Ginger

Species (Family)

Zingiber officinale Roscoe (Zingiberaceae)

Synonym(s)

Zingiber

Part(s) Used

Rhizome

Pharmacopoeial and Other Monographs

BHC 1992[G6]
BHP 1996[G9]
BP 2001[G15]
BPC 1973[G12]
ESCOP 1996[G52]
Martindale 32nd edition[G43]
Mills and Bone[G50]
PDR for Herbal Medicines 2nd edition[G36]
Ph Eur 2002[G28]
USP/NF19[G61]
WHO 1999 volume 1[G63]

Legal Category (Licensed Products)

GSL[G37]

Constituents[1,G2,G6,G37,G41,G64]

Carbohydrates Starch (major constituent, up to 50%).

Lipids 6–8%. Free fatty acids (e.g. palmitic acid, oleic acid, linoleic acid, caprylic acid, capric acid, lauric acid, myristic acid, pentadecanoic acid, heptadecanoic acid, stearic acid, linolenic acid, arachidic acid);[2] triglycerides, phosphatidic acid, lecithins; gingerglycolipids A, B and C.[3]

Oleo-resin Gingerol homologues (major, about 33%) including derivatives with a methyl side-chain,[4] shogaol homologues (dehydration products of gingerols), zingerone (degradation product of gingerols), 1-dehydrogingerdione,[5] 6-gingesulfonic acid[3] and volatile oils.

Volatile oils 1–3%. Complex, predominately hydrocarbons. β-Bisabolene and zingiberene (major); other sesquiterpenes include zingiberol, zingiberenol, *ar*-curcumene, β-sesquiphellandrene, β-sesquiphellandrol (*cis* and *trans*); numerous monoterpene hydrocarbons, alcohols and aldehydes (e.g. phellandrene, camphene, geraniol, neral, linalool, *d*-nerol).

Other constituents Amino acids (e.g. arginine, aspartic acid, cysteine, glycine, isoleucine, leucine, serine, threonine and valine), protein (about 9%), resins, diterpenes (galanolactone[6]), vitamins (especially nicotinic acid (niacin) and vitamin A), minerals.[2]

The material contains not less than 4.5% of alcohol (90%)-soluble extractive and not less than 10% of water-soluble extractive.[G15]

Food Use

Ginger is listed by the Council of Europe as a natural source of food flavouring (category N2). This category indicates that ginger can be added to foodstuffs in small quantities, with a possible limitation of an active principle (as yet unspecified) in the final product.[G16] It is used widely in foods as a spice. In the USA, ginger is listed as GRAS (Generally Recognised As Safe).[G41]

Herbal Use

Ginger is stated to possess carminative, diaphoretic and antispasmodic properties. Traditionally, it has been used for colic, flatulent dyspepsia, and specifically for flatulent intestinal colic.[7,G2,G6–G8,G32,G64] Modern interest in ginger is focused on its use in the prevention of nausea and vomiting, particularly motion (travel) sickness, as a digestive aid, and as an adjunctive treatment for inflammatory conditions, such as osteoarthritis and rheumatoid arthritis.

Dosage

Anti-emetic

Powdered rhizome Single dose of 1–2 g,[G6] 30 minutes before travel for prevention of motion sickness,[G52] or 0.5 g, two to four times daily.[G63]

Other uses

Powdered rhizome 0.25–1 g, three times daily.[G6]

Tincture 1.5–3 mL (1 : 5) three times daily,[G6] 1.7–5 mL daily.[G50]

Pharmacological Actions

Several pharmacological activities, including anti-emetic, antithrombotic, antimicrobial, anticancer, antioxidant and anti-inflammatory properties, have been documented for preparations of ginger in *in vitro* and/or animal studies. Also, ginger has been reported to have hypoglycaemic, hypo- and hypertensive, cardiac, prostaglandin and platelet aggregation inhibition, antihypercholesterolaemic, cholagogic and stomachic properties.

Clinical studies have focused mainly on the effects of ginger in the prevention of nausea and vomiting.

In vitro and animal studies

In vitro studies have demonstrated that constituents of ginger, such as 6-, 8- and 10-gingerols and galanolactone, have antiserotonergic activity.[6,8]

Anti-emetic activity and effects on gastrointestinal motility The older literature contains examples of studies documenting the antiemetic effects of ginger extract *in vivo* (e.g. dogs).[9] Oral administration of constituents of ginger (certain shogaols and gingerols at doses of 100 mg/kg body weight) inhibited emesis induced by oral administration of copper sulfate in leopard and ranid frogs.[10] Emetic latency was reported to be prolonged by over 150% by a trichloromethane extract of ginger at a dose of 1 g/kg body weight.

