from 0.00 to 1.1 mg/g (0.47) and 10-gingerol ranged from 0.00 to 1.40 mg/g (0.36). Tao et al. (2009) used high-performance liquid chromatography–tandem mass spectrometry for the quantitative analysis of 6-gingerol, 8-gingerol, 10-gingerol, 6-shogaol, 8-shogaol and 10-shogaol in ginger dietary supplements. Among the pure solvents tested for pressurised liquid extraction (PLE) of ginger, bioethanol yields the highest efficiency for recovering most constituents of gingerol-related compounds, while for a broad concentration spectrum of ethanol aqueous solutions, 70 % ethanol gave the best performance in terms of yield of total extract, complete constituent profile and recovery of most gingerol-related components (Hu et al. 2011). PLE with 70 % bioethanol operated at 1500 psi and 100 °C for 20 min (static extraction time: 5 min) was found as optimised extraction conditions, achieving 106.8 %, 109.3 % and 108.0 % yield of [6]-, [8]- and [10]-gingerol relative to the yield of corresponding constituent obtained by 8 h Soxhlet extraction (absolute ethanol as extraction solvent). Ginger extracts obtained using supercritical CO₂ and compressed propane afforded a maximum yield of 3.21 wt% for the CO₂ extraction and 2.75 wt% for the extraction using propane as solvent (Mesomo et al. 2012). When CO₂ was used as solvent, the pressure and temperature presented significant effect on the extraction yield. When propane was used, the most important variable was the pressure that presented a positive effect on the extraction yield. The chemical profiles were similar for the two solvents, in which the main compounds were α -

zingiberene, β -sesquiphellandrene, α -farnesene, geranial, β -bisabolene and β -eudesmol. Classes of gingerol-related compounds were detected during pulsed ultrafiltration from the chloroform partition of the methanol ginger root extract including 4 gingerols (6-, 8-, 10-, 12-gingerols), 4 shogaols (6-, 8-, 10-, 12-shogaols), 3 paradols (6-, 8-, 10-paradols), 2 gingerdiols (6-, 8-gingerdiols), 3 gingerdiones (6-, 8-, 10-gingerdiones) and 3 dehydrogingerols (6-dehydro-6-gingerol, 6-dehydro-8-gingerol, 6-dehydro-10-gingerol) (van Breemen et al. 2011). The main compounds present in ginger extracts obtained using supercritical CO₂ were α -zingiberene, β -sesquiphellandrene, α -farnesene, geranial, β -bisabolene and β -eudesmol (Mesomo et al. 2013).

In ginger, the concentration of flavonoids in the rhizomes increased (Halia Bentong 59.6 %; Halia Bara 60.1 %) with advancing growth periods (from 8 to 16 weeks) (Ghasemzadeh et al. 2010b). The concentration of flavonoids (mg/g DW) in the rhizomes of cv Halia Bentong and Halia Bara at 8 weeks and 16 weeks were, respectively, as follows: quercetin (0.505–0.803 mg, 0.641–0.865 mg), rutin (0.226–0.0311 mg, 0.423–0.324 mg), catechin (0.20–0.36 mg, 0.36–0.45 mg), epicatechin (0.049–0.077 mg, 0.020–0.091 mg), naringenin (0.031–0.046 mg, 0.015–0.020 mg) and kaempferol (0.023–0.045 mg, 0.048–0.060 mg). Both ginger varieties (Halia Bentong and Halia Bara) showed an increase in phenolic compounds (gallic acid, vanillic acid, ferulic acid, tannic acid, cinnamic acid and salicylic acid) and flavonoids (quercetin, rutin, catechin, epicatechin, kaempferol, naringenin, fisetin and morin) in response to CO₂ enrichment from 400 to 800 μ mol/mol CO₂ (Ghasemzadeh et al. 2010a). These increases were greater in rhizomes compared to leaves. High-performance liquid chromatography (HPLC) results showed that quercetin and gallic acid were the most abundant flavonoid and phenolic acid in Malaysian young ginger varieties. Under elevated CO₂ conditions, kaempferol and fisetin were among the flavonoid compounds, and gallic acid and vanillic acid were among the phenolic compounds whose levels increased in both varieties. Total flavonoids (TF), total phenolics (TP), total soluble carbohydrates (TSC), starch and

plant biomass increased significantly in all parts of the ginger varieties under elevated CO₂ (800 µmol/mol) (Ghasemzadeh and Jaafar 2011). The order of the TF and TP increment in the parts of the ginger plant was rhizomes > stems > leaves. More specifically, Halia Bara had a greater increase of TF (2.05 mg/g dry weight) and TP (14.31 mg/g dry weight) compared to Halia Bentong (TF: 1.42 mg/g dry weight; TP: 9.11 mg/g dry weight) in average over the whole plant.

Three unprecedented purine-containing compounds isolated from a methanolic extract of ginger rhizomes were named [6]-, [8]- and [10]-zingerines as they were 5-(6-amino-9H-purin-9-yl) analogues of [6]-, [8]- and [10]-gingerols, respectively, together with [6]-, [8]- and [10]-shogaols (Araya et al. 2011). Fresh ginger slices were found to contain 1,3-cyclohexadiene, 5-(1,5-dimethyl-4-hexyl)-2-methyl-, [*S*-(*R**,*S**)] (28.124 %), 2,6-octadienal, 3,7-dimethyl (15.713 %), α -farnesene (6.905 %), cyclohexene, 3-(1,5-dimethyl-4-hexenyl)-6-methylene-, [*S*-(*R**,*S**)] (7.645 %), β -phellandrene (7.53 %), camphene (6.675 %), 2,6-octadienal, 3,7-dimethyl-, (*Z*) (5.561 %), *R*- α -pinene (1.835 %), eucalyptol (5.658 %), benzene, 1-(5-dimethyl-4-hexenyl-4-methyl- (2.847 %), borneol (1.678 %), 1,6-cyclodecadiene, 1-methyl-5-methylene-8-(1-methylethyl)-, [*S*-(*E*,)]-(1.309 %) (Ding et al. 2012). Koo and Gang (2012) reported the identification and functional characterisation of 25 mono- and 18 sesquiterpene synthases from ginger. Novel terpene synthases, (–)-caryolan-1-ol synthase and α -zingiberene/ β -sesquiphellandrene synthase, which was responsible for the formation of the major sesquiterpenoids in ginger and turmeric rhizomes, were also discovered.

Volatiles/Essential Oil

Zingiberol plus citral, methyl heptenone, nonyl aldehyde, linalool, D-borneol, acetic acids combined as esters, traces of a phenol, cineol and new sesquiterpene alcohol called zingiberol were found in ginger oil (Brooks 1916). Zingiberol was shown to be a stereoisomeric mixture of β -eudesmol with *trans*- and *cis*-ring juncture (Varma et al. 1962). Also, juniper camphor

was found to possess a *cis*-ring juncture. A sesquiterpene, (–)- β -sesquiphellandrene, was isolated from ginger oil, and its structure was elucidated as (*l'**R*,6*S*)-2-methyl-6-(4'-methylene- cyclohex-2'-enyl)hept-2-ene (Connell and Sutherland 1966). Three new sesquiterpenes: sesquithujene, *cis*-sesquisabinene hydrate and 2-methyl-6-(*trans*-4'-methyl-4'-hydroxycyclohex-2'-enyl)-hept-2-ene (zingiberenol) were isolated from *Zingiber officinale* (Terhune et al. 1975). Four gas chromatographic peaks from ginger oil, consisting of α -terpineol, citral a, citral b, β -sesquiphellandrene, *ar*-curcumene, nerolidol and a sesquiterpene alcohol, accounted for 85 % of the taste panel's flavour response (Bednarczyk and Kramer 1975). Taste panel evaluations of the isolated components indicated that β -sesquiphellandrene and *ar*-curcumene were the prime contributors to the characteristic 'ginger' attribute. α -Terpineol, citral a and citral b contributed to the 'lemony' attribute of ginger oil and may therefore be desirable additives to whole ginger oil to intensify its 'lemony' character. Nerolidol contributed to the 'woody' or 'soapy' attribute and did not appear to be a good potential additive to ginger oil.

The major volatile flavour components of ginger rhizome identified were α -zingiberene (21.8 %), geranial (9.9 %), geraniol (9.4 %), β -bisabolene (7.9 %), neral (7.1 %), 1,8-cineole (6.2 %), α -terpineol (5.6 %), borneol (5.4 %), β -phellandrene (3.1 %), linalool (1.7 %), methyl nonyl ketone (1.6 %), camphene (1.4 %), menthyl acetate (1 %) and limonene (1 %) (Miyazawa and Kameoka 1988). The minor constituents (tr < 1 %) were α -pinene, β -pinene, δ -3-carene, β -myrcene, α -phellandrene, α -terpinene, γ -terpinene, 6 unknowns, *p*-cymene, terpinolene, 2-heptanol, 6-methyl-5-hepten-2-one, hexanol, *cis*-3-hexenol, 2,2,4-trimethylheptane, perillene, *trans*-2-octenal, *trans*-linalool oxide, citronellal, α -copaene, camphor, neo-isopulegol, β -thujone, bornyl acetate, camphene hydrate, terpinene-4-ol, β -caryophyllene, aromadendrene, isoborneol, citronellyl acetate, β -himachalene, α -muurolene, α -selinene, β -selinene, geranyl acetate, citronellol, sesquiphellandrene, α -curcumene, α -cadinene, sesquiterpene hydrocarbon, 6 sesquiterpene alcohols, calamenene, β -ionone, nerolidol, ethyl myristate, cedrol,

elemol, patchouli alcohol, *cis*-sesquiphellandrene hydrate, guaiol, β -bisabolol, juniper camphor, zingiberenol, β -eudesmol, farnesol, 9-oxonerolidol, dodecanoic acid, 4-phenylbenzaldehyde, 3-phenylbenzaldehyde and xanthorrhizol. Thirteen volatile components comprising monoterpenes, α -pinene, camphene, myrcene, β -phellandrene, 1,8-cineol, borneol, neral, geranial and geranyl acetate, and sesquiterpenes, α -curcumene, α -zingiberene, β -bisabolene and β -sesquiphellandrene, were found in Japanese fresh ginger (*Zingiber officinale*) (Tanabe et al. 1991).

Essential oil of ginger was found to contain the following: α -zingiberene and β -zingiberene (35.6 %), *ar*-curcumene (17.7 %), borneol (2.2 %), farnesene (1.8 %), citral a (1.4 %), γ -selinene (1.4 %), cineole (1.3 %), β -phellandrene (1.3 %), linalool (1.3 %), limonene (1.2 %), camphene (1.1 %), β -elemene (1.0 %), citral b (0.8 %), α -pinene (0.4 %), β -pinene (0.2 %), β -bisabolene (0.2 %), 2-nonanol (0.2 %), decyl aldehyde (0.2 %), alcohol A (0.2 %), alcohol B (0.1 %), myrcene (0.1 %), *p*-cymene (0.1 %), methyl heptenone (0.1 %), nonyl aldehyde (0.1 %), bornyl acetate (0.1 %), geraniol (0.1 %), cumene (trace <0.01 %) and 2-heptanol (tr) (Nigam et al. 1964). The qualitative and quantitative composition of ginger rhizome essential oils was found to be influenced by cultivars, stages of harvest maturity, growing location, methods of extractions and storage. Volatile constituents of ginger rhizomes produced by in-vitro shoot tip culture accumulated volatile oils similar to those formed in the original rhizome (Sakamura et al. 1968). In the oil from the rhizome grown in the modified Gamborg's B5 medium, the acyclic oxygenated monoterpenes predominated, while the oil from the rhizome grown in the modified Murashige–Skoog (MS) medium consisted mainly of sesquiterpenes. The essential oil from Australian-grown ginger was similar to that of oils from other areas (Cornell and Jordan 1971). The major constituents comprised sesquiterpene hydrocarbons based on the bisabolene carbon skeleton, monoterpene hydrocarbons and other substances. The oil contained a relatively high proportion of geranial and neral which imparted a distinctive 'citrus-like' aroma. The essential oil from the fresh ginger rhizome was characterised by the presence of acyclic

oxygenated monoterpenes mainly composed of neral, geraniol, geranial and geranyl acetate (Sakamura 1987). During storage the content of neral and geranial in the rhizome increased to *ca* 60 % of the essential oil, while the content of geraniol and geranyl acetate decreased to an undetectable amount. The change resulted from the conversion of geranyl acetate into geraniol, geranial and neral, successively. The content of geranial and neral decreased to a small extent through cultivation of the stored rhizome, whereas a large quantity of geraniol and geranyl acetate occurred in the newly propagated fresh rhizome. A ginger oil yield of 0.1–0.2 % comprising 25 constituents were identified in Fiji ginger essential oil (Smith and Robinson 1981). The oil was unusual in having a much higher neral (15 %) and geranial (27 %) content than oils reported from India, Australia, Japan and Africa. It also contained high 1,8-cineole (8 %), and other compounds identified included α -copaene, β -bourbonene, α -bergamotene, α -selinene, calamenene and cuparene. The content of [6]-gingerol and [6]-shogaol, the most important pungent compounds in the dried ginger, were 0.76 % and 0.11 %, respectively (Yonei et al. 1995). The volatile oil content obtained by high-pressure carbon dioxide extraction was about 50 %; the major volatile components were zingiberene which accounted for about 40 %, farnesene, β -sesquiphellandrene, camphene and 1,8-cineole. The volatile compounds were regarded as aromatic compounds in ginger flavour. The pungent compounds in the ginger extract was confirmed to be 6-, 8-, 10-geringerols and [6]-shogaol. The content of [6]-gingerol amounted to 40 % and the rest were < 2 %. It was found that the [6]-gingerol content of the extract could be controlled by manipulating the extraction conditions. Furthermore, a two-stage separation was performed in order to concentrate [6]-gingerol to produce a highly pungent ginger flavour. In the two-stage separation, the first separation was carried out under various pressures of 7.9–10.9 MPa at a constant temperature of 333 K, and the second separation conditions are kept the same as those for the one-stage separation.

Zingiber officinale oil from Mauritius was characterised by the presence of geranial (16.3 %), neral (10.3 %), zingiberene

(9.5 %), β -sesquiphellandrene (6.3 %) and *ar*-curcumene (5.1 %) (Gurib-Fakim et al. 2002). The rhizome essential oils of 16 of the 17 Australian ginger clones, including the tetraploid clones and their parent cultivar, were found to be of substantially similar composition (Wohlmuth et al. 2006). These oils were characterised by very high citral levels (51–71 %) and relatively low levels of the sesquiterpene hydrocarbons typical of ginger oil. The citral levels of most of these oils exceeded those previously reported for ginger oils. One clone, the cultivar ‘Jamaican’, yielded oil with a substantially different composition, lower citral content and higher levels of sesquiterpene hydrocarbons and pungent gingerols. The major components of ginger essential oil were *ar*-curcumene (59 %), β -myrcene (14 %), 1,8-cineol (8 %), citral (7.5 %) and zingiberene (7.5 %) (Nogueira de Melo et al. 2011). Ginger rhizome oil was predominated by monoterpenoids, with camphene (14.5 %), geranial (14.3 %) and geranyl acetate (13.7 %), the three most abundant constituents followed by neral (7.7 %), geraniol (7.3 %), 1,8-cineol (5.0 %), α -pinene (3.6 %), α -zingiberene (3.2 %), borneol (2.9 %), limonene (2.5 %), linalool (2.3 %), myrcene (2.0 %), *trans-trans*- α -farnesene (1.8 %), β -sesquiphellandrene (1.6 %), bornyl acetate (1.4 %), α -humulene (1.1 %), β -caryophyllene (1 %), bornyl acetate (1.4 %), α -terpineol (1.1 %) and *ar*-curcumene (1.0 %) (Sivasothy et al. 2011). Minor compounds (trace to < 1 %) were 2-heptanol, tricyclene, sabinene, β -pinene, 6-methyl-5-hepten-2-one, β -pinene, α -phellandrene, δ -3-carene, *p*-cymene, 2-heptyl acetate, γ -terpinene, terpinolene, 2-nonanone, *trans*-sabinene hydrate, camphor, camphene hydrate, citronellal, isoborneol, terpinene-4-ol, myrtenal, linalyl formate, β -citronellol, myrtenal, β -citronellol, 2-undecanone, myrtenyl acetate, neryl acetate, α -copaene, β -elemene, *allo*-aromadendrene, α -muurolene, α -elemol, *trans*-nerolidol, caryophyllene oxide, γ -eudesmol, β -eudesmol, α -bisabolol, *cis-cis*-farnesol and *trans-trans*-farnesal. The major constituents identified in ginger rhizome oil were zingiberene, β -sesquiphellandrene and *ar*-curcumene (Variyar et al. 1997, 2007).

Ding et al. (2012) found 19, 28, 21, 20, 31 and 20 novel volatile compounds (70 in total) in dried gingers treated by air-

drying (AD) at 50, 60 and 70 °C, microwave drying (MD) at 60 W, vacuum drying (VD) in 13.3 kPa at 60 °C and freeze-drying (FD) in 0.203 kPa at chamber temperature of 22 °C, respectively. Principal component analysis for the main volatiles indicated that drying increased the relative contents of benzene,1-(1,5-dimethyl-4-hexenyl)-4-methyl-; 1,3-cyclohexadiene,5-(1,5-dimethyl-4-hexenyl)-2-methyl-,*[S-(R*,S*)]*-; α -farnesene and cyclohexene,3-(1,5-dimethyl-4-hexenyl) -6-methylene-,*[S-(R*,S*)]*- while decreasing those of 2,6-octadienal,3,7-dimethyl-,*(Z)* and 2,6-octadienal,3,7-dimethyl-. Cluster analysis revealed that MD was the best drying method, followed by AD at 60 °C, VD, FD and AD at 50 and 70 °C. AD, MD and VD also resulted in the loss of cyclocompounds, alcohols (2-heptanol, eucalyptol, isoborneol and borneol), aldehydes (octanal; 6-octenal, 3,7-dimethyl, *(R)*6-octenol and 3,7-dimethyl-, *(R)*) and ketones (2-undecanone) which were more pronounced when temperature increased from 50 to 70°C in the case of AD. These cyclocompounds included tricycle[2.2.1.0(2,6)] heptane, 1,7,7-trimethyl-; bicycle[3.1.0]hexane, 4-methylene-1-(1-methylethyl)-; cyclohexene, 1-methyl-4(1-methylethylidene)-; cyclohexene,1-methyl-4-(1-methylidenene)-; bicycle[2.2.1]heptan-2-one,1,7,7-trimethyl-1,1(*R*)-; 3-cyclohexene-1-methanol, α,α -4-trimethyl-; and cyclohexane,1-ethenyl-1-methyl-2,4-bis(1-methylethenyl)-,*[1S-(1\alpha,2\beta,4\beta)]*-.

For ginger essential oil obtained by hydrodistillation, α -curcumene, geranial and camphene were the most abundant compounds. Pretreatment of ginger with α -amylase or viscozyme followed by extraction with acetone afforded higher yield of oleoresin (20 %) and gingerol (12.2 %) compared to control (15 % oleoresin, 6.4 % gingerol) (Nagendrachari et al. 2013). Extraction of ginger pretreated with enzymes followed by extraction with ethanol provided higher yield of gingerol (6.2–6.3 %) than the control (5.5 %) with comparable yields of the oleoresin (31–32 %). Also, ethanol extract of cellulase pretreated ginger had the maximum polyphenol content (37.5 mg/g). Apart from 6-gingerol, 6-paradol and 6- and 8-methyl shogaols were the other important bioactive constituents in the oleoresin from cellulase-treated ginger. Twenty-two terpenes were isolated

from steam-distilled ginger extract: α -pinene, β -pinene, β -myrcene, camphene, β -phellandrene, 1,8-cineole, α -terpinolene, 2-nonanone, linalool, borneol, α -terpineol, citronellol, neral, geraniol, geranial, bornyl acetate, geranyl acetate, *ar*-curcumene, zingiberene, germacrene D, β -bisabolene and β -sesquiphellandrene (Liu et al. 2012). Nine volatile compounds, (*E,E*)- α -farnesene, eucalyptol, L-linalool, borneol, citronellol, β -bisabolol, geranial, bornyl acetate and neryl acetate, were found to have significant positive contribution to gingery note, and atmospheric pressure sterilisation (95 °C, 30 min) was the most beneficial method to preserve these important volatile compounds and the most favourable method for sterilisation of clarified ginger flavour beverages (Liu et al. 2014). The essential oil content and constituents (zingiberene, limonene, linalool, geraniol, nerolidol, gingerol, shogaol) of sliced ginger, dried under various drying methods (sun-drying, solar tunnel drying), was found to increase, as the slice length increased and the maximum retention was obtained in the whole dry rhizomes (Jayashree et al. 2014).

Ibrahim and Zakaria (1987) reported the main volatile constituents of Malaysian ginger rhizome oil as bornyl acetate (5.10 %), camphene (4.62 %), limonene (2.70 %), linalyl acetate (2.52 %), α -pinene, (2.22 %), 1,8-cineole (2.04 %), β -bisabolene (1.20 %), linalool (1.14 %) and *ar*-curcumene (1.02 %). Malaysian *Zingiber officinale* variants, namely, *Z. officinale* var. *officinale* (young common ginger), *Zingiber officinale* var. *rubrum* (jahe merah), *Zingiber officinale* var. *rubrum* Theilade (halia bara) and *Zingiber officinale* var. *rubrum* Theilade (halia padi) rhizome oils were found to contain 22, 40, 19 and 17 components comprising 71.8 %, 89.7 %, 74.4 % and 84.1 % of the total rhizome oils, respectively (Abd Malek et al. 2005). The major components of the rhizome oils were found to be *Z. officinale* var. *officinale* (common ginger): zingiberene (16.70 %), (*E,E*)- α -farnesene (13.10 %), geranial (7.60 %), camphene (6.88 %), 1,8-cineole (6.52 %), β -sesquiphellandrene (6.49 %), neral (5.41 %) and *ar*-curcumene (2.62 %); *Z. officinale* var. *rubrum* (jahe merah): camphene (15.76 %), geranial (12.66 %), *ar*-curcumene (9.71 %), neral (7.42 %), β -bisabolene (5.23 %), β -

sesquiphellandrene (5.13 %), 1,8-cineole (4.47 %), α -pinene (3.72 %) and zingiberene (3.57 %); *Z. officinale* var. *rubrum* Theilade (halia bara): geranial (28.43 %), neral (14.20 %), geranyl acetate (8.77 %), zingiberene (3.71 %), α -phellandrene (2.91 %), borneol (2.74 %), β -bisabolene (2.15 %) and β -sesquiphellandrene (2.04 %); and *Z. officinale* var. *rubrum* Theilade (halia padi): geranial (28.62 %), neral (15.58 %), β -sesquiphellandrene (6.44 %), β -bisabolene (5.61 %), *cis*-Nerolidol (5.61 %), α -phellandrene (5.15 %), camphene (4.53 %), zingiberene (4.33 %), *ar*-curcumene (3.64 %) and pulegone (3.42 %).

Sri Lankan ginger varieties (Sidda and Chinese types) yielded relatively high percentages of oil (between 1.8 and 4.3 %) and total aroma volatiles (*ca* 5 mg/g for dried samples) (Macleod and Pieris 1984). Terpenes were the main aroma components (*ca* 99 % for all samples). Novel compounds found included *trans*- β -ocimene, thujyl alcohol, terpinen-4-ol, myrtenal, guaiane, α -cubebene, δ -cadinene and farnesol. On drying, both varieties of Sri Lankan ginger showed considerable decrease in monoterpene content and very high increase in sesquiterpene concentration. Sri Lankan dried ginger showed high levels of *ar*-curcumene together with reasonable levels of citral isomers and all other constituents previously claimed to be important to ginger aroma. Sri Lankan ginger would appear to be unusual in containing very low amounts of zingiberene but very high amounts of β -bisabolene. The essential oil yield of dried Vietnamese ginger was 2.7 % comprising 28 % monoterpene hydrocarbons, 37 % oxygenated monoterpenes, 25 % sesquiterpene hydrocarbons, 8 % oxygenated sesquiterpenes and 2 % non-terpenoid compounds (van Beek et al. 1987). The composition was most similar to that of a variety of fresh Sri Lankan ginger. The main component was geranial (16 %) which gave the ginger, together with neral, a lemony character. Furfural, 2,6-dimethylhept-5-enal, dihydroperillene, *p*-cymen-8-ol, *allo*-aromadendrene, γ -muurolene, lauric acid, methylisoeugenol, γ -eudesmol, farnesal and xanthorrhizol were also identified. Ginger essential oils (obtained by hydrodistillation) of fresh and dried rhizomes of Nigerian origin contained mainly mono- and sesquiterpenoids of which geranial, neral, 1,8-cineole,

zingiberene, β -bisabolene and β -sesquiphellandrene were the major components (Ekundayo et al. 1988). Among the 54 constituents identified, (*E*)(*E*)- α -farnesene, viridiflorol and (*E*)(*E*)-farnesal were found in ginger for the first time.

The volatile oil from shoukyo Japanese ginger rhizome contained α -zingiberene 21.8 %, geranial 9.9 %, geraniol 9.4 %, β -bisabolene 7.9 %, nerol 7.1 %, 1,8-cineol 6.2 %, α -terpineol 5.6 %, borneol 5.4 %, β -phellandrene 3.1 %, linalool 1.7 %, methyl nonyl ketone 1.6 %, camphene 1.4 %, limonene 1 % and menthyl acetate 1 %; those (<1 %) included α -pinene, β -myrcene, α -phellandrene, *p*-cymene, terpinolene, 2-heptanol, 6-methyl-5-hepten-2-one, 2,2,4-trimethylheptane, camphor, neo-isopulegol, bornyl acetate, camphene hydrate, terpinene-4-ol, β -caryophyllene, aromadendrene, citronellyl acetate, β -himachalene, α -muurolene, α -selinene, β -selinene, geranyl acetate, citronellol, sesquiphellandrene, *Z*-curcumene, sesquiterpene alcohol, β -ionone, nerolidol, elemol, *cis*-sesquisabien hydrate, guaial, β -bisabolol, juniper camphor, zingiberenol, β -eudesmol, five sesquiterpene alcohol, 3 unknown, α -cadinol, farnesol, 9-oxononerolidol and dodecanoic acid; those in traces (<0.1 %) were β -pinene, δ -3-carene, γ -terpinene, hexanol, *cis*-3-hexenol, perillene, *trans*-2-octenal, *trans*-linalool oxide, β -thujone, unknown, isoborneol, α -cadinene, sesquiterpene hydrocarbon, calamenene, ethyl myristate, cedorol, patchouli alcohol, 3 sesquiterpene alcohol, 1 sesquiterpene hydrocarbon, 3 unknown, 4-phenylbenzaldehyde, 3-phenylbenzaldehyde and xanthorrhizol (Miyazawa and Kameoka 1988).

Five major sesquiterpene hydrocarbons, viz. α -zingiberene, β -bisabolene, (*E,E*)- α -farnesene, β -sesquiphellandrene and *ar*-curcumene, were identified in 48 different ginger oils from nine countries spanning four continents (Van Beek and Lelyveld 1991). The major volatile components responsible for the flavour of Australian-grown ginger were neral and geranial, zingiberene, α -bisabolene and β -sesquiphellandrene which together accounted for 73 % of ginger supercritical CO₂ extract (Bartley and Foley 1994). Gingerol occurred in low concentration. Dried Nigerian ginger was hydrodistilled; the oil yield was 2.4 % and consisted of 64.4 % sesquiterpene

hydrocarbons, 6.6 % carbonyl compounds, 5.6 % alcohols, 2.4 % monoterpene hydrocarbons and 1.6 % esters (Onyenekwe and Hashimoto (1999)). The main compounds were zingiberene (29.5 %) and sesquiphellandrene (18.4 %). A number of constituents not previously reported in ginger oil were identified as 2,6-dimethyl hepten-L-ol, α -gurjunene, linalool oxide, isovaleraldehyde, 2-pentanone, cadinol, α - and γ -Calacorene, eremophyllene, *t*-muurolol, α -himachalene, α -cubebene acetic acid, pinanol, α -santalene, geranyl propionate, geranoic acid, (*E,E*)- α -farnesene, *n*-methyl pyrrole and geranic acid. Chau et al. (2001) described a fingerprint analysis by GC-MS of dried and fresh ginger rhizomes from China using chemometric techniques. For their studies, the percentages of the following compounds were taken into account: limonene, camphene, 1,8-cineole, neral, geranial, nerol, geraniol, α -terpineol, geranyl acetate, α -zingiberene, β -sesquiphellandrene, β -bisabolene, (*E,E*)- α -farnesene, *ar*-curcumene, nerolidol, zingiberenoids and sesquiphellandrols. From the methanol extracts of *Zingiber officinale* roots, the following phenolic compounds were isolated: [6]-gingerol, [8]-gingerol, [10]-gingerol, [6]-shogaol, [8]-shogaol, [10]-shogaol, dehydro-6-gingerdione, dehydro-10-gingerdione and [6]-paradol (Lee et al. 2011).

Volatiles liberated by enzymatic hydrolysis of the glycosidically bound fraction of the 80 % methanol extract from fresh ginger rhizomes are 2-heptanol, acetic acid; (*R*)-linalool, citronellol; terpinene-4-ol; α -terpineol; borneol, nerol; geraniol, 5-hydroxyborneol, 1,8-epoxy-*p*-menthan-2-ol; benzyl alcohol; 2-phenylethanol; 1,8-epoxy-*p*-menthan-3-ol; (*2E, 6E*)-3,7-dimethyl-8-hydroxyoctadien-1-ol; and (*2E, 6Z*)-3,7-dimethyl-8-hydroxyoctadien-1-ol (Sekiwa et al. 1999). Nine glucosides were isolated from fresh ginger rhizomes: 5-hydroxybornyl-*O*- β -D-glucopyranoside; 1,8-epoxy-*p*-menthan-3-yl- β -D-glucopyranoside; (*2E, 6E*)-3,7-dimethyl-8-hydroxyoctadien-1-yl- β -D-glucopyranoside; (*2E, 6Z*)-3,7-dimethyl-8-hydroxyoctadien-1-yl- β -D-glucopyranoside; heptan-2-yl- β -D-glucopyranoside; geranyl- β -D-glucopyranoside; neryl- β -D-glucopyranoside; (*R*)-linalyl- β -D-glucopyranoside and an unidentified (Sekiwa et al. 1999). The volatile compounds identified in Chinese ginger included α -

phellandrene, camphene, linalool, geranial, zingiberene, sesquiphellandrene, neral, α -bisabolene and α -curcumene (Song et al. 2003). Pino and Marbot (2004) identified *ar*-curcumene (22.1 %), zingiberene (11.7 %), β -bisabolene (11.2 %) and candina-1,4 diene (12.5 %) as the major components in the essential oils of Cuban ginger essential oils. The GC and GC-MS analysis of Mizoram, Chennai (Indian varieties) and Sikkim (Majhauley and Bhainsey varieties) ginger rhizome oils resulted in the identification and quantitation of 29, 29, 28 and 28 constituents representing 84.3 %, 86.6 %, 88.8 % and 86.8 % of the total oils, respectively (Raina et al. 2005). In all the four oils, zingiberene (10.5–16.6 %) was the major constituent. Among the four oils analysed, the Majhauley variety had an edge over the rest of three oils due to the higher content of zingiberene (16.6 %) followed by *E*-citral (12.0 %), *Z*-citral (8.8 %), camphene (7.6 %) and ocimene (6.5 %). The essential oil of Thai ginger was reported to contain zingiberene (30.81 %) as the major component followed by citral (5.4 %), myrcene (4.6 %), 1,8-cineol (3.9 %), α -pinene (3.6 %), β -phellandrene (2.8 %), γ -terpinene (2.5 %) and β -pinene (0.74 %) (Sultan et al. 2005).

Volatile compounds in supercritical fluid (SCF) extracts of Australian fresh and dried ginger were reported by Bartley and Jacobs (2000), respectively, as follows: octane (0.36, 0.07 %), hexanal (1.58, 0.87 %), α -pinene (0.35, 1.24 %), camphene (1.08, 2.89 %), β -pinene (0, 0.11 %), 6-methylene-5-hepten-2-one (0, 0.04 %), β -myrcene (0.3, 0.94%), octanal (0.42, 0.24%), octan-2-ol (0.13, 0.31%), limonene (0.27, 0.31%), β -phellandrene (1.30, 4.68%), heptyl acetate (0, 0.11%), terpinolene (0, 0.12%), linalool (0.41, 0.39), citronellal (0.02, 0.14%), isoborneol (0, 0.11%), borneol (0.73, 0.39%), decanal (0.96, 0.91%), citronellol (0.76, 0.47%), neral (1.46, 2.30%), geraniol (3.11, 1.14%), geranial (18.47, 3.90%), bornyl acetate (0, 0.04%), 2-undecanone (0.11, 0.24%), citronellyl acetate (0.47, 0.77%), α -copaene (0, 0.17%), geranyl acetate (3, 5.87%), δ -elemene (0.43, 0.6%), β -elemene (0, 0.14%), γ -elemene (0.16, 0.3%), (*Z*)- β -farnesene (0.15, 0.31%), (*E*)- β -farnesene (0.14, 0.17%), α -guaiene (0.02, 0.21%), *ar*-curcumene (1.54, 2.29%), germacrene *D* (0.74, 1.26%), zingiberene (13.44, 24.58%), (*E,E*)- α -farnesene (7.13,

14.19%), β -bisabolene (2.49, 3.32%), γ -cadinene (0.22, 0.19%), β -sesquiphellandrene (5.85, 7.64%), elemol (0.8, 0.44%), nerolidol (0.38, 0.38%), α -bisabolol (0.21, 0.15%), sesquisabinene hydrate (0.3, 0.29%), zingiberenol (0.15, 0.13%), guaiaol (0.22, 0.14%), zingerone (7.49, 3.42%), β -eudesmol (0.21, 0.11%), unidentified sesquiterpene alcohol (0.64, 0.30%), unidentified sesquiterpene alcohol (0.3, 0%), pentylcurcumene (0.05, 0.14%), 6-paradol (0.5, 0.17%), 6-shogaol (6.3, 2.35%), 6-gingerdione (1.92, 1%), 6-gingerol (1.09, 0%), 8-shogaol (2.09, 0.99%), 10-shogaol (1.18, 0.94%), 12-dihydroshogaol (0.79, 1.07%) and unidentified sesquiterpene alcohol (0.63, 0%). More than 90 volatile components were extracted from Chinese and Guinean gingers by steam distillation, accounting for about 89.55 and 93.57 % of total oil, respectively (Toure and Zhang 2007). Volatile components of steam-distilled ginger oil from China and Guinea were, respectively, reported as follows: ethane (1.14; 2.16%), α -pinene (0.30; 2.70%), camphene (0.07; 8.10%), β -pinene (1.30; 0.45%), β -myrcene (4.27; 1.37%), α -phellandrene (0.15; 0.23%), *p*-menth-2-en-1 (0.56; 2.93%), eucalyptol (0.13; 3.41%), 1,8-cineole (0.20; 1.43%), α -terpineol (1.03; 0.38%), linalool (3.85; 1.28%), citronellol (1.86; 0.54%), limonene oxide (0.14; 0.30%), borneol (0.13; 2.01%), terpineol (0.07; 0.26%), zingiberenol (0.14; 1.59%), linalool (0.53; 1.28%), *Z*-citral (0.18; 3.44%), citral (0.18; 3.44%), linalool (0.34; 3.31%), 2-undecanone (cas) (0.14; 0.36%), (+) cycloisativene (0.35; 0.30%), α -copaene (0.12; 0.49%), β -elemene (0.075; 0.89%), zingiberene (0.40; 19.58%), α -farnesene (0.74; 4.71%), aromadendrene (1.18; 0.64%), cubebene (0.08; 0.35%), zingiberene (0.40, 19.58%), β -bisabolene (0.74; 5.37%), β -sesquiphellandrene (1.55; 8.95%), elemol (31.1; 2.80%), *g*-elemene (7.46; 0.27%), germacrene *D* (1.63; 0.43%), sesquisabinene hydrate (7.77; 0.71%), zingiberenol (0.25; 3.22%), cubenol (0.15; 0.78%), cadinol (13.82; 0.32%), β -eudesmol (0.87; 1.46%), globulol (0.48; 0.27%), epiglobulol (0.09; 0.56%), epiglobulol-2 (0.20; 1.43%), (*Z,Z*)-farnesal (0.37; 0.44%), β -sinensal (0.74; 0.23%) and nerolidol (0.47; 0.46%). Also identified in the Chinese ginger were hexanal (cas), tricyclene, octanal, β -phellandrene, camphor, decanal (cas), endobornyl acetate, δ -elemene,

citronellyl acetate, geranyl acetate, β -farnesene, γ -cadinene, β -cubebene, δ -cadinene and farnesol.

Volatile constituents of ginger rhizomes were comparatively extracted using headspace solid-phase microextraction (HS-SPME), petrol ether extraction (PEE) and steam distillation extraction (SDE) (Yang et al. 2009). HS-SPME with polydimethylsiloxane (PDMS) fibre was more selective and particularly efficient for the isolation of volatile phytochemical composition and afforded a higher yield of total compounds than PEE and SDE. Thirty-eight constituents were identified from HS-SPME, 37 from PEE and 38 from SDE. Zingiberene (53.12%) were predominant components of ginger samples obtained by HS-SPME, whereas those levels were 39.01% in the same samples by PEE and 35.05% in those by SDE. The major compounds identified by GC-MS from HS-SPME were camphene (1.09%), myrcene (0.19%), β -phellandrene (3.34%), curcumene (4.90%), zingiberene (53.12%), farnesene (8.61%), β -bisabolene (5.98%) and β -sesquiphellandrene (13.03%). The major compounds identified by gas chromatographic analyses from PEE were camphene (3.02%), myrcene (0.61%), β -phellandrene (9.12%), curcumene (4.71%), zingiberene (39.01%), farnesene (7.57%), β -bisabolene (5.91%) and β -sesquiphellandrene (13.03%). The major compounds identified by gas chromatographic analyses from SDE were camphene (5.72%), myrcene (1.01%), β -phellandrene (15.12%), cineole (1.67%), (*E*)-citral (1.11%), curcumene (4.45%), zingiberene (35.05%), farnesene (6.51%), β -bisabolene (5.24%) and β -sesquiphellandrene (10.43%). Chamigrene and γ -elemene were only detected from HS-SPME; 4-(2,2-dimethyl-6-methylenecyclohexyl) butanal, zingiberene, β -cadin-4-en-10-ol and caprinaldehyde were detected only from PEE, while bicyclo[3.1.0]hexane, 4-methylene-1-(1-methylethyl), 2(10)-pinene, 2-heptanol, 6-methyl-, 3,3-dimethyl-1-octene and 3-cyclohexen-1-ol, 4-methyl-1-(1-methylethyl)- were only detected from SDE. Volatile phytochemical composition rhizomes of ginger were monoterpenes and sesquiterpene. Large amounts of sesquiterpenes and lesser amounts of monoterpenes were responsible for the characteristic aroma of ginger.

GC-MS analysis of ginger essential oil resulted in the identification of 7 compounds, representing 90.06% of the oil; the constituents were described as α -zingiberene (52.35%), β -pinene (14.20%), β -sesquiphellandrene (12.11%), santolina triene (6.06%), α -curcumene (2.71%), α -pinene (2.14%) and copaene (0.491%) (Wang et al. 2012). Singh et al. (2008) identified five major components in Indian ginger essential oil: geranial (25.9%), α -zingiberene (9.5%), (*E,E*)- α -farnesene (7.6%), neral (7.6%) and *ar*-curcumene (6.6%). Eighty-one constituents accounting for 95.24%, 97.1% and 97.03% for the essential oil of Sikkim ginger cultivars gorubathane, shingboi and thingra, respectively, were identified (Nampoochiri et al. 2012). The major compounds for gorubathane were zingiberene (32.2%), β -sesquiphellandrene (10.9%), (*E,E*)- α -farnesene (7.02%), geranial (5.86%), neral (2.64%) and camphene (2.5%); for thingra they were zingiberene (12.58%), *ar*-curcumene (9.8%), β -sesquiphellandrene (9.4%), β -bisabolene (7.18%), geranial (6.72%), neral (3.62%), α -bergamotene (3.04%), neryl acetate (2.89%) and (*E,E*)- α -farnesene (2.74%); and for shingboi they were geranial (20.07%) and neral (9.44%), *ar*-curcumene (6.56%), (*E,E*)- α -farnesene (6.29%), β -sesquiphellandrene (6.17%), β -bisabolene (5.91%), zingiberene (5.74%), camphene (2.54%), β -phellandrene (2.53%) and eudesma-3,7(11)-diene (1.89%). Forty-two constituents were identified from the essential oil of *Z. officinale* rhizomes produced in Yibin Province, China (Lin and Hua 1987). The main constituents were β -phellandrene (10.67%), α -zingiberene (44.26%), β -santalol (16.20%), β -bisabolene (10.51%), α -curcumene (1.94%) and zingiberol (0.29%). *E*-Nerolidol, β -eudesmol, *Z*-nerolidol, farnesol, elemol, perillaldehyde, neral and geranial were also detected.

The volatile oil of the fresh ginger rhizomes from the Delhi region, India, was composed mainly of β -germacrene *D* (25.4 %), linalool (11.8 %), camphene (9.4%), (*Z*)- β -farnesene (8.4 %), guaia-6,9-diene (8.3 %), limonene oxide (5.9 %), citronellal (3.6 %) and α -guaiene (3.5 %) (Husain Shahnaz et al. 2011). When the volatile oil was heated at 110° C for 24 h, β -germacrene *D* (19.7 %), linalool (13.4 %), camphene (10.1 %), limonene (8.2 %), guaia-6,9-diene (6.5 %), limonene-1,2-epoxide (4.9 %) and α -guaiene (3.2 %) were the major

constituents. Exposure of the volatile oil to sunlight for 48 h at 15°C showed the presence of β -germacrene *D* (21.4 %), linalool (14.5 %), camphene (8.7 %), *cis*-carveol (6.5 %), neral (5.8 %) and α -guaiene (3.2 %) as the main components. UV light exposure of the volatile oil for 24 h at 12°C exhibited the occurrence of β -caryophyllene (23 %), linalool (12.9 %), camphene (9 %), valencene (8.2 %), (*Z*)- β -farnesene (8.1 %) and nerol (6.6 %) as the prominent constituents. The predominant compounds of the silica gel-treated oil for 24 h at 12 °C included β -germacrene *D* (22 %), linalool (18.4 %), β -selinene (7.5 %), camphene (8.7 %), δ -cadinene (6.8 %), γ -cadinene (6.8 %), limonene oxide (6.6 %), citronellal (5.4 %) and α -guaiene (3.6 %). Treatment of the volatile oil with alumina neutral for 24 h at 12°C produced abundantly β -germacrene *D* (26.2 %), linalool (14 %), (*Z*)- β -farnesene (11 %), β -selinene (8.3 %), camphene (6.4 %), tagetonol (5.8 %), borneol (3.9 %) and α -selinene (3.3 %). Camphene (10.1–6.4 %) and linalool (14.5–11.8 %) were the major components present in all ginger oil samples. Fifty-one compounds, representing 95.1% of the oil, were identified in ginger from Nahan, Himachal Pradesh, India (Gupta et al. 2011). The oil contained relatively large amounts of the monoterpenoids 1,8-cineole (10.9%), linalool (4.8%), borneol (5.6%), α -terpineol (3.6%), neral (8.1%), geraniol (14.5%), geranial (9.5%), *trans*-dimethoxycitral (5.0%) and geranyl acetate (6.3%). Five compounds, namely, *trans*-linalool oxide, *trans*-linalool oxide acetate, (*Z*)-dimethoxycitral, (*E*)-dimethoxycitral and epi-zingiberenol, were also found. Sixty constituents accounting for 94.9% and 92.6% of Sikkim ginger cultivars Bhaisa and Majulay oils were identified (Sasidharan et al. 2012). The major compounds of Bhaisa oil were geranyl acetate (18.8%), zingiberene (16.3%) and geranial (8.2%), and those of Majulay oil were zingiberene (19.8%) and geranial (16.5%). Compared to other ginger cultivar oils, the Bhaisa oil had higher content of oxygenated compounds (43.1%). Kamaliroosta et al. (2013) found the following compounds in Iranian ginger essential oil: zingiberene (31.79%), *ar*-curcumenene (15.88%), β -sesquiphellandrene (15.57%), β -bisabolene (9.29%), α -farnesene (5.71%), γ -cadinene (3.57%), α -eudesmol (3.23%), 4,5-dimethyl-11-methylene tricyclo 7

(2.35%), nerolidol (2.01%), geranyl acetate (1.37%), germacrene B (1.10%), geraniol (0.97%), endo-borneol (0.97%), β -phellandrene (0.93%), camphene (0.73%) and δ -cadinene (0.64%).

Tang et al. (2012) identified 81 compounds accounting for 86.38% of ginger rhizome volatile oil. The major volatiles from ginger rhizome oil were ($\pm$)-3,7-dimethyl-1,6-octadien-3-ol (linalool) (8.8%), [*S*-(*R*^{*},*S*^{*})]-5-(1,5-dimethyl-4-hexenyl)-2-methyl-1,3-cyclohexadiene (α -zingiberene) (6.86%), β -phellandrene (6.76%), (*E*)-3,7-dimethyl-2,6-octadien-1-ol acetate (geraniol acetate) (6.2%), 3,7-dimethyl-2-octen-1-ol (5.34%), camphene (4.77%), 1-(1,5-dimethyl-4-hexenyl)-4-methyl- benzene (*ar*-curcumene) (4.63%), 3,7-dimethyl-2,6-octadienal (4.55%), eucalyptol (3.67%), [*S*-(*R*^{*},*S*^{*})]-3-(1,5-dimethyl-4-hexenyl)-6-methylene- cyclohexene (β -sesquiphellandrene) (3.61%), isoborneol (3.02%), α -farnesene (2.53%), D-limonene (2.33%), (*E*)-3,7-dimethyl-1,6-octadien-3-ol (2.1%), 3,7-dimethyl-2,6-octadienal (α -citral) (2.05%), cyclohexene, 1-methyl-4-(5-methyl-1-methylene-4-hexenyl)-, (*S*)-, (β - bisabolene) (1.79%), α,α -4-trimethyl-3-cyclohexene-1-methanol (1.43%), α -pinene (1.12%), β -myrcene (1.36%), cyclohexanemethanol, 4-ethenyl- α,α -4-trimethyl-3-(1-methylethenyl)-,[1*R*-(1 α ,3 α ,4 β)]- (elemol)(1.13%) and 3,7-dimethyl-6-octen-1-ol acetate (citronellol acetate) (1.03%). The minor components (<1.0%) were 2-heptanone; 2-heptanol; 1,7,7-trimethyl-tricyclo[2.2.1.0^{2,6}]heptane (tricyclene); (*1S*)-6,6-dimethyl-2-methylene-bicyclo[3.1.1]heptane ((-)- β -pinene); 4-methyl-1-(1-methylethyl)-bicyclo[3.1.0]hexane didehydro deriv.; 3-carene; 1-methyl-2-(1-methylethyl)-benzene (*O*-cymene); 1-methyl-4-(1-methylethyl)-benzene (*p*-cymene); acetic acid; sec-octyl ester; (*E*)-2-octenal; (*Z*)-3,7-dimethyl-1,3,6-octatriene (*cis*- β -ocimene); 1-methyl-4-(1-methylethyl)-1,4-cyclohexadiene (γ -terpinene); (1 α ,2 β ,5 α)-2-methyl-5-(1-methylethyl)-bicyclo [3.1.0]hexan-2-ol (*cis*-sabinene hydrate); 2-nonanone; *trans*-(-)-5-methyl-3-(1-methylethenyl)-cyclohexene (δ -elemene); 1,3,3-trimethyl-bicyclo[2.2.1]heptan-2-ol (fenchyl alcohol); *cis*-2-pinanol; exo-1,7,7-trimethyl-bicyclo[2.2.1]heptan-2-ol; *trans*-1-methyl-4-(1-methylethyl)-2-cyclohexen-1-ol; 7-methyl-3-methylene-6-octen-1-ol; (1*R*)-1,7,7-trimethyl-

bicyclo[2.2.1]heptan-2-one; *cis*-1-methyl-4-(1-methylethyl)-2-cyclohexen-1-ol; (*R*)-3,7-dimethyl-6-octenal; 4-(1-methylethyl)-2-cyclohexen-1-one; decanal; acetic acid octyl ester; acetic acid sec-octyl ester; 2-isopropyl-5-methyl-3-cyclohexen-1-one; (*Z*)-3,7-dimethyl-2,6-octadien-1-ol (*cis*-geraniol); 4-(1-methylethyl)-1,5-cyclohexadiene-1-methanol; 4-(1-methylethyl)-benzenemethanol (*p*-cymen-7-ol); bornyl acetate; 2-undecanone; 2-pentadecanol; ethanone 1-[3-methyl-3-(4-methyl-3-pentenyl)oxiranyl]-; (–)-myrtenyl acetate; copaene; (*Z*)-3,7-dimethyl-2,6-octadien-1-ol acetate (neryl acetate); [*1S*-(1 α ,2 β ,4 β)]-1-ethenyl-1-methyl-2,4-bis(1-methylethenyl)-cyclohexane (elemene); 2-methoxy-4-(1-propenyl)-phenol; 1H-cyclopenta[1,3]cyclopropa[1,2]benzene; octahydro-7-methyl-3-methylene-4-(1-methylethyl)-; [3a*S*-(3a α ,3b β ,4 β ,7 α ,7a*S**)]-; (β -cubebene); 2,6-dimethyl-6-(4-methyl-3-pentenyl)-bicyclo[3.1.1]hept-2-ene (α -bergamotene); humulene-(v1); 1H-cycloprop[e]azulene; 1a,2,3,4,4a,5,6,7b-octahydro-1,1,4,7-tetramethyl-; [1a*R*-(1a α ,4 α ,4a β ,7b α)]-(α -gurjunene); [*S*-(*R**,*S**)]-3-(1,5-dimethyl-4-hexenyl)-6-methylene-cyclohexene (β -sesquiphellandrene); [1a*R*-(1a α ; 4 α ,4a β ,7 α ,7a β ,7b α)]-decahydro-1,1,7-trimethyl-4-methylene-1H-cycloprop[e]azulene (*allo*-aromadendrene); *S* (–)-3,7,7-trimethyl-11-methylene- spiro[5.5]undec-2-ene; 3,7,11-trimethyl-2,6,10-dodecatrienal (*trans-trans*-farnesal); (*E,E*)-3,7,11-trimethyl-2,6,10-dodecatrien-1-ol acetate (*trans-trans*-farnesyl acetate); 9-hexadecenoic acid; eicosanoic acid; phytol; (*Z,Z*)-9,12-octadecadienoic acid; (*E*)-9-octadecenoic acid and heneicosane.

Essential oil compositions of ginger varieties grown in Ghana were determined as 1,8-cineol (0.86–10.6%), borneol (2.07–8.3%), α -terpineol (2.2–3.2%), neral (6.9–23.4%), geranial (10.7–34.6%), *ar*-curcumene (1.8–4.0%), α -zingiberene (5.3–16.4%), β -bisabolene (2.5–5.7%), β -sesquiphellandrene (2.1–6.2%) and zerumbone (3.1–86.9%) (Juliani et al. 2007). Three varieties, Gyankoba 1, krabonso 1 and Ofraanse 1, contained only 1,8-cineole and zerumbone. Forty-nine components were identified, comprising 95.9% of essential oil from ginger rhizome from Iran (Hassanpouraghdam et al. 2011). Sesquiterpenoids (61.3%) comprising sesquiterpene hydrocarbons (56.9%) and

oxygenated sesquiterpenes (4.4%) were the principal class of identified components, followed by monoterpenoids (25.4%) made up of monoterpene hydrocarbons (19.9%) and oxygenated monoterpenes (5.5%). α -Zingiberene, a sesquiterpene hydrocarbon (23.8%), was the major component of essential oil, followed by a great share of other mono- and sesquiterpene hydrocarbonic compounds such as *ar*-curcumene (9.2%), β -sesquiphellandrene (8.8%), sabinene (8.7%), (*E-E*)- α -farnesene (8.5%), camphene (6.3%) and α -pinene (2.6%). Citral (neral 2.2% + geranial 3.3%) (5.9%) had a minor share in the volatile oil profile. Borneol (2.3%), *E,E*-farnesol (1.5%) and 6-methyl-5-heptene-2-one (1.3%) were the other oxygenated compounds with the amounts exceeding one percent. The following compounds were isolated from Iranian ginger essential oil: zingiberene (31.75%), *ar*-curcumene (15.88%), β -sesquiphellandrene (15.57%), β -bisabolene (9.29%), α -farnesene (5.71%), γ -cadinene (3.56%), α -eudesmol (3.23%), 4,5-dimethyl-11-methylene tricycle 7 (2.35%), nerolidol (2.01%), 7- α -(1-hydroxyl-1-methylethyl) (2%), geranyl acetate (1.37%), germacrene B (1.1%), endo-borneol (0.97%), geraniol (0.97%), β -phellandrene (0.93%), camphene (0.73%) and δ -cadinene (0.64%) (Kamalirroosta et al. 2013). Compositions (%) of ginger oil from fresh young rhizomes, mature rhizomes, seed and aid-dried rhizomes and steam dry rhizomes were determined, respectively, as zingiberene (63, 17.1, 14.2, 3.8, 10.3%), *ar*-curcumene (13, 2.8, 5.2, 1.9, 18.1%), β -bisabolene (4.2, 6.8, 7.2, 1.8, 18.7%), farnesene (0.3, 0.5, 0.7, 0.2, 0.7%), β -sesquiphellandrene (2.8, 5.9, 6.4, 2.1, 14.1%), citral (12.6, 24.9, 46.0, 70.5, 7.0%), geraniol (8.6, 4.7, 2.4, 1.7, 1.9%), geranyl acetate (45, 6.7, 1.7, 0.8, – %), 1,8-cineole (1.6, 6.1, 1.7, 0.8, – %), camphene (0.1, 3.1, 0.6, –, 0.8%) and sabinene (0.7, 6.3, 1.7, 0.5, – %) (Takahashi et al. 2011).

From the essential oil from the sun-dried ginger of 46 cultivars, a total of 60 compounds constituting 71.15–94.57% of the total volatile oil constituents were identified (Kizhakkayil and Sasikumar 2014). The major compounds were zingiberene (6.79–29.60%), farnesene (0–14.40%), β -sesquiphellandrene (7.06–11.90%), α -curcumene (1.90–6.14%), β -cubebene (0–3.59%), β -bisabolene (0–7.34%), citral

(geranial) (4.13–12.50%), *Z*-citral (neral) (2.28–7.73%), β -phellandrene (0–4.08%), camphene (2.26–6.34%), β -myrcene (0.85–1.39%), linalool (0.61–2.94%), endo-borneol (0.33–2.37%), nerolidol (0.71–1.79%), α -pinene 0.61–1.73%, camphene (2.50–6.34%), β -myrcene (0.85–1.39%), β -phellandrene (0–4.57), 1,8-cineol (1.08–6.96%), β -citronellol (0.25–1.71%), *trans*-geraniol (0.12–2.11%), (–)-epiglobulol (0.46–1.28%) and viridiflorol (0–1.52%). Other minor components (<1% in all cultivars) were 2-heptanol, 2- β -pinene, 6-methyl-5-hepten-2-one, α -phellandrene, *cis*-ocimene, α -terpinolene, 2-nonanone, verbenone, camphor, citronellal, terpinene-4-ol, α -terpineol, myrtenal, *trans*-2-carene-4-ol, nerol, endobornyl acetate, 2-undecanone, citronellyl acetate, cyclosativene, α -copaene, geranyl acetate, β -elemene, γ -elemene, β -farnesene, *allo*-aromadendrene, β -selinene, α -muurulonene, torreyol, epi-bicyclosesquiphellandrene, elemol, ledol, germacrene B, juniper camphor, (–)-farnesol and β -eusdemol. Zingiberene was the major component present in the essential oils of all the 46 ginger accessions except the exotic ginger ‘Kintoki’, in which α -curcumene was the major component. The highest percentage of zingiberene was observed in the cultivar ‘Angamali’ (29.6%) and the lowest percentage in ‘Kintoki’ (6.79%). *Z*-citral (neral) and *E*-citral (geranial) were the important monoterpene aldehydes found in all the ginger genotypes except the exotic ginger ‘Brazil’. One of the major sesquiterpenes, farnesene, was absent in the essential oil of the ginger ‘Accession 50’ and present in all other accessions studied.

Out of 168 volatile components, 90 were identified by gas chromatographic retention and mass spectral data and 58 were tentatively identified by mass spectral (Chen and Ho 1988). A total of 140 and 136 volatile components were separated from ginger using GCMS, and 74 and 75 of them were tentatively identified, which accounted for about 62.82 and 47.11% of the total relative content for dried and fresh ginger, respectively (Gong et al. 2004). Major volatiles identified in ginger rhizomes included tricyclene, α -thujene (3-thujene), α -pinene, camphene, sabinene (4(10)-thujene), β -pinene, myrcene, α -phellandrene, 3-carene, β -phellandrene, 1,8-cineole

(eucalyptol), γ -terpinene, (*Z*)-sabinene hydrate, *p*-mentha-1,4(8)-diene (terpinolene), linalool, (*E*)-pinene hydrate ((*E*)-pinan-2-ol), γ -terpinene, 16, (*Z*)-sabinene hydrate, 17, *p*-mentha-1,4(8)-diene (terpinolene), 18, linalool, 19, (*E*)-pinene hydrate ((*E*)-pinan-2-ol), β -citronellal, borneol (endo-borneol), *p*-menth-1-en-8-ol (α -terpineol), β -citronellol (3,7-dimethyl-6-octen-1-ol), neral (β -citra), (*E*)-geraniol, geranial (α -citra), bornyl acetate, myrtenyl acetate (2-pinen-10-ol acetate), δ -elemene, citronellyl acetate, nerol acetate, unknown ((+)-cyclosativene-like), (+)-cyclosativene, α -copaene, geraniol acetate, β -elemene, unknown (7-epi-sesquithujene-like), (*E*)-caryophyllene (β -caryophyllene), β -copaene, γ -elemene, (*E*)- α -bergamotene, α -humulene (α -caryophyllene), (*E*)- β -farnesene, *allo*-aromadendrene, germacrene D, *ar*-curcumene, β -selinene (eudesma-4(14),11-diene), (–)- α -zingiberene, α -muurolene, (*E,E*)- α -farnesene, β -bisabolene, γ -cadinene, 7-epi- α -selinene, (–)- β -sesquiphellandrene, (*E*)- γ -bisabolene, α -elemol, unknown (*cis*-sesquisabinene hydrate-like), germacrene B, (*E*)-nerolidol, unknown *trans*-sesquisabinene hydrate-like 1, unknown *trans*-sesquisabinene hydrate-like 2, unknown *trans*-sesquisabinene hydrate-like 3 and epi- α -bisabolol/ α -bisabolol (Koo and Gang 2012).

Major volatiles identified in ginger roots included tricyclene, α -pinene, camphene, β -pinene, limonene, 1,8-cineole (eucalyptol), α -campholenal, (*E*)-pinocarveol (2(10)-pinen-3-ol), (*E*)-verbenol ((*E*)-2-pinen-4-ol), pinocarvone (2(10)-pinen-3-one), myrtenal, verbenone (2-pinen-4-ol), bornyl acetate, α -terpinyl acetate, α -copaene, β -elemene, (*E*)-caryophyllene (β -caryophyllene), (*E*)- α -bergamotene, α -humulene (α -caryophyllene), *allo*-aromadendrene, germacrene D, (–)- α -zingiberene, γ -amorphene, (*E,E*)- α -farnesene, β -bisabolene, (–)- β -sesquiphellandrene, caryophyllene oxide and humulene oxide II (Koo and Gang 2012). Sixty volatile compounds of ginger were identified by HS-SPME-GC-MS (Huang et al. 2012). The major volatile compounds were zingiberene (26.4–37.1%), β -phellandrene (7.4–12.9%), β -sesquiphellandrene (10.2–12.8%), geranial (0.9–8.1%), camphene (2.5–7.6%) and neral (0.2–4.8%). Other compounds included sabinene, β -pinene, octanal, α -phellandrene, *p*-cymene, limonene, (*E*)-2-octenal, γ -terpinene, terpinolene, α -

pinene, 2-heptanol, tricyclene, 3,4-dimethyl styrene, linalool, *trans*-3(10)-carene-2ol, 1,1-dimethyl-3-methylene-2-vinylcyclohexane, 2-methoxy-1,7,7-trimethyl-bicyclo[2,2,1]heptane, citronellal, camphor, borneol, 1-terpinen-4-ol, α -terpineol, myrtenal, citronellol, *trans*-geraniol, *cis*-*p*-menth-2,8-dienol, 2-undecanone, cyclosativene, α -copaene, β -elemene, α -*trans*-bergamotene, β -cubebene, β -farnesene, cedrene, *allo*-aromadendrene, β -himachalene, α -curcumene, α -farnesene, β -bisabolene, α -panasinsen, germacrene B, epiglobulol, cubenol, τ -eudesmol, caryophyllene oxide, τ -muurolol, α -cadinol, spathulenol, cedr-8-ene, β -cedren-9- α -ol, farnesal, *trans*-longipinocarveol, *E*-nuciferol and *cis*-lanceol. The volatiles of silica gel-dried ginger were similar to those of fresh ginger. Microwave-dried ginger had a higher content of zingiberene and satisfactory dehydration efficiency. The results showed that microwave and silica gel can be used in drying of ginger to maintain the taste and appearance of fresh ginger.

Essential oil in processed ginger was found to contain the pungent compounds 6-gingerol (0.09–0.32%), 6-shogaol (0.13–0.30%) and zingerone (0.001–0.004%) (Namera et al. 2012). Also present were terpenoids 1,8-cineol, α -pinene, β -pinene, camphene, decanal, geranial, geranyl acetate, curcumene, zingiberene, α -farnesene, β -sesquiphellandrene and β -bisabolene. Ginger root dietary supplements are often used to alleviate symptoms of nausea and vomiting associated with pregnancy.

Leaf Phytochemicals

In ginger, the concentration of flavonoids in the leaves decreased (Halia Bentong, 42.3%; Halia Bara 36.7%) with advancing growth periods (from 8 to 16 weeks) (Ghasemzadeh et al. 2010b). The concentrations of flavonoids (mg/g DW) in the leaves of cv Halia Bentong and Halia Bara at 8 weeks and 16 weeks were, respectively, as follows: quercetin (0.926–0.836 mg, 1.299–0.978 mg), rutin (0.152–0.054 mg, 0.211–0.205 mg), catechin (0.41–0.31 mg, 0.56–0.45 mg), epicatechin (0.113–0.092 mg, 0.19–0.11 mg), naringenin (0.054–0.049 mg, 0.04–0.039 mg) and kaempferol (0.051–

0.043 mg, 0.054–0.048 mg). The results of HPLC analysis indicated that synthesis and partitioning of quercetin, rutin, catechin, epicatechin and naringenin were high in ginger plants grown under $310 \mu\text{mol m}^{-2}\text{s}^{-1}$ (Ghasemzadeh et al. 2010c). The average value of flavonoids synthesis in leaves for both varieties increased (Halia Bentong 26.1%; Halia Bara 19.5%) when light intensity decreased. Photosynthetic rate and plant biomass increased in both varieties with increasing light intensity. A high photosynthesis rate ($12.25 \mu\text{mol CO}_2 \text{m}^{-2}\text{s}^{-1}$ in Halia Bara) and plant biomass (79.47 g in Halia Bentong) were observed at $790 \mu\text{mol m}^{-2}\text{s}^{-1}$. Quercetin occurred as an abundant flavonoid in both ginger varieties. Moreover, higher concentration of quercetin (1.12 mg/g dry weight) was found in Halia Bara leaves grown under $310 \mu\text{mol m}^{-2}\text{s}^{-1}$ with a low photosynthesis rate. Furthermore, a high content of salicylic acid (0.673 mg/g dry weight) was detected in Halia Bara leaves exposed under $790 \mu\text{mol m}^{-2}\text{s}^{-1}$ with a high photosynthesis rate. Salicylic acid was not detected in gingers grown under $310 \mu\text{mol m}^{-2}\text{s}^{-1}$. CO_2 levels of 800 $\mu\text{mol/mol}$ significantly increased anthocyanin, rutin, naringenin, myricetin, apigenin, fisetin and morin contents in ginger leaves (Ghasemzadeh et al. 2012). Meanwhile, the combined effect of salicylic acid (SA) and CO_2 enrichment enhanced anthocyanin and flavonoid production compared with single treatment effects. High anthocyanin content was observed in Halia Bara leaves treated with elevated CO_2 and SA. The highest chalcone synthase (CHS) activity was observed in plants treated with SA and CO_2 enrichment. Plants not treated with SA and kept under ambient CO_2 conditions showed the lowest CHS activity.

Ginger leaf oil was clearly dominated by β -caryophyllene (31.7%) followed by geranial (13.1%), neral (9.8%), caryophyllene oxide (6.3%), geraniol (4.4%), α -pinene (4.1%), *trans-trans*- α -farnesene (3.2%), β -phellandrene (2.6%), β -pinene (2.0%), myrcene (1.3%), α -muurolene (1.1%), linalool (1.1%) and geranyl acetate (1%) (Sivasothy et al. 2011). Other minor constituents (trace to < 1 %) were 2-heptanol, camphene, sabinene, 6-methyl-5-hepten-2-one, α -

phellandrene, δ -3-carene, *p*-cymene, 1,8-cineole, 2-heptyl acetate, *trans*- β -ocimene, γ -terpinene, citronellal, terpinene-4-ol, α -terpineol, myrtenal, linalyl formate, *trans*-2-decenal, 2-undecanone, α -copaene, germacrene D, α -selinene, isocaryophyllene, α -humulene, *allo*-aromadendrene, δ -cadinene, *trans*-nerolidol, caryophyllenedienol I, β -eudesmol, *cis-cis*-farnesol, *trans-trans*-farnesol, *trans-trans*-farnesal and phytol.

Major volatiles identified in ginger leaves included α -pinene, β -pinene, myrcene, α -phellandrene, β -phellandrene, 1,8-cineole (eucalyptol), (*E*)- β -ocimene, linalool, nonanal, *p*-menth-1-en-8-ol (α -terpineol), neral (β -citral), (*E*)-geraniol, geranial (α -citral), α -copaene, geraniol acetate, α -copaene, 43, geraniol acetate, (*E*)- α -bergamotene, α -humulene (α -caryophyllene), *allo*-aromadendrene, germacrene D, γ -amorphene, (*E,E*)- α -farnesene, (*E*)-nerolidol, humulene oxide II and epi- α -bisabolol/ α -bisabolol (Koo and Gang 2012).

Assays for enzymes in the phenylpropanoid pathway of the biosynthesis of curcuminoids and gingerols identified the corresponding enzyme activities in protein crude extracts from leaf, shoot and rhizome tissues from ginger and turmeric (Ramirez-Ahumada et al. 2006). These enzymes included phenylalanine ammonia lyase, polyketide synthases, *p*-coumaroyl shikimate transferase, *p*-coumaroyl quinate transferase, caffeic acid *O*-methyltransferase and caffeoyl-CoA *O*-methyltransferase which were evaluated because of their potential roles in controlling production of certain classes of gingerols and curcuminoids. All crude extracts possessed activity for all of these enzymes, with the exception of polyketide synthases. In ginger, a thioesterase activity in the crude protein extracts hydrolysed the precursor hydroxycinnamoyl-CoA substrates such as feruloyl-CoA preventing identification of gingerol synthase activity. In subsequent studies, Flores-Sanchez and Gang (2013) found that polyketide synthase activities could be better characterised by using lipase inhibitors to reduce thioesterase activities. Results of these analyses indicated that specific thioesterases do exist in these plants and that they could indeed be inhibited, with highest inhibition occurring with a mixture of these three

compounds (orlistat, a reduced form of lipstatin, and peptide 1 and peptide 2 from hydrolysates of soybean β -conglycinin), leading, for example, to a reduction of caffeoyl-CoA hydrolysis in leaves and rhizomes of ginger by 40-fold and 27-fold, respectively.

The main pharmacological actions of ginger and compounds isolated therefrom include immunomodulatory, antitumorigenic, anti-inflammatory, anti-apoptotic, anti-hyperglycaemic, anti-lipidemic and antiemetic actions (Ali et al. 2008). Ginger is a strong antioxidant substance and may either mitigate or prevent generation of free radicals.

Antioxidant Activity

Ginger hydroalcoholic extract was found to scavenge $\cdot\text{OH}$, $\text{O}_2^{\cdot-}$ and $\text{ABTS}^{\cdot+}$ radicals in a dose-dependent manner in-vitro (Jagetia et al. 2004). The non-volatile fraction of the dichloromethane extract of ginger rhizomes exhibited a strong antioxidative activity using linoleic acid as the substrate in ethanol-phosphate buffer solution (Kikuzaki and Nakatani 1993). The fraction was purified and afforded five gingerol-related compounds and eight diarylheptanoids. Among them, 12 compounds exhibited higher activity than α -tocopherol. Ginger (1% w/w) significantly lowered lipid peroxidation by maintaining the activities of the antioxidant enzymes: superoxide dismutase, catalase and glutathione peroxidase in rats (Ahmed et al. 2000a). The blood glutathione content was significantly increased in ginger-fed rats. Similar effects were also observed after natural antioxidant ascorbic acid (100 mg/kg, body wt) treatment. Concomitant dietary feeding of ginger 1%, w/w, significantly attenuated malathion-induced lipid peroxidation and oxidative stress in albino rats (Ahmed et al. 2000b). The results indicated the possible involvement of free radicals in organophosphate-induced toxicity and highlight the protective action of ginger. [6]-Gingerol exhibited dose-dependent inhibition of NO production and significant reduction of inducible NO synthase (iNOS) in LPS-stimulated J774.1 macrophages (Ippoushi et al. 2003). Additionally, [6]-gingerol effectively suppressed peroxynitrite-induced oxidation of dichlorodihydrofluorescein, oxidative

single-strand breaks in supercoiled pTZ 18U plasmid DNA and formation of 3-nitrotyrosine in bovine serum albumin (BSA) and J774.1 cells. The results indicated [6]-gingerol to be a potent inhibitor of NO synthesis and also an effective protector against peroxynitrite-mediated damage. Ginger extract exhibited significant activities in all antioxidant assays, namely, reducing power assay, superoxide anion scavenging activity assay, hydroxyl radical scavenging activity assay, nitric oxide scavenging activity assay, DPPH free radical scavenging assay and hydrogen peroxide method, compared to the standard antioxidant, ascorbic acid, in a dose-dependent manner (Amir et al. 2011). Its remarkable activities to scavenge reactive oxygen species (ROS) may be attributed to the high amount of hydrophilic phenolics. Ginger extracts obtained using supercritical CO₂ and compressed propane presented antioxidant effects (Mesomo et al. 2012). The highest antioxidant activity (931.67 mg of α -tocopherol/g of extract) was found for extracts obtained using supercritical CO₂ as solvent at 313.15 K and 16.5 MPa.

The antioxidant effect and the total phenols of ginger extract were studied. 2,2-Diphenyl-1-picrylhydrazyl radical (DPPH) scavenging of ginger alcohol extract reached 90.1 % and exceeded that of butylated hydroxytoluene (BHT); the IC₅₀ concentration for inhibition of DPPH was 0.64 μ g/ml (Stoilova et al. 2007). The antioxidant activity in a linoleic acid–water emulsion system determined by means of thiobarbituric acid-reactive substances (TBARS) was the highest—73.2% at 37 °C and 71.6 % when the formation of conjugated dienes was inhibited. At 80 °C the antioxidant activity at the highest concentration of a ginger extract was less efficient: 65.7 % for conjugated dienes formation and 68.2 % for TBARS. The ginger extract inhibited the hydroxyl radicals 79.6 % at 37 °C and 74.8 % at 80 °C, which showed a higher antioxidant activity than quercetin. The IC₅₀ concentration for inhibiting OH $\cdot$ at 37 °C was slower than that at 80 °C—1.90 and 2.78 μ g/ml, respectively. The ginger extract chelated Fe³⁺ in the solution. The total phenols of the alcohol extract were found to be 870.1 mg/g dry extract. The intake of daikon sprout (*Raphanus sativus*) or ginger (*Zingiber*

officinale) significantly decreased the concentration of urinary thiobarbituric acid-reactive substances (TBARS) in rats as compared with those before the intake (Ippoushi et al. 2007). Moreover, the intake of these vegetables reduced urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels in lipopolysaccharide (LPS)-treated rats as compared with those fed a basal diet only. The results showed that these vegetables suppress lipid peroxidation and the formation of malondialdehyde and protect DNA from LPS-induced oxidative damage in rats. In another study, concomitant dietary feeding of ginger (1%w/w) significantly attenuated lindane-induced lipid peroxidation, accompanied by modulation of oxygen free radical scavenging enzymes as well as reduced glutathione (GSH) and the GSH-dependent enzymes glutathione peroxidase (Gpx), glutathione reductase (GR) and glutathione *S*-transferase (GST) in the rats (Ahmed et al. 2008). The findings again suggested that a diet containing naturally occurring compounds like ginger was effective in exerting protective effects by modulating oxidative stress. The essential oil combination of *Curcuma longa* and *Zingiber officinale* showed strong antioxidant activity through 2,2-diphenyl-1-picrylhydrazil free radical scavenging, β -carotene-linoleic acid bleaching and total phenolic content assay (Prakash et al. 2012). In the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay, high dose of ginger extract showed strong antioxidative activity (Al-Tahtawy et al. 2011). In the DPPH test system, the IC₅₀ value of free radical scavenging activity of ginger essential oil was determined to be 0.0144% (v/v) (Wang et al. 2012). In the β -carotene bleaching test system, the IC₅₀ value of ginger essential oil was 0.55% (v/v). In reducing power, antioxidant standards showed the highest effects compared to ginger extracts, with oleoresin presenting more activity than essential oil: quercetin > ascorbic acid > BHA > oleoresin > essential oil (Bellik et al. 2013). Similar trend was observed for DPPH scavenging effect: gallic acid > quercetin > ascorbic acid > oleoresin > essential oil. For H₂O₂ scavenging activity, the results were quercetin > essential oil > gallic acid > oleoresin > ascorbic acid. Hydrodistillation of ginger dried roots afforded average

yields of 0.48 % for essential oil, and methanol extraction gave yields of 10.23% oleoresin. The content of total phenols was 67.6 mg GAE/g of dry extract

Leaves of *Z. officinale* had total phenolic content (TPC) of 291 mg GAE/100 g and ascorbic acid equivalent antioxidant capacity (AEAC) of 96 mg AA/100g and rhizome TPC of 157 mg GAE/100g and AEAC of 84 mg AA/100g (Chan et al. 2008). The antioxidant activity determined by the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay showed high activities (65.7%) in the leaves of cultivar Halia Bara at 8 weeks after planting (Ghasemzadeh et al. 2010b). The DPPH IC₅₀ values of the leaves at 8 weeks was 28 µg/ml for cv Halia Bara and 39 µg/ml for Halia Bentong. As CO₂ concentration was increased from 400 to 800 µmol/mol, free radical scavenging power (DPPH) increased about 30% in ginger variety Halia Bentong and 21.4% in variety Halia Bara, and the rhizomes exhibited more enhanced free radical scavenging power, with 44.9% in Halia Bentong and 46.2% in Halia Bara (Ghasemzadeh et al. 2010a). Leaves of both varieties also displayed good levels of flavonoid compounds and antioxidant activities. The highest free radical scavenging activity corresponded to Halia Bara treated with salicylic acid (SA) under high CO₂ conditions, while the lowest activity corresponded to Halia Bentong without SA treatment and under atmospheric CO₂ levels (Ghasemzadeh et al. 2012). As the level of CO₂ increased, the DPPH activity increased. Higher thiobarbituric acid (TBA) activity was also recorded in the extracts of Halia Bara treated with SA and grown under high CO₂ conditions. The antioxidant activity, as determined by the ferric-reducing antioxidant power (FRAP) activity, increased in young ginger grown under elevated CO₂ (Ghasemzadeh and Jaafar 2011). The FRAP values for the leaves, rhizomes and stems extracts of both varieties grown under two different CO₂ concentrations (400 and 800 µmol mol⁻¹) were significantly lower than those of vitamin C (3107.28 µmol Fe (II)/g) and α-tocopherol (953 µmol Fe (II)/g), but higher than that of BHT (74.31 µmol Fe (II)/g).

Ginger showed antioxidant activity and contained more than 50 antioxidants of two groups: gingerol-related compounds and diarylheptanoids (Masuda et al. 2004). Gingerol-related compounds substituted with an alkyl group bearing 10-, 12- or 14-carbon chain length were isolated from the dichloromethane extract of rhizome and showed antioxidant activity. The substituents on the alkyl chain might contribute to both DPPH radical scavenging effect and inhibitory effect on oxidation of methyl linoleate under aeration and heating by the Oil Stability Index (OSI) method, while inhibitory effects against the 2,2'-azobis(2-amidinopropane) dihydrochloride (AAPH)-induced peroxidation of liposome was somewhat influenced by the alkyl chain length; the antioxidant activity might be due to not only radical scavenging activity of antioxidants but also their affinity of the antioxidants to the substrates. The rhizome was reported to have antioxidant index 3.00 as evaluated by β -carotene bleaching method and to contain 5.87 mg% vitamin C, 0.0209 mg% vitamin E, 0.64 mg% total carotenes, 1.06 mg% total xanthophylls, 11.1 mg% tannins and 60.1 mg/% phenolics (Chanwitheesuk et al. 2005). Among 10 *Zingiber* species, *Z. officinale* had the highest total phenolic content of 7.70 mg GAE/g DW and exhibited the highest antioxidant activity in the DPPH assay with IC_{50} of 4.26 mg/ml IC_{50} and in the ABTS assay with IC_{50} of 7.04 mg/ml (Kantayos and Paisooksantivatana 2012). However, all the *Zingiber* species were not as strong as ascorbic acid. Ginger oleoresin, and especially that obtained by ethanol extraction, with a high [6]-gingerol content exhibited potent scavenging activity against 1,1-diphenyl-2-picrylhydrazyl radicals in comparison to essential oils of ginger and other Zingiberaceae plants (Takahashi et al. 2011). Most of the isolated diarylheptanoids from ginger rhizome were found to be better antioxidants than the positive control ascorbic acid in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay (Li et al. 2012b). Several ginger diarylheptanoids and epoxidic diarylheptanoids were effective DPPH radical scavengers and moderately effective at inhibiting xanthine oxidase (Peng et al. 2012). Almost all tested compounds inhibited lipid peroxidation. The results of in-vitro studies by Zhang et al. (2011) established the

possibility that polysaccharides extracted from ginger could be effectively employed as an ingredient in health or functional food to alleviate oxidative stress. A sample, G2 (extract with acid solution), showed significant inhibitory effects on superoxide radical, hydroxyl radical and DPPH radical; its reducing power and iron(II) chelation activity were also the strongest.

Of two glucosides 1-(4-*O*- β -D-glucopyranosyl-3-methoxyphenyl)-3,5-dihydroxydecane and 5-*O*- β -D-glucopyranosyl-3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)decane isolated from fresh ginger, the former elicited no antioxidative activities in the a linoleic acid model system, and by their DPPH radical scavenging assay, the latter glucoside elicited a strong activity as the aglycone 6-gingerdiol (Sekiwa et al. 2000). Ginger compounds 5-[4-hydroxy-6-(4-hydroxyphenethyl)tetrahydro-2H-pyran-2-yl]-3-methoxybenzene-1,2-diol, 5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)heptan-3-one and 1,5-epoxy-3-hydroxy-1-(4,5-dihydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)heptane exhibited strong superoxide anion radical scavenging activities in a phenazine methosulphate-NADH system (Tao et al. 2008). In a more biological system, these compounds were demonstrated to exhibit potent protection against lipid peroxidation in mouse liver microsomes exposed to oxidative condition. In the antioxidant activity assay, [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol exhibited substantial scavenging activities with IC₅₀ values of 26.3, 19.47, 10.47 and 8.05 μ M against DPPH radical; IC₅₀ values of 4.05, 2.5, 1.68 and 0.85 μ M against superoxide radical; and IC₅₀ values of 4.62, 1.97, 1.35 and 0.72 μ M against hydroxyl radical, respectively (Dugasani et al. 2010). The free radical scavenging activity of these compounds also enhanced with increasing concentration. At a concentration of 6 μ M, [6]-gingerol, [8]-gingerol, [10]-gingerol and [6]-shogaol significantly inhibited N-formyl-methionyl-leucyl-phenylalanine (f-MLP)-induced reactive oxygen species (ROS) production in human polymorphonuclear neutrophils. Bak et al. (2012) found that 6-shogaol-rich extract extracted from ginger powder with 95%

ethanol at 80 °C after drying at 80 °C may enhance antioxidant defence mechanism through the induction of Nrf2 and HO-1 regulated by mitogen-activated protein kinases (MAPK) p38 and PI3k/Akt pathway in HepG2 cells and in-vivo. In a mouse model, this extract decreased the diethylnitrosamine (DEN)-mediated elevations of serum aspartate transaminase and alanine transaminase as well as the DEN-induced hepatic lipid peroxidation. In addition, the administration of this extract to the mice also restored the DEN-reduced activity and protein expression of hepatic antioxidant enzymes such as superoxide dismutase, glutathione peroxidase and catalase.

