

Ginger (*Zingiber officinale*) Roots Treat Human Diseases

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Abstract: *Zingiber officinale*, commonly known as ginger, has a medicinal use as an anti-inflammatory agent for musculoskeletal diseases in Ayurvedic and Chinese medicine. *Z. officinale* is a member of the Zingiberaceae plant family, native to southern Asia, consisting of 49 genera and 1,300 species, 80–90 of which is Zingiber. It is a complex mixture of pharmacological compounds containing several hundred known constituents, including gingerols, beta-carotene, capsaicin, caffeic acid, curcumin, and salicylate. *Z. Officinale* possesses anti-emetic, positive inotropic and carminative properties to promote secretion of saliva and gastric juices and to inhibit platelet aggregation. Ginger contains a special group of compounds called diasyleheptanoids, which includes gingerenone. A very small amount of curcumin is also found in ginger. In addition to that it also contains small amounts of alkaloids, tannins, carotenoids, saponins, flavonoids, steroids, and cardinolides. The composition of fresh ginger oil contains more oxygenated compounds compared to dry ginger oil, making it more potent than dry ginger oil. There are more hydrocarbon compounds in dry ginger oil compared to fresh ginger oil. Monoterpene compounds are more active than sesquiterpene compounds. Dry ginger oil also has higher content of sesquiterpene hydrocarbons and have less activity compared to oxygenated compounds. Ginger oil (GEO) has been characterized to have a high content of sesquiterpene hydrocarbons, including β -sesquiphellandrene (27.16%), caryophyllene (15.29%), zingiberene (13.97%), α -farnesene (10.52%) and ar-curcumin (6.62%). The main stomachic constituents present in ginger are zinzibereine and gingeirol. A famous Ayurvedic drug trikatu, which is used against digestive disorders, contains ginger as the main constituent. Ginger acts as a purgative. Fresh ginger helps to remove constipation while dry ginger powder is a fecal astringent, meaning it dries up the watery portion of the feces and causes constipation. Ginger stimulates the flow of saliva, bile, and gastric secretions and is traditionally used to stimulate appetite, reduce flatulence, colic, and gastrointestinal spasms, and generally act as a digestive aid. Gingerols inhibit the growth of *Helicobacter pylori* associated with dyspepsia, peptic ulcer disease, and the development of gastric and colon cancer. These compounds demonstrate hypotensive and vasodilator properties and could be the causative agents in the reduction in blood pressure. Besides this, gingerdione has been shown to inhibit the production of 5-hydroxyeicosatetraenoic acid (5-HETE) and prostaglandins-F₂ (PGF₂) from arachidonic acid. Shogol appeared to be a preferential inhibitor of 5-HETE formation, while gingerol and dehydroparadol favored the inhibition of cyclooxygenase. Therefore, 6-gingerol exhibits preventive and/or therapeutic potential for the management of AD via augmentation of antioxidant capacity. An acetone extract containing gingerols, shogaols, and minor compounds like gingerenone A, gingerdiol, hexahydrocurcumin, and zingerone have been shown synergistically to produce dose-dependent anti-inflammatory effects. Gingerols and Gingerdiol are the main antifungal principles and extract of ginger powder is effective against several antifungal diseases. Ginger acts as anti-parasitic; proves the potential of methanolic extract of *Zingiber officinale* in the treatment of trypanosomiasis. Ginger is a powerful antineoplastic agent. Extracts of ginger suppress cell proliferation and act against resistance of cancerous cells. Ginger is having powerful antioxidant activity due to its oil which has protective effect on DNA damage. They have demonstrated this effect in much cell culture. Ginger oil has scavenging effects due to volatile oils and same has been proved in many studies. Ginger has preventive effect on lipid peroxidation and it inhibits or breaks its chain. Prostaglandin has been shown to have housekeeping and gastro-protective function by maintaining gastric mucosal integrity. It is effective in hepatitis C virus (HCV) infection where viral clearance is affected. The powerful anti-inflammatory action on prostaglandin synthesis help in menstrual cramps.

Keywords: *Zingiber officinale*, Ginger, Human Diseases.