The anti-emetic activity of ginger extracts has also been assessed in dogs.[11] Acetone and ethanolic extracts of ginger, administered intragastrically at doses of 25, 50, 100 and 200 mg/kg, protected against cisplatin-induced emesis (3 mg/kg administered intravenously 30 minutes before ginger extract), compared with control. However, ginger extracts were less effective in preventing emesis than the 5-HT_3 receptor antagonist granisetron, and were ineffective against apomorphine-induced emesis.

Compared with control, an acetone extract of ginger at doses of 200 and 500 mg/kg administered orally reversed the delay in gastric emptying induced by intraperitoneal cisplatin 10 mg/kg in rats.[12] Ginger juice (2 and 4 mL/kg) had a similar effect. A 50% ethanolic extract of ginger also reversed the cisplatin-induced delay in gastric emptying, although only at a dose of 500 mg/kg. In mice, oral administration of an acetone extract of ginger (75 mg/kg), 6-shogaol (2.5 mg/kg) and 6-, 8- and 10-gingerol (5 mg/kg) enhanced the transportation of a charcoal meal, indicating enhancement of gastrointestinal motility.[13]

Anti-ulcer activity The effect of ginger (acetone extract) and zingiberene on hydrochloric acid/ethanol-induced gastric lesions in rats has been examined.[14] (6)-Gingerol and zingiberene, both 100 mg/kg body weight by mouth, significantly inhibited gastric lesions by 54.5% and 53.6%, respectively. The total extract inhibited lesions by 97.5% at 1 g/kg. Oral administration of both aqueous and methanol ginger extracts to rabbits has been reported to reduce gastric secretions (gastric juice volume, acid and pepsin output).[15] Both extracts were found to be comparable with cimetidine (50 mg/kg) with respect to gastric juice volume; the aqueous extract was comparable with cimetidine and superior to the methanol extract for pepsin output, and the methanol extract superior to both the aqueous extract and comparable to cimetidine for acid output. In rats, 6-gingerol, 6-shogaol and 6-gingesulfonic acid at doses of 150 mg/kg protected against hydrochloric acid/ethanol-induced gastric lesions, compared with control.[3] 6-Gingesulfonic acid 300 mg/kg provided almost 100% protection against gastric lesions in this model. Other studies in rats found that oral administration of an ethanolic extract of ginger (500 mg/kg) inhibited gastric lesions induced by ethanol (80%), hydrochloric acid (0.6 mol/L), sodium hydroxide (0.2 mol/L), and 25% sodium chloride, compared with control.[16] The same dose of extract protected against gastric mucosal damage induced by the non-steroidal anti-inflammatory drugs (NSAIDs) indomethacin and aspirin in rats. In pylorus-ligated rats, oral administration of acetone and ethanol extracts of ginger inhibited gastric secretion.[17] These extracts, at doses of 62 mg/kg, also protected against the development of stress-induced lesions, although to a lesser extent than cimetidine.

Antiplatelet activity (6)-Gingerol, (6)- and (10)-dehydrogingerdione, (6)- and (10)-gingerdione have been reported to be potent inhibitors of prostaglandin biosynthesis (PG synthetase) *in vitro*, with the latter four compounds stated to be more potent than indomethacin.[18] Dose-dependent inhibition of platelet aggregation, *in vitro*, induced by ADP, adrenaline, collagen and arachidonic acid has been described for an aqueous ginger extract.[19] Ginger was also found to reduce platelet synthesis of prostaglandin-endoperoxides, thromboxane and prosta-

glandins. A good correlation was reported between concentrations of the extract required to inhibit platelet aggregation and concentrations necessary to inhibit platelet thromboxane synthesis.[19]

Anti-atherosclerotic and antioxidant activity Ginger oleo-resin, by intragastric administration, has been reported to inhibit elevation in serum and hepatic cholesterol concentrations in rats by impairing cholesterol absorption.[20] Antihypercholesterolaemic activity has also been documented for dried ginger rhizome when given to both rats fed a cholesterol-rich diet and those with existing hypercholesterolaemia.[21] Fresh ginger juice was not found to have an effect on serum cholesterol concentrations within 4 hours of administration. In addition, serum cholesterol concentrations were not greatly increased within 4 hours of cholesterol administration.