The relative antioxidant potencies of ginger compounds decreased in similar order of 1-dehydro-[6]-gingerdione, hexahydrocurcumin > 6-shogaol > 6-dehydroshogaol in both 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging and trolox equivalent antioxidant capacity (TEAC) assays (Li et al. 2012a). Ginger extracts (oleoresins and essential oil) exerted significant antioxidant activity, scavenging ABTS^{•+} free radical in a dose-dependent manner (Bellik 2014). In general, oleoresin showed higher antioxidant activity [IC₅₀ = 1.820 mg/mL] when compared to the essential oil [IC₅₀ = 110.14 mg/mL]. The antioxidant effect of Guangdong-ginger (GG) and Chu-ginger (CG) rhizome ethanolic extracts was more effective than aqueous extracts in Trolox equivalent antioxidant capacity and ferric-reducing ability of plasma (Yeh et al. 2014). Contrarily, ginger aqueous extracts were more effective in free radical scavenging activities and chelating abilities. Based on the results, the two ginger varieties exerted protective effects and could be used as a flavouring agent and a natural antioxidant.

The bioactive components of ginger rhizomes were characterised by spectroscopic analysis as zingerone and dehydrozingerone, which exhibited potent antioxidant activities (Kuo et al. 2005). Of the dehydrozingerone-derived analogues, 4-(2', 3'-dihydroxyphenyl)-(E)-3-buten-2-one inhibited Fe²⁺-induced lipid peroxidation in rat brain homogenate with an IC₅₀ = 6.3 µM. In the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical quencher assay, compounds

dehydrozingeron, 4-(2'-hydroxy-5'-methoxyphenyl)-(*E*)-3-buten-2-one, 4-(4'-hydroxy-3', 5'-dimethoxyphenyl)-(*E*)-3-buten-2-one, 4-(2', 3'- dihydroxyphenyl)-(*E*)-3-buten-2-one, 4-(2', 5'-dihydroxyphenyl)-(*E*)-3-buten-2-one and 4-(3', 4'-dihydroxyphenyl)-(*E*)-3-buten-2-one showed radical scavenging activity equal to or higher than those of the standard antioxidants, like α -tocopherol and ascorbic acid.

Anticancer Activity

Pre-application of ethanol ginger extract (GE) onto the skin of SENCAR mice resulted in significant inhibition of 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-caused induction of epidermal ornithine decarboxylase (ODC), cyclooxygenase and lipoxygenase activities and ODC mRNA expression in a dose-dependent manner (Katiyar et al. 1996). Preapplication of GE to mouse skin also afforded significant inhibition of TPA-caused epidermal oedema (56%) and hyperplasia (44%). In long-term tumour studies, topical application of GE 30 min prior to that of each TPA application to 7,12-dimethylbenz(*a*)anthracene-initiated SENCAR mice resulted in a highly significant protection against skin tumour incidence and its subsequent multiplicity. The animals pretreated with GE showed substantially lower tumour body burdens compared with non-GE-treated controls. Park et al. (1998) demonstrated that topical application of [6]-gingerol onto shaven backs of female ICR mice prior to each topical dose of 12-*O*-tetradecanoylphorbol-13-acetate (TPA) significantly inhibited 7,12-dimethylbenz[*a*]anthracene-induced skin papillomagenesis. The compound also suppressed TPA-induced epidermal ornithine decarboxylase activity and inflammation. In in-vivo studies, topical application of [6]-gingerol or [6]-paradol 30 min prior to 12-*O*-tetradecanoyl-phorbol-13-acetate (TPA) attenuated the skin papillomagenesis initiated by 7,12-dimethylbenz[*a*]anthracene in female ICR mice (Surh et al. 1998). Both substances also significantly inhibited the tumour promoter-stimulated inflammation, TNF- α production and activation of epidermal ornithine decarboxylase in mice. In another study, [6]-gingerol and [6]-paradol suppressed the superoxide production

stimulated by TPA in differentiated HL-60 cells. [6]-Paradol and its synthetic nonpungent analogue, [6]-dehydroparadol, significantly decreased the incidence and the multiplicity of skin tumours initiated by 7,12-dimethylbenz[a]anthracene (DMBA) and promoted by 12-*O*-tetradecanoylphorbol-13-acetate (TPA) (Chung et al. 2001). Topical application of [6]-paradol and its derivatives inhibited TPA-induced ear oedema and H₂O₂ production and myeloperoxidase activity in the dorsal skin of mice. Induction of TPA-induced mouse epidermal ornithine decarboxylase (ODC) activity and H₂O₂- and UV-induced formation of oxidised DNA bases in-vitro were also attenuated by the above compounds. Keum et al. (2002) found that [6]-paradol and other structurally related derivatives, [10]-paradol, [3]-dehydroparadol, [6]-dehydroparadol and [10]-dehydroparadol, with the exception of [3]-paradol dose-dependently induced apoptosis in an oral squamous carcinoma cell line, KB. [10]-paradol and [10]-dehydroparadol exhibited a similar extent of cytotoxicity to that of [6]-paradol. [6]-Dehydroparadol and [3]-dehydroparadol appeared to be more potent, with an IC₅₀ less than 40 µM. Treatment of KB cells with an apoptosis-inducing concentration of [6]-dehydroparadol caused induction of proteolytic cleavage of pro-caspase-3. [6]-Gingerol, a pungent ingredient of ginger, inhibited COX-2 expression in mouse skin stimulated with a prototype tumour promoter 12-*O*-tetradecanoylphorbol-13-acetate (TPA) by blocking the activation of p38 MAP kinase and NF-κβ signalling pathways (Kim et al. 2004).

Pungent vanilloid ketones from ginger, [6]-gingerol and [6]-paradol, were found to exert inhibitory effects (cytotoxic/cytostatic) on the viability and DNA synthesis of human promyelocytic leukaemia (HL-60) cells by inducing apoptosis (Lee and Surh 1998). [6]-gingerol and [6]-paradol inhibited epidermal growth factor-induced neoplastic cell transformation but through different mechanisms (Bode et al. 2001). 6-Gingerol, an antioxidant from ginger, induced apoptosis in promyelocytic leukaemia HL-60 cells, caused DNA fragmentation and inhibited Bcl-2 expression in HL-60 cell (Wang et al. 2002). The results suggested that the

inhibition of Bcl-2 expression in HL-60 cells might account for the mechanism of 6-gingerol-induced apoptosis and not its antioxidative activity. Wei et al. (2005) reported several diarylheptanoids, and gingerol-related compounds from ginger rhizome possessed significant cytotoxicity against human promyelocytic leukaemia HL-60 cells ($IC_{50} < 50 \mu M$) by induction of cell apoptosis. Structure–activity relationship analysis demonstrated that the following structural determinants contributed critically to the enhancement of the activity: (i) acetoxyl groups at 3- and/or 5-positions of the side chain, (ii) the appropriate longer alkyl side-chain length, (iii) the *ortho*-diphenoxyl functionality on the aromatic ring and (iv) the α,β -unsaturated ketone moiety in the side chain. The rhizome extracts that exhibited EBV activation inhibitory activity had no cytotoxic effect in Raji cells. Organic ginger extracts or standards containing gingerols (6-, 8- and 10-gingerols) were not cytotoxic, while extracts or standards containing predominantly shogaols (6-, 8- and 10-shogaols) were cytotoxic at concentrations above 20 $\mu g/ml$ in U937 (human leukemic monocyte lymphoma) cells (Lantz et al. 2007). Shieh et al. (2010) demonstrated that treatment of human leukaemia HL-60 cells with [8]-shogaol induced apoptosis in a time- and concentration-dependent manner by stimulation of reactive oxygen species (ROS) production and depletion of glutathione.

Studies suggested that 6-gingerol stimulated apoptosis in human colorectal cancer cells through upregulation of non-steroidal anti-inflammatory drug (NSAID)-activated gene-1 (NAG-1) and G_1 cell cycle arrest through downregulation of cyclin D1 (Lee et al. 2008). Multiple mechanisms appeared to be involved in 6-gingerol action, including protein degradation as well as β -catenin, PKC ϵ and GSK-3 β pathways. In-vitro studies showed that 6-gingerol had two types of antitumour effects: (1) direct colon cancer cell growth suppression and (2) inhibition of the blood supply of the tumour via angiogenesis (Brown et al. 2009). [6]-gingerol, isolated from ginger, enhanced the TRAIL-induced viability reduction of gastric cancer cells, while 6-gingerol alone affected viability only slightly (Ishiguro et al. 2007). [6]-Gingerol enhanced TRAIL-

induced viability reduction by inhibiting TRAIL-induced NF-kappaB activation, while [6]-shogaol alone reduced viability by damaging microtubules and induced mitotic arrest. Sang et al. (2009) found that shogaols ([6], [8] and [10]) had much stronger growth-inhibitory effects than gingerols ([6], [8] and [10]) on H-1299 human lung cancer cells and HCT-116 human colon cancer cells, especially when comparing [6]-shogaol with [6]-gingerol (IC₅₀ of approximately 8 versus approximately 150 µM). In addition, they found that [6]-shogaol had much stronger inhibitory effects on arachidonic acid release and nitric oxide (NO) synthesis than [6]-gingerol. The study of Deol and Kaur (2013) found ginger extract loaded alginate beads to be significantly better than free ginger extract in the therapeutic treatment of colon cancer in Wistar rats in terms of histopathology, oxidative stress, mitochondrial complex activity, β-glucuronidase and ammonia concentration determinations. In a phase II study, Zick et al. (2011) found that administration of ginger root extract had the potential to decrease eicosanoid levels in colon mucosa in people at normal risk for colorectal cancer, perhaps by inhibiting their synthesis from arachidonic acid. Ginger also appeared to be tolerable and safe. After ginger consumption, participants at increased risk for colorectal cancer (CRC) had a significantly reduced colonic cyclooxygenase COX-1 protein level (23.8%) compared with the placebo group (18.9%) (Jiang et al. 2013). Protein levels of 15-hydroxyprostaglandin dehydrogenase (15-PGDH) in the colon were unchanged. In participants who were at normal risk for CRC, neither protein levels of COX-1 nor 15-PGDH in the colon were altered by ginger consumption. Ginger significantly lowered COX-1 protein expression in participants at increased risk for CRC, but not in those at normal risk for CRC. Ginger did not alter 15-PGDH protein expression in either increased or normal-risk participants. Ginger had been shown to inhibit COX and to decrease the incidence and multiplicity of adenomas and PGE2 concentrations in subjects at normal risk for colorectal cancer (Zick et al. 2014). In a pilot randomised clinical study of 20 subjects, oral administration of ginger elicited no changes in eicosanoids. Ginger lacked the ability to decrease eicosanoid levels in people at increased risk for colorectal cancer. Ginger

did appear to be both tolerable and safe and could have chemopreventive effects through other mechanisms. The results of a pilot, randomised and placebo-controlled trial of 20 people at increased risk for colorectal cancer suggested that administration of ginger may reduce proliferation in the normal-appearing colorectal epithelium and increase apoptosis and differentiation relative to proliferation, especially in the differentiation zone of the crypts (Citronberg et al. 2013).

[6]-Gingerol exerted antitumourigenic effects on two human pancreatic cancer cell lines, HPAC expressing wild-type (wt) p53 and BxPC-3 expressing mutated p53 by inducing cell cycle arrest and cell death (Park et al. 2006). Chen et al. (2007) found that 6-shogaol could effectively induce apoptotic cell death of human hepatoma p53 mutant Mahlavu cells via an oxidative stress-mediated caspase-dependent mechanism followed by a severe depletion of intracellular glutathione (GSH) contents. Ginger extract significantly reduced the elevated expression of $\text{NF}\kappa\beta$ and $\text{TNF-}\alpha$ in rats with liver cancer (Mohd Habib et al. 2008). Ginger may act as an anticancer and anti-inflammatory agent by inactivating $\text{NF}\kappa\beta$ through the suppression of the pro-inflammatory $\text{TNF-}\alpha$. Ginger extracts at 500 $\mu\text{g/ml}$ reduced superoxide dismutase (SOD) activity significantly by 72.32% in human liver cancer (HepG2) cell line when compared to untreated cell lines (Hanif et al. 2005). Ginger extract also reduced significantly glutathione peroxidase (GPx) activities by 77.16 %, 87.35 % and 71.05 % in HepG2 cell line at 100, 200 and 500 $\mu\text{g/ml}$, respectively, when compared to untreated culture. Ginger extracts at 200 and 500 $\mu\text{g/ml}$ reduced catalase activities by 41.65 and 67.43 % in HepG2 cell line when compared to untreated culture, respectively. Ginger extract had no effect on glutathione and MDA contents in normal (WRL-68) and in liver cancer (HepG2) cell lines at all concentrations. The study showed that ginger extract may exert its anticancer effect by restoring the function of SOD, GPx and catalase in removing superoxide radicals and hydrogen peroxide that caused oxidative damage to cells.

[6]-Gingerol was found to have antiangiogenic activity in-vitro and in-vivo (Kim et al. 2005a). In-vitro, [6]-gingerol

inhibited both the VEGF- and bFGF-induced proliferation of human endothelial cells and caused cell cycle arrest in the G1 phase. It blocked capillary-like tube formation by endothelial cells and inhibited sprouting of endothelial cells in the rat aorta and formation of new blood vessel in the mouse cornea in response to VEGF. Intraperitoneal administration to mice reduced the number of lung metastasis, with preservation of apparently healthy behaviour.

Among the five isolated compounds [4]-, [6]-, [8]- and [10]-gingerols and [6]-shogaol from the chloroform-soluble fraction of the methanolic extract of dried ginger rhizomes, [6]-shogaol exhibited the most potent cytotoxicity against human A549 lung carcinoma, SK-OV-3 ovary malignant ascites, SK-MEL-2 skin melanoma and HCT15 colon adenocarcinoma tumour cells (Kim et al. 2008). [6]-Shogaol [1-(4-hydroxy-3-methoxyphenyl)-4-decen-3-one] inhibited the growth of human cancer cells and induced apoptosis in COLO 205 cells through modulation of mitochondrial functions regulated by reactive oxygen species (ROS) (Pan et al. 2008b). The growth arrest and DNA damage (GADD)-inducible transcription factor 153 (GADD153) mRNA and protein was markedly induced in a time- and concentration-dependent manner in response to [6]-shogaol. [6]-Shogaol inhibited proliferation of the transgenic mouse ovarian cancer cell lines, C1 (genotype: p53^{-/-}, c-myc, K-ras) and C2 (genotype: p53^{-/-}, c-myc, Akt), with ED₅₀ values of 0.58 µM (C1) and 10.7 µM (C2). Shogaol inhibited human non-small cell lung cancer A549 cell proliferation by inducing autophagic cell death, but not, predominantly, apoptosis (Hung et al. 2009). They also found that [6]-shogaol inhibited survival signalling through the AKT/mTOR signalling pathway. At concentrations of 5–100 µM, [6]-shogaol killed OC2 human oral cancer cells in a concentration-dependent manner (Chen et al. 2010). [6]-Shogaol induced a significant rise in [Ca²⁺] (i) in oral cancer OC2 cells by causing stored Ca²⁺ release from the thapsigargin-sensitive endoplasmic reticulum pool in an inositol 1,4,5-trisphosphate-dependent manner and by inducing Ca²⁺ influx via a phospholipase A2- and La³⁺-sensitive pathway. Wu et al. (2010) demonstrated that topical

application of [6]-shogaol more effectively inhibited 12-*O*-tetradecanoylphorbol 13-acetate (TPA)-stimulated transcription of iNOS and COX-2 mRNA expression in mouse skin than curcumin and 6-gingerol. The antitumour effect was mediated by the downregulation of inflammatory iNOS and COX-2 gene expression in mouse skin. Three compounds, [6]-shogaol, [10]-gingerol and an enone-diarylheptanoid analogue of curcumin, were identified to be cytotoxic in cell lines tested, with KB and HL60 cells most susceptible to [6]-shogaol and the curcumin analogue with $IC_{50} < 10 \mu M$ (Peng et al. 2012).

Studies showed that dietary supplementation of 1.0% ginger meal for 26 weeks exerted a protective effect on the post-initiation stage of N-butyl-N-(4-hydroxybutyl)-nitrosamine (BBN)-induced urothelial carcinogenesis (hyperplasia and neoplasia) in rats (Ihlaseh et al. 2006). Contrariwise, Bidinotto et al. (2006) found that ginger extract did not inhibit the development of BBN-induced mouse bladder tumours. Ginger by itself was not genotoxic, and it did not alter the DNA damage levels induced by the BBN/MNU treatment during the course of the exposure. The incidence and multiplicity of simple and nodular hyperplasia and transitional cell carcinoma (TCC) were increased by the BBN/MNU(N-methyl-N-nitrosourea) treatment, but dietary ginger had no significant effect on these responses. However, in Group G2 (BBN/MNU/2% ginger-treated group), there was an increased incidence of grade 2 TCC.

Whole ginger extract (GE) exerted significant growth-inhibitory and death-inductory effects in a spectrum of prostate cancer cells (Karna et al. 2012). Studies had confirmed that GE perturbed cell cycle progression, impaired reproductive capacity, modulated cell cycle and apoptosis regulatory molecules and induced a caspase-driven, mitochondrially mediated apoptosis in human prostate cancer cells. Remarkably, daily oral feeding of 100 mg/kg body weight of GE inhibited growth and progression of PC-3 xenografts by approximately 56 % in nude mice, as shown by measurements of tumour volume. Tumour tissue from GE-treated mice showed reduced proliferation index and widespread apoptosis

compared with controls, as determined by immunoblotting and immunohistochemical methods. Also, GE did not exert any detectable toxicity in normal, rapidly dividing tissues such as gut and bone marrow. Kurapati et al. (2012) found that the combined effects of *C. longa* and *Z. officinale* were much greater than their individual effects in inhibiting growth of PC-3M prostate cancer cell line, suggesting the role of multiple components and their synergistic mode of actions to elicit stronger beneficial effects.

The cytotoxic activity of ginger extracts was dose dependent (Nalbantsoy et al. 2010). IC₅₀ values for mouse fibroblast (L929) and HeLa cells were found to be 87.28 µg/ml and 74.32 µg/ml, respectively, for the chloroform extract, while the ethanol extract showed IC₅₀ values at 101 µg/ml and 33.78 µg/ml, respectively. Steaming of ginger enhanced the antiproliferative effects against human HeLa cancer cells 1.5- and 2-fold higher than dried or fresh ginger (Cheng et al. 2011). Twenty-two components were characterised in the steamed ginger. The contents of 6-, 8- and 10-gingerol and 6-shogaol are 11.5, 2.1, 2.6 and 0.4 mg/g in fresh ginger; 10.40, 1.87, 1.63 and 0.69 mg/g in dried ginger; and 4.27, 0.94, 1.13 and 4.63 mg/g in ginger steamed at 120°C for 4 h. The decreased concentration of gingerols and increased levels of shogaols contributed to the improved anticancer potential of the steamed ginger.

Treatment of HeLa cancer cells with [6]-gingerol elicited caspase-3-dependent apoptosis and autophagy (Chakraborty et al. 2012). It was found that [6]-gingerol had potential to bind with DNA and induced conformational changes of DNA. The over-expression of NFκβ, AKT and Bcl2 genes in HeLa cancer cells was downregulated by [6]-gingerol treatment. In contrast the expression levels of TNFα, Bax and cytochrome c were enhanced in [6]-gingerol-treated cells. Ginger diarylheptanoids curcumin, gingerenone A, 7-(3,4-dihydroxyphenyl)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)heptan-3-one, (*E*)-1,7-bis(4-hydroxy-3-methoxyphenyl)hept-1-ene-3,5-dione and (*E*)-7-(4-hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)-hept-1-ene-3,5-dione inhibited cervical HeLa cancer cells, and curcumin, gingerenone A, (*E*)-1,7-bis(4-

hydroxy-3-methoxyphenyl)hept-1-ene-3,5-dione and (*E*)-7-(4-hydroxy-3-methoxyphenyl)-1-(4-hydroxyphenyl)-hept-1-ene-3,5-dione inhibited gastric MNK-45 cancer cells (Li et al. 2012b). It was found that compound gingerenone A was markedly cytotoxic against HeLa and MNK-45 cell lines with IC₅₀ values of 6.4 and 7.8 µmol/L, respectively. Ginger inhibited growth and modulated secretion of angiogenic factors in ovarian cancer cells; [6]-shogaol was the most active of the individual ginger components tested (Rhode et al. 2007). Ginger essential oil exhibited the strong cytotoxicity towards two human cancer cells at low concentration (Wang et al. 2012). Its IC₅₀ values on human ovarian cancer cell HO-8910 and human hepatocarcinoma cell Bel-7402 were 0.00643 and 0.00256% (v/v), respectively. Liu et al. (2012) demonstrated that terpenoids present in the steam-distilled extract of ginger (SDGE) were potent inhibitors of proliferation of the endometrial cancer cell lines Ishikawa and ECC-1 at IC₅₀ of 1.25 µg/ml mediated by apoptosis by activating p53. Citral, a mixture of neral and geranial, inhibited the proliferation of Ishikawa and ECC-1 cells at an IC₅₀ 10 µM (2.3 µg/ml).

Hsu et al. (2010) found that dehydrogingerdione, an active constituent of dietary ginger, induced cell cycle arrest and apoptosis through reactive oxygen species/c-Jun N-terminal kinase pathways in human breast cancer cells. Shogaols ([6]-, [8]- and [10]-shogaol) inhibited phorbol 12-myristate 13-acetate (PMA)-stimulated MDA-MB-231 breast cancer cell invasion with an accompanying decrease in matrix metalloproteinase-9 (MMP-9) secretion (Ling et al. 2010). [6]-Shogaol was identified to display the greatest anti-invasive effect in association with a dose-dependent reduction in MMP-9 gene activation, protein expression and secretion and also NF-κβ transcriptional activity. Antioxidant-enriched ginger extract (rhizomes) exhibited the highest anticancer activity on MCF-7 breast cancer cells with IC₅₀ values of 34.8 and 25.7 µg/ml for varieties Fulbaria and Syedpuri, respectively (Rahman et al. 2011). IC₅₀ values for MDA-MB-231 were 32.53 and 30.20 µg/ml for rhizome extracts of Fulbaria and

Syedpuri, respectively. Treatment of breast cancer cell lines, MCF-7 and MDA-MB-231, with ginger resulted in sequences of events marked by apoptosis, accompanied by loss of cell viability, chromatin condensation, DNA fragmentation, activation of caspase-3 and cleavage of poly(ADP-ribose) polymerase (Elkady et al. 2012). It also inhibited the expression of the two prominent molecular targets of cancer, c-Myc and the human telomerase reverse transcriptase (hTERT). 4-Shogaol an active phytoconstituents isolated from dried red ginger inhibited metastasis of MDA-MB-231 human breast adenocarcinoma cells by decreasing the repression of NF- κ B/Snail/RKIP (Raf kinase inhibitor protein) pathways (Hsu et al. 2012). [6]-, [8]- and [10]-gingerols inhibited the proliferation of MDA-MB-231 tumour cell line with IC₅₀ of 666.2 μ M, 135.6 μ M and 12.1 μ M, respectively (da silva et al. 2012). These substances also inhibited human fibroblast (HF) cell proliferation, however in concentrations starting from 500 μ M.

The ethyl acetate fraction of ginger extract inhibited the expression of the two prominent molecular targets of cancer, the human telomerase reverse transcriptase (hTERT) and c-Myc, in A549 lung cancer cells in a time- and concentration-dependent manner (Tuntiwechapikul et al. 2010). Studies by Lv et al. (2012) showed that 6-gingerol was extensively metabolised in H-1299 human lung cancer cells, in CL-13 mouse lung cancer cells, in HCT-116 and HT-29 human colon cancer cells and in mice. The two major metabolites in H-1299 cells were purified and identified as (3*R*,5*S*)-6-gingerdiol (M1) and (3*S*,5*S*)-6-gingerdiol (M2). Both metabolites induced cytotoxicity in cancer cells after 24 h, with M1 having a comparable effect to 6-gingerol in H-1299 cells. In-vitro study results suggested that a combination of crude alkaloid extracts from *Rhazya stricta* and crude flavonoid extracts from *Z. officinale* was found to be a promising treatment for the prevention of human colorectal cancer cells (HCT116) (Elkady et al. 2014). The treatment synergistically suppressed the proliferation, colony formation and anchorage-independent growth of HCT116 cells by induction of apoptosis. The combined treatment downregulated expression levels of anti-

apoptotic proteins including Bcl-2, Bcl-X, Mcl-1, survivin and XIAP and upregulated expression levels of proapoptotic proteins such as Bad and Noxa. The combined treatment elevated expression levels of the oncosuppressor proteins, p53, p21 and p27, and reduced levels of the oncoproteins, cyclin D1, cyclin/cyclin-dependent kinase-4 and c-Myc.

Crude ethanolic ginger extract exerted cytotoxicity, toxicity and anticancer activity against oval-albumin and nitrosamine (OV/ DMN)-induced cholangiocarcinoma in hamsters (Plengsuriyakarn et al. 2012). In-vitro median IC₅₀ (concentration that inhibits cell growth by 50%) values for cytotoxicity and antioxidant activities of the crude ethanolic extract of ginger were 10.95, 53.15 and 27.86 µg/ml, respectively. The survival time and survival rate of the CCA-bearing hamsters were significantly prolonged by ginger extract compared to the control group (median of 54 vs 17 weeks). Acute and subacute toxicity tests indicated absence of any significant toxicity at the maximum dose of 5,000 mg/kg body weight given by intragastric gavage.

Fan et al. (2014) found that 6-gingerol suppressed the growth of osteosarcoma cells through apoptosis and AMP-activated protein kinase (AMPK) activation.

Antimutagenic/Mutagenic/Anticlastogenic Activities

Ginger juice was found to possess strong capacity of inactivating the mutagenicity of tryptophan pyrolysis products (Morita et al. 1978). Ginger was reported to contain antimutagenic factor(s) acting on tryptophan pyrolysate using the Ames strain's of *Salmonella* TA98 (Kada et al. 1978). However, when ginger rhizome juice was added to a solution of 2(2-furyl)-3(5-nitro-2-furyl)acryl amide (AF2) or N-methyl-N'-nitro-N-nitrosoguanidine (NTG), mutagenesis by these chemicals was markedly increased (Nakamura and Yamamoto 1982). The constituent [6]-gingerol was found to be the potent mutagen. The results suggested that the [6]-gingerol component may be mutagenically activated by the presence of AF2 and NTG. [6]-Shogaol was isolated from the ginger by

column chromatography on silica gel. [6]-Shogaol from ginger was found to be much less mutagenic (1×10^3 revertants/ 10^8 viable cells/700 μ M) than [6]-gingerol (1×10^7 of the same units) (Nakamura and Yamamoto 1983). Mutation frequencies of their related compounds were 4×10^1 for zingerone, 1×10^7 for 3-hydroxymyristic acid and 3×10^2 for 12-hydroxystearic acid. Curcumin and myristic, stearic and oleic acids had no mutagenicity, and diacetone alcohol and butyrol were suppressible for mutation. It was inferred from these results that the active part of [6]-gingerol was the aliphatic chain moiety containing a hydroxy group.

Nagabhushan et al. (1987) observed that ginger extract, gingerol and shogaol were mutagenic on metabolic activation in *Salmonella typhimurium* strains TA 100 and TA 1535, but zingerone was non-mutagenic in all the four strains with or without S9 mix. When mutagenicity of gingerol and shogaol was tested in the presence of different concentrations of zingerone, it was observed that zingerone suppressed mutagenic activity in both the compounds in a dose-dependent manner. Mukhopadhyay and Mukherjee (2000) found that ginger rhizome extract may contain substance(s) that suppressed clastogenesis in the bone marrow cells of mice. Ginger oil exerted a higher frequency of chromosomal aberrations. Studies found that EV.EXT 33, a patented *Zingiber officinale* extract, when administered to pregnant rats during the period of organogenesis, caused neither maternal nor developmental toxicity at daily doses of up to 1000 mg/kg body weight (Weidner and Sigwart 2000).

Antimicrobial Activity

The growth of both Gram-positive and Gram-negative bacteria was significantly inhibited by ethanol ginger extract (Mascolo et al. 1989). Gingerenone A exhibited a moderate anti-coccidium activity in-vitro and a strong antifungal effect to *Pyricularia oryzae* (Endo et al. 1990). Ficker et al. (2003) identified [6], [8] and [10]-gingerols and [6]-gingerdiol as the main antifungal principles from ginger. The compounds were active against 13 human pathogens at concentrations of <1

mg/mL. Two highly alkylated gingerols, [10]-gingerol and [12]-gingerol, effectively inhibited the growth of periodontal pathogens Gram-negative bacteria, *Porphyromonas gingivalis*, *Porphyromonas endodontalis* and *Prevotella intermedia* at a minimum inhibitory concentration (MIC) range of 6–30 µg/mL. These ginger compounds also killed the oral pathogens at a minimum bactericidal concentration (MBC) range of 4–20 µg/mL, but not the other ginger compounds 5-acetoxy-[6]-gingerol, 3,5-diacetoxy-[6]-gingerdiol and galanolactone. Four known components of ginger, [6]-dehydrogingerdione, [10]-gingerol, [6]-shogaol and [6]-gingerol, exhibited antibacterial activity against clinical drug-resistant *Acinetobacter baumannii* (Wang et al. 2010). Combined with tetracycline, they showed good resistance-modifying effects to modulate tetracycline resistance. Using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging method, these four ginger compounds demonstrated antioxidant properties, which were inhibited by MnO₂, an oxidant without antibacterial effects. After the antioxidant property was blocked, their antimicrobial effects were abolished significantly. These results indicated that ginger compounds had antioxidant effects that partially contributed to their antimicrobial activity.

Ginger extract exhibited antibacterial activity in-vitro against respiratory tract pathogens, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae* and *Haemophilus influenzae*, with minimum inhibitory concentration (MIC) of 0.0033–0.7 µg/ml and minimum bactericidal concentration (MBC) of 0.135–2.4 µg/ml (Akoachere et al. 2002). Ginger rhizome hydroalcoholic extract exhibited a dose-dependent antimicrobial activity against *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Escherichia coli* and *Candida albicans* (Jagetia et al. 2003). Studies showed that ginger extract exhibited higher antibacterial activity in-vitro than onion extract against *Staphylococcus aureus* and *Pseudomonas aeruginosa* (from high vaginal swab) two common pathogens of nosocomial (hospital-acquired) and urinary tract infections (Azu et al. 2007). Ginger ethanol and chloroform extracts inhibited the growth of *Klebsiella pneumoniae*, *Salmonella typhimurium*,

Bacillus cereus, *Enterococcus faecalis* and *Staphylococcus aureus* but had no effect on the growth of *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus epidermidis* (Nalbantsoy et al. 2010). Aqueous ginger extract inhibited growth of cariogenic bacteria *Streptococcus mutans*, *Lactobacillus acidophilus* and *Staphylococcus aureus* in-vitro (Patel et al. 2011). The combined extracts of ginger and honey were most effective against *Staphylococcus aureus* but least effective against *L. acidophilus*. Compared to tetracycline, the methanol and ethyl acetate extracts of ginger exhibited weak to moderate activity (based on inhibitory zone diameter) against *Bacillus cereus*, *Bacillus subtilis*, *Staphylococcus aureus* and *Escherichia coli* but were inactive against *Salmonella typhi* and *Streptococcus pyogenes* (Kaushik and Goyal 2011). The MIC of tetracycline against *S. aureus* was < 8 µg/ml, whereas the MIC of the methanol extract was 512 µg/ml and the MIC of the methanol extract against *Bacillus cereus*, *Bacillus subtilis*, *Staphylococcus aureus* and *Escherichia coli* was 4096 µg/ml or greater.

Ginger extracts obtained using supercritical CO₂ presented antibacterial effects against Gram-positive bacteria (Mesomo et al. 2013). The oil obtained by hydrodistillation differed from the other samples tested and had a lower capacity for inhibition of *Pseudomonas aeruginosa* bacteria than the supercritical extract. For the Gram-negative bacteria *Salmonella typhimurium* and *Shigella flexneri*, the oil showed slight inhibition.

In-vitro studies showed that ginger ethanol leaf and root extract exhibited antibacterial activity against *Staphylococcus aureus* and *Streptococcus pyogenes*, while the three antibiotics used (chloramphenicol, ampicillin and tetracycline) were less active compared to ginger extract (Sebiomo et al. 2011). Both ginger leaf and rhizome oils were moderately active against the Gram-positive bacteria, *Bacillus licheniformis*, *Bacillus spizizenii* and *Staphylococcus aureus*, and the Gram-negative bacteria, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas stutzeri* (Sivasothy et al. 2011). The sensitivity of the bacterial strains to the leaf oil decreased in the order *B. licheniformis* = *S. aureus* > *B. spizizenii* > *P. stutzeri* > *K.*

pneumoniae > *E. coli*, while for the rhizome oil, the order was *B. licheniformis* > *B. spizizenii* > *S. aureus* = *E. coli* > *K. pneumoniae* > *P. stutzeri*. Ginger rhizome extracts showed high antibacterial activity against Gram-positive bacteria: *Listeria monocytogenes*, *Staphylococcus aureus* and *Bacillus cereus*; the MIC of the last two species was 4 mg/ml (Nishikawa et al. 2013). The tetraploid ginger extract was more potent than diploid against *L. monocytogenes* (MIC diploid 8 mg/ml, tetraploid 4 mg/ml). The extracts were generally not active against the Gram-negative bacteria *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Salmonella enteritidis*, *Vibrio parahaemolyticus* and *Yersinia enterocolitica*. Crude ginger rhizomes and garlic cloves exhibited antibacterial activity against multi-drug-resistant clinical pathogens causing nosocomial infection (Karuppiah and Rajaram 2012). Except *Enterobacter* sp. and *Klebsiella* sp., all other isolates, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus* sp. and *Bacillus* sp., were susceptible when subjected to ethanolic extracts of garlic and ginger. The highest inhibition zone was observed with garlic (19.45 mm) against *Pseudomonas aeruginosa*.

[6]-Gingerol was the major constituent in both the diploid and tetraploid extracts (0.74–0.64% dw or 237–206 µg/ml). [6]-Dehydroparadol occurred in small amount, 0.07–0.09% dw, and zingerone was hardly detected. [6]-Gingerol demonstrated significant antibacterial activity against all bacteria tested with MIC value of 250 µg/ml against *S. aureus* and MIC 500 µg/ml against *Listeria monocytogenes*, *B. cereus*, *Pseudomonas aeruginosa* and *Vibrio parahaemolyticus*. [6]-Dehydroparadol and zingerone showed no activity against Gram-negative bacteria but some activity against Gram-positive bacteria.

Ethanol ginger powder extract exhibited pronounced inhibitory activity against *Candida albicans* (Supreetha et al. 2011). Ginger paste at room temperature exerted higher inhibition than ethanol alone, but cold ethanolic ginger extract showed the maximum inhibition zone at 24 h. Ginger essential oils, and particularly those from seed and air-dried rhizomes, had potent inhibitory activity against *Candida albicans*.

compared to ginger oleoresins obtained by ethanol and hypercritical carbon dioxide extraction and essential oils of five other plants in the family Zingiberaceae (Takahashi et al. 2011). Of the constituents, [6]-shogaol was most active against filament formation and growth of *C. albicans*, followed by citral and [6]-gingerol. *Escherichia coli* was the most susceptible to ginger oleoresin followed by *Bacillus subtilis* and *Staphylococcus aureus*, whereas ginger essential oil was more active on *Staphylococcus aureus* followed by *B. cereus* and *Escherichia coli* (Bellik 2014). *Candida albicans* was sensitive to both oleoresin and essential oil. *Aspergillus niger* was least, whereas *Penicillium* spp. had higher sensitivity to both ginger extracts; minimal inhibitory concentrations of the oleoresin and essential oil were 2 mg/mL and 869.2 mg/mL, respectively. The essential oil combination of *Curcuma longa* and *Zingiber officinale* significantly inhibited the growth and aflatoxin production by the toxigenic food-borne strain of *Aspergillus flavus* LHP-6 at 2.5 and 2.0 μ L/mL, respectively (Prakash et al. 2012). Ginger essential oil exhibited inhibitory activity against *Fusarium verticillioides*, with an MIC of 2500 μ g/mL, and at 4000 and 5000 μ g/mL reduced ergosterol biosynthesis by 57% and 100%, respectively (Yamamoto-Ribeiro et al. 2013). The inhibitory effect on fumonisin B1 (FB1) and fumonisin B2 (FB2) production was significant at concentrations of 4000 and 2000 μ g/mL, respectively. The predominant components of ginger oil were α -zingiberene (23.9%) and citral (21.7%).

Antiviral Activity

β -sesquiphellandrene from ginger rhizome exhibited antiviral activity against rhinovirus IB in-vitro with IC₅₀ value of 0.44 μ m (Denyer et al. 1994). Seven Zingiberaceous rhizomes, including *Z. officinale* (white and red cvs), were found to possess inhibitory activity towards Epstein–Barr virus early antigen (EBV-EA) activation, induced by 12-*O*-tetradecanoyl phorbol-13-acetate (TPA) (Vimala et al. 1999). Ginger compounds bisgingerdiones A and B, (5*R*)-5-acetoxy-1,7-bis(4-hydroxy-3-methoxyphenyl)heptan-3-one and methyl (*Z*)-neral acetal-[6]-gingerdiol showed weak cytotoxic and anti-

HIV-1 (human immunodeficiency virus1) activities (Feng et al. 2011). Fresh ginger dose-dependently inhibited human respiratory syncytial virus (HRSV)-induced plaque formation in both human upper (Hep-2) and lower (A549) respiratory tract cell lines (Chang et al. 2013). In contrast, dried ginger did not show any dose-dependent inhibition. 300 µg/ml fresh ginger could decrease the plaque counts to 19.7% (A549) and 27.0% (Hep-2) of that of the control group. Fresh ginger was more effective when given before viral inoculation, particularly on A549 cells. 300 µg/ml fresh ginger could decrease the plaque formation to 12.9% when given before viral inoculation. Fresh ginger dose-dependently inhibited viral attachment and internalisation. Fresh ginger of high concentration could stimulate mucosal cells to secrete IFN- β that possibly contributed to counteracting viral infection.

Anti-inflammatory Activity

Grzanna et al. (2005) in their review reported that ginger is an herbal medicinal product that shares pharmacological properties with non-steroidal anti-inflammatory drug. They stated that ginger suppressed prostaglandin synthesis through inhibition of cyclooxygenase-1 and cyclooxygenase-2 and suppressed leukotriene biosynthesis by inhibiting 5-lipoxygenase. Evidence was provided that showed ginger modulates biochemical pathways activated in chronic inflammation.

In addition to [6]-gingerol, four new constituents, [6]-dehydrogingerdione, [10]-dehydrogingerdione, [6]-gingerdione and [10]-gingerdione, were isolated as potent inhibitors of prostaglandin (PG) biosynthesis from ginger roots (Kiuchi et al. 1982). The IC₅₀ values of [6]-gingerol, [6]-dehydrogingerdione, [10]-dehydrogingerdione, [6]-gingerdione and [10]-gingerdione against PG synthetase were 5.5, 1.0, 2.3, 1.6 and 1.0 µM, respectively. In rats, the ethanolic ginger extract reduced carrageenan-induced paw swelling and yeast-induced fever (Mascolo et al. 1989) but was ineffective in suppressing the writhing induced by intraperitoneal acetic acid. A dose-dependent inhibition of

prostaglandin release effect was observed using rat peritoneal leucocytes. Ginger rhizome extract (50 and 100 mg/kg b.w.) significantly inhibited the carrageenan-induced rat paw oedema (Raji et al. 2002). A low dose of ginger (50 mg/kg) administered either orally or intraperitoneally (IP) did not produce any significant reduction in the serum thromboxane- B_2 levels when compared to saline-treated rats (Thomson et al. 2002). However, ginger administered orally caused significant changes in the serum prostaglandin- E_2 (PGE_2) at this dose. High doses of ginger (500 mg/kg) were significantly effective in lowering serum PGE_2 when given either orally or IP. However, TXB_2 levels were significantly lower in rats given 500 mg/kg ginger orally but not IP. A significant reduction in serum cholesterol was observed when a higher dose of ginger (500 mg/kg) was administered. At a low dose of ginger (50 mg/kg), a significant reduction in the serum cholesterol was observed only when ginger was administered IP. No significant changes in serum triglyceride levels were observed upon administration of either the low or high dose of ginger. The results suggested that ginger could be used as a cholesterol-lowering, antithrombotic and anti-inflammatory agent.

Ginger fractions from the dichloromethane extracts containing gingerols and/or gingerol derivatives showed excellent inhibition of LPS-induced PGE_2 production (Jolad et al. 2004). Topical application of [6]-gingerol inhibited phorbol 12-myristate 13-acetate -induced COX-2 expression in mouse skin (Kim et al. 2004; 2005b). [6]-Gingerol suppressed NF-kappa β DNA-binding activity in mouse skin and inhibited the phosphorylation of p38 mitogen-activated protein kinase which may account for its inactivation of NF-kappa β and suppression of COX-2 expression. [6]-Gingerol (50–100 mg/kg) produced an inhibition of paw edema induced by carrageenin (Young et al. 2005). A stable [6]-gingerol metabolite, RAC-[6]-dihydroparadol ([6]-DHP), and a closely related gingerol analogue, RAC-2-hydroxy-1-(4-hydroxy-3-methoxyphenyl)dodecan-3-one [a capsaicin/gingerol (capsarol) analogue referred to as ZTX42], significantly inhibited lipopolysaccharide-induced NO production in a

murine macrophage cell line, RAW 264.7, in a concentration-dependent manner, with an IC_{50} of 1.45 μ M and 7.24 μ M, respectively (Aktan et al. 2006). Both compounds suppressed NO production in murine macrophages by partially inhibiting iNOS enzymatic activity and reducing iNOS protein production, via attenuation of NF-kappaB-mediated iNOS gene expression. Crude organic extracts of ginger were capable of inhibiting LPS-induced PGE_2 ($IC_{50} < 0.1 \mu$ g/ml) production in U937 cells (Lantz et al. 2007). However, extracts were not nearly as effective at inhibiting $TNF-\alpha$ ($IC_{50} > 30 \mu$ g/ml). Ginger extracts containing either predominantly gingerols (6-, 8- and 10-gingerols) or shogaols (6-, 8- and 10-shogaols) were both highly active at inhibiting LPS-induced PGE_2 production ($IC_{50} < 0.1 \mu$ g/ml), while extracts that contained unknown compounds were less effective ($IC_{50} < 3.2 \mu$ g/ml). Extracts or standards containing predominantly gingerols were capable of inhibiting LPS-induced COX-2 expression, while shogaol containing extracts had no effect on COX-2 expression.

Ginger hexane extract significantly inhibited the excessive production of NO, PGE_2 , $TNF-\alpha$ and IL-1 β in LPS-stimulated BV2 cells (Jung et al. 2009). In addition, the extract attenuated the mRNA expressions and protein levels of inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2) and pro-inflammatory cytokines. The results indicated that ginger hexane extract exhibited anti-inflammatory activity by suppressing the transcription of inflammatory mediator genes through the MAPK and NF- κ B signalling pathways. Ginger compounds, [8]-gingerol, [10]-gingerol and [6]-shogaol, inhibited significantly and dose-dependently lipopolysaccharide-induced nitrite and prostaglandin E_2 production in RAW 264.7 cells (Dugasani et al. 2010). Pan et al. (2008a) showed that 6-shogaol downregulated inflammatory iNOS and COX-2 gene expression in LPS-stimulated murine macrophages by inhibiting the activation of NF-kappaB and interfering with the activation of PI3K/Akt/I kappaB kinases IKK and MAPK. Ginger compounds [6]-shogaol, 1-dehydro-[10]-gingerdione and [10]-gingerdione

significantly decreased lipopolysaccharide-induced nitric oxide production, and compounds [6]-shogaol and 1-dehydro-[10]-gingerdione significantly reduced inducible nitric oxide synthase expression in RAW 264.7 macrophage cell line (Koh et al. 2009). 1-Dehydro-[10]-gingerdione also showed significant stimulatory effects on phagocytosis.

Red ginger ethanol (RGE) extract (10–100 mg/kg) suppressed both the frequency of writhing and the increase in permeability of abdominal capillaries (Shimoda et al. 2010). In contrast, continuous treatment with RGE (10 mg/kg) significantly suppressed footpad oedema in a rat adjuvant arthritis model. RGE (3 and 10 µg/mL) significantly suppressed PGE(2) production, while it also suppressed NO production at 100 µg/mL in mouse leukemic monocytes (RAW264 cells) stimulated by lipopolysaccharide. [6]-Shogaol, gingerdiols and proanthocyanidins were identified as constituents of red ginger extract that inhibited NO production. Also they found a potent suppressive effect of RGE on acute and chronic inflammation, and inhibition of macrophage activation appeared to be involved in this anti-inflammatory effect.

Intraperitoneal administration of alcoholic ginger extract inhibited significantly carrageenan-, compound 48/80- or serotonin-induced rat paw oedema (Penna et al. 2003). Ginger extract was also effective in inhibiting 48/80-induced rat skin oedema at doses of 0.6 and 1.8 mg/site. The intraperitoneal administration of ginger extract (186 mg/kg(–1) body wt.) 1 h prior to serotonin injections reduced significantly the serotonin-induced rat skin oedema. Ginger rhizome ethanol extract (50–800 mg/kg p.o.) significantly inhibited fresh egg albumin-induced acute inflammation (Ojewole 2006). Oral administration of ginger essential oil (200–500 mg/kg) reduced the rolling and leukocyte adherence after 2 h of carrageenan injection (100 µg) into the scrotal chamber (Nogueira de Melo et al. 2011). The number of leukocytes migrated to the perivascular tissue 4 h after the irritant stimulus was also diminished. All doses tested (10^{-4} , 10^{-3} or 10^{-2} µL/mL) caused a significant reduction of leukocyte chemotaxis (35.89, 30.67 and 35.85 %, respectively) towards

casein stimuli. The data presented showed direct and systemic effects of ginger essential oil on leukocyte migration as an important mechanism of the anti-inflammatory action of ginger.

Except for the gingerdiols, at least some members of each class of the gingerol-related compounds (gingerols, shogaols, paradols, gingerdiols, gingerdiones and dehydrogingerols) showed specific binding to the active site of COX-2 (van Breemen et al. 2011). All 3 gingerdiones bound to COX-2, but only 2 gingerols, 2 shogaols, 2 paradols and 1 dehydrogingerol were COX-2 ligands. Among the gingerols, 10-gingerol and 12-gingerol, but not 6-gingerol or 8-gingerol, bound to COX-2, 8-shogaol and 10-shogaol were COX-2 ligands but not 6-shogaol or 12-shogaol, and 6-paradol and 8-paradol but not 10-paradol bound to COX-2. The paradols showed the highest affinity for COX-2 followed by the shogaols and then the gingerols and gingerdiones. Of much lower relative affinities for COX-2 were the dehydrogingerols and lastly the gingerdiols which showed no binding to COX-2. Ginger extract and purified 10-gingerol, 8-shogaol and 10-shogaol inhibited COX-2 with IC_{50} values of 7.5 μ M, 32 μ M, 17.5 μ M and 7.5 μ M, respectively. No inhibition of COX-1 was detected. Therefore, 10-gingerol, 8-shogaol and 10-shogaol inhibit COX-2 but not COX-1, which could explain, in part, the anti-inflammatory properties of ginger. Ginger compounds (*E*)-geranylferulic acid, (*Z*)-geranylferulic acid, [6]-gingerol, [8]-gingerol, [10]-gingerdione, 1-dehydro-[6]-gingerdione, 1-dehydro-[8]-gingerdione, [6]-paradol, [8]-paradol, [6]-gingeroldiacetate, 6-hydroxy-[6]-shogaol, galanolactone and *trans*- β -sesquiphellandrol were found to inhibit LPS-induced production of nitric oxide in murine macrophage RAW264.7 cells with IC_{50} values ranging from 5.5 to 28.5 μ M (Hong and Oh 2012). Ginger compounds hexahydrocurcumin, 1-dehydro-[6]-gingerdione, 6-dehydroshogaol and 6-shogaol could attenuate lipopolysaccharide (LPS)-elicited increase of prostaglandin E2 (PGE(2)) in murine macrophages (RAW 264.7) in a concentration-dependent manner but hexahydrocurcumin at 7 μ M and 6-shogaol at 7 μ M (Li et al. 2012a). The strongest inhibitory effect was observed for 6-

dehydroshogaol and 6-shogaol at 14 μ M with the inhibition of 53.3% and 48.9%, respectively. Furthermore, both 6-dehydroshogaol and 1-dehydro-[6]-gingerdione significantly suppressed the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) proteins in a concentration-dependent fashion. Studies by Saptarini et al. (2013) concluded that ginger's phenolic compounds 6-gingerol, 6-shogaol and 6-paradol could be developed as preferential COX-2 inhibitors.

Inhibitors of molecule-mediated cell adhesion might be novel therapeutic agents for the treatment of various inflammatory diseases (Lee et al. 2011). Of the compounds isolated from ginger root methanol extract, [10]-gingerol, [6]-shogaol, [8]-shogaol and dehydro-6-gingerdione inhibited direct binding between sICAM-1 (soluble intercellular adhesion molecule-1) and leukocyte function-associated antigen (LFA)-1 of the human monocytic THP-1 cells in a dose-dependent manner with IC₅₀ values of 57.6, 27.1, 65.4 and 62.0 μ M, respectively. [6]-Shogaol and dehydro-6-gingerdione had an inhibitory effect on direct binding between sVCAM-1 (soluble vascular cell adhesion molecule 1) and VLA-4 (very late antigen-4) of THP-1 cells. The results suggested that the phenolic compounds from *Z. officinale* roots were good candidates for therapeutic strategies aimed at inflammation. Myeloid differentiation protein 2 (MD-2), a co-receptor of toll-like receptor 4 (TLR4), was found to be a molecular target in the anti-inflammatory action of 1-dehydro-10-gingerdione (1D10G), a pungent constituent from ginger (Park et al. 2012). 1D10G inhibited lipopolysaccharide (LPS) binding to MD-2 with higher affinity than gingerol and shogaol from dietary ginger. Moreover, 1D10G downregulated TLR4-mediated expression of nuclear factor- κ B (NF- κ B) or activating protein 1 (AP1)-target genes such as tumour necrosis factor α (TNF- α) and interleukin-1 β , as well as those of interferon (IFN) regulatory factor 3 (IRF3)-target IFN- β gene and IFN- γ inducible protein 10 (IP-10) in LPS-activated macrophages.

Studies by Aimbire et al. (2007) suggested that ginger exerted an anti-inflammatory effect in rat lung by attenuating

rat trachea hyperreactivity and COX metabolites. Ginger extract and celecoxib attenuated rat trachea hyperreactivity 90 min and 48 h after LPS. Both reduced the serum level of prostaglandin (PGE₂) and thromboxane (TXA₂) 90 min after LPS and also reduced myeloperoxidase activity and the number of cells in rat bronchoalveolar lavage 48 h post-LPS. On lung parenchyma, ginger and celecoxib reduced the release of PGE₂ and TXA₂ 48 h post-LPS. Intraperitoneal injections of aqueous ginger extract before airway challenge of ovalbumin (OVA)-sensitised mice resulted in a marked decrease in the recruitment of eosinophils to the lungs as attested by cell counts in bronchoalveolar lavage (BAL) fluids and histological examination (Ahui et al. 2008). Resolution of airway inflammation induced was accompanied by a suppression of the Th2 cell-driven response to allergen in-vivo. The study provided evidence that ginger could suppress Th2-mediated immune responses and might thus provide a possible therapeutic application in allergic asthma.

Khan et al. (2014) found that ginger ameliorated ovalbumin-induced allergic asthma in mice via suppression of Th2-mediated immune response. Both ethanol and aqueous ginger extracts caused significant reduction in goblet cell hyperplasia, infiltration of inflammatory cells in airways, oedema with vascular congestion and total and differential count of eosinophils and neutrophils in BALF (bronchoalveolar liquid lavage). Protein levels of IL-4 and IL-5 in BALF, along with total serum IgE levels, were also significantly suppressed by both extracts.

Anti-inflammatory/ Anti-arthritic Activity

In-Vitro Studies

Studies found that treatment with ginger root extract inhibited inflammatory mediators nitric oxide (NO) and prostaglandin E₂ (PGE₂) production in sow osteoarthrotic cartilage explants (Shen et al. 2003) and in normal chondrocytes (NC) and osteoarthrotic chondrocytes (OC) isolated from sow cartilage explants (Shen et al. 2005). Both studies suggested an

important role for ginger root extract as an anti-arthritic agent. Hot water ginger extracts showed weak inhibitory activity against oxide (NO) production by LPS/IFN- γ -activated macrophages (Daikonya et al. 2013). The extract was divided into two groups according to the strength of the inhibitory activity. It was shown that [6]-gingerol, the main component of ginger, contributed to the distinction of the two groups and might be useful as a biomarker to evaluate an anti-inflammatory effect of ginger.

Animal Studies

Eugenol (33 mg/kg) and ginger oil (33 mg/kg) given prophylactically via oral route for 26 days caused significant suppression of both paw and joint swelling in male Sprague Dawley rats with adjuvant arthritis (Sharma et al. 1997a). Plasma kallikrein levels in the synovial tissue increased significantly in non-treated arthritic control rats and reduced to the normal levels in treated rat. The study demonstrated that eugenol and ginger oil had potent anti-inflammatory properties, and their anti-inflammatory effects may be related to reduction in kallikrein levels. Ginger extract at doses higher than 50 mg/kg/day intraperitoneally starting from the dose of booster immunisation and for 26 days ameliorated the clinical scores, disease incidence, joint temperature and swelling and cartilage destruction, together with the reduction of serum levels of IL-1 β , IL-2, IL-6, tumour necrosis factor α and anti-CII antibodies in collagen-induced arthritic rats (Fouda and Berika 2009). Moreover, ginger extract at the dose of 200 mg/kg/day was superior to 2 mg/kg/day of indomethacin in most of the measured parameters.

Turmeric and ginger rhizomes (at dose 200 mg/kg body weight) significantly suppressed (but with different degrees) the incidence and severity of arthritis by increasing/decreasing the production of anti-inflammatory/pro-inflammatory cytokines, respectively, and activating the antioxidant defence system in adjuvant-induced arthritic rats (Ramadan et al. 2011). The anti-arthritic activity of turmeric exceeded that of ginger and indomethacin (a non-steroidal anti-inflammatory drug), especially when the treatment started from the day of

arthritis induction. The percentage of disease recovery was 4.6–8.3% and 10.2 % more in turmeric compared with ginger and indomethacin, respectively. In another study, oral administration of ginger–turmeric rhizomes mixture was found to be more effective than indomethacin (a non-steroidal/anti-inflammatory drug) in alleviating the loss in body weight gain, the histopathological changes observed in ankle joints, blood leukocytosis and thrombocytosis, iron deficiency anaemia, serum hypoalbuminaemia and globulinaemia, the impairment of kidney functions and the risks for cardiovascular disease in adjuvant-induced human rheumatoid arthritic rats (Ramadan and El-Menshawy 2013).

Clinical Studies

Seven patients suffering from such rheumatic disorders reported relief in pain and associated symptoms upon ginger administration (Srivastava and Mustafa 1989). Srivastava and Mustafa (1992) reported that 56 patients (28 with rheumatoid arthritis, 18 with osteoarthritis and 10 with muscular discomfort) used powdered ginger against their afflictions. Among the arthritis patients, more than three-quarters experienced, to varying degrees, relief in pain and swelling. All the patients with muscular discomfort experienced relief in pain. None of the patients reported adverse effects during the period of ginger consumption which ranged from 3 months to 2.5 years. It was suggested that at least one of the mechanisms by which ginger elicited its ameliorative effects could be related to inhibition of prostaglandin and leukotriene biosynthesis. In a randomised, double-blind, placebo-controlled, multicentre, parallel-group, 6-week study of 261 patients with osteoarthritis (OA) of the knee and moderate to severe pain, administration of a highly purified and standardised ginger extract had a statistically significant effect on reducing symptoms of OA of the knee (Altman and Marcussen 2001). This effect was moderate. There was a good safety profile, with mostly mild gastrointestinal adverse events in the ginger extract group.

In a double-blind, parallel-group clinical trial of 52 patients with knee osteoarthritis, ginger was found to be as

effective as indomethacin in relieving symptoms of osteoarthritis with negligible side effects (Haghighi et al. 2006). Therefore, in patients with intolerance to indomethacin, ginger may be substituted to ginger and indomethacin. In a double-blind, placebo-controlled study group of 59 elderly persons with moderate to severe knee pain, six aroma massage sessions with ginger and orange oil over a 3-week period appeared to have potential as an alternative method for short-term knee pain relief (Yip and Tam 2008).

Antiemetic Activity

In-Vitro Studies

The in-vitro study of Abdel-Aziz et al. (2006) concluded that [6]-, [8]- and [10]-gingerol and [6]-shogaol exerted their antiemetic effect at least partly by acting on the 5-HT(3) receptor ion channel complex, probably by binding to a modulatory site distinct from the serotonin binding site. This may include indirect effects via receptors in the signal cascade behind the 5-HT(3) receptor channel complex such as substance P receptors and muscarinic receptors. Subsequent in-vitro studies by Pertz et al. (2011) concluded that the efficiency of ginger in reducing nausea and vomiting may be based on a weak inhibitory effect of gingerols ([6]-gingerol, [8]-gingerol and [10]-gingerol) and shogaols (e.g.[6]-shogaol) at cholinergic M (3) and serotonergic 5-HT (3) receptors. Serotonergic 5-HT (4) receptors, which play a role in gastroduodenal motility, appeared not to be involved in the action of these compounds.

In-Vivo Studies

All doses of ginger extract (0.05–0.2 g/kg bw) increased the contraction of the dog's intestine in-situ (Panthong and Tejasen 1975). The authors suggested that ginger extract acted by exerting a serotonin 5-HT-like action either by releasing 5-HT or by itself containing 5-HT. The acetone and 50% ethanolic ginger extract at the doses of 25, 50, 100 and 200 mg/kg p.o. exhibited significant protection, while aqueous

extract at these doses was ineffective against cisplatin emesis in healthy mongrel dogs (Sharma et al. 1997b). The acetone extract was more effective than ethanolic extract. However, both were less effective when compared to 5-HT₃ receptor antagonist—granisetron. Neither of the ginger extract was effective against apomorphine-induced emesis.

Clinical Studies

In a clinical study of 36 undergraduate men and women who reported very high susceptibility to motion sickness, powdered ginger rhizome was found to be superior to dimenhydrinate in reducing motion sickness (Mowrey and Clayson 1982).

In a double-blind crossover study of 8 healthy volunteers, ginger root reduced the induced vertigo significantly better than did placebo (Grøntved and Hentzer 1986). From their study Holtmann et al. (1989) concluded that neither the vestibular nor the oculomotor system, both of which were of decisive importance in the occurrence of motion sickness, was influenced by ginger. A CNS mechanism, characteristic of the conventional anti-motion sickness drugs, could thus be excluded as regards ginger root. They suggested that any reduction of motion sickness symptoms was derived from the influence of the ginger root agents on the gastric system. Grøntved et al. (1988) found that administration of ginger to naval cadets reduced the tendency to vomiting and cold sweating significantly better than placebo in a double-blind, randomised, placebo-controlled trial on the open sea. In a double-blind randomised study of 60 women who had undergone major gynaecological surgery, patients administered with metoclopramide or ginger at the time of premedication before surgery had significantly fewer incidents of nausea compared to placebo (Bone et al. 1990). In a double-blind randomised crossover trial of 30 women, administration of powdered root of ginger in daily doses of 1 g during 4 days was better than placebo in diminishing or eliminating the symptoms of hyperemesis gravidarum (Fischer-Rasmussen et al. 1991).

In another prospective, randomised, double-blind trial, the incidence of postoperative nausea and vomiting involving 120 women was similar in patients given metoclopramide and ginger (27% and 21%) and less than in those who received placebo (41%) (Phillips et al. 1993b). The requirements for postoperative analgesia, recovery time and time until discharge were the same in all groups. The authors concluded that ginger was an effective and promising prophylactic antiemetic that may be especially useful for day-case surgery. In a double-blind, randomised, crossover trial of 16 healthy volunteers, ingestion of ginger did not effect gastric emptying (Phillips et al. 1993a). The antiemetic effect of ginger was not associated with an effect on gastric emptying. Six, of the seven commonly used agents for prophylaxis of seasickness, namely, domperidone, cyclizine, dimenhydrinate with caffeine, ginger root and meclozine with caffeine, were found to be effective and may be recommended for prevention of seasickness in a study of 1489 volunteers; scopolamine TTS appeared to be the least attractive (Schmid et al. 1994)

Meyer et al. (1995) reported that psoralen, a drug given to patients before undergoing photopheresis therapy, caused nausea. They found that nausea was significantly reduced by ingesting three 530 mg capsules of ginger before taking psoralen. In a randomised, double-blind, placebo-controlled study of 70 eligible Thai women, ginger was found to be effective in relieving the severity of nausea and vomiting during pregnancy compared to placebo. No adverse effect of ginger on pregnancy outcome was detected (Vutyavanich et al. 2001). In a clinical study of 80 Thai female patients, administration of ginger was found to be effective in the prevention of nausea after outpatient gynaecological laparoscopy (Pongrojpraw and Chiamchanya 2003). Based on six months clinical experience and impressions, Geiger (2005) found that a 5% solution of the essential oil of *Zingiber officinale* in grape seed carrier oil, when applied nasocutaneously, could be administered safely for the effective prevention and therapeutic management of nausea in general anaesthesia patients at high risk for postoperative nausea and vomiting (PONV), with increased patient satisfaction and less expense to patients and hospital. He reported that the group

treated with the essential oil of ginger experienced approximately less than 20 % nausea in the in the post-anaesthesia recovery unit (PACU). Approximately, 80% of high-risk patients had no complaint of PONV and did not require any further intravenous therapy during recovery from anaesthesia through discharge from PACU. The non-ginger oil-treated patients in this clinical experience had a roughly 50/50 chance of PONV.

In a randomised, placebo-controlled, randomised trial of 120 patients in Thailand, administration of ginger an hour before major gynaecological surgery was found to reduce incidence of nausea and vomiting compared to placebo (Nanthakomon and Pongroj paw 2006). Side effects of ginger were not detected. In a seven-day clinical trial performed on 120 eligible pregnant women with symptoms of mild to moderate nausea and vomiting before 16 weeks gestation, ginger was found to be effective for the relief of mild to moderate nausea and vomiting (Saber i et al. 2014).

In the double-blind, placebo-controlled study, Wood et al. (1988) found that the medication of choice for the prevention of motion sickness was scopolamine 0.6 mg with D-amphetamine 10 mg. Three doses of ginger were all at the placebo level of efficacy. In a study of 28 human volunteers, Stewart et al. (1991) found that powdered ginger (500 mg) partially inhibited tachygastria in motion sickness, and it did not enhance the electrogastrogram (EGG) amplitude in motion sick subjects. They conclude that ginger did not possess anti-motion sickness activity, nor did it significantly alter gastric function during motion sickness. In a double-blind, randomised, controlled trial in 108 ASA 1 or 2 patients undergoing gynaecological laparoscopic surgery under general anaesthesia, ginger BP in dose of 0.5 or 1.0 g was ineffective in reducing the incidence of postoperative nausea and vomiting (Arfeen et al. 1995). In another study of 120 patients, administration of ginger powder, in the dose of 2 g, droperidol 1.25 mg or both, were ineffective in reducing the incidence of postoperative nausea and vomiting after day-case gynaecological laparoscopy (Visalyaputra et al. 1998). In a randomised, placebo-controlled study of 184 healthy women

undergoing gynaecologic laparoscopies, administration of ginger extract did not prevent postoperative nausea and vomiting after laparoscopic surgery (Eberhart et al. 2003).

In a randomised, double-blind, crossover study in 48 gynaecologic cancer patients receiving cisplatin-based chemotherapy, addition of ginger to standard antiemetic regimen provided no advantage in reducing nausea or vomiting in acute phase of cisplatin-induced emesis (Manusirivithaya et al. 2004). In delayed phase, ginger and metoclopramide had no statistically significant difference in efficacy. Restlessness, as a side effect, occurred more often in metoclopramide arm compared to ginger arm. In a randomised, double-blind, placebo-controlled phase II trial in 162 patients with cancer who were receiving chemotherapy and had experienced mild emesis, administration of encapsulated ginger provided no additional benefit for the reduction of the prevalence or severity of acute or delayed chemotherapy-induced nausea and vomiting when given with 5-HT₃ receptor antagonists and/or aprepitant (Zick et al. 2009). In a pilot, randomised, open-label clinical trial of 100 women (mean age = 51.83 ± 9.18 years), addition of ginger (1.5 g/day) to standard antiemetic therapy (granisetron plus dexamethasone) in patients with advanced breast cancer effectively reduced the prevalence of nausea 6–24 h postchemotherapy (Panahi et al. 2012). However, there is no other additional advantage for ginger in reducing prevalence or severity of acute or delayed chemotherapy-induced nausea and vomiting. In double-blind, multicentre trial, involving 744 cancer patients receiving chemotherapy and experiencing nausea, ginger supplementation at a daily dose of 0.5–1.0 g significantly helped in the reduction of the severity of acute chemotherapy-induced nausea in adult cancer patients (Ryan et al. 2012).

In a review of six double-blind randomised controlled trials with a total of 675 participants and a prospective observational cohort study, Borrelli et al. (2005) found ginger to be an effective treatment for nausea and vomiting in pregnancy. However, more observational studies, with a larger sample size, were needed to confirm the encouraging

preliminary data on ginger safety. In the systemic review and meta-analysis conducted by Viljoen et al. (2014), wherein twelve randomised control trials involving 1278 pregnant women were included, ginger was found to have potential benefits in reducing nausea symptoms in pregnancy. Ginger did not significantly affect vomiting episodes nor pose a risk for side effects or adverse events during pregnancy. Based on the results of the review, ginger could be considered a harmless and possibly effective alternative option for women suffering from nausea and vomiting during pregnancy.

Antiplatelet Activity

In-Vitro Studies

Studies showed that (+/-)-[6]- and (+/-)-[8]-gingerols potentiated the contraction induced by prostanoids, $\text{PGF}_{2\alpha}$, PGE_2 , PGI_2 (except PGD_2), and inhibited that produced by PGD_2 , thromboxane A_2 TXA_2 and leukotrienes C_4 and D_4 , suggesting the modulation of eicosanoid-induced responses of mouse and rat mesenteric blood vessels by (+/-)-[6]- or (+/-)-[8]-gingerols (Kimura et al. 1989a). Both ginger constituents *S*-(+)-[6]-gingerol and [6]-shogaol inhibited the contractile responses to noradrenaline in mouse mesenteric vein (Pancho et al. 1989). Crude ginger extract and *S*-(+)-[6]-gingerol potentiated the prostaglandin $\text{PGF}_2 \alpha$ -induced contraction, whereas processed ginger extract and [6]-shogaol inhibited the contraction. Earlier, studies in isolated portal veins of mice suggested that the inhibition of spontaneous contraction induced by (+/-)-[6]-gingerol, but not by (+/-)-[8]-gingerol, was due to the Ca^{2+} spike suppression (Kimura et al. 1988). Kimura et al. (1989b) found that the aliphatic hydroxyl group present in gingerol derivatives was necessary for potentiation of prostaglandin $\text{PGF}_2 \alpha$ - and the keto group for inhibition of noradrenalin-induced contraction in isolated mesenteric veins of mice. (+/-)-[8]-Gingerol potentiated $\text{PGF}_2 \alpha$ -induced contraction to a greater extent than (+/-)-[6]-gingerol and (+/-)-hexahydrocurcumine (HHC), but [6]-shogaol produced inhibition; noradrenaline (NA)-induced contraction was inhibited in the following order: [6]-shogaol > (+/-)-[8]-

gingerol > [6]-gingerdione > (+/-)-[6]-gingerol > *S*-(+)-[6]-gingerdiacetate (GDA) > [6]-dehydrogingerdione (DHG), whereas (+/-)-HHC had no significant inhibitory action. [6]-Gingerdione had different effects on PGF2 α -induced contraction, indicating inhibition just after preparation of the solution, no effect apparent after 2 h and potentiation after 5 h

Gingerols and related analogues (G1–G7) inhibited the arachidonic acid (AA)-induced platelet release reaction in a similar dose range as aspirin, with IC₅₀ values between 45.3 and 82.6 μ M. G1–G7 were also effective inhibitors of AA-induced human platelet aggregation (Koo et al. 2001). Maximum inhibitory (IC_{max}) values of 10.5 and 10.4 μ M for G3 and G4, respectively, were approximately 2-fold greater than aspirin (IC_{max} = 6.0 μ M). The remaining gingerols and related analogues maximally inhibited AA-induced platelet aggregation at approximately 20–25 μ M. The mechanism underlying inhibition of the AA-induced platelet release reaction and aggregation by G1–G7 may be via an effect on cyclooxygenase (COX) activity in platelets because representative gingerols and related analogues (G3–G6) potently inhibited COX activity in rat basophilic leukaemia (RBL-2H3) cells. Ginger constituents, [8]-paradol and [8]-shogaol, as well as two synthetic analogues, 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)decane and 5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)dodecane, showed strong inhibitory effects on COX-2 enzyme activity in intact cell (Tjendraputra et al. 2001). [8]-Gingerol, [8]-shogaol, [8]-paradol and gingerol analogues (1 and 5) exhibited antiplatelet activities with IC₅₀ values ranging from 3 to 7 μ M, while under similar conditions, the IC₅₀ value for aspirin was 20 μ M (Nurtjahja-Tjendraputra et al. 2003). The COX-1 inhibitory activity of [8]-paradol (IC₅₀ = 4 μ M) was more potent than the gingerol analogues (1 and 5) (IC₅₀ approximately 20 μ M). [8]-Paradol, a natural constituent of ginger, was found to be the most potent COX-1 inhibitor and anti platelet aggregation agent. Nie et al. (2008) used chicken thrombocyte extract to screen for antiplatelet aggregation compounds from ginger. There were four typical compounds that bound to the

thrombocytes: 6-gingerol, 8-gingerol, 6-shogaol and 10-gingerol, and all exhibited antiplatelet aggregation activities. Eight-gingerol displayed the best antiplatelet aggregation effect.

All the tested ginger compounds, [6]-dehydrogingerdione, [11]-isodehydrogingerdione, [6]-gingerol, [8]-gingerol, [10]-gingerol, [6]-shogaol, [8]-shogaol, hexahydrocurcumin, [6]-gingerdiol and 2,5-dihydroxybisabol-3,10-diene, displayed significant inhibitory effects on the aggregation of washed rabbit platelets stimulated by the agonists, including arachidonic acid (AA), collagen (Col), platelet-activating factor (PAF) and thrombin (Thr) (Liao et al. 2012). At 100 $\mu\text{g/mL}$ concentration, all the tested compounds caused complete inhibition of aggregation induced by AA (100 μM) except 2,5-dihydroxybisabol-3,10-diene which still displayed 67.9% inhibition at 100 $\mu\text{g/mL}$. Even at lower concentration, compounds [6]-dehydrogingerdione, [11]-isodehydrogingerdione, [6]-gingerol, [8]-gingerol, [6]-shogaol, [8]-shogaol, hexahydrocurcumin and [6]-gingerdiol still exhibited excellent inhibitory activity (100%) against AA-induced platelet aggregation at 1.0, 2.0, 5.0 and 20.0 $\mu\text{g/mL}$, respectively. Compound [6]-gingerol, displayed the most significant inhibition of platelet aggregation induced by AA with inhibitory percentages of 83.7, 66.3 and 16.7% at 0.5, 0.2 and 0.1 $\mu\text{g/mL}$, respectively. Similarly, compounds [6]-dehydrogingerdione, [11]-isodehydrogingerdione, [6]-gingerol, [8]-gingerol, [10]-gingerol, [6]-shogaol and [8]-shogaol at 100 $\mu\text{g/mL}$ showed the complete inhibition of aggregation induced by Col (10 $\mu\text{g/mL}$). However, the inhibitory activities of the tested compounds were not as effective as those induced by AA. At 5.0 $\mu\text{g/mL}$ only compound [6]-shogaol displayed excellent inhibition (100%) against Col-induced platelet aggregation. Compounds [6]-gingerol and [6]-shogaol exhibited the most significant inhibition of platelet aggregation induced by Col with inhibitory percentages of 15.6 and 28.1 % at 1.0 $\mu\text{g/mL}$, respectively. In contrast, the tested compounds did not show significant inhibition of aggregation induced by PAF (2 nM) and Thr (0.1 $\mu\text{g/mL}$). Only compound [6]-shogaol at 100 $\mu\text{g/mL}$ displayed complete inhibition of aggregation induced

by PAF. At 20.0 $\mu\text{g/mL}$ compound [6]-shogaol only inhibited the platelet aggregation induced by PAF with the percentage of 15.7%. All the tested compounds at 100 $\mu\text{g/mL}$ exhibited the inhibitory percentages lower than 29.5% against the platelet aggregation induced by Thr. Among the isolated ginger compounds, [6]-gingerol and [6]-shogaol exhibited potent antiplatelet aggregation bioactivity.

All 8 groups of synthesised derivatives based on the skeletons of gingerol and shogaol, the pungent principles from *Zingiber officinale* rhizomes, namely, [5]-, [6]-, [7]- and [9]-isodehydrogingerdiones; [5]-, [6]-, [7]-, [8]-, [9]- and [10]-dehydroshogaols; [5]-, [6]-, [7]-, [8]-, [9]- and [10]-shogaols; [5]-, [6]-, [7]-, [8]-, [9]- and [10]-paradols; [5]-, [6]-, [7]-, [8]-, [9]- and [10]-dehydroparadols; [5]-, [6]-, [7]-, [8]-, [9]- and [10]-epoxy-dehydroparadols; and [5]-, [6]-, [7]-, [8]-, [9]- and [10]-gingerols, displayed significant inhibitory effects on the aggregation of washed rabbit platelets stimulated by arachidonic acid (AA) (Shih et al. 2014). At a 10 $\mu\text{g/mL}$ concentration, most of the tested compounds with the exception of [5]-dehydrogingerol, [8]-dehydrogingerol and [9]-epoxy-dehydroparadol caused the inhibition percentages of aggregation induced by AA (100 μM) to be higher than 90%. In contrast, the activities of these synthetic derivatives against platelet-activating factor (PAF) and thrombin (Thr)-induced aggregation were insignificant. Among these derivatives, [5]-, [6]-, [7]-, [8]-, [9]- and [10]-paradols series were the most active compounds, and [6]-paradol displayed the most significant inhibition, with an IC_{50} value of 70 ng/mL . The [5]-, [6]-, [7]-, [8]-, [9]- and [10]-dehydroparadols were generally less potent than the corresponding [n]-paradols derivatives. The [5]-, [6]-, [7]-, [8]-, [9]- and [10]-shogaols series also displayed weaker inhibition of aggregation induced by AA (100 μM) compared to their related [n]-paradol derivatives; however, they were more active than the [5]-, [6]-, [7]-, [8]-, [9]- and [10]-dehydroparadols. The [5]-, [6]-, [7]-, [8]-, [9]- and [10]-dehydroshogaols with one more α,β -unsaturation $\text{C}=\text{C}$ bond exhibited further decreased inhibitory activity. However, their inhibition aggregation potency induced by collagen (Col) was generally more significant than

their [*n*]-paradol counterparts. Among the [*n*]-shogaols and [*n*]-dehydroshogaols, [10]-shogaol exhibited the most significant inhibition of aggregation induced by Col (10 μ M), with an IC₅₀ value lower than 5 μ g/mL. Among the compounds synthesised, [6]-paradol displayed the most significant inhibition of platelet aggregation induced by AA. The results of their study substantiated the antiplatelet aggregation activity of these synthetic derivatives related to shogaol and gingerol.

Animal Studies

Studies by Wu et al. (1993) found that the decoction, ether extract and liquid suspension of roasted ginger and charcoal of ginger all markedly reduced blood coagulation time in mice, while the decoction, ether extract of fresh ginger and dry ginger could not. The decoction of ginger charcoal exerted stronger effect than roasted ginger. The effect of decoction of ginger charcoal on blood coagulation time was dose-dependent.

Clinical Studies

Addition of 5 g of dry ginger in two divided doses with fatty meal(100g butter) (in 10 healthy individuals) significantly inhibited the platelet aggregation induced by ADP (adenosine diphosphate) and epinephrine, while in the placebo control group (10 healthy individuals), there was no significant alteration in platelet aggregation (Verma et al. 1993). Serum lipids, however, remained unchanged in both the group. In a randomised, double-blind study of eight healthy male volunteers, no differences were found between dried ginger (2g) and placebo capsules in bleeding time, platelet count, thromboelastography and whole blood platelet aggregometry (Lumb 1994). It was concluded that the effect of ginger on thromboxane synthetase activity was dose dependent, or only occurs with fresh ginger, and that up to 2 g of dried ginger was unlikely to cause platelet dysfunction when used therapeutically. In patients with coronary artery disease (CAD), powdered ginger administered in a dose of 4 g daily

for 3 months did not affect ADP- and epinephrine-induced platelet aggregation (Bordia et al. 1997). Also, no change in the fibrinolytic activity and fibrinogen level was observed. However, a single dose of 10 g powdered ginger administered to CAD patients produced a significant reduction in platelet aggregation induced by the two agonists. Ginger did not affect the blood lipids and blood sugar.

In a study in hypertensive patients and normal volunteers, ginger and nifedipine were found to possess synergistic effect on antiplatelet aggregation induced by collagen, ADP and epinephrine (Young et al. 2006). A combination of 1 g ginger with 10 mg nifedipine per day could be valuable for cardiovascular and cerebrovascular complication due to platelet aggregation.

Hepatoprotective Activity

Ethanol ginger extract showed protective effect against paracetamol-induced hepatotoxicity in rats at both oral dose levels of 200 mg/kg and 300 mg/kg, and the protective effect was better at the higher dose (Abdullah et al. 2004). The results showed that at 200 mg/kg, the extract reduced the plasma levels of superoxide dismutase (SOD) significantly, while at a higher dose of 300 mg/kg, it reduced plasma SOD, hepatic SOD and serum aspartate transaminase and increased the levels of plasma proteins significantly. Pretreatment of rats with ginger ethanol extract attenuated in a dose-dependent manner, carbon tetrachloride (CCl₄) and acetaminophen-induced increases in the activities of aspartate and alanine aminotransferases (AST and ALT), alkaline phosphatase (ALP), succinate and lactate dehydrogenases (SDH and LDH) in the blood serum (Yemitan and Izegebu 2006). The protective effect of the extract on CCl₄- and acetaminophen-induced hepatic damage was confirmed by histopathological examination of the liver. Administration of ginger extracts (petroleum ether, chloroform and ethanol) protected rats against liver fibrosis induced by CCl₄ (Motawi et al. 2011). Treatments with the ginger extracts significantly increased glutathione (GSH), SOD, SDH, LDH, glucose-6-phosphatase

(G-6-Pase), acid phosphatase (AP) and 5'-nucleotidase (5' NT). However, malondialdehyde (MDA), AST and ALT as well as cholestatic markers, ALP, γ -glutamyl transferase (GGT) and total bilirubin were significantly decreased. Extracts of ginger, particularly the ethanol, resulted in an attractive candidate for the treatment of liver fibrosis induced by CCl₄.

Pretreatment of aqueous ginger extract significantly protected against acetaminophen hepatotoxicity as evident from the decreased activities of serum transaminase and ALP and the enhancement in hepatic antioxidant status in rats (Ajith et al. 2007a). Oral administration of aqueous ginger extract (3 mg/animal/day) along with paraben for 30 days caused significant amelioration in paraben-induced lipid peroxidation and increased significantly the activities of enzymatic (superoxide dismutase, glutathione peroxidase, catalase) and contents of non-enzymatic (glutathione and ascorbic acid) antioxidants in the liver of mice, as compared with those given paraben alone (Asnani and Verma 2009). Earlier they reported an addition of aqueous extract of ginger significantly and dose-dependently reduced paraben (100 μ g/mL)-induced lipid peroxidation in liver and kidney homogenates in-vitro (Asnani and Verma 2007).

Ethanol significantly decreased the superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and glutathione content, while increasing malondialdehyde (MDA) levels were estimated in the rat hepatic tissue; treatment with 1 % dietary ginger for 4 weeks reversed the effect, suggesting that ginger may have protective role against the ethanol-induced hepatotoxicity (Mallikarjuna et al. 2008). Studies showed that the water extracts of thyme and ginger had detoxifying and antioxidant effects on injuries of alcohol abuse on the liver and brain of mice (Shati and Elsaid 2009). Both extracts ameliorated the decrease in total antioxidant capacity and glutathione peroxidase activity caused by alcohol abuse and attenuated the alcohol-elevated liver function enzymes such as L- γ -glutamyl transpeptidase and butyrylcholinesterase activities. Therefore, it is recommended to use them to avoid alcohol toxicity. Concurrent

administration of ginger extract and atorvastatin ameliorated the hepatotoxic effect of atorvastatin by lowering serum cholesterol and decreasing serum aminotransferases, hepatic MDA and nitric oxide in rats (Heeba and Abd-Elghany 2010). Histopathological study revealed that ginger reduced liver lesions induced by atorvastatin. It was concluded that combination regimens containing ginger extract and low dose of statins could be advantageous in treating hypercholesterolaemic patients susceptible to liver function abnormalities. Dietary administration of ground ginger to rats exposed to heavy metals in the drinking water for six weeks affected the bioavailability, elimination and uptake of these metals in a time-dependent way with highest beneficial reducing effect to Cd followed by Hg and least protection to Pb in the liver (Nwokocha et al. 2012).

