GINGER

Zingiber officinale Roscoe

Family

Zingiberaceae (the ginger family). There are about 52 genera and 1300 species of ginger around the world.[1]

Parts Used

Rhizome.

Description

Ginger is a perennial plant native to the tropics. The subterranean, digitately branched rhizome (the edible and medicinal portion of the plant) produces reed like stems up to 1.5 meters in height with pale green sheathing leaves. Ginger root is characterised by its knotted, beige exterior and its yellow interior. Flower stems, shorter than the leaf stems, bear a few yellow-green flowers with a deep purple, yellow marked lip.[2]

Traditional Use

Ginger is one of the oldest, most popular and most versatile of spices. Known as the 'universal medicine' in Ayurveda, ginger has been indispensable to Indian and Chinese medicine, and cuisine, since antiquity and it was one of the earliest spices to reach the West. An old Indian proverb says 'every good quality is contained in ginger' and it still remains one of the most popular herbs of our time. It was a favoured remedy with the American 19th Century Eclectic physicians for digestive problems and menstrual complaints. Ginger became so important in British food and medicine that not only the spice but also the plant was transported to Australia on the First Fleet. In the early 19th century Chinese immigrants to Australia also brought with them ginger plants. Chinese sailors chewed ginger to prevent sea sickness and it was widely used in Ancient China to treat arthritis.

Gingerbread is thought to have originated from the Ancient Greek traders who learnt of the Asian practice of using ginger as a digestive aid. They brought it to Greece where it was wrapped in sweetened bread after big meals and eaten as a stomach settling dessert. From here gingerbread evolved into ginger ale which is still a popular home remedy for diarrhoea, nausea and vomiting.[3,4]

A close relative of turmeric *(Curcuma longa)* ginger has been widely studied with positive results for a variety of issues making it one of the more accepted herbs in Western medicine. Traditionally ginger has been used to treat a broad range of diseases including stomach ache, diarrhoea, nausea (especially associated with pregnancy, motion sickness and post-surgery), asthma, respiratory disorders, toothache, gingivitis and arthritis. Modern science has supported some of these uses particularly its remarkable ability to prevent the nausea of motion and morning sickness.[5]

Reproductive health guru Ruth Trickey says ginger is an important herb in the first stage of acute infectious illness where it is traditionally used in conjunction with other herbs to facilitate a sweat. "The outcome of using ginger is to cause a lowering of the temperature, an effect similar to that of aspirin. It is possible that the observed benefits are also related to an anti-infective effect, as some components (sesquiterpenes) are known to have activity against the rhinoviruses which are implicated in the common cold." Regarding its use in gynaecology Trickey says the warming properties of ginger make it useful for period pain that is improved by the application of heat or warm drinks. She says ginger is also useful for the many women who experience nausea and vomiting with their period. Ginger can aggravate the hot flushing of menopause so Trickey recommends its use for premenstrual and menstrual migraines but not when these occur around menopause.[6]

Constituents

Ginger contains a volatile oil and resin known collectively as oleoresin which contains sesqueterpines, such as zingiberene, and pungent phenolic components such as gingerol, shogaol and zingerone. Among them, the gingerols and shogaols are considered as the major bioactive constituents of fresh and dried ginger, respectively. The distinctive odour and flavour of ginger are due to these volatile oils and also nonvolatile phenolic compounds which have pungent properties. Interestingly, 6-gingerol, a natural analogue of curcumin derived from the root of ginger exhibits a biologic activity profile similar to that of curcumin. Ginger powder is a source of phosphorus (168mg/100g), magnesium (214mg/100g), potassium (1320mg/100g), manganese (33.3mg/100g), zinc (3.64mg/100g), iron (19.8mg/100g) and niacin (9.62mg/100g).[7,8,9]

Actions

Antiemetic, carminative, digestive stimulant, antidiarrhoeal, anti-inflammatory, antispasmodic, anodyne, analgesic, antioxidant, stimulating diaphoretic, stimulating expectorant, antimicrobial, circulatory stimulant, immunomodulatory.