INTRODUCTION

Worldwide, over 25 varieties of ginger are grown. Zingiber, ISR- Varada 2, Suprabha, Suruchi, Suravi, Himagiri, IISR Mahima, IISR Rejatha, Rio-de-Janerio, Nadia, and China are some of the important cultivars grown across the world (Shasikaran. et al., 2008). Ginger is also grown as a decorative plant. Patterned foliage, deliciously perfumed flowers in a rainbow palette of colors and surprising seedpods make the ginger plant an interesting and noteworthy ornamental plant. *Cautleya*, *Globba*, *Roscoea*, *Kaempferia*, and *Siphonochilus* are grown for ornamental and medicinal purpose but not for spice (Branney, 2005).

As ginger resembles fingers, pregnant women in China are advised to avoid ginger during pregnancy, as they might give birth to babies with more than five fingers. But after birth a woman

may take it for strength, to clean out all poison from her body, and to protect the newborn (Wong, 2001). In Malaysia and Indonesia, ginger soup is given to new mothers for 30 days after their delivery to help them sweat out impurities. In Arabian medicine, ginger is considered an aphrodisiac. Some Africans believe that eating ginger regularly will help repel mosquitoes and women of central Africa make belts of ginger roots to attract the attention of their husbands. Ginger flowers are traditionally worn by Hawaiian dancers (Gilani, 2005).

It is also used to make candy called Shoga no satozuke. In the traditional Korean Kimchi, ginger is finely minced and added to the ingredients of the spicy paste just before the fermenting process (Kim. et al., 2005). Some African ginger varieties contain 5.98 and 3.72g /100 proteins and fat (Shrin

Adel, 2010). Soluble and insoluble fibers are also found in ginger. Ginger is a good source of essential micronutrients such as potassium, magnesium, copper, manganese and silicon. Potassium and manganese help to build resistance to disease and protect the lining of heart, blood vessels and urinary passages. Silicon promotes healthy skin, hair, teeth, and nails and helps to assimilate calcium. Small amount of vitamins A, E and some amounts of B- vitamins and Vitamin C are also found in ginger rhizome (Adel and Prakash, 2010). Ginger is a complex substance consisting of more than 60 compounds (Srivastava. *et al.*, 2000).

Ginger contains a special group of compounds called diasyleheptanoids, which includes gingerenone. A very small amount of curcumin is also found in ginger. In addition to that it also contains small amounts of alkaloids, tannins, carotenoids, saponins, flavonoids, steroids, and cardinolides (Shrin Adel, 2010).

The composition of fresh ginger oil contains more oxygenated compounds compared to dry ginger oil, making it more potent than dry ginger oil. There are more hydrocarbon compounds in dry ginger oil compared to fresh ginger oil. Monoterpene compounds are more active than sesquiterpene compounds. Dry ginger oil also has higher content of sesquiterpene hydrocarbons and they are reported to have less activity compared to oxygenated compounds (Srivastava. *et al.*, 2000 Sasidharan and Menon, 2010). Ginger oil (GEO) has been characterized to have a high content of sesquiterpene hydrocarbons, including β -sesquiphellandrene (27.16%), caryophyllene (15.29%), zingiberene (13.97%), α -farnesene (10.52%) and ar-curcumin (6.62%) (El-Baroty. *et al.*, 2010).

The main stomachic constituents present in ginger are zinzibereine and gingeirol. A famous Ayurvedic drug trikatu, which is used against digestive disorders, contains ginger as the main constituent (Malhotra. *et al.*, 2003). Ginger acts as a purgative. Fresh ginger helps to remove constipation while dry ginger powder is a fecal astringent, meaning it dries up the watery portion of the feces and causes constipation (Malhotra. *et al.*, 2003).

Ginger stimulates the flow of saliva, bile, and gastric secretions and therefore is traditionally used to stimulate appetite, reduce flatulence, colic, and gastrointestinal spasms, and generally act as a

digestive aid (Blumenthal. *et al.*, 2000). Gingerols inhibit the growth of *Helicobacter pylori* associated with dyspepsia, peptic ulcer disease, and the development of gastric and colon cancer (Mahady. *et al.*, 2005).

These compounds demonstrate hypotensive and vasodilator properties and could be the causative agents in the reduction in blood pressure (Ajay *et al.*, 2003).