Administration of ginger rhizome ethanol extract significantly reduced the impact of thioacetamide-induced hepatotoxicity in rats (Abdulaziz Bardi et al. 2013). Fibrosis of the liver tissues was significantly reduced. The ginger extract showed antiproliferative activity (IC_{50} 38–60 μ g/mL) when tested on HepG2 cells. *Z. officinale* and *C. longa* oils (200 mg/kg) exhibited hepatoprotective activity in acute ethanol-induced fatty liver acute in male Wistar rats, and *Z. officinale* oil was identified to have better effects than *C. longa* oil (Nwozo et al. 2014). The oils decreased activities of serum enzymes, serum triglyceride (TG) level, total cholesterol (TC) and hepatic MDA, while they significantly restored the level of reduced glutathione (GSH), glutathione *S*-transferase (GST) and SOD activities. Histological examination of rat tissues supported the biochemical results.

Gastroprotective/Antiulcer Activity

Orally administered acetone ginger extract at 1000 mg/kg and zingiberene, the main terpenoid from the extract, at 100 mg/kg significantly inhibited HCl-/ethanol-induced gastric lesions in rats by 97.5 and 53.6%, respectively (Yamahara et al. 1988). 6-Gingerol, the pungent principle, at 100 mg/kg significantly inhibited gastric lesions by 54.5%. Ginger extract in the dose

of 500 mg/kg orally exerted highly significant cytoprotection against 80% ethanol, 0.6M HCl, 0.2M NaOH and 25% NaCl induced gastric lesions in rats (Al-Yahya et al. 1989). The extract also prevented the occurrence of gastric ulcers induced by non-steroidal anti-inflammatory drugs (NSAIDs) and hypothermic restraint stress. Oral administration of 4.5 g/kg roasted ginger decoction to rats exhibited ulcer inhibiting tendency on three gastric ulcer models except the indomethacin-induced model, while the dry ginger had no such effects (Wu et al. 1990a). The LD₅₀ value of roasted ginger decoction administered orally was 170.6 g/kg, but it was over 250 g/kg with dry ginger, suggesting that the water-soluble constituents of the dry ginger had changed in the roasting process.

The following low polar constituents, β -sesquiphellandrene, β -bisabolene, *ar*-curcumene and [6]-shogaol isolated from dried ginger rhizome, exhibited antiulcer effect in HCl-/ethanol-induced gastric lesions in rats (Yamahara et al. 1992). Gingesulphonic acid, isolated from the rhizome, exhibited antiulcer effect against HCl-/ethanol-induced gastric lesions in rats (Yoshikawa et al. 1992). 6-Gingesulphonic acid showed weaker pungency and more potent antiulcer activity than 6-gingerol and 6-shogaol. Studies demonstrated that ginger root extracts containing the gingerols inhibited the growth of *Helicobacter pylori* CagA+ strains in-vitro, and this activity may contribute to its chemopreventive effects in dyspepsia and peptic ulcer disease and the development of gastric and colon cancer (Mahady et al. 2003). The methanol extract of ginger rhizome inhibited the growth of all 19 strains in-vitro with a minimum inhibitory concentration range of 6.25–50 μ g/ml. One fraction of the crude extract, containing the gingerols, was active and inhibited the growth of all HP strains with an MIC range of 0.78–12.5 μ g/ml and with significant activity against the CagA+ strains.

Higher oral doses of ginger rhizome hydroalcoholic extracts (350 and 700 mg/kg) were effective in reducing ulcer severity, area and index as well as mucosal inflammation severity, extent and total colitis index in acetic acid-induced

acute colitis in rats compared to controls (Minaiyan et al. 2008). Rectally administered ginger extract, only at high dose (700 mg/kg), was effective in reducing ulcer index and total colitis index. Pretreatment of rats with ginger extract before induction of ulcerative colitis by intra-rectal acetic acid administration ameliorated colonic mucosal injury and adverse biochemical changes, which were comparable to that of the standard sulfasalazine, especially at the highest dose level (El-Abhar et al. 2008). Results showed a valuable effect of ginger extract against acetic acid-induced ulcerative colitis possibly by its antioxidant and anti-inflammatory properties. Ginger extract (GE) loaded floating beads (FBs) (200 mg/kg) were significantly better than free GE and better than or equivalent to cimetidine (10 mg/kg) in antiulcer activity in cold-restraint stress-induced gastric ulcers in albino rats (Singh and Kaur 2011). They established that GE FBs afforded sustained curative effect. Administration of turmeric essential oil (TEO) and ginger essential oil (GEO) inhibited ethanol-induced ulcer by 84.7% and 85.1%, respectively, as seen from the ulcer index, and ameliorated ethanol-induced lesions such as necrosis, erosion and haemorrhage of the stomach of rats (Liju et al. 2015). Reduced antioxidant enzymes such as GPx, SOD, catalase and GSH produced by ethanol administration were significantly increased by simultaneous administration of TEO and GEO. Oral administration of ginger volatile oil to rats with acetic acid-induced ulcerative colitis effectively reduced symptoms of experimental colitis in a dose-dependent manner (Rashidian et al. 2014). Higher oral doses of volatile oil (200 and 400 mg/kg) reduced ulcer severity, ulcer area and ulcer index. In contrast, evaluation of microscopic scores showed that the dose of 400 mg/kg of volatile oil was effective to reduce inflammation severity and inflammation extent compared to the control group. Aqueous ginger extract exhibited gastroprotective activity against indomethacin-induced gastric damage in rats (Zaman et al. 2014). The percent inhibition of gastric ulcers was 40.91%, 57, 58% and 65.91% by ginger 200mg/kg, ginger 400 mg/kg and omeprazole, respectively.

Renoprotective Activity

Z. officinale ethanol extract significantly and dose-dependently protected the nephrotoxicity induced by cisplatin in rats (Ajith et al. 2007b). Cisplatin elevated serum urea, creatinine and malondialdehyde (MDA) were reduced by ginger treatment. Cisplatin reduced renal antioxidant enzyme activities such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and the level of reduced glutathione (GSH) were normalised by ginger. The protective effect of *Z. officinale* (250 mg/kg body wt) was found to be better than that of vitamin E (250 mg/kg body wt). The results also demonstrated that combination of *Z. officinale* (250 mg/kg) and vitamin E (250 mg/kg) showed a better protection compared to their 250 mg/kg alone-treated groups. Aqueous ethanol ginger extract (200 and 400 mg/kg, p.o.) protected against doxorubicin (DXN)-induced (15 mg/kg, i.p.) acute renal damage in rats (Ajith et al. 2008). DXN elevated serum urea, creatinine and malondialdehyde (MDA) levels were reduced by ginger. Renal antioxidant enzyme activities such as SOD and CAT GPx and levels of GSH and GST activity were restored by ginger. Studies by Ademiluyi et al. (2012) found that pretreatment with ginger and turmeric rhizome (2% and 4%) prior to gentamycin administration significantly protected the kidney and attenuated oxidative stress by modulating renal damage and antioxidant indices in rats.

Ginger extract was found to prevent degeneration of the renal cells and reduce the severity of tubular damage caused by gentamicin-induced toxicity in Wistar rats (Nasri et al. 2013). Oral administration of gingerols from ginger protected Wistar rats against gentamicin-induced nephrotoxicity (Rodrigues et al. 2014). Gingerol-treated rats showed amelioration in renal function parameters and reduced lipid peroxidation and nitrosative stress, in addition to an increment in the levels of glutathione (GSH) and superoxide dismutase (SOD) activity. Gingerols also promoted significant reductions in mRNA transcription for TNF- α , IL-2 and IFN- γ . These effects were dose dependent. Administration of ginger extract ameliorated lead-induced renal toxicity in male rats by enhancing the levels of glutathione, glutathione peroxidase, glutathione S-transferase and catalase (Reddy et al. 2014). In addition, histological studies showed lesser renal changes in

lead plus ginger extract-treated rat groups than that of lead alone-treated rat groups.

Antidiabetic Activity

Ethanollic ginger extract produced blood glucose lowering in rabbits (Mascolo et al. 1989). Ginger exhibited amylase and glucosidase enzyme inhibitory activity in-vitro (Abeysekara et al. 2007). Glucosidase and amylase activities in cooked rice were inhibited by addition of ginger which causes significant reduction in glucose percentages (36.86–26.875 and 49.045–35.35), respectively. The results were comparable to that of acarbose on glucosidase activity. The results indicated ginger to be a potential plant-based amylase and glucosidase inhibitor in carbohydrate digestion. Three gingerol derivatives showed inhibitory activities against human and mouse 11 β -HSD1 (11 β -hydroxysteroid dehydrogenases) with IC₅₀ values between 1.09 and 1.30 μ M (Feng et al. 2011). Inhibiting 11 β -HSD1 activity had been reported to afford a promising therapeutic strategy in the treatment of type II diabetes and related diseases (Tu et al. 2008). In-vivo studies showed that dietary ginger was effective against the development of diabetic cataract in streptozotocin-induced diabetic rats mainly through its antiglycating potential and to a lesser extent by inhibition of the polyol pathway (Saraswat et al. 2010). Ethyl acetate extract of ginger rhizome exhibited antidiabetic activity with its antioxidant, antiglycation and potential to express or transport Glut4 receptors from internal vesicles (Rani et al. 2012). It exerted DPPH radical scavenging activity with IC₅₀ value of 4.59 μ g/ml and antiglycation potential with IC 290.84 μ g/ml. It enhanced glucose uptake in L6 mouse myoblast and myotubes. Li et al. (2013b) found that (*S*)-[6]-gingerol time-dependently enhanced glucose uptake in L6 myotubes by activating threonine172 phosphorylated AMPK α , suggesting its potential for development as an antidiabetic agent. In another study, gingerols of ginger rhizome extract, in particular (*S*)-[8]-gingerol, strongly enhanced glucose uptake (Li et al. 2012d). The activity of (*S*)-[8]-gingerol was found to be associated primarily with an increase in surface distribution

of GLUT4 protein on the L6 myotube plasma membrane. The enhancement of glucose uptake in L6 rat skeletal muscle cells by the gingerol pungent principles of the ginger extract supports the potential of ginger and its pungent components for the prevention and management of hyperglycaemia and type II diabetes. Studies found that the polyphenol extracts of alligator pepper, ginger and nutmeg displayed good antioxidant as well as antiglycation potential and were safe for consumption (Kazeem et al. 2012). Results obtained showed that polyphenol extract of ginger had the highest antioxidant potential with IC_{50} 0.075 and 0.070 mg/mL for DPPH and superoxide anion radical scavenging assay, while alligator pepper displayed the highest antiglycation activity with IC_{50} 0.125 mg/mL. However, nutmeg extract exhibited the weakest cytotoxic and phytotoxic potential with LD_{50} 4359.70 and 1490 μ g/mL, respectively.

In normoglycaemic rats, serotonin (5-hydroxytryptamine) (1 mg/kg, i.p.) produced hyperglycaemia and hypoinsulinaemia, which was significantly prevented by ginger juice (Akhani et al. 2004). Ginger treatment produced a significant increase in insulin levels and a decrease in fasting glucose levels in streptozotocin (STZ)-induced type I diabetic rats. In an oral glucose tolerance test, ginger treatment significantly decreased the area under the curve of glucose and increased the area under the curve of insulin in STZ-diabetic rats. Ginger treatment also caused a decrease in serum cholesterol, serum triglyceride and blood pressure in diabetic rats. Ginger rhizome ethanol extract (50–800 mg/kg p.o.) caused dose-related, significant hypoglycaemia in normal (normoglycaemic) and diabetic rats (Ojewole 2006).

Intraperitoneal administration of aqueous ginger extract (500 mg/kg) for 7 weeks to streptozotocin (STZ)-induced diabetic rats significantly lowered serum glucose, cholesterol and triacylglycerol levels compared with the control diabetic rats (Al-Amin et al. 2006). The ginger treatment also resulted in a significant reduction in urine protein levels, water intake and urine output. In addition, the ginger-treated diabetic rats sustained their initial weights during the treatment period. The results indicated that raw ginger possessed hypoglycaemic,

hypocholesterolaemic and hypolipidaemic potential. Additionally, raw ginger was effective in reversing the diabetic proteinuria observed in the diabetic rats. Oral administration of both methanol and aqueous ginger extracts increased fertility index, sexual organs weight, serum testosterone level and sperm motility and count in alloxan-diabetic rats (Shalaby and Hamowieh 2010). Treatment with ginger extracts caused alleviation of the testicular lesions (mild to moderate degenerative changes of spermatogenic cells, diffuse oedema and incomplete arrest of spermatogenesis) that appeared in non-treated diabetic rats.

In a randomised, double-blind, placebo-controlled study of 64 diabetic type II patients, ginger supplementation significantly reduced the levels of pro-inflammatory cytokines (IL-6 and TNF- α) and the acute phase protein hs-CRP in DM2 patients (Mahluji et al. 2013). The results indicated that ginger supplementation in oral administration reduced inflammation in type II diabetic patients.

Antihyperlipidemic Activity

The marked rise in serum and tissue cholesterol, serum triglycerides, serum lipoproteins and phospholipids that followed 10 weeks of cholesterol feeding was significantly reduced by the ethanolic ginger extract, and results were compared with gemfibrozil, a standard orally effective hypolipidaemic drug (Bhandari et al. 1998). The severity of aortic atherosclerosis as judged by gross grading was more marked in pathogenic, i.e. the hypercholesterolaemic, group, while animals receiving ginger extract along with cholesterol showed a lower degree of atherosclerosis. The results confirmed ginger to be an antihyperlipidaemic agent. Oral administration of dietary ethanol ginger extract to streptozotocin (STZ)-induced diabetic rats for 20 days lowered serum total cholesterol and triglycerides and increased the HDL cholesterol levels when compared with pathogenic diabetic rats (Bhandari et al. 2005). Ginger extract lowered the STZ-induced elevated liver and pancreatic thiobarbituric acid-reactive substances (TBARS) values. The results showed that ginger extract protected tissues from lipid peroxidation and

significantly lowered lipids in diabetic dyslipidaemic rats. Treatment with 250 mg/kg of methanol and ethyl acetate ginger extracts for 8 weeks produced significant reduction in body weight and glucose, insulin and lipid levels as compared to gold thioglucose-induced obese control mice (Goyal and Kadnur 2006). The reduction in elevated glucose along with elevated insulin levels indicated that the treatment with *Z. officinale* improved insulin sensitivity.

Administration of ginger rhizome ethanol extract to high-fat diet-fed rats significantly reduced the elevated rise in body weights, glucose, insulin, total cholesterol, LDL cholesterol, triglycerides, free fatty acids and phospholipids in serum of the rats (Nammi et al. 2009). However, no significant change in serum HDL cholesterol was observed either with high-fat diet or ginger-treated control group compared to both control groups. They found that in parallel, ginger extract upregulated both LDL receptor mRNA and protein level and downregulated HMG-CoA reductase protein expression in the liver of high-fat diet rats (Nammi et al. 2010). The metabolic control of body lipid homeostasis was in part due to enhanced cholesterol biosynthesis and reduced expression of LDL receptor sites following long-term consumption of high-fat diets. Administration of high dose of ginger extract to albino mice caused a significant reduction in the levels of cholesterol, triglycerides and phospholipids and both levels of VLDL and LDL cholesterol and triglycerides in serum and tissue of aorta (Al-Tahtawy et al. 2011).

Analgesic Activity

Both [6]-gingerol and [6]-shogaol alleviated writhing symptom at 1.75–3.5 mg/kg in rats. In 140 mg/kg oral administration, the effect of [6]-shogaol was more intense (Suekawa et al. 1984). Ginger rhizome extract (50 and 100 mg/kg b.w.) significantly reduced the number of writhing induced by acetic acid in Swiss mice (Raji et al. 2002). Ginger oleoresin could significantly reduce mouse locomotor activity, prolong pentobarbital-induced sleep time of mice, delay latency of convulsion induced by strychnine, reduce the number of writhing and stretching induced by the acetic acid

and delay latency of reaction to the thermal stimulus (Jiang and Zhou 2010). The authors concluded that ginger oleoresin had significant inhibitory effect on mouse central nervous system (CNS).

Intraperitoneal administration of [6]-gingerol (25 mg/kg–50 mg/kg) produced an inhibition of acetic acid-induced writhing response and formalin-induced licking time in the late phase (Young et al. 2005). Ginger rhizome ethanol extract (50–800 mg/kg i.p.) produced dose-dependent, significant analgesic effects against ‘hot plate’ and acetic acid-induced nociceptive pain in mice (Ojewole 2006). The double-blind, placebo-controlled, randomised experiments with 34 and 40 volunteers demonstrated that daily consumption of raw and heat-treated ginger resulted in moderate to large reductions in muscle pain following exercise-induced muscle injury (Black et al. 2010). The findings agreed with those showing hypoalgesic effects of ginger in osteoarthritis patients and further demonstrated ginger’s effectiveness as a pain reliever.

Ginger (50 and 100 mg/kg) completely prevented the development of morphine analgesic tolerance and physical dependence in rats (Darvishzadeh-Mahani et al. 2012). In addition, concomitant treatment of morphine with 100 and 150 mg/kg ginger attenuated almost all of the naloxone-induced withdrawal signs which included weight loss, abdominal contraction, diarrhoea, petosis, teeth chattering and jumping. In addition, morphine-induced L-type calcium channel over-expression in spinal cord was reversed by 100 mg/kg ginger.

Antidepressant Activity

Administration of dehydrozingerone (DHZ), a phenolic compound isolated from ginger rhizomes, 30 min prior to testing, reduced the immobility time in the tail suspension test (1–40 mg/kg) and the forced swim test (10–40 mg/kg), with no change in locomotor activity in the open field test (Martinez et al. 2014). The study found that DHZ had a potent antidepressant effect, which appeared to involve the serotonergic and noradrenergic systems. DHZ had antioxidant

activity on in-vitro lipid peroxidation induced by sodium nitroprusside in all brain regions tested.

Anxiolytic Activity

Intraperitoneal administration of mice with ginger extracts at 200 and 400 mg/kg body weight elicited significant increase in the time spent in the centre of the field in the open field test, indicating the extracts possessed promising anxiolytic activity (Harsha and Anilakumar 2012).

Studies showed that Zingicomb[®] (ZC), a combination preparation of *Zingiber officinale* and *Ginkgo biloba*, exerted anxiolytic-like effects in the elevated plus maze (EPM), possibly related to 5-HT antagonistic properties of its components (Hasenöhrl et al. 1996). Further they found that the anxiolytic-like effects of ZC were specific in that only the mixture ratio of ginger and ginkgo adjusted for the phytopharmakon was active in the EPM (Hasenöhrl et al. 1998). Also, ZC did not interfere negatively with the performance on an inhibitory avoidance and a water maze task, as opposed to diazepam. The results revealed a dissociation between anxiolytic and memory-disrupting effects for chemically defined 5-HT antagonists, especially for those acting at 5-HT₃ receptors. Pre-trial administration of Zingicomb (ZC) to rats enhanced conditioned inhibitory avoidance (Topic et al. 2002a). When tested 24 h after training, rats which had received 10 mg/kg ZC exhibited significantly longer step-through latencies than vehicle-treated animals. Also, they found that administration of ZC enhanced Morris water maze performance by facilitating spatial learnings and reduced oxidative stress in brain tissue of aged rats (Topic et al. 2002b).

Effect on Cortical Brain Activity

In the electro-encephalogram of cortex, the low-amplitude fast wave pattern was observed for 5 min after intravenous administration of (6)-shogaol in rats and then changed to the drowsy pattern, which was restored after 60 min (Suekawa et al. 1984).

Neuroprotective Activity

From ginger rhizome, four isolated shogaols protected IMR32 human neuroblastoma and normal human umbilical vein endothelial cells from β -amyloid (25–35) insult at $EC_{50} = 4.5$ – $81 \mu\text{M}$ (Kim et al. 2002) and 10 synthesised shogaols protected cells from β -amyloid insult using PC12 rat pheochromocytoma and IMR-32 human neuroblastoma cells (Kim and Kim 2004). The efficacy of cell protection from β -amyloid (25–35) insult by these shogaols was shown to improve as the length of the side chain increases.

In isolated rat stomach fundus, ginger extract showed a spasmogenic effect (0.03–5.00 m/mL); it relaxed the tissue at concentrations $> \text{or} = 5 \text{ mg/mL}$ (Ghayur et al. 2008). The stimulant effect was resistant to blockade by hexamethonium and methysergide, but sensitive to atropine, indicating activity via muscarinic receptors. In atropinised (0.1 μM) preparations, ginger extract (0.3–3.0 mg/mL) relaxed high K^+ (80 mM)-induced contractions, indicating Ca^{2+} antagonism in addition to the muscarinic effect. Ginger extract (0.1–0.3 mg/mL), similar to verapamil (0.03–0.10 μM), shifted the contractions induced by externally administered Ca^{2+} to the right, thus suggesting an inhibitory interaction between ginger extract and voltage-operated Ca^{2+} channels. Ginger extract (0.1–3.0 $\mu\text{g/mL}$) also potentiated acetylcholine peak responses in stomach fundus, similar to physostigmine, a cholinesterase inhibitor. Ginger extract, in an in-vitro assay, showed specific inhibition of butyrylcholinesterase (BuChE) rather than acetylcholinesterase enzyme. Different pure compounds of ginger also showed spasmolytic activity in stomach fundus, with 6-gingerol being the most potent. 6-Gingerol also showed a specific anti-BuChE effect. This study showed a unique combination of muscarinic, possible Ca^{2+} antagonist and BuChE inhibitory activities of dried ginger, indicating its benefit in dementia, including Alzheimer's disease. Incubation of the brain tissue homogenate in the presence of Fe caused a significant increase in the malondialdehyde (MDA) contents of rat brain; however, the aqueous extract from both red and white varieties of ginger caused a significant decrease in the

MDA contents of the brain in a dose-dependent manner (Obboh et al. 2012). However, the aqueous extract of red ginger had a significantly higher inhibitory effect on both Fe^{2+} -induced lipid peroxidation in the rat brain homogenates than that of white ginger. This higher inhibitory effect of red ginger could be attributed to its significantly higher phytochemical content, Fe^{2+} chelating ability, OH scavenging ability and reducing power. However, part of the mechanisms through which the extractable phytochemicals in ginger (red and white) protected the brain may be through their antioxidant activity and Fe^{2+} chelating and OH scavenging ability.

Oral administration of ginger extract exhibited neuroprotective effect against oxidative stress-related brain damage, on brain damage and memory impairment induced by focal cerebral ischaemia in male adult Wistar rats (Wattanathorn et al. 2011). Administration of ginger extract mitigated 3,4-methylenedioxymethamphetamine (MDMA)-induced spatial memory impairment and apoptosis in the hippocampus of male rats (Mehdizadeh et al. 2012). In the Morris water maze, escape latency and travelled distances decreased significantly in the MDMA plus ginger group relative to the MDMA group. Also, downregulation of Bcl-2 and upregulation of Bax were observed in the MDMA plus ginger group in comparison to the MDMA group. Administration of ginger extract significantly improved the ability of mice to recognise novel objects, indicating improvements in learning and memory (Lim et al. 2014). The results suggested that ginger extract had a synaptogenic effect via nerve growth factor (NGF)-induced extracellular-signal-regulated kinase (ERK)/cyclic AMP response element-binding protein (CREB) activation in the mouse hippocampus, resulting in memory enhancement.

An enone-dione analogue of 6-shogaol (compound 2) was isolated and identified to be most effective at protecting PC12 cells from H_2O_2 -induced damage (Peng et al. 2012).

Azam et al. (2014) employed computational molecular docking studies to investigate the binding interactions between active ginger components and various anti-Alzheimer drug

targets. They found ginger components to have potential to be developed into promising leads for the design and development of novel multi-targeted anti-Alzheimer's drugs.

Studies demonstrated that *Z. officinale* possessed antioxidant, radioprotective and neuromodulatory properties that could be effectively utilised for behavioural radioprotection and for efficiently mitigating radiation-induced conditioned taste aversion in both male and female rats (Haksar et al. 2006). The methanolic extract of dry ginger was found to have antioxidant activity, cholinesterase inhibition, anti-amyloidogenic potential and neuroprotective properties (Mathew and Subramanian 2014). Ginger extract contained 18 mg/g gallic acid equivalents of total phenolic content and 4.18 mg quercetin equivalents/g of dry material and expressed high antioxidant activity with an IC₅₀ value of 70 microg/mL in DPPH assay and 845.4 µM Fe(II) equivalents/g dry weight in FRAP assay, respectively. In Ellman's assay for the cholinesterase inhibitory activity, GE had an IC₅₀ value of 41 µg/mL and 52 µg/mL for inhibition of acetyl- and butyrylcholinesterase, respectively. Also, ginger extract increased the cell survival against amyloid β (Aβ)-induced toxicity in primary adult rat hippocampal cell culture. Aggregation experiments with the thioflavin T binding studies showed that ginger extract effectively prevented the formation of Aβ oligomers and dissociated the preformed oligomers. The findings suggested that methanolic ginger extract influenced multiple therapeutic molecular targets of Alzheimer's disease (AD) and could be considered as an effective non-toxic nutraceutical supplement for AD.

Sixty middle-aged, healthy women participants were randomly assigned to receive a placebo or standardised ginger extract at doses of 400 and 800 mg once daily for 2 months (Saenghong et al. 2012). It was found that the ginger-treated groups had significantly decreased P300 latencies, increased N100 and P300 amplitudes and exhibited enhanced working memory. The results indicated ginger to be a potential cognitive enhancer for middle-aged women.

Anticonvulsant Activity

In the pentylenetetrazole-induced convulsion test, 7 mg/kg of [6]-shogaol (i.v.) prolonged the time to tonic extension and death in mice (Suekawa et al. 1984). In the strychnine-induced convulsion test, 3.5–7 mg/kg of [6]-gingerol (i.v.) prolonged the time to tonic extension and death. Oral administration of ginger ethanol extract (50, 100 and 200 mg/kg) in Swiss albino rats exerted anticonvulsant effect against maximal electroshock seizures (Venkatanarayana et al. 2013). Ginger-treated rats showed significant decrease in the duration of tonic hindlimb extension, suggesting anticonvulsant effect. Animal studies showed that the hydroethanolic extract of ginger had anticonvulsant effects against intravenous pentylenetetrazole-induced clonic seizure in mice, possibly through an interaction with inhibitory and excitatory system, antioxidant mechanisms, oxidative stress and calcium channel inhibition (Hosseini and Mirazi 2014).

Antitussive Activity

[6]-Shogaol exhibited an antitussive activity in i.v. administration in mice; its ED_{50} value was 1.75 mg/kg (Suekawa et al. 1984). [6]-Shogaol showed an intense antitussive effect in comparison with dihydrocodeine phosphate ($ED_{50} = 5.36$ mg/kg, i.v.)

Anti-dysmenorrhoea Activity

In a double-blind comparative clinical trial of 150 students (18 years old and over) with primary dysmenorrhoea, administration of ginger was found to be as effective as mefenamic acid and ibuprofen in relieving pain in women with primary dysmenorrhoea (Ozgoli et al. 2009). In a randomised, placebo-controlled trial of 120 students with moderate or severe primary, treatment with ginger for 5 days had a statistically significant effect on relieving intensity and duration of pain compared to placebo (Rahnama et al. 2012). In another clinical trial of 70 female university students, ginger was found to be effective in minimising the pain

severity in primary dysmenorrhoea compared to placebo (Jenabi 2013). In a recent randomised, placebo-controlled trial of 150 high school students, compared with placebo, participants receiving ginger and zinc sulphate reported more alleviation of period pain during the intervention (Kashefi et al. 2014). In another recent study of 120 female students with moderate to severe primary dysmenorrhoea, ginger was found to be as effective as mefenamic acid on pain relief in primary dysmenorrhoea (Shirvani et al. 2015). No adverse effects of ginger were found.

Spasmolytic /Spontaneous Motor Inhibition Activity

In the gastrointestinal system, (6)-shogaol intensively inhibited the traverse of charcoal meal through the intestine in contrast with (6)-gingerol after i.v. administration of 3.5 mg/kg, but (6)-shogaol facilitated such an intestinal function after oral administration of 35 mg/kg (Suekawa et al. 1984). Both (6)-shogaol and (6)-gingerol suppressed gastric contraction in-situ, and the suppression by the former was more intensive than that by the latter. Borrelli et al. (2004) found that ginger possessed both prejunctional and postjunctional inhibitory effects on ileal contractility; the prejunctional inhibitory effect of ginger on enteric excitatory transmission could involve a capsazepine-sensible site (possibly vanilloid receptors).

Among the isolated ginger compounds [6]-dehydrogingerdione, [11]-isodehydrogingerdione, [6]-gingerol, [8]-gingerol, [10]-gingerol, [6]-shogaol, [8]-shogaol, hexahydrocurcumin, [6]-gingerdiol and 2,5-dihydroxybisabol-3,10-diene -, [10]-gingerol depressed markedly the contractions induced, but not active against the phasic and tonic contractions caused by norepinephrine (3 μ M) (Liao et al. 2012). Since [10]-gingerol inhibited the Ca^{2+} -dependent contractions in high K^{+} medium, it may be a blocker of voltage-dependent Ca^{2+} channels.

Ginger oil and its constituent citral, but not camphene, suppressed rat tracheal contraction induced by carbachol (Mangprayool et al. 2013). Eucalyptol, another constituent,

showed a relaxing effect on rat airway. Since the content of eucalyptol in ginger oil was relatively low, the contribution of eucalyptol to the bronchodilatory effect of ginger oil was small. It was found that propranolol, but not indomethacin and L-NAME, reversed bronchodilatory effects of both ginger oil and citral, suggesting that a possible mechanism involved β -adrenergic receptor. Aqueous ginger extract decreased the basal tonus and contractile force of the isolated rabbit duodenum, whereas histamine increased the basal tonus and contractile force (Ahui et al. 2013)

Antipyretic Activity

Intravenous (i.v.) administration of [6]-shogaol (at 1.75–3.5 mg/kg) exerted antipyretic effect in mice (Suekawa et al. 1984). In oral administration, a smaller effect was seen at 140 mg/kg with both [6]-shogaol and [6]-gingerol.

Gastroparesis

Ameliorative/Antidiarrhoeal/Antipurgative Activity

The acetone and 50% ethanolic extract of ginger in the doses of 100, 200 and 500 mg/kg (p.o.) and ginger juice in the doses of 2 and 4 ml/kg significantly reversed cisplatin-induced delay in gastric emptying in rats (Sharma and Gupta 1998). The ginger juice and acetone extract were more effective than the 50% ethanolic extract. The reversal produced by the ginger acetone extract was similar to that caused by the 5-HT₃ receptor antagonist ondansetron; however, ginger juice produced better reversal than ondansetron. Ginger rhizome showed significant ameliorative effect on the BaCl₂-induced delay of gastric emptying in rat (Hashimoto et al. 2002). Its active constituents 6-gingesulphonic acid and shogasulphonic acid A significantly improved the delay of gastric emptying on both BaCl₂-induced and N^G-nitro-L-arginine (L-NNA)-induced model in rat.

Acetone extract of ginger at 75 mg/kg p.o. significantly inhibited serotonin (5-HT)-induced diarrhoea in ddY mice (Huang et al. 1990). On fractionation, fractions 2 and 3, which was especially effective, were further purified, and [6]-shogaol, [6]-dehydrogingerdione, [8]-gingerol and [10]-gingerol were found to have an anticathartic action. [6]-Shogaol was more potent than [6]-dehydrogingerdione, [8]-gingerol and [10]-gingerol. Studies by Huang et al. (1991) found that the anti-5-HT (5-hydroxytryptamine; serotonin) effects of galanolactone, a diterpenoid isolated from ginger, were related to antagonism of 5-HT₃ receptors. The inhibitory effect of galanolactone on the 5-HT response in the rat stomach fundus and rabbit aortic strips was less than that in the guinea pig ileum.

Kankyo (steamed and dried ginger rhizome) extract was found to be effective against castor oil-induced diarrhoea (Hashimoto et al. 2002). Its active constituents [6]-gingerol and [6]-shogaol also exhibited similar activity. *Z. officinale* exhibited its antidiarrhoeal activity by affecting bacterial and host cell metabolism (Daswani et al. 2010). It had no effect on the production and action of *Escherichia coli* heat-labile and heat-stable toxins.

Gastrointestinal Transit Ameliorative Activity

Oral administrations of the acetone extract of ginger at 75 mg/kg, [6]-shogaol at 2.5 mg/kg or [6]-, [8]- or [10]-gingerol at 5 mg/kg enhanced the transport of a charcoal meal in mice (Yamahara et al. 1990). The effects of these substances were similar to or slightly weaker than those of metoclopramide and domperidone. The results of a double-blind, randomised controlled pilot study involving 45 patients with irritable bowel syndrome (IBS) suggested that ginger was well tolerated but did not perform better than placebo (van Tilburg et al. 2014).

Androgenic Reproductive Activity

Studies by Morakinyo et al. (2008) indicated that ginger aqueous extract possessed pro-fertility properties in male rats which might be a product of both its potent antioxidant properties and androgenic activities. Ginger extract caused a significant increase in the weight of the testis and epididymis. There were dose- and duration-dependent increases in sperm count and motility. There was also a significant increase in serum testosterone level. Malondialdehyde levels were significantly reduced. Ghilissi et al. (2013) found that dietary ginger decreased blood glucose and malondialdehyde (MDA) level, increased reproductive organ weights and testosterone level, improved semen quantity and motility and ameliorated the superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) activities as well as testis lactate dehydrogenase (LDH), alkaline phosphatase (ALP) and aspartate and lactate aminotransferase (AST and ALT) activities. Intake of ginger roots improved the antioxidant and androgenic reproductive function of male diabetic rats in addition to its antidiabetic property. In another study, administration of combined ginger and cinnamon to streptozotocin (STZ)-induced diabetic rats for 56 days exerted significant beneficial effects on the sperm viability, motility, and serum total testosterone, follicle-stimulating hormone (FSH), luteinising hormone (LH) and serum antioxidants' level (total antioxidant capacity, SOD, catalase and GPX) and could be effective for maintaining healthy sperm parameters and male reproductive function in diabetics (Khaki et al. 2014).

In contrast, in an in-vitro study, addition of metholic ginger extract to human semen fluid was found to induce toxic effects on sperm parameters such as motility, grading and morphology (Jorsaraei et al. 2008). Studies by Isaac et al. (2014) found that the usage of ginger by the males should be moderate, as high consumption may have some side effects on male fertility. They found that high consumption of ginger extract (500 mg/kg) for 2 weeks caused deleterious changes in the testes of male Wistar rats. Histological sections of the ginger-treated groups showed distortion of germinal and supporting cells, disintegration of matured sperm cells in the lumen, distortion

of seminiferous tubules, widened interstitial spaces indicating shrinkage of tubules and destruction of leydig cells.

Cholagogic Activity

The acetone extracts of ginger caused an increase in bile secretion (Yamahara et al. 1985). [6]-Gingerol and [10]-gingerol were found to be mainly responsible for the cholagogic effect of ginger.

Wound Healing Activity

Ginger component 10-shogaol exhibited antioxidant activity and promoted human normal epidermal keratinocytes and dermal fibroblast cell growths. 10-Shogaol enhanced growth factor production in transforming growth factor- β (TGF- β), platelet-derived growth factor- $\alpha\beta$ (PDGF- $\alpha\beta$) and vascular endothelial growth factors (VEGF) of both cells. In the in-vitro wound healing assay for 12 or 24 h, with 10-shogaol, the fibroblasts and keratinocytes migrated more rapidly than the vehicle control group. The results substantiated 10-shogaol as an antioxidant for human skin cell growth and a migration enhancer with potential to be a novel wound repair agent.

Cardiotonic Activity

Crude methanol extracts of ginger rhizome showed potent, positive inotropic effects on the guinea pig isolated left atria (Shoji et al. 1982). Gingerols were found as active principles of the cardiotonic activity. In the cardiovascular system, both (6)-shogaol and (6)-gingerol produced depressor response at lower doses on the blood pressure; at high doses, both drugs produced three phase pattern (Suekawa et al. 1984).

Hypotensive Activity

Intraventricular injection of (6)-shogaol (0.1–0.5 μ g) caused a pressor response in a dose-dependent manner in rats (Suekawa et al. 1986b). (6)-Shogaol (0.5 mg/kg, i.v.)-induced pressor response was markedly reduced by a spinal destruction to the sacral cord level. In the hindquarters of rats which were

perfused with rats' blood, (6)-shogaol caused two pressor responses on the perfusion pressure. The first pressor response, which was accompanied by a rise in systemic blood pressure, was reduced by hexamethonium but was not entirely eliminated by phentolamine. However, the pressor response disappeared with spinal destruction to the sacral cord level. The second pressor response, which occurred when the systemic blood pressure regained its original pressure, was not affected by hexamethonium, phentolamine or spinal destruction. When (6)-shogaol (0.5 mg/kg, i.v.) was administered to anaesthetised rats, blood pressure showed a tri-phasic response which was comprised of a rapid fall, followed by a rise and a delayed fall (Suekawa et al. 1986a). In hindquarters perfused with a nutrient solution, (6)-shogaol (10^{-5} g)-induced peripheral pressor response was also not affected by α -adrenoceptor blockades and Ca antagonists, but was inhibited by the combination of an α -adrenoceptor blockade and a Ca antagonist. Furthermore, this peripheral pressor response was eliminated by the removal of Ca ion from the perfusate. (6)-Shogaol did not exhibit a pressor response in an artery and a vein of the tail or an artery of the femur perfused with a nutrient solution. (6)-Shogaol-induced peripheral pressor response in hindquarters was markedly potentiated during the perfusion of norepinephrine (5×10^{-6} g/ml), but this potentiation was prevented by pretreatment with reserpine (5 mg/kg, i.p.). Moreover, repeated injections of (6)-shogaol caused a tachyphylaxis in mesenteric and tail vascular beds and a slight tachyphylaxis in hindquarters.

The crude extract of ginger induced a dose-dependent (0.3–3 mg/kg) fall in the arterial blood pressure of anaesthetised rats (Ghayur and Gilani 2005). In guinea pig paired atria, ginger extract exhibited a cardiodepressant activity on the rate and force of spontaneous contractions. In rabbit thoracic aorta preparation, ginger extract relaxed the phenylephrine-induced vascular contraction at a dose 10 times higher than that required against K (80 mM)-induced contraction. Ca^{2+} channel-blocking (CCB) activity was confirmed when ginger extract shifted the Ca^{2+} dose–response curves to the right similar to the effect of verapamil. It also

inhibited the phenylephrine (1 microM) control peaks in normal Ca^{2+} and Ca^{2+} -free solution, indicating that it acts at both the membrane-bound and the intracellular Ca^{2+} channels. When tested in endothelium-intact rat aorta, it again relaxed the K-induced contraction at a dose 14 times less than that required for relaxing the PE-induced contraction. The vasodilator effect of ginger extract was endothelium-independent because it was not blocked by L-NAME (0.1 mM) or atropine (1 μM) and also was reproduced in the endothelium-denuded preparations at the same dose range. These data indicated that the blood pressure-lowering effect of ginger was mediated through blockade of voltage-dependent calcium channels. Ghayur et al. (2005) reported that the hypotensive, endothelium-dependent and independent vasodilator and cardio-suppressant and stimulant effects of aqueous ginger extract, which tested positive for saponins, flavonoids, amines, alkaloids and terpenoids, induced a dose-dependent (3.0–10.0 mg/kg) fall in the arterial blood pressure (BP) of anaesthetised rats which was partially blocked by atropine (1 mg/kg). In isolated endothelium-intact rat aorta, ginger extract (0.01–5.0 mg/ml) relaxed the phenylephrine (1 microM)-induced contractions, effect partially blocked by atropine (1 microM). An atropine-resistant and L-NAME-sensitive vasodilator activity was also noted from ginger phenolic constituents 6-, 8- and 10-gingerol, while 6-shogaol showed a mild vasodilator effect. In guinea pig atria, ginger extract (0.1–5.0 mg/ml) inhibited the force and rate of atrial contractions, but pretreatment with atropine blocked the inhibitory effect, and a stimulatory effect was unmasked which was resistant to propranolol and verapamil but sensitive to ryanodine, blocker of Ca^{++} release from intracellular stores. Later at doses ≥ 1.0 mg/ml, the extract completely suppressed the atrial tissue, effect resistant to glibenclamide, pyrilamine, aminophylline and L-NAME. These data indicate that the aqueous ginger extract lowered BP through a dual inhibitory effect mediated via stimulation of muscarinic receptors and blockade of Ca^{++} channels and elucidated the mechanistic basis for the use of ginger in hypertension and palpitations.

Milk-Clotting and Proteolytic Activities

Ginger was found to be a new source of proteolytic enzyme named Zingibain (Thompson et al. 1973). With bovine serum albumin (BSA) as substrate, a relatively high proteolytic activity occurred over a pH range of 4.5–6.0, with an optimum pH of 5.0. The optimum temperature for proteolysis of BSA was 60°C during a 10 min reaction time, with rapid denaturation of the enzyme occurring at 70° C. The analyses of soluble peptide amino acids or terminal amino acids suggested that the proteolysis of collagen was many folds greater than that of actomyosin. The combined proteolysis of these two muscle protein fractions by the ginger protease resulted in significantly more tender meat. Ginger proteases in ginger rhizome were extracted from the ginger acetone powder and purified (Ohtsuki et al. 1995). The proteases were fractionated into three components by the isoelectric focusing, having *pI* value of 4.5, 4.6 and 4.8, respectively. All these proteases had a molecular mass of 29,000. Some divalent metal ions, such as Hg^{2+} , Cu^{2+} , Cd^{2+} and Zn^{2+} , strongly inhibited these purified enzymes. Two ginger proteases (GP-I and GP-II) were isolated from the ginger rhizome (Choi and Laursen 2000). GP-II was found to be a 221 amino acid glycoprotein possessing two N-linked oligosaccharide chains (8% glycosylated by weight) at Asn99 and Asn156 (Choi et al. 1999). The cysteine protease (GP-II) from ginger rhizome was found to have an unusual specificity for proline; it cleaved peptides and proteins with proline at the P(2) position. GP-II had two predicted glycosylation sites which were occupied by the glycans (Man)₃(Xyl)₁(Fuc)₁(GlcNAc)₂ and (Man)₃(Xyl)₁(Fuc)₁(GlcNAc)₃, in a ratio of approximately 7:1 (Choi and Laursen 2000). Both glycans were xylose containing biantennary complex types that shared the common core structural unit, $\text{Man1} \rightarrow 6(\text{Man1} \rightarrow 3) (\text{Xyl1} \rightarrow 2)\text{Man1} \rightarrow 4\text{GlcNAc1} \rightarrow 4 (\text{Fuc1} \rightarrow 3)\text{GlcNAc}$ for the major form, with an additional N-acetylglucosamine residue being linked, in the minor form, to one of the terminal mannose units of the core structure. Two additional cysteine proteases, GP2 and GP3, were isolated from ginger rhizomes (Kim et al. 2007). GP2 was virtually identical to a previously identified ginger

protease GP-II by Choi and Laursen (2000). The collagenase activity of ginger proteases (GP) was better than other plant cysteine proteases such as papain and bromelain based on its ability to hydrolyse native collagen. Ginger protease was found to have a molecular weight of 34.8 kDa compared with papain 25.1 kDa (Adulyatham and Owusu-Apenten 2005). Sodium ascorbate stabilised ginger protease solutions by 20-fold at 5 °C. The authors also described an efficient method for partially purifying the stabilised protease leading to 940-fold maximum purification.

The milk-clotting activity (MCA) and proteolytic activity (PA) of ginger proteases were stable after storage at 4 °C for 24 h (Su et al. 2009). The ascorbic acid addition significantly stabilised the MCA and PA of ginger proteases. The protease inhibition test suggested that ginger proteases belonged to the cysteine type. The biochemical characteristics of ginger proteases suggested their potential for making new milk curd products. A milk coagulating protease was purified ~ 10.2-fold to apparent homogeneity from ginger rhizomes in 34.9% recovery (Hashim et al. 2011). It was found to be a glycoprotein with 3% carbohydrate content with molecular mass ~ 36 kDa and a member of the cysteine proteases and exhibited a pI of 4.3. The purified enzyme differed in molecular mass, pI, carbohydrate content and N-terminal sequence from previously reported ginger proteases. These results indicated that the purified protease may have potential application as a rennet substitute in the dairy industry. Zingibain, a milk-clotting enzyme, was extracted from *Zingiber officinale* rhizomes (Gagaoua et al. 2014). The enzyme was found to be a monomeric protein of 33.8kDa and its isoelectric point is 4.38. The enzyme exhibited maximal proteolytic activity at a temperature of 60°C and pH 7.0. It was found to be stable at 40–65°C during 2h. The enzyme was found to be highly stable against numerous metal ions, and its activity was enhanced by Ca^{2+} , K^{+} and Na^{+} . It was completely inhibited by heavy metal ions such as Cu^{2+} and Hg^{2+} and partially by Cd^{+} . Zingibain milk-clotting activity (MCA) was found to be highly stable when stored under freezing temperature of –20°C for 30 days compared to 4°C. A

protease was isolated from Bentong ginger rhizome (Nafi et al. 2013; 2014). Ginger protease was completely inhibited by heavy metal cations, i.e. Cu^{2+} and Hg^{2+} , and a thiol-blocking agent or inhibitor, N-ethyl maleimide (NEM), indicating that the protease was most probably a cysteine protease. The enzyme had an optimum temperature of 60°C and the optimum pH ranged between pH 6–8. Monovalent cations (K^+ and Na^+) had no significant effect on the activity of the protease, but divalent and trivalent cations showed moderate inhibitory effect. Detergents such as sodium dodecyl sulphate increased the activity of ginger protease, while Tween 80 and Tween 20 slightly reduced the activity.

Ginger powder had been used to improve meat tenderness and flavour in chicken kabab, an Indian traditional food (Bhaskar et al. 2006), while ginger rhizome extract was reported to improve the properties of patties made from goat meat (chevon) (Pawar et al. 2007).

Adaptogenic Activity

Pretreatment of Swiss mice with ginger rhizome ethanol extract significantly ameliorated the stress-induced variations in these biochemical levels and blood cell counts in both acute (swimming endurance physical stress) and chronic cold-restraint stress models (Lakshmi and Sudhakar 2010). Ginger extract-treated animals showed increase in swimming endurance time and increase in anoxia tolerance time in physical and anoxia stress models, respectively. Treatment groups also reverted back increase in liver, adrenal gland weights and atrophy of spleen caused by cold chronic stress and swimming endurance stress models. The results indicated that ethanolic extract of *Z. officinale* had significant adaptogenic activity against a variety of biochemical and physiological perturbations in different stress models.

In a randomised, placebo-controlled study of 32 obese males (body mass index ≥ 30 , aged 18–30 years) randomised to one of the four groups—a placebo ($n = 8$), resistance training plus placebo ($n = 8$), resistance training plus ginger supplementation ($n = 8$) and ginger supplementation only ($n =$

8)—10 weeks of either ginger supplementation or progressive resistance training protected against oxidative stress, and therefore, both of these interventions could be beneficial for obese individuals; however, when combined, the effects were negated (Atashak et al. 2014).

Radioprotective Activity

Preclinical studies carried out in the last decade had shown that ginger and its phytochemicals dehydrozingerone and zingerone possess radioprotective effects in laboratory animals and in cultured cells in-vitro (Baliga et al. 2012). The hydroalcoholic extract of ginger rhizome when administered either through intraperitoneal or oral route was effective in protecting against γ -radiation-induced sickness and mortality. The phytochemicals dehydrozingerone and zingerone present in ginger were also shown to protect mice against radiation-induced sickness and mortality. Mechanistic studies had indicated that the free radical scavenging and antioxidant, anti-inflammatory and anticlastogenic effects may contribute towards the observed protection. Additionally, studies with tumour-bearing mice had also shown that zingerone selectively protects the normal tissues against the tumouricidal effects of radiation.

Administration of *Zingiber* extract 1 h before 2-Gy γ -irradiation was effective in blocking the saccharin avoidance response for five post-treatment observational days, both in a dose- and time-dependent manner, with 200 mg/kg b.w. i.p. being the most effective dose (Sharma et al. 2005). The highest saccharin intake in all the groups was observed on the fifth post-treatment day. The 1000- μ g/ml and 2000- μ g/ml concentration of ginger extract showed the highest efficiency in scavenging free radicals and in inhibiting lipid peroxidation induced by radiation (2 Gy) and ascorbate-ion stress in brain homogenate. The lipid peroxidation and superoxide anion scavenging ability of the extract further supported its radioprotective properties. The results clearly established the neurobehavioral efficacy of ginger extract, and the antioxidant properties appeared to be a contributing factor in its overall ability to modulate radiation-induced conditioned taste

aversion. Dichloromethane extracts of turmeric and ginger protected human keratinocytes from UVB toxicity (Thongrakard et al. 2013). These extracts stimulated the synthesis of thioredoxin 1, an antioxidant protein, and could protect human HaCaT keratinocytes from UV-induced DNA damage and cytotoxicity.

Pretreatment intraperitoneal administration of mice with ginger rhizome hydroalcoholic extract (ZOE) reduced the severity of radiation sickness and the mortality at all doses (Jagetia et al. 2003). The ZOE treatment protected mice from GI syndrome as well as bone marrow syndrome. The dose reduction factor for ZOE was found to be 1.15. The optimum protective dose of 10 mg/kg ZOE was 1/50 of the LD₅₀ (500 mg/kg). Irradiation of the animals resulted in a dose-dependent elevation in the lipid peroxidation and depletion of GSH on day 31 post-irradiation; both effects were lessened by pretreatment with ZOE. In another study, pretreatment of mice with ginger rhizome hydroalcoholic extract (ZOE) reduced the severity of symptoms of radiation sickness and mortality at all the exposure doses and also increased the number of survivors in a ZOE + irradiation group compared to the concurrent double-distilled water + irradiation group (Jagetia et al. 2004). The ZOE treatment protected mice against gastrointestinal-related deaths as well as bone marrow-related deaths. The dose reduction factor was found to be 1.2. The administration of ZOE after exposure to irradiation was not effective, as no survivors lasted up to 30 days post-irradiation. Treatment of mice with ZOE before irradiation caused a significant depletion in lipid peroxidation followed by a significant elevation in GSH concentration in the livers of mice at 31 days post-irradiation. The mechanism of action of ZOE was determined by evaluating its free radical scavenging capability. Ginger hydroalcoholic extract was found to scavenge $\cdot\text{OH}$, $\text{O}_2^{\cdot-}$ and $\text{ABTS}^{\cdot+}$ radicals in a dose-dependent manner in-vitro.

Antiparasitic Activity

Gingerol (5.0 ppm) completely abolished the infectivity of *Schistosoma mansoni* miracidia in mice (Adewunmi et al. 1990). Ginger compounds [6]-shogaol and [6]-gingerol could kill *Anisakis simplex* larvae at a minimal effective dose of 62.5 and 250 µg/ml, respectively (Goto et al. 1990). However, the concentration of [6]-gingerol in fraction 1 was greater than 20 times that of [6]-shogaol, making the former the most active component in the ginger fraction. Furthermore, synergistic effects between [6]-gingerol and a small amount of [6]-shogaol were observed. In saline solution containing [6]-shogaol (62.5 µg/ml), greater than 90% of larvae lost spontaneous movement within 4 h and were destroyed completely within 16 h. Lin et al. (2010b) reported that ginger compounds [10]-shogaol, [6]-shogaol, [10]-gingerol and [6]-gingerol exhibited larvicidal activity against *Anisakis simplex*. The above compounds kill or reduce spontaneous movement in *A. simplex* larvae. The maximum lethal efficacy of [10]-shogaol and [10]-gingerol was approximately 80% and 100%, respectively. Ginger root extract fraction F1 strongly inhibited the proliferation of *Toxoplasma gondii*-infected C6 cells and *T. gondii* in a dose-dependent manner compared with sulfadiazine (Choi et al. 2013). After *T. gondii* invasion, C6 cells induced the activation of caspase-3, bax, p53 and p21 related to programmed cell death, and F1 effectively suppressed the expression of caspase-3, bax, p53 and p21 causing cell death of the infected host cells. In addition, INF-γ, and IL-8 levels, and the viability of *T. gondii*-infected mice treated with F1 (500 µg/ml) were not changed or increased during the period of the experiment. These results demonstrated that F1 not only induce anti-*T. gondii* effects causing the inactivation of apoptotic proteins in infected host cells through the direct inhibition of *T. gondii* but also had antiparasitic properties which inhibited inflammatory cytokine secretion in-vivo.

Twelve subcutaneous injections of ginger rhizome extract given at 100 mg/kg reduced microfilarial concentration in blood by a maximum of 98% in dogs naturally infected with the nematode parasite, *Dirofilaria immitis* (Datta and Sukul 1987). Fifty-five days after the last injection, there was 83% reduction in microfilarial concentration, suggesting partial

destruction of adult worms. Constituents from ginger rhizome [6]-gingerol, [10]-shogaol, [10]-gingerol, [6]-shogaol and hexahydrocurcumin killed *Angiostrongylus cantonensis* larvae or reduced their spontaneous movements in a time- and dose-dependent manner (Lin et al. 2010a). The larvicidal effect or ability to halt spontaneous parasite movement of these ginger constituents at various concentrations was reached from 24 to 72 h, respectively. [10]-Gingerol was found to have a greater maximum larvicidal effect and loss of spontaneous movements than hexahydrocurcumin, mebendazole and albendazole.

Using *Zingiber officinale* extract at the concentration of 10 mg/ml, the time of paralysis and death of *Pheretima posthuma* was found to be 13.20 min and 32.40 min, respectively; at concentration of 20 mg/ml, it was 7.50 min for paralysis and 24.20 min for death; and at 50 mg/ml, the time of paralysis and death was 6.40 min and 17.5 min, respectively (Singh et al. 2011). In case of combination of the plant extracts (*Curcuma longa* and *Zingiber officinale*), the time of paralysis and death was 10.6 min and 31.8 min, respectively, at concentration of 10 mg/ml. At concentration of 20 mg/ml, the time of paralysis and death was 6.8 min and 27 min, respectively, and at 50 mg/ml concentration, the time of paralysis and death was 4.8 min and 16.3 min, respectively. Ginger and curcumin extracts exhibited anthelmintic activity in-vitro against *Ascaridia galli* in dose- and time-dependent manner (Bazh and El-Bahy 2013). Ginger in all concentrations used exhibited a higher death rate observed than curcumin.

Ginger compounds gingerenone A, [6]-dehydrogingerdione, [4]-shogaol, 5-hydroxy-[6]-gingerol, [6]-shogaol, [6]-gingerol, [10]-shogaol, [10]-gingerol, hexahydrocurcumin, 3*R*,5*S*-[6]-gingerdiol and 3*S*,5*S*-[6]-gingerdiol exhibited anthelmintic activity against the parasite *Hymenolepis nana* (Lin et al. 2014). The cestocidal activity or ability to halt spontaneous parasite movement (oscillation/peristalsis) by the above constituents occurred from 24 to 72 h in a time- and dose-dependent manner, respectively. [10]-Shogaol and [10]-gingerol exerted maximum lethal efficacy and loss of spontaneous movement than the others at 24–72 h, but [10]-gingerol had less loss of

spontaneous movement efficacy than [10]-shogaol. After exposure to 200 μ M [10]-shogaol, 100% of *H. nana* died compared to 100% dying at 24 h for [10]-gingerol, showing that [10]-gingerol had less lethal efficacy than [10]-shogaol. In addition, these constituents of ginger showed effects against peroxy radical under cestocidal activity. In-vivo, oral administration of ginger extract to *H. nana*-infected mice BALB/c mice significantly reduced worm number, and cytokine production by in-vitro Con A-stimulated spleen cell assay showed that INF- γ and IL-2 were significantly increased by ginger extract. IL-4, IL-5, IL-6, IL-10 and IL-13 were significantly decreased by the extract.

Crude powder (CP) and crude aqueous extract (CAE) of dried ginger (1–3 g/kg) exhibited anthelmintic activity when administered to sheep naturally infected with mixed species of gastrointestinal nematodes (Iqbal et al. 2006). Both CP and CAE exhibited a dose- and a time-dependent anthelmintic effect with respective maximum reduction of 25.6 % and 66.6 % in eggs per gram (EPG) of faeces on day 10 of post-treatment. Levamisole (7.5 mg/kg), a standard anthelmintic agent, exhibited 99.2 % reduction in EPG.

Insecticidal (Larvicidal) Activity

Constituents of ginger ether extract 4-gingerol (1), (6)-dehydrogingerdione (2) and (6)-dihydrogingerdione (3) exhibited larvicidal activities against fourth instar larvae of *Aedes aegypti* (LC₅₀ 4.25, 9.80, 18.20 ppm) and *Culex quinquefasciatus* (LC₅₀ 5.52, 7.66, 27.24 ppm), respectively (Rahuman et al. 2008). The results showed that the most effective compound was 4-gingerol.

Molluscicidal Activity

Gingerol and shogaol exhibited potent molluscicidal activity on *Biomphalaria glabrata* (Adewunmi et al. 1990). Gingerol (5.0 ppm) completely abolished the infectivity of cercariae in *B. glabrata* in mice.

Testicular Protective Activity

Rasyidah et al. (2014) found that treatment with ethanolic ginger extract ameliorated formalin-induced testicular toxicity in rats. Inhalation exposure to 10 % formalin for 4h/day, 5 days/week for 8 weeks significantly induced oxidative stress in the rat testis. Treatment with ginger extract ameliorated the oxidative stress by increasing superoxide dismutase (SOD) and catalase (CAT) and decreasing malondialdehyde. Pretreatment of ginger extract ameliorated aspartame induced testicular toxicity in rats (Hozayen et al. 2014). The extract ameliorated aspartame reduced glutathione level, glutathione *S*-transferase and catalase activities in the testes and reduced aspartame elevated lipid peroxidation.

Antihypothermic Activity

Acetone extract of ginger at 100 mg/kg p.o. significantly inhibited serotonin (5-HT)-induced hypothermia (Huang et al. 1990). On fractionation, fractions 1 and 2 showed significant activity. Fraction 2 was further purified and [6]-shogaol which was obtained from fraction 2–2, at 10 mg/kg p.o., was shown to inhibit 5-HT-induced hypothermia.

Antityrosinase Activity

The bioactive components of ginger rhizomes were characterised by spectroscopic analysis as zingerone and dehydrozingerone, which exhibited potent tyrosinase inhibition activities (Kuo et al. 2005). Of the dehydrozingerone-derived analogues, compound 4-(2', 4'-dihydroxyphenyl)-(E)-3-buten-2-one displayed superior inhibition of tyrosinase activity relative to other examined analogues. Compounds dehydrozingerone [4-(4'-hydroxy-3'-methoxyphenyl)-(E)-3-buten-2-one], 4-(4'-hydroxy-3', 5'-dimethoxyphenyl)-(E)-3-buten-2-one and 4-(2',3'-dihydroxyphenyl)-(E)-3-buten-2-one exhibited non-competitive inhibition against oxidation of 3,4-dihydroxyphenylalanine (L-DOPA). It was observed that both number and position of hydroxyl groups on aromatic ring and

a double bond between C-3 and C-4 played a critical role in exerting the antioxidant and antityrosinase activity

Skin Permeation Enhancement Activity

The skin permeation of diclofenac sodium was remarkably enhanced in the presence of three essential oils extracted from rhizomes of *Zingiber officinale*, *Zingiber cassumunar* and *Curcuma zedoaria* (Songkro et al. 2008). Overall, the rank order of the enhancing activities of these oils was *Zingiber officinale* > *Zingiber cassumunar* > *Curcuma zedoaria*. Furthermore, the essential oil at 5% appeared to give the greatest enhancement. For the in-vivo skin irritation study, the essential oils at concentrations of 1 and 5% in hydroalcoholic mixture and at 100% were found to cause skin irritation in different degrees. The most severe skin damage was observed with the 1 % of these oils, whereas the 5% of these oils were classified as mild irritants.

Toxicological Studies

Ginger was non-toxic up to a dose of 1500 mg/kg body weight, the highest drug dose that could be tested for acute toxicity (Jagetia et al. 2004). Subchronic oral administration of ginger oil for 13 weeks at doses of 100, 250 and 500 mg/kg per day to rats did not produce any treatment-related changes in haematological parameters, hepatic and renal functions, serum electrolytes or histopathology of selected organs (Jeena et al. 2011). The major component of ginger oil was found to be zingiberene (31.08%), and initial studies indicated the presence of zingiberene in the serum after oral dosing. These results confirmed that ginger oil was not toxic to male and female rats following subchronic oral administrations of up to 500 mg/kg per day (no observed adverse effect level [NOAEL]).

The administration of ginger in a dose of 50 mg/ kg for 28 days produced bradycardia with waviness in cardiac muscle fibres in rats (Elkhishin and Awwad 2009). Ginger in a dose of 500 mg/kg produced both hypotension and bradycardia with degenerative changes in cardiac myocyte tissue. It was

concluded that a single dose of 2500 mg/kg ginger could be a toxic by causing severe hypotension and bradycardia with induction of pre-necrotic changes in cardiac tissue. The hypotensive and bradycardic effects of ginger may be partially due to induction of vasodilatation by increasing nitric oxide release or synthesis and partially due to a calcium channel-blocking effect. Also, a cholinomimetic effect could be contributed in the cardiovascular effects of ginger. While the in-vitro results revealed ginger to be a partial vasorelaxant as it produced a relaxant effect on rabbit's aortic strip precontracted with phenylephrine. Preincubation with L-nitroarginine methyl ester (L-NAME) significantly attenuated the ginger-induced relaxation indicating that the vasodilator effect of ginger was partially mediated through nitric oxide synthesis or release from L-NAME.

Pharmacokinetic Studies

Oral or intraperitoneal dosage (100 mg/kg) of zingerone, a pungent principle of ginger, resulted in the urinary excretion of most metabolites within 24 h, mainly as glucuronide and/or sulphate conjugates (Monge et al. 1976). While zingerone itself accounted for roughly 50–55% of the dose, reduction to the corresponding carbinol (11–13%) also occurred. Side-chain oxidation occurred at all three available sites, and oxidation at the 3-position, giving rise to C6-C2 metabolites, predominated. Appreciable (40% in 12 h) biliary excretion occurred. Biliary studies and studies in-vitro using caecal microorganisms indicated that several *O*-demethylated metabolites found in the urine were of bacterial origin.

In a study of human volunteers, after oral dosing of ginger, no participant had detectable free 6-gingerol, 8-gingerol, 10-gingerol or 6-shogaol, but 6-gingerol, 8-gingerol, 10-gingerol and 6-shogaol glucuronides were detected (Zick et al. 2008). 6-Gingerol, 8-gingerol, 10-gingerol and 6-shogaol were absorbed after p.o. dosing and could be detected as glucuronide and sulphate conjugates. 6-gingerol, 8-gingerol, 10-gingerol and 6-shogaol were simultaneously determined in rat plasma after oral administration of ginger oleoresin (Wang et al. 2009). Calibration curves ($1/x^2$ weighted) offered

satisfactory linearity ($R^2 > 0.995$) in a wide linear range (0.0104–13.0 µg/mL for 6-gingerol, 0.00357–4.46 µg/mL for 8-gingerol, 0.00920–11.5 µg/mL for 10-gingerol and 0.00738–9.22 µg/mL for 6-shogaol). The lower limit of quantification (LLOQ) was in a range of 3.57–10.4 ng/mL. Glucuronide of 6-gingerol was determined after β -glucuronidase hydrolysis for more information, and the intestinal glucuronidation was further confirmed by comparison of plasma samples of hepatic portal vein and femoral vein. The recovery of all 6-, 8- and 10-gingerols and 6-shogaol in human plasma was $\geq 99\%$ at 5.0 µg/mL (Zick et al. 2010). The lower limit of quantitation was 0.1 µg/mL except for 10-gingerol which was 0.25 µg/mL. After oral dosing of 2.0 g ginger extracts in human, free 10-gingerol and 6-shogaol were detected in plasma with peak concentrations (9.5 and 13.6 ng/mL, respectively) at 1 h after oral administration, but no free 6-gingerol and 8-gingerol were detected in plasma from 0.25 to 24 h (Yu et al. 2011). The peak concentrations of glucuronide metabolites of 6-, 8- and 10-gingerols and 6-shogaol were 0.47, 0.17, 0.37 and 0.73 µg/mL at 1 h, respectively. The peak concentrations of the sulphate metabolites of 6-, 8- and 10-gingerols and 6-shogaol were 0.28, 0.027, 0.018 and 0.047 µg/mL at 1 h, respectively. Very low concentrations (2–3 ng/mL) of 10-gingerol glucuronide and sulphate were found in colon tissues. Pharmacokinetic analysis showed that half-lives of these four analytes and their metabolites were 1–3 h in human plasma. No accumulation was observed for 6-, 8- and 10-gingerols and 6-shogaol and their metabolites in both plasma and colon tissues after multiple daily dosing.

Contraindications

Ginger in quantities of 6 g or more may cause gastric irritations by causing a significant increase in exfoliation of gastric surface epithelial cells in human subjects (Desai et al. 1990). 6 g ginger given intragastrically showed a mean significant increase in DNA-p/min in gastric aspirates.

Traditional Medicinal Uses

Ginger is a medicinal plant that has been widely used in Chinese, Ayurvedic and Unani Tibb herbal medicines all over the world, since antiquity, for a wide array of unrelated ailments that include arthritis, rheumatism, sprains, muscular aches, pains, sore throats, cramps, constipation, indigestion, vomiting, hypertension, dementia, fever, infectious diseases and helminthiasis (Ali et al. 2008). Ginger root has been used traditionally for the treatment of gastrointestinal ailments such as motion sickness, dyspepsia and hyperemesis gravidarum (Mahady et al. 2003). Hot ginger infusion is used for stoppage of menses due to cold and ginger is also used as a rubefacient (Grieve 1971).

Ginger (Chinese name: Shengjiang), derived from the rhizomes of *Zingiber officinale* Roscoe, is a well-known spice and is most frequently prescribed as a traditional Chinese medicine for its stomachic, antiemetic, antidiarrhoeal, expectorant, antiasthmatic, haemostatic and cardiologic properties for the treatment of several gastrointestinal and respiratory diseases (Shih et al. 2014). The most famous traditional medicinal application of *Z. officinale* is to promote blood circulation for the removal of blood stasis, a mechanism that is related to antiplatelet aggregation activity (Shih et al. 2014; Liao et al. 2012). Ginger root (*Zingiber officinale*) has been used traditionally for the treatment of gastrointestinal ailments such as motion sickness, dyspepsia and hyperemesis gravidarum (Mahady et al. 2003). Red ginger (*Zingiber officinale* var. *Rubra*) has been prescribed as an analgesic for arthritis pain in Indonesian traditional medicine (Shimoda et al. 2010). Ginger is reported in Ayurvedic and Tibb systems of medicine to be useful in rheumatic disorders (Srivastava and Mustafa 1989; 1992). The rhizome of *Zingiber officinale* is a traditional medicine with carminative effect and anti-nausea, anti-inflammatory and anticarcinogenic properties (Pan et al. 2008a, b). Ginger is used in Korea, China and Japan as a traditional medicine for treating vomiting, gastric or duodenal ulcers, dyspepsia, nausea, diarrhoea and cough (But et al. 1997). In Africa, dried ginger is used much as it is in Asia (Iwu 1990). The Chinese pharmacopeia lists ginger for epigastric pain with cold feeling, vomiting and diarrhoea accompanied by cold extremities and faint pulse, dyspnea and

cough with copious frothy expectoration (Tu 1992). Ginger has been used commonly in the traditional system of medicine for the treatment of respiratory disorders (Khan et al. 2014). Dried and fresh ginger have been used in Indian traditional medicine for relief from arthritis, rheumatism, sprains, muscular aches and pains, congestion, coughs, sinusitis, sore throats, diarrhoea, indigestion, loss of appetite, fever, flu, etc. (Nampoochiri et al. 2012). *Z. officinale* and its variants are used in folk medicine to treat stomach discomfort and tumours (Theilade 1996). Ginger essential oil has been used in folk medicine for manifold conditions including as an analgesic, anti-inflammatory and antirheumatic (Nogueira de Melo et al. 2011).

Ojewole (2006) reported folkloric, ethnomedical uses of ginger in the treatment and/or management of painful, arthritic inflammatory conditions, as well as in the management and/or control of type II diabetes mellitus in some rural Africa communities. Ginger is a common medicinal plant used by women from Agnalazaha littoral forest (Southeastern Madagascar) (Razafindraibe et al. 2006). The rhizome and leaf are used to treat cough, diarrhoea, nausea during pregnancy and evacuation of the placenta.

In Ethiopia, ginger rhizome is used to treat malaria, abdominal pains and cold (ginger chewed with *Lepidium sativum*) and as a stimulant (Getahun 1976); ginger is chewed and swallowed for tonsillitis (Megersa et al. 2013); ginger rhizome and garlic are pounded and eaten with honey for malaria, the same with *Vernonia amygdalina* twigs, which are also pounded and eaten with honey for intestinal parasites (Amenu 2007, cited by Megersa et al. 2013). In Ethiopia (Butajira District), ginger rhizome is chewed for stomach ache, and a cold decoction of ginger rhizome and tea is taken for cough (Gedif and Hahn 2003). The Shinasha, Agew-awi and Amhara peoples in northwest Ethiopia used ginger rhizome to treat tuberculosis (Giday et al. 2007). In the region of Debre Libanos monastery and Dek Island in Lake Tana, Ethiopia, ginger rhizome is chewed for stomach ache (Teklehaymanot 2009; Teklehaymanot et al. 2007). In Wonago Woreda, Ethiopia, ginger is chewed and swallowed to treat

stomach ache (Mesfin et al. 2009). A concoction of ginger rhizome, garlic and chilli fruit and coffee leaves is taken orally for headache by the Sheko ethnic group of Ethiopia (Giday et al. 2010). In North Shewa Zone, Amhara Region, Ethiopia, a ginger decoction is used for constipation, cough, asthma, common cold and diarrhoea (Lulekal et al. 2013). In Senegal, ginger rhizome is used for remedy of cough and indigestion (Pousset 1989).

The Waluguru people in east Uluguru Mountains Tanzania ingest pressed ginger, ginger juice and salt to treat cough and hernia (Mahonge et al. 2006). In Tanzania, ginger root decoction is orally taken for coughs (Amri and Kisangau 2012). In Morocco, an infusion of ginger rhizome powder is used as antitussive, analgesic, appetite stimulant, aphrodisiac and antipyretic and for digestive disorders, diabetes and pulmonary disease (Bnouham et al. 2002). In Egypt, a decoction of ginger rhizome is used to remedy voice problems in common cold (Sameh and Abdelhalim 2011). In the Suba District, Kenya, ginger is chewed for sore throat, and a decoction is taken to treat malaria (Nagata et al. 2011).

In Sierra Leone (Moyamba District), ginger rhizomes are pounded with a single fruit of *Capsicum annum* and the poultice rubbed as a remedy for fever and colds in children (Lebbie and Guries 1995). In Ghana (district of Bosomtwe-Atwima-Kwanwoma), ginger rhizome is used as poultice for chronic wounds and boils (Agyare et al. 2009). In Western Uganda, ginger rhizomes are chewed to induce labour during childbirth (Kamatenesi-Mugisha and Oryem-Origa 2007), and ginger rhizome is pounded and used in tea or boiled in porridge or milk and ingested to treat sexual impotence and erectile dysfunction (Kamatenesi-Mugisha and Oryem-Origa 2005). A decoction of fresh ginger rhizome is taken orally to treat coughs by the local communities around the Northern sector of Kibale National Park, Uganda (Namukobe et al. 2011). In Libya, ginger is used as aphrodisiac (De Natale 2012). In Gabon, maceration of pounded roots is taken or the rhizome is chewed to treat coughing and pounded rhizome is used to treat diaper rash in children (Bourobou-Bourobou et al. 2009).

In Nigeria (Bauchi State), ginger rhizome is used to treat coughs and diarrhoea (Adamu et al. 2005) and is chewed to treat toothache (Etkin 1981). The Ondo people in Nigeria employ ginger rhizome for headache, stomach ache, aerophagia, malaria (Odugbemi et al. 2007), yellow fever and indigestion (Gill and Akinwumi 1986). In Southwestern Nigeria, a concoction of ginger rhizome is ingested for cancer (Ashidi et al. 2010); ginger rhizome is macerated and used to treat diabetes (Abo et al. 2008). In Akwa Ibom State, Nigeria, ginger rhizome is chewed to treat cough, stomach ache and catarrh (Ajibesin et al. 2008). In Ijesa Land of Osun State, Nigeria, ginger stem is used for piles (Kayode et al. 2008). In Lagos State, Nigeria, ginger is used for cough, typhoid fever, malaria, asthma, obesity, piles, cold, rheumatism, hepatitis, liver diseases and digestive disorders and as stimulant (Olowokudejo et al. 2008). In Nigeria (Ogun State), ginger rhizome is taken once daily for typhoid, and a mixture of onion, ginger rhizome and root/bark of *Garcinia kola* is taken twice daily for asthma (Erinoso and Aworinde 2012). In the Niger Delta area of Nigeria, ginger rhizome is employed for toothache, congested nostrils, coughs, cold, influenza and flu, asthma, stomach ailments, rheumatism, piles, hepatitis and liver problems (Ndukwu and Ben-Nwadibia n.d).

In the municipality of Nkonkobe, South Africa, fresh or dried ginger is chewed to relieve throat infections (Dyubeni and Buwa 2012). Ginger is used to treat abdominal pains and to manage opportunistic fungal infections (Aspergillosis) in HIV/AIDS patients in the Amathole District of the Eastern Cape Province, South Africa (Otang et al. 2013). Ginger rhizome juice is taken orally to treat intestinal worm infestation in the Republic of Guinea (Keita et al. 1999).

In the Congo basin, a decoction of *Abrus precatorius*, *Mondia whitei*, *Allium sativum* and *Zingiber officinale* is used to treat cough; ginger rhizome is cooked with tomatoes, lemons, fish and a bit of salt to treat intestinal worms; leaves of *Ocimum basilicum* and *Mondia whitei*, *Allium sativum*, *Dorstenia psilurus* and ginger are pounded, boiled, filtered and taken to treat hookworms; pounded mixture of *Cyperus articulatus*, ginger, *Cola acuminata* (seeds), *Mangifera indica*

(barks), *Allium sativum*, *Piper nigrum* (fruits), *Capsicum frutescens* (fruits), *Aframomum melegueta* (fruits), *Croton mubango* (barks), unrolled leaf of tobacco, roots of *Landolphia owariensis*, *Mondia whitei* and *Aframomum alboviolaceum* is allowed to stand overnight and drunk to cure haemorrhoids; ginger rhizomes are pounded with traditional salt and the resulting paste is introduced into the anus as a suppository to treat haemorrhoids; pounded ginger rhizomes are used to relieve abdominal pain by rectal administration; ginger rhizomes are pounded with salt, and the aqueous maceration is used as enema or taken orally for blennorrhoea, and a decoction of rhizome with pepper and salt is ingested as an aphrodisiac and appetite stimulant (Kembelo 2003). In the Democratic republic of Congo (e.g. Zaïre), the leaves are macerated and ingested to treat piles and backache (Nyakabwa and Dibaluka 1990). In Benin, ginger rhizome is used to treat headache, cough, joint pains and hernia and is used as a restorative/stimulant and aphrodisiac (Souza and Dossa 1988).

In Malaysia, ginger is taken as a warm, stimulating carminative and applied to the skin as an efficient rubefacient and counterirritant (Burkill 1966). Ginger is chewed or sucked as an antiemetic, and a decoction is taken to treat stomach ache and given to women after childbirth. The Medical Book of Malayan Medicine recommended ginger for intestinal problems in tonics, for congestion of the liver, in a panacea for puerperal infections and for headache and extreme bodily pains, while *halia padi* is recommended for coughs and diseases of the female generative system. Ginger pickle is used in a draught for puerperal infection and in a lotion for rheumatism. Ginger plaster is used externally on the abdomen to treat intestinal troubles. Ginger races, 'halia bara'. 'halia padi' and 'halia udang,' enter into a powder compound which is externally applied over a Malay woman's body after childbirth, together with a lotion made with vinegar. Also bathing in ginger water is carried out for fever. The Chinese people take a hot drink of ginger and brown sugar for its diuretic effect. A liniment containing *Datura*, ginger and onion is used for pain along the spinal cord; 'halia bara' is also applied to sore gums. 'Halia bara' is used with pepper as an abortifacient. The Malays consumed the leaves as food for

indigestion and those of 'halia udang' for rheumatism. Leaves pounded may be used as a poultice for headache and ginger juice may be sprinkled over a child's face for ague. Young shoots may be made into a lotion for rheumatism.

In the Philippines, pounded ginger rhizome, alone or mixed with oil, is used as revulsive and antirheumatic (Stuart 2014). For rheumatism, roasted rhizome is pounded and mixed with oil and applied locally. As digestive aid and for flatulence and tympanism, decoction of the rhizome is drunk as tea. For sore throat and hoarseness, warm decoction of the rhizome is drunk as ginger tea (salabat); a piece of small rhizome is chewed for the same. Chewing ginger is said to diminish biliousness and delirium; relieve sore throat, hoarseness and aphonia; and increase the flow of saliva. In Chinese folk medicine, pulverised fresh ginger is used for baldness and vitiligo. Juice from fresh root is used for treatment of burns (Stuart 2014).

Menaut (1929) recorded that in Indochina, the rhizomes were prescribed for tuberculosis, general fatigue and affections of the uterus, and ginger cataplasm was good for furuncles and, when mixed with oil, was antirheumatic. Dalziel (1955) asserts that the leaves, pounded and warmed, are applied as a poultice to bruises.

According to Nadkarni (2001), ginger has stomachic, carminative, stimulant, diaphoretic, sialogogue and digestive properties. Dry ginger is much used in India as a carminative adjunct along with black pepper and long pepper. Ginger is extremely valuable in dyspepsia, flatulence, colic, vomiting, spasms and other painful affections of the stomach and the bowels unattended by fever. It is also very effective for colds, coughs, asthma, dyspepsia and indigestion. Ginger taken with rocksalt before meals is said to clean the throat, increase the appetite and produce an agreeable sensation. People suffering from biliousness and delirium, sore throat, hoarseness and loss of voice are sometimes benefited by chewing a piece of ginger, thus producing a copious flow of saliva. Drying ginger is generally used as a corrective adjunct to purgatives to prevent nausea and griping. The juice expressed from fresh ginger in gradually increasing doses is a strong diuretic in

cases of general dropsy. Ginger juice is rubbed on and around the navel to cure all kinds of diarrhoea.

Other Uses

Landscape Plant

Ginger is often used in landscaping around subtropical homes.

Weedicide Activity

The rhizome, stem and leaf aqueous extracts of ginger at concentrations of 10, 20, 40 and 80 g/L inhibited seed germination, seedling growth, water uptake and lipase activity of soybean and chive compared with the control, and the degree of inhibition increased with the incremental extracts concentration (Han et al. 2008). The degree of toxicity of different ginger plant parts can be classified in order of decreasing inhibition as stem > leaf > rhizome. The results of this study suggested that rhizome, stem and leaf of ginger may contain water-soluble allelochemicals which could inhibit seed germination and seedling growth of soybean and chive.

Pest and Disease Control

Agarwal et al. (2001) isolated five compounds, gingerol, gingerone, dihydrogingerone, dehydrozingerone and dehydroshogaol, from ginger rhizome, all of which were reported to significantly inhibit hyphal growth of the potato pathogen *Rhizoctonia solani*. Dehydrozingerone imparted maximum antifungal activity ($EC_{50} = 86.49$ mg/l). The tested compounds also showed moderate insect growth regulatory (IGR) and antifeedant activity against *Spilosoma obliqua*. [6]-Dehydroshogaol exhibited maximum IGR activity ($EC_{50} = 3.55$ mg/ml). Studies showed that vacuum-distilled *Aframomum melegueta* and *Z. officinale* extracts were repellent towards adult maize weevil, *Sitophilus zeamais*, in both the absence and the presence of maize grains (Ukeh et al. 2009). Three major compounds in the behaviourally active

fractions of ginger were identified as 1,8-cineole, neral and geranial in a ratio of 5.48:1:2.13.

Comments

The leading ginger-producing countries in the world (tonnes) in 2012 are India 70,300; China 425,000; Nepal 255,208; Nigeria 156,000; Thailand 150,000; Indonesia 113,851; and Japan 55,000 tonnes (FAO [2014](#)).

Studies by Wang et al. ([2014](#)) found that 25.4 % of geographic accessions of ginger in China were mixploid with diploid and tetraploid cells, and 74.6 % of the accessions were diploid. No solid tetraploid or other polyploidy occurred in nature. Mixploid ginger was typed as a ‘giant ginger’ with stronger stems, fatter fingers, bigger rhizomes and fewer shoots, and the diploid was typed as ‘small ginger’ with thinner stems, more shoots and a smaller single finger and rhizomes. The single finger mass of ginger was the most important key morphological character distinguishing the mixploid from the diploid. Ginger from different geographical regions could be discriminated using key characteristic fingerprint based on gingerol derivatives using HPLC-DAD combined with chemometrics (Yudthavorasit et al. [2014](#)). The proposed method would be useful for quality control of ginger in case of origin labelling and to assess food authenticity issues.

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Zingiber spectabile

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Scientific Name

Zingiber spectabile Griffith

Synonyms

No synonyms recorded.