Pharmacological Activity

Ginger's long and established history of medicinal use in humans has inspired ongoing clinical trials to scientifically assess the effectiveness of ginger as an adjuvant therapy, or as a complementary and alternative medicine, in a number of indications especially related to nausea and vomiting. Other clinical studies have assessed the effects of ginger preparations on gastrointestinal motility, platelet function and inflammatory conditions such as osteoarthritis. A selection of some of the most recent of these studies are described below.

Antiemetic Activity

Ginger has demonstrated antiemetic activity in both experimental models and human studies. This action first received scientific validation in 1982 and since then many other studies have confirmed its value in this area. Ginger's mechanism of action in reducing nausea and vomiting is unknown although some authors advocate that it shows an antiemetic effect by reducing stomach contractions and increasing the intestinal system activity while other authors state that it prevents nausea and vomiting by having an inhibitory effect on 5-HT serotonin receptors in a way similar to antiemetic drugs.[10,11,12,13]

A 2015 review discussed recent clinical trials that investigated ginger as a treatment for multiple

types of nausea and vomiting and the potential mechanisms of action. The researchers identified nine studies and seven reviews that investigated ginger for morning sickness, postoperative nausea and vomiting, chemotherapy induced and antiretroviral induced nausea and vomiting. All studies reported that ginger provided a significant reduction in nausea and vomiting. These results suggest that ginger is a promising treatment for nausea and vomiting in a variety of clinical settings and possesses a clinically relevant mechanism although further studies are required to address the limitations.[14] An earlier meta-analysis demonstrated that a fixed dose of at least 1g of ginger is more effective than placebo for the prevention of postoperative nausea and vomiting and in postoperative vomiting.[15]

Nausea and Vomiting in Pregnancy

There are many studies, including observational studies, randomised controlled trials as well as multiple systematic reviews, including a Cochrane review, that suggest that ginger powder or extract may be safe and effective in treating nausea and vomiting of pregnancy which ranks high among the most common complaints during the early weeks of pregnancy.[16]

A 2018 systematic review focused on randomised controlled trials and assessed complementary medicine on nausea and vomiting of pregnancy of which ten clinical trials with 1059 participants were about ginger. According to the results the majority of methods employed were effective in reducing the incidence of nausea and vomiting of pregnancy with ginger being among those that could be recommended with more reliability. Other meta-analyses have also supported the safe effectiveness of ginger on nausea and vomiting of pregnancy. As mentioned the exact mechanism of ginger in reducing nausea and vomiting of pregnancy is unknown but constituents such as 6-gingerol, 6-shogaol and galano-lactogen have antiserotonin-3 (5HT3) effects. The recommended dose of ginger in most studies is 250mg every four hours.[17]

French researchers conducted a 2018 review to assess the effectiveness and safety of ginger consumption during early pregnancy. A total of 15 studies and three prospective clinical studies were included. For 1g of fresh ginger root per day for four days results show a significant decrease in nausea and vomiting and no risk for the mother or her baby. The available evidence suggests that ginger is a safe and effective treatment for nausea and vomiting in pregnancy.[18]

A 2014 systemic review said there were potential benefits of ginger in reducing nausea symptoms in pregnancy. Based on evidence from this review ginger could be considered a harmless and possibly effective alternative option for women suffering from nausea and vomiting during pregnancy.[19]

In another 2014 review reporting on the prevalence of herbal products used by pregnant women and evaluating the evidence of efficacy and safety of the most popular remedies ginger was the most investigated remedy and it was consistently reported to ameliorate nausea and vomiting in pregnancy.[20]

An earlier study into the safety of ginger use during pregnancy found it does not seem to increase the risk of congenital malformations, stillbirth or perinatal death, preterm birth, low birth weight or low Apgar score. The large Norwegian population based cohort study consisted of 68,522 women. Among the participants 1020 (1.5%) women reported using ginger during pregnancy.[21]

Another clinical trial suggests that ginger at a dose of 250mg taken four times per day is as effective as the higher dose of B6 40mg twice per day for reducing pregnancy induced nausea.[22]

Chemotherapy and Drug Induced Nausea and Vomiting

In a 2018 meta-analysis of 10 randomised controlled trials ginger displayed significant efficacy with regard to controlling chemotherapy induced nausea and vomiting in experimental groups.[23]