An ethanol (50%) extract of ginger administered orally at a dose of 500 mg/kg to hyperlipidaemic rabbits led to a significant reduction in blood serum cholesterol concentrations, compared with those in control rabbits.[22] In a study in rabbits fed cholesterol for 10 weeks, administration of an ethanolic extract of ginger (200 mg/kg orally) decreased raised serum and tissue concentrations of cholesterol, serum triglycerides and serum lipoproteins.[23]

An ethanolic ginger extract, standardised to contain 40 mg/g gingerols, shogaols and zingerone, and 90 mg/g total polyphenols, was reported to inhibit low-density lipoprotein oxidation and to reduce the development of atherosclerosis in atherosclerotic mice, when compared with control.[24] In rats fed a high-fat diet for 10 weeks, an aqueous preparation of ginger powder administered orally at doses of 35 and 70 mg/kg demonstrated antioxidant activity, as measured by raised tissue concentrations of thiobarbituric acid reactive substances and hydroperoxides, and reduced activities of superoxide dismutase and catalase.[25]

The antioxidant activity of ginger constituents has been documented *in vitro*.[26]

Anti-inflammatory activity Constituents of ginger have been shown to have anti-inflammatory activity *in vitro*. In a study in intact human airway epithelial cells (A549 cells), 8-paradol and 8-shogaol inhibited cyclooxygenase 2 (COX-2) enzyme activity in a concentration-dependent manner (IC_{50} values ranged from 1 to 25 μmol/L).[27] In other studies, an acetone extract of ginger inhibited inflammation of the chorioallantoic membrane of fertilised hen's eggs in a concentration-dependent manner.[28] In another assay, the extract exhibited anti-inflammatory properties by inhibiting the release of nitric oxide in a concentration-dependent manner.[28] Ginger oil has demonstrated anti-inflammatory activity in a study in rats with severe chronic adjuvant arthritis induced by injection of 0.05 mL of a suspension of dead *Mycobacterium tuberculosis* bacilli.[29] Ginger oil 33 mg/kg administered orally for 26 days caused a significant suppression of paw and joint swelling, compared with control (no ginger oil).

Other studies documenting anti-inflammatory activity for ginger constituents have been summarised.[26]

Antimicrobial activity *In vitro* activity against rhinovirus IB has been reported for sesquiterpenes isolated from ginger rhizomes.[1] The most active compound was β-sesquiphellandrene (IC_{50} 0.44 μmol/L). *In vitro* anthelmintic activity against *Ascaridia galli* Schrank has been documented for the volatile oil of *Zingiber purpureum* Roxb.[30] Activity exceeding that of piperazine citrate was exhibited by the oxygenated compounds fractionated from the volatile oil.

Anticancer activity Extracts of ginger or constituents of ginger have been shown to have cancer chemopreventive and cytotoxic or cytostatic activity *in vitro* and *in vivo* (animals). Application of an ethanolic extract of fresh ginger in a mouse skin tumorigenesis model (SENCAR mice) resulted in significant inhibition of 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced induction of epidermal ornithine decarboxylase, cyclooxygenase and lipoxygenase activities in a concentration-dependent manner.[31] Preapplication of ginger extract also inhibited TPA-induced epidermal oedema and hyperplasia. Application of ginger extract 30 minutes before application of two tumour inducers to the skin of SENCAR mice protected against skin tumour incidence, compared with control. In another mouse model, topical application of 6-gingerol or 6-paradol before application of tumour inducers attenuated skin papillomagenesis.[32] Other studies documenting the cancer chemopreventive potential of ginger and its constituents have been summarised.[26]

In vitro, incubation of 6-gingerol with human promyelocytic leukaemia (HL-60) cells resulted in inhibitory effects on cell viability and DNA synthesis.[33] Microscopic examination of the incubated cells provided evidence of the induction of apoptosis by 6-gingerol.

Other activities In rats, the anxiolytic effects of pretreatment with a combination preparation of standardised extracts of ginger and *Ginkgo biloba* administered intragastrically at doses between 0.5

and 100 mg/kg were assessed in the elevated plus-maze test.[34] The combination was found to have an anxiolytic effect at lower doses, but appeared to have an anxiogenic effect at higher doses.