Family

Zingiberaceae

Common/English Names

Beehive Ginger, Black Gingerwort, Champagne Beehive, Malaysian Ginger, Nodding Ginger

Vernacular Names

German: Ansehnlicher Ingwer, Nickender Ingwer

Malaysia: Tepus Tanah, Tepus Tundok, Chadak, Tepai, Tepus Halia, Tepus Haliya Puar, Langkinang (Temuan Orang Asli)

Portuguese: Gengibre-magnífico, Sorvetão

Spanish: Microfono

Thai: Changoe, Dakngoe

Origin/Distribution

The plant is found in Peninsular Malaysia and Peninsular Thailand.

Agroecology

Its habitat is in the warm and wet tropical rainforest, occurring along trails, streams and edges of forests up to 1000 m elevation. It thrives in full shade to partial shade, in moist, humus-rich, well-drained fertile soil.

Edible Plant Parts and Uses

Leaves and rhizomes are sometimes used for flavouring (Burkill 1966; Tanaka 1976). The leaves and rhizomes are used to flavour food. Its young rhizomes are sliced, soaked in vinegar and used as an appetiser (Jones 1993). The young tender shoots are eaten as ulam, fresh as salad.

Botany

Zingiber spectabile is a clumping herbaceous plant with branched underground fleshy rhizome. Leafy pseudostems are 2–3.5 m high, and basal leafless stem is up to 1 m high. Leaf sheath is sparsely pilose with scarious margin, and ligule is deeply bilobed and is broad and pale green in colour. Leaf lamina is lanceolate and is 30–50 cm by 6–10 cm long and glabrous or slightly hairy at the base. Inflorescence is a cylindrical spike, beehive like, 10–30 cm by 6–7 cm long with rounded apex borne by a radical erect scape, which is 20–40 cm long (Plate 1). Bracts are obovate, turning red from yellow through orange, fleshy and curved outwards with edge incurved forming pouches (Plate 2); bracteole is linear and 40 mm long; calyx is up to 35 mm long and cream to pinkish in colour; corolla is 70 mm long and yellow in colour; dorsal

lobes are larger than lateral lobes; labellum is 40–60 mm long and dark purple with yellow spots; mid-lobe is shorter than lateral corolla lobes; apex is cleft; stylode is slender and free to base, not surrounding the style; stigma is not dilated, round, white in colour and fringed with hairs; filament is absent; and anther is yellow, anther appendage is purple and 1.5 cm long. Its fruit is an ellipsoid capsule, 3 cm by 1 cm long and sparsely pilose. Seeds are up to six in each loculus, are black when ripe, are ellipsoid, are 6 mm long and covered 2/3 from base by a white aril with fimbriate or lobed edge.



Plate 1 Large flower spikes at the terminal of long scapes



Plate 2 Flower spike with yellow bracts turning red and mucilage in the pouches

Nutritive/Medicinal Properties

Rhizome Phytochemicals

Nine sesquiterpenes, zerumbone, humulene, humulene 9,10-epoxide (humulene epoxide III), buddledone A, humulene 6,7-epoxide (humulene epoxide II), 6-methoxy-2*E*,9*E*-humuladien-8-one, zerumbone oxide (zerumbone epoxide), humulene 2,3;6,7-diepoxy or a racemate and kobusone, and eight flavonoids, kaempferol-3-*O*-methylether, kaempferol-3-*O*-(3,4-*O*-diacetyl- α -rhamnopyranoside), kaempferol-3-*O*-(2,3-*O*-diacetyl- α -rhamnopyranoside), kaempferol-3-*O*-(2,4-*O*-diacetyl- α -rhamnopyranoside), kaempferol-3-*O*-(4-*O*-acetyl- α -L-rhamnopyranoside), kaempferol-3-*O*-(3-*O*-acetyl- α -rhamnopyranoside), kaempferol-3-*O*-(2-*O*-acetyl- α -rhamnopyranoside) and kaempferol-3-*O*- α -L-rhamnopyranoside, were isolated from *Zingiber spectabile* rhizome (Sadhu et al. 2007).

Zerumbone was isolated from fresh rhizomes of *Zingiber zerumbet* Smith in yields of 0.3–0.4 % by simple steam distillation and recrystallisation (Kitayama et al. 1999). Several zerumbone dibromide derivatives were derived from zerumbone and found to be selective inhibitors of the growth of Gram-positive bacteria (Kitayama et al. 2001b). The achiral sesquiterpene zerumbone was found to have unique functionality and reactivity, making it a potential starting material for conversion to useful compounds such as paclitaxel, provided that it can easily be transformed to chiral derivatives such as zerumbone (Kitayama et al. 2002). Asymmetric epoxidation of zerumbone yielded single bisepoxides (=)-3 and (-)-3 with nearly 100 % enantiomeric purity (Kitayama et al. 2001a). Zerumbone and its 6,7-epoxide reacted with ammonia and dimethylamine regio- and stereospecifically, affording four monoamines (Kitayama et al. 2003).

A dimeric flavonol glycoside for which the name was designated as spectraflavoside A with the structure kaempferol-3-*O*-(4''-*O*-acetyl)- α -l-rhamnopyranoside-(I-6,II-8)-kaempferol-3-*O*-(4''-*O*-acetyl)- α -L-rhamnopyranoside, along

with kaempferol and its four acetylramnosides kaempferol-3-*O*-(3'',4''-di-*O*-acetyl)- α -L-rhamnopyranoside, kaempferol-3-*O*-(2'',3''-di-*O*-acetyl)- α -L-rhamnopyranoside, kaempferol-3-*O*-(2'',4''-di-*O*-acetyl)- α -L-rhamnopyranoside and kaempferol-3-*O*-(4''-*O*-acetyl)- α -L-rhamnopyranoside, kaempferol, demethoxycurcumin and curcumin, was isolated from *Zingiber spectabile* rhizome (Sivasothy et al. 2012b).

Nineteen constituents were identified in the rhizome essential oil and labda-8(17),12-diene-15,16-dial (24.3 %), terpinen-4-ol (23.7 %), α -terpineol (13.1 %) and β -pinene (10.3 %) as the major components (Sirat and Leh 2001). *Z. spectabile* rhizome oil was more pungent than the leaf oil (Sivasothy et al. 2012a). Fifty-six constituents accounting for 91.0 % of the sample were identified in the rhizome oil. The rhizome oil was found to be rich in sesquiterpenoids (76.4 %) but with a higher proportion of oxygen-containing compounds. Zerumbone was the most abundant component, accounting for more than half of the sample (59.1 %). Except for α -humulene (6.2 %), humulene epoxide II (5.4 %), caryophyllene oxide (2.1 %), γ -eudesmol (1.9 %) and β -caryophyllene (1.0 %), the other sesquiterpenoids were present at concentrations <1.0 %. Forty-one monoterpenoids (14.6 %) were identified as minor components, with only 1,8-cineole being present at appreciable quantity of 5.8 %.

Leaf Phytochemicals

Z. spectabile leaf oil was found to be rich in monoterpenoids being mainly characterised by α -pinene (7.44–11.42 %), β -pinene (35.85–49.35 %) and β -phellandrene (16.59–18.45 %) (Vahairut-Lechat et al. 1996). Fifty-four compounds constituting 87.2 % of the sample were identified in the essential oil of *Z. spectabile* leaves which was dominated by 19 sesquiterpenoids (53.4 %) made up largely of β -caryophyllene (21.3 %), β -elemene (12.5 %), caryophyllene oxide (6.6 %) and germacrene D (2.9 %) (Sivasothy et al. 2012a). Twenty-six monoterpenoids (29.3 %) were identified, with appreciable amounts of α -pinene (7.7 %), β -pinene (7.6 %), *trans*- β -ocimene (2.7 %) and δ -3-carene (2.0 %). Six

aliphatic aldehydes (4.0 %) and three aliphatic alcohols (0.5 %) accounted for the remaining identified compounds

Stem Phytochemicals

Z. spectabile stem oil was found to be rich in monoterpenoids being mainly characterised by α -pinene (10.78–13.69 %), β -pinene (23.52–26.17 %) and β -phellandrene (23.11–38.05 %) (Vahairut-Lechat et al. 1996).

Flower Phytochemicals

Z. spectabile inflorescence oil was found to be rich in β -phellandrene (45.3 %), α -pinene (13.4 %) and β -pinene (11.0 %) (Zoghbi and Andrade 2005).

Pharmacological Properties

Zerumbone present in zingiberaceous species including *Z. spectabile* had been reported to possess multiple biomedical properties, such as antiproliferative, antioxidant, anti-inflammatory and anticancer activities (Rahman et al. 2014a, b). Zerumbone showed strong reactivity with good chemo-, regio- and stereoselectivity (Kitayama 2011). It could be converted into various compounds with various structures and has potential uses in natural material-related diversity-oriented synthesis.

Antioxidant Activity

Leaves of *Z. spectabile* had total phenolic content (TPC) of 242 mg GAE/100 g and ascorbic acid equivalent antioxidant capacity (AEAC) of 121 mg AA/100 g and rhizome TPC of 157 mg GAE/100 g and AEAC of 124 mg AA/100 g (Chan et al. 2008). Ferrous ion-chelating (FIC) abilities of leaves were higher than for the rhizomes. Among the ten *Zingiber* species, *Z. spectabile* had the lowest total phenolic content of 1.34 mg GAE/g DW and exhibited the lowest antioxidant activity in the DPPH (2,2-diphenyl-1-picrylhydrazyl) assay with IC₅₀ of 39.34 mg/ml and in the ABTS (2,2'-azinobis-(3-

ethylbenzothiazoline-6-sulphonic acid) diammonium salt) assay with IC₅₀ of 60.80 mg/ml (Kantayos and Paisooksantivatana 2012).

The dimeric flavonol glycoside, spectraflavoside A isolated from the rhizome, was found to be a potent iron-chelating agent (Sivasothy et al. 2012b). Of the compounds isolated from the rhizome, the highest antioxidant activity in all assays was demonstrated by kaempferol (>89 %), followed by curcumin and demethoxycurcumin (Sivasothy et al. 2013). These two curcuminoids were found to have the potential in extending the shelf life of different food products as compared with other tested compounds due to the higher antioxidant activities that ranged from 56.27 % in the FRAP assay to 77.27 % in the β -carotene bleaching assay.

Anticancer Activity

In-Vitro Studies

Hoffman et al. (2002) proposed a redox-regulated mechanism to account for zerumbone's ability to suppress cancer cell proliferation. Prasannan et al. (2010) reported zerumbone to be multitargeted in nature via various key signalling pathways and thus to have desirable modulating property for different cancer therapies. Zerumbone inhibited the proliferation of human colonic adenocarcinoma cell lines (LS174T, LS180, COLO205 and COLO320DM) in a dose-dependent manner, while the growth of normal human dermal (2F0-C25) and colon (CCD-18Co) fibroblasts was less affected (Murakami et al. 2002). It also induced apoptosis in COLO205 cells, as detected by dysfunction of the mitochondria transmembrane, annexin V-detected translocation of phosphatidylserine and chromatin condensation. Zerumbone effectively suppressed 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced superoxide anion generation from both NADPH oxidase in dimethylsulfoxide-differentiated HL-60 human acute promyelocytic leukaemia cells and xanthine oxidase in AS52 Chinese hamster ovary cells. Xian et al. (2007) demonstrated that zerumbone significantly suppressed the proliferation of promyelocytic leukaemia NB4 cells among several leukaemia

cell lines, but not human umbilical vein endothelial cells (HUVECs), by inducing G2/M cell cycle arrest followed by apoptosis via Fas/CD95- and mitochondria-mediated pathways with IC₅₀ of 10 µM. Zerumbone exerted cytotoxic effect via apoptosis against cancer cells of T-cell acute lymphoblastic leukaemia, CEM-ss with an IC₅₀ of 8.4 µg/ml (Abdelwahab et al. 2011).

Zerumbone caused cell cycle arrest in colonic HT-29 cancer cells at G0/G1 for 10 and 12.5 mM and G2/M for 25 mM after 24 h at concentrations of 10–25 mM of zerumbone, and a concentration-dependent increase in apoptosis (2–6 % of viable cells) was observed after 48 h using the same concentration range (Kirana et al. 2003). Sadhu et al. (2007) reported zerumbone to potently inhibit the growth of colon carcinoma SW480 cells in-vitro with an IC₅₀ value of 13 µg/mL. Yodkeeree et al. (2009) found that zerumbone potentiated tumour necrosis factor-related apoptosis-inducing ligand (TRAIL)-induced apoptosis in human HCT116 colon cancer cells through the reactive oxygen species-mediated activation of extracellular signal-regulated kinase 1/2 and p38 mitogen-activated protein kinase leading to death receptors DR4 and DR5 induction and resulting in enhancement of the anticancer effects of TRAIL. Edagawa et al. (2014) demonstrated that the stress response gene transcription factor 3 (ATF3) was required for endoplasmic reticulum stress-mediated death receptor 5 (DR5) induction upon zerumbone and celecoxib in human p53-deficient colorectal cancer cells. Exogenous expression of ATF3 caused a more rapid and elevated expression of DR5, resulting in enhanced sensitivity to apoptotic cell death by tumour necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL)/zerumbone or TRAIL/celecoxib. Cell proliferation, vascular endothelial growth factor (VEGF) expression and NF-κB activity in six gastric cancer AGS cell lines were all significantly inhibited by zerumbone (Tsuboi et al. 2014). Moreover, the tube formation area of HUVECs was increased by coculture with AGS cells, and this effect was inhibited by zerumbone. Both VEGF expression and NF-κB activity in AGS cells were reduced by treatment with zerumbone, thereby inhibiting

angiogenesis. The results indicated that zerumbone may become a new antiangiogenic and antitumour drug in the treatment of gastric cancer. Five zerumbone derivatives showed potent antiproliferative activity against cholangiocarcinoma KKKU-100 cell line with an IC₅₀ value of 16.44 μ M (Songsiang et al. 2010).

Zerumbone significantly displayed antiproliferative effect towards human cancer cell lines including the human liver cancer HepG2 cell line (IC₅₀ of 3.45 μ g/ml), human breast cancer MCF-7 cell line IC₅₀ of 3.73 μ g/ml), human ovarian cancer Caov-3 cell line (IC₅₀ of 4.73 μ g/ml) and human cervix cancer HeLa cell line (IC₅₀ of 5.43 μ g/ml) (Alwi et al. 2007). The action of zerumbone appeared to be cytoselective as its effect on the proliferation of non-malignant Chang liver cells generated IC₅₀ value that was much higher than that obtained for all zerumbone-treated cancer cell lines (10.96 μ g/ml). The antiproliferative effect of zerumbone was also shown to occur via apoptosis. Zerumbone significantly increased apoptosis of the HepG2 cells in a time-course manner, and its effect was generally more potent than cisplatin. Results of MTT assay showed that zerumbone exerted less effect on normal Chinese hamster ovary cells compared to cancer cells; lower IC₅₀ values for apoptosis were observed on human cervix cancer HeLa cells (Abdelwahab et al. 2009). Cytological observations showed nuclear and chromatin condensation, cell shrinkage, multinucleation, abnormalities of mitochondrial cristae, membrane blebbing, holes, cytoplasmic extrusions and formation of apoptotic bodies. Also, zerumbone increased the cellular level of caspase-3 on the treated HeLa cells.

Zerumbone was found to induce the apoptotic process in human liver cancer HepG2 cells through the up- and downregulation of Bax/Bcl-2 protein independently of functional p53 activity (Sakinah et al. 2007). Zerumbone significantly showed an antiproliferative activity upon HepG2 cells with an IC₅₀ of 3.45 μ g/ml. It also inhibited the proliferation of non-malignant Chang liver and MDBK cell lines; however, the IC₅₀ obtained was higher compared to the IC₅₀ for HepG2 cells (>10 μ g/ml). Kamalidehghan et al.

(2012) found that DNA fragmentation was not associated with apoptosis in zerumbone-induced human hepatocellular liver carcinoma (HepG2) cells. Encapsulation of zerumbone with hydroxypropyl- β -cyclodextrin (HP- β -CD) enhanced its solubility, making it more tolerable in the human body (Muhammad Nazri et al. 2013). The encapsulated complex was found to induce apoptosis in liver hepatocellular HepG2 cells, via caspase 8/BID cleavage switch and modulating Bcl2/Bax ratio.

Zerumbone was also found to inhibit interleukin-6 and induced apoptosis and cell cycle arrest in ovarian and cervical cancer cells Caov-3 and HeLa, respectively, in a dose-dependent manner (Abdelwahab et al. 2012). Zerumbone (10 ~ 50 μ M) induced death of human glioblastoma multiforme (GBM8401) cells in a dose-dependent manner by suppressing I κ B kinase α (IKK α), protein kinase B (Akt) and forkhead box protein O1 (FOXO1) phosphorylation and caspase-3 activation (Weng et al. 2012).

Treatment with zerumbone induced apoptosis of pancreatic carcinoma PANC-1 cells through p53 signalling pathway (Zhang et al. 2012). Shamoto et al. (2014) showed in in-vitro studies zerumbone suppressed pancreatic cancer PaCa-associated angiogenesis through mRNA expression and protein secretion of angiogenic factors and nuclear factor- κ B (NF- κ B) activity.

Exposure of human renal clear cell carcinoma (RCC) 786-0 and 769-P cell lines to zerumbone resulted in cell viability inhibition, accompanied by DNA fragmentation and increased apoptotic index (Sun et al. 2013). The zerumbone-induced apoptosis might be related to the activation of the caspase cascade and deregulation of the Gli-1/Bcl-2 pathway. Zerumbone suppressed signal transducer and activator of transcription 3 (STAT3) activation in a dose- and time-dependent manner in renal cell carcinoma (RCC) cells (Shanmugam et al. 2014). When administered i.p., zerumbone inhibited STAT3 activation in tumour tissues and the growth of human RCC xenograft tumours in athymic nu/nu mice without any side effects.

Zerumbone downregulated the expression of CXCR4 on HER2-overexpressing breast cancer cells in a dose- and time-dependent manner (Sung et al. 2008). The downregulation of CXCR4 was not due to proteolytic degradation but rather to transcriptional regulation, as indicated by downregulation of mRNA expression, inhibition of nuclear factor-kappaB activity and suppression of chromatin immunoprecipitation activity. Suppression of CXCR4 expression by zerumbone correlated with the inhibition of CXCL12-induced invasion of both breast and pancreatic cancer cells. Zerumbone treatment caused a dose-dependent decrease in viability of MCF-7 and MDA-MB-231 human breast cancer cells in association with G(2)/M phase cell cycle arrest and Bax/Bak-mediated apoptosis induction in-vitro and retarded growth of MDA-MB-231 orthotopic xenografts in-vivo (Sehrawat et al. 2012). Zerumbone decreased interleukin IL-1 β -induced IL-8 and MMP-3 expression and IL-1 β -induced cell migration and invasion in human triple negative breast cancer Hs578T and MDA-MB231 cells (Han et al. 2014). Inhibition of cell migration as well as apoptosis induction of human breast cancer MDA-MB-231 cells resulting from zerumbone exposure was significantly augmented by the knockdown of Notch2 protein (Sehrawat et al. 2014). The study found that Notch2 activation by zerumbone inhibited its pro-apoptotic and anti-migratory response at least in breast cancer cells.

Results of studies using mouse epidermal JB6 cells by Shin et al. (2011) suggested that upregulation of heme oxygenase-1 (HO-1) expression by zerumbone was mediated through activation of NF-E2-related factor 2 (Nrf2), which provided a mechanistic basis for the chemopreventive effects of this sesquiterpene on mouse skin carcinogenesis.

Studies by Takada et al. (2005) found that zerumbone inhibited the activation of nuclear factor NF-kappaB and NF-kappaB-regulated gene expression induced by carcinogens such as okadaic acid, cigarette smoke condensate, phorbol myristate acetate and H₂O₂ and that this inhibition may provide a molecular basis for the prevention and treatment of cancer by zerumbone. Zerumbone's inhibition of expression of these NF-kappaB-regulated genes also correlated with the

suppression of tumour necrosis factor (TNF)-induced invasion activity. Studies by Sobhan et al. (2013) confirmed that mitochondrial permeabilisation and cytochrome c-dependent caspase activation dominated in zerumbone-induced cell death. They found, in general, mammary epithelial cells, endothelial progenitor cells and smooth muscle cells were relatively resistant to zerumbone-induced cell death with lesser reactive oxygen species (ROS) accumulation than cancer cells.

Animal Studies

Murakami et al. (2004b) found that pretreatment of zerumbone markedly suppressed dimethylbenz[a]anthracene-induced tumour incidence, tumour diameter and tumour number in ICR mice. Their results revealed zerumbone to be a promising agent for the prevention of both tumour-initiating and tumour-promoting processes, through induction of antioxidative and phase II drug-metabolising enzymes as well as attenuation of pro-inflammatory signalling pathways. Zerumbone at a dosage of 2 mg/kg inhibited the growth of P-388D cells, induced DNA fragmentation in culture and significantly prolonged the life of P-388D-bearing CDF mice (Huang et al. 2005). In addition, zerumbone inhibited the growth of a human leukaemia cell line, HL-60 cells, in a time- and concentration-dependent manner, by inducing G2/M cell cycle arrest in HL-60 cells in a time- and concentration-dependent manner and decreasing the cyclin B1/cdk 1 protein level.

Kim et al. (2009) found dietary administration of zerumbone effectively suppressed mouse colon and lung carcinogenesis through multiple modulatory mechanisms such as growth inhibition, induction of apoptosis, suppression of inflammation and expression of NF-kappaB and heme oxygenase (HO)-1 that were involved in carcinogenesis in the colon and lung.

In-vivo studies indicated that zerumbone at 16 mg/kg and cisplatin at 10 mg/kg exerted a regressing effect on cervical intraepithelial neoplasia (Abdul et al. 2009). This combination modulated the serum level of interleukin 6 when compared with that in mice treated with isotonic sodium chloride

solution. Treatment of zerumbone resulted in regression of cervical intraepithelial neoplasia by apoptosis resembling cisplatin effect in cervical tissues from female BALB/c mice treated prenatally with diethylstilboestrol (Abdelwahab et al. 2010). Zerumbone modulated the expression of Bax protein and Bcl-2 gene.

Rahman et al. (2013) reported that in-vitro drug release of zerumbone from zerumbone-loaded nanostructured lipid carrier (ZER-NLC) was 46.7 % and for a pure zerumbone dispersion was 90.5 % over 48 h. Using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay in human T-cell acute lymphoblastic leukaemia (Jurkat) cells, the half maximal inhibitory concentration (IC_{50}) of ZER-NLC was 5.64 $\mu\text{g/mL}$ and for free zerumbone was 5.39 $\mu\text{g/mL}$ after 72 h of treatment. The results strongly suggested that ZER-NLC had potential as a sustained-release drug carrier system for the treatment of leukaemia. They also showed that the antiproliferative effect of ZER-NLC on acute human lymphoblastic leukaemia (Jurkat) cells was through the intrinsic apoptotic pathway via activation of caspase-3 and caspase-9, release of cytochrome c from the mitochondria into the cytosol and subsequent cleavage of poly(adenosine diphosphate-ribose) polymerase (PARP) (Rahman et al. 2014a).

Antimutagenic/Antigenotoxic Activity

In novel bioassay systems, in which either phorbol ester-stimulated, differentiated HL-60 human leukaemia cells or lipopolysaccharide (LPS)-stimulated RAW 264.7 murine macrophages were cocultured with AS52 Chinese hamster ovary cells, compounds like auraptene, nobiletin and zerumbone from Asian vegetables, and fruits were found to be highly antimutagenic (Murakami and Ohigashi 2006). They suggested that the co-culture systems may be useful for identifying potentially anticarcinogenic inhibitors of reactive oxygen and nitrogen oxide species (RONS) generation. Two zerumbone analogues azazerumbone 1 and azazerumbone 2 exhibited strong protection against sodium azide-induced

mutagenicity of *Salmonella typhimurium* strains TA 98 and TA 1531 (Santosh Kumar et al. 2013). Azazerumbone 2 showed higher antimutagenic activity than azazerumbone 1.

Chromosomal aberration assay showed that zerumbone was not clastogenic in cultured human peripheral blood lymphocytes (PBL), when compared to untreated control, but micronucleus test results showed a dose-dependent increase in micronucleus formation (Al-Zubairi et al. 2010). The overall clastogenic effect of zerumbone on human PBL was statistically not significant. It was concluded that zerumbone was a cytotoxic but not a clastogenic substance in human PBL.

Antiviral Activity

Z. spectabile methanol extract inhibited Epstein–Barr virus (EBV) activation induced by a phorbol ester promoter, 12-*O*-hexadecanoylphorbol-13-acetate (HPA) (Koshimizu et al. 1988). Zerumbone exhibited HIV-1 inhibitory and cytotoxic activities (Dai et al. 1997). Zerumbone was found to be a potent inhibitor of tumour promoter 12-*O*-tetradecanoylphorbol-13-acetate-induced Epstein–Barr virus activation with an IC_{50} value of 0.14 μ M (Murakami et al. 1999). Alpha-humulene lacking the carbonyl group at the 8-position in zerumbone was inactive ($IC_{50} > 100 \mu$ M), while 8-hydroxy-alpha-humulene was markedly active ($IC_{50} = 0.95 \mu$ M). Zerumbone was found to suppress tumour promoter 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced Epstein–Barr virus activation in a potent manner (Muakami et al. 2002).

Antimicrobial Activity

Zingiber spectabile rhizome oil exhibited weak activity against *Escherichia coli*, *Salmonella enteritidis*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella flexneri*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA), but the leaf oil was inactive against all the tested bacteria (Sivasothy et al. 2012a). Two curcuminoids curcumin and demethoxycurcumin from

the rhizome inhibited in-vitro growth of eight food-borne bacteria: *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Salmonella typhimurium*, *Vibrio parahaemolyticus*, *Bacillus cereus*, *Bacillus licheniformis* and *Staphylococcus aureus* with minimum inhibitory concentration (MIC) ranging from 62.50 to 500 µg/ml (Sivasothy et al. 2013). *Vibrio parahaemolyticus* and *Staphylococcus aureus* were the most sensitive bacteria. Curcumin exhibited in-vitro antibacterial activity with MIC values 175 µg/ml, 129 µg/ml, 219 µg/ml, 217 µg/ml, 163 µg/ml, 293 µg/ml and 216 µg/ml against *Pseudomonas aeruginosa*, *Bacillus subtilis*, methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli*, *Enterococcus faecalis* and *Klebsiella pneumoniae*, respectively (Gunes et al. 2014).

Zerumbone ring-opening derivative, 4 ($10E/10Z = 3/2$), inhibited autophosphorylation of the essential histidine kinase YycG existing in *Bacillus subtilis* constituting a two-component system (Kitayama et al. 2004). However, it did not inhibit drug-resistant bacterium such as MRSA (methicillin-resistant *Staphylococcus aureus*) and VRE (vancomycin-resistant *Enterococcus*) (Kitayama et al. 2007). Two zerumbone analogues azazerumbone 1 and azazerumbone 2 were synthesised from zerumbone oxime (Santosh Kumar et al. 2013). Azazerumbone 2 exhibited better antibacterial activity especially against *Bacillus cereus* than zerumbone. *Yersinia enterocolitica* was found to be the most resistant.

Antiosteoporotic Activity

Zerumbone inhibited RANKL (receptor activator of nuclear factor-kappaB (NF-kappaB) ligand)-induced NF-kappaB activation in mouse monocyte, an osteoclast precursor cell, and also inhibited the osteoclast formation induced by human breast tumour cells and by multiple myeloma cells (Sung et al. 2009). In-vivo, zerumbone decreased osteolysis in a dose-dependent manner in MDA-MB-231 breast cancer tumour-bearing athymic nude mice. The results indicated zerumbone to be an effective blocker of RANKL-induced NF-kappaB activation and of osteoclastogenesis induced by RANKL and

tumour cells, suggesting its potential as a therapeutic agent for osteoporosis and cancer-associated bone loss.

Hepatoprotective Activity

Fakurazi et al. (2008) reported that pretreatment of zerumbone for 2 weeks significantly suppressed ethanol-induced fatty liver development and injury in rats following ethanol 50 % (v/v) administration. They also found that pretreatment of rats with zerumbone for 14 days was protected against paracetamol hepatic intoxication (Fakurazi et al. 2009). Twenty-four hours after paracetamol administration, the levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) were found to be reduced in rats that were pretreated with zerumbone compared to group that was treated with paracetamol only. Correspondingly, there was no hepatocellular necrosis observed in rats that were pretreated with zerumbone.

The study by Taha et al. (2010) showed that zerumbone protected the rat liver from the carcinogenic effects of diethylnitrosamine (200 mg/kg) and dietary 2-acetylaminofluorene by reducing oxidative stress, inhibiting proliferation and inducing mitochondria-regulated apoptosis. Erenoğlu et al. (2011) reported that treatment with curcumin reduced bile duct ligation-induced cholestatic liver injury, bile duct proliferation and fibrosis in male Wistar rats.

After treatment of Syrian golden hamsters fed on high-fat diet with zerumbone, the plasma levels of total cholesterol (TC) and triglycerides (TGs) and the contents of TC and TG in hepatic tissue as well as homeostasis model assessment of insulin resistance were lowered, especially in the zerumbone-treated group (Tzeng et al 2013a). Also, steatosis and inflammation in the liver of zerumbone-treated groups were improved. Zerumbone exhibited the ability to decrease hepatic mRNA levels of sterol regulatory element-binding protein-1c and its lipogenic target genes, such as fatty acid synthase, acetyl-CoA carboxylase 1 and stearoyl-CoA desaturase 1. The hepatic mRNA expression of peroxisome proliferator-activated receptor α , together with its target genes including

carnitine palmitoyltransferase-1, acyl-CoA oxidase and acyl-CoA oxidase 1, was also upregulated by zerumbone. The results implied a potential application of zerumbone in the treatment of nonalcoholic fatty liver disease.

Antidiabetic cum Nephropathic Activity

Zerumbone treatment of streptozotocin-induced diabetic nephropathic rats was found to markedly improve histological architecture in the diabetic kidney (Tzeng et al. 2013b). Hyperglycaemia induced p38 mitogen-activated protein kinase activation, leading to increased infiltration of macrophages and increased levels of interleukin (IL)-1, IL-6 and tumour necrosis factor- α were reversed by zerumbone treatment, which also decreased the expression of intercellular adhesion molecule-1, monocyte chemoattractant protein-1, transforming growth factor- β 1 and fibronectin in the diabetic kidneys.

Antihyperlipidemic Activity

Oral administration of zerumbone to high-fat diet (HFD)-induced hyperlipidemic hamsters for 8 weeks decreased plasma levels of TC, TG and LDL-C, as well as the concentrations of hepatic lipids, with a simultaneous increase in faecal lipids (Tzeng et al. 2014). The ratios of LDL-C/HDL-C and TC/HDL-C were elevated by zerumbone. Zerumbone was effective in ameliorating dyslipidemia by modulating the gene expression involving in the lipolytic and lipogenic pathways of lipid metabolism.

Antiatherosclerotic Activity

Eguchi et al. (2007) reported that zerumbone suppressed 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced lectin-like ox-LDL receptor-1 (LOX-1) mRNA expression in THP-1 human monocyte-like cells. Further, zerumbone attenuated the expression of SR-A, SR-PSOX and CD36 but not that of CD68 or CLA-1, leading to a blockade of DiI-acLDL uptake, while it also inhibited the transcriptional activities of activator protein-1 and nuclear factor-kappaB. The results indicated

zerumbone to be a potential phytochemical for regulating atherosclerosis with reasonable action mechanisms.

Anti-pancreatic Activity

In-vivo studies showed that pretreatment of zerumbone ameliorated the inflammatory parameters of cholecystokinin octapeptide-induced experimental pancreatitis in Wistar rats probably by interfering with I-kappaB degradation, but in the applied dose, it failed to influence the histology of the disease (Szabolcs et al. 2007). Treatment of pancreatic rat with zerumbone attenuated the severity of acute necrotizing pancreatitis and pancreatitis-induced hepatic injury, via inhibiting NF- κ B activation and downregulating the expression of ICAM-1 and IL-1 β (Deng et al. 2012).

Anti-inflammatory Activity

Studies by Murakami et al. (2003) found that oral feeding of zerumbone significantly lowered the levels of interleukin IL-1 β [inhibitory rate (IR) = 34 %], tumour necrosis factor (TNF)- α (IR = 29 %) and prostaglandin PGE(2) (IR = 73 %) and suppressed dextran sodium sulphate (DSS)-induced colitis, whereas nimesulide suppressed the histological changes induced by DSS without affecting inflammatory biomarkers. However, their treatment in combination, with different modes of actions, was most effective for suppressing these inflammatory biomarkers. Zerumbone suppressed expression of pro-inflammatory genes (COX-2 and iNOS) and induced detoxification genes (GSTP1 and NQO1) in RAW 264.7 macrophages (Ohnishi et al. 2009). Zerumbone and zerumbone 2,3-epoxide inhibited NF- κ B activation and NO production in LPS (lipopolysaccharide)-stimulated RAW 264.7 cells. The IC₅₀ of these compounds was 1.97 μ M and 30.11 μ M in the NF- κ B activation assay and 3.58 μ M and 34.7 μ M in the nitric oxide production assay, respectively (Giang et al. 2009). The combined lipopolysaccharide- and interferon- γ -stimulated protein expressions of inducible nitric oxide synthase and cyclooxygenase (COX)-2, together with the release of tumour necrosis factor- α , in RAW 264.7 mouse

macrophages were markedly diminished by zerumbone (Murakami et al. 2002). These suppressive events were accompanied with a combined decrease in the medium concentrations of nitrite and prostaglandin E(2), while the expression level of COX-1 was unchanged. It was demonstrated that intraperitoneal administration of zerumbone at a dose of 5, 10, 50 and 100 mg/kg produced significant dose-dependent inhibition of paw edema induced by carrageenan (Sulaiman et al. 2010). It was also demonstrated that zerumbone at similar doses significantly suppressed granulomatous tissue formation in cotton pellet-induced granuloma test.

Radioprotective Activity

The study by Aktas et al. (2012) demonstrated that curcumin prevented follicular atresia in ionising radiation-induced apoptosis in ovarian follicles in mice exposed to whole body ionising radiation. Pretreatment with zerumbone before radiation inhibited the binding affinity between HSP27 and apoptotic molecules, such as cytochrome c and PKC δ , and induced sensitization in-vitro and in an in-vivo xenografted nude mouse system (Choi et al. 2011). The results suggested that altered cross-linking of HSP27 by ZER is a good strategy for abolishing HSP27-mediated resistance.

Locomotor Reduction Activity

Zerumbone; α -humulene (2); tetrahydrozerumbone stereoisomers, viz. (2*R*)-tetrahydrozerumbone, (2*S*)-tetrahydrozerumbone and (2*RS*)-tetrahydrozerumbone; and its tetrahydrozerumbone derivatives, viz. (1*RS*,2*RS*)-*cis*-tetrahydrozerumbol, (1*RS*,2*RS*)-*trans*-tetrahydrozerumbol, (1*RS*,2*RS*)-*cis*-tetrahydrozerumbyl acetate, and (1*RS*,2*RS*)-*trans*-tetrahydrozerumbyl acetate, were obtained from the rhizome of *Z. zerumbet* (Ogawa et al. 2014). Inhalation of zerumbone and its tetrahydrozerumbone derivatives by mice resulted in the reduction of spontaneous locomotor activity compared with the control group. The oxygen-containing functional groups and the configurations at C1 and C2

contributed to the spontaneous locomotor activity reduction of zerumbone and tetrahydrozerumbone derivatives. The reduction of locomotor activity may indicate sedative, anxiolytic, relaxative or soporific effects which needed to be clarified.

Anticataract/Photoprotective Activity

Dietary zerumbone at 100 mg/kg after UVB exposure was effective against UVB-induced cataractogenesis by decreasing lens opacity scores and malondialdehyde (MDA) levels and enhancing the endogenous antioxidant GSH (glutathione), GR (GSH reductase) and SOD (superoxide dismutase) levels in the lens of female ICR mice (Chen et al. 2011a). Also, they found that dietary zerumbone prevented UVB-induced corneal damages by inhibition of NF- κ B, iNOS and TNF- α , with concomitant reduction of MDA accumulation and increase of GSH and GR levels in the mouse model (Chen et al. 2011b). Results of their study suggested that dietary zerumbone may be used as a prophylactic agent against UVB-induced photokeratitis.

Antinociceptive/Analgesic Activity

Intraperitoneal administration of zerumbone produced significant dose-dependent antinociceptive effect in acetic acid-induced abdominal writhing test and hot plate test in mice (Sulaiman et al. 2009). Further, the antinociceptive effect of zerumbone in the hot plate test was reversed by the nonselective opioid receptor antagonist naloxone, suggesting that the opioid system was involved in its analgesic mechanism of action. Zerumbone administered through intraperitoneal route (i.p.) produced dose-related antinociception when assessed on acetic acid-induced abdominal writhing test in mice (Perimal et al. 2011). Furthermore, i.p. administration of zerumbone exhibited significant inhibition of the neurogenic pain induced by intraplantar (i.pl.) injection of capsaicin and bradykinin. Likewise, zerumbone given by i.p. route reduced the nociception produced by i.pl. injection of glutamate and

phorbol myristate acetate. It was strongly suggested that the l-arginine-nitric oxide-cGMP-PKC-K(+) ATP channel pathways, the TRPV1 and kinin B2 receptors play an important role in the zerumbone-induced antinociception.

Immunomodulatory Activity

Lymphocyte proliferation assay showed that zerumbone was able to activate mice thymocytes, splenocytes and human peripheral blood mononuclear cells (PBMC) in a dose-dependent manner and the best concentration was 7.5 µg/ml (Keong et al. 2010). Flow cytometry analysis showed the highest population of PBMC entered into G2/M phase after treatment for 72 h with 7.5 µg/ml zerumbone. The production of human interleukin-2 and human interleukin-12 cytokines in culture supernatant from zerumbone-activated lymphocytes was prominently upregulated at 24 h and decreased from 48 to 72 h.

Proteolytic Activity

Zerumbone was found to possess potential for activating intracellular proteolysis mechanisms of the ubiquitin-proteasome system and autophagy (Ohnishi et al. 2013). It was found that protein modifications by zerumbone caused mild proteo-stress, thereby activating intracellular proteolysis machineries to maintain protein homeostasis. The authors considered these effects on proteolysis mechanisms to be hormesis, which could provide beneficial functions through mild biological stresses.

Adverse Issues

Zerumbone was found to markedly induce the expression of pro-inflammatory genes interleukin (IL)-1alpha, IL-1beta, IL-6 and tumour necrosis factor (TNF)-alpha in each cell line in concentration- and time-dependent manners in human colon adenocarcinoma cell lines, Caco-2, Colo320DM and HT-29 (Murakami et al. 2004a). The production of pro-inflammatory

cytokines in cancerous tissues in the colon may cause side effects.

Pharmacokinetic Study

Recovery of zerumbone and its analogue α -humulene was above 90 % using HPLC (Eid et al. 2010). Following intravenous and intraperitoneal administration of zerumbone (ZER) (20 mg/kg) prepared in hydroxypropyl- β -cyclodextrin (HP- β -CD) and sodium carboxymethyl cellulose (CMC) resulted in a clear significant difference in pharmacokinetic parameters of ZER in ZER/HP- β -CD complex compared with ZER in CMC preparation (Eid et al. 2011).

Traditional Medicinal Uses

This species is widely used in Malay traditional medicine. Pounded leaves have been used for poulticing swellings and a cold leaf infusion used to wash infected eyelids (Burkill 1966). *Z. spectabile* is employed in the treatment of various ailments and in the preparation of traditional medicine. The pounded leaves are applied as a poultice to inflamed eyes and on to the body to reduce swelling (Jones 1993). The rhizomes are used as a germicide, stimulant and tonic and in the treatments of cancer, cough and asthma (Sadhu et al. 2007). The Temuan native in Peninsular Malaysia used the juice from the leaves to treat eye ailment and swelling (Faridah and Nurulhuda 1999)

Other Uses

The plant is cultivated as an ornamental, and its large, unique and attractive inflorescences are esteemed as popular cut flowers.

Comments

Refer to notes on *Zingiber zerumbet* in *Edible Medicinal and Non-medicinal Plants: Volume 8, Flowers* (Lim 2014).

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Medical Glossary and Scientific Glossary

Medical Glossary

AAD

Allergic airway disease, an inflammatory disorder of the airways caused by allergens.

AAPH

2,2'-Azobis(2-amidinopropane) dihydrochloride, a water-soluble azo compound used extensively as a free radical generator, often in the study of lipid peroxidation and the characterisation of antioxidants.

Abeta aggregation

Amyloid beta protein (Abeta) aggregation is associated with Alzheimer's disease (AD); it is a major component of the extracellular plaque found in AD brains.

Abdominal distension

Referring to generalised distension of most or all of the abdomen. Also referred to as stomach bloating often caused by a sudden increase in fibre from consumption of vegetables, fruits and beans.

Ablation therapy

The destruction of small areas of myocardial tissue, usually by application of electrical or chemical energy, in the treatment of some tachyarrhythmias.

Abortifacient

A substance that causes or induces abortion.

Abortivum

A substance inducing abortion.

Abscess

A swollen infected, inflamed area filled with pus in body tissues.

ABTS

2,2-Azinobis-3-ethylthiazoline-6-sulphonic acid, a type of mediator in chemical reaction kinetics of specific enzymes.

ACAT

Acyl CoA: cholesterol acyltransferase.

ACE

See Angiotensin-converting enzyme.

ACTH (adrenocorticotrophic hormone)

Also known as 'corticotropin', is a polypeptide tropic hormone produced and secreted by the anterior pituitary gland.

Acetogenins

Natural products from the plants of the family Annonaceae, are very potent inhibitors of the NADH-ubiquinone reductase (complex I) activity of mammalian mitochondria.

Acetyl-CoA carboxylase (ACC)

Enzyme that catalyses the biotin-dependent carboxylation of acetyl-CoA to produce malonyl-CoA.

Acetylcholinesterase (AChE)

Is an enzyme that degrades (through its hydrolytic activity) the neurotransmitter acetylcholine, producing choline.

Acne vulgaris

Also known as chronic acne, usually occurring in adolescence, with comedones (blackheads), papules (red pimples), nodules (inflamed acne spots) and pustules (small inflamed pus-filled lesions) on the face, neck and upper part of the trunk.

Acidosis

Increased acidity, an excessively acid condition of the body fluids.

Acquired immunodeficiency syndrome (AIDS)

An epidemic disease caused by an infection by human immunodeficiency virus (HIV-1, HIV-2), retrovirus that causes immune system failure and debilitation and is often accompanied by infections such as tuberculosis.

Acridone

An organic compound based on the acridine skeleton, with a carbonyl group at the 9 position.

ACTH

Adrenocorticotrophic hormone (or corticotropin), a polypeptide tropic hormone produced and secreted by the anterior pituitary gland. It plays a role in the synthesis and secretion of gluco- and mineralo-corticosteroids and androgenic steroids.

Activating transcription factor (ATF)

A protein (gene) that binds to specific DNA sequences regulating the transfer or transcription of information from DNA to mRNA.

Activator protein-1 (AP-1)

A heterodimeric protein transcription factor that regulates gene expression in response to a variety of stimuli, including cytokines, growth factors, stress and bacterial and viral infections. AP-1 in turn regulates a number of cellular processes including differentiation, proliferation and apoptosis.

Actoprotective

Increasing the body's physical performance.

Actoprotectors

Preparations that increase the mental performance and enhance body stability against physical loads without increasing oxygen consumption. Actoprotectors are regarded as a subclass of adaptogens that hold a significant capacity to increase physical performance.

Acute otitis media

(AOM) see Otitis media.

Acyl-CoA dehydrogenases

A group of enzymes that catalyses the initial step in each cycle of fatty acid β -oxidation in the mitochondria of cells.

Adaptogen

A term used by herbalists to refer to a natural herb product that increases the body's resistance to stresses such as trauma, stress and fatigue.

Adaptogenic

Increasing the resistance of the body to stress.

Addison's disease

Is a rare endocrine disorder. It occurs when the adrenal glands cannot produce sufficient hormones (corticosteroids). It is also known as chronic adrenal insufficiency, hypocortisolism or hypocorticism.

Adenocarcinoma

A cancer originating in glandular tissue.

Adenoma

A benign tumour from a glandular origin.

Adenoidectomy

Surgical removal of the adenoids.

Adenopathy

Abnormal enlargement or swelling of the lymph node.

Adenosine receptors

A class of purinergic, G protein-coupled receptors with adenosine as endogenous ligand. In humans, there are four adenosine receptors. A_1 receptors and A_{2A} play roles in the heart, regulating myocardial oxygen consumption and coronary blood flow, while the A_{2A} receptor also has broader anti-inflammatory effects throughout the body. These two receptors also have important roles in the brain, regulating the release of other neurotransmitters such as dopamine and glutamate, while the A_{2B} and A_3 receptors

are located mainly peripherally and are involved in inflammation and immune responses.

ADH

See Alcohol dehydrogenase.

Adipocyte

A fat cell involved in the synthesis and storage of fats.

Adipocytokine

Bioactive cytokines produced by adipose tissues

Adiponectin

A protein in humans that modulates several physiological processes, such as metabolism of glucose and fatty acids and immune responses.

Adipose tissues

Body fat, loose connective tissue composed of adipocytes (fat cells).

Adoptogen

Containing smooth pro-stressors which reduce reactivity of host defence systems and decrease damaging effects of various stressors due to increased basal level of mediators involved in the stress response.

Adrenal glands

Star-shaped endocrine glands that sit on top of the kidneys.

Adrenalectomised

Having had the adrenal glands surgically removed.

Adrenergic

Having to do with adrenaline (epinephrine) and/or noradrenaline (norepinephrine).

Adrenergic receptors

A class of G protein-coupled receptors that are targets of the noradrenaline (norepinephrine) and adrenaline (epinephrine).

Adulterant

An impure ingredient added into a preparation.

Advanced glycation end products (AGEs)

Resultant products of a chain of chemical reactions after an initial glycation reaction. AGEs may play an important adverse role in process of atherosclerosis, diabetes, aging and chronic renal failure.

Aegilops

An ulcer or fistula in the inner corner of the eye.

Aerophagia

Excessive air swallowing.

Afferent

Something that so conducts or carries towards, such as a blood vessel, fibre, or nerve.

Agammaglobulinaemia

An inherited disorder in which there are very low levels of protective immune proteins called immunoglobulins. *cf.* x-linked agammaglobulinaemia.

Agalactia

Lack of milk after parturition (birth).

Age-related macular degeneration

(AMD) a medical condition of elderly adults that results in a loss of vision in the centre of the visual field (the macula) because of damage to the retina.

Agglutinin

A protein substance, such as an antibody, that is capable of causing agglutination (clumping) of a particular antigen.

Agglutination

Clumping of particles.

Agonist

A drug that binds to a receptor of a cell and triggers a response by the cell.

Agoraphobia

An anxiety disorder characterised by anxiety in situations where the sufferer perceives certain environments (openness or crowdedness) as dangerous or uncomfortable.

Ague

A fever (such as from malaria) that is marked by paroxysms of chills, fever and sweating that recurs with regular intervals.

AHR

AhR, aryl hydrocarbon receptor, a cytosolic protein transcription factor.

AIDS

See Acquired immunodeficiency syndrome.

Akathisia

A movement disorder in which there is an urge or need to move the legs to stop unpleasant sensations. Also called restless leg syndrome, the disorder is often caused by long-term use of antipsychotic medications.

AKT

Serine/threonine kinase (also known as protein kinase B or PKB) plays a critical regulatory role in diverse cellular processes, including cancer progression and insulin metabolism.

Akt signalling pathway

Akt are protein kinases involved in mammalian cellular signalling and inhibit apoptotic processes.

Akt/FoxO pathway

Cellular processes involving Akt and FoxO transcription factors that play a role in angiogenesis and vasculogenesis.

Akt/GSK-3 β /eNOS phosphorylation

Amplifies serotonin 5-HT_{2B} receptor blockade mediated anti-hypertrophic effects.

Alanine transaminase (ALT)

Also called serum glutamic pyruvate transaminase (SGPT) or alanine aminotransferase (ALAT), an enzyme present in hepatocytes (liver cells). When a cell is damaged, it leaks this enzyme into the blood.

ALAT (alanine aminotransferase)

See Alanine transaminase.

Albumin

Water-soluble proteins found in egg white, blood serum, milk, various animal tissues and plant juices and tissues.

Albuminaria

Excessive amount of albumin in the urine, a symptom of severe kidney disease.

Alcohol dehydrogenase (ADH)

An enzyme involved in the breakdown of alcohol.

Aldose reductase , aldehyde reductase

An enzyme in carbohydrate metabolism that converts glucose to sorbitol.

Aldosterone

Is a steroid hormone. Its main role is to regulate salt and water in the body, thus having an effect on blood pressure.

Aldosteronism

A condition in which there is excessive secretion of aldosterone, which disturbs the balance of sodium, potassium and water in the blood and so leads to high blood pressure.

Aldosteronopenia

Deficiency of aldosterone production with normal secretion of cortisol.

Alexipharmic

An antidote, remedy for poison.

Alexiteric

A preservative against contagious and infectious diseases and the effects of poisons.

Algesic

Endogenous substances involved in the production of pain that is associated with inflammation, e.g. serotonin, bradykinin and prostaglandins.

Alkaline phosphatase (ALP)

An enzyme in the cells lining the biliary ducts of the liver. ALP levels in plasma will rise with large bile duct obstruction, intrahepatic cholestasis or infiltrative diseases of the liver. ALP is also present in bone and placental tissues.

Alkalosis

Is a condition in which the body fluids have excess base (alkali).

Allergenic

Having the properties of an antigen (allergen), immunogenic.

Allergic

Pertaining to, caused, affected with, or the nature of the allergy.

Allergic conjunctivitis

Inflammation of the tissue lining the eyelids (conjunctiva) due to allergy.

Allergy

A hypersensitivity state induced by exposure to a particular antigen (allergen) resulting in harmful immunologic reactions on subsequent exposures. The term is usually used to refer to hypersensitivity to an environmental antigen (atopic allergy or contact dermatitis) or to drug allergy.

Allodynia

A painful response to a normally innocuous stimulus.

Allogeneic

Cells or tissues which are genetically different because they are derived from separate individuals of the same species. Also refers to a type of immunological reaction that occurs when cells are transplanted into a genetically different recipient.

Allografts

Or homografts, a graft between individuals of the same species, but of different genotypes.

Alloknesis

Itch produced by innocuous mechanical stimulation.

Allostasis

The process of achieving stability, or homeostasis, through physiological or behavioural change.

Alopecia

Is the loss of hair on the body.

Alopecia areata

Type of hair loss that typically causes patches of baldness.

ALP

See Alkaline phosphatase.

Alpha-adrenoceptor

Receptors postulated to exist on nerve cell membranes of the sympathetic nervous system in order to explain the specificity of certain agents that affect only some sympathetic activities (such as vasoconstriction and relaxation of intestinal muscles and contraction of smooth muscles).

Alpha amylase (α -amylase)

A major form of amylase found in humans and other mammals that cleaves alpha-bonds of large, alpha-linked

polysaccharides, such as starch and glycogen, yielding glucose and maltose.

ALT

See Alanine transaminase.

Alterative

A medication or treatment which gradually induces a change and restores healthy functions without sensible evacuations.

Alveolar macrophage

A vigorously phagocytic macrophage on the epithelial surface of lung alveoli that ingests carbon and other inhaled particulate matters. Also called coniphage or dust cell.

Alzheimer's disease

A degenerative, organic, mental disease characterised by progressive brain deterioration and dementia, usually occurring after the age of 50.

Amastigote

Refers to a cell that does not have any flagella, used mainly to describe a certain phase in the life cycle of trypanosome protozoans.

Amenorrhea

The condition when a woman fails to have menstrual periods.

Amidolytic

Cleavage of the amide structure.

Amoebiasis

State of being infected by amoeba such as *Entamoeba histolytica* .

Amoebicidal

Lethal to amoeba.

AMPK (5' AMP-activated protein kinase)

Or 5' adenosine monophosphate-activated protein kinase, enzyme that plays a role in cellular energy homeostasis.

Amygdalitis

Inflammation of one or both tonsils, tonsilitis .

Amyloid beta (A β or Abeta)

A peptide of 39–43 amino acids that appear to be the main constituent of amyloid plaques in the brains of Alzheimer's disease patients.

Amyloidosis

A disorder that results from abnormal deposition of the protein, amyloid, in various tissues of the body.

Amyotrophic lateral sclerosis

Or ALS, is a disease of the motor neurons in the brain and spinal cord that control voluntary muscle movement.

Amyotrophy

Progressive wasting of muscle tissues. *adj.* amyotrophic.

Anaemia

A blood disorder in which the blood is deficient in red blood cells and in haemoglobin.

Anaesthesia

Condition of having sensation temporarily suppressed.

Anaesthetic

A substance that decreases partially or totally nerve the sense of pain.

Analeptic

A central nervous system (CNS) stimulant medication.

Analgesia

Term describing relief, reduction or suppression of pain. *adj.* analgetic.

Analgesic

A substance that relieves or reduces pain.

Anamnesis

Patient's account of their medical history.

Anaphoretic

An antiperspirant.

Anaphrodisiac

Or antiaphrodisiac is something that reduces or blunts the libido.

Anaphylaxis

A severe, life-threatening allergic response that may be characterised by symptoms such as reduced blood pressure, wheezing, vomiting or diarrhoea.

Anaphylactic

adj. see Anaphylaxis.

Anaphylotoxins

Are fragments (C3a, C4a or C5a) that are produced during the pathways of the complement system. They can trigger release of substances of endothelial cells, mast cells or phagocytes, which produce a local inflammatory response.

Anaplasia

A reversion of differentiation in cells and is characteristic of malignant neoplasms (tumours).

Anaplastic

adj. see Anaplasia.

Anasarca

Accumulation of great quantity of fluid in body tissues.

Anencephaly

A cephalic disorder that results from a neural tube defect that occurs when the cephalic (head) end of the neural tube fails to close, resulting in the absence of a major portion of the brain, skull and scalp.

Androgen

Male sex hormone in vertebrates. Androgens may be used in patients with breast cancer to treat recurrence of the disease.

Androgenic alopecia

Hair loss in men and women.

Android adiposity

Centric fat distribution patterns with increased disposition towards the abdominal area, visceral fat—apple shaped. *cf.* gynoid adiposity.

Andrology

Branch of medicine concerned with the reproductive diseases in men.

Aneugen

An agent that affects cell division and the mitotic spindle apparatus, causing the loss or gain of whole chromosomes, thereby inducing aneuploidy. *adj.* aneugenic.

Angina pectoris, angina

Chest pain or chest discomfort that occurs when the heart muscle does not get enough blood.

Angioedema

Rapid swelling of the dermis, subcutaneous tissues, mucosa and submucosal tissues caused by small blood vessels leaking fluid into these tissues.

Angiogenic

adj. see Angiogenesis.

Angiogenesis

A physiological process involving the growth of new blood vessels from pre-existing vessels.

Angiotensin

An oligopeptide hormone in the blood that causes blood vessels to constrict and drives blood pressure up. It is part

of the renin–angiotensin system.

Angiotensin-converting enzyme (ACE)

An exopeptidase, a circulating enzyme that participates in the body's renin–angiotensin system (RAS) which mediates extracellular volume (i.e. that of the blood plasma, lymph and interstitial fluid) and arterial vasoconstriction.

Angioplasty

Medical procedure used to open obstructed or narrowed blood vessel resulting usually from atherosclerosis.

Anguillulosis

A parasitosis caused by the intestinal nematode *Strongyloides stercoralis* (round worm).

Anisakiasis

A human parasitic infection of the gastrointestinal tract caused by the consumption of raw or undercooked seafood containing larvae of the nematode *Anisakis simplex*.

Anisonucleosis

A morphological manifestation of nuclear injury characterised by variation in the size of the cell nuclei.

Ankylosing spondylitis (AS)

Is a type of inflammatory arthritis that targets the joints of the spine.

Annexin V or annexin A5

Is a member of the annexin family of intracellular proteins that binds to phosphatidylserine (PS) in a calcium-dependent manner.

Annexitis

Also called adnexitis, a pelvic inflammatory disease involving the inflammation of the ovaries or fallopian tubes.

Anodyne

A substance that relieves or soothes pain by lessening the sensitivity of the brain or nervous system. Also called an

analgesic.

Anoikis

Apoptosis that is induced by inadequate or inappropriate cell-matrix interactions.

Anophthalmia

Medical term for the absence of one or both eyes.

Anorectal

Relating to the rectum and anus.

Anorectics

Appetite suppressants, substances which reduce the desire to eat. Used on a short-term basis clinically to treat obesity. Also called anorexigenics.

Anorexia

Lack or loss of desire to eat.

Anorexia nervosa

Is a psychiatric disorder characterised by an unrealistic fear of weight gain, self-starvation and conspicuous distortion of body image.

Anorexic

Having no appetite to eat.

Anorexigenics

See Anorectics.

Anosmia

Inability to perceive odour, reduced sense of smell.

Anoxia

Absence of oxygen supply.

Antagonist

A substance that acts against and blocks an action.

Antalgic

A substance used to relieve a painful condition.

Antecubital vein

This vein is located in the antecubital fossa—the area of the arm in front of the elbow.

Anterior uveitis

Is the most common form of ocular inflammation that often causes a painful red eye.

Anthelmintic

An agent or substance that is destructive to worms and used for expulsion of internal parasitic worms in animals and humans.

Anthocyanins

A subgroup of antioxidant flavonoids, are glucosides of anthocyanidins, which are beneficial to health. They occur as water-soluble vacuolar pigments that may appear red, purple or blue according to pH in plants.

Anthrax

A bacterial disease of cattle and sheep that can be transmitted to man through unprocessed wool.

Anthropometric

Pertaining to the study of human body measurements.

Antiamoebic

A substance that destroys or suppresses parasitic amoebae.

Antiamyloidogenic

Compounds that inhibit the formation of Alzheimer's β -amyloid fibrils (fA β) from amyloid β -peptide (A β) and destabilise fA β .

Antianaphylactic

Agent that can prevent the occurrence of anaphylaxis (life-threatening allergic response).

Antiangiogenic

A drug or substance used to stop the growth of tumours and progression of cancers by limiting the pathologic

formation of new blood vessels (angiogenesis).

Antiarrhythmic

A substance to correct irregular heartbeats and restore the normal rhythm.

Antiasmatic

Drug that treats or ameliorates asthma.

Antiatherogenic

That protects against atherogenesis, the formation of atheromas (plaques) in arteries.

Antibacterial

Substance that kills or inhibits bacteria.

Antibiliary

An agent or substance which helps remove excess bile from the body.

Antibiotic

A chemical substance produced by a microorganism which has the capacity to inhibit the growth of or to kill other microorganisms.

Antiblennorrhagic

A substance that treats blenorrhagia a conjunctival inflammation resulting in mucus discharge.

Antibody

A gamma globulin protein produced by a kind of white blood cell called the plasma cell in the blood used by the immune system to identify and neutralise foreign objects (antigen).

Anticarcinomic

A substance that kills or inhibits carcinomas (any cancer that arises in epithelium/tissue cells).

Anticephalalgic

Headache relieving or preventing.

Anticestodal

A chemical destructive to tapeworms.

Anticholesterolemic

A substance that can prevent the build-up of cholesterol.

Anticlastogenic

Having a suppressing effect of chromosomal aberrations.

Anticoagulant

A substance that thins the blood and acts to inhibit blood platelets from sticking together.

Antidepressant

A substance that suppresses depression or sadness.

Antidiabetic

A substance that prevents or alleviates diabetes. Also called antidiabetogenic.

Antidiarrhoeal

Having the property of stopping or correcting diarrhoea, an agent having such action.

Antidipsotropic

Antialcohol abuse; medication to reduce alcohol consumption.

Antidote

A remedy for counteracting a poison.

Antidopaminergic

A term for a chemical that prevents or counteracts the effects of dopamine.

Antidrepanocytary

Anti-sickle cell anaemia.

Antidysenteric

An agent used to reduce or treat dysentery and diarrhoea.

Antidyslipidemic

Agent that will reduce the abnormal amount of lipids and lipoproteins in the blood.

Anti-oedematous

Reduces or suppresses oedema.

Antiemetic

An agent that stops vomiting and nausea.

Anti-epileptic

A drug used to treat or prevent convulsions, anticonvulsant.

Antifebrile

A substance that reduces fever, also called antipyretic.

Antifeedant

Preventing something from being eaten.

Antifertility

Agent that inhibits formation of ova and sperm and disrupts the process of fertilisation (antizygotic).

Anti-fibrosis

Preventing/retarding the development of fibrosis, i.e. excessive growth and activity of fibroblasts.

Antifilarial

Effective against human filarial worms.

Antifungal

An agent that kills or inhibits the growth of fungi.

Antigen

A substance that prompts the production of antibodies and can cause an immune response. *adj.* antigenic.

Antigenotoxic

An agent that inhibits DNA adduct formation, stimulates DNA repair mechanisms and possesses antioxidant functions.

Antiganacratia

Anti-menstruation.

Antigastralgie

Preventing or alleviating gastric colic.

Antihaematic

Agent that stops vomiting.

Antihaemorrhagic

An agent which stops or prevents bleeding.

Antihepatotoxic

Counteracting injuries to the liver.

Antitherpetic

Having activity against herpes simplex virus (HSV).

Antihistamine

An agent used to counteract the effects of histamine production in allergic reactions.

Antihyperalgesia

The ability to block enhanced sensitivity to pain, usually produced by nerve injury or inflammation, to nociceptive stimuli. *adj.* antihyperalgesic.

Antihypercholesterolemia

Term to describe lowering of cholesterol level in the blood or blood serum.

Antihypercholesterolemic

Agent that lowers cholesterol level in the blood or blood serum.

Antihyperlidemic

Promoting a reduction of lipid levels in the blood, or an agent that has this action.

Antihypersensitive

A substance used to treat excessive reactivity to any stimuli.

Antihypertensive

A drug used in medicine and pharmacology to treat hypertension (high blood pressure).

Anti-inflammatory

A substance used to reduce or prevent inflammation.

Antileishmanial

Inhibiting the growth and proliferation of *Leishmania* , a genus of flagellate protozoans that are parasitic in the tissues of vertebrates.

Antileprotic

Therapeutically effective against leprosy.

Antilithiatic

An agent that reduces or suppresses urinary calculi (stones) and acts to dissolve those already present.

Antileukaemic

Anticancer drugs that are used to treat leukaemia.

Antilithogenic

Inhibiting the formation of calculi (stones).

Antimalarial

An agent used to treat malaria and/or kill the malaria-causing organism, *Plasmodium* spp.

Antimelanogenesis

Obstruct production of melanin.

Antimicrobial

A substance that destroys or inhibits growth of disease-causing bacteria, viruses, fungi and other microorganisms.

Antimitotic

Inhibiting or preventing mitosis.

Antimutagenic

An agent that inhibits mutations.

Antimycotic

Antifungal.

Antineoplastic

Said of a drug intended to inhibit or prevent the maturation and proliferation of neoplasms that may become malignant, by targeting the DNA.

Antineuralgic

A substance that stops intense intermittent pain, usually of the head or face, caused by neuralgia.

Antinociception

Reduction in pain: a reduction in pain sensitivity produced within neurons when an endorphin or similar opium-containing substance opioid combines with a receptor.

Antinociceptive

Having an analgesic effect.

Antioxytotic

Inhibiting premature labour. *cf.* tocolytic.

Antinutrient

Are natural or synthetic compounds that interfere with the absorption of nutrients and are commonly found in food sources and beverages.

Antioestrogen

A substance that inhibits the biological effects of female sex hormones.

Antiophidian

Antivenoms of snake.

Antiosteoporotic

Substance that can prevent osteoporosis.

Antiovulatory

Substance suppressing ovulation.

Antioxidant

A chemical compound or substance that inhibits oxidation and protects against free radical activity and lipid oxidation such as vitamin E, vitamin C or beta-carotene (converted

to vitamin B) and carotenoids and flavonoids which are thought to protect body cells from the damaging effects of oxidation. Many foods including fruit and vegetables contain compounds with antioxidant properties. Antioxidants may also reduce the risks of cancer and age-related macular degeneration (AMD).

Antipaludic

Antimalarial.

Antiperiodic

Substance that prevents the recurrence of symptoms of a disease, e.g. malaria.

Antiperspirant

A substance that inhibits sweating. Also called antisudorific, anaphoretic.

Antiphlogistic

A traditional term for a substance used against inflammation, an anti-inflammatory.

Antiplatelet agent

Drug that decreases platelet aggregation and inhibits thrombus formation.

Antiplasmodial

Suppressing or destroying plasmodia.

Antiproliferative

Preventing or inhibiting the reproduction of similar cells.

Antiprostatic

Drug to treat the prostate.

Antiprotozoal

Suppressing the growth or reproduction of protozoa.

Antipruritic

Alleviating or preventing itching.

Antipyretic

A substance that reduces fever or quells it. Also known as antithermic.

Antirheumatic

Relieving or preventing rheumatism.

Antiscorbutic

A substance or plant rich in vitamin C that is used to counteract scurvy.

Antisecretory

Inhibiting or diminishing secretion.

Antisense

Refers to antisense RNA strand because its sequence of nucleotides is the complement of message sense. When mRNA forms a duplex with a complementary antisense RNA sequence, translation of the mRNA into the protein is blocked. This may slow or halt the growth of cancer cells.

Antiseptic

Preventing decay or putrefaction, a substance inhibiting the growth and development of microorganisms.

Anti-sickling agent

An agent used to prevent or reverse the pathological events leading to sickling of erythrocytes in sickle cell conditions.

Antispasmodic

A substance that relieves spasms or inhibits the contraction of smooth muscles; smooth muscle relaxant, muscle relaxer.

Antispermatogetic

Preventing or suppressing the production of semen or spermatozoa.

Antisudorific

See Antiperspirant.

Antisyphilitic

A drug (or other chemical agents) that is effective against syphilis.

Antithermic

A substance that reduces fever and temperature. Also known as antipyretic.

Antithrombotic

Preventing or interfering with the formation of thrombi.

Antitoxin

An antibody with the ability to neutralise a specific toxin.

Antitumoral

Substance that acts against the growth, development or spread of a tumour.

Antitussive

A substance that depresses coughing.

Antiulcerogenic

An agent used to protect against the formation of ulcers or is used for the treatment of ulcers.

Antivenin

An agent used against the venom of a snake, spider or other venomous animals or insects.

Antivinous

An agent or substance that treats addiction to alcohol.

Antiviral

Substance that destroys or inhibits the growth and viability of infectious viruses.

Antivomitive

A substance that reduces or suppresses vomiting.

Antizygotic

See Antifertility.

Anuria

Absence of urine production and excretion. *adj.* anuric.

Anxiogenic

Substance that causes anxiety.

Anxiolytic

A drug prescribed for the treatment of symptoms of anxiety.

APAF-1

Apoptotic protease-activating factor 1.

Apelin

Also known as APLN, a peptide which in humans is encoded by the APLN gene.

Aperient

A substance that acts as a mild laxative by increasing fluids in the bowel.

Aperitif

An appetite stimulant.

Aphonia

Loss of the voice resulting from disease, injury to the vocal cords, or various psychological causes, such as hysteria.

Aphrodisiac

An agent that increases sexual activity and libido and/or improves sexual performance.

Aphthae

White, painful oral ulcer of unknown cause.

Aphthous ulcer

Also known as a canker sore, is a type of oral ulcer, which presents as a painful open sore inside the mouth or upper throat.

Aphthous stomatitis

A canker sore, a type of painful oral ulcer or sore inside the mouth or upper throat, caused by a break in the mucous

membrane. Also called aphthous ulcer.

Aplastic anaemia

(AA) is a disease in which the bone marrow and the blood stem cells that reside there are damaged and do not make enough new blood cells.

Apnoea

Suspension of external breathing.

Apoprotein

The protein moiety of a molecule or complex, as of a lipoprotein.

Apolipoprotein A-I (APOA1)

A major protein component of high-density lipoprotein (HDL) in plasma. The protein promotes cholesterol efflux from tissues to the liver for excretion.

Apolipoprotein B (APOB)

Is the primary apolipoprotein of low-density lipoproteins (LDL or 'bad cholesterol'), which is responsible for carrying cholesterol to tissues.

Apolipoprotein E (APOE)

The apolipoprotein found on intermediate density lipoprotein and chylomicron that binds to a specific receptor on liver and peripheral cells.

Apoplexy

Unconsciousness or incapacity of the brain to function resulting from a cerebral haemorrhage or stroke.

Apoptogenic

Ability to cause death of cells.

Apoptosis

Death of cells.

Appendicitis

Is a condition characterised by inflammation of the appendix.
Also called epityphlitis.

Appetite stimulant

A substance to increase or stimulate the appetite. Also called aperitif.

aPPT (activated partial thromboplastin time)

A blood test, a measure of the part of the blood clotting pathway.

Apurinic lyase

A DNA enzyme that catalyses a chemical reaction.

Arachidonate cascade

Includes the cyclooxygenase (COX) pathway to form prostanoids and the lipoxygenase (LOX) pathway to generate several oxygenated fatty acids, collectively called eicosanoids.

ARE

Antioxidant response element, is a transcriptional control element that mediates expression of a set of antioxidant proteins.

Ariboflavinosis

A condition caused by the dietary deficiency of riboflavin that is characterised by mouth lesions, seborrhea and vascularisation.

Aromatase

An enzyme involved in the production of oestrogen that acts by catalysing the conversion of testosterone (an androgen) to estradiol (an oestrogen). Aromatase is located in oestrogen-producing cells in the adrenal glands, ovaries, placenta, testicles, adipose (fat) tissue and brain.

Aromatic

Having a pleasant, fragrant odour.

Aromatherapy

A form of alternative medicine that uses volatile liquid plant materials, such as essential oils and other scented compounds from plants for the purpose of affecting a person's mood or health.

ARPE-19 cells

A human retinal pigment epithelial cell line with differentiated properties.

Arrhythmias

Abnormal heart rhythms that can cause the heart to pump less effectively. Also called dysrhythmias.

Arsenicosis

See Arsenism.

Arsenism

An incommunicable disease resulting from the ingestion of groundwater containing unsafe levels of arsenic, also known as arsenicosis.

Arteriogenic erectile dysfunction

A penis dysfunction caused by the narrowing of the arteries in the penis, decreasing blood inflow to it, thus making erection impossible.

Arteriosclerosis

Imprecise term for various disorders of arteries, particularly hardening due to fibrosis or calcium deposition, often used as a synonym for atherosclerosis.

Arthralgia

Is pain in the joints from many possible causes.

Arthritis

Inflammation of the joints of the body.

Arthrodynia

An affection characterised by pain in or about a joint.

Arthus reaction

An allergic reaction of the immediate hypersensitive type that results from the union of antigen and antibody, with complement present in blood vessel walls.

Aryl hydrocarbon receptor (AhR)

A ligand-activated transcription factor best known for mediating the toxicity of dioxin and other exogenous contaminants and is responsible for their toxic effects, including immunosuppression.

ASAT or AST

Aspartate aminotransferase; see Aspartate transaminase.

ASBT

Apical sodium-dependent bile acid transporter, belongs to the solute carrier family (SLC) of transporters and is an important carrier protein expressed in the small intestine.

Ascaris

A genus of parasitic intestinal round worms.

Ascites

Abnormal accumulation of fluid within the abdominal or peritoneal cavity.

Ascorbic acid

See Vitamin C.

Aspartate transaminase (AST)

Also called serum glutamic oxaloacetic transaminase (SGOT) or aspartate aminotransferase (ASAT) is similar to ALT in that it is another enzyme associated with liver parenchymal cells. It is increased in acute liver damage but is also present in red blood cells and cardiac and skeletal muscle and is therefore not specific to the liver.

Asphyxia

Failure or suppression of the respiratory process due to obstruction of airflow to the lungs or due to the lack of oxygen in inspired air.

Asphyxiation

The process of undergoing asphyxia.

Asthenia

A nonspecific symptom characterised by loss of energy, strength and feeling of weakness.

Asthenopia

Weakness or fatigue of the eyes, usually accompanied by headache and dimming of vision. *adj.* asthenopic.

Asthenozoospermia (asthenospermia)

Reduced sperm motility.

Asthma

A chronic illness involving the respiratory system in which the airway occasionally constricts, becomes inflamed and is lined with excessive amounts of mucus, often in response to one or more triggers.

Astringent

A substance that contracts blood vessels and certain body tissues (such as mucous membranes) with the effect of reducing secretion and excretion of fluids and/or has a drying effect.

Astrocytes

Collectively called astroglia, are characteristic star-shaped glial cells in the brain and spinal cord.

Ataxia

(Loss of coordination) results from the degeneration of nerve tissue in the spinal cord and of nerves that control muscle movement in the arms and legs.

Ataxic polyneuropathy

Is a syndrome characterised by problems with coordination and balance (sensory ataxia) and disturbances in nerve function (sensory neuropathy), bilateral optic atrophy and bilateral sensorineural deafness.

Ataxia telangiectasia and Rad3-related protein (ATR)

Also known as serine/threonine-protein kinase ATR, FRAP-related protein 1 (FRP1), is an enzyme encoded by the ATR gene. It is involved in sensing DNA damage and activating the DNA damage checkpoint, leading to cell cycle arrest

Atelectasis

The collapse or closure of the lung resulting in reduced or absent gas exchange.

ATF-2

Activating transcription factor 2.

Athlete's foot

A contagious skin disease caused by parasitic fungi affecting the foot and hands, causing itching, blisters and cracking. Also called dermatophytosis.

Atherogenic

Having the capacity to start or accelerate the process of atherogenesis.

Atherogenesis

The formation of lipid deposits in the arteries.

Atheroma

A deposit or degenerative accumulation of lipid-containing plaques on the innermost layer of the wall of an artery.

Atherosclerosis

The condition in which an artery wall thickens as the result of a build-up of fatty materials such as cholesterol.

Atherothrombosis

Medical condition characterised by an unpredictable, sudden disruption (rupture or erosion/fissure) of an atherosclerotic plaque, which leads to platelet activation and thrombus formation.

Athymic mice

Laboratory mice lacking a thymus gland.

Atonic

Lacking normal tone or strength.

Atony

Insufficient muscular tone.

Atopic dermatitis

An inflammatory, non-contagious, pruritic skin disorder of unknown aetiology; often called eczema.

Atresia

A congenital medical condition in which a body orifice or passage in the body is abnormally closed or absent.

Atretic follicle

Follicular atresia is the breakdown of the ovarian follicles.

Atretic ovarian follicles

An involuted or closed ovarian follicle.

Atrial fibrillation

Is the most common cardiac arrhythmia (abnormal heart rhythm) and involves the two upper chambers (atria) of the heart; the most serious consequence of atrial fibrillation is ischemic stroke.

Atrioventricular node

A node of specialised heart muscle located in the septal wall of the right atrium; receives impulses from the sinoatrial node and directs them to the walls of the ventricles.

Attention-deficit hyperactivity disorder (ADHD, ADD or AD/HD)

Is a neurobehavioural developmental disorder, primarily characterised by the coexistence of attentional problems and hyperactivity.

Auditory brainstem response (ABR)

Also called brainstem evoked response (BSER), is an electrical signal evoked from the brainstem of a human by the presentation of a sound such as a click.

Augmerosen

A drug that may kill cancer cells by blocking the production of a protein that makes cancer cells live longer. Also called bcl-2 antisense oligonucleotide.

Auricular

Of or relating to the auricle or the ear in general.

Aurones

[2-Benzylidenebenzofuran-3(2H)-ones] are the secondary plant metabolites and are a subgroup of flavonoids. See Flavonoids.

Autoantibodies

Antibodies manufactured by the immune system that mistakenly target and damage specific tissues and organs of the body.

Autolysin

An enzyme that hydrolyses and destroys the components of a biological cell or a tissue in which it is produced.

Autonomic disorder

A neurological disease in which the autonomic nervous system ceases to function properly.

Autonomic neuropathy

Is a nerve disorder due to damage to the autonomic nerves that affects involuntary body functions, including heart rate, blood pressure, perspiration and digestion.

Autophagy

Digestion of the cell contents by enzymes in the same cell.

Autopsy

Examination of a cadaver to determine or confirm the cause of death .

Avenanthramides

Low molecular weight, soluble phenolic compounds found in oats.

Avidity index

Describes the collective interactions between antibodies and a multivalent antigen.

Avulsed teeth

Is tooth that has been knocked out.

Ayurvedic

Traditional Hindu system of medicine based largely on homeopathy and naturopathy.

Azoospermia

Is the medical condition of a male not having any measurable level of sperm in his semen.

Azotaemia

A higher than normal blood level of urea or other nitrogen-containing compounds in the blood.

B Cell-activating factor (BAFF)

Also called tumour necrosis factor ligand superfamily member 13B. It plays an important role in the proliferation and differentiation of B cells.

Babesia

A protozoan parasite (malaria-like) of the blood that causes a haemolytic disease known as babesiosis.

Babesiosis

Malaria-like parasitic disease caused by *Babesia* , a genus of protozoal piroplasms.

Back tonus

Normal state of balanced tension in the tissues of the back.

Bactericidal

Lethal to bacteria.

BAFF

A cytokine that belongs to the tumour necrosis factor (TNF) ligand family.

Balanitis

Is an inflammation of the glans (head) of the penis.

BALB/c mice

Balb/c mouse was developed in 1923 by McDowell. It is a popular strain and is used in many different research disciplines, but most often in the production of monoclonal antibodies.

Balm

Aromatic oily resin from certain trees and shrubs used in medicine.

Barbiturates

Are drugs that act as central nervous system depressants and can therefore produce a wide spectrum of effects, from mild sedation to total anaesthesia. They are also effective anxiolytics, hypnotics and anticonvulsants.

Baroreceptor

A type of interoceptor that is stimulated by pressure changes, as those in blood vessel wall.

Barrett's oesophagus (Barrett oesophagitis)

A disorder in which the lining of the oesophagus is damaged by stomach acid.

Basophil

A type of white blood cell with coarse granules within the cytoplasm and a bilobate (two-lobed) nucleus.

Bax/Bad

Proapoptotic proteins.

BCL-2

A family of apoptosis regulator proteins in humans encoded by the B cell lymphoma 2 (BCL-2) gene.

BCL-2 antisense oligonucleotide

See Augmereson.

BCR/ABL

A chimeric oncogene, from fusion of BCR and ABL cancer genes associated with chronic myelogenous leukaemia.

Bechic

A remedy or treatment of cough.

Bed nucleus of the stria terminalis (BNST)

Act as a relay site within the hypothalamic-pituitary-adrenal axis and regulate its activity in response to acute stress.

Belching , or burping

Refers to the noisy release of air or gas from the stomach through the mouth.

Beriberi

Is a disease caused by a deficiency of thiamine (vitamin B₁) that affects many systems of the body, including the muscles, heart, nerves and digestive system.

Beta-carotene

Naturally occurring retinol (vitamin A) precursor obtained from certain fruits and vegetables with potential antineoplastic and chemopreventive activities. As an antioxidant, beta-carotene inhibits free radical damage to DNA. This agent also induces cell differentiation and apoptosis of some tumour cell types, particularly in early stages of tumorigenesis, and enhances immune system activity by stimulating the release of natural killer cells, lymphocytes and monocytes.

Beta-catenin

Is a multifunctional oncogenic protein that contributes fundamentally to cell development and biology. It has been implicated as an integral component in the Wnt signalling pathway.

Beta cells

A type of cell in the pancreas in areas called the islets of Langerhans.

Beta glucans

Polysaccharides of D -glucose monomers linked by β -glycosidic bonds, (1 $\rightarrow$ 3), (1 $\rightarrow$ 4)- β - D -glucan, soluble, viscous component of fibres found in cereals like oats.

Beta-thalassemia

An inherited blood disorder that reduces the production of haemoglobin.

Beta-lactamase

Enzymes produced by some bacteria that are responsible for their resistance to beta-lactam antibiotics like penicillins.

BHT

Butylated hydroxytoluene (phenolic compound), an antioxidant used in foods, cosmetics, pharmaceuticals and petroleum products.

BID

The only known Bcl-2 family member that can function as an agonist of proapoptotic Bcl-2-related proteins such as Bax and Bak.

Bifidobacterium

Is a genus of Gram-positive, nonmotile, often branched anaerobic bacteria. Bifidobacteria are one of the major genera of bacteria that make up the gut flora. Bifidobacteria aid in digestion are associated with a lower incidence of allergies and also prevent some forms of tumour growth. Some bifidobacteria are being used as probiotics.

Bifidogenic

Promoting the growth of (beneficial) bifidobacteria in the intestinal tract.

Bile

Fluid secreted by the liver and discharged into the duodenum where it is integral in the digestion and absorption of fats.

Bilharzia, bilharziosis

See Schistosomiasis.

Biliary

Relating to the bile or the organs in which the bile is contained or transported.

Biliary infections

Infection of organ(s) associated with bile, comprise:

- (a) acute cholecystitis, an acute inflammation of the gallbladder wall
- (b) cholangitis, inflammation of the bile ducts

Biliousness

Old term used in the eighteenth and nineteenth centuries pertaining to bad digestion, stomach pains, constipation and excessive flatulence.

Bilirubin

A breakdown product of haem (a part of haemoglobin in red blood cells) produced by the liver that is excreted in bile which causes a yellow discoloration of the skin and eyes when it accumulates in those organs.

Biotin

Also known as vitamin B7. See Vitamin B7.