A 2017 trial suggests ginger supplementation could be an effective adjuvant treatment for chemotherapy induced nausea. The results of the trial demonstrated that adjuvant ginger supplementation is associated with better chemotherapy induced, nausea related, quality of life and less cancer related fatigue. The aim of this particular clinical trial was to address significant methodological limitations in previous trials. In the double-blind, randomised, placebo controlled trial 51 patients received either 1.2g of standardised ginger extract or placebo per day, in addition to standard

antiemetic therapy, during the first three cycles of chemotherapy.[24]

An earlier study by the same authors reviewed the proposed mechanisms of action for ginger in chemotherapy induced nausea and vomiting. The constituents gingerol and shogaol interact with several pathways that are directly implicated in chemotherapy induced nausea and vomiting in addition to pathways that could play secondary roles by exacerbating symptoms. These properties include 5-HT3, substance P and acetylcholine receptor antagonism; anti-inflammatory properties; and modulation of cellular redox signalling, vasopressin (antidiuretic hormone) release, gastrointestinal motility and gastric emptying rate. The review outlined these proposed mechanisms by discussing the results of clinical, *in vitro* and animal studies both within the chemotherapy context and in other relevant fields. The evidence indicated that ginger possesses multiple properties that could be beneficial in reducing chemotherapy induced nausea and vomiting.[25]

The authors also reviewed the potential effect of ginger on platelet aggregation. Due to the observed *in vitro* effects of ginger on the arachidonic acid cascade, excessive bleeding and interactions with platelet therapy during cancer chemotherapy are of clinical concern. While the results of *in vitro* studies are consistent these results are not always translatable to the complex human system. While *in vitro* data, as well as some clinical studies and epidemiological evidence suggest that ginger inhibits platelet aggregation, the evidence is ambiguous with multiple limitations, particularly within the clinical data, which prevents firm recommendations being made. Limitations include the lack of standardisation of ginger preparations used, significant variations in dosage and time frame studied, and the high level of bias in the study designs used. Therefore, further research is needed to clearly define the safety, or otherwise, of ginger in patient population at increased risk of bleeding.[26]

A double-blind, multicentre trial with 576 patients indicated that supplementing with ginger (0.5g to 1.0g liquid ginger root extract) significantly aids in reduction of the severity of acute chemotherapy induced nausea in adult cancer patients.[27]

In another study researchers observed reductions in the prevalence of nausea in 100 patients with breast cancer when 1.5g powdered dried ginger root in three divided doses every eight hours was added to an antiemetic therapy for four days following chemotherapy.[28]

A combination study found that 1.5g per day of ginger taken with granisetron plus dexamethasone (standard antiemetic therapy in chemotherapy in patients with advanced breast cancer) was more effective at reducing chemotherapy induced nausea and vomiting than granisetron plus dexamethasone alone. A significantly lower prevalence of nausea, vomiting and retching was observed in the six to 24 hour post chemotherapy period.[29]

Ginger (500mg twice daily) was effective in ameliorating antiretroviral induced nausea and vomiting in a placebo controlled randomised controlled trial involving 102 HIV positive patients.[30]

Motion Sickness

A double-blind, randomised, placebo controlled crossover study showed positive benefits with ginger pretreatment on prolonging time before nausea, shortening recovery time and effectively reducing nausea. This study used pretreatment doses of 1000mg and 2000mg, which were also shown to reduce tachygastria (electrical activity in the stomach) and plasma vasopressin (antidiuretic hormone). The researchers hypothesised that ginger ameliorates the nausea associated with motion sickness by preventing the development of gastric dysrhythmias and the elevation of plasma vasopressin.[31]

Postoperative Nausea

According to a thorough 2018 meta-analysis ginger decreases the severity of postoperative nausea and vomiting and may lower the incidence. This in turn may reduce antiemetic drug demand suggesting that ginger may be a useful alternative to antiemetic medications to alleviate postoperative nausea and vomiting. Ginger was also found to be safe and well tolerated. Ten randomised trials including a total of 918 patients were pooled for the statistical analysis.[32]