Besides this, gingerdione has been shown to inhibit the production of 5-hydroxyeicosatetraenoic acid (5-HETE) and prostaglandins-F₂ (PGF₂) from arachidonic acid. Shogol appeared to be a preferential inhibitor of 5-HETE formation, while gingerol and dehydroparadol favored the inhibition of cyclooxygenase (Nurtjahja-Tjendraputra *et al.*, 2003, Thomson. *et al.*, 2002). Therefore, 6-gingerol exhibits preventive and/or therapeutic potential for the management of AD via augmentation of antioxidant capacity (Lee. *et al.*, 2011). An acetone extract containing gingerols, shogaols, and minor compounds like gingerenone A, -gingerdiol, hexahydrocurcumin, and zingerone have been shown synergistically to produce dose-dependent anti-inflammatory effects (Young *et al.*, 2005).

Udea. *et al.*, (2010) investigated the ability of ginger extract to induce an immune response in RAW-264 cells after repeated oral administration to mice. They revealed that ginger extract augmented the serum corticosterone level and gradually induced tolerance and anti-inflammatory activity in mice.

A highly non-polar fraction of a ginger extract has been shown to possess anticonvulsant, anxiolytic, and anti-emetic activities in animals (Vishwakarma. *et al.*, 2002).

Ginger was found very effective in reversing the diabetic proteinuria and lowering serum glucose, cholesterol, and triacylglycerol levels in the ginger-treated diabetic rats compared with the control diabetic rats (Al-Amin, *et al.*, 2006). Singh. *et al.*, (2009) suggested that (6)-gingerol is an effective anti-diabetic agent via its ability to enhance insulin sensitivity and to decrease hyperlipidemia in type 2 diabetic animals. Furthermore, it is also beneficial against oxidative stress, thereby being helpful in delaying or preventing complications of diabetes and aging. Ginger ethanolic extract has shown in sulintropic action similar to chlorpropamide, a sulphonylurea

drug, and enhanced insulin sensitivity at the cellular level (Ojewole. *et al.*, 2006). Also, ethanolic ginger extract reduced plasma cholesterol and inhibited LDL oxidation in atherosclerotic apoE-deficient mice (Fuhrman. *et al.*, 2000). Moreover, addition of ginger (1 %) to a normal diet prevented the formation of free radicals and maintained the integrity of rat erythrocytes (Ahemed. *et al.*, 2000). The antioxidant potency of ginger has been attributed to gingerols that prevent the production of reactive oxygen species (Ali. *et al.*, 2008). At least two active components, 2-(4-hydroxy-3-methoxyphenyl) ethanol and 2-(4-hydroxy-3-methoxyphenyl) ethanoic acid, of ginger have shown aldose reductase inhibitor properties (Ali. *et al.*, 2008). Also, ginger inhibited serotonin-induced hyperglycemia and hypoinsulinemia by blocking its receptors (Al-Amin. *et al.*, 2006). Madko *et al.*, (2011) reported that a ginger, garlic and turmeric mixture significantly decreased serum total lipid and total cholesterol levels in healthy rats, which may be beneficial as a prophylaxis against hypercholesterolemia.

The aqueous extract of ginger possesses both antiglycating activity and ALR2 (aldolase reductase) inhibition (Saraswat. *et al.*, 2010, Saraswat. *et al.*, 2008). Regular consumption of ginger delays the progression and maturation of cataracts. This could be attributed to its ability to prevent the multiple changes associated with the accumulation of AGE (i.e., reduction in the carbonyl stress, inhibition of osmotic stress by reducing the activity of polyol pathway, and prevention of oxidative stress) (Saraswat, 2009).

Angiotensin I converting enzyme (ACE) is a metalloproteinase that catalyses two reactions, leading to constriction of blood vessels and hence blood pressure regulation (Schmaier, 2002). Ginger exhibited relevant ACE inhibitory activities indicating potential anti-hypertension activity likely related to non-phenolic compounds (Ranilla. *et al.*, 2010).

Ginger extract raises the thymus index, spleen index, and percentage of phagocytosis significantly, thus improving immunologic function (Schitteck. *et al.*, 2001). Dermicidin is a protein manufactured in the body's sweat glands, secreted into the sweat, and transported to the skin's surface where it provides protection against invading microorganisms, including bacteria, such as *E. coli* and *Staphylococcus aureus* (a common cause of skin infections), and fungi, including

Candida albicans (Alternative Medical Review, 2003, Schitteck. *et al.*, 2001).