Bitter

A medicinal agent with a bitter taste and used as a tonic, alterative or appetiser.

Blackhead

See Comedone.

Blackwater fever

Dangerous complication of malarial whereby the red blood cells burst in the blood stream (haemolysis) releasing haemoglobin directly into the blood.

Blain

See Chilblain.

Blastocyst

Blastocyst is an embryonic structure formed in the early embryogenesis of mammals, after the formation of the morula, but before implantation.

Blastocystotoxic

Agent that suppresses further development of the blastocyst through to the ovum stage.

Blebbing

Bulging, e.g. membrane blebbing also called membrane bulging or ballooning.

Bleeding diathesis

Is an unusual susceptibility to bleeding (haemorrhage) due to a defect in the system of coagulation.

Blennorrhagia

Gonorrhoea.

Blennorrhoea

Inordinate discharge of mucus, especially a gonorrhoeal discharge from the urethra or vagina.

Blepharitis

Inflammation of the eyelids.

Blepharospasm

Involuntary twitching, blinking closure or squeezing of the eyelids.

Blister

Thin vesicle on the skin containing serum and caused by rubbing, friction or burn.

Blood–brain barrier (BBB)

Is a separation of circulating blood and cerebrospinal fluid (CSF) in the central nervous system (CNS). It allows essential metabolites, such as oxygen and glucose, to pass from the blood to the brain and central nervous system

(CNS) but blocks most molecules that are more massive than about 500 Da.

Blood stasis syndrome

Blood stagnation or slowing of blood, an important underlying pathology of many disease processes according to traditional Chinese medicine.

BMPs (bone morphogenetic proteins)

A family of secreted signalling molecules that can induce ectopic bone growth.

BNIP3

A pro-apoptotic BH3-only protein which is associated with mitochondrial dysfunction and cell death.

Boil

Localised pyrogenic, painful infection, originating in a hair follicle.

Borborygmus

Rumbling noise caused by the muscular contractions of peristalsis, the process that moves the contents of the stomach and intestines downwards.

Bowman–Birk inhibitors

Type of serine proteinase inhibitor.

Bouillon

A broth in French cuisine.

Bradycardia

As applied to adult medicine, is defined as a resting heart rate of under 60 beats per minute.

Bradyphrenia

Referring to the slowness of thought common to many disorders of the brain.

Brain-derived neurotrophic factor (BDNF)

A protein member of the neurotrophin family that plays an important role in the growth, maintenance, function and survival of neurons. The protein molecule is involved in the modulation of cognitive and emotional functions and in the treatment of a variety of mental disorders.

Bright's disease

Chronic nephritis.

Bronchial inflammation

See Bronchitis.

Bronchiectasis

A condition in which the airways within the lungs (bronchial tubes) become damaged and widened.

Bronchitis

Is an inflammation of the main air passages (bronchi) to the lungs.

Bronchoalveolar lavage (BAL)

A medical procedure in which a bronchoscope is passed through the mouth or nose into the lungs and fluid is squirted into a small part of the lung and then recollected for examination.

Bronchopneumonia

Or bronchial pneumonia; inflammation of the lungs beginning in the terminal bronchioles.

Broncho-pulmonary

Relating to the bronchi and lungs.

Bronchospasm

Is a difficulty in breathing caused by a sudden constriction of the muscles in the walls of the bronchioles as occurs in asthma.

Brown fat

Brown adipose tissue (BAT) in mammals; its primary function is to generate body heat in animals or newborns that do not

shiver.

Bubo

Inflamed, swollen lymph node in the neck or groin.

Buccal

Of or relating to the cheeks or the mouth cavity.

Bulbectomy

Removal of the olfactory bulb.

Bulimia

An emotional disorder characterised by a distorted body image and an obsessive desire to lose weight, in which bouts of extreme overeating are followed by fasting or self-induced vomiting or purging.

Bullae

Blisters; circumscribed, fluid-containing, elevated lesions of the skin, usually more than 5 mm in diameter.

Bursa

A fluid-filled sac or saclike cavity situated in areas subjected to friction.

Bursitis

Condition characterised by inflammation of one or more bursae (small sacs) of synovial fluid in the body.

C fibre s

Afferent fibres found in the nerve of the somatic sensory system.

c-FOS

A cellular proto-oncogene belonging to the immediate early gene family of transcription factors.

C-jun NH(2)-terminal kinase

Enzymes that belong to the family of the MAPK superfamily of protein kinases. These kinases mediate a plethora of cellular responses to such stressful stimuli, including

apoptosis and production of inflammatory and immunoregulatory cytokines in diverse cell systems. *cf* MAPK.

c-Jun-I (Ser 73)

Substrate of JNK-1 activated by phosphorylation at Ser73.

c-Jun-I (Ser 63)

Substrate of JNK-1 activated by phosphorylation at Ser63.

C-reactive protein

A protein found in the blood the levels of which rise in response to inflammation.

c-Src

A cellular non-receptor tyrosine kinase.

CAAT element-binding proteins-alpha (c/EBP-alpha)

Regulates gene expression in adipocytes in the liver.

Cachexia

Physical wasting with loss of weight, muscle atrophy, fatigue and weakness caused by disease.

Caco-2 cell line

A continuous line of heterogeneous human epithelial colorectal adenocarcinoma cells.

Cadaver

A dead body, corpse.

Ca²⁺ ATPase

(PMCA) is a transport protein in the plasma membrane of cells that serves to remove calcium (Ca²⁺) from the cell.

Calcitonin gene-related peptide

(CGRP) is a 37-amino acid neuropeptide that is abundant in the sensory neurons which innervate bone.

Calcium (Ca)

Is the most abundant mineral in the body found mainly in bones and teeth. It is required for muscle contraction, blood vessel expansion and contraction, secretion of hormones and enzymes and transmitting impulses throughout the nervous system. Dietary sources include milk, yoghurt, cheese, Chinese cabbage, kale, broccoli, some green leafy vegetables, fortified cereals, beverages and soybean products.

Calcium ATPase

Is a form of P-ATPase which transfers calcium after a muscle has contracted.

Calcium channel blockers (CCBs)

A class of drugs and natural substances that disrupt the calcium (Ca^{2+}) conduction of calcium channels.

Calciuria

Abnormal presence of calcium in the urine.

Calculosis

The tendency or deposition to form calculi or stones.

Calculus (calculi)

Hardened, mineral deposits that can form a blockage in the urinary system.

Calculi infection

Most calculi arise in the kidney when urine becomes supersaturated with a salt that is capable of forming solid crystals. Symptoms arise as these calculi become impacted within the ureter as they pass towards the urinary bladder.

Calefacient

Substance that gives a sensation of warmth.

Caligo

Dimness or obscurity of sight, dependent upon a speck on the cornea.

Calmodulin

Is a calcium-modulated protein that can bind to and regulate a multitude of different protein targets, thereby affecting many different cellular functions.

cAMP-dependent pathway

Cyclic adenosine monophosphate is a G protein-coupled receptor triggered signalling cascade used in cell communication in living organisms.

CAMP factor

Diffusible, heat-stable, extracellular protein produced by Group B *Streptococcus* that enhances the haemolysis of sheep erythrocytes by *Staphylococcus aureus*. It is named after Christie, Atkins and Munch-Petersen, who described it in 1944.

Campylobacteriosis

Is a gastrointestinal disease (gastroenteritis) caused by bacteria called *Campylobacter* which is frequently associated with the consumption of contaminated poultry.

Cancer

a malignant neoplasm or tumour in any part of the body.

Candidiasis

Infections caused by members of the fungus genus *Candida* that range from superficial, such as oral thrush and vaginitis, to systemic and potentially life-threatening diseases.

Canker

See Chancre.

Cannabinoid receptor family

Includes CB1 cannabinoid receptors found predominantly in the brain and nervous system and CB2 cannabinoid receptors mainly associated with immune tissues and expressed at low levels in the brain.

Cannabinoid receptor type 2 (CB 2 receptor)

A G protein-coupled receptor from the cannabinoid receptor family that is mainly expressed on T cells of the immune system, on macrophages and B cells and in haematopoietic cells.

Carboxypeptidase

An enzyme that hydrolyses the carboxy-terminal (C-terminal) end of a peptide bond. It is synthesised in the pancreas and secreted into the small intestine.

Carbuncle

Is an abscess larger than a boil, usually with one or more openings draining pus onto the skin.

Carcinogenesis

Production of carcinomas. *adj.* carcinogenic.

Carcinoma

Any malignant cancer that arises from epithelial cells.

Carcinosarcoma

A rare tumour containing carcinomatous and sarcomatous components.

Cardiac

Relating to, situated near or affecting the heart.

Cardiac asthma

Acute attack of dyspnoea with wheezing resulting from a cardiac disorder.

Cardiac hypertrophy

Is a thickening of the heart muscle (myocardium) resulting in a decrease chamber size, including the left and right ventricles. Common causes of cardiac hypertrophy include high blood pressure (hypertension) and heart valve stenosis.

Cardialgia

Heartburn.

Cardinolides

Cardiac glycosides with a five-membered lactone ring in the side chain of the steroid aglycone.

Cardenolide glycoside

Cardenolides that contain structural groups derived from sugars.

Cardioactive

Having an effect on the heart.

Cardiogenic shock

Is characterised by a decreased pumping ability of the heart that causes a shock-like state associated with an inadequate circulation of blood due to primary failure of the ventricles of the heart to function effectively.

Cardiomyocytes

Cardiac muscle cells.

Cardiomyopathy

Heart muscle disease.

Cardiopathy

Disease or disorder of the heart.

Cardioplegia

Stopping the heart so that surgical procedures can proceed in a still and bloodless field.

Cardiotonic

Something which strengthens, tones or regulates heart functions without overt stimulation or depression.

Cardiovascular

Pertaining to the heart and blood vessels.

Caries

Tooth decay, commonly called cavities.

Cariogenic

Leading to the production of caries.

Carminative

Substance that stops the formation of intestinal gas and helps expel gas that has already formed, relieving flatulence or colic by expelling gas.

Carnitine palmitoyltransferase I (CPT1)

Also known as carnitine acyltransferase I or CAT1, is a mitochondrial enzyme, involved in converting long-chain fatty acid into energy.

Carotenes

Are a large group of intense red and yellow pigments found in all plants; these are hydrocarbon carotenoids (subclass of tetraterpenes) and the principal carotene is beta-carotene which is a precursor of vitamin A.

Carotenoids

A class of natural fat-soluble pigments found principally in plants, belonging to a subgroup of terpenoids containing eight isoprene units forming a C40 polyene chain. Carotenoids play an important potential role in human health by acting as biological antioxidants. See also Carotenes.

Carotenodermia

Yellow skin discoloration caused by excess blood carotene.

Carpopedal spasm

Spasm of the hand or foot, or of the thumbs and great toes.

Capases

Cysteine–aspartic acid proteases, are a family of cysteine proteases, which play essential roles in apoptosis (programmed cell death), necrosis and inflammation.

Catalase (CAT)

Enzyme in living organism that catalyses the decomposition of hydrogen peroxide to water and oxygen.

Catalepsy

Indefinitely prolonged maintenance of a fixed body posture;
seen in severe cases of catatonic schizophrenia.

Catamenia

Menstruation.

Cataplasia

Degenerative reversion of cells or tissue to a less differentiated form.

Cataplasm

A medicated poultice or plaster. A soft moist mass, often warm and medicated, that is spread over the skin to treat an inflamed, aching or painful area, to improve the circulation.

Cataractogenesis

Formation of cataracts.

Catarrh, catarrhal

Inflammation of the mucous membranes especially of the nose and throat.

Catechins

Are polyphenolic antioxidant plant metabolites. They belong to the family of flavonoids; tea is a rich source of catechins. See Flavonoids.

Catecholamines

Hormones that are released by the adrenal glands in response to stress.

Cathartic

Is a substance which accelerates defaecation.

Caustic

Having a corrosive or burning effect.

Cauterisation

A medical term describing the burning of the body to remove or close a part of it.

Caveolae

Tiny (50–100nm) invaginations of the plasma membrane of the cell.

CB-1 receptor

Cannabinoid receptor type 1 held to be one of the most widely expressed G protein-coupled receptors in the brain.

CCAAT/enhancer-binding proteins (C/EBP)

Family of transcription factors that interact with CCAAT (cytidine–cytidine–adenosine–adenosine–thymidine) box motif.

CCAAT/enhancer-binding protein (C/EBP)- α

A key adipogenic transcription factor.

cdc2 kinase

A member of the cyclin-dependent protein kinases (CDKs).

CDKs

Cyclin-dependent protein kinases, a family of serine/threonine kinases that mediate many stages in mitosis.

CD4T cell

Helper T cell with CD4 receptor that recognises antigens on the surface of a virus-infected cell and secretes lymphokines that stimulate B cells and killer T cells.

CD 28

Is one of the molecules expressed on T cells that provide co-stimulatory signals, which are required for T cell (lymphocytes) activation.

CD31

Also known as PECAM-1 (platelet endothelial cell adhesion molecule-1), a member of the immunoglobulin superfamily, that mediates cell-to-cell adhesion.

CD36

An integral membrane protein found on the surface of many cell types in vertebrate animals.

CD40

An integral membrane protein found on the surface of B lymphocytes, dendritic cells, follicular dendritic cells, haematopoietic progenitor cells, epithelial cells and carcinomas.

CD68

A glycoprotein expressed on monocytes/macrophages which binds to low-density lipoprotein.

Cecal ligation

Tying up the cecum.

Celiac disease

An autoimmune disorder of the small intestine, triggered in genetically susceptible individuals by ingested gluten from wheat, rye, barley and other closely related cereal grains.

Peptides resulting from partially digested gluten of wheat, barley or rye cause inflammation of the small intestinal mucosa.

Cell adhesion molecules (CAM)

Glycoproteins located on the surface of cell membranes involved with binding of other cells or with the extracellular matrix.

Cellular respiration

Is the set of the metabolic reactions and processes that take place in organisms' cells to convert biochemical energy from nutrients into adenosine triphosphate (ATP) and then release waste products. The reactions involved in respiration are catabolic reactions that involve the oxidation of one molecule and the reduction of another.

Cellulitis

A bacterial infection of the skin that tends to occur in areas that have been damaged or inflamed.

Central nervous system

Part of the vertebrate nervous system comprising the brain and spinal cord.

Central serous chorioretinopathy

(CSCR) is a disease in which a serous detachment of the neurosensory retina occurs over an area of leakage from the choriocapillaris through the retinal pigment epithelium.

Central venous catheter

A catheter placed into the large vein in the neck, chest or groin.

Cephalagia

Pain in the head, a headache.

Cephalic

Relating to the head.

Ceramide oligosides

Oligosides with an *N*-acetyl-sphingosine moiety.

Cercariae

A free swimming larva of the parasitic schistosome worm that has a tail and suckers on its head for penetration into a host.

Cerebral embolism

A blockage of blood flow through a vessel in the brain by a blood clot that formed elsewhere in the body and travelled to the brain.

Cerebral ischemia

Is the localised reduction of blood flow to the brain or parts of the brain due to arterial obstruction or systematic hyperfusion.

Cerebral infarction

Is the ischemic kind of stroke due to a disturbance in the blood vessels supplying blood to the brain.

Cerebral tonic

Substance that can alleviate poor concentration and memory, restlessness, uneasiness and insomnia.

Cerebrosides

Are glycosphingolipids which are important components in animal muscle and nerve cell membranes.

Cerebrovascular disease

Is a group of brain dysfunctions related to disease of the blood vessels supplying the brain.

Cervical spondylotic myelopathy

A common cause of spinal cord dysfunction in older persons.

Cerumen

Ear wax, a yellowish waxy substance secreted in the ear canal of humans and other mammals.

cFLIP

Cellular FLICE-inhibitory protein, an inhibitor of death ligand-induced apoptosis.

cGMP

Cyclic guanosine monophosphate is a cyclic nucleotide derived from guanosine triphosphate (GTP). cGMP is a common regulator of ion channel conductance, glycogenolysis and cellular apoptosis. It also relaxes smooth muscle tissues.

CGRP calcitonin gene-related peptide

A vasodilator neuropeptide that is expressed in a subgroup of small neurons in the dorsal root, trigeminal and vagal ganglia. This neuropeptide has been postulated to play a role in the pathophysiology of migraine.

Chalcones

A subgroup of flavonoids.

Chancre

A painless lesion formed during the primary stage of syphilis.

Chaperones

Are proteins that assist the non-covalent folding or unfolding and the assembly or disassembly of other macromolecular structures.

Chemoembolisation

A procedure in which the blood supply to the tumour is blocked surgically or mechanically and anticancer drugs are administered directly into the tumour.

Chemokines

Are chemotactic cytokines, which stimulate migration of inflammatory cells towards tissue sites of inflammation.

Chemonociceptors

Nociceptors or sensory peripheral neurons that are sensitive to chemical stimuli.

Chemosensitiser

A drug that makes tumour cells more sensitive to the effects of chemotherapy .

Chemosis

Oedema of the conjunctiva of the eye.

Chickenpox

Is also known as varicella and is a highly contagious illness caused by primary infection with varicella zoster virus (VZV). The virus causes red, itchy bumps on the body.

Chilblains

Small, itchy, painful lumps that develop on the skin. They develop as an abnormal response to cold. Also called perniosis or blain.

Chlorosis

Iron deficiency anaemia characterised by greenish yellow colour.

Cholagogue

Is a medicinal agent which promotes the discharge of bile from the system.

Cholecalcifereol

A form of vitamin D, also called vitamin D3. See Vitamin D.

Cholecyst

Gallbladder.

Cholecystitis

Inflammation of the gallbladder.

Cholecystokinin

A peptide hormone that plays a key role in facilitating digestion in the small intestine.

Cholera

An infectious gastroenteritis caused by enterotoxin-producing strains of the bacterium *Vibrio cholera* and characterised by severe, watery diarrhoea.

Choleretic

Stimulation of the production of bile by the liver.

Cholestasis

A condition caused by rapidly developing (acute) or long-term (chronic) interruption in the excretion of bile from the liver to the duodenum.

Cholesterol

A soft, waxy, steroid substance found among the lipids (fats) in the bloodstream and in all our body's cells.

Cholethiasis

Presence of gall stones (calculi) in the gallbladder.

Choline

A water-soluble, organic compound, usually grouped within the vitamin B complex. It is an essential nutrient and is needed for physiological functions such as structural integrity and signalling roles for cell membranes, cholinergic neurotransmission (acetylcholine synthesis).

Cholinergic

Activated by or capable of liberating acetylcholine, especially in the parasympathetic nervous system.

Cholinergic system

A system of nerve cells that uses acetylcholine in transmitting nerve impulses.

Cholinomimetic

Having an action similar to that of acetylcholine; called also parasympathomimetic.

Chronotropic

Affecting the time or rate, as the rate of contraction of the heart.

Choriocarcinoma

A quick-growing malignant, trophoblastic, aggressive cancer that occurs in a woman's uterus (womb).

Choroidal neovascularisation

(CNV) is the creation of new blood vessels in the choroid layer of the eye.

Chromium (Cr)

Is required in trace amounts in humans for sugar and lipid metabolism. Its deficiency may cause a disease called chromium deficiency. It is found in cereals, legumes, nuts and animal sources.

Chromoblastomycosis

A chronic fungal infection of the skin and the subcutaneous tissue caused by traumatic inoculation of a specific group of dematiaceous fungi (such as *Fonsecaea pedrosoi*, *Phialophora verrucosa*, *Fonsecaea compacta*) through the skin.

Chromosome

Long pieces of DNA found in the centre (nucleus) of cells.

Chronic

Persisting over extended periods.

Chronic anterior uveitis

Inflammation of the iris and middle coat of the eyeball.

Chronic obstructive pulmonary disease (COPD)

A progressive disease that makes it hard to breathe.

Chronic venous insufficiency (CVI)

A medical condition where the veins cannot pump enough oxygen-poor blood back to the heart.

Chronotropic

Affecting the rate of rhythmic movements (e.g. heartbeat).

Chyle

A milky bodily fluid consisting of lymph and emulsified fats, or free fatty acids.

Chylomicrons

Are large lipoprotein particles that transport dietary lipids from the intestines to other locations in the body.

Chylomicrons are one of the five major groups of lipoproteins (chylomicrons, VLDL, IDL, LDL, HDL) that enable fats and cholesterol to move within the water-based solution of the bloodstream.

Chylorus

Milky (having fat emulsion).

Chyluria

Also called chylous urine, is a medical condition involving the presence of chyle (emulsified fat) in the urine stream, which results in urine appearing milky.

Chymase

Member of the family of serine proteases found primarily in mast cell.

Chymopapain

An enzyme derived from papaya, used in medicine and to tenderise meat.

Cicatrizant

The term used to describe a product that promotes healing through the formation of scar tissue.

C-Kit receptor

A protein tyrosine kinase receptor that is specific for stem cell factor. This interaction is crucial for the development of haematopoietic, gonadal and pigment stem cells.

Cirrhosis

Chronic liver disease characterised by replacement of liver tissue by fibrous scar tissue and regenerative nodules/lumps leading progressively to loss of liver function.

Clastogen

Is an agent that can cause one of two types of structural changes and breaks in chromosomes that results in the gain, loss, or rearrangements of chromosomal segments.
adj. clastogenic.

Claudication

Limping, impairment in walking.

Climacterium

Refers to menopause and the bodily and mental changes associated with it.

Clonic seizures

Consist of rhythmic jerking movements of the arms and legs, sometimes on both sides of the body.

Clonus

A series of involuntary muscular contractions and relaxations.

Clyster

Enema.

C-myc

Codes for a protein that binds to the DNA of other genes and is therefore a transcription factor.

CNS depressant

Anything that depresses, or slows, the sympathetic impulses of the central nervous system (i.e. respiratory rate, heart rate).

Coagulopathy

A defect in the body's mechanism for blood clotting, causing susceptibility to bleeding.

Cobalamin

Vitamin B12. See Vitamin B12.

Co-carcinogen

A chemical that promotes the effects of a carcinogen in the production of cancer.

Cold

An acute inflammation of the mucous membrane of the respiratory tract, especially of the nose and throat caused by a virus and accompanied by sneezing and coughing.

Collagen

Protein that is the major constituent of cartilage and other connective tissues; comprises the amino acids, hydroxyproline, proline, glycine and hydroxylysine.

Collagenases

Enzymes that break the peptide bonds in collagen.

Colibacillosis

Infection with *Escherichia coli* .

Colic

A broad term which refers to episodes of uncontrollable, extended crying in a baby who is otherwise healthy and well fed.

Colitis

Inflammatory bowel disease affecting the tissue that lines the gastrointestinal system.

Collyrium

A lotion or liquid wash used as a cleanser for the eyes, particularly in diseases of the eye.

Colorectal

Relating to the colon or rectum.

Coma

A state of unconsciousness from which a patient cannot be aroused.

Comedone

A blocked, open sebaceous gland where the secretions oxidise, turning black . Also called blackhead .

Comitogen

Agent that is considered not to induce cell growth alone but to promote the effect of the mitogen.

Concoction

A combination of crude ingredients that is prepared or cooked together.

Condyloma, condylomata acuminata

Genital wart, venereal wart, anal wart or anogenital wart, a highly contagious sexually transmitted infection caused by epidermotropic human papillomavirus (HPV).

Congestive heart failure

Heart failure in which the heart is unable to maintain adequate circulation of blood in the tissues of the body or to pump out the venous blood returned to it by the venous circulation.

Conglutination

Becoming stuck together.

Conjunctival hyperemia

Enlarged blood vessels in the eyes.

Conjunctivitis

Sore, red and sticky eyes caused by eye infection.

Conn's syndrome

Extremely rare condition characterised by adenoma, carcinoma or hyperplasia of the zona glomerulosa of the adrenal cortex, resulting in excessive production of aldosterone and leading to sodium retention and hydrogen loss.

Constipation

A very common gastrointestinal disorder characterised by the passing of hard, dry bowel motions (stools) and difficulty of bowel motion.

Constitutive androstane receptor (CAR, NR113)

Is a nuclear receptor transcription factor that regulates drug metabolism and homoeostasis.

Consumption

Term used to describe wasting of tissues including but not limited to tuberculosis.

Consumptive

Afflicted with or associated with pulmonary tuberculosis.

Contraceptive

An agent that reduces the likelihood of or prevents conception.

Contraindication

A condition which makes a particular treatment or procedure inadvisable.

Contralateral muscle

Muscle of opposite limb (leg or arm).

Contralateral rotation

Rotation occurring or originating in a corresponding part on an opposite side.

Contusion

Another term for a bruise. A bruise, or contusion, is caused when blood vessels are damaged or broken as the result of a blow to the skin.

Convulsant

A drug or physical disturbance that induces convulsion.

Convulsion

Rapid and uncontrollable shaking of the body.

Coolant

That which reduces body temperature.

Copper (Cu)

Is essential in all plants and animals. It is found in a variety of enzymes, including the copper centres of cytochrome C oxidase and the enzyme superoxide dismutase (containing copper and zinc). In addition to its enzymatic roles, copper is used for biological electron transport. Because of its role in facilitating iron uptake, copper deficiency can often produce anaemia-like symptoms. Dietary sources include curry powder, mushroom, nuts, seeds, wheat germ, whole grains and animal meat.

Copulation

To engage in coitus or sexual intercourse. *adj.* copulatory.

Cor pulmonale

Or pulmonary heart disease is enlargement of the right ventricle of the heart as a response to high blood pressure or increased resistance in the lungs.

Cordial

A preparation that is stimulating to the heart.

Corn

Or callus, is a patch of hard, thickened skin on the foot that is formed in response to pressure or friction.

Corpora lutea

A yellow, progesterone-secreting body that forms from an ovarian follicle after the release of a mature egg.

Corticosteroids

A class of steroid hormones that are produced in the adrenal cortex, used clinically for hormone replacement therapy, for suppressing ACTH secretion, for suppression of immune response and as antineoplastic, anti-allergic and anti-inflammatory agents.

Corticosterone

A 21-carbon steroid hormone of the corticosteroid type produced in the cortex of the adrenal glands.

Cortisol

Is a corticosteroid hormone made by the adrenal glands and plays an essential role in homeostasis.

Cornification

Is the process of forming an epidermal barrier in stratified squamous epithelial tissue.

Coryza

A word describing the symptoms of a head cold. It describes the inflammation of the mucus membranes lining the nasal cavity which usually gives rise to the symptoms of nasal congestion and loss of smell, among other symptoms.

COX-1

See Cyclooxygenase-1.

COX-2

See Cyclooxygenase - 2.

CpG islands

Genomic regions that contain a high frequency of CpG sites.

CpG sites

The cytosine–phosphate–guanine nucleotide that links two nucleosides together in DNA.

cPLA(2)

Cytosolic phospholipases A2, these phospholipases are involved in cell signalling processes, such as inflammatory response.

CPY1B1, CPY1A1

A member of the cytochrome P450 superfamily of haem-thiolate monooxygenase enzymes.

Creatin

A nitrogenous organic acid that occurs naturally in vertebrates and helps to supply energy to muscle.

Creatine phosphokinase (CPK, CK)

Enzyme that catalyses the conversion of creatine and consumes adenosine triphosphate (ATP) to create phosphocreatine and adenosine diphosphate (ADP).

CREB

cAMP response element binding, a protein that is a transcription factor that binds to certain DNA sequences called cAMP response elements.

Crohn disease

An inflammatory disease of the intestines that affect any part of the gastrointestinal tract.

CRP (C-reactive protein)

A substance produced by the liver that increases in the presence of inflammation in the body.

Crossover study

A longitudinal, balance study in which participants receive a sequence of different treatments or exposures.

Croup

Is an infection of the throat (larynx) and windpipe (trachea) that is caused by a virus (also called laryngotracheobronchitis).

Cryptococcal meningitis

A fungal infection of the membranes covering the brain and spinal cord (meninges).

Cryptochidism (cryptochism)

A developmental defect characterised by the failure of one or both testes to move into the scrotum as the male fetus develops.

Curettage

Surgical procedure in which a body cavity or tissue is scraped with a sharp instrument or aspirated with a cannula.

Cutaneous

Pertaining to the skin.

CXC8

Also known as interleukin 8, IL-8.

Cyanogenesis

Generation of cyanide . *adj.* cyanogenetic.

Cyclooxygenase (COX)

An enzyme that is responsible for the formation of prostanoids —prostaglandins, prostacyclins and thromboxanes that are each involved in the inflammatory response. Two different COX enzymes existed, now known as COX-1 and COX-2.

Cyclooxygenase-1 (COX-1)

Is known to be present in most tissues. In the gastrointestinal tract, COX-1 maintains the normal lining of the stomach. The enzyme is also involved in kidney and platelet function.

Cyclooxygenase-2 (COX-2)

Is primarily present at sites of inflammation.

Cysteine proteases

Are enzymes that degrade polypeptides possessing a common catalytic mechanism that involves a nucleophilic cysteine thiol in a catalytic triad. They are found in fruits like papaya, pineapple and kiwifruit.

Cystitis

A common urinary tract infection that occurs when bacteria travel up the urethra, infect the urine and inflame the

bladder lining.

Cystorrhea

Discharge of mucus from the bladder.

Cytochrome bc-1 complex

Ubihydroquinone: Cytochrome c oxidoreductase.

Cytochrome P450 3A CYP3A

A very large and diverse superfamily of haem-thiolate proteins found in all domains of life. This group of enzymes catalyses many reactions involved in drug metabolism and synthesis of cholesterol, steroids and other lipids.

Cytokine

Non-antibody proteins secreted by certain cells of the immune system which carry signals locally between cells. They are a category of signalling molecules that are used extensively in cellular communication.

Cytopathic

Any detectable, degenerative changes in the host cell due to infection.

Cytoprotective

Protecting cells from noxious chemicals or other stimuli.

Cytosolic

Relates to the fluid of the cytoplasm in cells.

Cytostatic

Preventing the growth and proliferation of cells.

Cytotoxic

Of or relating to substances that are toxic to cells; cell killing.

D - Galactosamine

An amino sugar with unique hepatotoxic properties in animals.

Dandruff

Scurf, dead, scaly skin among the hair.

Dartre

Condition of dry, scaly skin

Debility

Weakness, relaxation of muscular fibre.

Debridement

Is the process of removing nonliving tissue from pressure ulcers, burns and other wounds.

Debriding agent

Substance that cleans and treats certain types of wounds, burns and ulcers.

Deciduogenic

Relating to the uterus lining that is shed off at childbirth.

Deciduoma

Decidual tissue induced in the uterus (as by trauma) in the absence of pregnancy.

Deciduomata

Plural of deciduoma.

Decidual stromal cells

Like endometrial glands and endothelium, express integrins that bind basement components.

Decoction

A medical preparation made by boiling the ingredients.

Decongestant

A substance that relieves or reduces nasal or bronchial congestion.

Deep venous thrombosis

Is a blood clot that forms in a vein deep inside a part of the body.

Defibrinated plasma

Blood whose plasma component has had fibrinogen and fibrin removed.

Degranulation

Cellular process that releases antimicrobial cytotoxic molecules from secretory vesicles called granules found inside some cells.

Delayed after depolarisations (DADs)

Abnormal depolarisation that begins during phase 4—after depolarisation is completed, but before another action potential would normally occur.

Delirium

Is common, sudden severe confusion and rapid changes in brain function that occur with physical or mental illness; it is reversible and temporary.

Demulcent

An agent that soothes internal membranes. Also called emollient.

Dendritic cells

Are immune cells and form part of the mammalian immune system, functioning as antigen-presenting cells.

Dentition

A term that describes all of the upper and lower teeth collectively.

Deobstruent

A medicine which removes obstructions; also called an aperient.

Deoxypyridinoline (Dpd)

A crosslink product of collagen molecules found in bone and excreted in urine during bone degradation.

Depilatory

An agent for removing or destroying hair.

Depressant

A substance that diminishes functional activity, usually by depressing the nervous system.

Depurative

An agent used to cleanse or purify the blood; it eliminates toxins and purifies the system.

Dermatitis

Inflammation of the skin causing discomfort such as eczema.

Dermatitis herpetiformis

An autoimmune chronic blistering skin disorder characterised by blisters filled with a watery fluid.

Dermatophyte

A fungus parasitic on the skin.

Dermatosis

Is a broad term that refers to any disease of the skin, especially one that is not accompanied by inflammation.

Dermonecrotic

Pertaining to or causing necrosis of the skin.

Dermopathy

A skin disorder characterised by discoloured patches and small papules that often become pigmented and ulcerated and result in scars, most commonly occurring on the shins of people with diabetes mellitus.

Desmutagen

Substances that inactivate mutagens (cancer-causing agents).

Desquamation

The shedding of the outer layers of the skin.

Desquamative gingivitis

Red, painful, glazed and friable gingivae which may be a manifestation of some mucocutaneous conditions such as lichen planus or the vesiculobullous disorders.

Detoxifier

A substance that promotes the removal of toxins from a system or organ.

Diabetes

A metabolic disorder associated with inadequate secretion or utilisation of insulin and characterised by frequent urination and persistent thirst. See Diabetes mellitus.

Diabetes mellitus (DM)

(Sometimes called ‘sugar diabetes’) is a set of chronic, metabolic disease conditions characterised by high blood sugar (glucose) levels that result from defects in insulin secretion, or action, or both. Diabetes mellitus appears in two forms.

Diabetes mellitus type I

(Formerly known as juvenile onset diabetes) caused by deficiency of the pancreatic hormone insulin as a result of destruction of insulin-producing beta cells of the pancreas. Lack of insulin causes an increase of fasting blood glucose that begins to appear in the urine above the renal threshold.

Diabetes mellitus type II

(Formerly called non-insulin-dependent diabetes mellitus or adult-onset diabetes) the disorder is characterised by high blood glucose in the context of insulin resistance and relative insulin deficiency in which insulin is available but cannot be properly utilised.

Diabetic autonomic neuropathy

(DAN) is a serious and common complication of diabetes involving damage of the autonomic nerves. Major clinical manifestations of DAN include resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis, erectile dysfunction, sudomotor dysfunction, impaired neurovascular function, ‘brittle diabetes’ and hypoglycaemic autonomic failure.

Diabetic foot

Any pathology that results directly from diabetes mellitus or any long-term or chronic complication of diabetes

mellitus.

Diabetic neuropathy

A neuropathic disorder that is associated with diabetes mellitus. It affects all peripheral nerves including pain fibres, motor neurons and the autonomic nervous system.

Diabetic retinopathy

Damage to the retina caused by complications of diabetes mellitus, which can eventually lead to blindness.

Diads

Two adjacent structural units in a polymer molecule.

Dialysis

Is a method of removing toxic substances (impurities or wastes) from the blood when the kidneys are unable to do so.

Diaphoresis

Is profuse sweating commonly associated with shock and other medical emergency conditions.

Diaphoretic

A substance that induces perspiration. Also called sudorific.

Diaphyseal

Pertaining to or affecting the shaft of a long bone (diaphysis).

Diaphysis

The main or midsection (shaft) of a long bone.

Diarrhoea

A profuse, frequent and loose discharge from the bowels.

Diastolic

Referring to the time when the heart is in a period of relaxation and dilatation (expansion). *cf.* systolic.

Dieresis

Surgical separation of parts.

Dietary fibre

Is a term that refers to a group of food components that pass through the stomach and small intestine undigested and reach the large intestine virtually unchanged. Scientific evidence suggest that a diet high in dietary fibre can be of value for treating or preventing such disorders as constipation, irritable bowel syndrome, diverticular disease, hiatus hernia and haemorrhoids. Some components of dietary fibre may also be of value in reducing the level of cholesterol in blood and thereby decreasing a risk factor for coronary heart disease and the development of gallstones. Dietary fibre is beneficial in the treatment of some diabetics.

Digalactosyl diglycerides

Are the major lipid components of chloroplasts.

Diosgenin

A steroid-like substance that is involved in the production of the hormone progesterone, extracted from roots of *Dioscorea* yam.

Dipsia

Sensation of dryness in the mouth and throat related to a desire to drink.

Dipsomania

Pathological use of alcohol.

Discussient

An agent (as a medicinal application) which serves to disperse morbid matter.

Disinfectant

An agent that prevents the spread of infection, bacteria or communicable disease.

Distal sensory polyneuropathy (DSPN)

Or peripheral neuropathy, is the most common neurological problem in HIV disease. DSPN also represents a complex

symptom that occurs because of peripheral nerve damage related to advanced HIV disease.

Diuresis

Increased urination .

Diuretic

A substance that increases urination (diuresis).

Diverticular disease

Is a condition affecting the large bowel or colon and is thought to be caused by eating too little fibre.

Diverticulitis

Common, sometimes painful digestive disease which involves the formation of pouches (diverticula) within the bowel wall.

DMBA

7,12-Dimethylbenzanthracene. A polycyclic aromatic hydrocarbon found in tobacco smoke that is a potent carcinogen.

DNA

Deoxyribonucleic acid, a nucleic acid that contains the genetic instructions used in the development and functioning of all known living organisms.

DOCA

Desoxycorticosterone acetate — a steroid chemical used as replacement therapy in Addison's disease.

Dopamine

A catecholamine neurotransmitter that occurs in a wide variety of animals, including both vertebrates and invertebrates.

Dopaminergic

Relating to, or activated by the neurotransmitter, dopamine.

Double blind

Refers to a clinical trial or experiment in which neither the subject nor the researcher knows which treatment any particular subject is receiving.

Douche

A localised spray of liquid directed into a body cavity or onto a part.

DPPH

2,2-Diphenyl-1-picryl-hydrazyl—a crystalline, stable free radical used as an inhibitor of free radical reactions.

Dracunculiasis

Also called guinea worm disease (GWD), is a parasitic infection caused by the nematode, *Dracunculus medinensis*.

Dropsy

An old term for the swelling of soft tissues due to the accumulation of excess water. *adj.* dropsical.

Drug metabolising enzymes

Play central roles in the biotransformation, metabolism and/or detoxification of xenobiotics or foreign compounds that are introduced to the human body.

Drusen

Tiny yellow or white deposits of extracellular materials in the retina of the eye or on the optic nerve head.

Dry eye syndrome

Also called keratoconjunctivitis sicca, occurs when there are not enough tears on the front of the eyes.

DT diaphorase

Also called DTD or NAD(P)H Quinone oxidoreductase, is an obligate two-electron reductase which bioactivates chemotherapeutic quinones.

Dysarthria

Is a motor speech disorder.

Dysbiosis

Also called dysbacteriosis, refers to a condition with microbial imbalances on or inside the body.

Dysentery

(Formerly known as flux or the bloody flux) is a disorder of the digestive system that results in severe diarrhoea containing mucus and blood in the faeces. It is caused usually by a bacterium called *Shigella* .

Dysesthesia

An unpleasant abnormal sensation produced by normal stimuli.

Dysgeusia

Distortion of the sense of taste.

Dyshomeostasis

An imbalance or other breakdown of a homeostasis system.

Dyskinesia

The impairment of the power of voluntary movement, resulting in fragmentary or incomplete movements. *adj.* dyskinetic.

Dyslipidemia

Abnormality in or abnormal amount of lipids and lipoproteins in the blood.

Dysmenorrhoea

Is a menstrual condition characterised by severe and frequent menstrual cramps and pain associated with menstruation.

Dysmotility syndrome

A vague, descriptive term used to describe diseases of the muscles of the gastrointestinal tract (oesophagus, stomach, small and large intestines).

Dysosmia

Qualitative alteration or distortion of the perception of smell.

Dyspareunia

Painful sexual intercourse.

Dyspedia

Indigestion followed by nausea.

Dyspepsia

Refers to a symptom complex of epigastric pain or discomfort.

It is often defined as chronic or recurrent discomfort centred in the upper abdomen and can be caused by a variety of conditions. *cf.* functional dyspepsia.

Dysphagia

Difficulty in swallowing.

Dysphonia

A voice disorder, an impairment in the ability to produce voice sounds using the vocal organs.

Dysplasia

Refers to abnormality in development.

Dyspnoea

Shortness of breath, difficulty in breathing.

Dysrhythmias

See Arrhythmias.

Dystocia

Abnormal or difficult childbirth or labour.

Dystonia

A neurological movement disorder characterised by prolonged, repetitive muscle contractions that may cause twisting or jerking movements of muscles.

Dysuria

Refers to difficult and painful urination.

E - Cadherin

Has traditionally been categorised as a tumour suppressor.

E-Selectin

Also known as endothelial leucocyte adhesion molecule-1 (ELAM-1), CD62E, a member of the selectin family. It is transiently expressed on vascular endothelial cells in response to IL-1 beta and TNF-alpha.

EC 50

Median effective concentration that produces desired effects in 50 % of the test population.

Ecboolic

A drug (as an ergot alkaloid) that tends to increase uterine contractions and that is used especially to facilitate delivery.

Ecchymosis

Skin discolouration caused by the escape of blood into the tissues from ruptured blood vessels.

ECG

See electrocardiography.

EC-SOD

Extracellular superoxide dismutase, a tissue enzyme mainly found in the extracellular matrix of tissues. It participates in the detoxification of reactive oxygen species by catalysing the dismutation of superoxide radicals.

Ectopic heartbeats

Small changes in an otherwise normal heartbeat that lead to extra or skipped heartbeats.

Ectrodactyly

Involves the absence of one or more central digits of the hand or foot.

Eczema

Is broadly applied to a range of persistent skin conditions. These include dryness and recurring skin rashes which are characterised by one or more of these symptoms: redness,

skin oedema, itching and dryness, crusting, flaking, blistering, cracking, oozing or bleeding.

Eczematous rash

Dry, scaly, itchy rash.

ED 50

Is defined as the dose producing a response that is 50 % of the maximum obtainable.

Edema

Formerly known as dropsy or hydropsy, is characterised as swelling caused by abnormal accumulation of fluid beneath the skin, or in one or more cavities of the body. It usually occurs in the feet, ankles and legs, but it can involve the entire body.

Edematogenic

Producing or causing edema.

EGFR proteins

Epidermal growth factor receptor (EGFR) proteins. Protein kinases are enzymes that transfer a phosphate group from a phosphate donor onto an acceptor amino acid in a substrate protein.

EGR-1

Early growth response 1, a human gene.

Eicosanoids

Are signalling molecules made by oxygenation of arachidonic acid, a twenty-carbon essential fatty acid, and include prostaglandins and related compounds.

Elastase

A serine protease that also hydrolyses amides and esters.

Electrocardiography

Or ECG, is a transthoracic interpretation of the electrical activity of the heart over time captured and externally recorded by skin electrodes.

Electromyogram (EMG)

A test used to record the electrical activity of muscles. An electromyogram (EMG) is also called a myogram.

Electuary

A medicinal paste composed of powders, or other medical ingredients, incorporated with sweeteners to hide the taste, suitable for oral administration.

Elephantiasis

A disorder characterised by chronic thickened and oedematous tissue on the genitals and legs due to various causes.

11 β -Hydroxysteroid dehydrogenase

(HSD-11 β or 11 β -HSD) is the name of a family of enzymes that catalyse the conversion of inert 11 keto-products (cortisone) to active cortisol, or vice versa.

Embrocation

Lotion or liniment that relieves muscle or joint pains.

Embryonation

Formation of embryo in the egg.

Embryotoxic

Term that describes any chemical which is harmful to an embryo.

Emesis

Vomiting, throwing up.

Emetic

An agent that induces vomiting. *cf.* antiemetic

Emetocathartic

Causing vomiting and purging.

Emmenagogue

A substance that stimulates, initiates and/or promotes menstrual flow. Emmenagogues are used in herbal

medicine to balance and restore the normal function of the female reproductive system.

Emollient

An agent that has a protective and soothing action on the surfaces of the skin and membranes.

Emphysema

A long-term, progressive disease of the lungs that primarily causes shortness of breath.

Emulsion

A preparation formed by the suspension of very finely divided oily or resinous liquid in another liquid.

Encephalitis

Inflammation of the brain caused by a virus.

Encephalocele

A neural tube defect characterised by saclike protrusions of the brain tissue through a congenital fissure in the skull.

Encephalomalacia

Cerebral softening, a localised softening of the brain substance, due to haemorrhage or inflammation.

Encephalopathy

A disorder or disease of the brain.

Endocrine

adj. of or relating to endocrine glands or the hormones secreted by them.

Endocytosis

Is the process by which cells absorb material (molecules such as proteins) from outside the cell by engulfing it with their cell membrane.

Endometrial cancer

Cancer that arises in the endometrium, the lining of the uterus (womb).

Endometriosis

Is a common and often painful disorder of the female reproductive system in which the endometrium, the tissue that normally lines the womb (uterus), grows outside the uterus. The two most common symptoms of endometriosis are pain and infertility.

Endometritis

Refers to inflammation of the endometrium, the inner lining of the uterus.

Endometrium

The inner lining of the uterus.

Endoplasmic reticulum

Is a network of tubules, vesicles and sacs around the nucleus that are interconnected.

Endostatin

A naturally occurring 20-kDa C-terminal protein fragment derived from type XVIII collagen. It is reported to serve as an antiangiogenic agent that inhibits the formation of the blood vessels that feed cancer tumours.

Endosteum

The thin layer of cells lining the medullary cavity of a bone.

Endosteul

Pertaining to the endosteum.

Endothelial progenitor cells

Population of rare cells that circulate in the blood with the ability to differentiate into endothelial cells, the cells that make up the lining of blood vessels.

Endothelin

Any of a group of vasoconstrictive peptides produced by endothelial cells that constrict blood vessels and raise blood pressure.

Endotoxaemia

The presence of endotoxins in the blood, which may result in shock. *adj* . endotoxemic.

Endotoxin

Toxins associated with certain bacteria, unlike an ‘exotoxin’ that is not secreted in soluble form by live bacteria, but is a structural component in the bacteria which is released mainly when bacteria are lysed.

Enema

Liquid injected into the rectum either as a purgative or medicine. Also called clyster.

Enophthalmos

A condition in which the eye falls back into the socket and inhibits proper eyelid function.

eNOS

(Endothelial nitric oxide synthase) the enzyme responsible for most of the vascular nitric oxide produced.

Enteral

Term used to describe the intestines or other parts of the digestive tract.

Enteralgia

Pain in the intestines; intestinal colic.

Enteral administration

Involves the oesophagus, stomach and small and large intestines (i.e. the gastrointestinal tract).

Enteritis

Refers to inflammation of the small intestine.

Enterocolic disorder

Inflamed bowel disease.

Enterocytes

Tall columnar cells in the small intestinal mucosa that are responsible for the final digestion and absorption of

nutrients.

Enterohaemorrhagic

Causing bloody diarrhoea and colitis, said of pathogenic microorganisms.

Enterohepatonephropathy

Hepatorenal lesions accompanied by renal failure.

Enterolactone

A lignin formed by the action of intestinal bacteria on lignan precursors found in plants; acts as a phytoestrogen.

Enteropooling

Increased fluids and electrolytes within the lumen of the intestines due to increased levels of prostaglandins.

Enterotoxigenic

Of or being an organism containing or producing an enterotoxin.

Enterotoxin

Is a protein toxin released by a microorganism in the intestine.

Entheogen

A substance taken to induce a spiritual experience.

Enuresis

Bed-wetting, a disorder of elimination that involves the voluntary or involuntary release of urine into bedding, clothing or other inappropriate places.

Envenomation

Is the entry of venom into a person's body, and it may cause localised or systemic poisoning.

Eosinophilia

The state of having a high concentration of eosinophils (eosinophil granulocytes) in the blood.

Eosinophils

(Or, less commonly, acidophils) are white blood cells that are one of the immune system components.

Epidermal growth factor receptor (EGFR)

Belongs to the ErbB family of receptor tyrosine kinases (RTK). EGFR are involved in the pathogenesis and progression of different carcinoma types.

Epididymis

A structure within the scrotum attached to the backside of the testis and whose coiled duct provides storage, transit and maturation of spermatozoa.

Epididymitis

A medical condition in which there is inflammation of the epididymis.

Epidural haematoma

Accumulation of blood in the potential space between dura and bone and may be intracranial or spinal.

Epigastralgia

Pain in the epigastric region.

Epigastric discomfort

Bloated abdomen, swelling of abdomen, abdominal distension.

Epilepsy

A common chronic neurological disorder that is characterised by recurrent unprovoked seizures.

Epileptiform

Resembling epilepsy or its manifestations. *adj.* epileptiformic.

Epileptogenesis

A process by which a normal brain develops epilepsy, a chronic condition in which seizures occur. *adj.* epileptogenic.

Episiotomy

A surgical incision through the perineum made to enlarge the vagina and assist childbirth.

Epithelial–mesenchymal transition or transformation (EMT)

A process by which epithelial cells lose their cell polarity and cell–cell adhesion and gain migratory and invasive properties to become mesenchymal cells.

Epithelioma

A usually benign skin disease most commonly occurring on the face, around the eyelids and on the scalp.

Epitope

A single antigenic site on a protein against which an antibody reacts.

Epitrochlearis

The superficial-most muscle of the arm anterior surface.

Epistaxis

Acute haemorrhage from the nostril, nasal cavity or nasopharynx (nosebleed).

Epstein–Barr virus

Herpesvirus that is the causative agent of infectious mononucleosis. It is also associated with various types of human cancers.

ERbeta

Oestrogen receptor beta, a nuclear receptor which is activated by the sex hormone, oestrogen.

Ergocalciferol

A form of vitamin D, also called vitamin D2. See Vitamin D.

Ergogenic

Increasing capacity for bodily or mental labour, especially by eliminating fatigue symptoms.

Ergonic

Increasing capacity for bodily or mental labour, especially by eliminating fatigue symptoms.

ERK (extracellular signal regulated kinases)

Widely expressed protein kinase intracellular signalling molecules which are involved in functions including the regulation of meiosis, mitosis and postmitotic functions in differentiated cells.

Eructation

The act of belching or of casting up wind from the stomach through the mouth.

Eruption

A visible rash or cutaneous disruption.

Eryptosis

Suicidal death of erythrocytes, characterised by cell shrinkage, membrane blebbing, activation of proteases and phosphatidylserine exposure at the outer membrane leaflet.

Erysipelas

Is an intensely red *Streptococcus* bacterial infection that occurs on the face and lower extremities.

Erythema

Abnormal redness and inflammation of the skin, due to vasodilation.

Erythema multiforme

Is a skin disorder due to an allergic reaction or infection; characterised by fever, general ill feeling, skin itching, joint aches and multiple skin lesions.

Erythematous

Characterised by erythema.

Erythroderma

Exfoliative dermatitis.

Erythroleukoplakia

An abnormal patch of red and white tissue that forms on mucous membranes in the mouth and may become cancer. Tobacco (smoking and chewing) and alcohol may increase the risk of erythroleukoplakia.

Erythropoiesis

Is the process whereby erythroid precursor cells proliferate and differentiate into red blood cells.

Erythropoietin (EPO)

A hormone produced by the kidney that promotes the formation of red blood cells (erythrocytes) in the bone marrow.

Eschar

A slough or piece of dead tissue that is cast off from the surface of the skin.

Escharotic

Capable of producing an eschar; a caustic or corrosive agent.

Estradiol

Is the predominant sex hormone present in females, also called oestradiol.

Estrogenic

Relating to oestrogen or producing oestrus.

Euglycaemia

Normal blood glucose concentration.

Eupeptic

Conducive to digestion.

Exanthema

Sudden widespread rash.

Exanthematous

Characterised by or of the nature of an eruption or rash.

Excitotoxicity

Is the pathological process by which neurons are damaged and killed by glutamate and similar substances.

Excipient

A pharmacologically inert substance used as a diluent or vehicle for the active ingredients of a medication.

Exencephaly

A type of cephalic disorder wherein the brain is located outside of the skull.

Exfoliative cheilitis

Is a reactive process, in which upper, lower or both lips become chronically inflamed, crusted and sometimes fissured.

Exocytosis

The cellular process by which cells excrete waste products or chemical transmitters.

Exophthalmos or exophthalmia or proptosis

Is a bulging of the eye anteriorly out of the orbit. *adj.* exophthalmic.

Exotoxin

A toxin secreted by a microorganism and released into the medium in which it grows.

Expectorant

An agent that increases bronchial mucous secretion by promoting liquefaction of the sticky mucous and expelling it from the body.

Experimental allergic encephalomyelitis (EAE)

Is an animal model of brain inflammation.

Exteroceptive

Responsiveness to stimuli that are external to an organism.

Extrapyramidal side effects

Are a group of symptoms (tremor, slurred speech, akathisia, dystonia, anxiety, paranoia and bradyphrenia) that can occur in persons taking antipsychotic medications.

Extravasation

Discharge or escape, as of blood from the vein into the surrounding tissues; discharge or escape from a vessel or channel.

Eyelid oedema

Swollen eyelid caused by inflammation or excess fluid.

Fabry disease

Is a rare X-linked (inherited) lysosomal storage disease caused by alpha-galactosidase A deficiency, which can cause a wide range of systemic symptoms such as pain in the extremities, papules on the lower body parts, cornea clouding, fatigue, neuropathy, renal and cardiac complications.

FAC chemotherapy

Fluorouracil, doxorubicin (adriamycin) and cyclophosphamide chemotherapy.

FADD

Fas-associated protein with death domain; the protein encoded by this gene is an adaptor molecule which interacts with other death cell surface receptors and mediates apoptotic signals.

Familial amyloid polyneuropathy (FAP)

Also called Corino de Andrade's disease, a neurodegenerative autosomal dominant genetically transmitted, fatal, incurable disease.

Familial adenomatous polyposis (FAP)

Is an inherited condition in which numerous polyps form mainly in the epithelium of the large intestine.

Familial dysautonomia

A genetic disorder that affects the development and survival of autonomic and sensory nerve cells.

Fanconi syndrome

Is a disease of the proximal renal tubes in which certain substances normally absorbed into the bloodstream by the kidneys are released into the urine instead.

FasL or CD95L

Fas ligand is a type II transmembrane protein that belongs to the tumour necrosis factor (TNF) family.

FAS, fatty acid synthase (FAS)

A multienzyme that plays a key role in fatty acid synthesis.

Fas molecule

A member of the tumour necrosis factor receptors, which mediates apoptotic signal in many cell types.

Fauces

The passage leading from the back of the mouth into the pharynx.

Favus

A chronic skin infection, usually of the scalp, caused by the fungus *Trichophyton schoenleinii* and characterised by the development of thick, yellow crusts over the hair follicles. Also termed tinea favosa.

Febrifuge

An agent that reduces fever. Also called an antipyretic.

Febrile

Pertaining to or characterised by fever.

Febrile neutropenia

The development of fever, often with other signs of infection, in an individual with neutropenia, an abnormally low number of neutrophil granulocytes in the blood.

Felon

A purulent infection in the bulbous distal end of a finger.

Fetotoxic

Toxic to the fetus.

Fibrates

Hypolipidemic agents primarily used for decreasing serum triglycerides, while increasing high-density lipoprotein (HDL).

Fibril

A small slender fibre or filament.

Fibrin

Insoluble protein that forms the essential portion of the blood clot.

Fibrinolysis

A normal ongoing process that dissolves fibrin and results in the removal of small blood clots.

Fibrinolytic

Causing the dissolution of fibrin by enzymatic action.

Fibroblast

Type of cell that synthesises the extracellular matrix and collagen, the structural framework (stroma) for animal tissues, and plays a critical role in wound healing.

Fibrogenic

Promoting the development of fibres.

Fibromyalgia

A common and complex chronic, body-wide pain disorder that affects people physically, mentally and socially. Symptoms include debilitating fatigue, sleep disturbance and joint stiffness. Also referred to as FM or FMS.

Fibronectin

A high molecular weight (~440kDa) glycoprotein of the extracellular matrix (ECM) that adheres to membrane-

spanning receptor proteins called integrins.

Fibrosarcoma

A malignant tumour derived from fibrous connective tissue and characterised by immature proliferating fibroblasts or undifferentiated anaplastic spindle cells.

Fibrosis

The formation of fibrous tissue as a reparative or reactive process.

Filarial

Pertaining to a thread-like nematode worm.

Filariasis

A parasitic and infectious tropical disease that is caused by thread-like filarial nematode worms in the superfamily Filarioidea.

Fistula

An abnormal connection between two organs inside of the body.

Fistula-in-ano

A track connecting the internal anal canal to the skin surrounding the anal orifice.

5'-Nucleotidase

(5'-Ribonucleotide phosphohydrolase) an intrinsic membrane glycoprotein present as an ectoenzyme in a wide variety of mammalian cells, hydrolyses 5'-nucleotides to their corresponding nucleosides.

5-HT_{1A} receptor

A serotonin protein that binds to 5-hydroxytryptamine (5-HT) with high affinity to exert subtle control over emotion and behaviour.

Flash electroretinogram or flash ERG (fERG)

Is a test which measures the electrical response of the eye's light-sensitive cells (rods and cones). It also checks other

cell layers in the retina.

Flatulence

Is the presence of a mixture of gases known as flatus in the digestive tract of mammals expelled from the rectum.

Excessive flatulence can be caused by lactose intolerance, certain foods or a sudden switch to a high fibre.

Flavans

A subgroup of flavonoids. See Flavonoids.

Flavanols

A subgroup of flavonoids, are a class of flavonoids that use the 2-phenyl-3,4-dihydro-2H-chromen-3-ol skeleton. These compounds include the catechins and the catechin gallates. They are found in chocolate, fruits and vegetables. See Flavonoids.

Flavanones

A subgroup of flavonoids, constitute >90% of total flavonoids in citrus. The major dietary flavanones are hesperetin, naringenin and eriodictyol.

Flavivirus

A family of viruses transmitted by mosquitoes and ticks that cause some important diseases, including dengue, yellow fever, tick-borne encephalitis and West Nile fever.

Flavones

A subgroup of flavonoids based on the backbone of 2-phenylchromen-4-one (2-phenyl-1-benzopyran-4-one). Flavones are mainly found in cereals and herbs.

Flavonoids

(Or bioflavonoids) are a group of polyphenolic antioxidant compounds that occur in plant as secondary metabolites. They are responsible for the colour of fruit and vegetables. Twelve basic classes (chemical types) of flavonoids have been recognised: flavones, isoflavones, flavans, flavanones, flavanols, flavanolols, anthocyanidins, catechins (including proanthocyanidins),

leucoanthocyanidins, chalcones, dihydrochalcones and aurones. Apart from their antioxidant activity, flavonoids are known for their ability to strengthen capillary walls, thus assisting circulation and helping to prevent and treat bruising, varicose veins, bleeding gums and nosebleeds and heavy menstrual bleeding, and are also anti-inflammatory.

Flourine

F is an essential chemical element that is required for the maintenance of healthy bones and teeth and to reduce tooth decay. It is found in seaweeds, tea, water, seafood and dairy products.

Fluorosis

A dental health condition caused by a child receiving too much fluoride during tooth development.

Flux

An excessive discharge of fluid.

FMD (flow-mediated dilation)

A measure of endothelial dysfunction which is used to evaluate cardiovascular risk. Also called FMVD (flow-mediated vasodilation).

Focal adhesion kinase (FAK)

Is a protein tyrosine kinase which is recruited at an early stage to focal adhesions and which mediates many of the downstream regulatory responses.

Follicle-stimulating hormone (FSH)

A hormone produced by the pituitary gland. In women, it helps control the menstrual cycle and the production of eggs by the ovaries.

Follicular atresia

The breakdown of the ovarian follicles.

Fomentation

Treatment by the application of war, moist substance.

Fontanelle

Soft spot on an infant's skull.

Forkhead box-O transcription factors (FOXOs)

Are a family of transcription factors that play important roles in regulating the expression of genes involved in cell growth, proliferation, differentiation and longevity. It also plays an important role in tumour suppression by regulating the expression of genes involved in stress resistance, DNA damage repair, cell cycle arrest and apoptosis.

Framboesia

See Yaws.

FRAP

Ferric reducing ability of plasma, an assay used to assess antioxidant property.

Fibrillation

Is the rapid, irregular and unsynchronised contraction of muscle fibres, especially with regard to the heart.

5-Dihydroaldosterone

A hormone secreted by the adrenal cortex that regulates electrolyte and water balance by increasing the renal retention.

Friedreich's ataxia

Is a genetic inherited disorder that causes progressive damage to the nervous system resulting in symptoms ranging from muscle weakness and speech problems to heart disease. *cf.* ataxia.

Fulminant hepatitis

Acute liver failure.

Functional dyspepsia

A non-ulcer condition that causes an upset stomach or pain or discomfort in the upper belly, near the ribs.

Functional food

Is any fresh or processed food claimed to have a health-promoting or disease-preventing property beyond the basic function of supplying nutrients. Also called medicinal food.

Furuncle

Is a skin disease caused by the infection of hair follicles usually caused by *Staphylococcus aureus* , resulting in the localised accumulation of pus and dead tissue.

Furunculosis

Skin condition characterised by persistent, recurring boils.

G protein-coupled receptor kinases (GRKs , GPCRKs)

A family of protein kinases which regulate the activity of G protein-coupled receptors (GPCRs) by phosphorylating their intracellular domains after their associated G proteins have been released and activated.

GABA

Gamma aminobutyric acid, required as an inhibitory neurotransmitter to block the transmission of an impulse from one cell to another in the central nervous system, which prevents over-firing of the nerve cells. It is used to treat both epilepsy and hypertension.

GADD 152

A proapoptotic gene.

Galctifuge

Or lactifuge, causing the arrest of milk secretion.

Galactagogue

A substance that promotes the flow of milk.

Galactophoritis

Inflammation of the milk ducts.

Galactopoietic

Increasing the flow of milk; milk producing.

Gallbladder

A small, pear-shaped muscular sac, located under the right lobe of the liver, in which bile secreted by the liver is stored until needed by the body for digestion. Also called cholecyst, cholecystitis.

Gallic acid equivalent (GAE)

Measures the total phenol content in terms of the standard gallic acid by the Folin–Ciocalteu assay.

Galphai proteins or G alpha I proteins

Are heterotrimeric guanine nucleotide-regulatory (G) proteins associated with a variety of intracellular membranes and specific plasma membrane domains.

Gamma GT (GGT)

Gamma-glutamyl transpeptidase, a liver enzyme.

Gap junction intercellular communication

Is considered to be the sole means by which low molecular weight factors inside a cell can pass directly into the interior of neighbouring cells. Gap junctions are considered to play an essential role in the maintenance of homeostasis.

Gastralgia

(Heartburn) pain in the stomach or abdominal region. It is caused by excess of acid, or an accumulation of gas, in the stomach.

Gastric

Pertaining to or affecting the stomach.

Gastric emptying

Refers to the speed at which food and drink leave the stomach.

Gastritis

Inflammation of the stomach.

Gastrocnemius muscle

The big calf muscle at the rear of the lower leg.

Gastrodynia

Pain in the stomach.

Gastroparesis

Also called **delayed gastric emptying** , a medical condition consisting of a paresis (partial paralysis) of the stomach, resulting in food remaining in the stomach for an abnormally long time.

Gastropromkinetic

See Prokinetic.

Gastrotonic (gastroprotective)

Substance that strengthens, tones or regulates gastric functions (or protects from injury) without overt stimulation or depression .

Gavage

Forced feeding.

Gene silencing

Suppression of the expression of a gene.

Genotoxic

Describes a poisonous substance which harms an organism by damaging its DNA, thereby capable of causing mutations or cancer.

Genotoxin

A chemical or another agent that damages cellular DNA, resulting in mutations or cancer.

Geriatrics

Is a subspecialty of internal medicine that focuses on healthcare of elderly people.

Gestational hypertension

Development of arterial hypertension in a pregnant woman after 20 weeks of gestation.

Ghrelin

A gastrointestinal peptide hormone secreted by epithelial cells in the stomach lining; it stimulates appetite and gastric emptying and increases cardiac output.

Gingival index

An index describing the clinical severity of gingival inflammation as well as its location.

Gingivitis

Refers to gingival inflammation induced by bacterial biofilms (also called plaque) adherent to tooth surfaces.

Gin-nan sitotoxism

Toxicity caused by ingestion of ginkgotoxin and characterised mainly by epileptic convulsions, paralysis of the legs and loss of consciousness.

GIP

Gastric inhibitory polypeptide also known as the glucose-dependent insulintropic peptide, a member of the secretin family of hormones.

Glaucoma

A group of eye diseases in which the optic nerve at the back of the eye is slowly destroyed, leading to impaired vision and blindness.

Gleet

A chronic inflammation (as gonorrhoea) of a bodily orifice usually accompanied by an abnormal discharge.

Glial cells

Support non-neuronal cells in the central nervous system that maintain homeostasis, form myelin and provide protection for the brain's neurons.

Glioma

Is a type of tumour that starts in the brain or spine. It is called a glioma because it arises from glial cells.

Glioblastoma

Common and most lethal form of brain tumour.

Glioblastoma multiforme

Most common and most aggressive type of primary brain tumour in humans, involving glial cells.

Glomerulonephritis (GN)

A renal disease characterised by inflammation of the glomeruli, or small blood vessels in the kidneys. Also known as glomerular nephritis. *adj.* glomerulonephritic.

Glomerulopathy

Any disease of the renal glomeruli.

Glomerulosclerosis

A hardening (fibrosis) of the glomerulus in the kidney.

Glossal

Pertaining to the tongue.

GLP-1

Glucagon-like peptide-1.

Glucagon-like peptide-1

(GLP-1) is derived from the transcription product of the proglucagon gene, reduces insulin requirement in diabetes mellitus and promotes satiety.

Gluconeogenesis

A metabolic pathway that results in the generation of glucose from non-carbohydrate carbon substrates such as lactate. *adj.* gluconeogenic.

Glucose-6-phosphate dehydrogenase (G6PD or G6PDH)

Is a cytosolic enzyme in the pentose phosphate metabolic pathway.

Glucose transporter type 4 (GLUT 4)

Insulin-regulated glucose transporter found in adipose tissues and striated muscles that modulates insulin-related translocation into the cell.

Glucose transporters

(GLUT or SLC2A family) are a family of membrane proteins found in most mammalian cells.

Glucosuria or glycosuria

Is the excretion of glucose into the urine.

Glucosyltransferase

An enzyme that enables the transfer of glucose.

Glucuronidation

A phase II detoxification pathway occurring in the liver in which glucuronic acid is conjugated with toxins.

Glutamic oxaloacetic transaminase (GOT)

Catalyses the transfer of an amino group from an amino acid (Glu) to a 2-keto-acid to generate a new amino acid and the residual 2-keto-acid of the donor amino acid.

Glutamic pyruvate transaminase (GPT)

See Alanine aminotransferase.

Glutathione (GSH)

A tripeptide produced in the human liver and plays a key role in intermediary metabolism, immune response and health. It plays an important role in scavenging free radicals and protects cells against several toxic oxygen-derived chemical species.

Glutathione peroxidase (GPX)

The general name of an enzyme family with peroxidase activity whose main biological role is to protect the organism from oxidative damage.

Glutathione S-transferase (GST)

A major group of detoxification enzymes that participate in the detoxification of reactive electrophilic compounds by catalysing their conjugation to glutathione.

Glycaemic index (GI)

Measures carbohydrates according to how quickly they are absorbed and raise the glucose level of the blood.

Glycaemic load (GL)

Is a ranking system for carbohydrate content in food portions based on their glycaemic index and the amount of available carbohydrate, i.e. $GI \times \text{available carbohydrate} \div 100$. Glycaemic load combines both the quality and quantity of carbohydrate in one 'number'. It's the best way to predict blood glucose values of different types and amounts of food.

Glycation or glycosylation

A chemical reaction in which glycosyl groups are added to a protein to produce a glycoprotein.

Glycogenolysis

Is the catabolism of glycogen by removal of a glucose monomer through cleavage with inorganic phosphate to produce glucose-1-phosphate.

Glycometabolism

Metabolism (oxidation) of glucose to produce energy.

Glycosuria

Or glucosuria is an abnormal condition of osmotic diuresis due to excretion of glucose by the kidneys into the urine.

Glycosylases

A family of enzymes involved in base excision repair.

Goitre

An enlargement of the thyroid gland leading to swelling of the neck or larynx.

Goitrogen

Substance that suppresses the function of the thyroid gland by interfering with iodine uptake, causing enlargement of the thyroid, i.e. goitre.

Goitrogenic

adj. causing goitre.

Gonadotroph

A basophilic cell of the anterior pituitary specialised to secrete follicle-stimulating hormone or luteinising hormone.

Gonatropins

Protein hormones secreted by gonadotrope cells of the pituitary gland of vertebrates.

Gonorrhoea

A common sexually transmitted bacterial infection caused by the bacterium *Neisseria gonorrhoeae* .

Gout

A disorder caused by a build-up of a waste product, uric acid, in the bloodstream. Excess uric acid settles in joints causing inflammation, pain and swelling.

G protein-coupled receptors (GPCRs)

Constitute the largest family of cell surface molecules involved in signal transmission. These receptors play key physiological roles and their dysfunction results in several diseases .

Granulation

The condition or appearance of being granulated (becoming grain-like).

Gravel

Sand-like concretions of uric acid, calcium oxalate and mineral salts formed in the passages of the biliary and urinary tracts.

Gripe water

Is a home remedy for babies with colic, gas, teething pain or other stomach ailments. Its ingredients vary and may include alcohol, bicarbonate, ginger, dill, fennel and chamomile.

Grippe

An epidemic catarrh; older term for influenza.

GSH

See Glutathione.

GSH-Px

Glutathione peroxidase, general name of an enzyme family with peroxidase activity whose main biological role is to protect the organism from oxidative damage.

GSSG

Glutathione disulfides are biologically important intracellular thiols, and alterations in the GSH/GSSG ratio are often used to assess exposure of cells to oxidative stress.

GSTM

Glutathione S transferase M1, a major group of detoxification enzymes.

GSTM 2

Glutathione S transferase M2, a major group of detoxification enzymes.

G2-M cell cycle

The phase where the cell prepares for mitosis and where chromatids and daughter cells separate.

Guillain–Barre syndrome

Is a serious disorder that occurs when the body's defence (immune) system mistakenly attacks part of the nervous system, leading to nerve inflammation, muscle weakness and other symptoms.

Gynecomastia

Enlargement of the gland tissue of the male breast, resulting from an imbalance of hormones.

Gynecopathy

Any or various diseases specific to women.

Gynoid adiposity

Fat distribution mainly to the hips and thighs, pear shaped.

Haemagogic

Promoting a flow of blood.

Haematemesis, hematemesis

Is the vomiting of blood.

Haematinic

Improving the quality of the blood, its haemoglobin level and the number of erythrocytes.

Haematochezia

Passage of stools containing blood.

Haematochyluria, hematochyluria

the discharge of blood and chyle (emulsified fat) in the urine; see also Chyluria.

Haematoma, hematoma

A localised accumulation of blood in a tissue or space composed of clotted blood.

Haematometra, hematometra

A medical condition involving bleeding of or near the uterus.

Haematopoiesis, hematopoiesis

Formation of blood cellular components from the haematopoietic stem cells.

Haematopoietic

adj. relating to the formation and development of blood cells.

Haematuria, Hematuria

Is the presence of blood in the urine. Haematuria is a sign that something is causing abnormal bleeding in a person's genitourinary tract.

Haeme oxygenase

(HO-1, encoded by Hmox1) is an inducible protein activated in systemic inflammatory conditions by oxidant stress, an

enzyme that catalyses degradation of haem.

Haemochromatosis

iron overload in the body with a hereditary or primary cause.

Haemodialysis, hemodialysis

A method for removing waste products such as potassium and urea, as well as free water from the blood when the kidneys are in renal failure.

Haemolysis

Lysis of red blood cells and the release of haemoglobin into the surrounding fluid (plasma). *adj.* haemolytic.

Haemoptysis, hemoptysis

Is the coughing up of blood from the respiratory tract. The blood can come from the nose, mouth, throat and the airway passages leading to the lungs.

Haemorrhage, hemaorrhage

bleeding, discharge of blood from blood vessels.

Haemorrhoids, hemorrhoids

A painful condition in which the veins around the anus or lower rectum are enlarged, swollen and inflamed. Also called piles.

Haemostasis, hemostasis

A complex process which causes the bleeding process to stop.

Haemostatic, hemostatic

Something that stops bleeding.

Halitosis

(Bad breath) a common condition caused by sulphur-producing bacteria that live within the surface of the tongue and in the throat.

Hallucinogen

Drug that produces hallucinogen.

Hallucinogenic

Inducing hallucinations.

Hallux abducto valgus

Commonly called bunion is an abnormal bending of the big toe towards the other toes of the foot.

Haplotype

A set of alleles of closely linked loci on a chromosome that tend to be inherited together.

Hapten

A small molecule that can elicit an immune response only when attached to a large carrier such as a protein.

HATs

Histone acetyl transferases, enzymes that regulate the acetylation of histones and transcription factors, playing a major role in the growth and differentiation of cells.

HbA1c

Glycosylated haemoglobin.

HBeAg

Hepatitis B e antigen.

HBsAg

Hepatitis B s antigen.

HBD-2 (human β -defensin 2)

A member of the defensin family of antimicrobial peptides that plays important roles in the innate and adaptive immune system of both vertebrates and invertebrates.

Heartburn

Burning sensation in the stomach and oesophagus caused by excessive acidity of the stomach fluids.

Heat rash

Any condition aggravated by heat or hot weather such as intertrigo.

Heat shock chaperones (HSC)

Ubiquitous molecules involved in the modulation of protein conformational and complexation states, associated with heat stress or other cellular stress responses.

Heat shock proteins (HSP)

A group of functionally related proteins, the expression of which is increased when the cells are exposed to elevated temperatures or other cellular stresses.

Helminthiasis

A disease in which a part of the body is infested with worms such as pinworm, roundworm or tapeworm.

Haemagglutination

A specific form of agglutination that involves red blood cells.

Haemagglutination–inhibition test

Measures the ability of soluble antigen to inhibit the agglutination of antigen-coated red blood cells by antibodies.

Haemagglutinin

Refers to a substance that causes red blood cells to agglutinate.

Haemangioma

Blood vessel.

Haematocrit

Is a blood test that measures the percentage of the volume of the whole blood that is made up of red blood cells.

Haematopoietic

Pertaining to the formation of blood or blood cells.

Haematopoietic stem cell

Is a cell isolated from the blood or bone marrow that can renew itself and can differentiate to a variety of specialised cells.

Haem oxygenase-1 (HO-1)

An enzyme that catalyses the degradation of haem; an inducible stress protein, confers cytoprotection against oxidative stress in-vitro and in-vivo.

Hemiplegia

Paralysis of the arm, leg and trunk on the same side of the body.

Haemoglobinopathies

Genetic defects that produce abnormal haemoglobins and anaemia.

Haemolytic anaemia

Anaemia due to haemolysis, the breakdown of red blood cells in the blood vessels or elsewhere in the body.

Hemorheology

Study of blood flow and its elements in the circulatory system.
adj. hemorheological.

Haemorrhagic colitis

An acute gastroenteritis characterised by overtly bloody diarrhoea that is caused by *Escherichia coli* infection.

Haemolysin

Certain proteins and lipids that cause lysis of red blood cells by damaging their cell membranes.

Haemolytic uremic syndrome

Is a disease characterised by haemolytic anaemia, acute renal failure (uraemia) and a low platelet count.

Hepa-1c1c7

A type of hepatoma cells.

Hepatalgia

Pain or discomfort in the liver area.

Hepatectomy

The surgical removal of part or all of the liver.

Hepatic

Relating to the liver.

Hepatic cirrhosis

Affecting the liver, characterised by hepatic fibrosis and regenerative nodules.

Hepatic encephalopathy

Is the loss of brain function that occurs when the liver is unable to remove toxins from the blood.

Hepatic fibrosis

Is overly profuse wound healing in which excessive connective tissue builds up in the liver.

Hepatitis

Inflammation of the liver.

Hepatitis A

(Formerly known as infectious hepatitis) is an acute infectious disease of the liver caused by the hepatovirus hepatitis A virus.

Hepatocarcinogenesis

Represents a linear and progressive cancerous process in the liver in which successively more aberrant monoclonal populations of hepatocytes evolve.

Hepatocellular carcinoma (HCC)

Also called malignant hepatoma, is a primary malignancy (cancer) of the liver.

Hepatocytolysis

Cytotoxicity (dissolution) of liver cells.

Hepatoma

Cancer of the liver.

Hepatomegaly

Condition of enlarged liver.

Hepatopathy

A disease or disorder of the liver.

Hepatoprotective

(Liver protector) a substance that helps protect the liver from damage by toxins, chemicals or other disease processes.

Hepatoregenerative

A compound that promotes hepatocellular regeneration, repairs and restores liver function to optimum performance.

Hepatotonic

(Liver tonic) a substance that is tonic to the liver—usually employed to normalise liver enzymes and function.

Hernia

Occurs when part of an internal organ bulges through a weak area of muscle.

HER-2

Human epidermal growth factor receptor 2, a protein giving higher aggressiveness in breast cancer, also known as ErbB-2, ERBB2.

Herpes

A chronic inflammation of the skin or mucous membrane characterised by the development of vesicles on an inflammatory base.

Herpes circinatus

Dermatitis herpetiformis (resembling herpes).

Herpes simplex virus 1 and 2 (HSV-1 and HSV-2)

Are two species of the herpesvirus family which cause a variety of illnesses/infections in humans such as cold sores, chickenpox or varicella, shingles or herpes zoster (VZV), cytomegalovirus (CMV) and various cancers and can cause brain inflammation (encephalitis). HSV-1 is commonly associated with herpes outbreaks of the face known as cold sores or fever blisters, whereas HSV-2 is more often associated with genital herpes. They are also

called human herpesvirus 1 and 2 (HHV-1 and HHV-2) and are neurotropic and neuroinvasive viruses; they enter and hide in the human nervous system, accounting for their durability in the human body.

Herpes zoster

Or simply zoster, commonly known as shingles and also known as zona, is a viral disease characterised by a painful skin rash with blisters.

Herpes zoster ophthalmicus (HZO)

Is a viral ocular disease characterised by a painful skin rash in one or more dermatome distributions of the fifth cranial nerve, shared by the eye and orbit.

Heterophobia

Term used to describe irrational fear of, aversion to, or discrimination against heterosexuals.

HDL-C (HDL cholesterol)

High-density lipoprotein cholesterol, also called ‘good cholesterol’. See also High-density lipoprotein.

Hiatus hernia

Occurs when the upper part of the stomach pushes its way through a tear in the diaphragm.

High-density lipoprotein (HDL)

Is one of the five major groups of lipoproteins which enable cholesterol and triglycerides to be transported within the water-based blood stream. HDL can remove cholesterol from atheroma within arteries and transport it back to the liver for excretion or reutilisation—which is the main reason why HDL-bound cholesterol is sometimes called ‘good cholesterol’, or HDL-C. A high level of HDL-C seems to protect against cardiovascular diseases. *cf.* LDL.

HGPRT, HPRT (hypoxanthine-guanine phosphoribosyl transferase)

An enzyme that catalyses the conversion of 5-phosphoribosyl-1-pyrophosphate and hypoxanthine, guanine or 6-

mercaptopurine to the corresponding 5'-mononucleotides and pyrophosphate. The enzyme is important in purine biosynthesis as well as central nervous system functions.

Hippocampus

A ridge in the floor of each lateral ventricle of the brain that consists mainly of grey matter.

Hippocampal

Pertaining to the hippocampus.

Hirsutism

A condition where women have excess facial and body hair that is dark and coarse.

Histaminergic

Liberated or activated by histamine, relating to the effects of histamine at histamine receptors of target tissues.

Histaminergic receptors

Are types of G protein-coupled receptors with histamine as their endogenous ligand.

Histone acetyltransferases (HAT)

Are enzymes that acetylate conserved lysine amino acids on histone proteins by transferring an acetyl group from acetyl CoA to form *N*-acetyl lysine. HATs act as transcriptional coactivators.

Histone lysine demethylases (KDMs)

Enzymes that play a key role in the amplification of hypoxia-inducible-factor signalling and expression of proangiogenic genes in cancer and neurological disorders.

HIV

See Human immunodeficiency virus.

Hives

(Urticaria) is a skin rash characterised by circular wheals of reddened and itching skin.

HLA

Human leucocyte antigen system, name of the major histocompatibility complex (MHC) in humans.

HLA-DQB1

Human leucocyte antigen beta chain.

HLA-DR

A major histocompatibility complex (MHC) class II cell surface receptor encoded by the human leucocyte antigen complex on chromosome 6 region 6p21.31.

HMG-CoAr

3-Hydroxy-3-methyl-glutaryl-CoA reductase or HMGCR is the rate-controlling enzyme (EC 1.1.1.88) of the mevalonate pathway.

HMG-CoA

3-Hydroxy-3-methylglutaryl-coenzyme A, an intermediate in the mevalonate pathway.

Hodgkin's disease

Disease characterised by enlargement of the lymph glands, spleen and anaemia.

Homeodomain transcription factor

A protein domain encoded by a homeobox. Homeobox genes encode transcription factors which typically switch on cascades of other genes.

Homeostasis

The maintenance of a constant internal environment of a cell or an organism, despite fluctuations in the external.

Homeotherapy

Treatment or prevention of disease with a substance similar but not identical to the causative agent of the disease.

Homocysteine

An amino acid in the blood.

Homograft

See Allograft.

Hormesis a

Term used by toxicologists to refer to a biphasic dose response to an environmental agent characterised by a low-dose stimulation or beneficial effect and a high-dose inhibitory or toxic effect.

Hormonal (female)

Substance that has a hormone-like effect similar to that of oestrogen and/or a substance used to normalise female hormone levels.

Hormonal (male)

Substance that has a hormone-like effect similar to that of testosterone and/or a substance used to normalise male hormone levels.

HRT

Hormone replacement therapy, the administration of the female hormones, oestrogen and progesterone and sometimes testosterone.