Based on a 2017 simple randomised, double-blind, single dose, parallel group clinical trial study researchers recommend administration of 500mg oral ginger one hour before an operation to control the severity of postoperative nausea and vomiting

in patients undergoing laparoscopic gall bladder removal. In this study ginger was compared with ondansetron (Zofran: used to prevent nausea and vomiting in some cases). The participants included 100 patients with cholelitiasis who were candidates for laparoscopic cholecystectomy.[33]

Ginger can be used for the prevention of nausea and vomiting during caesarean section under spinal anesthesia a 2016 study concluded. In this double-blind randomised clinical trial 92 pregnant women, each of whom underwent a caesarean section under spinal anesthesia, were divided in two groups: a control group and an intervention group. The intervention group received 25 drops of ginger extract in 30mL of water and the control group received 30mL of water one hour before surgery.[34]

Powdered ginger (2g) was administered to 239 women undergoing elective caesarean section at term in order to evaluate the effects on intra- and post-operative nausea and vomiting. Ginger reduced the number of episodes of intraoperative nausea compared to placebo but had no effect on the incidence of nausea, vomiting or pain during or after elective caesarean section.[35]

Gastrointestinal Activity

In a double-blind randomised controlled trial involving 24 healthy volunteers ginger (1.2g in three capsules) was found to accelerate gastric emptying and stimulate antral (stomach cavity) contractions, a result that was confirmed in a follow up double-blind randomised controlled trial using the same amount of ginger in 11 patients with functional dyspepsia.[36,37]

Anti-inflammatory, Antispasmodic, Anodyne and Analgesic Activity

In the early 1970s it was discovered that nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the biosynthesis of prostaglandins. Not long after, ginger was found to contain constituents that inhibit prostaglandins synthesis too. This finding provided a sound scientific rationale for its anti-inflammatory effects. Subsequent studies revealed that some of the constituents of ginger have pharmacological properties similar to the novel class of dual acting NSAIDs. Compounds in this class can inhibit arachidonic acid metabolism through both the cyclooxygenase (COX) and lipoxygenase (LOX) pathways and have notably fewer side effects than conventional NSAIDs. Different animal studies revealed that orally prescribed dried ginger or ginger extract can reduce acute inflammation. Several clinical studies support the value of ginger for the treatment of osteoarthritis, and in some cases, a significant reduction in knee pain was reported. In some of these trials ginger relieved pain and swelling to varying degrees in patients with osteoarthritis, rheumatoid arthritis and muscular pain without causing serious adverse effects even after long periods of use.[38]

In a 2017 randomised, double-blind clinical trial on 67 healthy adults with at least one impacted lower third molar (an acute pain model) were randomly allocated into three groups, Ibuprofen, ginger and placebo, to investigate the onset of analgesic action. The results showed that ginger is as effective as Ibuprofen in the management of postsurgical complications including pain.[39]

A recent review concluded that constituents in ginger could provide symptomatic relief in rheumatoid arthritis and may also provide total relief by stopping bone destruction.[40]

A recent meta-analysis of five trials on 593 patients found ginger to be modestly efficacious and reasonably safe for the symptomatic treatment of osteoarthritis. Patients given ginger were more than twice as likely to discontinue treatment compared to placebo.[41]

Ginger has been shown to be effective in reducing pain on movement, handicap and knee circumference in patients with inflammation of the knee joint. A double-blind, placebo controlled, crossover study showed that 250mg of the ginger extract taken four times daily for six months was significantly more effective than placebo in reducing pain and disability in 29 osteoarthritis patients.[42]

Following a 2018 prospective clinical study on 23 patients who took ginger it could be recommended as an adjunct to routine medical treatment for decreasing side effects following tonsillectomy. Ginger relieved pain, accelerated wound healing and patients had earlier oral intake which ensures they recover rapidly and shortens their hospital stay.[43]

A 2018 study found that ginger was as effective as Novafen (a strong analgesic) at relieving pain in girls with primary dysmenorrhoea. This crossover clinical trial study was done on 168 girls receiving 200mg of

ginger at the beginning of pain every six hours for two cycles.[44]

A recent study concluded that in treating symptoms of dysmenorrhoea ginger is superior to muscle relaxation exercises. One gram of ginger was administered twice a day with warm water after meals during the first three days of menstruation.[45]