Ginger extract and several of its constituent's exhibit antimicrobial activity in vitro and in vivo and anti schistosomal activity (Akoachere. *et al.*, 2002). At the same time, dry ginger oil (DG) was more active towards *Candida* and weaker against *Aspergillus niger*, *Penicillium* spp, and *Saccharomyces cerevisiae* (Sasidharan and Menon, 2010).

Ginger is a good source of antioxidant and most of the antioxidant components exhibit higher activities in alcoholic media. Hence, apart from its medicinal properties, ginger can also be used as antioxidants supplement (Adil and Prasad, 2010).

The anticancer properties of ginger are attributed to the presence of certain constituents such as [6]-gingerol and [6]-paradol, as well as some other constituents like shogaols and zingerone (Park. *et al.*, 2006). As suggested by Cancer Prevention Research, gingerols, the main active components in ginger, inhibit the growth of human colorectal cancer cells (Bode. *et al.*, 2003). Multiple mechanisms appear to be involved in gingerol action, including protein degradation as well as beta-catenin, PKCepsilon, and GSK-3beta pathways (Lee. *et al.*, 2008).

Ginger extracts have been shown to have antioxidant, anti-inflammatory, and anti-tumor effects on cells (Rhode. *et al.*, 2006). A pro-inflammatory state is thought to be an important contributing factor in the development of ovarian cancer (Rhode. *et al.*, 2006). However, ginger may be of special benefit for ovarian cancer patients because cancer cells exposed to ginger do not become resistant to its cancer-destroying effects (Rhode. *et al.*, 2006).

Ginger has been found to significantly inhibit mammary tumorigenesis and tumor growth in laboratory mice when fed in drinking water. [6]-gingerol, a component of ginger, has been shown to inhibit cell adhesion, invasion, and motility in ER-negative (estrogen independent) human breast cancer cells in the laboratory (Lee. *et al.*, 2007).

Ginger is on the Food and Drug Administrations (FDA) list of generally recognized as safe (GRAS) (Alternative Medical Review, 2003).

The use of ginger extract for improving the qualities of tough meat could prove to be a boon to the meat industry (Naveen. *et al.*, 2001).

El-Baroty et al (2010) reported that cinnamon and ginger essential oils can be used as a preventer of cellular damage due to spoilage bacteria and fungi. Both oils and bioactive components (at concentration levels 20 - 100 µg/ml) could be employed as natural food preservatives to prevent lipid peroxidation, which causes food spoilage.

Ginger is useful when taken internally, if menstrual pain is due to ischemic cramp (lack of uterine blood supply) (Alternative Medical Review, 2003). It is also good in the form of hot compresses for abdominal cramps, headaches, and joint stiffness.

Ginger therapy is also not recommended in children less than two years (Heck. *et al.*, 2000 and Vaes. *et al.*, 2000).

Zingiber officinale, commonly known as ginger, has a long tradition of medicinal use as an anti-inflammatory agent for musculoskeletal diseases in Ayurvedic and Chinese medicine (Ali *et al.*, 2008). *Z. officinale* is a member of the Zingiberaceae plant family, native to southern Asia, consisting of 49 genera and 1,300 species, 80–90 of which is Zingiber. It is a complex mixture of pharmacological compounds containing several hundred known constituents, including gingerols, beta-carotene, capsaicin, caffeic acid, curcumin, and salicylate (Altman and Marcussen, 2001). Previous investigations of varying quality have suggested that *Z. Officinale* possesses anti-emetic, positive inotropic and carminative properties to promote secretion of saliva and gastric juices and to inhibit platelet aggregation (Altman and Marcussen, 2001).

Several of its chemical constituents, including gingerols, shogaols, paradols, and zingerone, have demonstrated anti-inflammatory actions in vitro, inhibiting leukotriene synthesis, the activity of cyclooxygenase enzymes (COX⁻¹ and COX⁻²), production of interleukins (Il-1 and Il-12), and tumor necrosis factor alpha in activated macrophages (Iwaskai et al., 2006 and Lanz *et al.*, 2007). In addition, it has been suggested that *Z. officinale* and its constituents particularly shogaols have agonizevallinoid (capsaicin) receptors TRPV1, which are involved in the central and peripheral processing of noxious stimuli (Iwaskai. *et al.*, 2006 and Black. *et al.*, 2010).