HSF-1 factor

Major regulator of heat shock protein transcription in eukaryotes.

HSP27

Is an ATP-independent, 27kDa heat shock protein chaperone that confers protection against apoptosis.

HSP70

Heat shock protein chaperone that confers protection against heat-induced apoptosis.

HSP90

A 90kDa heat shock protein chaperone that has the ability to regulate a specific subset of cellular signalling proteins that have been implicated in disease processes.

HSPD 1

Heat shock 60kDa protein 1

hTERT (TERT)

Telomerase reverse transcriptase is a catalytic subunit of the enzyme telomerase in humans. It exerts a novel protective function by binding to mitochondrial DNA, increasing respiratory chain activity and protecting against oxidative stress-induced damage.

HT29 cells

Are human intestinal epithelial cells which produce the secretory component of immunoglobulin A (IgA) and carcinoembryonic antigen (CEA).

Human cytomegalovirus (HCMV)

A DNA herpesvirus which is the leading cause of congenital viral infection and mental retardation.

Human factor X

A coagulation factor also known by the eponym Stuart–Prower factor or as thrombokinase, is an enzyme involved in blood coagulation. It synthesised in the liver and requires vitamin K for its synthesis.

Human immunodeficiency virus (HIV)

A retrovirus that can lead to acquired immunodeficiency syndrome (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections.

Humoral immune response (HIR)

Is the aspect of immunity that is mediated by secreted antibodies (as opposed to cell-mediated immunity, which involves T lymphocytes) produced in the cells of the B lymphocyte lineage (B cell).

HUVEC

Human umbilical vein endothelial cells.

Hyaluronidase

Enzymes that catalyse the hydrolysis of certain complex carbohydrates like hyaluronic acid and chondroitin sulphates.

Hydatidiform

A rare mass or growth that forms inside the uterus at the beginning of a pregnancy.

Hydrocele

Abnormal accumulation of fluid inside the scrotum.

Hydrocholeretic

An agent that stimulates an increased output of bile of low specific gravity.

Hydrogogue

A purgative that causes an abundant watery discharge from the bowel.

Hydronephrosis

Is distension and dilation of the renal pelvis and calyces, usually caused by obstruction of the free flow of urine from the kidney.

Hydrophobia

A viral neuroinvasive disease that causes acute encephalitis (inflammation of the brain) in warm-blooded animals. Also called rabies.

Hydropsy

See Dropsy.

Hydrothorax

Accumulation of serous fluid in the pleural cavity.

Hyperaemia

The increase of blood flow to different tissues in the body.

Hyperalgesia

An increased sensitivity to pain (enhanced pricking pain), which may be caused by damage to nociceptors or

peripheral nerves.

Hyperammonemia, hyperammonaemia

A metabolic disturbance characterised by an excess of ammonia in the blood.

Hypercalciuria

(*Idiopathic*) presence of excess calcium in the urine without obvious cause.

Hypercholesterolemia

High levels of cholesterol in the blood that increase a person's risk for cardiovascular disease leading to stroke or heart attack.

Hyperdipsia

Intense thirst that is relatively temporary.

Hyperemia

Is the increased blood flow that occurs when tissue is active.

Hyperemesis

Severe and persistent nausea and vomiting (morning sickness) during pregnancy.

Hyperemesis gravidarum

Is a pregnancy complication characterised by severe nausea, vomiting, weight loss and electrolyte disturbance.

Hyperfibrinogenemia

Excessive fibrinogen in the blood.

Hyperglycaemia hyperglycaemic

High blood sugar; is a condition in which an excessive amount of glucose circulates in the blood plasma.

Hyperglycaemic

A substance that raises blood sugar levels .

Hyperhomocysteinemia

Is a medical condition characterised by an abnormally large level of homocysteine in the blood.

Hyperinsulinemia

A condition in which there are excess levels of circulating insulin in the blood; also known as prediabetes.

Hyperkalemia

Is an elevated blood level of the electrolyte potassium.

Hyperkeratosis

Abnormal thickening of the outer layer of the skin. *adj.* hyperkeratotic.

Hyperknesis

Enhanced itch to pricking.

Hyperleptinemia

Increased serum leptin level.

Hyperlipoproteinemia

A metabolic disorder characterised by abnormally elevated concentrations of lipid/lipoprotein in the plasma; also known as hyperlipidaemia and hyperlipemia.

Hypermenorrhea

Abnormally heavy or prolonged menstruation.

Hypermethylation

An increase in the inherited methylation of cytosine and adenosine residues in DNA.

Hypermineralocorticoidism

Excessive mineralocorticoid activity.

Hyperoxaluria

An excessive urinary excretion of oxalate.

Hyperphagia

Or polyphagia abnormally large ingestion of food beyond that needed for basic energy requirements.

Hyperpiesia

Persistent and pathological high blood pressure for which no specific cause can be found.

Hyperplasia

Increased cell production in a normal tissue or organ.

Hyper-pre-beta-lipoproteinaemia

Increased concentrations of pre-beta-lipoproteins in the blood.

Hyperpropulsion

Using water pressure as a force to move objects; used to dislodge calculi in the urethra.

Hyperpyrexia

Is an abnormally high fever.

Hypertension

Commonly referred to as 'high blood pressure' or HTN, is a medical condition in which the arterial blood pressure is chronically elevated.

Hypertensive

Characterised or caused by increased tension or pressure as abnormally high blood pressure.

Hypertonia

Abnormal increase in muscle tension and a reduced ability of the muscle to stretch.

Hypertriglyceridaemia or hypertriglycaemia

A disorder that causes high triglycerides in the blood.

Hypertrophy

Enlargement or overgrowth of an organ.

Hyperuricaemia

Is a condition characterised by abnormally high level of uric acid in the blood.

Hypoadiponectinemia

The state of having too low level of adiponectin, a major metabolic endocrine, responsible for regulating things like glucose uptake and lipolysis (the breakdown of fat deposits); low adiponectin is a risk factor for both type II diabetes and metabolic syndrome.

Hypoalbuminemia

A medical condition where levels of albumin in blood serum are abnormally low.

Hypocalcaemic tetany

A disease caused by an abnormally low level of calcium in the blood and characterised by hyperexcitability of the neuromuscular system and results in carpopedal spasms.

Hypochlorhydria

Refer to states where the production of gastric acid in the stomach is absent or low.

Hypocholesterolemic

(Cholesterol reducer) a substance that lowers blood cholesterol levels.

Hypocitraturia

Low amount of citrate in the urine, an important risk factor for kidney stone formation.

Hypocorticism

See Addison's disease.

Hypocortisolism

See Addison's disease.

Hypoesthesia

(Or hypesthesia) refers to a reduced sense of touch or sensation, or a partial loss of sensitivity to sensory stimuli.

Hypoglycaemic

An agent that lowers the concentration of glucose (sugar) in the blood.

Hypogonadism syndrome

Characterised by defects of the gonads, a diminished functional activity of the gonads—the testes and ovaries in males and females, respectively.

Hypokalemia

Medical condition in which the concentration of potassium (K^+) in the blood is low.

Hypoparathyroidism

An uncommon condition in which your body secretes abnormally low levels of parathyroid hormone (PTH). PTH plays a key role in modulating the balance of calcium and phosphorus levels in the body.

Hypoperfusion

Decreased blood flow through an organ, characterised by an imbalance of oxygen demand and oxygen delivery to tissues.

Hypophagic

Undereating.

Hypophysectomy

The surgical removal of the hypophysis (pituitary gland).

Hypospadias

An abnormal birth defect in males in which the urethra opens on the under surface of the penis.

Hypotensive

Characterised by or causing diminished tension or pressure, as abnormally low blood pressure.

Hypothermia

A condition in which an organism's temperature drops below that required for normal metabolism and body functions.

Hypothermic

Relating to hypothermia, with subnormal body temperature.

Hypoxaemia

Is the reduction of oxygen specifically in the blood.

Hypoxia

A shortage of oxygen in the body. *adj.* hypoxic.

Hypoxia-inducible factors (HIFs)

Transcription factors that respond to changes in available oxygen in the cellular environment, specifically, to deficiency in oxygen.

ICAM-1 (inter-cellular adhesion molecule 1)

Also known as CD54 (cluster of differentiation 54), is a protein that in humans is encoded by the ICAM1 gene.

IC₅₀

The median maximal inhibitory concentration; a measure of the effectiveness of a compound in inhibiting biological or biochemical function.

I.C.V.

(Intra-cerebroventricular) injection of chemical into the right lateral ventricle of the brain.

Iceterus

Jaundice, yellowish pigmentation of the skin.

Ichthyosis

Dry, rectangular, fishlike scales on the skin.

Ichthyotoxic

A substance which is poisonous to fish.

Icteric hepatitis

An infectious syndrome of hepatitis characterised by jaundice, nausea, fever, right-upper quadrant pain, enlarged liver and transaminitis (increase in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST)).

Icterus neonatorum

Jaundice in newborn infants.

Idiopathic

Of no apparent physical cause.

Idiopathic mesenteric phlebosclerosis

(IMP) a rare disease, characterised by thickening of the wall of the right hemicolon with calcification of mesenteric veins.

Idiopathic sudden sensorineural hearing loss (ISSHL)

Is a sudden hearing loss where clinical assessment fails to reveal a cause.

I.g.

Gastric intubation, insertion of Levin tube through the nasal passage to the stomach.

IgE

Immunoglobulin E, a class of antibody that plays a role in allergy.

IGFs

Insulin-like growth factors, polypeptides with high sequence similarity to insulin.

IgG

Immunoglobulin G—the most abundant immunoglobulin (antibody) and is one of the major activators of the complement pathway.

IgM

Immunoglobulin M, primary antibody against A and B antigens on red blood cells.

IKAP

Is a scaffold protein of the IkarKappaBeta kinase complex and a regulator for kinases involved in pro-inflammatory cytokine signalling.

IKappa B

Or IκB-beta, a protein of the NF-Kappa-B inhibitor family.

Ileus

A temporary disruption of intestinal peristalsis due to nonmechanical causes.

Immune modulator

A substance that affects or modulates the functioning of the immune system.

Immunodeficiency

A state in which the immune system's ability to fight infectious disease is compromised or entirely absent.

Immunogenicity

The property enabling a substance to provoke an immune response, *adj.* immunogenic.

Immunoglobulin class switching Ig class switching

A biological mechanism that changes a B cell's production of antibody from one class to another.

Immunomodulatory

Capable of modifying or regulating one or more immune functions.

Immunoreactive

Reacting to particular antigens or haptens.

Immunostimulant

Agent that stimulates an immune response.

Immunosuppression

Involves a process that reduces the activation or efficacy of the immune system.

Immunotoxin

A man-made protein that consists of a targeting portion linked to a toxin.

Impaired glucose tolerance

(IGT) a prediabetic state of dysglycaemia associated with insulin resistance, increased risk of cardiovascular pathology and also a risk factor for mortality.

Impetigo

A contagious, bacterial skin infection characterised by blisters that may itch, caused by a *Streptococcus* bacterium or *Staphylococcus aureus* and mostly seen in children.

Impotence

A sexual dysfunction characterised by the inability to develop or maintain an erection of the penis.

Incontinence (faecal)

The inability to control bowel's movement.

Incontinence (urine)

The inability to control urine excretion.

Incretin

A group of gastrointestinal hormones that cause an increase in the amount of insulin released from the beta cells of the islets of Langerhans after a meal; members include GIP and GLP-1.

Index of structural atypia (ISA)

Index of structural abnormality.

Induration

Hardened, as a soft tissue that becomes extremely firm, sclerosis.

Infarct

An area of living tissue that undergoes necrosis as a result of obstruction of local blood supply.

Infarction

Is the process of tissue death (necrosis) caused by blockage of the tissue's blood supply.

Inflammasomes

Are large intracellular caspase-1-activating multiprotein complexes that play a central role in innate immunity.

Inflammation

A protective response of the body to infection, irritation or other injuries, aimed at destroying or isolating the injuries and characterised by redness, pain, warmth and swelling.

Influenza

A viral infection that affects mainly the nose, throat, bronchi and, occasionally, lungs.

Infusion

A liquid extract obtained by steeping something (e.g. herbs) that are more volatile or dissolve readily in water, to release their active ingredients without boiling.

Inguinal hernia

A hernia into the inguinal canal of the groin.

Inhalant

A medicinal substance that is administered as a vapour into the upper respiratory passages.

iNOS, inducible nitric oxide synthases

Through its product, nitric oxide (NO), may contribute to the induction of germ cell apoptosis. It plays a crucial role in early sepsis-related microcirculatory dysfunction.

Inotropic

Affecting the force of muscle contraction.

Insecticide

An agent that destroys insects. *adj* . insecticidal.

Insomnia

A sleeping disorder characterised by the inability to fall asleep and/or the inability to remain asleep for a reasonable amount of time.

Insulin

A peptide hormone composed of 51 amino acids produced in the islets of Langerhans in the pancreas causes cells in the liver, muscle and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle.

Insulin deficiency is often the cause of diabetes and exogenous insulin is used to control diabetes.

Insulin homeostasis

Blood sugar regulation.

Insulin-like growth factors (IGFs)

Polypeptides with high sequence similarity to insulin. They are part of a complex system that cells employ to communicate with their physiologic environment.

Insulin mimetic

To act like insulin.

Insulin resistance

A condition where the natural hormone insulin becomes less effective at reducing blood sugars.

Insulinogenic

Associated with or stimulating the production of insulin.

Insulinotropic

Stimulating or affecting the production and activity of insulin.

Integrase

An enzyme produced by a retrovirus (such as HIV) that enables its genetic material to be integrated into the DNA of the infected cell.

Intercellular adhesion molecule (ICAM)

A part of the immunoglobulin superfamily. They are important in inflammation, in immune responses and in intracellular signalling events.

Interferons (IFNs)

Are natural cell-signalling glycoproteins known as cytokines produced by the cells of the immune system of most vertebrates in response to challenges such as viruses, parasites and tumour cells.

Interleukins

A group of naturally occurring proteins and is a subset of a larger group of cellular messenger molecules called cytokines, which are modulators of cellular behaviour.

Interleukin-1 (IL-1)

A cytokine that could induce fever, control lymphocytes, increase the number of bone marrow cells and cause degeneration of bone joints. Also called endogenous pyrogen, lymphocyte-activating factor, haemopoietin-1 and mononuclear cell factor, among others that IL-1 is composed of two distinct proteins, now called IL-1 α and IL-1 β .

Interleukin 1 beta (IL-1 β)

A cytokine protein produced by activated macrophages. Cytokine is an important mediator of the inflammatory response and is involved in a variety of cellular activities, including cell proliferation, differentiation and apoptosis.

Interleukin 2 (IL-2)

A type of cytokine immune system signalling molecule that is instrumental in the body's natural response to microbial infection.

Interleukin-2 receptor (IL-2R)

A heterotrimeric protein expressed on the surface of certain immune cells, such as lymphocytes, that binds and responds to a cytokine called IL-2.

Interleukin-6 (IL-6)

An interleukin that acts as both a pro-inflammatory and anti-inflammatory cytokine.

Interleukin 8 (I-8)

A cytokine produced by macrophages and other cell types such as epithelial cells and is one of the major mediators of the inflammatory response.

Intermediate-density lipoproteins (IDL)

Is one of the five major groups of lipoproteins (chylomicrons, VLDL, IDL, LDL and HDL) that enable fats and

cholesterol to move within the water-based solution of the bloodstream. IDL is further degraded to form LDL particles and, like LDL, can also promote the growth of atheroma and increase cardiovascular diseases.

Intermittent claudication

An aching, crampy, tired and sometimes burning pain in the legs that comes and goes, caused by peripheral vascular disease. It usually occurs when walking and disappears after rest.

Interoceptive

Relating to stimuli arising from within the body.

Interstitium

The space between cells in a tissue.

Interstitial

Pertaining to the interstitium.

Intertrigo

An inflammation (rash) caused by microbial infection in skin folds.

Intima

Innermost layer of an artery or vein.

Intimal hyperplasia

The thickening of the tunica intima of a blood vessel as a complication of a reconstruction procedure.

Intoxicant

Substance that produces drunkenness or intoxication.

Intracavernosal

Within the corpus cavernosum, columns of erectile tissues forming the body of the penis.

Intraperitoneal (i.p.)

The term used when a chemical is contained within or administered through the peritoneum (the thin, transparent

membrane that lines the walls of the abdomen).

Intrathecal (i.t.)

Through the theca of the spinal cord into the subarachnoid space.

Intromission

The act of putting one thing into another.

Intubation

Refers to the placement of a tube into an external or internal orifice of the body.

Iodine (I)

Is an essential chemical element that is important for hormone development in the human body. Lack of iodine can lead to an enlarged thyroid gland (goitre) or other iodine deficiency disorders including mental retardation and stunted growth in babies and children. Iodine is found in dairy products, seafood, kelp, seaweeds, eggs, some vegetables and iodised salt.

IP

See Intraperitoneal.

IP3R3

(Inositol 1,4,5-triphosphate receptor type 3) is an intracellular calcium release channel that mediates calcium release from the endoplasmic reticulum.

Iron (Fe)

Is essential to most life forms and to normal human physiology. In humans, iron is an essential component of proteins involved in oxygen transport and for haemoglobin. It is also essential for the regulation of cell growth and differentiation. A deficiency of iron limits oxygen delivery to cells, resulting in fatigue, poor work performance and decreased immunity. Conversely, excess amounts of iron can result in toxicity and even death. Dietary sources include certain cereals, dark green leafy vegetables, dried fruit, legumes, seafood, poultry and meat.

Ischemia

An insufficient supply of blood to an organ, usually due to a blocked artery.

Ischuria

Retention or suppression of urine.

Isoflavones

A subgroup of flavonoids in which the basic structure is a 3-phenyl chromane skeleton. They act as phytoestrogens in mammals. See Flavonoids.

Isomers

Substances that are composed of the same elements in the same proportions and hence have the same molecular formula but differ in properties because of differences in the arrangement of atoms.

Isoprostanes

Unique prostaglandin-like compounds generated in-vivo from the free radical-catalysed peroxidation of essential fatty acids.

Jamu

Traditional Indonesian herbal medicine.

Janus kinase (JAK)-signal transducer and activator of transcription (STAT) signalling

Are essential molecules in cytokine signal transduction pathways involved in cancer development and progression.

Jaundice

Refers to the yellow colour of the skin and whites of the eyes caused by excess bilirubin in the blood.

JNK

(Jun N-terminal kinase), also known as stress-activated protein kinase (SAPK), belongs to the family of MAP kinases.

Jurkat cells

A line of T lymphocyte cells that are used to study acute T cell leukaemia.

KB cell

A cell line derived from a human carcinoma of the nasopharynx, used as an assay for antineoplastic (antitumour) agents.

Kainate receptors

Or KARs, are non-NMDA (N-methyl- D -aspartate) ionotropic receptors which respond to the neurotransmitter glutamate.

Kaliuresis

The presence of excess potassium in the urine.

Kallikreins

Peptidases (enzymes that cleave peptide bonds in proteins), a subgroup of the serine protease family; they liberate kinins from kininogens. Kallikreins are targets of active investigation by drug researchers as possible biomarkers for cancer.

Kaposi sarcoma

A cancerous tumour of the connective tissues caused by the human herpesvirus 8 and is often associated with AIDS.

Kaposi sarcoma herpesvirus (KSHV)

Also known as human herpesvirus 8, is a gamma 2 herpesvirus or rhadinovirus. It plays an important role in the pathogenesis of Kaposi sarcoma (KS), multicentric Castleman disease (MCD) of the plasma cell type and primary effusion lymphoma and occurs in HIV patients.

Karyolysis

Dissolution and disintegration of the nucleus when a cell dies.

Karyorrhexis

Destructive fragmentation of the nucleus of a dying cell whereby its chromatin disintegrates into formless granules.

Keloids

Benign dermal tumours characterised by fibroblastic proliferation and excessive accumulation of collagen.

Keratin

A sulphur-containing protein which is a major component in skin, hair, nails, hooves, horns and teeth.

Keratinocyte

Is the major constituent of the epidermis, constituting 95% of the cells found there.

Keratinophilic

Having an affinity for keratin.

Keratitis

Inflammation of the cornea.

Keratoconjunctivitis sicca

Also called keratitis sicca, xerophthalmia or dry eye syndrome (DES), is an eye disease characterised by a deficiency of aqueous tear film over the surface of the eye and in the lining of the lids.

Keratolysis

Softening and separation of the horny layer of the epidermis.

Keratolytic

Pertaining to keratolysis.

Keratomalacia

An eye disorder that leads to a dry cornea.

Kidney stones

(Calculi) are hardened mineral deposits that form in the kidney.

Kinin

Is any of various structurally related polypeptides, such as bradykinin, that act locally to induce vasodilation and contraction of smooth muscle.

Kininogen

Either of two plasma α_2 -globulins that are kinin precursors.

Ki-67

Human protein associated with cell proliferation.

Knockout

Gene knockout is a genetic technique in which an organism is engineered to carry genes that have been made inoperative.

Konzo

Is an epidemic paralytic disease occurring in outbreaks in remote rural areas of low-income African countries.

Kunitz protease inhibitors

A type of protein contained in legume seeds which functions as a protease inhibitor.

Kupffer cells

Are resident macrophages of the liver and play an important role in its normal physiology and homeostasis as well as participating in the acute and chronic responses of the liver to toxic compounds.

L - Dopa

(L - 3,4- Dihydroxyphenylalanine) is an amino acid that is formed in the liver and converted into dopamine in the brain.

Labour

Process of childbirth involving muscular contractions.

Lacrimation

Secretion and discharge of tears.

Lactagogue

An agent that increases or stimulates milk flow or production. Also called a galactagogue.

Lactate dehydrogenase (LDH)

Enzyme that catalyses the conversion of lactate to pyruvate.

Lactation

Secretion and Production of milk.

Lactic acidosis

Is a condition caused by the build-up of lactic acid in the body.
It leads to acidification of the blood (acidosis) and is considered a distinct form of metabolic acidosis.

LAK cell

A lymphokine-activated killer cell, i.e. a white blood cell that has been stimulated to kill tumour cells.

Lamella

In cell biology, it refers to numerous plate or disc-like structures at both a tissue and cellular level.

Laminin

A glycoprotein component of connective tissue basement membrane that promotes cell adhesion.

Laparoscopic cholecystectomy

Is a procedure in which the gallbladder is removed by laparoscopic techniques.

Laparotomy

A surgical procedure involving an incision through the abdominal wall to gain access into the abdominal cavity.
adj. laparotomised.

Larvacidal

An agent which kills insect or parasite larva.

Laryngitis

Is an inflammation of the larynx.

Laxation

Bowel movement.

Laxatives

Substances that are used to promote bowel movement.

LC 50

Median lethal concentration; see LD 50.

LD 50

Median lethal dose—the dose required to kill half the members of a tested population. Also called LC 50 (median lethal concentration).

LDL

See Low-density lipoprotein.

LDL cholesterol

See Low-density lipoprotein.

LDL receptor (LDLr)

A low-density lipoprotein receptor gene.

Lectins

Are sugar-binding proteins that are highly specific for their sugar moieties, which agglutinate cells and/or precipitate glycoconjugates. They play a role in biological recognition phenomena involving cells and proteins.

Leiomyoma

Benign smooth muscle neoplasm that is very rarely (0.1%) premalignant.

Leishmaniasis

A disease caused by protozoan parasites that belong to the genus *Leishmania* and is transmitted by the bite of certain species of sand fly.

Lenitive

Palliative; easing pain or discomfort.

Lenticular opacity

Also known as or related to cataract.

Leprosy

A chronic bacterial disease of the skin and nerves in the hands and feet and, in some cases, the lining of the nose. It is

caused by the *Mycobacterium leprae*. Also called Hansen's disease.

Leptin

Is a 16-kDa protein hormone with important effects in regulating body weight, metabolism and reproductive function.

Lequesne algofunctional index

Is a widespread international instrument (ten-question survey) and recommended by the World Health Organization (WHO) for outcome measurement in hip and knee diseases such as osteoarthritis.

Leucocyte

White blood corpuscles, colourless, without haemoglobin that helps to combat infection.

Leucocytopenia

Abnormal decrease in the number of leucocytes (white blood cells) in the blood.

Leucocytosis

Increase in white blood cell count above its normal range.

Leucoderma

A skin abnormality characterised by white spots, bands and patches on the skin; they can also be caused by fungus and tinea. Also see Vitiligo.

Leucomyelopathy

Any diseases involving the white matter of the spinal cord.

Leucopenia

A decrease in the number of circulating white blood cells.

Leucorrhoea

Commonly known as whites, refers to a whitish discharge from the female genitals.

Leukemia, leukaemia

A cancer of the blood or bone marrow and is characterised by an abnormal proliferation (production by multiplication) of blood cells, usually white blood cells (leucocytes).

Leukemogenic

Relating to leukaemia, causing leukaemia.

Leukoplakia

Condition characterised by white spots or patches on mucous membranes, especially of the mouth and vulva.

Leukotriene

A group of hormones that cause the inflammatory symptoms of hay-fever and asthma.

Leydig cells

Also called interstitial cells of Leydig, are found adjacent to the seminiferous tubules in the testicle. They produce testosterone in response to luteinising hormone.

Levarterenol

See Norepinephrine.

LexA repressor

Or repressor LexA, is repressor enzyme that represses SOS response genes coding for DNA polymerases required for repairing DNA damage

Libido

Sexual urge.

Lichen planus

A chronic mucocutaneous disease that affects the skin, tongue and oral mucosa.

Ligroin

A volatile, inflammable fraction of petroleum, obtained by distillation and used as a solvent.

Limbic system

Complex set of brain structures, including the hypothalamus, amygdala, hippocampus, anterior thalamic nuclei, septum, limbic cortex and fornix that control various functions such as emotion, behaviour, motivation, memory and olfaction.

Liniment

Liquid preparation rubbed on skin, used to relieve muscular aches and pains.

Linterised starch

Starch that has undergone prolonged acid treatment.

Lipodiatic

Having lipid and lipoprotein lowering property.

Lipodystrophy

A medical condition characterised by abnormal or degenerative conditions of the body's adipose tissue.

Lipofuscin

Finely granular yellow-brown pigment granules composed of lipid-containing residues of lysosomal digestion.

Lipogenesis

Is the process by which acetyl-CoA is converted to fats; *adj.* lipogenic.

Lipolysis

Is the breakdown of fat stored in fat cells in the body.

Liposomes

Artificially prepared vesicles made of lipid bilayer.

Lipotoxicity

Refers to tissue diseases that may occur when fatty acids spill over in excess of the oxidative needs of those tissues and enhances metabolic flux into harmful pathways of nonoxidative metabolism.

Lipotropic

Refers to compounds that help catalyse the breakdown of fat during metabolism in the body, e.g. chlorine and lecithin.

Lipoxygenase

A family of iron-containing enzymes that catalyse the dioxygenation of polyunsaturated fatty acids in lipids containing a *cis,cis*- 1,4-pentadiene structure.

Lithiasis

Formation of urinary calculi (stones) in the renal system (kidneys, ureters, the urinary bladder, urethra) can be of any one of several compositions.

Lithogenic

Promoting the formation of calculi (stones).

Lithontriptic

Removes stones from the kidney, gallbladder.

Liver X receptors

Nuclear hormones that function as central transcriptional regulators for lipid homeostasis.

Lochia

Vaginal discharge containing blood, mucus and uterine tissues, during the postpartum period

Lotion

A liquid suspension or dispersion of chemicals for external application to the body.

Lovo cells

Colon cancer cells.

Low-density lipoprotein (LDL)

Is a type of lipoprotein that transports cholesterol and triglycerides from the liver to peripheral tissues. High levels of LDL cholesterol can signal medical problems like cardiovascular disease, and it is sometimes called ‘bad cholesterol’.

LRP1

Low-density lipoprotein receptor-related protein-1, plays a role in intracellular signalling functions as well as in lipid metabolism.

LTB4

A type of leukotriene, a major metabolite in neutrophil polymorphonuclear leucocytes. It stimulates polymorphonuclear cell function (degranulation, formation of oxygen-centred free radicals, arachidonic acid release and metabolism). It induces skin inflammation.

Luciferase

Is a generic name for enzymes commonly used in nature for bioluminescence.

Lumbago

Is the term used to describe general lower back pain.

Lung abscess

Necrosis of the pulmonary tissue and formation of cavities containing necrotic debris or fluid caused by microbial infections.

Lusitropic

An agent that affects diastolic relaxation.

Lutein

A carotenoid, occurs naturally as yellow or orange pigment in some fruits and leafy vegetables. It is one of the two carotenoids contained within the retina of the eye. Within the central macula, zeaxanthin predominates, whereas in the peripheral retina, lutein predominates. Lutein is necessary for good vision and may also help prevent or slow down atherosclerosis, the thickening of arteries, which is a major risk for cardiovascular disease.

Luteinising hormone (LH)

A hormone produced by the anterior pituitary gland. In females, it triggers ovulation. In males, it stimulates the production of testosterone to aid sperm maturation.

Luteolysis

Is the structural and functional degradation of the corpus luteum (CL) that occurs at the end of the luteal phase of both the estrous and menstrual cycles in the absence of pregnancy. *adj* . luteolytic.

Luteotropic

Stimulating the formation of the corpus luteum.

Lymphadenitis

The inflammation or enlargement of a lymph node caused by microbial infection.

Lymphadenitis, cervical

Inflammation of the lymph nodes in the neck, usually caused by an infection.

Lymphatitis

Inflammation of lymph vessels and nodes.

Lymphadenopathy

A term meaning 'disease of the lymph nodes'—lymph node enlargement.

Lymphadenomegaly

Is the enlargement of the lymph node/nodes.

Lymphangitis

An inflammation or bacterial infection of the lymphatic channels, mostly commonly caused by the bacterium *Streptococcus pyogenes* in humans.

Lymphoblastic

Pertaining to the production of lymphocytes.

Lymphocyte

A small white blood cell (leucocyte) that plays a large role in defending the body against disease. Lymphocytes are responsible for immune responses. There are two main types of lymphocytes: B cells and T cells. Lymphocytes secrete products (lymphokines) that modulate the

functional activities of many other types of cells and are often present at sites of chronic inflammation.

Lymphocyte B cells

The B cells make antibodies that attack bacteria and toxins.

Lymphocyte T cells

T cells attack body cells themselves when they have been taken over by viruses or have become cancerous.

Lymphoma

A type of cancer involving cells of the immune system, called lymphocytes.

Lymphopenia

Abnormally low in the number of lymphocytes in the blood.

Lysosomes

Are small, spherical organelles containing digestive enzymes (acid hydrolases) and other proteases (cathepsins).

mTOR, the mammalian (or mechanistic) target of rapamycin

Regulates a wide range of cellular and developmental processes by coordinating signalling responses to mitogens, nutrients and various stresses.

Maceration

Softening or separation of parts by soaking in a liquid.

Macrophage

A type of large leucocyte that travels in the blood but can leave the bloodstream and enter tissue; like other leucocytes it protects the body by digesting debris and foreign cells.

Macular degeneration

A disease that gradually destroys the macula, the central portion of the retina, reducing central vision.

Macules

Small circumscribed changes in the colour of skin that are neither raised (elevated) nor depressed.

Maculopapular

Describes a rash characterised by raised, spotted lesions.

Magnesium (Mg)

Is the fourth most abundant mineral in the body and is essential to good health. It is important for normal muscle and nerve function, steady heart rhythm, immune system and strong bones. Magnesium also helps regulate blood sugar levels, promotes normal blood pressure and is known to be involved in energy metabolism and protein synthesis and plays a role in preventing and managing disorders such as hypertension, cardiovascular disease and diabetes.

Dietary sources include legumes (e.g. soya bean and by-products), nuts, whole unrefined grains, fruit (e.g. banana, apricots), okra and green leafy vegetables.

MAK cell

Macrophage-activated killer cell, activated macrophage that is much more phagocytic than monocytes.

Malaise

A feeling of weakness, lethargy or discomfort as of impending illness.

Malaria

Is an infection of the blood by *Plasmodium* parasite that is carried from person to person by mosquitoes. There are four species of malaria parasites that infect man.

Plasmodium falciparum

So-called malignant tertian fever, is the most serious disease, *Plasmodium vivax*, causing a relapsing form of the disease, *Plasmodium malariae* and *Plasmodium ovale*.

Malassezia

A fungal genus (previously known as *Pityrosporum*) classified as yeasts, naturally found on the skin surfaces of many animals including humans. It can cause

hypopigmentation on the chest or back if it becomes an opportunistic infection.

Mammalian target of rapamycin (mTOR)

Pathway that regulates mitochondrial oxygen consumption and oxidative capacity.

Mammogram

An X-ray of the breast to detect tumours.

Mandibular

Relating to the mandible, the human jaw bone.

Manganese

Is an essential element for health. It is an important constituent of some enzymes and an activator of other enzymes in physiologic processes. Manganese superoxide dismutase (MnSOD) is the principal antioxidant enzyme in the mitochondria. Manganese-activated enzymes play important roles in the metabolism of carbohydrates, amino acids and cholesterol. Manganese is the preferred cofactor of enzymes called glycosyltransferases which are required for the synthesis of proteoglycans that are needed for the formation of healthy cartilage and bone. Dietary source includes whole grains, fruit, legumes (soybean and by-products), green leafy vegetables, beetroot and tea.

MAO activity

Monoamine oxidase activity.

MAPK (mitogen-activated protein kinase)

These kinases are strongly activated in cells subjected to osmotic stress, UV radiation, dysregulated K⁺ currents, RNA-damaging agents and a multitude of other stresses, as well as inflammatory cytokines, endotoxin and withdrawal of a trophic factor. The stress-responsive MAPKs mediate a plethora of cellular responses to such stressful stimuli, including apoptosis and production of inflammatory and immunoregulatory cytokines in diverse cell systems.

Marasmus

Is one of the three forms of serious protein–energy malnutrition.

Mastalgia

Breast pain.

Mastectomy

Surgery to remove a breast.

Masticatory

A substance chewed to increase salivation. Also called sialogue.

Mastitis

A bacterial infection of the breast which usually occurs in breastfeeding mothers.

Matrix metalloproteinases (MMP)

A member of a group of enzymes that can break down proteins, such as collagen, that are normally found in the spaces between cells in tissues (i.e. extracellular matrix proteins). Matrix metalloproteinases are involved in wound healing, angiogenesis and tumour cell metastasis. See also Metalloproteinase.

MBC

Minimum bacterial concentration—the lowest concentration of antibiotic required to kill an organism.

MCP-1

Monocyte chemotactic protein-1, plays a role in the recruitment of monocytes to sites of infection and injury. It is a member of small inducible gene (SIG) family.

MDA

Malondialdehyde is one of the most frequently used indicators of lipid peroxidation.

Measles

An acute, highly communicable rash illness due to a virus transmitted by direct contact with infectious droplets or,

less commonly, by airborne spread.

Mechanonociceptors

Sensory neurons that are mechanically sensitive found in all of the paraspinal connective tissues including ligament, joint capsule, annulus fibrosus of the intervertebral disc, muscle, tendon and skin. They respond to a noxious (damaging) mechanical load.

Medial preoptic area

Is located at the rostral end of the hypothalamus; it is important for the regulation of male sexual behaviour.

Megaloblastic anaemia

An anaemia that results from inhibition of DNA synthesis in red blood cell production, often due to a deficiency of vitamin B12 or folate, and is characterised by many large immature and dysfunctional red blood cells (megaloblasts) in the bone marrow.

Melaene (melena)

Refers to the black, 'tarry' faeces that are associated with gastrointestinal haemorrhage.

Melanogenesis

Production of melanin by living cells.

Melanoma

Malignant tumour of melanocytes which are found predominantly in skin but also in the bowel and the eye and appear as pigmented lesions.

Melatonin

A hormone produced in the brain by the pineal gland; it is important in the regulation of the circadian rhythms of several biological functions.

Menarche

The first menstrual cycle, or first menstrual bleeding, in female human beings.

Menorrhagia

Heavy or prolonged menstruation, too frequent menstrual periods.

Menopausal

Refers to permanent cessation of menstruation.

Menses

See Menstruation.

Menstruation

The approximately monthly discharge of blood from the womb in women of childbearing age who are not pregnant. Also called menses. *adj.* menstrual.

Mesangial cells

Are specialised cells around blood vessels in the kidneys, at the mesangium.

Mesencephalon

Midbrain .

Mesothelioma

Is an aggressive cancer affecting the membrane lining of the lungs and abdomen.

Metabolic syndrome

(MetS) represents a combination of cardiometabolic risk factors, including visceral obesity, glucose intolerance or type 2 diabetes, elevated triglycerides, reduced HDL cholesterol and hypertension.

Metabonome

Complete set of metabolically regulated elements in cells.

Metabolomics

Is the scientific study of chemical processes involving metabolites.

Metalloproteinase

Enzymes that break down proteins and require zinc or calcium atoms for proper function.

Metallothionein

(MT) a family of cysteine-rich, low molecular weight (500 to 14000 Da) proteins.

Meta-analysis

A statistical procedure that combines the results of several studies that address a set of related research hypotheses.

Metaphysis

Is the portion of a long bone between the epiphyses and the diaphysis of the femur.

Metaphyseal

Pertaining to the metaphysis.

Metaplasia

Transformation of one type of one mature differentiated cell type into another mature differentiated cell type.

Metastasis

Is the movement or spreading of cancer cells from one organ or tissue to another.

Metetrus

The quiescent period of sexual inactivity between oestrus cycles.

Methaemoglobinemia

Is a disorder characterised by the presence of a higher than normal level of methaemoglobin (ferric $[\text{Fe}^{3+}]$ rather than ferrous $[\text{Fe}^{2+}]$ haemoglobin) in red blood cells. This results in a decreased availability of oxygen to the tissues.

Metropathy

Any disease of the uterus especially of the myometrium.

Metroptosis

The slipping or falling out of place of an organ (as the uterus)

Metrorrhagia

Uterine bleeding at irregular intervals, particularly between the expected menstrual periods.

Mevinolin

A potent inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase).

MHC

Acronym for major histocompatibility complex, a large cluster of genes found on the short arm of chromosome 6 in most vertebrates that encodes MHC molecules. MHC molecules play an important role in the immune system and autoimmunity.

MHC 11 molecules

Class II MHC molecules belong to a group of molecules known as the immunoglobulin supergene family, which includes immunoglobulins, T cell receptors, CD4, CD8 and others.

MIC

Minimum inhibitory concentration, lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism.

Micelle

A submicroscopic aggregation of molecules.

Micellisation

Formation process of micelles.

Michael acceptors

See Michael reaction.

Michael donors

See Michael reaction.

Michael reaction

Conjugate addition of a carbon nucleophile to an α,β -unsaturated acceptor; a thermodynamically controlled reaction between unusually acidic donors (β -ketoesters or

β -diketones) and unhindered α,β -unsaturated acceptors. Stable enolates, active methylenes such as malonates and nitroalkanes are Michael donors, and activated olefins such as α,β -unsaturated carbonyl compounds are Michael acceptors.

Microangiopathy

(Or microvascular disease) is an angiopathy affecting small blood vessels in the body.

Microfilaria

A pre-larval parasitic worm of the family Onchocercidae, found in the vector and in the blood or tissue fluid of human host.

Micronuclei

Small particles consisting of acentric fragments of chromosomes or entire chromosomes, which lag behind at anaphase of cell division.

Microphthalmia-associated transcription factor (MITF)

A basic helix-loop-helix leucine zipper transcription factor protein that plays a role in the development, survival and function of melanocytes and osteoclast.

Microsomal PGE2 synthase

Is the enzyme that catalyses the final step in prostaglandin E2 (PGE2) biosynthesis.

Microvasculature

The finer vessels of the body, as the arterioles, capillaries and venules.

Micturition

Urination, act of urinating.

Migraine

A neurological syndrome characterised by altered bodily perceptions; severe, painful headaches; and nausea.

Mimosine

Is an alkaloid, β -3-hydroxy-4 pyridone amino acid; it is a toxic nonprotein free amino acid and is an antinutrient.

Mineral apposition rate

MAR, rate of addition of new layers of mineral on the trabecular surfaces of bones.

Mineralcorticoids

A group of steroid hormones that are secreted by the adrenal cortex and regulate the balance of water and electrolytes (sodium, potassium) in the body.

Miscarriage

Spontaneous abortion.

Mitochondrial complex I

The largest enzyme in the mitochondrial respiratory oxidative phosphorylation system.

Mitochondrial permeability transition (MPT)

Is an increase in the permeability of the mitochondrial membranes to molecules of less than 1500 Da in molecular weight. MPT is one of the major causes of cell death in a variety of conditions.

Mitogen

An agent that triggers mitosis and elicits all the signals necessary to induce cell proliferation.

Mitogenic

Able to induce mitosis or transformation.

Mitogenicity

Process of induction of mitosis.

Mitomycin

A chemotherapy drug that is given as a treatment for several different types of cancer, including breast, stomach, oesophagus and bladder cancers.

Mitosis

Cell division in which the nucleus divides into nuclei containing the same number of chromosomes.

Mitral valve prolapse

The most common heart valve abnormality. Symptoms could include palpitations, shortness of breath, cough, fatigue, dizziness or anxiety, migraine headaches and chest discomfort.

MMP

Matrix metalloproteinases, a group of peptidases involved in the degradation of the extracellular matrix (ECM).

Mnemonic

Pertaining to memory.

Molecular docking

Is a key tool in structural molecular biology and computer-assisted drug design.

Molluscidal

Destroying molluscs like snails.

Molt 4 cells

MOLT4 cells are lymphoblast-like in morphology and are used for studies of apoptosis, tumour cytotoxicity and tumorigenicity, as well as for antitumour testing.

Molybdenum (Mo)

Is an essential element that forms part of several enzymes such as xanthine oxidase involved in the oxidation of xanthine to uric acid and use of iron. Molybdenum concentrations also affect protein synthesis, metabolism and growth. Dietary sources include meat, green beans, eggs, sunflower seeds, wheat flour, lentils and cereal grain.

Monoamine oxidase A (MAOA)

Is an isozyme of monoamine oxidase. It preferentially deaminates norepinephrine (noradrenaline), epinephrine (adrenaline), serotonin and dopamine.

Monoaminergic

Of or pertaining to neurons that secrete monoamine neurotransmitters (e.g. dopamine, serotonin).

Monoclonal antibodies

Are produced by fusing single antibody-forming cells to tumour cells grown in culture.

Monocyte

Large white blood cell that ingests microbes, other cells and foreign matter.

Monogalactosyl diglyceride

Are the major lipid components of chloroplasts.

Monorrhagia

Is heavy bleeding and that is usually defined as periods lasting longer than 7 days or excessive bleeding.

Morbidity

A diseased state or symptom or can refer either to the incidence rate or to the prevalence rate of a disease.

Morelloflavone

A biflavonoid extracted from *Garcinia dulcis* , has shown antioxidative, antiviral and anti-inflammatory properties.

Morphine

The major alkaloid of opium and a potent narcotic analgesic.

MTTP

Microsomal triglyceride transfer protein that is required for the assembly and secretion of triglyceride-rich lipoproteins from both enterocytes and hepatocytes.

MUC 5AC

Mucin 5AC, a secreted gel-forming protein mucin with a high molecular weight of about 641kDa.

Mucositis

Painful inflammation and ulceration of the mucous membranes lining the digestive tract.

Mucous

Relating to mucus.

Mucolytic

Capable of reducing the viscosity of mucus, or an agent that so acts.

Mucus

Viscid secretion of the mucous membrane.

Multidrug resistance (MDR)

Ability of a living cell to show resistance to a wide variety of structurally and functionally unrelated compounds.

Muscarinic receptors

Are G protein-coupled acetylcholine receptors found in the plasma membranes of certain neurons and other cells.

Musculotropic

Affecting or acting upon muscular tissue.

Mutagen

An agent that induces genetic mutation by causing changes in the DNA.

Mutagenic

Capable of inducing mutation (used mainly for extracellular factors such as X-rays or chemical pollution).

Myalgia

Muscle pain.

Myc

Codes for a protein that binds to the DNA of other genes and is therefore a transcription factor, found on chromosome 8 in human.

Mycosis

An infection or disease caused by a fungus.

Mydriasis

Abnormal, excessive dilation of the pupil caused by disease or drug.

Myelocyte

Is a young cell of the granulocytic series, occurring normally in bone marrow, but not in circulating blood.

Myeloid leukaemia (chronic)

A type of cancer that affects the blood and bone marrow, characterised by excessive number of white blood cells.

Myeloma

Cancer that arises in the plasma cells, a type of white blood cells.

Myelopathy

Refers to pathology of the spinal cord.

Myeloperoxidase (MPO)

Is a peroxidase enzyme most abundantly present in neutrophil granulocytes (a subtype of white blood cells). It is an inflammatory enzyme produced by activated leucocytes that predicts risk of coronary heart disease.

Myeloproliferative disorder

Disease of the bone marrow in which excess cells are produced.

Myelosuppressive

Causing bone marrow suppression.

Myelotoxicity

State of being toxic to myeloid tissues, the bone marrow.

Myiasis

Parasitic infestation of the body of a live mammal by fly larvae.

Myocardial

Relating to heart muscle tissues.

Myocardial infarction (MI)

Is the rapid development of myocardial necrosis caused by a critical imbalance between oxygen supply and demand of the myocardium.

Myocardial ischemia

An intermediate condition in coronary artery disease during which the heart tissue is slowly or suddenly starved of oxygen and other nutrients.

Myocardial lipidosis

Is the accumulation of fat droplets in myocardial fibres.

Myoclonus

Brief, involuntary twitching of a muscle or a group of muscles.

Myogenesis

The formation of muscular tissue, especially during embryonic development.

Myoglobin

A red, iron- and oxygen-binding protein which carries and stores oxygen in muscle tissues; this haemoprotein resembles a single subunit of haemoglobin.

Myoglobinuria

Is the presence of myoglobin in the urine, usually associated with rhabdomyolysis or muscle destruction.

Myopathy

A muscular disease wherein the muscle fibres do not function for any one of many reasons, resulting in muscular weakness.

Myopia

Near- or short-sightedness.

Myosarcoma

A malignant muscle tumour.

Myotonia dystrophica

An inherited disorder of the muscles and other body systems characterised by progressive muscle weakness, prolonged muscle contractions (myotonia), clouding of the lens of the eye (cataracts), cardiac abnormalities, balding and infertility.

Myotube

A developing skeletal muscle fibre or cell with a tubular appearance and a centrally located nucleus.

Myringosclerosis

Also known as tympanosclerosis or intratympanic tympanosclerosis, is a condition caused by calcification of collagen tissues in the tympanic membrane of the middle ear.

Mytonia

A symptom of certain neuromuscular disorders characterised by the slow relaxation of the muscles after voluntary contraction or electrical stimulation.

N -Nitrosmorpholine

A human carcinogen.

N -Nitrosoproline

An indicator for *N* -nitrosation of amines.

Nicotinamide adenine dinucleotide phosphate (NADP)

A coenzyme comprising nicotinamide mononucleotide coupled by pyrophosphate linkage to adenosine 2',5'-bisphosphate; it acts as an electron carrier in numerous reactions, being alternately oxidised (NADP⁺) and reduced (NADPH).

NADPH

The reduced form of nicotinamide adenine dinucleotide phosphate that serves as an electron carrier.

NAFLD

Non-alcoholic fatty liver disease.

Narcosis

A state of stupor, drowsiness or unconsciousness produced by drugs.

Narcotic

An agent that produces narcosis; in moderate doses it dulls the senses, relieves pain and induces sleep; in excessive dose it causes stupor, coma, convulsions and death.

Nasopharynx

Upper part of the alimentary continuous with the nasal passages.

Natriorexia

Excessive intake of sodium evoked by sodium depletion. *adj.* natriorexic, natriorexigenic.

Natriuresis

The discharge of excessive large amount of sodium through urine. *adj.* natriuretic.

Natural killer cells (NK cells)

A type of cytotoxic lymphocyte that constitutes a major component of the innate immune system.

Natural killer T (NKT) cells

A heterogeneous group of T cells that share properties of both T cells and natural killer (NK) cells.

Nausea

Sensation of unease and discomfort in the stomach with an urge to vomit.

Necropsy

See Autopsy.

Necrosis

Morphological changes that follow cell death, usually involving nuclear and cytoplasmic changes.

Neointima

A new or thickened layer of arterial intima formed especially on a prosthesis or in atherosclerosis by migration and proliferation of cells from the media.

Neonatal

adj. of or relating to newborn infants or an infant.

Neoplasia

Abnormal growth of cells, which may lead to a neoplasm, or tumour.

Neoplasm

Tumour; any new and abnormal growth, specifically one in which cell multiplication is uncontrolled and progressive. Neoplasms may be benign or malignant.

Neoplastic transformation

Conversion of a tissue with a normal growth pattern into a malignant tumour.

Neovascularisation

Is the development of tiny, abnormal, leaky blood vessels inside the eye.

Neovasculature

Formation of new blood vessels.

Nephrectomised

Kidneys surgically removed.

Nephrectomy

Surgical removal of the kidney.

Nephric

Relating to or connected with a kidney.

Nephrin

Is a protein necessary for the proper functioning of the renal filtration barrier.

Nephritic syndrome

Is a collection of signs (known as a syndrome) associated with disorders affecting the kidneys, more specifically glomerular disorders.

Nephritis

Is inflammation of the kidney.

Nephrolithiasis

Process of forming a kidney stone in the kidney or lower urinary tract.

Nephropathy

A disorder of the kidney.

Nephrotic syndrome

Nonspecific disorder in which the kidneys are damaged, causing them to leak large amounts of protein from the blood into the urine.

Nephrotoxicity

Poisonous effect of some substances, both toxic chemicals and medication, on the kidney.

Nerve growth factor (NGF)

A small protein that induces the differentiation and survival of particular target neurons (nerve cells).

Nervine

A nerve tonic that acts therapeutically upon the nerves, particularly in the sense of a sedative that serves to calm ruffled nerves.

Neural tube defects (NTDs)

Are common birth defects of the brain and spinal cord.

NEU 4 sialidase

This protein belongs to a family of glycohydrolytic enzymes, which remove terminal sialic acid residues from various sialo derivatives, such as glycoproteins, glycolipids, oligosaccharides and gangliosides.

Neuralgia

Is a sudden, severe painful disorder of the nerves.

Neuraminidase

Glycoside hydrolase enzymes that cleaves the glycosidic linkages of neuraminic acids.

Neuraminidase inhibitors

A class of antiviral drugs targeted at the influenza viruses whose mode of action consists of blocking the function of the viral neuraminidase protein, thus preventing the virus from reproducing.

Neurasthenia

A condition with symptoms of fatigue, anxiety, headache, impotence, neuralgia and impotence.

Neurasthenic

A substance used to treat nerve pain and/or weakness (i.e. neuralgia, sciatica, etc).

Neurectomy

Surgical cutting through or removal of a nerve or a section of a nerve.

Neurite

Refers to any projection from the cell body of a neuron.

Neuritis

An inflammation of the nerve characterised by pain, sensory disturbances and impairment of reflexes. *adj* . neuritic.

Neuritogenesis

The formation of neuritis. *a dj* . neuritogenic.

Neuroblastoma

A common extracranial cancer that forms in nerve tissues, common in infancy.

Neuroendocrine

adj. of, relating to, or involving the interaction between the nervous system and the hormones of the endocrine glands.

Neurogenesis

Process by which neurons are generated from neural stem and progenitor cells.

Neurogenic

Originating from the nerves of the nervous system.

Neurolathyrism

Is a neurodegenerative disease that is caused by heavy consumption of *Lathyrus* legumes, resulting in weakness and paralysis of the legs.

Neuroleptic

Refers to the effects on cognition and behaviour of antipsychotic drugs that reduce confusion, delusions, hallucinations and psychomotor agitation in patients with psychoses.

Neuroma

Is a growth or tumour of nerve tissue.

Neuropathy

A collection of disorders that occurs when the peripheral nervous systems are damaged causing pain and numbness in the hands and feet.

Neuropharmacological

Relating the effects of drugs on the neurosystem .

Neuroradiology

Is a subspecialty of radiology focusing on the diagnosis and characterisation of abnormalities of the central and peripheral nervous system . *adj.* neuroradiologic.

Neurotrophic

Relating to the nutrition and maintenance of nervous tissue (neurons).

Neutropenia

a disorder of the blood, characterised by abnormally low levels of neutrophils.

Neutrophil

Type of white blood cell, specifically a form of granulocyte.

Neurophin

Protein that induces the survival, development and function of neurons.

NF -Kappa B (NF -kB)

Nuclear factor kappa-B, is an ubiquitous rapid response transcription factor in cells involved in immune and inflammatory reactions.

Niacin

Vitamin B3. See Vitamin B3.

Niacinamide

An amide of niacin, also known as nicotinamide. See Vitamin B3.

NIH3T3 cells

A mouse embryonic fibroblast cell line used in the cultivation of keratinocytes.

Nidation

Implantation.

Niosomes

Are novel, vesicular, drug delivery systems composed of nonionic surfactants instead of phospholipids; they are capable of entrapping hydrophilic and hydrophobic drugs.

Nitrogen (N)

Is an essential building block of amino and nucleic acids and proteins and is essential to all living organisms. Protein-rich vegetables like legumes are rich food sources of nitrogen.

NK cells

Natural killer cells, a type of cytotoxic lymphocyte that constitutes a major component of the innate immune system.

NK1.1+ T (NKT) cells

A type of natural killer T (NKT) cells. See Natural killer T cells.

NMDA receptor

N -Methyl- D -aspartate receptor, the predominant molecular device for controlling synaptic plasticity and memory function. A brain receptor activated by the amino acid glutamate, which when excessively stimulated may cause cognitive defects in Alzheimer's disease.

Nociceptive

Causing pain, responding to a painful stimulus.

Nociceptors

Specialised peripheral sensory neurons that respond to potentially damaging stimuli by sending nerve signals to the spinal cord and brain.

Non-osteogenic

Fibromata of bone, a benign tumour of bone which shows no evidence of ossification.

Non-alcoholic fatty liver disease

One cause of a fatty liver, occurring when fat is deposited (steatosis) in the liver not due to excessive alcohol use

Nootropics

Are substances which are claimed to boost human cognitive abilities (the functions and capacities of the brain). Also popularly referred to as 'smart drugs', 'smart nutrients', 'cognitive enhancers' and 'brain enhancers'.

Noradrenalin

See Norepinephrine.

Norepinephrine

A substance, both a hormone and neurotransmitter, secreted by the adrenal medulla and the nerve endings of the sympathetic nervous system to cause vasoconstriction and

increases in heart rate, blood pressure and the sugar level of the blood. Also called levarterenol, noradrenalin.

Normoglycaemic

Having the normal amount of glucose in the blood.

Normotensive

Having normal blood pressure.

Nosebo

A harmless substance that when taken by a patient is associated with unpleasant or harmful effects due to negative expectations or the psychological state of the person.

Nosocomial infections

Infections which are a result of treatment in a hospital or a healthcare service unit, but secondary to the patient's original condition.

NPC1L1

Niemann–Pick C1-like 1 gene that plays a major role in cholesterol homeostasis. It is critical for the uptake of cholesterol across the plasma membrane of the intestinal enterocyte.

Nrf2

Nuclear erythroid 2-related factor 2, a transcription factor that activates ARE-containing genes.

Nrf2/ARE pathway

Plays an important role in inducing phase II detoxifying enzymes and antioxidant proteins and has been considered a potential target for cancer chemoprevention because it eliminates harmful reactive oxygen species or reactive intermediates generated from carcinogens.

Nuclear factor erythroid 2-related factor 2 (Nrf2)

A transcription factor that plays a major role in response to oxidative stress by binding to antioxidant-responsive

elements that regulate many hepatic phase I and II enzymes as well as hepatic efflux transporters.

Nucleosomes

Fundamental repeating subunits of all eukaryotic chromatin, consisting of a DNA chain coiled around a core of histones.

Nulliparous

Term used to describe a woman who has never given birth.

Nyctalopia

Night blindness, impaired vision in dim light and in the dark, due to impaired function of certain specialised vision cells.

Nystagmus

Fast, involuntary movements of the eyes.

Nycturia

Excessive urination at night; especially common in older men.

Obsessive–compulsive disorder (OCD)

A common psychiatric disorder defined by the presence of obsessive thoughts and repetitive compulsive actions; self-grooming.

Occludin

A novel integral membrane protein localising at tight junctions. *cf.* tight junction.

Occlusion

Closure or blockage (as of a blood vessel).

Occlusive peripheral arterial disease (PAOD)

Also known as peripheral vascular disease (PVD), or peripheral arterial disease (PAD), refers to the obstruction of large arteries not within the coronary, aortic arch vasculature, or the brain. PVD can result from atherosclerosis, inflammatory processes leading to stenosis, an embolism, or thrombus formation.

Oculomotor nerve

The third of twelve paired cranial nerves.

Odds ratio

A statistical measure of effect size, describing the strength of association or nonindependence between two binary data values.

Odontalgia

Toothache. *adj.* odontalgic.

Odontopathy

Any disease of the teeth.

Oedema

See Edema.

Oestrogen

Female hormone produced by the ovaries that play an important role in the estrous cycle in women.

Oestrogen receptor (ER)

Is a protein found in high concentrations in the cytoplasm of breast, uterus, hypothalamus and anterior hypophysis cells; ER levels are measured to determine a breast CA's potential for response to hormonal manipulation.

Oestrogen receptor positive (ER+)

Means that oestrogen is causing the tumour to grow and that the breast cancer should respond well to hormone suppression treatments.

Oestrogen receptor negative (ER-)

Tumour is not driven by oestrogen and needs another test to determine the most effective treatment.

Oestrus

Sexual excitement or heat of female; or period of this characterised by changes in the sex organs.

Oligoarthritis

An inflammation of two, three or four joints.

Oligoasthenoteratozoospermia

A combination of asthenozoospermia (reduced sperm motility) and oligozoospermia (low spermatozoon count).

Oligonucleosome

A series of nucleosomes.

Oligospermia or oligozoospermia

Refers to semen with a low concentration of sperm, commonly associated with male infertility .

Oliguria

Decreased production of urine.

Oligoanuria

Insufficient urine volume to allow for administration of necessary fluids, etc.

Omega-3 fatty acids

Are essential polyunsaturated fatty acids that have in common a final carbon–carbon double bond in the n–3 position. Dietary sources of omega-3 fatty acids include fish oil and certain plant/nut oils. The three most nutritionally important omega-3 fatty acids are alpha-linolenic acid, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Research indicates that omega-3 fatty acids are important in health promotion and disease and can help prevent a wide range of medical problems, including cardiovascular disease, depression, asthma and rheumatoid arthritis.

Omega-6 fatty acids

Are essential polyunsaturated fatty acids that have in common a final carbon–carbon double bond in the n–6 position. Omega-6 fatty acids are considered essential fatty acids (EFAs) found in vegetable oils, nuts and seeds. They are essential to human health but cannot be made in the body. Omega-6 fatty acids—found in vegetable oils, nuts and seeds—are a beneficial part of a heart-healthy eating. Omega-6 and omega-3 PUFA play a crucial role in heart

and brain function and in normal growth and development. Linoleic acid (LA) is the main omega-6 fatty acid in foods, accounting for 85% to 90% of the dietary omega-6 PUFA. Other omega-6 acids include gamma-linolenic acid or GLA, sometimes called gamoleic acid, eicosadienoic acid, arachidonic acid and docosadienoic acid.

Omega-9 fatty acids

Are not essential polyunsaturated fatty acids that have in common a final carbon-carbon double bond in the n-9 position. Some n-9s are common components of animal fat and vegetable oil. Two n-9 fatty acids important in industry are:

Oleic acid (18, 1, n-9), which is a main component of olive oil

Erucic acid (22, 1, n-9), which is found in rapeseed, wallflower seed and mustard seed

Oncogenes

Genes carried by tumour viruses that are directly and solely responsible for the neoplastic (tumorous) transformation of host cells.

Oncosis

Accidental cell death, also referred to swelling necrosis.

Ophthalmia

Severe inflammation of the eye, or the conjunctiva or deeper structures of the eye. Also called ophthalmitis.

Ophthalmia (sympathetic)

Inflammation of both eyes following trauma to one eye.

Ophthalmopathy

An autoimmune disease where the thyroid gland is overactive leading to ocular manifestations.

Opiate

Drug derived from the opium plant.

Opioid receptors

A group of G protein-coupled receptors located in the brain and various organs that bind opiates or opioid substances.

Oppilation

Obstruction particularly of the lower intestines.

Optic placode

An ectodermal placode from which the lens of the embryonic eye develops; also called lens placode.

ORAC (oxygen radical absorbance capacity)

A method of measuring antioxidant capacities in biological samples.

Oral submucous fibrosis

A chronic debilitating disease of the oral cavity characterised by inflammation and progressive fibrosis of the submucosa tissues.

Oral thrush

An infection of yeast fungus, *Candida albicans* , in the mucous membranes of the mouth.

Orchidectomy

Surgery to remove one or both testicles.

Orchidectomised

With the testis removed.

Orchitis

An acute painful inflammatory reaction of the testis secondary to infection by different bacteria and viruses.

Orexigenic

Increasing or stimulating the appetite.

Orofacial dyskinesia

Abnormal involuntary movements involving muscles of the face, mouth, tongue, eyes and, occasionally, the neck—may be unilateral or bilateral and constant or intermittent.

Oropharyngeal

Relating to the oropharynx.

Oropharynx

Part of the pharynx between the soft palate and the epiglottis.

Osmophobia

A fear, aversion or psychological hypersensitivity to odours.

Ostalgia, ostealgia

Pain in the bones. Also called osteodynia.

Osteoarthritis

Is the deterioration of the joints that becomes more common with age.

Osteoarthrosis

Chronic noninflammatory bone disease.

Osteoblast

A mononucleate cell that is responsible for bone formation.

Osteoblastic

Relating to osteoblasts.

Osteocalcin

A noncollagenous protein found in bone and dentin, also refers to as bone gamma-carboxyglutamic acid-containing protein.

Osteoclasts

A kind of bone cell that removes bone tissue by removing its mineralised matrix.

Osteoclastogenesis

The production of osteoclasts.

Osteodynia

Pain in the bone.

Osteogenic

Derived from or composed of any tissue concerned in bone growth or repair.

Osteomalacia

Refers to the softening of the bones due to defective bone mineralisation.

Osteomyelofibrosis

A myeloproliferative disorder in which fibrosis and sclerosis finally lead to bone marrow obliteration.

Osteopenia

Reduction in bone mass, usually caused by a lowered rate of formation of new bone that is insufficient to keep up with the rate of bone destruction.

Osteoporosis

A disease of bone that leads to an increased risk of fracture.

Osteoprotegerin

Also called osteoclastogenesis inhibitory factor (OCIF), a cytokine, which can inhibit the production of osteoclasts.

Osteosarcoma

A malignant bone tumour. Also called osteogenic sarcoma.

Otalgia

Earache, pain in the ear.

Otic placode

A thickening of the ectoderm on the outer surface of a developing embryo from which the ear develops.

Otitis

Inflammation of the inner or outer parts of the ear.

Otitis media

Inflammation of the middle ear.

Otorrhea

Running drainage (discharge) exiting the ear.

Otopathy

Disease of the ear.

Ovariectomised

With one or two ovaries removed.

Ovariectomy

Surgical removal of one or both ovaries.

Oxidation

The process of adding oxygen to a compound, dehydrogenation or increasing the electro-negative charge.

Oxidoreductase activity

Catalysis of an oxidation–reduction (redox) reaction, a reversible chemical reaction. One substrate acts as a hydrogen or electron donor and becomes oxidised, while the other acts as hydrogen or electron acceptor and becomes reduced.

Oxygen radical absorbance capacity (ORAC)

A method of measuring antioxidant capacities in biological samples.

Oxytocic

adj. hastening or facilitating childbirth, especially by stimulating contractions of the uterus.

Oxytocin

Is a mammalian hormone that also acts as a neurotransmitter in the brain. It is best known for its roles in female reproduction. It is released in large amounts after distension of the cervix and vagina during labour and after stimulation of the nipples, facilitating birth and breastfeeding, respectively*****.

Oxyuriasis

Infestation by pinworms.

Ozoena

Discharge of the nostrils caused by chronic inflammation of the nostrils.

p.o.

Per os, oral administration.

P-Glycoprotein (P-gp, ABCB1, MDR1)

A cell membrane-associated drug-exporting protein that transports a variety of drug substrates from cancer cells.

P-Selectin

Also known as CD62P, GMP-140, LSECAM-3 and PADGEM, a member of the selectin family. It is expressed by activated platelets and endothelial cells.

P65 transcription factor

Is a protein that in humans is encoded by the RELA gene. Its alternative name is nuclear factor NF-kappa-B p65 subunit.

P300/CBP

Are transcriptional coactivators that play critical roles in integrating multiple signal-dependent transcription events and may have specific roles in tumour suppression pathways.

p21waf1/cip1

Encodes a cyclin-dependent kinase inhibitor that is transcriptionally activated by the p53 tumour suppressor gene, transforming growth factor beta 1 (TGF-beta 1), AP2 and other pathways, all regulating apoptosis and the cell cycle.

Palliative

Relieving pain without alleviating the underlying problem.

Palinostmia

Olfactory perservation.

Palpebral ptosis

The abnormal drooping of the upper lid, caused by partial or total reduction in levator muscle function.

Palpitation

Rapid pulsation or throbbing of the heart.

Paludism

State of having symptoms of malaria characterised by high fever and chills.

Pancreatectomised

Having undergone a pancreatectomy.

Pancreatectomy

Surgical removal of all or part of the pancreas.

Pancreatitis

Inflammation of the pancreas.

Pancytopenia

A haematological condition in which there is a reduction in the number of red and white blood cells, as well as platelets.

Pantothenic acid

Vitamin B5. See Vitamin B5.

Papain

A protein-degrading enzyme used medicinally and to tenderise meat.

Papilloma

A benign epithelial tumour growing outwardly like in fingerlike fronds.

Papule

A small, solid, usually inflammatory elevation of the skin that does not contain pus.

Paradontosis

Is the inflammation of gums and other deeper structures, including the bone.

Parageusia

Abnormal sense of taste.

Paralytic

Person affected with paralysis, pertaining to paralysis.

Paraoxonase

An enzyme that protects against oxidation of low-density lipoprotein and affects the risk of coronary artery disease.

Paraplegia

An impairment in motor or sensory function of the lower extremities.

Parasitemia

Presence of parasites in blood. *adj.* parasitemic.

Parasympathetic nervous system

Subsystem of the nervous systems that slows the heart rate and increases intestinal and gland activity and relaxes the sphincter muscles.

Parasympathomimetic

Having an action resembling that caused by stimulation of the parasympathetic nervous system.

Parenteral administration

Administration by intravenous, subcutaneous or intramuscular routes.

Paresis

A condition characterised by partial loss of movement, or impaired movement.

Paresthesia

A sensation of tingling, burning, pricking or numbness of a person's skin with no apparent long-term physical effect. Also known as 'pains and needles'.

Parotitis

Inflammation of salivary glands.

Paroxysm

A sudden outburst of emotion or action and a sudden attack, recurrence or intensification of a disease.

Paroxysmic

Relating to an abnormal event of the body with an abrupt onset and an equally sudden return to normal.

PARP

See Poly-(ADP-ribose) polymerase.

Pars compacta

Is a portion of the substantia nigra (a brain structure located in the midbrain).

Parturition

Act of childbirth.

Pathognomonic

Distinctively characteristic of a particular disease.

PCAF

P300/CBP-associated factor, a histone acetyl transferase (HAT) that plays an important role in the remodelling of chromatin and the regulation of gene expression, transcription, cell cycle progression and differentiation.

PCE/PCN ratio

Polychromatic erythrocyte/normochromatic erythrocyte ratio used as a measure of cytotoxic effects.

PCNA

Proliferating cell nuclear antigen, an auxiliary protein of DNA polymerase delta involved in modulating eukaryotic DNA replication.

pCREB

Phosphorylated cAMP (adenosine 3 ' 5 ' cyclic monophosphate)-response element binding protein.

PDEF

Acronym for prostate-derived ETS factor, an ETS (epithelial-specific E26 transforming sequence) family member that has been identified as a potential tumour suppressor.

PDGR receptor (platelet-derived growth factor receptor)

Are cell surface tyrosine kinase receptors for members of the platelet-derived growth factor (PDGF) family.

PDGFs

Platelet-derived growth factors constitute a group of growth factors that play a significant role in blood vessel formation and the growth of blood vessels.

Pectoral

Pertaining to or used for the chest and respiratory tract.

Pectoralagia

Pain experienced in the thorax or chest.

pERK

Phosphorylated extracellular signal-regulated kinase, protein kinases involved in many cell functions.

P53

Also known as protein 53 or tumour protein 53, is a tumour suppressor protein that in humans is encoded by the TP53 gene.

Peliosis

See Purpura.

Pellagra

Is a systemic nutritional wasting disease caused by a deficiency of vitamin B3 (niacin).

Pemphigus

Describes a group of autoimmune disorders in which there is blistering of the skin and/or mucosal surfaces.

Pemphigus neonatorum

Staphylococcal scalded skin syndrome, a bacterial disease of infants, characterised by elevated vesicles or blebs on a normal or reddened skin.

Peptic ulcer

A sore in the lining of the stomach or duodenum, the first part of the small intestine.

Peptide YY

A short (36-amino acid) pancreatic protein released by cells in the ileum and colon in response to feeding.

Percutaneous

Pertains to a medical procedure where access to inner organs or tissues is done via needle puncture of the skin.

Perfusion

To force fluid through the lymphatic system or blood vessels to an organ or tissue.

Periapical periodontitis

Is the inflammation of the tissue adjacent to the tip of the tooth's root.

Perifuse

To flush a fresh supply of bathing fluid around all of the outside surfaces of a small piece of tissue immersed in it.

Perilipins

Highly phosphorylated adipocyte proteins that are localised at the surface of the lipid droplet.

Perimenopause

Is the phase before menopause actually takes place, when ovarian hormone production is declining and fluctuating.
adj . perimenopausal.

Perineum

The region between the thighs inferior to the pelvic diaphragm.

Perineal

Pertaining to the perineum.

Periodontal ligament (PDL)

Is a group of specialised connective tissue fibres that essentially attach a tooth to the bony socket.

Periodontitis

Is a severe form of gingivitis in which the inflammation of the gums extends to the supporting structures of the tooth.
Also called pyorrhea.

Perioral paresthesias

Are sensations of numbness and tingling around the mouth.

Peripheral arterial disease (PAD)

Is a disease in which plaque builds up in the arteries that carry blood to your head, organs and limbs.

Peripheral neuropathy

Refers to damage to nerves of the peripheral nervous system.

Peripheral neuropathic pain (PNP)

Refers to situations where nerve roots or peripheral nerve trunks have been damaged by mechanical and/or chemical stimuli that exceeded the physical capabilities of the nervous system. Symptoms may include pain, paresthesia, dysesthesia, spasm, weakness, hypoesthesia or anaesthesia.

Peripheral vascular disease (PVD)

See Peripheral artery occlusive disease.

Peristalsis

A series of organised, wave-like muscle contractions that occur throughout the digestive tract.

PERK

A transmembrane protein kinase of the PEK family resident in the endoplasmic reticulum (ER) membrane and is linked to insulin processing.

Perlingual

Through or by way of the tongue.

Perniosis

An abnormal reaction to cold that occurs most frequently in women, children and the elderly. Also called chilblains.

Per os (P.O.)

Oral administration.

Peroxisome proliferator-activated receptors (PPARs)

A family of nuclear receptors that are involved in lipid metabolism, differentiation, proliferation, cell death and inflammation.

Peroxisome proliferator-activated receptor alpha (PPAR-alpha)

A nuclear receptor protein, transcription factor and a major regulator of lipid metabolism in the liver.

Peroxisome proliferator-activated receptor gamma (PPAR-γ)

A type II nuclear receptor protein that regulates fatty acid storage and glucose metabolism.

Pertussis

Whooping cough, severe cough.

Peyers patches

Patches of lymphoid tissue or lymphoid nodules on the walls of the ileal-small intestine.

PGE-2

Prostaglandin E2, a hormone-like substance that is released by blood vessel walls in response to infection or inflammation that acts on the brain to induce fever.

Phagocytes

Are the white blood cells that protect the body by ingesting (phagocytosing) harmful foreign particles, bacteria and dead or dying cells. *adj.* phagocytic.

Phagocytosis

Is a process the human body uses to destroy dead or foreign cells.

Phantosmia

A form of olfactory hallucination.

Pharmacognosis

The branch of pharmacology that studies the composition, use and history of drugs.

Pharmacodynamics

Branch of pharmacology dealing with the effects of drugs and the mechanism of their action.

Pharmacokinetics

Branch of pharmacology concerned with the movement of drugs within the body including processes of absorption, distribution, metabolism and excretion in the body.

Pharmacopoeia

Authoritative treatise containing directions for the identification of drug samples and the preparation of compound medicines, published by the authority of a government or a medical or pharmaceutical society and in a broader sense is a general reference work for pharmaceutical drug specifications.

Pharyngitis, pharyngolaryngitis

Inflammation of the pharynx and the larynx.

Pharyngolaryngeal

Pertaining to the pharynx and larynx.

Pharyngopathy

Disease of the pharynx.

Phase II drug metabolising enzymes

Play an important role in biotransformation of endogenous compounds and xenobiotics to more easily excretable forms as well as in the metabolic inactivation of pharmacologically active compounds. Phase II drug metabolising enzymes are mainly transferases.

Phenolics

Class of chemical compounds consisting of a hydroxyl group (–OH) bonded directly to an aromatic hydrocarbon group.

Pheochromocytoma

Is a rare neuroendocrine tumour that usually originates from the adrenal glands' chromaffin cells, causing overproduction of catecholamines, powerful hormones that induce high blood pressure and other symptoms.

Phlebitis

Is an inflammation of a vein, usually in the legs.

Phlegm

Abnormally viscid mucus secreted by the mucosa of the respiratory passages during certain infectious processes.

Phlegmon

A spreading, diffuse inflammation of the soft or connective tissue due to infection by streptococci bacteria.

Phonophobia

Fear of loud sound.

Phoroglucinol

A white, crystalline compound used as an antispasmodic, analytical reagent and decalcifier of bone specimens for microscopic examination.

Phosphatidylglycerol

Is a glycerophospholipid found in pulmonary active surface lipoprotein and consists of an L -glycerol 3-phosphate backbone ester bonded to either saturated or unsaturated fatty acids on carbons 1 and 2.

Phosphatidylinositol 3-kinases (PI 3-kinases or PI3Ks)

A group of enzymes involved in cellular functions such as cell growth, proliferation, differentiation, motility, survival and intracellular trafficking, which in turn are involved in cancer.

Phosphatidylserine

A phosphoglyceride phospholipid that is one of the key building blocks of cellular membranes, particularly in the nervous system. It is derived from soy lecithin.

Phosphaturia

A urinary tract condition of excessive urine phosphorus, causing urine to appear cloudy or murky colour; also called hypophosphatemia.

Phosphodiesterases

A diverse family of enzymes that hydrolyse cyclic nucleotides and thus play a key role in regulating intracellular levels of the second messengers, cAMP and cGMP, and hence cell function.

Phosphoenolpyruvate C kinase (PEPCK)

An enzyme in the lyase family used in the metabolic pathway of gluconeogenesis.

Phospholipase

An enzyme that hydrolyses phospholipids into fatty acids and other lipophilic substances.

Phospholipase A2 (PLA2)

A small lipolytic enzyme that releases fatty acids from the second carbon group of glycerol. Plays an essential role in the synthesis of prostaglandins and leukotrienes.

Phospholipase C

Enzymes that cleaves phospholipase.

Phospholipase C gamma (PLC gamma)

Enzymes that cleaves phospholipase in cellular proliferation and differentiation, and its enzymatic activity is upregulated by a variety of growth factors and hormones.

Phosphorus (P)

Is an essential mineral that makes up 1% of a person's total body weight and is found in the bones and teeth. It plays an important role in the body's utilisation of carbohydrates and fats; in the synthesis of protein for the growth,

maintenance, and repair of cells and tissues. It is also crucial for the production of ATP, a molecule the body uses to store energy. Main sources are meat and milk; fruits and vegetables provide small amounts.

Photoaging

Is the term that describes damage to the skin caused by intense and chronic exposure to sunlight resulting in premature aging of the skin.

Photocarcinogenesis

Represents the sum of a complex of simultaneous and sequential biochemical events that ultimately lead to the occurrence of skin cancer caused by exposure to the sun.

Photodermatoses

Skin disorders caused by exposure to sunlight.

Photophobia

Abnormal visual intolerance to light.

Photopsia

An affection of the eye, in which the patient perceives luminous rays, flashes, coruscations, etc.

Photosensitivity

Sensitivity towards light.

Phthisis

An archaic name for tuberculosis.

Phytohemagglutinin

A lectin found in plant that is involved in the stimulation of lymphocyte proliferation.

Phytonutrients

Certain organic components of plants that are thought to promote human health. Fruits, vegetables, grains, legumes, nuts and teas are rich sources of phytonutrients.

Phytonutrients are not 'essential' for life. Also called phytochemicals.

Phytosterols

A group of steroid alcohols, cholesterol-like phytochemicals naturally occurring in plants like vegetable oils, nuts and legumes.

Pica

The persistent eating of substances with no nutrition, such as dirt, chalk, sand, ice, clay or paint.

Piebaldism

Rare autosomal dominant disorder of melanocyte development characterised by distinct patches of skin and hair that contain no pigment.

Piles

See Haemorrhoids.

PI3K

Phosphoinositide 3-kinase.

PI3K/AKT signalling pathways

Are involved in the modulation of cell survival, cell cycle progression and cellular growth in cancer.

Pityriasis lichenoides

Is a rare skin disorder of unknown aetiology characterised by multiple papules and plaques.

Pityriasis versicolor

Common fungal infection of the skin; the fungus interferes with the normal pigmentation of the skin, resulting in small, discoloured patches.

PKC

Protein kinase C, a membrane-bound enzyme that phosphorylates different intracellular proteins and raised intracellular Ca levels.

PKC delta inhibitors

Protein kinase C delta inhibitors that induce apoptosis of haematopoietic cell lines.

Placebo

A sham or simulated medical intervention.

Placode

A platelike epithelial thickening in the embryo where some organ or structure later develops.

Plantar verruca

Wart occurring on the sole of the foot.

Plasma

The yellow-coloured liquid component of blood, in which blood cells are suspended.

Plasma kallikrien

A serine protease, synthesised in the liver and circulated in the plasma.

Plasmalemma

Plasma membrane.

Plasmin

A proteinase enzyme that is responsible for digesting fibrin in blood clots.

Plasminogen

The proenzyme of plasmin, whose primary role is the degradation of fibrin in the vasculature.

Plasminogen activator inhibitor-1 (PAI-1)

Also known as endothelial plasminogen activator inhibitor or serpin E1, is a serine protease inhibitor (serpin) that functions as the principal inhibitor of tissue plasminogen activator (tPA) and urokinase (uPA), the activators of plasminogen and hence fibrinolysis (the physiological breakdown of blood clots).

Plaster

Poultice.

Platelet-activating factor (PAF)

Is an acetylated derivative of glycerophosphorylcholine, released by basophils and mast cells in immediate hypersensitive reactions and macrophages and neutrophils in other inflammatory reactions. One of its main effects is to induce platelet aggregation.

Platelet - derived growth factor (PDGF)

Is one of the numerous growth factors or proteins that regulate cell growth and division.

PLC gamma

Phospholipase C gamma plays a central role in signal transduction.

Pleurisy

Is an inflammation of the pleura, the lining of the pleural cavity surrounding the lungs, which can cause painful respiration and other symptoms. Also known as pleuritis.

Pneumonia

An inflammatory illness of the lung caused by bacteria or viruses.

Pneumotoxicity

Damage to lung tissues.

Poliomyelitis

Is a highly infectious viral disease that may attack the central nervous system and is characterised by symptoms that range from a mild non-paralytic infection to total paralysis in a matter of hours; also called polio or infantile paralysis.

Pollakiuria

Extraordinary daytime urinary frequency.

Poly-(ADP-ribose) polymerase (PARP)

A protein involved in a number of cellular processes, especially DNA repair and programmed cell death.

Polyarthrititis

Is any type of arthritis which involves five or more joints.

Polychromatic erythrocyte (PCE)

An immature red blood cell containing RNA that can be differentiated by appropriate staining techniques from a normochromatic erythrocyte (NCE), which lacks RNA.

Polycystic kidney disease

Is a kidney disorder passed down through families in which multiple cysts form on the kidneys, causing them to become enlarged.

Polycystic ovary syndrome

Imbalance of woman's sex hormone; this imbalance may cause changes in menstrual cycle, excessive hair growth, acne, obesity, reduced fertility and an increased risk of diabetes. The ovaries are larger and have many cysts or follicles that rarely grow to maturity or produce eggs capable of being fertilised.

Polycythaemia

A type of blood disorder characterised by the production of too many red blood cells.

Polymorphnuclear

Having a lobed nucleus. Used especially of neutrophilic white blood cells.

Polyneuritis

Widespread inflammation of the nerves.

Polyneuritis gallinarum

A nervous disorder in birds and poultry.

Polyneuropathy

Simultaneous malfunction of many peripheral nerves throughout the body.

Polyp

A growth that protrudes from a mucous membrane.

Polyphagia

Medical term for excessive hunger or eating.

Polyposis

Describes a condition where there are a lot of polyps.

PolyQ disease

Polyglutamine repeat diseases are neurodegenerative ailments elicited by glutamine-encoding CAG nucleotide expansions within endogenous human genes.