A similar clinical trial assessing the effectiveness of ginger in providing relief to 70 women with primary dysmenorrhoea found that at the end of the study period 82.85% of the participants in the experimental group reported symptom improvement compared to 47.05% of the participants in the placebo group.[46]

Ginger is as effective as mefenamic acid (an NSAID) on pain relief in primary dysmenorrhoea. In this recent randomised clinical trial 122 women with moderate to severe primary dysmenorrhoea were randomly allocated to the ginger and mefenamic groups. The mefenamic group received 250mg capsules every eight hours and the ginger group received 250mg capsules every six hours from the onset of menstruation until pain relief lasted two cycles.[47]

Ginger was tested in primary dysmenorrhoea in comparison with ibuprofen and mefenamic acid. Ginger was as effective as the pharmaceuticals and no significant differences were found between the study groups in relief, stability or aggravation of symptoms. This was a double-blind comparative clinical trial on 150 women. The ginger group took 250mg capsules of ginger powder four times a day for three days from the start of their menstrual period. Members of the other groups received 250mg mefenamic acid or 400mg ibuprofen capsules, respectively, on the same protocol.[48]

A randomised controlled trial based on a sample of 120 students with moderate or severe primary dysmenorrhoea found that treatment with 500mg of ginger three times a day (1.5g daily) for five days had a statistically significant effect on relieving the intensity and duration of pain.[49]

In a double-blind, placebo controlled clinical trial of healthy volunteers daily consumption of 2g of raw or heated ginger for 11 days was found to reduce eccentric exercise induced muscle pain when compared to placebo.[50]

The addition of ginger to NSAIDs may contribute to the treatment of migraine a 2018 double-blind placebo controlled randomised clinical trial concluded. Previous studies have demonstrated the analgesic effects of ginger in different conditions but evidence about its efficacy in migraine treatment is scarce. Thirty adults with episodic migraine (one to six migraine attacks per month) with or without aura received 400mg of ginger in addition to an intravenous drug (100mg of ketoprofen) to treat the migraine attack. Patients treated with ginger showed significantly better clinical response and ginger treatment promoted reduction in pain and improvement on functional status at all times assessed.[51]

Antioxidant, Antiproliferative and Chemoprotective Activity

A double-blind randomised controlled trial involving 60 healthy middle-aged women who received 800mg of ginger per day for one month or placebo found that when compared to placebo active treatment resulted in statistically significant improvements in attention, cognitive processing and working memory, including speed of recall and quality of memory. As a result the researchers suggested ginger is a potential brain tonic to enhance cognitive function for middle-aged women.[52]

A 2013 *in vitro* study indicated that the use of ginger extract might be a safe approach for acute monocytic leukemia. Ginger in methanol showed distinctive anticancer activities when examined for its antiproliferative activities against acute monocytic leukemia cells.[53]

In a recent study *in vitro* and *in vivo* anticancer activity has been demonstrated for whole ginger extract in the management of prostate cancer. Whole ginger extract exerted significant growth inhibitory and death inducing effects in a spectrum of prostate cancer cells. Comprehensive studies have confirmed that ginger disturbed 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. Daily oral feeding of 100mg/kg body weight of ginger inhibited growth

and progression of prostate cancer transplants in approximately 56% of mice. Tumour tissue from ginger treated mice showed reduced proliferation index and widespread apoptosis compared with controls. Although the constituent phytochemicals present in ginger, in particular gingerols, shogaols and paradols, are being rigorously tested for their anticancer properties it is becoming increasingly recognisable that the gainful effects of herbs, fruits and vegetables are due to an additive and/or synergistic interplay of the composite mixture of phytochemicals present in whole foods rather than the constituent single agents alone. In the context of ginger sufficient evidence suggests that achievable plasma concentrations of individual phytochemicals are in a very low micromolar range (2µg/ml or less). In addition these phytochemicals are found primarily in the form of their non-active glucuronide or sulphate metabolites and therefore the anticancer effects observed with much higher concentrations *in vitro* may not be relevant *in vivo*. The researchers suggest that there is sufficient accumulating evidence which suggests that the repertoire of phytochemicals present in dietary agents works together through complementary and overlapping mechanisms to present optimal cancer chemopreventive and therapeutic benefits. It was with this mindset that the researchers did their study. In light of the accumulating data that suggests that the synergistic effects of the constituent phytochemicals in plants are accountable for their actions, the remarkable anticancer activity of whole ginger without any detectable toxicity, certainly underscores the importance of using whole extracts.[54]