A hypoglycaemic effect in both non-diabetic and alloxan-induced diabetic rabbits and rats has been documented for fresh ginger juice administered orally. The effect was stated to be significant in the diabetic animals.[35]

The pharmacological actions of (6)-shogaol and capsaicin have been compared.[36] Both compounds caused rapid hypotension followed by a marked pressor response, bradycardia, and apnoea in rats after intravenous administration. The pressor response was thought to be a centrally acting mechanism. Contractile responses in isolated guinea-pig trachea with both compounds, and positive inotropic and chronotropic responses in isolated rat atria with (6)-shogaol were thought to involve the release of an unknown active substance from nerve endings.[36] A potent, positive inotropic action on isolated guinea-pig atria has been documented and gingerols were identified as the cardiotonic principles.[37]

A cholagogic action in rats has been described for an acetone extract of ginger administered intraduodenally.[38] (6)-Gingerol and (10)-gingerol were reported to be the active components, the former more potent with a significant increase in bile secretion still apparent 4 hours after administration.

Utero-activity has been described for a phenolic compound isolated from *Zingiber cassumunar* Roxb.[39] The compound was found to exhibit a dose-related relaxant effect on the non-pregnant rat uterus *in situ*; the uterine response from pregnant rats was stated to vary with the stage of pregnancy, the post-implantation period being the most sensitive. The compound was thought to act by a similar mechanism to that of papaverine.[39]

Clinical studies

Clinical trials of ginger have focused mainly on its effects on the prevention and treatment of nausea and vomiting of various causes. Other clinical studies have assessed the effects of ginger preparations on gastrointestinal motility and on platelet function, and in vertigo and inflammatory conditions, such as osteoarthritis. Several of these studies are described below.

Nausea and vomiting and effects on gastrointestinal motility Ginger has been reported to be effective as a prophylactic against seasickness.[40,41] Ingestion of powdered ginger root 1 g was found to significantly reduce the tendency to vomit and experience cold sweating in 40 naval cadets, compared with 39 cadets who received placebo.[40] Powdered ginger root 1.88 g has been reported to be superior to dimenhydrinate 100 mg in preventing the gastrointestinal symptoms of motion sickness induced by a rotating chair.[41] However, a second study reported ginger (500 mg powdered, 1 g powdered/fresh) to be ineffective in the prevention of motion sickness induced by a rotating chair.[42] The study concluded hyoscine 600 µg and dexamphetamine 10 mg to be the most effective combination, with dimenhydrinate 50 mg as the over-the-counter motion sickness medication of choice.[42]

A systematic review of 6 randomised controlled trials of ginger preparations included three trials involving patients with post-operative nausea and vomiting, and three further trials in patients with seasickness (motion sickness), morning sickness (emesis of pregnancy) and cancer chemotherapy-induced nausea (one trial in each condition).[43] Two of the three studies assessing the effects of ginger in post-operative nausea and vomiting found that ginger was more effective than placebo and as effective as metoclopramide in reducing nausea. However, when the data from the three studies were pooled, the difference between the ginger and placebo groups was statistically non-significant.[43]

A randomised, double-blind, crossover trial involving women with nausea of pregnancy assessed the effects of capsules of powdered ginger root 250 mg, or placebo, administered orally four times daily for four days.[44] It was reported that symptom relief was significantly greater during treatment with ginger than with placebo, and that significantly more women stated a preference for ginger treatment than for placebo (as later disclosed). A more recent randomised, double-blind trial involving 70 women with nausea and vomiting of pregnancy assessed the effectiveness of capsules of powdered fresh ginger root 250 mg four times daily, or placebo, for four days.[45] At the end of the study, ginger recipients had significantly lower scores for nausea and fewer vomiting episodes than did the placebo group.

Studies involving healthy volunteers have investigated the effects of ginger on gastric emptying as a possible mechanism for the anti-emetic effects of ginger. A randomised, double-blind, placebo-controlled, crossover trial involving 16 volunteers assessed the effects of capsules containing powdered ginger 1 g for one week, followed by a one-week washout period before crossing over to the opposite arm of the study.[46] Gastric emptying was measured using a paracetamol absorption technique by comparing the effects of ginger administration on mean and peak plasma paracetamol concentrations. The

results indicated that the rate of absorption of oral paracetamol was not affected by simultaneous ingestion of ginger. Another randomised, double-blind, placebo-controlled trial involving 12 healthy volunteers assessed the effects of ginger rhizome extract on fasting and postprandial gastroduodenal motility.[47] The results of this study indicated that oral administration of ginger improved gastroduodenal motility in both the fasting state and after a test meal.