Polyuria

A condition characterised by the passage of large volumes of urine with an increase in urinary frequency.

Pomade

A thick oily dressing.

Porphyria

A disorder wherein the body cannot convert naturally occurring compounds (prophyrins) into haem which contains iron.

Porphyrin

Any of a class of water-soluble, nitrogenous biological pigments, derivatives of which include the haemoproteins.

Postherpetic neuralgia

(PHN) is neuralgia (pain in the nerves) caused by the varicella herpes zoster virus. The pain may last for more than a month or more after a shingles infection occurred.

Postpartum depression

Depression after pregnancy; also called postnatal depression.

Postprandial

After mealtime.

Postural hypotension

Also called orthostatic hypotension—a condition of low blood pressure that can cause dizziness.

Potassium (K)

Is an element that is essential for the body's growth and maintenance. It is necessary to keep a normal water balance between the cells and body fluids, for cellular enzyme activities, and plays an essential role in the response of nerves to stimulation and in the contraction of muscles. Potassium is found in many plant foods and fish (tuna, halibut): chard, mushrooms, spinach, fennel, kale, mustard greens, Brussels sprouts, broccoli, cauliflower, cabbage winter squash, eggplant, cantaloupe, tomatoes, parsley, cucumber, bell pepper, turmeric, ginger root, apricots, strawberries, avocado and banana.

Poultice

Is a soft moist mass, often heated and medicated, that is spread on cloth over the skin to treat an aching, inflamed or painful part of the body. Also called cataplasm.

PPARs

Peroxisome proliferator-activated receptors—a group of nuclear receptor proteins that function as transcription factors regulating the expression of genes.

PR interval

Is the time (in seconds) from the beginning of the P wave (onset of atrial depolarisation) to the beginning of the QRS complex.

Prebiotics

A category of functional food, defined as non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improve host health. *cf.* probiotics.

Pre-eclampsia

Toxic condition of pregnancy characterised by high blood pressure, abnormal weight gain, proteinuria and oedema.

Prenidatory phase

Preimplantation phase.

Prepubertal

Before puberty; pertaining to the period of accelerated growth preceding gonadal maturity.

Pregnane X receptor

(PXR, NR1I2) is a ligand-activated transcription factor that plays a role not only in drug metabolism and transport but also in various other biological processes .

Pregnenolone

A steroid hormone produced by the adrenal glands, involved in the steroidogenesis of other steroid hormones like progesterone, mineralocorticoids, glucocorticoids, androgens and oestrogens.

Prenidatory

Referring to the time period between fertilisation and implantation.

Prenylated flavones

Flavones with an isoprenyl group in the 8 position, has been reported to have good anti-inflammatory properties.

Presyncopal sensation

State consisting of light-headedness, muscular weakness, blurred vision and feeling faint.

Primiparous

Relating to a woman who has given birth once.

Proangiogenic

Promote angiogenesis (formation and development of new blood vessels).

Probiotication

Enhancement with beneficial probiotic bacteria such as *Lactobacillus* species that can prevent the growth of intestinal pathogenic microflora.

Probiotics

Are dietary supplements and live microorganisms containing potentially beneficial bacteria or yeasts that are taken into the alimentary system for healthy intestinal functions. *cf.* prebiotics.

Proctitis

An inflammation of the rectum that causes discomfort, bleeding and, occasionally, a discharge of mucus or pus.

Procyanidin

Also known as proanthocyanidin, oligomeric proanthocyanidin, leukocyanidin and leucoanthocyanin, is a class of flavanols found in many plants. It has antioxidant activity and plays a role in the stabilisation of collagen and maintenance of elastin.

Progestational

Of or relating to the phase of the menstrual cycle immediately following ovulation, characterised by secretion of progesterone.

Proglottid

One of the segments of a tapeworm.

Prognosis

Medical term to describe the likely outcome of an illness.

Prokinetic

Or gastropromkinetic, substance that enhances gastrointestinal motility by increasing the frequency of contractions in the small intestine or making them stronger.

Prolactin

A hormone produced by the pituitary gland; it stimulates the breasts to produce milk in pregnant women. It is also present in males, but its role is not well understood.

Prolapse

A common condition where the bladder, uterus and/or bowel protrudes into the vagina.

Prolapsus

To fall or slip out of place.

Prolapus ani

Eversion of the lower portion of the rectum and protruding through the anus, common in infancy and old age.

Proliferating cell nuclear antigen (PCNA)

A new marker to study human colonic cell proliferation.

Proliferative vitreoretinopathy (PVR)

Is a blinding retinal condition. It involves the formation of pathological membranes, which dislodges the retina and thereby compromises an individual's ability to see.

Prolyl-4-hydroxylase (P4H)

Key enzyme in collagen synthesis.

Promastigote

The flagellate stage in the development of trypanosomatid protozoa, characterised by a free anterior flagellum.

Promyelocytic leukaemia

A subtype of acute myelogenous leukaemia (AML), a cancer of the blood and bone marrow.

Pro-oxidants

Chemicals that induce oxidative stress, either through creating reactive oxygen species or inhibiting antioxidant systems.

Prophylaxis

Prevention or protection against disease.

Proptosis

See Exophthalmos.

Prostacyclin

A prostaglandin that is a metabolite of arachidonic acid, inhibits platelet aggregation and dilates blood vessels.

Prostaglandins

A family of C 20 lipid compounds found in various tissues, associated with muscular contraction and the inflammation response such as swelling, pain, stiffness, redness and warmth.

Prostaglandin E2 (PEG-2)

One of the prostaglandins, a group of hormone-like substances that participate in a wide range of body functions such as the contraction and relaxation of smooth muscle, the dilation and constriction of blood vessels, control of blood pressure and modulation of inflammation.

Prostaglandin E synthase

An enzyme that in humans is encoded by the glutathione-dependent PTGES gene.

Prostanoids

Term used to describe a subclass of eicosanoids (products of COX pathway) consisting of the prostaglandins (mediators of inflammatory and anaphylactic reactions), the thromboxanes (mediators of vasoconstriction) and the prostacyclins (active in the resolution phase of inflammation.)

Prostanoid EP 4

A prostaglandin receptor that may be involved in the neonatal adaptation of circulatory system, osteoporosis as well as initiation of skin immune responses.

Prostate

A gland that surrounds the urethra at the bladder in the male.

Prostate cancer

A disease in which cancer develops in the prostate, a gland in the male reproductive system. Symptoms include pain, difficulty in urinating, erectile dysfunction and other symptoms.

Prostate-specific antigen (PSA)

A protein produced by the cells of the prostate gland.

Protein kinase C (PKC)

A family of enzymes involved in controlling the function of other proteins through the phosphorylation of hydroxyl groups of serine and threonine amino acid residues on these proteins. PKC enzymes play important roles in several signal transduction cascades.

Protein tyrosine phosphatase (PTP)

A group of enzymes that remove phosphate groups from phosphorylated tyrosine residues on proteins.

Proteinase

A protease (enzyme) involved in the hydrolytic breakdown of proteins, usually by splitting them into polypeptide chains.

Proteinuria

Means the presence of an excess of serum proteins in the urine.

Proteolysis

Cleavage of the peptide bonds in protein forming smaller polypeptides. *adj.* proteolytic.

Proteomics

The large-scale study of proteins, particularly their structures and functions.

Prothrombin

Blood-clotting protein that is converted to the active form, factor IIa, or thrombin, by cleavage.

Prothyroid

Good for thyroid function.

Protheolithic

Proteolytic. See Proteolysis.

Proto-oncogene

A normal gene which, when altered by mutation, becomes an oncogene that can contribute to cancer.

Prurigo

A general term used to describe itchy eruptions of the skin.

Pruritis

Defined as an unpleasant sensation on the skin that provokes the desire to rub or scratch the area to obtain relief; itch, itching. *adj* . pruritic.

PSA

Prostate-specific antigen, a protein which is secreted into ejaculate fluid by the healthy prostate. One of its functions is to aid sperm movement.

Pseudoaldosteronism

Is a medical condition characterised by hypertension, reduced aldosterone secretion, hypokalemia and metabolic acidosis and associated with low plasma renin activity.

Pseudohyperaldosteronism (also pseudoaldosteronism)

Is a medical condition that mimics hyperaldosteronism. Like hyperaldosteronism, it produces hypertension associated with low plasma renin activity and metabolic alkalosis associated with hypokalemia.

Pseudohypoaldosteronism

A hereditary disorder of infancy characterised by severe salt and water depletion and other signs of aldosterone deficiency, although aldosterone secretion is normal or increased; causes include aldosterone receptor defects and renal dysfunction.

Psoriasis

A common chronic, non-contagious autoimmune dermatosis that affects the skin and joints.

Psychoactive

Having effects on the mind or behaviour.

Psychonautics

Exploration of the psyche by means of approaches such as meditation, prayer, lucid dreaming, brain wave

entrainment, etc.

Psychotomimetic

Hallucinogenic.

Psychotropic

Capable of affecting the mind, emotions and behaviour.

PTEN

Phosphatase and tensin homolog, a tumour suppressor gene.

Ptosis

Also known as drooping eyelid; caused by weakness of the eyelid muscle and damage to the nerves that control the muscles or looseness of the skin of the upper eyelid.

P13-K

Is a lipid kinase enzyme involved in the regulation of a number of cellular functions such as cell growth, proliferation, differentiation, motility, survival and intracellular trafficking, which in turn are involved in cancer.

P13-K/AKT signalling pathway

Shown to be important for an extremely diverse array of cellular activities—most notably cellular proliferation and survival.

Pthysis

Silicosis with tuberculosis.

Ptosis

Drooping of the upper eye lid.

PTP

Protein tyrosine phosphatase.

PTPIB

Protein tyrosine phosphatase 1B.

P21

Also known as cyclin-dependent kinase inhibitor 1 or CDK-interacting protein 1, is a potent cyclin-dependent kinase inhibitor.

Puerperal

Pertaining to childbirth.

Puerperium

Postpartum period.

Pulmonary embolism

A blockage (blood clot) of the main artery of the lung.

Purgative

A substance used to cleanse or purge, especially causing the immediate evacuation of the bowel.

Purpura

Is the appearance of red or purple discolourations on the skin that do not blanch on applying pressure. Also called peliosis.

Purulent

Containing pus discharge.

Purulent sputum

Sputum containing, or consisting of, pus.

Pustule

Small, inflamed, pus-filled lesions.

Pyelitis

Acute inflammation of the pelvis of the kidney caused by bacterial infection.

Pyelonephritis

An ascending urinary tract infection that has reached the pyelum (pelvis) of the kidney.

Pyoderma

Bacterial skin infection.

Pyodermatitis

Refers to inflammation of the skin.

Pyorrhea

See Periodontitis.

Pyretic

Referring to fever.

Pyrexia

Fever of unknown origin.

Pyridoxal

A chemical form of vitamin B6. See Vitamin B6.

Pyridoxamine

A chemical form of vitamin B6. See Vitamin B6.

Pyridoxine

A chemical form of vitamin B6. See Vitamin B6.

Pyrolysis

Decomposition or transformation of a compound caused by heat. *adj.* pyrolytic.

PYY peptide

A 36-amino acid peptide secreted by L cells of the distal small intestine and colon that inhibits gastric and pancreatic secretion.

QSR complex

Series of deflections in an electrocardiogram that represent electrical activity generated by ventricular depolarisation prior to contraction of the ventricle.

QT interval

Is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. A prolonged QT interval is a biomarker for ventricular tachyarrhythmias and a risk factor for sudden death.

Quorum sensing (QS)

The control of gene expression in response to cell density, is used by both Gram-negative and Gram-positive bacteria to regulate a variety of physiological functions.

Radiculitis

Inflammation of the radicle of a nerve.

Radiodermatitis

A skin disease associated with prolonged exposure to ionising radiation.

Radiolysis

The dissociation of molecules by radiation.

Radioprotective

Serving to protect or aiding in protecting against the injurious effect of radiations.

RAD23B

UV excision repair protein RAD23 homolog B

RAGE

Is the receptor for advanced glycation end products, a multiligand receptor that propagates cellular dysfunction in several inflammatory disorders, in tumours and in diabetes.

RANKL

Receptor activator of nuclear factor kappa-B ligand, a type II membrane protein and a member of the tumour necrosis factor (TNF) superfamily.

RAS

See Renin–angiotensin system or recurrent aphthous stomatitis.

Rash

A temporary eruption on the skin; see Urticaria.

Reactive oxygen species

Species such as superoxide, hydrogen peroxide and hydroxyl radical. At low levels, these species may function in cell signalling processes. At higher levels, these species may damage cellular macromolecules (such as DNA and RNA) and participate in apoptosis (programmed cell death).

Rec A

Is a 38-kDa *Escherichia coli* protein essential for the repair and maintenance of DNA.

Receptor for advanced glycation end products (RAGE)

Is a member of the immunoglobulin superfamily of cell surface molecules; mediates neurite outgrowth and cell migration upon stimulation with its ligand, amphoterin.

Reticulocyte

Non-nucleated stage in the development of the red blood cell.

Reticulocyte lysate

Cell lysate produced from reticulocytes, used as an in-vitro translation system.

Recticuloendothelial system

Part of the immune system, consists of the phagocytic cells located in reticular connective tissue, primarily monocytes and macrophages.

Recurrent aphthous stomatitis, or RAS

Is a common, painful condition in which recurring ovoid or round ulcers affect the oral mucosa.

Redox homeostasis

Is considered as the cumulative action of all free radical reactions and antioxidant defences in different tissues.

Refrigerant

A medicine or an application for allaying heat, fever or its symptoms.

Renal calculi

Kidney stones.

Renal interstitial fibrosis

Damage sustained by the kidneys' renal tubules and interstitial capillaries due to accumulation of extracellular waste in the wall of the small arteries and arterioles.

Renal resistive index (RRI)

Measures the resistance of renal arterial flow to the kidney.

Renin

Also known as an angiotensinogenase, is an enzyme that participates in the body's renin–angiotensin system (RAS). It regulates the body's mean arterial blood pressure.

Renin–angiotensin system (RAS)

Also called the renin–angiotensin–aldosterone system (RAAS), is a hormone system that regulates blood pressure and water (fluid) balance.

Reperfusion

The restoration of blood flow to an organ or tissue that has had its blood supply cut off, after a heart attack.

Reporter gene

A transfected gene that produces a signal, such as green fluorescence, when it is expressed.

Resistin

A cysteine-rich protein secreted by adipose tissue of mice and rats.

Resolutive

A substance that induces subsidence of inflammation.

Resolvent

Reduce inflammation or swelling.

Respiratory burst

Is the rapid release of reactive oxygen species (superoxide radical and hydrogen peroxide) from different cells.

Resorb

To absorb or assimilate a product of the body such as an exudate or cellular growth.

Restenosis

Is the reoccurrence of stenosis, a narrowing of a blood vessel, leading to restricted blood flow.

Resveratrol

Is a phytoalexin produced naturally by several plants when under attack by pathogens such as bacteria or fungi. It is a potent antioxidant found in red grapes and other plants.

Reticuloendothelial system

Part of the immune system that consists of the phagocytic cells located in reticular connective tissue. Also called macrophage system or mononuclear phagocyte system.

Retinal ischemia

Is a common cause of visual impairment and blindness.

Retinitis pigmentosa (RP)

An inherited, degenerative eye disease that causes severe vision impairment and may lead to blindness.

Retinol

A form of vitamin A; see Vitamin A.

Retinoblastoma protein

A tumour suppressor protein that is dysfunctional in several major cancers.

Retinopathy

A general term that refers to some form of noninflammatory damage to the retina of the eye.

Revulsive

Counterirritant, used for swellings.

Reye's syndrome

A potentially fatal disease that has numerous detrimental effects to many organs, especially the brain and liver, and

occurs commonly in children after a viral infection.

Rhabdomyolysis

Breakdown of muscle fibres leading to the release of muscle fibre content (myoglobin) into the bloodstream.

Rheumatic

Pertaining to rheumatism or to abnormalities of the musculoskeletal system.

Rheumatism, rheumatic disorder, rheumatic diseases

Refers to various painful medical conditions which affect bones, joints, muscles and tendons. Rheumatic diseases are characterised by the signs of inflammation—redness, heat, swelling and pain.

Rheumatoid arthritis (RA)

Is a chronic, systemic autoimmune disorder that most commonly causes inflammation and tissue damage in joints (arthritis) and tendon sheaths, together with anaemia.

Rhinitis

Irritation and inflammation of some internal areas of the nose and the primary symptom of rhinitis is a runny nose.

Rhinopathy

Disease or malformation of the nose.

Rhinoplasty

Is surgery to repair or reshape the nose.

Rhinorrhea

Commonly known as a runny nose, characterised by an unusually significant amount of nasal discharge.

Rhinosinusitis

Inflammation of the nasal cavity and sinuses.

Rho GTPases

Rho-guanosine triphosphate hydrolase enzymes are molecular switches that regulate many essential cellular processes,

including actin dynamics, gene transcription, cell cycle progression and cell adhesion.

Ribosome-inactivating proteins

Proteins that are capable of inactivating ribosomes.

Rickets

Is a softening of the bones in children potentially leading to fractures and deformity.

Ringworm

Dermatophytosis, a skin infection caused by fungus.

Roborant

Restoring strength or vigour, a tonic.

Rotavirus

The most common cause of infectious diarrhoea (gastroenteritis) in young children and infants, one of several viruses that causes infections called stomach flu.

Rubefacient

A substance for external application that produces redness of the skin, e.g. by causing dilation of the capillaries and an increase in blood.

Ryanodine receptor

Intracellular Ca ++ channels in animal tissues like muscles and neurons.

S.C.

Abbreviation for subcutaneous, beneath the layer of skin.

S-T segment

The portion of an electrocardiogram between the end of the QRS complex and the beginning of the T wave. Elevation or depression of the S-T segment is the characteristics of myocardial ischemia or injury and coronary artery disease.

Salve

Medical ointment used to soothe the head or body surface.

Sapraemia

See Septicaemia.

Sarcoma

Cancer of the connective or supportive tissue (bone, cartilage, fat, muscle, blood vessels) and soft tissues.

Sarcopenia

Degenerative loss of skeletal muscle mass and strength associated with aging.

Sarcoplasmic reticulum

A special type of smooth endoplasmic reticulum found in smooth and striated muscle.

SARS

Severe acute respiratory syndrome, the name of a potentially fatal new respiratory disease in humans which is caused by the SARS coronavirus (SARS-CoV)

Satiety

State of feeling satiated, fully satisfied (appetite or desire).

Scabies

A transmissible ectoparasite skin infection characterised by superficial burrows, intense pruritus (itching) and secondary infection.

Scarlatina

Scarlet fever, an acute, contagious disease caused by infection with group A streptococcal bacteria.

Schwann cells

Or neurolemmocytes, are the principal supporting cells of the peripheral nervous system; they form the myelin sheath of a nerve fibre.

Schistosomiasis

Is a parasitic disease caused by several species of fluke of the genus *Schistosoma* . Also known as bilharzia, bilharziasis or snail fever.

Schizophrenia

A psychotic disorder (or a group of disorders) marked by severely impaired thinking, emotions and behaviours.

Sciatica

A condition characterised by pain deep in the buttock often radiating down the back of the leg along the sciatic nerve.

Scleroderma

A disease of the body's connective tissue. The most common symptom is a thickening and hardening of the skin, particularly of the hands and face.

Scrofula

A tuberculous infection of the skin on the neck caused by the bacterium *Mycobacterium tuberculosis*.

Scrophulosis

See Scrofula.

Scurf

Abnormal skin condition in which small flakes or scales become detached.

Scurvy

A state of dietary deficiency of vitamin C (ascorbic acid) which is required for the synthesis of collagen in humans.

Sebotropic

Having an affinity for or a stimulating effect on sebaceous glands; promoting the excretion of sebum.

Sebum

Oily secretion of the sebaceous glands.

Secretagogue

A substance that causes another substance to be secreted.

Sedative

Having a soothing, calming or tranquilising effect; reducing or relieving stress, irritability or excitement.

Seizure

The physical findings or changes in behaviour that occur after an episode of abnormal electrical activity in the brain.

Selectins

Are a family of cell adhesion molecules, e.g. selectin E, selectin L and selectin P.

Selenium (Se)

A trace mineral that is essential to good health but required only in tiny amounts; it is incorporated into proteins to make selenoproteins, which are important antioxidant enzymes. It is found in avocado, brazil nut, lentils, sunflower seeds, tomato, whole grain cereals, seaweed, seafood and meat.

Sensorineural bradyacuasia

Hearing impairment of the inner ear resulting from damage to the sensory hair cells or to the nerves that supply the inner ear.

Sepsis

Potentially fatal whole-body inflammation caused by severe infection.

Sequela

An abnormal pathological condition resulting from a disease, injury or trauma.

Serine proteinase

Peptide hydrolases which have an active centre histidine and serine involved in the catalytic process.

Serotonergic

Liberating, activated by, or involving serotonin in the transmission of nerve impulses.

Serotonin

A monoamine neurotransmitter synthesised in serotonergic neurons in the central nervous system.

Sepsis

Is a potentially fatal medical condition characterised by a whole-body inflammatory response (called a systemic inflammatory response syndrome or SIRS) that is triggered by an infection.

Septicaemia

A systemic disease associated with the presence and persistence of pathogenic microorganisms or their toxins in the blood.

Sequelae

A pathological condition resulting from a prior disease, injury or attack.

Sexual potentiator

Increases sexual activity and potency and enhances sexual performance due to increased blood flow and efficient metabolism.

Sexually transmitted diseases (STD)

Infections that are transmitted through sexual activity.

SGOT , serum glutamic oxaloacetic transaminase

An enzyme that is normally present in liver and heart cells. SGOT is released into blood when the liver or heart is damaged. Also called aspartate transaminase (AST).

SGPT , serum glutamic pyruvic transaminase

An enzyme normally present in serum and body tissues, especially in the liver; it is released into the serum as a result of tissue injury, also called alanine transaminase (ALT).

Shiga-like toxin

A toxin produced by the bacterium *Escherichia coli* which disrupts the function of ribosomes, also known as verotoxin.

Shiga toxigenic Escherichia coli (STEC)

Comprises a diverse group of organisms capable of causing severe gastrointestinal disease in humans.

Shiga toxin

A toxin produced by the bacterium *Shigella dysenteriae* , which disrupts the function of ribosomes.

Shingles

Skin rash caused by the zoster virus (same virus that causes chicken pox) and is medically termed herpes zoster.

Sialogogue

Salivation promoter, a substance used to increase or promote the excretion of saliva.

Sialoproteins

Glycoproteins that contain sialic acid as one of their carbohydrates.

Sialorrhea

Excessive production of saliva.

Sialylation

Reaction with sialic acid or its derivatives; used especially with oligosaccharides.

Sialyltransferases

Enzymes that transfer sialic acid to nascent oligosaccharide.

Sickle cell disease

Is an inherited blood disorder that affects red blood cells. People with sickle cell disease have red blood cells that contain mostly haemoglobin S, an abnormal type of haemoglobin. Sometimes these red blood cells become sickle shaped (crescent shaped) and have difficulty passing through small blood vessels.

Side stitch

Is an intense stabbing pain under the lower edge of the ribcage that occurs while exercising.

Signal transduction cascade

Refers to a series of sequential events that transfer a signal through a series of intermediate molecules until final regulatory molecules, such as transcription factors, and is modified in response to the signal.

Silicon (Si)

Is required in minute amounts by the body and is important for the development of healthy hair and the prevention of nervous disorders. Lettuce is the best natural source of silicon.

Sinapism

Signifies an external application, in the form of a soft plaster, or poultice.

Sinusitis

Inflammation of the nasal sinuses.

SIRC cells

Statens Seruminstitut rabbit cornea (SIRC) cell line.

SIRT 1

Stands for sirtuin (silent mating type information regulation 2 homolog) 1. It is an enzyme that deacetylates proteins that contribute to cellular regulation.

Sirtuin

Also called Sir2 proteins, a class of proteins that possess either histone deacetylase or mono-ribosyltransferase activity.

6-Keto-PGF1 alpha

A physiologically active and stable hydrolysis product of epoprostenol, found in nearly all mammalian tissues.

Sjögren's syndrome

An autoimmune disease that mainly affects the eyes and salivary glands, but can affect different parts of the body. Symptoms include dry and itchy eyes, a dry mouth, thirst and swallowing difficulties.

Skp1

(S-Phase kinase-associated protein 1) is a core component of SCF ubiquitin ligases and mediates protein degradation.

Smads

A family of intracellular proteins that mediate signalling by members of the TGF-beta (transforming growth factor beta) superfamily.

Smad2/3

A key signalling molecule for TGF-beta.

Smad7

A TGFβ type 1 receptor antagonist.

Smallpox

Is an acute, contagious and devastating disease in humans caused by *Variola* virus and has resulted in high mortality over the centuries.

Snuff

Powder inhaled through the nose.

SOCE (store - operated Ca^{2+})

Is a receptor-regulated Ca^{2+} entry pathway.

SOD

Superoxide dismutase, is an enzyme that repairs cells and reduces the damage done to them by superoxide, the most common free radical in the body.

Sodium (Na)

Is an essential nutrient required for health. Sodium cations are important in neuron (brain and nerve) function and in influencing osmotic balance between cells and the interstitial fluid and in maintenance of total body fluid homeostasis. Extra intake may cause a harmful effect on health. Sodium is naturally supplied by salt intake with food.

Soleus muscle

Smaller calf muscle lower down the leg and under the gastrocnemius muscle.

Somites

Mesodermal structures formed during embryonic development that give rise to segmented body parts such as the muscles of the body wall.

Soporific

A sleep-inducing drug.

SOS response

A global response to DNA damage in which the cell cycle is arrested and DNA repair and mutagenesis are induced.

Soyasapogenins

Triterpenoid products obtained from the acid hydrolysis of soyasaponins, designated soyasapogenols A,B, C, D and E.

Soyasaponins

Bioactive saponin compounds found in many legumes.

Spasmogenic

Inducing spasm.

Spasmolytic

Checking spasms; see Antispasmodic.

Spastic paraparesis

A disorder that causes gradual weakness with muscle spasms (spastic weakness) in the legs.

Spermatogenic

Giving rise to sperms.

Spermatorrhoea

Medically an involuntary ejaculation/drooling of semen usually nocturnal emissions.

Spermidine

An important polyamine in DNA synthesis and gene expression.

Spina bifida

A congenital birth defect caused by the incomplete closing of the embryonic neural tube.

Sphingolipid

A member of a class of lipids derived from the aliphatic amino alcohol, sphingosine.

Spinocerebellar ataxia

(SCA) is a progressive, degenerative, genetic disease with multiple types.

Spleen

Organ that filters blood and prevents infection.

Spleen tyrosine kinase (SYK)

Is an enigmatic protein tyrosine kinase functional in a number of diverse cellular processes such as the regulation of immune and inflammatory responses.

Splenitis

Inflammation of the spleen.

Splenocyte

Is a monocyte, one of the five major types of white blood cell, and is characteristically found in the splenic tissue.

Splenomegaly

Is an enlargement of the spleen.

Spongiosis

Abnormal accumulation of fluid in the epidermis.

Sprain

To twist a ligament or muscle of a joint without dislocating the bone.

Sprue

Is a chronic disorder of the small intestine caused by sensitivity to gluten, a protein found in wheat and rye and to a lesser extent oats and barley. It causes poor absorption by the intestine of fat, protein, carbohydrates, iron, water and vitamins A, D, E and K.

Sputum

Matter coughed up and usually ejected from the mouth, including saliva, foreign material and substances such as mucus or phlegm, from the respiratory tract.

SREBP-1

See Sterol regulatory element-binding protein-1.

Stanch

To stop or check the flow of a bodily fluid like blood from a wound.

Statin

A type of lipid-lowering drug.

STAT3

Signal transducer and activator of transcription 3, a transcription factor, plays a key role in many cellular processes such as cell growth and apoptosis.

Status epilepticus

Refers to a life-threatening condition in which the brain is in a state of persistent seizure.

STD

Sexually transmitted disease.

Steatorrhea

Is the presence of excess fat in faeces which appear frothy, foul smelling and floats because of the high fat content.

Steatohepatitis

Liver disease, characterised by inflammation of the liver with fat accumulation in the liver.

Steatosis

Refer to the deposition of fat in the interstitial spaces of an organ like the liver, fatty liver disease.

Stereotypy

Excessive repetitive or ritualistic movement, posture or utterance.

Sterility

Inability to produce offspring, also called asepsis.

Sternutatory

Causing or tending to cause sneezing.

Steroidogenic

Relating to steroidogenesis.

Steroidogenesis

The production of steroids, as by the adrenal glands.

Sterol regulatory element-binding protein-1 (SREBP1)

Is a key regulator of the transcription of numerous genes that function in the metabolism of cholesterol and fatty acids.

Stimulant

A substance that promotes the activity of a body system or function.

Stomachic

(Digestive stimulant) an agent that stimulates or strengthens the activity of the stomach; used as a tonic to improve the appetite and digestive processes.

Stomatitis

Oral inflammation and ulcers, may be mild and localised or severe, widespread and painful.

Stomatology

Medical study of the mouth and its diseases.

Stool

Faeces.

Strangury

Is the painful passage of small quantities of urine which are expelled slowly by straining with severe urgency; it is usually accompanied with the unsatisfying feeling of a remaining volume inside and a desire to pass something that will not pass.

Straub tail

Condition in which an animal carries its tail in an erect (vertical or nearly vertical) position.

STREPs

Sterol regulatory element-binding proteins, a family of transcription factors that regulate lipid homeostasis by controlling the expression of a range of enzymes required for endogenous cholesterol, fatty acid, triacylglycerol and phospholipid synthesis.

Stria terminalis

A structure in the brain consisting of a band of fibres running along the lateral margin of the ventricular surface of the thalamus.

Striae gravidarum

A cutaneous condition characterised by stretch marks on the abdomen during and following pregnancy.

Stricture

An abnormal constriction of the internal passageway within a tubular structure such as a vessel or duct

Strongyloidiasis

An intestinal parasitic infection in humans caused by two species of the parasitic nematode *Strongyloides*. The nematode or round worms are also called thread worms.

Styptic

A short stick of medication, usually anhydrous aluminium sulphate (a type of alum) or titanium dioxide, which is used for stanching blood by causing blood vessels to

contract at the site of the wound. Also called haemostatic pencil. See Antihæmorrhagic.

Subarachnoid hæmorrhage

Is bleeding in the area between the brain and the thin tissues that cover the brain.

Substance P

A neuropeptide that functions as a neurotransmitter and neuromodulator and is associated with the sensation of pain.

Substantia nigra

Is a dark coloured brain structure located in the midbrain that plays an important role in reward, addiction and movement.

Sudatory

Medicine that causes or increases sweating. Also see Sudorific.

Sudorific

A substance that causes sweating.

Sulphur

Sulphur is an essential component of all living cells. Sulphur is important for the synthesis of sulphur-containing amino acids, all polypeptides, proteins and enzymes such as glutathione, an important sulphur-containing tripeptide which plays a role in cells as a source of chemical reduction potential. Sulphur is also important for hair formation. Good plant sources are garlic, onion, leeks and other alliaceous vegetables and brassicaceous vegetables like cauliflower, cabbages, Brussels sprout, kale; legumes, beans, green and red gram and soybeans; horse radish; water cress; and wheat germ.

Superior mesenteric artery (SMA)

Arises from the anterior surface of the abdominal aorta, just inferior to the origin of the celiac trunk, and supplies the

intestine from the lower part of the duodenum to the left colic flexure and the pancreas.

Superoxidase mutase (SOD)

Antioxidant enzyme.

Suppuration

The formation of pus, the act of becoming converted into and discharging pus.

Supraorbital

Located above the orbit of the eye.

Sural nerve

Sensory nerve comprising collateral branches off of the common tibial and common fibular nerve.

SYK, spleen tyrosine kinase

Is a human protein and gene. Syk plays a similar role in transmitting signals from a variety of cell surface receptors including CD74, Fc receptor and integrins.

Sympathetic nervous system

The part of the autonomic nervous system originating in the thoracic and lumbar regions of the spinal cord that in general inhibits or opposes the physiological effects of the parasympathetic nervous system, as in tending to reduce digestive secretions or speed up the heart.

Sympathomimetic

Mimicking the effects of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system.

Synaptic plasticity

The ability of neurons to change the number and strength of their synapses.

Synaptogenesis

The formation of synapses.

Synaptoneuroosomes

Purified synapses containing the pre- and postsynaptic termini.

Synaptosomes

Isolated terminal of a neuron.

Syncope

Fainting, sudden loss of consciousness followed by the return of wakefulness.

Syndactyly

Webbed toes, a condition where two or more digits are fused together.

Syneresis

Expulsion of liquid from a gel, as contraction of a blood clot and expulsion of liquid.

Syngeneic

Genetically identical or closely related, so as to allow tissue transplant; immunologically compatible.

Synovial

Lubricating fluid secreted by synovial membranes, as those of the joints.

Synoviocyte

Located in the synovial membrane; there are two types. Type A cells are more numerous, have phagocytic characteristics and produce degradative enzymes. Type B cells produce synovial fluid, which lubricates the joint and nourishes the articular cartilage.

Syphilis

Is perhaps the best known of all the STDs. Syphilis is transmitted by direct contact with infection sores, called chancres, syphilitic skin rashes or mucous patches on the tongue and mouth during kissing, necking, petting or sexual intercourse. It can also be transmitted from a pregnant woman to a fetus after the fourth month of pregnancy.

System lupus erythematosus

A long-term autoimmune disorder that may affect the skin, joints, kidneys, brain and other organs. Symptoms may include chest pain, fatigue, fever, hair loss, nail disease, mouth sores, sensitivity to sunlight, skin rash (butterfly rash).

Systolic

The blood pressure when the heart is contracting. It is specifically the maximum arterial pressure during contraction of the left ventricle of the heart.

T cells

Or T lymphocytes, a type of white blood cell that plays a key role in the immune system and attacks virus-infected cells, foreign cells and cancer cells.

Tachyarrhythmia

Any disturbance of the heart rhythm in which the heart rate is abnormally increased.

Tachycardia

A fast heart rate applied to adults to rates over 100 beats per minute.

Tachykinins

Neuropeptide transmitters that are widely distributed and active in the central nervous system and periphery, rapidly acting secretagogues, and cause smooth muscle contraction and vasodilation (hypotension).

Tachyphylaxis

A decreased response to a medicine given over a period of time so that larger doses are required to produce the same response.

Tachypnea

Abnormally fast breathing.

Taenia

A parasitic tapeworm or flatworm of the genus *Taenia*.

Taeniaceae

An agent that kills tapeworms.

Tardive dyskinesia

A disorder characterised by repetitive, involuntary, purposeless movements in the body such as grimacing, tongue protrusion, lip smacking, puckering and pursing of the lips and rapid eye blinking. Rapid, involuntary movements of the limbs, torso and fingers may also occur.

Tau

Is a class of microtubule-associated protein (MAP) in neuronal and glial cells.

Tau-1 (Ser198/199/202), pS396 (Ser396) and pS214 (Ser214) epitopes

Serine phosphorylation sites of tau-1.

Tau phosphorylation

Plays an important role in neurodegenerative diseases and regulated by protein kinases and phosphatases.

TBARS

See thiobarbituric acid reactive substances.

TCA cycle

See Tricarboxylic acid cycle .

TCID₅₀

Median tissue culture infective dose; that amount of a pathogenic agent that will produce pathological change in 50% of cell cultures.

Telencephalon

The cerebral hemispheres, the largest divisions of the human brain.

Teletherapy

A noninvasive procedure using external beam radiotherapy treatments.

Telomerase

Enzyme that acts on parts of chromosomes known as telomeres.

Temporomandibular joint disorder (TMJD or TMD syndrome)

A disorder characterised by acute or chronic inflammation of the temporomandibular joint that connects the mandible to the skull.

Tendonitis

Is inflammation of a tendon.

Tenesmus

A strong desire to defaecate.

Teras

(Medicine) a grossly malformed and usually nonviable fetus.
plural terata.

Teratogen

Is an agent that can cause malformations of an embryo or fetus. *adj.* teratogenic.

Testicular torsion

Twisting of the spermatic cord, which cuts off the blood supply to the testicle and surrounding structures within the scrotum.

Tetanus

An acute, potentially fatal disease caused by tetanus bacilli multiplying at the site of an injury and producing an exotoxin that reaches the central nervous system producing prolonged contraction of skeletal muscle fibres. Also called lockjaw.

Tete

Acute dermatitis caused by both bacterial and fungal infections.

Tetraparesis

Weakness of muscles of all four limbs.

Tetter

Any of a number of skin diseases.

TGF-beta

Transforming growth factor beta is a protein that controls proliferation, cellular differentiation and other functions in most cells.

Th cells or T helper cells

A subgroup of lymphocytes that helps other white blood cells in immunologic processes.

Th 1 cells

Helper cells that play an important role in the immune system.

Th 17 cells

A subset of T helper cells producing interleukin 17.

Thalassemia major

Is a genetic blood disorder that causes the body to manufacture an abnormal form of haemoglobin.

Thelarche

The beginning of secondary (postnatal) breast development, usually occurring at the beginning of puberty in girls.

Thermogenic

Tending to produce heat, applied to drugs or food (fat burning food).

Thermogenesis

Is the process of heat production in organisms.

Thermonociceptors

Or thermal nociceptors, sensory receptors that are stimulated by noxious heat or cold at various temperatures.

Thiobarbituric acid reactive substances (TBARS)

A well-established method for screening and monitoring lipid peroxidation.

Thixotropy

The property exhibited by certain gels of becoming fluid when stirred or shaken and returning to the semisolid state upon standing .

Thoracodynia

Pain in the chest.

3- β -HSD

(Or 3- β -hydroxysteroid dehydrogenase/ δ -5-4 isomerase) is an enzyme that catalyses the synthesis of progesterone from pregnenolone.

3-Nitrotyrosine (3-NT) protein

Used as a marker for oxidative damage or nitrosative stress.

Thrombocythaemia

A blood condition characterised by a high number of platelets in the blood.

Thrombocytopenia

A condition when the bone marrow does not produce enough platelets (thrombocytes) like in leukaemia.

Thromboembolism

Formation in a blood vessel of a clot (thrombus) that breaks loose and is carried by the blood stream to plug another vessel. *cf.* deep vein thrombosis.

Thrombogenesis

Formation of a thrombus or blood clot.

Thrombophlebitis

Occurs when there is inflammation and clot in a surface vein.

Thromboplastin

An enzyme liberated from blood platelets that converts prothrombin into thrombin as blood starts to clot, also called thrombokinase.

Thrombosis

The formation or presence of a thrombus (clot).

Thromboxanes

Any of several compounds, originally derived from prostaglandin precursors in platelets that stimulate aggregation of platelets and constriction of blood vessels.

Thromboxane B2

The inactive product of thromboxane.

Thrombus

A fibrinous clot formed in a blood vessel or in a chamber of the heart.

Thrush

A common mycotic infection caused by yeast, *Candida albicans*, in the digestive tract or vagina. In children it is characterised by white spots on the tongue.

Thymocytes

Are T cell precursors which develop in the thymus.

Thyrotoxicosis

Or hyperthyroidism—an overactive thyroid gland, producing excessive circulating free thyroxine and free triiodothyronine, or both.

Tight junction

Associated areas of two cells whose membranes join together forming a virtually impermeable barrier to fluid.

TIMP-3

A human gene belongs to the tissue inhibitor of matrix metalloproteinases (MMP) gene family. See MMP.

Tincture

Solution of a drug in alcohol.

Tinea

Ringworm, fungal infection on the skin.

Tinea favosa

See Favus.

Tinea cruris

Ringworm of the groin.

Tinea imbricata

(Also called Tokelau) an eruption characterised by concentric rings of overlapping scales forming papulosquamous patches scattered over the body; it occurs in tropical climates especially prevalent in southwest Polynesia and is caused by the fungus *Trichophyton concentricum* .

Tinea pedis

Fungal infection of the foot, also called athlete's foot.

Tinnitus

A noise in the ears, as ringing, buzzing, roaring, clicking, etc.

Tisane

An herbal infusion used as tea or for medicinal purposes.

Tissue plasminogen activator (t-PA)

A serine protease involved in the breakdown of blood clots.

TNF alpha

Cachexin or cachectin and formally known as tumour necrosis factor-alpha, a cytokine involved in systemic inflammation. Primary role of TNF is in the regulation of immune cells. TNF is also able to induce apoptotic cell death, to induce inflammation and to inhibit tumorigenesis and viral replication.

Tocolytics

Medications used to suppress premature labour.

Tocopherol

Fat-soluble organic compounds belonging to vitamin E group .
See Vitamin E.

Tocotrienol

Fat-soluble organic compounds belonging to vitamin E group .
See Vitamin E.

Tolerogenic

Producing immunological tolerance.

Toll-like receptors (TLRs)

A class of proteins that play a key role in the innate immune system.

Tonic

Substance that acts to restore, balance, tone, strengthen or invigorate a body system without overt stimulation or depression

Tonic–clonic seizure

A type of generalised seizure that affects the entire brain.

Tonsillitis

An inflammatory condition of the tonsils due to bacteria, allergies or respiratory problems.

TOP2A

Topoisomerase II alpha enzyme.

Topoisomerases

A class of enzymes involved in the regulation of DNA supercoiling.

Topoisomerase inhibitors

A new class of anticancer agents with a mechanism of action aimed at interrupting DNA replication in cancer cells.

Torsade de Pointes

An uncommon condition of the heart. It is a polymorphic ventricular tachycardia occurring in the context of QT prolongation.

Total parenteral nutrition (TPN)

Is a method of feeding that bypasses the gastrointestinal tract.

Toxaemia

Is the presence of abnormal substances in the blood, but the term is also used for a serious condition in pregnancy that involves hypertension and proteinuria. Also called pre-eclampsia.

Tracheitis

Is a bacterial infection of the trachea; also known as bacterial tracheitis or acute bacterial tracheitis.

Trachoma

A contagious disease of the conjunctiva and cornea of the eye, producing painful sensitivity to strong light and excessive tearing.

TRAIL

Acronym for tumour necrosis factor-related apoptosis-inducing ligand, is a cytokine that preferentially induces apoptosis in tumour cells.

Tranquiliser

A substance drug used in calming person suffering from nervous tension or anxiety.

Transaminase

Also called aminotransferase, is an enzyme that catalyses a type of reaction between an amino acid and an α -keto acid.

Transaminitis

Increase in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) to > 5 times the upper limit of normal.

Transcatheter arterial chemoembolisation (TACE)

Is an interventional radiology procedure involving percutaneous access to the hepatic artery and passing a catheter through the abdominal artery aorta followed by radiology. It is used extensively in the palliative treatment of unresectable hepatocellular carcinoma (HCC).

Transcriptional activators

Are proteins that bind to DNA and stimulate transcription of nearby genes.

Transcriptional coactivator PGC-1

A potent transcriptional coactivator that regulates oxidative metabolism in a variety of tissues.

Transcriptome

Is a set of all RNA molecules, including mRNA, rRNA, tRNA and other non-coding RNA transcribed in one cell or a population of cells.

Transcriptome profiling

To identify genes involved in peroxisome assembly and function.

Transoesophageal echocardiogram

Uses sound wave (ultrasound) technology to examine heart function.

Transforming growth factor beta (TGF- β)

A protein that controls proliferation, cellular differentiation and other functions in most cells.

Transient receptor potential ankyrin 1 (TRPA1)

Is a Ca(2+)-permeant, non-selective cationic channel that may play a role in nociception.

Transient receptor potential vanilloid 1 (TRPV1)

Receptor also known as capsaicin receptor and vanilloid receptor, is a Ca²⁺-permeable non-selective cation channel localised on a subset of primary sensory neurons and can be activated by physical and chemical stimuli.

TRAP 6

Thrombin receptor-activating peptide with 6 amino acids.

Tremorine

A chemical that produces a tremor resembling Parkinsonian tremor.

Tremulous

Marked by trembling, quivering or shaking.

Triacylglycerols

Or triacylglyceride, is a glyceride in which the glycerol is esterified with three fatty acids.

Tricarboxylic acid cycle (TCA cycle)

A series of enzymatic reactions in aerobic organisms involving oxidative metabolism of acetyl units and producing high-energy phosphate compounds, which serve as the main source of cellular energy. Also called citric acid cycle, Krebs cycle.

Trichophytosis

Infection by fungi of the genus *Trichophyton*.

Trigeminal neuralgia (TN)

Is a neuropathic disorder of one or both of the facial trigeminal nerves, also known as prosopalgia.

Triglycerides

A type of fat (lipids) found in the blood stream.

Trismus

Continuous contraction of the muscles of the jaw, specifically as a symptom of tetanus, or lockjaw; inability to open mouth fully.

TrkB receptor

Also known as TrkB tyrosine kinase, a protein in humans that acts as a catalytic receptor for several neutrophils.

Trolox equivalent

Measures the antioxidant capacity of a given substance, as compared to the standard, Trolox also referred to as TEAC (Trolox equivalent antioxidant capacity).

Trypanocidal

Destructive to trypanosomes.

Trypanosomes

Protozoan of the genus *Trypanosoma*.

Trypanosomiasis

Human disease or an infection caused by a trypanosome.

Trypsin

An enzyme of pancreatic juice that hydrolyses proteins into smaller polypeptide units.

Trypsin inhibitor

Small protein synthesised in the exocrine pancreas which prevents conversion of trypsinogen to trypsin, so protecting itself against trypsin digestion.

TRPV1

See Transient receptor potential vanilloid 1.

Tuberculosis (TB)

Is a bacterial infection of the lungs caused by a bacterium called *Mycobacterium tuberculosis* , characterised by the formation of lesions (tubercles) and necrosis in the lung tissues and other organs.

Tubulopathy

Any disease of the renal tubules of the nephron.

Tumorigenesis

Formation or production of tumours .

Tumour

An abnormal swelling of the body other than those caused by direct injury.

Tussis

A cough.

Tympanic membrane

Ear drum.

Tympanitis

Infection or inflammation of the inner ear.

Tympanophonia

Increased resonance of one's own voice, breath sounds, arterial murmurs, etc., noted especially in disease of the middle ear.

Tympanosclerosis

See Myringosclerosis.

Tyrosinase

A copper containing enzyme found in animals and plants that catalyses the oxidation of phenols (such as tyrosine) and the production of melanin and other pigments from tyrosine by oxidation.

Ubiquitin ligase

Also called an E3 ubiquitin ligase, is a protein that targets other proteins to be broken down (degraded) within cells.

UCP1

An uncoupling protein found in the mitochondria of brown adipose tissue used to generate heat by non-shivering thermogenesis .

UCP: 2 enzyme

Uncoupling protein 2 enzyme, a mitochondrial protein expressed in adipocytes.

Ulcer

An open sore on an external or internal body surface usually accompanied by disintegration of tissue and pus.

Ulcerative colitis

Is one of two types of inflammatory bowel disease—a condition that causes the bowel to become inflamed and red.

Ulemorrhagia

Bleeding of the gums.

Ulitis

Inflammation of the gums.

Unguent

Ointment.

Unilateral ureteral obstruction

Unilateral blockage of urine flow through the ureter of one kidney, resulting in a backup of urine, distension of the renal pelvis and calyces and hydronephrosis.

Uraemia

An excess in the blood of urea, creatinine and other nitrogenous end products of protein and amino acid metabolism, more correctly referred to as azotaemia.

Urethra

Tube conveying urine from the bladder to the external urethral orifice.

Urethritis

Is an inflammation of the urethra caused by infection.

Uricaemia

An excess of uric acid or urates in the blood.

Uricosuric

Promoting the excretion of uric acid in the urine.

Urinary

Pertaining to the passage of urine.

Urinary incontinence

Sudden and strong need to urinate because of poor bladder control.

Urinogenital

Relating to the genital and urinary organs or functions.

Urodynia

Pain on urination.

Urokinase

Also called urokinase-type plasminogen (u-PA), is a serine protease enzyme in human urine that catalyses the conversion of plasminogen to plasmin. It is used clinically as a thrombolytic agent.

Urokinase-type plasminogen (u-PA)

Plays a key role in tumour invasion and metastasis; also see Urokinase.

Urolithiasis

Formation of stone in the urinary tract (kidney bladder or urethra).

Urticant

A substance that causes wheals to form.

Urticaria

(Or hives) is a skin condition, commonly caused by an allergic reaction, that is characterised by raised red skin welts.

Uterine

Relating to the uterus.

Uterine myomas

Also called fibroids, tumours that grown from the uterine wall.

Uterine prolapse

Occurs when weakened or damaged muscles and ligaments allow the uterus to slip into the vagina.

Uterine relaxant

An agent that relaxes the muscles in the uterus.

Uterine stimulant

An agent that stimulates the uterus (and often employed during active childbirth).

Uterotonic

Giving muscular tone to the uterus.

Uterotrophic

Causing an effect on the uterus.

Uterus

Womb.

Vaginal dystrophy

A condition in which the outer part of the vagina becomes dry and the skin thickens or thins.

Vaginitis

Infectious or non-infectious inflammation of the vaginal mucosa.

Vaginopathy

Any disease of the vagina.

Vagotomy

The surgical cutting of the vagus nerve to reduce acid secretion in the stomach.

Vagus nerve

A cranial nerve, that is, a nerve connected to the brain. The vagus nerve has branches to most of the major organs in the body, including the larynx, throat, windpipe, lungs, heart and most of the digestive system.

Variola

Or smallpox, a contagious disease unique to humans, caused by either of two virus variants, *Variola major* and *Variola minor*. The disease is characterised by fever, weakness and skin eruption with pustules that form scabs that leave scars.

Varicose veins

Are veins that have become enlarged and twisted.

Vasa vasorum

Is a network of small blood vessels that supply large blood vessels. *pl.* vasa vasori.

Vascular cell adhesion molecule (VCAM)

A part of the immunoglobulin superfamily. They are important in inflammation, immune responses and intracellular signalling events.

Vascular endothelial growth factor (VEGF)

A polypeptide chemical produced by cells that stimulates the growth of new blood vessels.

Vasculitis

Group of disorders that destroy blood vessels by inflammation.

Vasculogenesis

The process of blood vessel formation occurring by a de novo production of endothelial cells.

Vasoconstrictor

Drug that causes constriction of blood vessels.

Vasodilator

Drug that causes dilation or relaxation of blood vessels.

Vasodilatory

Causing the widening of the lumen of blood vessels.

Vasomotor symptoms

Menopausal symptoms characterised by hot flushes and night sweats.

Vasospasm

Refers to a condition in which blood vessels spasm, leading to vasoconstriction and subsequently to tissue ischemia and death (necrosis).

VCAM-1 (vascular cell adhesion molecule-1)

Also known as CD106, contains six or seven immunoglobulin domains and is expressed on both large and small vessels only after the endothelial cells are stimulated by cytokines.

VEGF

Vascular endothelial growth factor.

Venereal disease (VD)

Term given to the diseases syphilis and gonorrhoea.

Venule

A small vein, especially one joining capillaries to larger veins.

Vermifuge

A substance used to expel worms from the intestines.

Verotoxin

S Shiga-like toxin produced by *Escherichia coli* , which disrupts the function of ribosomes, causing acute renal failure.

Verruca

A contagious and painful wart on the sole of the foot.

Verruca plana

Is a reddish-brown or flesh-coloured, slightly raised, flat-surfaced, well-demarcated papule on the hand and face, also called flat wart.

Verruca vulgaris

Small painless warts on the skin caused by the human papillomavirus.

Vertigo

An illusory, sensory perception that the surroundings or one's own body is revolving; dizziness.

Very low-density lipoprotein (VLDL)

A type of lipoprotein made by the liver. VLDL is one of the five major groups of lipoproteins (chylomicrons, VLDL, intermediate-density lipoprotein, low-density lipoprotein, high-density lipoprotein (HDL)) that enable fats and cholesterol to move within the water-based solution of the bloodstream. VLDL is converted in the bloodstream to low-density lipoprotein (LDL).

Vesical calculus

Calculi (stones) in the urinary bladder

Vesicant

A substance that causes tissue blistering.

Vestibular

Relating to the sense of balance.

Vestibular disorders

Includes symptoms of dizziness, vertigo and imbalance; it can be result from or worsened by genetic or environmental conditions.

Vestibular schwannoma

Also called acoustic neuroma is a benign tumour that may develop from an overproduction of Schwann cells that press on the hearing and balance nerves in the inner ear.

Vestibular system

Includes parts of the inner ear and brain that process sensory information involved with controlling balance and eye movement.

Vibrissa

Stiff hairs that are located especially about the nostrils.

Vimentin

A type III intermediate filament protein that is expressed in mesenchymal cells.

Viremia

A medical condition where viruses enter the bloodstream and hence have access to the rest of the body.

Visceral fat

Intra-abdominal fat, is located inside the peritoneal cavity, packed in between internal organs and torso.

Visual entopia

Visual disturbances

Vitamin

Any complex, organic compound, found in various food or sometimes synthesised in the body, required in tiny

amounts and are essential for the regulation of metabolism, normal growth and function of the body.

Vitamin A

Retinol, fat-soluble vitamins that play an important role in vision, bone growth, reproduction, cell division and cell differentiation, and help regulate the immune system in preventing or fighting off infections. Vitamin A that is found in colourful fruits and vegetables is called provitamin A carotenoid. They can be made into retinol in the body. Deficiency of vitamin A results in night blindness and keratomalacia.

Vitamin B1

Also called thiamine, water-soluble vitamins, dissolve easily in water and, in general, are readily excreted from the body they are not readily stored; consistent daily intake is important. It functions as coenzyme in the metabolism of carbohydrates and branched chain amino acids and other cellular processes. Deficiency results in beriberi disease.

Vitamin B2

Also called riboflavin, an essential water-soluble vitamin that functions as coenzyme in redox reactions. Deficiency causes ariboflavinosis.

Vitamin B3

Comprises niacin and niacinamide, water-soluble vitamin that functions as coenzyme or co-substrate for many redox reactions and is required for energy metabolism. Deficiency causes pellagra.

Vitamin B5

Also called pantothenic acid, a water-soluble vitamin that functions as coenzyme in fatty acid metabolism. Deficiency causes paresthesia.

Vitamin B6

water-soluble vitamin, exists in three major chemical forms: pyridoxine, pyridoxal and pyridoxamine. Vitamin B6 is needed in enzymes involved in protein metabolism, red

blood cell metabolism, efficient functioning of nervous and immune systems and haemoglobin formation. Deficiency causes anaemia and peripheral neuropathy.

Vitamin B 7

Also called biotin or vitamin H, an essential water-soluble vitamin, is involved in the synthesis of fatty acids, amino acids and glucose, in energy metabolism. Biotin promotes normal health of sweat glands, bone marrow, male gonads, blood cells, nerve tissue, skin and hair. Deficiency causes dermatitis and enteritis.

Vitamin B9

Also called folic acid, an essential water-soluble vitamin. Folate is especially important during periods of rapid cell division and growth such as infancy and pregnancy. Deficiency during pregnancy is associated with birth defects such as neural tube defects. Folate is also important for production of red blood cells and prevents anaemia. Folate is needed to make DNA and RNA, the building blocks of cells. It also helps prevent changes to DNA that may lead to cancer.

Vitamin B12

A water-soluble vitamin, also called cobalamin as it contains the metal cobalt. It helps maintain healthy nerve cells and red blood cells and DNA production. Vitamin B12 is bound to the protein in food. Deficiency causes megaloblastic anaemia.

Vitamin C

Also known as ascorbic acid is an essential water-soluble vitamin. It functions as cofactor for reactions requiring reduced copper or iron metalloenzyme and as a protective antioxidant. Deficiency of vitamin C causes scurvy.

Vitamin D

A group of fat-soluble, prohormone vitamin, the two major forms of which are vitamin D2 (or ergocalciferol) and vitamin D3 (or cholecalciferol). Vitamin D obtained from sun exposure, food and supplements is biologically inert

and must undergo two hydroxylations in the body for activation. Vitamin D is essential for promoting calcium absorption in the gut and maintaining adequate serum calcium and phosphate concentrations to enable normal growth and mineralisation of bone and prevent hypocalcaemic tetany. Deficiency causes rickets and osteomalacia. Vitamin D has other roles in human health, including modulation of neuromuscular and immune function, reduction of inflammation and modulation of many genes encoding proteins that regulate cell proliferation, differentiation and apoptosis.

Vitamin E

Is the collective name for a group of fat-soluble compounds and exists in eight chemical forms (alpha-, beta-, gamma- and delta-tocopherol and alpha-, beta-, gamma- and delta-tocotrienol). It has pronounced antioxidant activities stopping the formation of reactive oxygen species when fat undergoes oxidation and helps prevent or delay the chronic diseases associated with free radicals. Besides its antioxidant activities, vitamin E is involved in immune function, cell signalling, regulation of gene expression and other metabolic processes. Deficiency is very rare but can cause mild haemolytic anaemia in newborn infants.

Vitamin K

A group of fat-soluble vitamin and consists of vitamin K₁ which is also known as phyloquinone or phytomenadione (also called phytonadione) and vitamin K₂ (menaquinone, menatetrenone). Vitamin K plays an important role in blood clotting. Deficiency is very rare but can cause bleeding diathesis.

Vitamin P

A substance or mixture of substances obtained from various plant sources, identified as citrin or a mixture of bioflavonoids, thought to but not proven to be useful in reducing the extent of haemorrhage.

Vitiligo

A chronic skin disease that causes loss of pigment, resulting in irregular pale patches of skin. It occurs when the melanocytes, cells responsible for skin pigmentation, die or are unable to function . Also called leucoderma.

Vitreoretinopathy

See Proliferative vitreoretinopathy.

VLA-4

Very late antigen-4, expressed by most leucocytes, but it is observed on neutrophils under special conditions.

VLDL

See Very low-density lipoproteins.

Vomitive

Substance that causes vomiting.

Vulnerary

(Wound healer) a substance used to heal wounds and promote tissue formation.

Vulva-vaginal erythema

Abnormal redness and inflammation of the skin in the vagina.

Wart

An infectious skin tumour caused by a viral infection.

Welt

See Wheal.

Wheal

A firm, elevated swelling of the skin. Also called a weal or welt.

White fat

White adipose tissue (WAT) in mammals, store of energy. *cf.* brown fat.

Whitlow

Painful infection of the hand involving one or more fingers that typically affects the terminal phalanx.

Whooping cough

Acute infectious disease usually in children caused by a *Bacillus* bacterium and accompanied by catarrh of the respiratory passages and repeated bouts of coughing.

Wnt proteins

Are a diverse family of secreted lipid-modified signalling glycoproteins that are 350–400 amino acids in length

Wnt signalling pathway

Is a network of proteins involved in embryogenesis and cancer and also in normal physiological processes.

X-Linked agammaglobulinemia

Also known as X-linked hypogammaglobulinemia, XLA, Bruton-type agammaglobulinemia, Bruton syndrome or sex-linked agammaglobulinemia; a rare x-linked genetic disorder that affects the body's ability to fight infection.

Xanthine oxidase

A flavoprotein enzyme containing a molybdenum cofactor (Moco) and (Fe_2S_2) clusters, involved in purine metabolism. In humans, inhibition of xanthine oxidase reduces the production of uric acid and prevents hyperuricaemia and gout.

Xanthones

Unique class of biologically active phenol compounds with the molecular formula $\text{C}_{13}\text{H}_8\text{O}_2$ possessing antioxidant properties, discovered in the mangosteen fruit.

Xenobiotics

A chemical (as a drug, pesticide or carcinogen) that is foreign to a living organism.

Xenograft

A surgical graft of tissue from one species to an unlike species.

Xerophthalmia

A medical condition in which the eye fails to produce tears.

Xerostomia

Dryness in the mouth due to lack of saliva production.

Yaws

An infectious tropical infection of the skin, bones and joints caused by the spirochete bacterium *Treponema pertenue*, characterised by papules and papilloma with subsequent deformation of the skins, bone and joints; also called framboesia.

yGCN5

A histone acetyl transferase (HAT) that plays a role in regulation of transition, cell cycle progression and differentiation.

Yellow fever

Is a viral disease that is transmitted to humans through the bite of infected mosquitoes. Illness ranges in severity from an influenza-like syndrome to severe hepatitis and haemorrhagic fever. Yellow fever virus (YFV) is maintained in nature by mosquito-borne transmission between nonhuman primates.

Zeaxanthin

A common carotenoid, found naturally as coloured pigments in many fruit vegetables and leafy vegetables. It is important for good vision and is one of the two carotenoids contained within the retina of the eye. Within the central macula, zeaxanthin predominates, whereas in the peripheral retina, lutein predominates.

Zinc (Zn)

Is an essential mineral for health. It is involved in numerous aspects of cellular metabolism: catalytic activity of enzymes, immune function, protein synthesis, wound healing, DNA synthesis and cell division. It also supports normal growth and development during pregnancy,

childhood and adolescence and is required for proper sense of taste and smell. Dietary sources include beans, nuts, pumpkin seeds, sunflower seeds, whole wheat bread and animal sources.

ZK1

Kruppel-type zinc finger protein — binds DNA and, through this binding, regulates gene transcription.

ZO1 protein

A high molecular weight tight junction-associated protein.

Scientific Glossary

Abaxial

Facing away from the axis, as of the surface of an organ.

Abortive

Imperfectly formed.

Abscission

Shedding of leaves, flowers or fruits following the formation of the abscission zone.

Acaulescent

Lacking a stem, or stem very much reduced.

Accrescent

Increasing in size after flowering or with age.

Achene

A dry, small, one-seeded, indehiscent fruit formed from a superior ovary of one carpel as in sunflower.

Acid soil

Soil that maintains a pH of less than 7.0.

Acidulous

Acid or sour in taste.

Actinomorphic

Having radial symmetry, capable of being divided into symmetrical halves by any plane, referring to a flower, calyx or corolla.

Aculeate

Having sharp prickles.

Acuminate

Tapering gradually to a sharp point.

Acute

(Botany) tapering at an angle of less than 90° before terminating in a point as of leaf apex and base.

Adaxial

Side closest to the stem axis.

Adelphous

Having stamens united together by their filaments.

Adherent

Touching without organic fusion as of floral parts of different whorls.

Adnate

United with another unlike part as of stamens attached to petals.

Adpressed

Lying close to another organ but not fused to it.

Adventitious

Arising in abnormal positions, e.g. roots arising from the stem, branches or leaves, buds arising elsewhere than in the axils of leaves.

Adventive

Not native to and not fully established in a new habitat or environment; locally or temporarily naturalised, e.g. an adventive weed.

Aestivation

Refers to positional arrangement of the floral parts in the bud before it opens.

Akinete

A thick-walled dormant cell derived from the enlargement of a vegetative cell. It serves as a survival structure.

Alfisols

Soil with a clay-enriched subsoil and relatively high native fertility, having undergone only moderate leaching, containing aluminium, iron and with at least 35% base saturation, meaning that calcium, magnesium and potassium are relatively abundant.

Alkaline soil

Soil that maintains a pH above 7.0, usually containing large amounts of calcium, sodium and magnesium, and is less soluble than acidic soils.

Alkaloids

Naturally occurring bitter, complex organic-chemical compounds containing basic nitrogen and oxygen atoms and having various pharmacological effects on humans and other animals.

Alternate

Leaves or buds that are spaced along opposite sides of stem at different levels.

Allomorphic

With a shape or form different from the typical.

Alluvial soil

A fine-grained fertile soil deposited by water flowing over flood plains or in river beds.

Alluvium

Soil or sediments deposited by a river or other running water.

Amplexicaul

Clasping the stem as base of certain leaves.

Anatomising

Interconnecting network as applied to leaf veins.

Andisols

Are soils formed in volcanic ash and containing high proportions of glass and amorphous colloidal materials.

Androdioecious

With male flowers and bisexual flowers on separate plants.

Androecium

Male parts of a flower; comprising the stamens of one flower.

Androgynophore

A stalk bearing both the androecium and gynoecium above the perianth of the flower.

Androgynous

With male and female flowers in distinct parts of the same inflorescence.

Andromonoecious

Having male flowers and bisexual flowers on the same plant.

Angiosperm

A division of seed plants with the ovules borne in an ovary.

Annual

A plant which completes its life cycle within a year.

Annular

Shaped like or forming a ring.

Annulus

Circle or ringlike structure or marking; the portion of the corolla which forms a fleshy, raised ring.

Anthelate

An open, paniculate cyme.

Anther

The part of the stamen containing pollen sac which produces the pollen.

Antheriferous

Containing anthers.

Anthesis

The period between the opening of the bud and the onset of flower withering.

Anthocarp

A false fruit consisting of the true fruit and the base of the perianth.

Anthocyanidins

Are common plant pigments. They are the sugar-free counterparts of anthocyanins.

Anthocyanins

A subgroup of antioxidant flavonoids, are glucosides of anthocyanidins. They occur as water-soluble vacuolar pigments that may appear red, purple or blue according to pH in plants.

Antipetala

Situated opposite petals.

Antisepala

Situated opposite sepals.

Antrorse

Directed forward and upward.

Apetalous

Lacking petals as of flowers with no corolla.

Apical meristem

Active growing point. A zone of cell division at the tip of the stem or the root.

Apically

Towards the apex or tip of a structure.

Apiculate

Ending abruptly in a short, sharp, small point.

Apiculum

A short, pointed, flexible tip.

Apocarpous

Carpels separate in single individual pistils.

Apopetalous

With separate petals, not united to other petals.

Aposepalous

With separate sepals, not united to other sepals.

Appendiculate

Having small appendages

Appressed

Pressed closely to another structure but not fused or united.

Aquatic

A plant living in or on water for all or a considerable part of its life span.

Arachnoid

(Botany) formed of or covered with long, delicate hairs or fibres.

Arborescent

Resembling a tree; applied to nonwoody plants attaining tree height and to shrubs tending to become tree-like in size.

Arbuscular mycorrhiza (AM)

A type of mycorrhiza in which the fungus (of the phylum Glomeromycota) penetrates the cortical cells of the roots of a vascular plant and forms unique structures such as arbuscules and vesicles. These fungi help plants to capture

nutrients such as phosphorus and micronutrients from the soil.

Archegonium

A flask-shaped female reproductive organ in mosses, ferns and other related plants.

Areolate

With areolae.

Areole

(Botany) a small, specialised, cushion-like area on a cactus from which hairs, glochids, spines, branches or flowers may arise; an irregular angular specs marked out on a surface, e.g. fruit surface. *pl.* areolae.

Aril

Specialised outgrowth from the funiculus (attachment point of the seed) (or hilum) that encloses or is attached to the seed. *adj.* arillate.

Arillode

A false aril; an aril originating from the micropyle instead of from the funicle or chalaza of the ovule, e.g. mace of nutmeg.

Aristate

Bristlelike part or appendage, e.g. awns of grains and grasses.

Aristulate

Having a small, stiff, bristlelike part or appendage; a diminutive of aristate

Articulate

Jointed; usually breaking easily at the nodes or point of articulation into segments.

Ascending

Arched upwards in the lower part and becoming erect in the upper part.

Ascospore

Spore produced in the ascus in ascomycete fungi.

Ascus

Is the sexual spore-bearing cell produced in ascomycete fungi.
pl . asci.

Asperulous

Refers to a rough surface with short, hard projections.

Attenuate

Tapered or tapering gradually to a point.

Auricle

An ear-like appendage that occurs at the base of some leaves or corolla.

Auriculate

Having auricles.

Awn

A hair-like or bristlelike appendage on a larger structure.

Axil

Upper angle between a lateral organ, such as a leaf petiole, and the stem that bears it.

Axile

Situated along the central axis of an ovary having two or more locules, as in axile placentation.

Axillary

Arising or growing in an axil.

Baccate

Beery-like, pulpy or fleshy.

Barbate

Bearded, having tufts of hairs.

Barbellae

Short, stiff, hair-like bristles. *adj.* barbellate.

Bark

Is the outermost layers of stems and roots of woody plants.

Basal

Relating to, situated at, arising from or forming the base.

Basaltic soil

Soil derived from basalt, a common extrusive volcanic rock.

Basidiospore

A reproductive spore produced by basidiomycete fungi.

Basidium

A microscopic, spore-producing structure found on the hymenophore of fruiting bodies of basidiomycete fungi.

Basifixed

Attached by the base, as certain anthers are to their filaments.

Basionym

The synonym of a scientific name that supplies the epithet for the correct name.

Beak

A prominent apical projection, especially of a carpel or fruit.
adj. beaked.

Bearded

Having a tuft of hairs.

Berry

A fleshy or pulpy indehiscent fruit from a single ovary with the seed(s) embedded in the fleshy tissue of the pericarp.

Biconvex

Convex on both sides.

Biennial

Completing the full cycle from germination to fruiting in more than one, but not more than two years.

Bifid

Forked, divided into two parts.

Bifoliolate

Having two leaflets.

Bilabiate

Having two lips as of a corolla or calyx with segments fused into an upper and lower lip.

Bipinnate

Twice pinnate; the primary leaflets being again divided into secondary leaflets.

Bipinnatisect

Refers to a pinnately compound leaf, in which each leaflet is again divided into pinnae.

Biserrate

Doubly serrate; with smaller, regular, asymmetric teeth on the margins of larger teeth.

Bisexual

Having both sexes, as in a flower bearing both stamens and pistil, hermaphrodite or perfect.

Biternate

Twice ternate; with three pinnae each divided into three pinnules.

Blade

Lamina; part of the leaf above the sheath or petiole.

Blotched

See Variegated.

Bole

Main trunk of tree from the base to the first branch.

Brachyblast

A short, axillary, densely crowded branchlet or shoot of limited growth, in which the internodes elongate little or

not at all.

Bracket fungus

Shelf fungus.

Bract

A leaflike structure, different in form from the foliage leaves, associated with an inflorescence or flower. *adj.* bracteate.

Bracteate

Possessing bracts.

Bracteolate

Having bracteoles.

Bracteole

A small, secondary, bract-like structure borne singly or in a pair on the pedicel or calyx of a flower. *adj.* bracteolate.

Bran

Hard outer layer of grain and comprises the aleurone and pericarp. It contains important antioxidant, vitamins and fibre.

Bristle

A stiff hair.

Bulb

A modified underground axis that is short and crowned by a mass of usually fleshy, imbricate scales. *adj.* bulbous.

Bulbil

A small bulb or bulb-shaped body, especially one borne in the leaf axil or an inflorescence and usually produced for asexual reproduction.

Bullate

Puckered, blistered.

Burr

Type of seed or fruit with short, stiff bristles or hooks or may refer to a deformed type of wood in which the grain has been misformed.

Bush

Low, dense shrub without a pronounced trunk.

Buttress

Supporting, projecting outgrowth from base of a tree trunk as in some Rhizophoraceae and Moraceae.

Caducous

Shedding or falling early before maturity refers to sepals and petals.

Caespitose

Growing densely in tufts or clumps; having short, closely packed stems.

Calcareous

Composed of or containing lime or limestone.

Calcrete

A hardpan consisting gravel and sand cemented by calcium.

Callus

A condition of thickened raised mass of hardened tissue on leaves or other plant parts often formed after an injury but sometimes a normal feature. A callus also can refer to an undifferentiated plant cell mass grown on a culture medium. *n.* callosity . *pl.* calli, callosities. *adj.* callose.

Calyptra

The protective cap or hood covering the spore case of a moss or related plant.

Calyptrate

Operculate, having a calyptra.

Calyx

Outer floral whorl usually consisting of free sepals or fused sepals (calyx tube) and calyx lobes. It encloses the flower while it is still a bud. *adj.* calycine.

Calyx lobe

One of the free upper parts of the calyx which may be present when the lower part is united into a tube.

Calyx tube

The tubular fused part of the calyx, often cup shaped or bell shaped, when it is free from the corolla.

Campanulate

Shaped like a bell refers to calyx or corolla.

Canaliculate

Having groove or grooves.

Candelabrifform

Having the shape of a tall branched candle stick.

Canescent

Covered with short, fine whitish or greyish hairs or down.

Canopy

Uppermost leafy stratum of a tree.

Cap

See Pileus.

Capitate

Growing together in a head. Also means enlarged and globular at the tip.

Capitulum

A flower head or inflorescence having a dense cluster of sessile, or almost sessile, flowers or florets.

Capsule

A dry, dehiscent fruit formed from two or more united carpels and dehiscing at maturity by sections called valves to

release the seeds. *adj.* capsular.

Carinate

Keeled.

Carpel

A simple pistil consisting of ovary, ovules, style and stigma.

adj. carpellary.

Carpogonium

Female reproductive organ in red algae. *pl.* carpogonia.

Carpophore

Part of the receptacle which is lengthened between the carpels as a central axis; any fruiting body or fruiting structure of a fungus.

Cartilaginous

Sinewy, having a firm, tough, flexible texture (in respect of leaf margins).

Caruncle

(Bot) fleshy structure attached to the seed of certain plants.

Caryopsis

A simple dry, indehiscent fruit formed from a single ovary with the seed coat united with the ovary wall as in grasses and cereals.

Cataphyll

A reduced or scarcely developed leaf at the start of a plant's life (i.e. cotyledons) or in the early stages of leaf development.

Catkin

A slim, cylindrical, pendulous flower spike usually with unisexual flowers.

Caudate

Having a narrow, tail-like appendage.

Caudex

Thickened, usually underground base of the stem.

Caulescent

Having a well-developed aerial stem.

Cauliflory

Botanical term referring to plants which flower and fruit from their main stems or woody trunks. *adj.* cauliflorous.

Cauline

Borne on the aerial part of a stem.

Chaffy

Having thin, membranous scales in the inflorescence as in the flower heads of the sunflower family.

Chalaza

The basal region of the ovule where the stalk is attached.

Chamaephyte

A low-growing perennial plant whose dormant overwintering buds are borne at or just above the surface of the ground.

Chartaceous

Papery, of paper-like texture.

Chasmogamous

Describing flowers in which pollination takes place while the flower is open.

Chatoyant

Having a velvety sheen or lustre.

Chloroplast

A chlorophyll-containing organelle (plastid) that gives the green colour to leaves and stems. Plastids harness light energy that is used to fix carbon dioxide in the process called photosynthesis.

Chromoplast

Plastid containing coloured pigments apart from chlorophyll.

Chromosomes

Thread-shaped structures that occur in pairs in the nucleus of a cell, containing the genetic information of living organisms.

Cilia

Hairs along the margin of a leaf or corolla lobe.

Ciliate

With a fringe of hairs on the margin as of the corolla lobes or leaf.

Ciliolate

Minutely ciliate.

Cilium

A straight, usually erect hair on a margin or ridge. *pl.* cilia.

Cincinnus

A monochasial cyme in which the lateral branches arise alternately on opposite sides of the false axis.

Circinnate

Spirally coiled, with the tip innermost.

Circumscissile

Opening by a transverse line around the circumference as of a fruit.

Cladode

The modified photosynthetic stem of a plant whose foliage leaves are much reduced or absent. *cf.* cladophyll, phyllode.

Cladophyll

A photosynthetic branch or portion of a stem that resembles and functions as a leaf, like in asparagus. *cf.* cladode, phyllode.

Clamp connection

In the basidiomycetes fungi, a lateral connection or outgrowth formed between two adjoining cells of a hypha and arching over the septum between them.

Clavate

Club shaped thickened at one end referring to fruit or other organs.

Claw

The conspicuously narrowed basal part of a flat structure.

Clay

A naturally occurring material composed primarily of fine-grained minerals like kaolinite, montmorillonite-smectite or illite which exhibit plasticity through a variable range of water content and which can be hardened when dried and/or fired.

Clayey

Resembling or containing a large proportion of clay.

Cleft

Incised halfway down.

Cleistogamous

Refers to a flower in which fertilisation occurs within the bud, i.e. without the flower opening. *cf.* chasmogamous.

Climber

Growing more or less upwards by leaning or twining around another structure.

Clone

All the plants reproduced, vegetatively, from a single parent, thus having the same genetic make-up as the parent.

Coccus

One of the sections of a distinctly lobed fruit which becomes separate at maturity; sometimes called a mericarp. *pl.* cocci.

Coenocarpium

A fleshy, multiple pseudocarp formed from an inflorescence rather than a single flower.

Coherent

Touching without organic fusion, referring to parts normally together, e.g. floral parts of the same whorl. *cf.* adherent, adnate, connate.

Collar

Boundary between the above- and below-ground parts of the plant axis.

Colliculate

Having small elevations.

Column

A structure formed by the united style, stigma and stamen(s) as in Asclepiadaceae and Orchidaceae.

Comose

Tufted with hairs at the ends as of seeds.

Composite

Having two types of florets as of the flowers in the sunflower family, Asteraceae.

Compost

Organic matter (like leaves, mulch, manure, etc.) that breaks down in soil releasing its nutrients.

Compound

Describe a leaf that is further divided into leaflets or pinnae or flower with more than a single floret.

Compressed

Flattened in one plane.

Conceptacles

Specialised cavities of marine algae that contain the reproductive organs.

Concolorous

Uniformly coloured, as in upper and lower surfaces. *cf.*
discolorous

Conduplicate

Folded together lengthwise.

Cone

A reproductive structure composed of an axis (branch) bearing sterile bract-like organs and seed- or pollen-bearing structures. Applied to Gymnospermae, Lycopodiaceae, Casuarinaceae and also in some members of Proteaceae.

Conic

Cone shaped, attached at the broader end.

Conic–capitate

A cone-shaped head of flowers.

Connate

Fused to another structure of the same kind . *cf.* . adherent, adnate, coherent.

Connective

The tissue separating two lobes of an anther.

Connivent

Converging.

Conspecific

Within or belonging to the same species.

Contorted

Twisted.

Convolute

Refers to an arrangement of petals in a bud where each has one side overlapping the adjacent petal.

Cordate

Heart shaped as of leaves.

Core

Central part.

Coriaceous

Leathery texture as of leaves.

Corm

A short, swollen, fleshy, underground plant stem that serves as a food storage organ used by some plants to survive winter or other adverse conditions

Cormel

A miniature, new corm produced on a mature corm.

Corn silk

The long, filamentous styles that grow as a silky tuft or tassel at the tip of an ear of corn.

Corolla

The inner floral whorl of a flower, usually consisting of free petals or petals fused forming a corolla tube and corolla lobes. *adj.* corolline.

Corona

A crown-like section of the staminal column, usually with the inner and outer lobes as in the **Stapelieae** .

Coroniform

Crown shaped, as in the pappus of Asteraceae.

Cortex

The outer of the stem or root of a plant, bounded on the outside by the epidermis and on the inside by the endodermis containing undifferentiated cells.

Corymb

A flat-topped, short, broad inflorescence, in which the flowers, through unequal pedicels, are in one horizontal plane and the youngest in the centre. *adj.* corymbose

Costa

A thickened, linear ridge or the midrib of the pinna in ferns.
adj. costate.

Costapalmate

Having definite costa (midrib) unlike the typical palmate leaf, but the leaflets are arranged radially like in a palmate leaf.

Cotyledon

The primary seed leaf within the embryo of a seed.

Cover crop

Crop grown in between trees or in fields primarily to protect the soil from erosion, to improve soil fertility and to keep off weeds.

Crenate

Round toothed or scalloped as of leaf margins.

Crenulate

Minutely crenate, very strongly scalloped.

Crested

Frilled and ruffled edge.

Crispate

Weakly undulating edge.

Crisped

With a curled or twisted edge.

Cristate

Having or forming a crest or crista.

Crozier

Shaped like a shepherd's crook.

Crustaceous

Like a crust; having a hard crust or shell.

Cucullate

Having the shape of a cowl or hood, hooded.

Culm

The main aerial stem of the Graminae (grasses, sedges, rushes and other monocots).

Culm sheath

The plant casing (similar to a leaf) that protects the young bamboo shoot during growth, attached at each node of culm.

Cultigen

Plant species or race known only in cultivation.

Cultivar

Cultivated variety; an assemblage of cultivated individuals distinguished by any characters significant for the purposes of agriculture, forestry or horticulture and which, when reproduced, retains its distinguishing features.

Cuneate

Wedge-shaped, obtriangular.

Cupular

Cup shaped, having a cupule.

Cupule

A small cup-shaped structure or organ, like the cup at the base of an acorn.

Cusp

An elongated, usually rigid, acute point. *cf.* mucro.

Cuspidate

Terminating in or tipped with a sharp firm point or cusp. *cf.* mucronate.

Cuspidulate

Constricted into a minute cusp. *cf.* cuspidate.

Cyathiform

In the form of a cup, a little widened at the top.

Cyathium

A specialised type of inflorescence of plants in the genera *Euphorbia* and *Chamaesyce* in which the unisexual flowers are clustered together within a bract-like envelope.
pl. cyathia.

Cylindric

Tubular or rod shaped.

Cylindric–acuminate

Elongated and tapering to a point.

Cymbiform

Boat shaped and elongated and having the upper surface decidedly concave.

Cyme

An inflorescence in which the lateral axis grows more strongly than the main axis with the oldest flower in the centre or at the ends. *adj.* cymose

Cymule

A small cyme or one or a few flowers.

Cystidium

A relatively large cell found on the hymenium of a basidiomycete, for example, on the surface of a mushroom.

Cystocarp

Fruitlike structure (sporocarp) developed after fertilisation in the red algae.

Deciduous

Falling off or shedding at maturity or a specific season or stage of growth.

Decorticate

To remove the bark, rind or husk from an organ; to strip of its bark; to come off as a skin.

Decompound

As of a compound leaf; consisting of divisions that are themselves compound.

Decumbent

Prostrate, laying or growing on the ground but with ascending tips. *cf.* ascending, procumbent.

Decurrent

Having the leaf base tapering down to a narrow wing that extends to the stem.