Antimicrobial Activity

Ginger interferes with the colonisation of cells by enterogenic bacteria thus reducing diarrhoea and reducing bacterial load.[55]

Campylobacter jejuni is one of the most common bacterial causes of diarrhoea in the industrialised world and there are increasing reports of *Campylobacter jejuni* drug resistance against standard antibiotics. In a 2011 study an ethanol extract of ginger displayed one of the highest antiadhesion activity against *Campylobacter jejuni* in the herbal extracts screened.[56]

Antiobesity and Antidiabetic Activity

All of the relevant human, animal and *in vitro* studies were included in a 2018 study which systematically reviewed the effects of ginger on obesity management. Twenty-seven articles (six *in vitro*, 17 animal and four human studies) were reviewed. There was agreement among researchers on the efficient weight lowering effect of ginger in animal models of obesity whereas the results of the available limited clinical studies showed no or slight changes of measurements and body composition in subjects with obesity however most of the animal studies used ginger extract or its bioactive compounds in high doses instead of ginger powder used in the human trials. Given the lack of clinical data the researchers suggested more randomised controlled clinical trials are needed to make a definitive conclusion. It was suggested ginger could modulate obesity through various potential mechanisms including increasing thermogenesis, increasing lipolysis, suppression of lipogenesis, inhibition of intestinal fat absorption and controlling appetite.[57]

A randomised, double-blind placebo controlled trial of 88 diabetic participants recently found that 1g of ginger taken three times daily for eight weeks significantly improved fasting blood sugar, fasting insulin and insulin sensitivity.[58]

Hypolipidaemic Activity

According to a double-blind controlled clinical trial study of 85 volunteers, ginger (3g capsules per day in three divided doses) demonstrated clinically significant lipid lowering effects compared to controls. After 45 days of treatment triglyceride and cholesterol levels were reduced as well as a reduction in low density lipoprotein levels and an increase in high density lipoprotein levels.[59]

Indications

- Prophylaxis and treatment of nausea and vomiting for morning sickness in pregnancy, motion sickness, postoperative and drug induced nausea
- Digestive disorders including nausea, vomiting, dyspepsia, colic, gastritis, lack of appetite, diarrhoea especially bacterial diarrhoeal conditions with cramping (cholera, dysentery,

E. coli etc.) and gastrointestinal discomfort such as stomach cramping, bloating, indigestion, flatulence
- Inflammation including joint pain, osteoarthritis, rheumatoid arthritis
- Migraines
- To support mild feverish conditions such as colds and influenza
- Relief of mild bronchitis and other conditions requiring expectoration
- Ear infections
- Cardiovascular health
- Relief of dysmenorrhoea (due to stagnation) especially when it is improved by the application of heat or warm drinks
- Conditions requiring improved peripheral circulation
- Flavouring agent and adjuvant in formulations to promote the activity of the other herbs

Energetics

Hot, drying, pungent.

Use in Pregnancy

No adverse effects on pregnancy were observed in multiple studies of ginger for nausea and vomiting. Doses up to 2g per day of dried ginger root have been used safely.[60]

Contraindications

None known.

Drug Interactions

Avoid with nifedipine (sold under the brand name Adalat among others, a calcium channel blocker medication used to manage angina and high blood pressure) and tacrolimus (an immunosuppressive drug). Caution with antidiabetic and anticoagulant/antiplatelet (such as warfarin) drugs. Limited research suggests ginger may reduce severity of anaesthetic-induced post-operative nausea and vomiting if taken pre-treatment. Combining with antiemetic drugs and chemotherapy (e.g. cisplatin) may be beneficial but medical supervision is recommended.

Administration and Dosage

Liquid Extract:	1:2
Alcohol:	90%
Weekly Dosage:[61]	5 to 10mL

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