A randomised, double-blind, placebo-controlled, crossover trial involving eight healthy volunteers tested the effects of powdered ginger root 1 g on experimentally induced vertigo.[48] One hour after ginger or placebo administration, participants' vestibular system was stimulated by water irrigation of the left ear. It was reported that ginger significantly reduced vertigo, when compared with placebo

Other effects In a randomised, double-blind, placebo-controlled, crossover trial involving 75 patients with osteoarthritis of the knee or hip, the effects of capsules of ginger extract 170 mg three times daily were compared with those of ibuprofen 400 mg three times daily, or placebo, for three weeks with a one-week washout period between each treatment period.[49] At the end of the study, data for the 56 evaluable participants indicated that there was no strong evidence of an effect for ginger extract over that of placebo on parameters of pain.

A reduction in joint pain and improvement in joint movement in seven rheumatoid arthritis sufferers has been documented for ginger, with a dual inhibition of cyclooxygenase and lipoxygenase pathways reported as a suggested mechanism of action.[50,51] Patients took either fresh ginger in amounts ranging from 5 to 50 g or powdered ginger 0.1–1.0 g daily.

A placebo-controlled study assessed the effects of two doses of ginger powder (4 g daily for three months, and 10 g as a single dose) on platelet aggregation and fibrinolytic activity in patients with coronary artery disease (CAD).[52] The results indicated that long-term administration of ginger powder did not affect ADP- and epinephrine (adrenaline)-induced platelet aggregation and had no effects on fibrinolytic activity or fibrinogen concentrations, compared with placebo administration. By contrast, administration of a single dose of ginger powder to 10 patients with CAD produced a significant reduction in platelet aggregation, compared with placebo administration ($n = 10$ patients with CAD).

In a study involving seven women, oral raw ginger 5 g reduced thromboxane B_2 concentrations in serum collected after clotting,[50] thus indicating a reduction in eicosanoid synthesis (associated with platelet aggregation).

Side-effects, Toxicity

None documented for ginger. Ginger oil is stated to be non-irritating and non-sensitising although dermatitis may be precipitated in hypersensitive individuals. Phototoxicity is not considered to be of significance.[53] Ginger oil is stated to be of low toxicity[G58] with acute LD_{50} values (rat, by mouth; rabbit, dermal) reported to exceed 5 g/kg.[53]

Mutagenic activity has been documented for an ethanolic ginger extract, gingerol and shogaol in *Salmonella typhimurium* strains TA100 and TA1535 in the presence of metabolic activation (S9 mix) but not in TA98 or TA1538 with or without S9 mix.[54] Zingerone was found to be non-mutagenic in all four strains with or without S9 mix, and was reported to suppress mutagenic activity of gingerol and shogaol. Ginger juice has been reported to exhibit antimutagenic activity, whereas mutagenic activity has been described for (6)-gingerol in the presence of known chemical mutagens.[55] It was suggested that certain mutagens may activate the mutagenic activity of (6)-gingerol so that it is not suppressed by antimutagenic components present in the juice.[55]

Contra-indications, Warnings

Ginger has been reported to possess both cardiotonic and antiplatelet activity *in vitro* and hypoglycaemic activity in *in vivo* studies. Excessive doses may therefore interfere with existing cardiac, antidiabetic or anticoagulant therapy. An oleo-resin component, (6)-shogaol has been reported to affect blood pressure (initially decrease then increase) *in vivo*.

Pregnancy and lactation Ginger is reputed to be an abortifacient[G30] and uteroactivity has been documented for a related species. Doses of ginger that greatly exceed the amounts used in foods should not be taken during pregnancy or lactation.

Pharmaceutical Comment

The chemistry of ginger is well documented with respect to the oleo-resin and volatile oil. Oleo-resin components are considered to be the main active principles in ginger and documented pharmacological actions generally support the traditional uses. In addition, a number of other pharmacological activities have been documented, including hypoglycaemic, antihypercholesterolaemic, anti-ulcer and inhibition of prostaglandin synthesis, all of which

require further investigation. The use of ginger as a prophylactic remedy against motion sickness is contentious. It seems likely that ginger may act by a local action on the gastro-intestinal tract, rather than by a centrally mediated mechanism.

References

See also General References G2, G3, G5, G6, G9, G12, G15, G16, G18, G21, G29, G31, G32, G36, G41, G43, G50, G52, G58, G61, G63 and G64.

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