Decussate

Having paired organs with successive pairs at right angles to give four rows as of leaves.

Deflexed

Bent downwards.

Degumming

Removal of gum deposits (phosphatides, entrained oil and meal particles) from crude edible oils traditionally done with water. Water degumming process also removes hydrophilic substances such as sugars from the oil.

Dehisce

To split open at maturity, as in a capsule.

Dehiscent

Splitting open at maturity to release the contents. *cf.* indehiscent.

Deltate

Triangular shape.

Deltoid

Shaped like an equilateral triangle.

Dendritic

Branching from a main stem or axis like the branches of a tree.

Dentate

With sharp, rather coarse teeth perpendicular to the margin.

Denticulate

Finely toothed.

Diageotropic

The tendency of growing parts, such as roots, to grow at right angle to the line of gravity.

Diadelphous

Having stamens in two bundles as in Papilionaceae flowers.

Dichasium

A cymose inflorescence in which the branches are opposite and approximately equal. *pl.* dichasia. *adj.* dichasial.

Dichotomous

Divided into two parts.

Dicotyledon

Angiosperm with two cotyledons.

Didymous

Arranged or occurring in pairs as of anthers, having two lobes.

Digitate

Having digits or fingerlike projections.

Dikaryophyses

Or dendrophydia, irregularly, strongly branched terminal hyphae in the hymenomycetes (class of basidiomycetes) fungi.

Dimorphic

Having or occurring in two forms, as of stamens of two different lengths or a plant, having two kinds of leaves.

Dioecious

With male and female unisexual flowers on separate plants. *cf.* monoecious.

Diploid

a condition in which the chromosomes in the nucleus of a cell exist as pairs, one set being derived from the female parent and the other from the male.

Diplobiontic life cycle

Life cycle that exhibits alternation of generations, which features spore-producing multicellular sporophytes and gamete-producing multicellular gametophytes. Mitoses occur in both the diploid and haploid phases.

Diplontic life cycle

Or gametic meiosis, wherein instead of immediately dividing meiotically to produce haploid cells, the zygote divides mitotically to produce a multicellular diploid individual or a group of more diploid cells.

Diplochory

Seed dispersal involving two or more modes.

Dipterocarpous

Trees of the family Dipterocarpaceae, with two-winged fruit found mainly in tropical lowland rainforest.

Disc

(Botany) refers to the usually disc-shaped receptacle of the flower head in Asteraceae; also the fleshy nectariferous organ usually between the stamens and ovary; also used for the enlarged style end in Proteaceae.

Disc floret

The central, tubular four- or five-toothed or lobed floret on the disc of an inflorescence, as of flower head of Asteraceae.

Disciform

Flat and rounded in shaped. *cf.* discoid, radiate.

Discoid

Resembling a disc; having a flat, circular form; disc shaped. *cf.* disciform, radiate.

Discolorous

Having two colours, as of a leaf which has different colours on the two surfaces. *cf.* concolorous.

Disomic

Having one or more chromosomes present twice but without the entire genome doubled.

Dispersal

Dissemination of seeds.

Distal

Site of any structure farthest from the point of attachment. *cf.* proximal.

Distichous

Referring to two rows of upright leaves in the same plane.

Ditheous

Having two thecae.

Divaricate

Diverging at a wide angle.

Domatium

A part of a plant (e.g. a leaf) that has been modified to provide protection for other organisms. *pl.* domatia.

Dormancy

A resting period in the life of a plant during which growth slows or appears to stop.

Dorsal

Referring to the back surface.

Dorsifixed

Attached to the back as of anthers.

Drupaceous

Resembling a drupe.

Drupe

A fleshy fruit with a single seed enclosed in a hard shell (endocarp) which is tissue embedded in succulent tissue (mesocarp) surrounded by a thin outer skin (epicarp). *adj.* drupaceous.

Drupelet

A small drupe.

Ebracteate

Without bracts.

Echinate

Bearing stiff, stout, bristly, prickly hairs.

Edaphic

Refers to plant communities that are distinguished by soil conditions rather than by the climate.

Eglandular

Without glands. *cf.* glandular.

Elaioplasts

A type of leucoplast that is specialised for the storage of lipids in plants.

Elaiosome

Fleshy lipid-rich structures that are attached to the seeds of many plant species.

Ellipsoid

A three-dimensional shape; elliptic in outline.

Elliptic

Having a two-dimensional shape of an ellipse or flattened circle .

Elongate

Extended, stretched out.

Emarginate

Refers to leaf with a broad, shallow notch at the apex. *cf.* retuse.

Embryo

(Botany) a minute rudimentary plant contained within a seed or an archegonium, composed of the embryonic axis (shoot end and root end).

Endemic

Prevalent in or peculiar to a particular geographical locality or region.

Endocarp

The hard innermost layer of the pericarp of many fruits.

Endosperm

Tissue that surrounds and nourishes the embryo in the angiosperm seed. It contains starchy carbohydrates, proteins and small amounts of vitamins and minerals.

Endospermous

Refers to seeds having an endosperm.

Ensiform

Shaped like the blade of a sword, long and narrow with sharp edges and a pointed tip.

Endotrophic

As of mycorrhiza obtaining nutrients from inside.

Ensilage

The process of preserving green food for livestock in an undried condition in airtight conditions. Also called silaging.

Entire

Having a smooth, continuous margin without any incisions or teeth as of a leaf.

Entisols

Soils that do not show any profile development other than an A horizon.

Ephemeral

Transitory, short lived.

Epicalyx

A whorl of bracts, subtending and resembling a calyx.

Epicarp

Outermost layer of the pericarp of a fruit.

Epicormic

Attached to the corm.

Epicotyl

The upper portion of the embryonic axis, above the cotyledons and below the first true leaves.

Epigeal

Above ground with cotyledons raised above ground.

Epiparasite

An organism parasitic on another that parasitizes a third.

Epipetalous

Borne on the petals, as of stamens.

Epiphyte

A plant growing on, but not parasitic on, another plant, deriving its moisture and nutrients from the air and rain, e.g. some Orchidaceae. *adj.* epiphytic.

Epithet

Name.

Equitant

In a loose fan pattern.

Erect

Upright, vertical.

Essential oils

Volatile products obtained from a natural source; refers to volatile products obtained by steam or water distillation in a strict sense.

Etiolation

To cause (a plant) to develop without chlorophyll by preventing exposure to sunlight.

Eutrophic

Having waters rich in mineral and organic nutrients that promote a proliferation of plant life, especially algae, which reduces the dissolved oxygen content and often causes the extinction of other organisms.

Excentric

Off the true centre.

Excrecence

Abnormal outgrowth.

Excurrent

Projecting beyond the tip, as the midrib of a leaf or bract.

Exserted

Sticking out, protruding beyond some enclosing organ, as of stamens which project beyond the corolla or perianth.

Exstipulate

Without stipules. *cf.* stipulate.

Extra-floral

Outside the flower.

Extrose

Turned outwards or away from the axis as of anthers. *cf.* introrse, latrorse.

Falcate

Sickle shaped, crescent shaped.

Fascicle

A cluster or bundle of stems, flowers and stamens. *adj.*
fasciculate.

Fasciclude

Staminode bundles.

Fastigate

A tree in which the branches grow almost vertically .

Ferrosols

Soils with an iron oxide content of greater than 5%.

Ferruginous

Rust coloured, reddish-brown.

Fertile

Having functional sexual parts which are capable of
fertilisation and seed production. *cf.* sterile.

Filament

The stalk of a stamen supporting and subtending the anther.

Filiform

Having the form of or resembling a thread or filament.

Fimbriate

Fringed.

Fixed oils

Non-volatile oils, triglycerides of fatty acids.

Flaccid

Limp and weak.

Flag leaf

The uppermost leaf on the stem.

Flaky

In the shape of flakes or scales.

Flexuous

Zigzagging, sinuous, bending, as of a stem.

Floccose

Covered with tufts of soft woolly hairs.

Floral tube

A flower tube usually formed by the basal fusion of the perianth and stamens.

Floret

One of the small individual flowers of sunflower family or the reduced flower of the grasses, including the lemma and palea.

Flower

The sexual reproductive organ of flowering plants, typically consisting of gynoecium, androecium and perianth or calyx and/or corolla and the axis bearing these parts.

Fluted

As of a trunk with grooves and folds.

Fodder

Plant material, fresh or dried fed to animals.

Foliaceous

Leaflike.

Foliage

Leaves of the plant.

Foliar

Pertaining to a leaf.

Foliolate

Pertaining to leaflets, used with a number prefix to denote the number of leaflets.

Foliose

Leaflike.

Follicle

(Botany) a dry fruit, derived from a single carpel and dehiscing along one suture.

Forb

Any herb that is not grass or grass-like.

Foveolate

Surface pitted with shallow depressions.

Free central placentation

The arrangement of ovules on a central column that is not connected to the ovary wall by partitions, as in the ovaries of the carnation and primrose.

Frond

The leaf of a fern or cycad.

Fruit

Ripened ovary with adnate parts.

Frutescent

Shrubby.

Fugacious

Shedding off early.

Fulvous

Yellow, tawny.

Funiculus

(Botany) short stalk which attaches the ovule to the ovary wall.

Fuscescent

Dusky.

Fusiform

A three-dimensional shape; spindle shaped, i.e. broad in the centre, but tapering at both thick ends.

Galea

A part of the calyx or corolla having the form of a helmet.

Gall flower

Short-styled flower that does not develop into a fruit but is adapted for the development of a specific wasp within the fruit, e.g. in the fig.

Gamete

A reproductive cell that fuses with another gamete to form a zygote. Gametes are haploid (they contain half the normal (diploid) number of chromosomes); thus when two fuse, the diploid number is restored.

Gametophyte

The gamete-producing phase in a plant characterised by alternation of generations.

Gamosepalous

With sepals united or partially united.

Genome

Complete set of genetic material of an organism.

Geniculate

Bent like a knee, refer to awns and filaments.

Geocarpic

Where the fruit is pushed into the soil by the gynophore and matures.

Geophyte

A plant that stores food in an underground storage organ, e.g. a tuber, bulb or rhizome, and has subterranean buds which form aerial growth.

Geotextile

Are permeable fabrics which, when used in association with soil, have the ability to separate, filter, reinforce, protect or drain.

Germ

Of cereal is the embryo of the seed or kernel. It contains vitamins B and E, folic acid, some protein, minerals and

polyunsaturated fats.

Glabrescent

Becoming glabrous.

Glabrous

Smooth, hairless without pubescence.

Gland

A secretory organ, e.g. a nectary, extra-floral nectary or a gland tipped, hair-like or wartlike organ. *adj.* glandular. *cf.* eglandular.

Glaucous

Pale blue-green in colour, covered with a whitish bloom that rubs off readily.

Gley soils

A hydric soil which exhibits a greenish-blue-grey soil colour due to wetland conditions.

Globose

Spherical in shape.

Globular

A three-dimensional shape; spherical or orbicular; circular in outline.

Glochids

Tiny, finely barbed hair-like spines found on the areoles of some cacti and other plants.

Glochidiate

Having glochids.

Glochidote

Plant having glochids .

Glume

One of the two small, sterile bracts at the base of the grass spikelet, called the lower and upper glumes, due to their

position on the rachilla. Also used in Apiaceae, Cyperaceae for the very small bracts on the spikelet in which each flower is subtended by one floral glume. *adj.* glumaceous.

Grits

Consist of coarsely ground corn, or sometimes alkali-treated corn.

Groats

Hulled, whole grains of various cereals, such as oats, wheat, barley or buckwheat; it includes the cereal germ, fibre-rich bran portion and endosperm of the grain.

Guttation

The appearance of drops of xylem sap on the tips or edges of leaves of some vascular plants, such as grasses and bamboos.

Guttule

Small droplet.

Gymnosperm

A group of spermatophyte seed-bearing plants with ovules on scales, which are usually arranged in cone-like structures and not borne in an ovary. *cf.* angiosperm.

Gynoecium

The female organ of a flower; a collective term for the pistil, carpel or carpels.

Gynomonoecious

Having female flowers and bisexual flowers on the same plant. *cf.* andromonoecious.

Gynophore

Stalk that bears the pistil/carpel.

Habit

The general growth form of a plant, comprising its size, shape, texture and stem orientation, the locality in which the plant

grows..

Halophyte

A plant adapted to living in highly saline habitats. Also a plant that accumulates high concentrations of salt in its tissues.

adj. halophytic.

Hapaxanthic

Refer to palms which flower only once and then die. c.f. pleonanthic.

Haploid

Condition where nucleus or cell has a single set of unpaired chromosomes; the haploid number is designated as n.

Haplontic life cycle

Or zygotic meiosis wherein meiosis of a zygote, immediately after karyogamy, produces haploid cells which produces more or larger haploid cells ending its diploid phase.

Hastate

Having the shape of an arrowhead but with the basal lobes pointing outwards at right angles as of a leaf.

Hastula

A piece of plant material at the junction of the petiole and the leaf blade; the hastula can be found on the top of the leaf, adaxial or the bottom, abaxial or both sides.

Heartwood

Wood from the inner portion of a tree.

Heliophilous

Sun loving, tolerates high level of sunlight.

Heliotropic

Growing towards sunlight.

Herb

A plant which is nonwoody or woody at the base only, the above-ground stems usually being ephemeral. *adj.*

herbaceous.

Herbaceous

Resembling a herb, having a habit of a herb.

Hermaphrodite

Bisexual, bearing flowers with both androecium and gynoecium in the same flower. *adj.* hermaphroditic.

Heterocyst

A differentiated cyanobacterial cell that carries out nitrogen fixation.

Heterogamous

Bearing separate male and female flowers, or bisexual and female flowers, or florets in an inflorescence or flower head, e.g. some Asteraceae in which the ray florets may be neuter or unisexual and the disc florets may be bisexual. *cf.* homogamous.

Heteromorphous

Having two or more distinct forms. *cf.* homomorphous.

Heterophyllous

Having leaves of different forms.

Heterosporous

Producing spores of two sizes, the larger giving rise to megagametophytes (female) and the smaller giving rise to microgametophytes (male). Refer to the ferns and fern allies. *cf.* homosporous.

Heterostylous

Having styles of two different lengths or forms.

Heterostyly

The condition in which flowers on polymorphous plants have styles of different lengths, thereby facilitating cross-pollination.

Hilar

Of or relating to a hilum .

Hilum

The scar on a seed, indicating the point of attachment to the funiculus.

Hirsute

Bearing long coarse hairs.

Hispid

Bearing stiff, short, rough hairs or bristles.

Hispidulous

Minutely hispid.

Histosol

Soil comprising primarily of organic materials, having 40 cm or more of organic soil material in the upper 80 cm.

Hoary

Covered with a greyish layer of very short, closely interwoven hairs.

Holdfast

An organ or structure of attachment, especially the basal, root-like formation by which certain seaweeds or other algae are attached to a substrate.

Holocarpic

Having the entire thallus developed into a fruiting body or sporangium.

Homochromous

Having all the florets of the same colour in the same flower head *cf.* heterochromous.

Homogamous

Bearing flowers or florets that do not differ sexually. *cf.* heterogamous.

Homogeneous endosperm

Endosperm with even surface that lacks invaginations or infoldings of the surrounding tissue.

Homomorphous

Uniform, with only one form. *cf.* heteromorphous.

Homosporous

Producing one kind of spores. Refer to the ferns and fern allies. *cf.* heterosporous.

Hormogonium

A part of a filament of a cyanobacterium that detaches and grows by cell division into a new filament. *pl.* hormogonia.

Hurd fibre

Long pith fibre of the stem.

Hyaline

Colourless, almost transparent.

Hybrid

The first-generation progeny of the sexual union of plants belonging to different taxa.

Hybridisation

The crossing of individuals from different species or taxa.

Hydathode

A type of secretory tissue in leaves, usually of Angiosperms, that secretes water through pores in the epidermis or margin of the leaf.

Hydrophilous

Water loving; requiring water in order to be fertilised, referring to many aquatic plants.

Hygrochastic

Applied to plants in which the opening of the fruits is caused by the absorption of water.

Hygrophilous

Living in water or moist places.

Hymenial cystidia

The cells of the hymenium develop into basidia or asci, while in others some cells develop into sterile cells called cystidia.

Hymenium

Spore-bearing layer of cells in certain fungi containing asci (ascomycetes) or basidia (basidiomycetes).

Hypanthium

Cup-like receptacles of some dicotyledonous flowers formed by the fusion of the calyx, corolla and androecium that surrounds the ovary which bears the sepals, petals and stamens. *adj.* relating to or of the nature of a hypanthium.

Hypha

Is a long, branching filamentous cell of a fungus and also of unrelated Actinobacteria. *pl.* hyphae.

Hypocotyl

The portion of the stem below the cotyledons.

Hypodermis

The cell layer beneath the epidermis of the pericarp.

Hypogeal

Below ground as of germination of seed.

Hysteresis

Refers to systems that may exhibit path dependence.

Imbricate

Closely packed and overlapping. *cf.* valvate.

Imparipinnate

Pinnately compound with a single terminal leaflet and hence with an odd number of leaflets. *cf.* paripinnate.

Inceptisols

Old soils that have no accumulation of clays, iron, aluminium or organic matter.

Incised

Cut jaggedly with very deep teeth.

Included

Referring to stamens which do not project beyond the corolla or to valves which do not extend beyond the rim of a capsular fruit. *cf.* exserted.

Incurved

Curved inwards; curved towards the base or apex.

Indefinite

Numerous and variable in number.

Indehiscent

Not opening or splitting to release the contents at maturity as of fruit. *cf.* dehiscent.

Indumentum

covering of fine hairs or bristles commonly found on external parts of plants.

Indurate

To become hard, often the hardening developed only at maturity.

Indusium

An enclosing membrane, covering the sorus of a fern. Also used for the modified style end or pollen-cup of some Goodeniaceae (including Brunoniaceae). *adj.* indusiate.

Inferior

Said of an ovary or fruit that has sepals, petals and stamens above the ovary. *cf.* superior.

Inflated

Enlarged and hollow except in the case of a fruit which may contain a seed. *cf.* swollen.

Inflexed

Bent or curved inwards or downwards, as petals or sepals.

Inflorescence

A flower cluster or the arrangement of flowers in relation to the axis and to each other on a plant.

Infracoliar

Located below the leaves.

Infraspecific

Referring to any taxon below the species rank.

Infructescence

The fruiting stage of an inflorescence.

Infundibulum

Funnel-shaped cavity or structure.

Inrolled

Curved inwards.

Integuments

Two distinct tissue layers that surround the nucellus of the ovule, forming the testa or seed coat when mature.

Intercalary

Of growth, between the apex and the base; of cells, spores, etc., between two cells.

Interfoliar

Inter-leaf.

Internode

Portion of the stem, culm, branch or rhizome between two nodes or points of attachment of the leaves.

Interpetiolar

As of stipules positioned between petioles of opposite leaves.

Intrastaminal

Within the stamens.

Intricate

Entangled, complex.

Introduced

Not indigenous; not native to the area in which it now occurs.

Introrse

Turned inwards or towards the axis or pistil as of anthers. *cf.* extrorse, latrorse.

Involucre

A whorl of bracts or leaves that surround one to many flowers or an entire inflorescence.

Involute

Having the margins rolled inwards, referring to a leaf or other flat organ.

Jugate

Of a pinnate leaf; having leaflets in pairs.

Juvenile

Young or immature, used here for leaves formed on a young plant which are different in morphology from those formed on an older plant.

Keel

A longitudinal ridge, at the back of the leaf. Also the two lower fused petals of a 'pea' flower in the Papilionaceae, which form a boat-like structure around the stamens and styles, also called carina. *adj.* keeled. *cf.* standard, wing.

Labellum

The modified lowest of the three petals forming the corolla of an orchid, usually larger than the other two petals, and often spurred.

Lacerate

Irregularly cleft.

Laciniate

Fringed; having a fringe of slender, narrow, pointed lobes cut into narrow lobes.

Lamella

A gill-shaped structure: fine sheets of material held adjacent to one another.

Lamina

The blade of the leaf or frond.

Lanate

Woolly, covered with long hairs which are loosely curled together like wool.

Lanceolate

Lance shaped in outline, tapering from a broad base to the apex.

Landrace: landrace

Plants adapted to the natural environment in which they grow, developing naturally with minimal assistance or guidance from humans and usually possess more diverse phenotypes and genotypes. They have not been improved by formal breeding programmes.

Laterite

Reddish-coloured soils rich in iron oxide, formed by weathering of rocks under oxidising and leaching conditions, commonly found in tropical and subtropical regions. *adj.* lateritic.

Latex

A milky, clear or sometimes coloured sap of diverse composition exuded by some plants.

Latrorse

Turned sideways, i.e. not towards or away from the axis as of anthers dehiscing longitudinally on the side. *cf.* extrorse, introrse.

Lax

Loose or limp, not densely arranged or crowded.

Leaflet

One of the ultimate segments of a compound leaf.

Lectotype

A specimen chosen after the original description to be the type.

Lemma

The lower of two bracts (scales) of a grass floret, usually enclosing the palea, lodicules, stamens and ovary.

Lenticel

Is a lens shaped opening that allows gases to be exchanged between air and the inner tissues of a plant, commonly found on young bark, or the surface of the fruit.

Lenticellate

Dotted with lenticels.

Lenticular

Shaped like a biconvex lens. *cf.* lentiform.

Lentiform

Shaped like a biconvex lens, *cf.* lenticular.

Leptomorphic

Temperate, running bamboo rhizome; usually thinner than the culms they support and the internodes are long and hollow.

Liane

A woody climbing or twining plant.

Ligneous

Woody.

Lignotuber

A woody, usually underground, tuberous rootstock often giving rise to numerous aerial stems.

Ligulate

Small and tongue shaped or with a little tongue-shaped appendage or ligule, star shaped as of florets of Asteraceae.

Ligule

A strap-shaped corolla in the flowers of Asteraceae; also a thin membranous outgrowth from the inner junction of the grass leaf sheath and blade. *cf.* ligulate.

Limb

The expanded portion of the calyx tube or the corolla tube, or the large branch of a tree.

Linear

A two-dimensional shape, narrow with nearly parallel sides.

Linguiform

Tongue shaped. *cf.* ligulate.

Lipotubuloids

Are cytoplasmic domains containing aggregates of lipid bodies surrounded by a network of microtubules, which join one lipid body with the others.

Lithosol

A kind of shallow soils lacking well-defined horizons and composed of imperfectly weathered fragments of rock.

Littoral

Of or on a shore, especially seashore.

Loam

A type of soil made up of sand, silt and clay in relative concentration of 40–40–20% respectively.

Lobed

Divided but not to the base.

Loculicidal

Opening into the cells, when a ripe capsule splits along the back.

Loculus

Cavity or chamber of an ovary. *pl.* loculi.

Lodicules

Two small structures below the ovary which, at flowering, swell up and force open the enclosing bracts, exposing the stamens and carpel.

Lorate

Strap shaped with obtuse tip.

Lyrate

Pinnately lobed, with a large terminal lobe and smaller lateral ones which become progressively smaller towards the base.

Macronutrients

Chemical elements which are needed in large quantities for growth and development by plants and include nitrogen, phosphorus, potassium and magnesium.

Maculate

Spotted.

Mallee

A growth habit in which several to many woody stems arise separately from a lignotuber; usually applied to certain low-growing species of *Eucalyptus*.

Mangrove

A distinctive vegetation type of trees and shrubs with modified roots, often viviparous, occupying the saline coastal habitats that are subject to periodic tidal inundation.

Marcescent

Withering or to decay without falling off.

Margin

The edge of the leaf blade.

Medulla

The pith in the stems or roots of certain plants; or the central portion of a thallus in certain lichens.

Megasporangium

The sporangium containing megaspores in fern and fern allies.
cf. microsporangium.

Megaspore

The large spore which may develop into the female gametophyte in heterosporous ferns and fern allies. *cf.* microspore.

Megasporophyll

A leaflike structure that bears megasporangia.

Megastrobilus

Female cone, seed cone or ovulate cone and contains ovules within which, when fertilised by pollen, become seeds.
The female cone structure varies more markedly between the different conifer families.

Meiosis

The process of cell division that results in the formation of haploid cells from diploid cells to produce gametes.

Mericarp

A one-seeded portion of an initially syncarpous fruit (schizocarp) which splits apart at maturity. *cf.* coccus .

Meristem

The region of active cell division in plants, from which permanent tissue is derived. *adj.* meristematic

-merous

Used with a number prefix to denote the basic number of the three outer floral whorls, e.g. a five-merous flower may have 5 sepals, 10 petals and 15 stamens.

Mesic

Moderately wet.

Mesocarp

The middle layer of the fruit wall derived from the middle layer of the carpel wall. *cf.* endocarp, exocarp and pericarp.

Mesophytes

Terrestrial plants which are adapted to neither a particularly dry nor particularly wet environment.

Micropyle

The small opening in a plant ovule through which the pollen tube passes in order to effect fertilisation.

Microsporangium

The sporangium containing microspores in pteridophytes. *cf.* megasporangium.

Microspore

A small spore which gives rise to the male gametophyte in heterosporous pteridophytes. Also for a pollen grain. *cf.* megaspore.

Midvein

The main vascular supply of a simple leaf blade or lamina. Also called midrib.

Mitosis

Is a process of cell division which results in the production of two daughter cells from a single parent cell.

Mollisols

Soils with deep, high organic matter, nutrient-enriched surface soil (a horizon), typically between 60 and 80 cm thick.

Monadelphous

Applied to stamens united by their filaments into a single bundle.

Monocarpic

Refer to plants that flower, set seeds and then die.

Monochasial

A cyme having a single flower on each axis.

Monocotyledon

Angiosperm having one cotyledon.

Monoecious

Having both male and female unisexual flowers on the same individual plant. *cf.* dioecious.

Monoembryonic seed

The seed contains only one embryo, a true sexual (zygotic) embryo. Polyembryonic seed.

Monolete

A spore that has a simple linear scar.

Monopodial

With a main terminal growing point producing many lateral branches progressively. *cf.* sympodial.

Monostichous

Forming one row.

Monotypic

Of a genus with one species or a family with one genus; in general, applied to any taxon with only one immediately subordinate taxon.

Montane

Refers to highland areas located below the subalpine zone.

Mucilage

A soft, moist, viscous, sticky secretion. *adj.* mucilaginous.

Mucous

(Botany) slimy.

Mucro

A sharp, pointed part or organ, especially a sharp terminal point, as of a leaf.

Mucronate

Ending with a short, sharp tip or mucro, resembling a spine. cf. cuspidate, muticous.

Mucronulate

With a very small mucro; a diminutive of mucronate.

Mulch

Protective cover of plant (organic) or non-plant material placed over the soil, primarily to modify and improve the effects of the local microclimate and to control weeds.

Multiple fruit

A fruit that is formed from a cluster of flowers.

Muricate

Covered with numerous short hard outgrowths. cf. papillose.

Muriculate

With numerous minute hard outgrowths; a diminutive of muricate.

Muticous

Blunt, lacking a sharp point. cf. mucronate.

MYB proteins

Are a superfamily of transcription factors that play regulatory roles in developmental processes and defence responses in plants.

Mycorrhiza

The mutualistic symbiosis (non-pathogenic association) between soilborne fungi with the roots of higher plants.

Mycorrhiza (vesicular arbuscular)

Endomycorrhiza living in the roots of higher plants producing inter- and intracellular fungal growth in root cortex and forming specific fungal structures, referred to as vesicles and arbuscules. abbrev. VAM.

Myrmecochory

Seed dispersal by ants.

Native

A plant indigenous to the locality or region.

Naviculate

Boat shaped.

Necrotic

Applied to dead tissue.

Nectariferous

Having one or more nectaries.

Nectary

A nectar secretory gland; commonly in a flower, sometimes on leaves, fronds or stems.

Nervation

Venation, a pattern of veins or nerves as of leaf.

Nixtamalisation

Refers to a process for the preparation of maize (corn), or other grains, in which the grains are soaked and cooked in an alkaline solution, usually limewater, and hulled.

Node

The joint between segments of a culm, stem, branch or rhizome; the point of the stem that gives rise to the leaf and bud.

Nodule

A small knoblike outgrowth, as those found on the roots of many leguminous, containing *Rhizobium* bacteria which fixes nitrogen in the soil.

Nom. ambig.

Nomen ambiguum (Latin) ambiguous name used in different senses which has become a long-persistent source of error.

Nom. cons.

Nomen nonservandum (Latin) name conserved in International Code of Botanical Nomenclature.

Nom. dub.

Nomen dubium (Latin) an invalid proposed taxonomic name because it is not accompanied by a definition or description of the taxon to which it applies.

Nom. illeg.

Nomen illegitimum (Latin) illegitimate taxon deemed as superfluous at its time of publication either because the taxon to which it was applied already has a name, or because the name has already been applied to another plant.

Nom. invalid.

Nomen invalidum (Latin) invalid name according to International Code of Botanical Nomenclature.

Nom. nud.

Nomen nudum (Latin) the name of a taxon which has never been validated by a description.

Nom. rej.

Nomen rejiciendum (Latin) name rejected in International Code of Botanical Nomenclature.

Notho-

(Subsp. or var.) prefix to the rank of a hybrid taxon below the rank of species.

Nucellus

Central portion of an ovule in which the embryo sac develops.

Nucellar embryony

A form of seed reproduction in which the nucellar tissue which surrounds the embryo sac can produce additional embryos (polyembryony) which are genetically identical to the parent plant. This is found in many citrus species and in mango.

Nut

A dry indehiscent one-celled fruit with a hard pericarp.

Nutlet

A small, one-seeded, indehiscent lobe of a divided fruit.

Ob-

Prefix meaning inversely or opposite to.

Obconic

A three-dimensional shape; inversely conic; cone shaped, conic with the vertex pointing downwards.

Obcordate

Inversely cordate, broad and notched at the tip; heart shaped but attached at the pointed end.

Obdeltate

Inversely deltate; deltate with the broadest part at the apex.

Ob lanceolate

Inversely lanceolate, lance shaped but broadest above the middle and tapering towards the base as of leaf.

Oblate

Having the shape of a spheroid with the equatorial diameter greater than the polar diameter; being flattened at the poles.

Oblong

Longer than broad with sides nearly parallel to each other.

Obovate

Inversely ovate, broadest above the middle.

Obpyramidal

Resembling a four-sided pyramid attached at the apex with the square base facing away from the attachment.

Obpyriform

Inversely pyriform, resembling a pear which is attached at the narrower end. *cf.* pyriform.

Obspathulate

Inversely spathulate; resembling a spoon but attached at the broadest end. *cf.* spathulate.

Obtriangular

Inversely triangular; triangular but attached at the apex. *cf.* triangular.

Obtrullate

Inversely trullate; resembling a trowel blade with the broadest axis above the middle. *cf.* trullate.

Obtuse

With a blunt or rounded tip, the converging edges separated by an angle greater than 90°.

-oid

Suffix denoting a three-dimensional shape, e.g. spheroid.

Ochraceous

A dull yellow colour.

Ocreate

Having a tube-like covering around some stems, formed of the united stipules; sheathed.

Oleaginous

Oily.

Oligotrophic

Lacking in plant nutrients and having a large amount of dissolved oxygen throughout.

Operculum

A lid or cover that becomes detached at maturity by abscission, e.g. in *Eucalyptus*, also a cap or lid covering the bud and formed by fusion or cohesion of sepals and/or petals. *adj.* operculate.

Opposite

Describing leaves or other organs which are borne at the same level but on opposite sides of the stem. *cf.* alternate.

Orbicular

Of circular outline, disc-like.

Order

A taxonomic rank between class and family used in the classification of organisms, i.e. a group of families believed to be closely related.

Orifice

An opening or aperture.

Organosols

Soils not regularly inundated by marine waters and containing a specific thickness of organic materials within the upper part of the profile.

Orth. var.

Orthographic variant, i.e. an incorrect alternate spelling of a name.

Ovary

The female part of the pistil of a flower which contains the ovules (immature seeds).

Ovate

Egg shaped, usually with reference to two dimensions.

Ovoid

Egg shaped, usually with reference to three dimensions.

Ovule

The young, immature seed in the ovary which becomes a seed after fertilisation. *adj.* ovular.

Ovulode

A sterile reduced ovule borne on the placenta, commonly occurring in Myrtaceae.

Oxisols

Refer to ferralsols.

Pachymorphic

Describes the short, thick rhizomes of clumping bamboos with short, thick and solid internode (except the bud-bearing internodes, which are more elongated). *cf.* sympodial.

Palate

(Botany) a raised appendage on the lower lip of a corolla which partially or completely closes the throat.

Palea

The upper of the two membranous bracts of a grass floret, usually enclosing the lodicules, stamens and ovary. *pl.* paleae. *adj.* paleal. *cf.* lemma.

Paleate

Having glumes.

Palm heart

Refers to soft, tender inner core and growing bud of certain palm trees which are eaten as vegetables. Also called heart of palm, palmito, burglar's thigh, chonta or swamp cabbage.

Palmate

Describing a leaf which is divided into several lobes or leaflets which arise from the same point. *adv.* palmately.

Palmito

See Palm heart.

Palustrial

Paludal, swampy, marshy.

Palustrine

Marshy, swampy.

Palustrine herb

Vegetation that is rooted below water but grows above the surface in wetland system.

Panduriform

Fiddle shaped, usually with reference to two dimensions.

Panicle

A compound, indeterminate, racemose inflorescence in which the main axis bears lateral racemes or spikes. *adj.* paniculate.

Pantropical

Distributed throughout the tropics.

Papilionaceous

Butterfly-like, said of the pea flower or flowers of Papilionaceae, flowers which are zygomorphic with imbricate petals, one broad upper one, two narrower lateral ones and two narrower lower ones.

Papilla

A small, superficial protuberance on the surface of an organ being an outgrowth of one epidermal cell. *pl.* papillae. *adj.* papillose, *pappous* .

Papillate

Having papillae.

Papillose

Covered with papillae.

Pappus

A tuft (or ring) of hairs, bristles or scales borne above the ovary and outside the corolla as in Asteraceae often persisting as a tuft of hairs on a fruit. *adj.* pappose, pappous.

Papyraceous

Resembling parchment or paper.

Parenchyma

Undifferentiated plant tissue composed of more or less uniform cells.

Parietal

Describes the attachment of ovules to the outer walls of the ovaries.

Paripinnate

Pinnate with an even number of leaflets and without a terminal leaflet. *cf.* imparipinnate.

- partite

Divided almost to the base into segments, the number of segments written as a prefix.

Patelliform

Shaped like a limpet shell; cap shaped and without whorls.

Patent

Diverging from the axis almost at right angles.

Peat

Is an accumulation of partially decayed vegetation matter.

Pectin

A group of water-soluble colloidal carbohydrates of high molecular weight found in certain ripe fruits.

Pectinate

Pinnatifid with narrow segments resembling the teeth of a comb.

Pedicel

The stalk of the flower or stalk of a spikelet in Poaceae. *adj.* pedicellate.

Pedicellate

Having pedicel.

Peduncle

A stalk supporting an inflorescence. *adj.* pedunculate

Pellucid

Allowing the passage of light; transparent or translucent.

Pellucid dotted

Copiously dotted with immersed, pellucid, resinous glands.

Peltate

With the petiole attached to the lower surface of the leaf blade.

Pendant

Hanging down.

Pendulous

Drooping, as of ovules.

Penniveined or penninerved

Pinnately veined.

Pentamerous

In five parts.

Perennial

A plant that completes its life cycle or lives for more than two years. *cf.* annual, biennial.

Perfoliate

A leaf with the basal lobes united around—and apparently pierced by—the stem.

Pergamentaceous

Parchment-like.

Perianth

The two outer floral whorls of the angiosperm flower; commonly used when the calyx and the corolla are not readily distinguishable (as in monocotyledons).

Pericarp

(Botany). The wall of a ripened ovary; fruit wall composed of the exocarp, mesocarp and endocarp.

Persistent

Remaining attached; not falling off. *cf.* caduceus.

Petal

Free segment of the corolla. *adj.* petaline. *cf.* lobe.

Petiolar

Relating to the petiole.

Petiolate

Having petiole.

Petiole

Leaf stalk. *adj.* petiolate.

Petiolulate

Supported by its own petiolule.

Petiolule

The stalk of a leaflet in a compound leaf. *adj.* petiolulate.

pH

Is a measure of the acidity or basicity of a solution. It is defined as the cologarithm of the activity of dissolved hydrogen ions (H⁺).

Phenology

The study of periodic plant life cycle events as influenced by seasonal and interannual variations in climate.

Phyllary

A bract of the involucre of a composite plant, term for one of the scalelike bracts beneath the flower head in Asteraceae.

Phylloclade

A flattened, photosynthetic branch or stem that resembles or performs the function of a leaf, with the true leaves represented by scales.

Phyllode

A petiole that functions as a leaf. *adj.* phyllodineous. *cf.* cladode.

Phyllopodia

Refer to the reduced, scalelike leaves found on the outermost portion of the corm where they seem to persist longer than typical sporophylls as in the fern *Isoetes* .

Phytoremediation

Describes the treatment of environmental problems (bioremediation) through the use of plants which mitigate the environmental problem without the need to excavate the contaminant material and dispose of it elsewhere.

Pileus

(Botany) cap of mushroom.

Piliferous

(Botany) bearing or producing hairs, as of an organ with the apex having long, hair-like extensions.

Pilose

Covered with fine soft hairs.

Pinna

A primary division of the blade of a compound leaf or frond.
pl. pinnae.

Pinnate

Bearing leaflets on each side of a central axis of a compound leaf; divided into pinnae.

Pinnatifid, pinnatilobed

A pinnate leaf parted approximately halfway to midrib; when divided to almost to the midrib described as deeply pinnatifid or pinnatisect.

Pinnatisect

Lobed or divided almost to the midrib.

Pinnule

A leaflet of a bipinnate compound leaf.

Pistil

Female part of the flower comprising the ovary, style and stigma.

Pistillate

Having one or more pistils; having pistils but no stamens.

Placenta

The region within the ovary to which ovules are attached. *pl.* placentae.

Placentation

The arrangement of the placentae and ovules in the ovary.

Plano-

A prefix meaning level or flat.

Pleonanthic

Refer to palms in which the stem does not die after flowering.

Plicate

Folded like a fan.

Plumose

Feather-like, with fine hairs arising laterally from a central axis; feathery.

Pneumatophore

Modified root which allows gaseous exchange in mud-dwelling shrubs, e.g. mangroves.

Pod

A dry one- to many-seeded dehiscent fruit, as applied to the fruit of Fabaceae, i.e. Caesalpiniaceae, Mimosaceae and Papilionaceae.

Podzol, podsolic soil

Any of a group of acidic, zonal soils having a leached, light-coloured, grey and ashy appearance. Also called spodosol.

Pollen cone

Male cone or microstrobilus or pollen cone is structurally similar across all conifers; extending out from a central axis are microsporophylls (modified leaves). Under each microsporophyll is one or several microsporangia (pollen sacs).

Pollinia

The paired, waxy pollen masses of flowers of orchids and milkweeds.

Polyandrous

(Botany) having an indefinite number of stamens.

Polyembryonic seed

Seeds contain many embryos, most of which are asexual (nucellar) in origin and genetically identical to the maternal parent.

Polygamous

With unisexual and bisexual flowers on the same or on different individuals of the same species.

Polymorphic

With different morphological variants.

Polypetalous

(Botany) having a corolla composed of distinct, separable petals.

Pome

A fleshy fruit where the succulent tissues are developed from the receptacle.

Pore

A tiny opening.

Premorse

Abruptly truncated, as though bitten or broken off as of a leaf.

Procumbent

Trailing or spreading along the ground but not rooting at the nodes, referring to stems. *cf.* ascending, decumbent, erect.

Pro hyb.

(Latin) as a hybrid.

Pro parte

(Latin) in part

Pro parte majore

(Latin) for the greater part.

Pro parte minore

(Latin) for a small part.

Pro sp.

(Latin) as a species.

Pro subsp.

(Latin) as a subspecies.

Pro syn.

(Latin) as a synonym.

Prophyll

A plant structure that resembles a leaf.

Prostrate

Lying flat on the ground.

Protandrous

Relating to a flower in which the anthers release their pollen before the stigma of the same flower becomes receptive.

Proximal

End of any structure closest to the point of attachment. *cf.* distal.

Pruinose

Having a thick, waxy, powdery coating or bloom.

Pseudocarp

A false fruit, largely made up of tissue that is not derived from the ovary but from floral parts such as the receptacle and calyx.

Pseudostem

The false, herbaceous stem of a banana plant composed of overlapping leaf bases.

Pteridophyte

A vascular plant which reproduces by spores; the ferns and fern allies.

Puberulent

Covered with minute hairs or very fine down; finely pubescent.

Puberulous

Covered with a minute down.

Pubescent

Covered with short, soft hairs.

Pulvinate

Having a swell, pulvinus at the base as a leaf stalk.

Pulvinus

Swelling at the base of leaf stalk.

Pulviniform

Swelling or bulging.

Punctate

Marked with translucent dots or glands.

Punctiform

Marked by or composed of points or dots.

Punctulate

Marked with minute dots; a diminutive of punctate.

Purpurascent

Purple or becoming purple.

Pusticulate

Characterised by small pustules.

Pyrene

The stone or pit of a drupe, consisting of the hardened endocarp and seed.

Pyriform

Pear shaped, a three-dimensional shape; attached at the broader end. *cf.* obpyriform.

Pyxidium

Seed capsule having a circular lid (operculum) which falls off to release the seed.

Raceme

An indeterminate inflorescence with a simple, elongated axis and pedicellate flowers, youngest at the top. *adj.* racemose.

Rachilla

The main axis of a grass spikelet.

Rachis

The main axis of the spike or other inflorescence of grasses or a compound leaf.

Radiate

Arranged around a common centre; as of an inflorescence of Asteraceae with marginal, female or neuter, ligulate ray florets and central, perfect or functionally male, tubular, disc florets. *cf.* disciform, discoid.

Radical

Arising from the root or its crown, or the part of a plant embryo that develops into a root.

Ray

The marginal portion of the inflorescence of Asteraceae and Apiaceae when distinct from the disc. Also, the spreading branches of a compound umbel.

Receptacle

The region at the end of a pedicel or on an axis which bears one or more flowers. *adj.* receptacular.

Recurved

Curved downwards or backwards.

Reflexed

Bent or turned downward.

Regosol

Soil that is young and undeveloped, characterised by medium to fine-textured unconsolidated parent material that maybe alluvial in origin and lacks a significant horizon layer formation.

Reniform

Kidney shaped in outline.

Repand

With slightly undulate margin.

Replicate

Folded back, as in some corolla lobes.

Resinous

Producing sticky resin.

Resupinate

Twisted through 180°.

Reticulate

Having the appearance of a network.

Retrorse

Bent or directed downwards or backwards. *cf.* antrorse.

Retuse

With a very blunt and slightly notched apex. *cf.* emarginated.

Revolute

With the margins inrolled on the lower (abaxial) surface.

Rhizine

A root-like filament or hair growing from the stems of mosses or on lichens.

Rhizoid

Root-like filaments in a moss, fern, fungus, etc., that attach the plant to the substratum.

Rhizome

A prostrate or underground stem consisting of a series of nodes and internodes with adventitious roots and which generally grows horizontally.

Rhizophore

A stilt-like outgrowth of the stem which branches into roots on contact with the substrate.

Rhombic

Shaped like a rhombus.

Rhomboid

Shaped like a rhombus.

Rib

A distinct vein or linear marking, often raised as a linear ridge.

Riparian

Along the river margins, interface between land and a stream.

Rosette

A tuft of leaves or other organs arranged spirally like petals in a rose, ranging in form from a hemispherical tuft to a flat whorl. *adj.* rosetted, rosulate.

Rostrate

Beaked; the apex tapered into a slender, usually obtuse point.

Rostrum

A beak-like extension.

Rosulate

Having a rosette.

Rotate

Wheel shaped; refers to a corolla with a very short tube and a broad upper part which is flared at right angles to the tube.
cf. salverform .

Rotundate

Rounded; especially at the end or ends.

Rugae

Refers to a series of ridges produced by folding of the wall of an organ.

Rugose

Deeply wrinkled.

Rugulose

Finely wrinkled.

Ruminate

(Animal) chew repeatedly over an extended period .

Ruminate endosperm

Uneven endosperm surface that is often highly enlarged by ingrowths or infoldings of the surrounding tissue. *cf.* homogeneous endosperm.

Rz value

Is a numerical reference to the mesh/emulsion equalisation on the screen.

Saccate

Pouched.

Sagittate

Shaped like an arrow head.

Saline soils

Soils that contain excessive levels of salts that reduce plant growth and vigour by altering water uptake and causing ion-specific toxicities or imbalances.

Salinity

Is characterised by high electrical conductivities and low sodium ion concentrations compared to calcium and magnesium

Salverform

Applies to a gamopetalous corolla having a slender tube and an abruptly expanded limb.

Samara

An indehiscent, winged, dry fruit.

Sand

A naturally occurring granular material composed of finely divided rock and mineral particles range in diameter from 0.0625µm to 2 mm. *adj.* sandy

Saponins

Are plant glycosides with a distinctive foaming characteristic. They are found in many plants, but get their name from the soapwort plant (*Saponaria*) .

Saprophytic

Living on and deriving nourishment from dead organic matter.

Sapwood

Outer woody layer of the tree just adjacent to and below the bark.

Sarcotesta

Outermost fleshy covering of Cycad seeds below which is the sclerotesta.

Scabrid

Scurfy, covered with surface abrasions, irregular projections or delicate scales.

Scabrous

Rough to the touch because of scattered rough hairs.

Scale

Dry bract or leaf.

Scandent

Refer to plants, climbing.

Scape

Erect flowering stem, usually leafless, rising from the crown or roots of a plant. *adj.* scapose.

Scapigerous

With a scape.

Scarious

Dry, thin and membranous.

Schizocarp

A dry fruit which splits into longitudinally multiple parts called mericarps or cocci. *adj.* schizocarpous.

Sclerotesta

The innermost fleshy coating of cycad seeds, usually located directly below the sarcotesta.

Scorpoid

Refers to a cymose inflorescence in which the main axis appears to coil.

Scutellum

(Botany) any of various parts shaped like a shield.

Scutiform

Shaped like a shield.

Secondary venation

Arrangement of the lateral veins arising from the midrib in the leaf lamina.

Secund

With the flowers all turned in the same direction.

Sedge

A plant of the family Apiaceae, Cyperaceae.

Segmented

Constricted into divisions.

Seminal root

Or seed root originates from the scutellar node located within the seed embryo and is composed of the radicle and lateral seminal roots.

Senescence

Refers to the biological changes which take place in plants as they age.

Sepal

Free segment of the calyx. *adj.* sepaline.

Septum

A partition or cross wall. *pl.* septa. *adj.* septate.

Seriate

Arranged in rows.

Sericeous

Silky; covered with close-pressed, fine, straight silky hairs.

Serrate

Tooth like a saw; with regular, asymmetric teeth pointing forward.

Serrated

Toothed margin.

Serratures

Serrated margin.

Serrulate

With minute teeth on the margin.

Sessile

Without a stalk.

Seta

A bristle or stiff hair. *pl.* setae. *adj.* setose, setaceous.

Setaceous

Bristlelike.

Setate

With bristles.

Setiform

Bristle shaped.

Setulose

With minute bristles.

Sheathing

Clasping or enveloping the stem.

Shrub

A woody plant usually less than 5 m high and with many branches without a distinct main stem except at ground level.

Silicula

A broad, dry, usually dehiscent fruit derived from two or more carpels which usually dehisce along two sutures. *cf.* siliqua.

Siliqua

A silicula which is at least twice as long as broad.

Silt

Is soil- or rock-derived granular material of a grain size between sand and clay, grain particles ranging from 0.004 to 0.06 mm in diameter. *adj.* silty.

Simple

Refer to a leaf or other structure that is not divided into parts. *cf.* compound.

Sinuate

With deep wavy margin.

Sinuous

Wavy.

Sinus

An opening or groove, as occurs between the bases of two petals.

Sodicity

Is characterised by low electrical conductivities and high sodium ion concentrations compared to calcium and magnesium.

Sodic soils

Contains high levels of sodium salts that affects soil structure, inhibits water movement and causes poor germination and crop establishment and plant toxicity.

Soil pH

Is a measure of the acidity or basicity of the soil. See pH.

Solitary

Usually refer to flowers which are borne singly and not grouped into an inflorescence or clustered.

Sorocarp

Fruiting body formed by some cellular slime moulds and has both stalk and spore mass.

Sorophore

Stalk bearing the sorocarp.

Sorosis

Fleshy multiple fruit formed from flowers that are crowded together on a fleshy stem, e.g. pineapple and mulberry.

Sorus

A discrete aggregate of sporangia in ferns. *pl.* sori

Spadix

Fleshy spikelike inflorescence with an unbranched, usually thickened axis and small embedded flowers often surrounded by a spathe. *pl.* spadices.

Spathe

A large bract ensheathing an inflorescence or its peduncle. *adj.* spathaceous.

Spatheate

Like or with a spathe.

Spathulate

Spatula or spoon shaped; broad at the tip and narrowed towards the base.

Spicate

Borne in or forming a spike.

Spiculate

Spikelet bearing.

Spike

An unbranched, indeterminate inflorescence with sessile flowers or spiklets. *adj.* spicate, spiciform.

Spikelet

A small or secondary spike characteristics of the grasses and sedges and, generally, composed of two glumes and one or more florets. Also applied to the small spikelike inflorescence or inflorescence units commonly found in Apiaceae.

Spine

A stiff, sharp, pointed structure, formed by modification of a plant organ. *adj.* spinose.

Spinescent

Ending in a spine; modified to form a spine

Spinulate

Covered with small spines.

Spinulose

With small spines over the surface.

Spodosol

See Podzol.

Sporidia

Asexual spores of smut fungi.

Sporangium

A spore bearing structure found in ferns, fern allies and gymnosperms. *pl.* sporangia. *adj.* sporangial.

Sporocarp

A stalked specialised fruiting structure formed from modified sporophylls, containing sporangia or spores as found in ferns and fern allies.

Sporophore

A spore-bearing structure, especially in fungi.

Sporophyll

A leaf or bract which bears or subtends sporangia in the fern allies, ferns and gymnosperms.

Sporophyte

The spore-producing phase in the life cycle of a plant that exhibits alternation of generations.

Spreading

Bending or spreading outwards and horizontally.

Spur

A tubular or saclike extension of the corolla or calyx of a flower.

Squama

Structure shaped like a fish scale. *pl.* squamae.

Squamous

Covered in scales.

Squarrose

Having rough or spreading scalelike processes.

Stamen

The male part of a flower, consisting typically of a stalk (filament) and a pollen-bearing portion (anther). *adj.* staminal, staminate.

Staminate

Unisexual flower bearing stamens but no functional pistils.

Staminode

A sterile or abortive stamen, often reduced in size and lacked anther. *adj.* staminodial.

Standard

Refers to the adaxial petal in the flower of Papilionaceae. cf. keel, wing.

Starch

A polysaccharide carbohydrate consisting of a large number of glucose units joined together by glycosidic bonds α -1-4 linkages.

Stellate

Star shaped, applies to hairs.

Stem

The main axis of a plant, developed from the plumule of the embryo and typically bearing leaves.

Sterile

Lacking any functional sexual parts which are capable of fertilisation and seed production.

Stigma

The sticky receptive tip of an ovary with or without a style which is receptive to pollen.

Stilt root

A supporting root arising from the stem some distance above the ground as in some mangroves, sometimes also known as a prop root.

Stipe

A stalk that supports some other structures like the frond, ovary or fruit.

Stipel

Secondary stipule at the base of a leaflet. *pl.* stipellae. *adj.* stipellate.

Stipitate

Having a stalk or stipe, usually of an ovary or fruit.

Stipulated

Having stipules.

Stipule

Small leaflike, scalelike or bristlelike appendages at the base of the leaf or on the petiole. *adj.* stipulate.

Stolon

A horizontal, creeping stem rooting at the nodes and giving rise to another plant at its tip.

Stoloniferous

Bearing stolon or stolons.

Stoma

A pore in the epidermis of the leaf or stem for gaseous exchange. *pl.* stomata.

Stone

The hard endocarp of a drupe, containing the seed or seeds.

Stramineous

Chaffy; straw-like.

Striae

Parallel longitudinal lines or ridges. *adj.* striate.

Striate

Marked with fine longitudinal parallel lines or ridges.

Strigose

Bearing stiff, straight, closely appressed hair; often the hairs have swollen bases.

Strobilus

A cone-like structure formed from sporophylls or sporangiophores. *pl.* strobili.

Strophile

An appendage at the hilum of certain plant seeds.

Strophiolate

Furnished with a strophile or caruncle.

Style

The part of the pistil between the stigma and ovary.

Sub-

A prefix meaning nearly or almost, as in subglobose or subequal.

Subcarnose

Nearly fleshy.

Subfamily

Taxonomic rank between the family and tribe.

Subglobose

Nearly spherical in shape.

Subretuse

Faintly notched at the apex.

Subsessile

Nearly stalkless or sessile.

Subshrub

Intermediate between a herb and shrub.

Subspecies

A taxonomic rank subordinate to species.

Substrate

Surface on which a plant or organism grows or attached to.

Subtend

Attached below of something.

Subulate

Narrow and tapering gradually to a fine-point, awl shaped.

Succulent

Fleshy, juicy, soft in texture and usually thickened.

Suckers

Young plants sprouting from the underground roots of a parent plant and appearing around the base of the parent plant.

Suffrutescent stem

Stem woody at the base.

Sulcate

Grooved longitudinally with deep furrows.

Sulcus

A groove or depression running along the internodes of culms or branches.

Superior

Refers to the ovary that is free and mostly above the level of insertion of the sepals and petals. *cf.* inferior.

Suture

Line of dehiscence.

Swidden

Slash-and-burn or shifting cultivation.

Syconium

A type of pseudocarp formed from a hollow receptacle with small flowers attached to the inner wall. After fertilisation the ovaries of the female flowers develop into one-seeded achenes, e.g. fig.

Symbiosis

Describes close and often long-term mutualistic and beneficial interactions between different organisms.

Sympetalous

Having petals united.

Sympodial

Refers to a specialised lateral growth pattern in the apical meristem. *cf* monopodial.

Synangium

An organ composed of united sporangia, divided internally into cells, each containing spores. *pl.* synangia.

Syncarp

An aggregate or multiple fruit formed from two or more united carpels with a single style. *adj.* syncarpous.

Syncarpous

Carpels fused forming a compound pistil.

Synteny

Presence of two or more genetic loci on the same chromosome.

Tannins

Group of plant-derived phenolic compounds.

Taxon

The taxonomic group of plants of any rank, e.g. a family, genus, species or any infraspecific category. *pl.* taxa.

Tendrils

A slender, thread-like organ formed from a modified stem, leaf or leaflet which, by coiling around objects, supports a

climbing plant.

Tepal

A segment of the perianth in a flower in which all the perianth segments are similar in appearance and are not differentiated into calyx and corolla; a sepal or petal.

Tetrasporangium

A sporangium containing four haploid spores as found in some algae.

Terete

Having a circular shape when cross-sectioned or a cylindrical shape that tapers at each end.

Terminal

At the apex or distal end.

Ternate

In threes as of leaf with three leaflets.

Testa

A seed coat, outer integument of a seed.

Thallus

Plant body of algae, fungi and other lower organisms.

Thyrse

A dense, panicle-like inflorescence, as of the lilac, in which the lateral branches terminate in cymes.

Tomentose

Refers to plant hairs that are bent and matted forming a woolly coating.

Tomentellose

Mildly tomentose.

Torus

Receptacle of a flower.

Transpiration

Evaporation of water from the plant through leaf and stem pores.

Tree

That has many secondary branches supported clear of the ground on a single main stem or trunk.

Triangular

Shaped like a triangle, three angled and three sided.

Tribe

A category intermediate in rank between subfamily and genus.

Trichome

A hair-like outgrowth of the epidermis.

Trichotomous

Divided almost equally into three parts or elements.

Tridentate

Three toothed or three pronged.

Trifid

Divided or cleft into three parts or lobes.

Trifoliate

Having three leaves.

Trifoliolate

A leaf having three leaflets.

Trifurcate

Having three forks or branches.

Trigonous

Obtusely three angled; triangular in cross section with plane faces.

Tripartite

Consisting of three parts.

Tripinnate

Relating to leaves, pinnately divided three times with pinnate pinnules.

Tripliveined

Main laterals arising above base of lamina.

Triploid

Describing a nucleus or cell that has three times (3n) the haploid number (n) of chromosomes.

Triveined

Main laterals arising at the base of lamina.

Triquetrous

Three edged; acutely three angled.

Trullate

With the widest axis below the middle and with straight margins; ovate but margins straight and angled below middle, trowel, angular, ovate shaped.

Truncate

With an abruptly transverse end as if cut off.

Tuber

A stem, usually underground, enlarged as a storage organ and with minute scalelike leaves and buds. *adj.* tuberous.

Tubercle

A wartlike protuberance. *adj.* tuberculate.

Tuberculate

Bearing tubercles; covered with warty lumps.

Tuberisation

Formation of tubers in the soil.

Tuft

A densely packed cluster arising from an axis. *adj.* tufted.

Turbinate

Having the shape of a top; cone shaped, with the apex downwards, inversely conic.

Turgid

Distended by water or other liquid.

Turion

The tender young, scaly shoot such as asparagus, developed from an underground bud without branches or leaves.

Turnery

Articles made by the process of turning.

Twining

Winding spirally.

Ultisols

Mineral soils with no calcareous material, having less than 10% weatherable minerals in the extreme top layer of soil and with less the 35% base saturation throughout the soil.

Umbel

An inflorescence of pedicellate flowers of almost equal length arising from one point on top of the peduncle. *adj.* umbellate.

Umbellet

A secondary umbel of a compound umbel. *cf.* umbellule.

Umbellule

A secondary umbel of a compound umbel. *cf.* umbellet.

Uncinate

Bent at the end like a hook; unciform.

Undershrub

Subshrub; a small, usually sparsely branched woody shrub less than 1 m high. *cf.* shrub.

Undulate

With an edge/margin or edges wavy in a vertical plane; may vary from weakly to strongly undulate or crisped. *cf.* crisped.

Unifoliolate

A compound leaf which has been reduced to a single, usually terminal leaflet.

Uniform

With one form, e.g. having stamens of a similar length or having one kind of leaf. *cf.* dimorphic.

Uniseriate

Arranged in one row or at one level.

Unisexual

With one sex only, either bearing the anthers with pollen, or an ovary with ovules, referring to a flower, inflorescence or individual plant. *cf.* bisexual.

Urceolate

Shaped like a jug, urn or pitcher.

Utricle

A small bladdery pericarp.

Vaginate

Forming or enclosed in a sheath.

Valvate

Meeting without overlapping, as of sepals or petals in bud. *cf.* imbricate.

Valve

One of the sections or portions into which a capsule separates when ripe.

Variant

Any definable individual or group of individuals which may or may not be regarded as representing a formal taxon after examination.

Variegate, variegated

Diverse in colour or marked with irregular patches of different colours, blotched.

Variety

A taxonomic rank below that of subspecies.

Vein

(Botany) a strand of vascular bundle tissue.

Veinlets

Small veins.

Velum

A flap of tissue covering the sporangium in the fern, *Isoetes* .

Velutinous

Having the surface covered with a fine and dense silky pubescence of short fine hairs; velvety. *cf.* sericeous

Venation

Distribution or arrangement of veins in a leaf.

Veneer

Thin sheet of wood.

Ventral

(Botany) facing the central axis, opposed to dorsal.

Vernation

The arrangement of young leaves or fronds in a bud or at a stem apex. *cf.* circinnate.

Verrucose

Warty.

Verticil

A circular arrangement, as of flowers, leaves or hairs, growing about a central point; a whorl.

Verticillaster

False whorl composed of a pair of opposite cymes as in Lamiaceae.

Verticillate

Whorled, arranged in one or more whorls.

Vertisol

A soil with a high content of expansive montmorillonite clay that forms deep cracks in drier seasons or years.

Vertosols

Soils that both contain more than 35% clay and possess deep cracks wider than 5mm during most years.

Vesicle

A small bladdery sac or cavity filled with air or fluid. *adj.* vesicular.

Vestigial

The remaining trace or remnant of an organ which seemingly lost all or most of its original function in a species through evolution.

Vestiture

Covering; the type of hairiness, scaliness or other covering commonly found on the external parts of plants. *cf.* indumentums .

Vibratile

Capable of to and fro motion.

Villose

Covered with long, fine, soft hairs, finer than in pilose.

Villous

Covered with soft, shaggy unmatted hairs.

Vine

A climbing or trailing plant.

Violaxanthin

Is a natural xanthophyll pigment with an orange colour found in a variety of plants like pansies.

Viscid

Sticky, being of a consistency that resists flow.

Viviparous

Describes seeds or fruit which sprout before they fall from the parent plant.

Whorl

A ringlike arrangement of leaves, sepals, stamens or other organs around an axis.

Winged

Having a flat, often membranous expansion or flange, e.g. on a seed, stem or one of the two lateral petals of a papilionaceous flower or one of the petal-like sepals of Polygalaceae. *cf.* keel, standard.

Xanthophylls

Are yellow, carotenoid pigments found in plants. They are oxidised derivatives of carotenes.

Xeromorphic

Plant with special modified structure to help the plant to adapt to dry conditions.

Xerophyte

A plant which naturally grows in dry regions and is often structurally modified to withstand dry conditions.

Zygomorphic

Having only one plane of symmetry, usually the vertical plane, referring to a flower, calyx or corolla. *cf.* actinomorphic.

Zygote

The first cell formed by the union of two gametes in sexual reproduction. *adj.* zygotic.

Scientific Name Index

A

Abroma augusta

Abrus precatorius

Acanthamoeba

A. castellanii

A. culbertsoni

A. polyphaga

Achasma loroglossum

Acinetobacter baumannii

Acorus

Actinomyces viscosus

Aedes aegypti

Aeromonas sp.

Aframomum

A. alboviolaceum

A. melegueta

Agaricus bisporus

Aggregatibacter actinomycetemcomitans

Agrobacterium rhizogenes

Albizia myriophylla

Allium sativum

Aloe vera

Alpinia

A. alba

A. allughas

A. bifida

A. caerula

A. calcarata

A. carnea
A. conchigera
A. cristata
A. fimbriata
A. fluvitialis
A. galanga
A. galangal
A. galanga var. *galanga*
A. galanga var. *pyramidata*
A. hookeriana
A. humilis
A. javanica
A. laosensis
A. latilabris
A. malaccensis
A. malaccensis var. *malaccensis*
A. nigra
A. nutans var. *longiramosa*
A. nutans var. *sericea*
A. officinarum
A. oxyphylla
A. purpurata
A. pyramidata
A. rheedei
A. schumanniana
A. sericea
A. sessilis
A. speciosa

A. sumatrana

A. viridiflora

A. zerumbet

Alternaria alternata

Amomum

A. angustifolium

A. cassumunar

A. compactum

A. curcuma

A. galanga

A. latifolium

A. medium

A. montanum

A. nutans

A. xanthorrhiza

A. zedoaria

A. zerumbet

A. zingiber

A. zinziba

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Angiostrongylus cantonensis

Anisakis simplex

Anopheles

A. aconitus

A. barbirostris

A. dirus

A. gambiae

A. minimus

Armigeres subalbatus

Artemia salina nauplii

Artemisia

A. cina

A. iwayomogi

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Ascaridia galli

Ascaris suum

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A. ficuum

A. flavus

A. fumigatus

A. japonicus

A. niger

A. ochraceus

A. oryzae

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A. terreus

A. tubingensis

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Averrhoa bilimbi

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B. licheniformis

B. macerans

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B. polymyxa

B. pumilus

B. spizizenii

B. subtilis

Bacteroides

B. fragilis

Bactrocera dorsalis

Biomphalaria glabrata

Bixa orellana

Blumea balsamifera

Boesenbergia

B. cochinchinensis

B. pandurata

B. rotunda

Boswellia serrata

Bothrops jararaca

Buekia malaccensis

Bursaphelenchus xylophilus

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C. maculatus

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C. glabrata

C. guilliermondii

C. krusei

C. kruseii

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C. annum

C. frutescens

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Carissa carandas

Cassumunar roxburghii

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C. latibre

C. latilabre

C. malaccense

C. speciosum

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Cinnamomum camphora

Citrobacter sp.

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Clostridia

Clostridium perfringens

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Croton mubang o

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C. pipiens pallens

C. quinquefasciatus

C. tritaeniorhynchus

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C. aeruginosa
C. amada
C. angustifolia
C. aromatica
C. australasica
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C. caesia
C. caulina
C. domestica
C. kwangsiensis
C. longa
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C. longifolia
C. malabarica
C. mangga
C. ochrorhiza
C. officinalis
C. pallida
C. phaeocaulis
C. pierreana
C. pseudomontana
C. purpurascens
C. raktakanta
C. rotunda
C. sichuanensis
C. soloensis
C. speciosa
C. tinctoria

C. wenyujin
C. xanthorrhiza
C. zanthorrhiza
C. zedoaria
C. zerumbet
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E. aerogenes
E. cloacae

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E. faecium

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E. floccosum

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Erwinia

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E. carotovora ssp. *carotovora*

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F. graminearum

F. moniliforme

F. oxysporum

F. sambucinum

F. semitectum

F. solani

F. sulphureum

F. verticillioides

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G. officinalis
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Garcinia
G. kola
G. mangostana
Gastrochilus
G. panduratus
G. rotundus
Gendarussa
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Giardia
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G. lamblia
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Glycyrrhiza glabra
Grangea maderaspatana
Grewia asiatica

H

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Haemophilus influenzae
Harpagophytum procumbens
Hedychium coronarium
Helicobacter pylori
Hellenia alba
Helminthosporium oryzae
Heritiera alba

Hitchenia caulina

Hornstedtia scottiana

Houttuynia cordata

Hymenolepis nana

Hyoscyamus vulgaris

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Jaegera montana

Jaltomata procumbens

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K. cochinchinensis

K. galanga

K. galanga var. *latifolia*

K. humilis

K. latifolia

K. longa

K. marginata

K. ovata

K. pandurata

K. parviflora

K. plantaginifolia

K. procumbens

K. rotunda

K. versicolor

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L. conchigera

L. galanga

L. hookeriana

L. javanica

L. malaccensis

L. officinarum

L. pyramidata

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Methicillin-resistant *Staphylococcus aureus* (MRSA strain)

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Nigella sativa

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O. sanctum

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P. chaba
P. nigrum
P. ribesioides
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Plectranthus amboinicus
Plodia interpunctella
Plutella xylostella
Poncirus trifoliata
Porphyromonas
P. endodontalis
P. gingivalis
Prevotella intermedia
Propionibacterium acnes
Proteus sp.
P. mirabilis
P. vulgaris
Pseudallescheria boydii
Pseudomonas
P. cepacia
P. stutzeri
Pseudomonas aeruginosa
Pseudoxanthomonas sp.
Pueraria thomsonii
Punica granatum
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S. stenotomum subsp. *stenotomum*
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S. tuberosum subsp. *andigenum*

S. tuberosum subsp. *tuberosum*

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S. tuberosum var. *tuberosum*

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S. epidermis

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T. angustata var. *gracilis*

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T. angustifolia f. *submersa*
T. angustifolia subsp. *angustata*
T. angustifolia subsp. *australis*
T. angustifolia subsp. *domingensis*
T. angustifolia subsp. *javanica*
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T. angustifolia var. *brownii*
T. angustifolia var. *calumetensis*
T. angustifolia var. *domingensis*
T. angustifolia var. *elatior*
T. angustifolia var. *elongata*
T. angustifolia var. *longispicata*
T. angustifolia var. *spathacea*
T. angustifolia var. *virginica*
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T. bracteata
T. brownii
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T. domingensis
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T. domingensis var. *sachetiae*
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Z. cassumunar var. *subglabrum*

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Z. galanga

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Z. officinale
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Z. officinale f. *rubens*
Z. officinale var. *cholmondeleyi*
Z. officinale var. *macrorhizonum*
Z. officinale var. *officinale*
Z. officinale var. *rubens*
Z. officinale var. *Rubra*
Z. officinale var. *rubrum*
Z. officinale var. *sichuanense*
Z. ottensii
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Z. purpureum var. *palamauense*
Z. sichuanense
Z. spectabile
Z. sylvestre
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Z. zerumbet var. *amaricans*
Z. zerumbet var. *aromaticum*
Z. zerumbet var. *zerumbet*

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A/ Bangkok/93/03 (H1N1)

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Adenocarcinomas of duodenum

Adenomas

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A/Fukushima/13/43 (H3N2)

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Am-Ada (Assamese)

Andigena

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Arsenic Bowen's disease of skin

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Blue ginger

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Bonglai (Malaysia)

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Cochin turmeric
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COLO205, human colonic adenocarcinoma cell lines
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Creeping false holly

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Dark Blue Temu

Dengue virus Den2 Ns2b/Ns3

Dengue-2 virus NS3

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Galangal resurrection lily
Galangal root
Gandh Tora (Assamese)
Garlic
Gastric cancer AGS cell lines
Gastric MNK-45 cancer cells
Gentil achochil chocke
Giant Curcuma
Ginger
Googol Bon
Greater Galangal
Green Ginger
Guatemalan potato moth

H

Hainan Resurrection Lily
Halia (Malaysia)
Halia bara
Halia padi
Halia udang
Hati Ghah (Assamese)
H1299 cells
HCT15 colon adenocarcinoma tumour cells
HCT-116 human colon cancer cells
HeLa cancer cell line
Hepatitis B virus (HBV)
Hepatitis C virus

Hepatocyte carcinoma (HepG2)

Hep3B (p53 null)

Hep3B human hepatoma cells

HepG2

- cell lines

- hepatocarcinoma cell

- human hepatocarcinomatic cell lines

- MCF-7 and SF-268

- MCF-7, MDA-MB-231 and HeLa cells

- MCF-7, T98G and B16-F10 tumour cell lines

- p53 wild type

Herpes simplex virus (HSV)

Herpes simplex virus type 1 (HSV-1)

H-1299 human lung cancer cells

Hidden lily

Hidden lily ginger

H4IIE rat hepatoma

Hill turmeric

Himalayan Crocus

HL-60 cell line (human promyelocytic leukaemia)

H1N1 and H3N2 influenza A viruses

HPAC expressing wild-type (wt) p53

HT-29

- human colon adenocarcinoma cells

- human colon cancer cell lines

- (p53 mutated; ras wild type) human colon cancer cell lines

HT1080 human fibrosarcoma cell

HuH-7 (p53 mutant)

Hui Dam (Thai)

Human acute myelogenous leukaemia HL-60 cells

Human A549 lung carcinoma

Human breast cancer cell line

MCF-7

MCF-7/ADR

MDA-MB-231

Human breast carcinoma-derived MCF-7

Human cancer cell lines

Ca Ski

HCT-116

MCF-7

Human cell lines

cervical (HeLa)

liver (HepG2)

lymphoma (U937)

stomach (AGS and KATO III) cancer cells

Human cervical cancer (HeLa) cells

Human cholangiocarcinoma CL-6 cell line

Human colon cancer cell line HCT-11

Human colon (HCT-15 and HT-29) cancer cells

Human colon carcinoma cell line

Human colon HCT-116 (p53 wild type; ras mutated)

Human colorectal cancer cells

Human colorectal cancer cells (HCT116)

Human epithelial carcinoma HeLa cells

Human fibrosarcoma HT 1080 cells

Human gastric adenocarcinoma SGC-7901cell

Human gastric carcinoma AGS cells

Human glioblastoma multiforme (GBM8401) cells

Human HCT116 colon cancer cells

Human head and neck cancer HN4 cells

Human head lice

Human HeLa cancer cells

Human hepatocarcinoma cell Bel-7402

Human hepatocellular carcinoma (HepG2)
cell line

Huh-7 and Hep3B cells

p53 mutant Mahlavu cells

SMMC-7721 cells

Human immunodeficiency virus type I (HIV-1)

Human immunodeficiency virus type I (HIV1-LTR lacZ)

Human Jurkat cells (cell line used for studying T-cell
leukaemia)

Human Jurkat lymphoblastoid cells

Human LAN5 NB neuroblastoma cells

Human leukaemia cell line K-562

Human leukaemia HL-60 cells

Human leukemic HL-60 and U937 cells

Human liver cancer (HepG2) cell line

Human lung adenocarcinoma A549 cells

Human lung cancer cell line A549 cells

Human mammalian cancer (MCF-7) cells

Human mammary carcinoma

Human multiple myeloma cells

Human non-small cell lung cancer A549 cell

Human ovarian cancer Caov-3 cell line

Human ovarian cancer cell HO-8910

Human ovarian cancer OVCAR-3 cells

Human ovarian cancer SiHa cells

Human pancreatic cancer cell lines

BxPC3

Capan1

E3LZ10.7

Panc1

PL5 and PL8

Su86.86

Human pancreatic PANC-1 cancer cells

Human papillomavirus (HPV)

Human papillomavirus HPV18

Human papillomavirus-positive cervical cancer HeLa

Human promyelocytic leukaemia (HL-60) cancer cell lines

Human prostate cancer LNCaP and PC-3 cells

Human prostate tumour DU-145 cell line

Human renal clear cell carcinoma (RCC) 786-0 and 769-P cell lines

Human T-cell acute lymphoblastic leukaemia (Jurkat) cells

Human triple negative breast cancer Hs578T and MDA-MB231 cells

I

Indian arrowroot

Indian Crocus

Indian ginger

Indian Saffron

India root

Influenza A virus (IAV)

Influenza B virus

Influenza viral strains, H1N1 and H9N2

Influenza viruses A/PR/8/34 (H1N1)

Irish potato

J

Jahe merah

Jaltomate

Jamaican Ginger

Japanese encephalitis virus

Java Galangal

Javanese turmeric

Javan Turmeric

Java turmeric

Jiddo

Joint-whip Ginger

K

K562 (human erythromyeloblastoid leukaemia cell line)

Kantan Hutan

Karphul

KB and HL60 cells

Kencur

Kentjur

Khaa

Khamin (Thai)

Khamin chan

Khamin Khao (Thai)
Khamin oi
Koneng Pinggang
Kra Chaai
Krachai
Krachai (Thai)
Krachai dam
Kua
Kunci pepet
Kunir putih
Kunir Tinggang (Indonesia)
Kunyit
Kunyit Hitam

L

L1210 (murine leukaemia)
Lampoyang
Lampoyang (Malaysia)
Lampoyang Hitam
Lampuayng Wangi
Lampunyang Badak (Indonesia)
Lampuyang Pahit
Lampuyang Pahit (Malay)
Lampuyan Pahit
Languas
Laos root
Laurel
L929 cells

Leaves
Lemon iron bark
Lempoyang
Lempui (Malaysia)
Lempuyan Emprit (Indonesia)
Lempuyang Gajah
Lempuyang Pait
Lempuyang Wangi (Indonesia)
Lempuyan Kapur
Lengkuas Ranting (Malay)
Lenguas
Lenguas (Indonesia, Malaysia)
Lesser Alpinia
Lesser Bulrush
Lesser galangal
Lesser ginger
Lesser grain borer
Lesser Reed-Mace
Leukaemia (KBM-5)
Leukaemic CEMss cancer cells
Leukemic (K562)
Lewis lung carcinoma
Light galangal
Light ginger
Liver fluke
LNCaP (androgen dependent)
Long pepper
Long Rooted Curcuma

Long turmeric

Long zedoary

LS180, human colonic adenocarcinoma cell lines

LS174T, human colonic adenocarcinoma cell lines

Lung cancer A549 cells

Lung cancer A549/DDP cells

Lung carcinoma A549

Lymphoblastic leukaemia IC cancer cell lines

M

Maca

Maize

Maize weevil

Malacca galangal

Malaysian ginger

Mammary adenocarcinoma

Mango ginger

Mango turmeric

Mantle cell lymphoma (MCL)

Marba

Mashua

MCF-7

MCF-7/Adriamycin (ADR) multidrug-resistant human breast cancer cells

MCF-7 and MDA-MB-231 human breast cancer cells

MCF-7 human breast cancer cells

MDA-MB-231 human breast cancer cells

MDA-MB-468 human breast cell lines

MDBK cell lines

Measles virus

Melanoma B16F10 cells

Melanoma tumours

MG-63 osteosarcoma cells

Monoterpenoids

Mosquitoes

Moth

Mouse colon adenoma

Multiple myeloma MM1 cells and head

Murine adenocarcinoma colon26 cells

Mussel galangal

Myeloma

N

Nail-Rod

Narrow-leaf cattail

Narrow-leaved cumbungi

Nasopharyngeal carcinoma (KB)

Nasopharyngeal epidermoid cell line (KB) lung cell line (A549)

Native ginger

NB4 promyelocytic leukemic cells

NCI H460 (lung cancer)

Neck squamous cell carcinoma LICR-LON-HN5 cells

Neuroblastoma cell lines (IMR-32, SK-N-SH, NB-39)

Neuroblastoma cell line SH-SY5Y

Nodding Ginger

Non-hormone-dependent breast cancer (MDA-MB-231)

Non-small cell lung cancer (A549)

Non-small-cell lung carcinoma (NSCLC) cells

O

Oca

OC2 human oral cancer cells

Oral leukoplakia

Oral squamous carcinoma (HSC-2 and HSC-4)

Oral squamous carcinoma cell line, KB

Orange

Oriental fruit fly

Oseltamivir-resistant A/PR/8/34 (H1N1)

Oseltamivir-resistant novel H1N1 (H274Y mutant)

Osteosarcoma multidrug resistance (MDR) cells

Ovarian and cervical cancer cells Caov-3 and HeLa

Ovarian cancer (CaOV3)

Ovarian cancer cells (SKOV-3)

Ovary (OVACAR)

P

Pancreatic (PSN-1)

Pancreatic carcinoma PANC-1 cells

Pancreatic tumour cell line BxPc-3

Panglai Hideung (Indoneisa)

Papa Cimarrona

Papa Del Monte

Papa Morda

Patagonian Capucine

PC-3 and Colo-320DM human tumour cell lines

PC-3 M prostate cancer cell line

PC-3 prostate cancer cell line

PC-3 (androgen independent) prostate cancer cells

Peacock ginger

Peruvian Capucine

Peruvian Nasturtium

Phlai

Phrikgnek (Assamese)

Phrilang Dung (Assamese)

Pine wood nematode

Pink Ginger

Pink porcelain lily

Pink Shell *Heliconia*

Plai

PLC/PRF/5 (p53 mutant)

Poliovirus

Potato

Potato tuberworm moth

Prostate adenocarcinoma (PC3)

Prostate cancer DU-145 cell line

Prostate cancer PC3 cells

Prostate tumour cell line LNCaP

Puar Putih

Q

Queen palm

R

Raji cancer cell line

RBL-2H3 (basophilic leukaemia cell) cancer cell lines

Red flour beetle
Red spider mite
Reed mace
Renal cell carcinoma (RCC) cells
Respiratory syncytial virus (RSV)
Resurrection ginger
Resurrection lily
Rhinovirus IB
Riềng ắm (Vietnamese)
Riềng Đẹp
Riềng Malacca (Vietnamese)
Riềng Nếp (Vietnamese)
Riềng Rừng (Vietnamese)
Riềng Thuoc (Vietnamese)
Rosemary
Round-rooted galangal
Roundworm
Round zedoary
Ry (Vietnamese)

S

Sacha Pappa
Salam
Sand Ginge
Sarcoma 180 ascites
SCC-15 oral squamous cell carcinoma (OSCC) cells
Scented Flag
Scotts Ginger

Scrub typhus
Sembung
Setwall
SF-268 (CNS)
Shampoo ginger
Shell flower
Shell ginger
Shell plant
Siamese galangal
Siamese ginger
SiHa
SK-BR-3
SK-MEL-2 skin melanoma
SK-OV-3 ovary malignant ascites
Small bulrush
Smaller galangal
Small Reed-Mace
Snap ginger
SNU638 stomach cancer
Solid tumour (sarcoma 180)
Soybean
Spice ginger
Spud
Stem ginger
Stinkbug
SW620 colon cancer cells
Sweet potato
Sweet Thai ginger

T

T-acute lymphoblastic leukaemia CEMss cells

Tareng (Mishing)

T-cell acute lymphoblastic leukaemia

T-cell leukaemia (Jurkat)

T47D

Temu Kunchi (Indonesia, Malaysia)

Temu Kuning (Malaysia)

Temu Kunyit (Malaysia)

Temulawak

Temu Lawak (Malaysia)

Temu Mangga (Malaysia)

Temu Pauh

Temu Putri

Temu Tis

Tepus (Malaysia)

Tepus Halia (Malaysia)

Tepus Putih

Tepus Tanah

T98G

Thai galangal

Thai ginger

Tharai (Bodo)

Tharmit Tharve Am Haladhi

THP-1 AMoL (human acute monocytic leukaemia) cells

Tomato

Tora (Assamese)

Triple-negative breast cancer (TNBC) cells

Tropical Crocus

True ginger

Tuber Nasturtium

Tuberous Nasturtium

Tuberous Nasutium

Tuberous Rooted Nasturtium

Turmeric

Turmeric Common

Two human pancreatic cancer cell lines

U

U937 (human leukemic monocyte lymphoma) cells

Ulluco

Urinary bladder cancer

V

Variegated ginger

Variegated Shell ginger

W

White Ginger Lily

White potato

White termite

White turmeric

Wild Ginger

Wild potato

Wild turmeric

Y

Yeasts

Yellow ginger

Yellow zedoary

Yinbun

Yoshida AH-130 ascites hepatoma

Z

Zedoary

Zedoary turmeric

Zerumbert Ginger