There is a growing literature that has focused on assessing the value of the analgesic and anti-inflammatory properties of *Z. officinale* in human participants, including a recent review that

evaluated the effectiveness of *Z. officinale* in the management of osteoarthritis (Leach and Kumar, 2008).

The rhizome of ginger plant has been used as a spice since several years across the globe. It was found that, ginger was one of wildy used herbs in traditional Chinese, Ayurveda, Europe and America (Avato. *et al.*, 2000; Kamtchoung *et al.*, 2000; Afzal *et al.*, 2011; Grzanna. *et al.*, 2005).

The mode of administration of ginger is oral, intra muscular (IM) and topically (Barnes. *et al.*, 2002; Chrubasik. *et al.*, 2005; Shukla and Singh, 2007). Historically, it has been used to treat nausea, vomiting, rheumatism, baldness, respiratory diseases and bleeding disorders (Young. *et al.*, 2006; Kim. *et al.*, 2005; Kelly. *et al.*, 2009).

It is cultivated from Asia to Africa and used everywhere as a cooking spice. It is also useful in case of chills. In India, it is widely consumed in dose of 8-10 g as a flavouring agent (Kelly. *et al.*, 2009).

Ginger enhances blood circulation throughout the body by stimulation of the heart muscle and by diluting circulating blood. This enhances cellular metabolism and helps to relief cramp and tension (Ernst and Pittler, 2000; Chaiyakunapruk. *et al.*, 2006).

It helps to reduce atrial blood pressure by blocking calcium channel or by acting on muscarinic receptor (Ernst and Pittler, 2004; Portoni *et al.*, 2003; Ozgoli and Goli, 2009; Vutyavanich *et al.*, 2001).

It also helps to increase serum HDL-cholesterol (Ernst and Pittler, 2004; Portoni. *et al.*, 2003; Ozgoli and Goli, 2009; Vutyavanich. *et al.*, 2001; Al-Awwadi, 2010; 2013).

Ginger is also very useful in cases of ulcerogenesis due to its antioxidant activities (Gull. *et al.*, 2012; Dugasani. *et al.*, 2010; Halvorsen. *et al.*, 2002).

It stimulates peripheral anti-cholinergic and ant-histaminic receptors and antagonises 5-hydroxytreptamine receptors in the GIT (Gull. *et al.*, 2012; Dugasani. *et al.*, 2010; Halvorsen. *et al.*, 2002).

It is also used to treat nausea after surgery and same has been proved in several randomised clinical trials. This effect is seen due to its action on the 5-HT3 receptor (Ajith. *et al.*, 2007; Krim. *et al.*, 2013; Waggas, 2009; Sabina. *et al.*, 2011; Ahmed. *et al.*, 2008).

The German Commission and Europe does not consider it as safe due to lack of published data (El-Sharaky. *et al.*, 2009; Nasri. *et al.*, 2013; Ajith. *et al.*, 2008 ; El-Abhar. *et al.*, 2008; Kyung. *et al.*, 2006).

It was found that Gingerols and Paradol have good anti-platelet and COX⁻¹ inhibitor properties (Mehdizadeh. *et al.*, 2012; Jagetia. *et al.*, 2004; Jagetia. *et al.*, 2003).

It also decreases cholesterol and triglyceride level. Long term usage helps to increase high-density lipoprotein cholesterol concentrations (Afzal. *et al.*, 2011; Kim. *et al.*, 2007; Li. *et al.*, 2012).

It is having proven history of treatment of rheumatic conditions (Avato. *et al.*, 2000; Afzal. *et al.*, 2011; Ha. *et al.*, 2012).

It also has been reported that ginger suppresses leukotriene biosynthesis by inhibiting 5-lipoxygenase (Ernst and Pittler, 2004; Nasri. *et al.*, 2013; Tjendraputra. *et al.*, 2001).

Ginger is showing anti-inflammatory effect by suppression of PG synthesis and also interference in cytokine signalling (Uz. *et al.*, 2009; Mahmoud. *et al.*, 2012).

In many countries, ginger is used to preserve food (Ernst and Pittler, 2004; Liao. *et al.*, 2012; Chen. *et al.*, 2009).

Ginger has shown antiviral effect; however, more published literature is needed to prove efficacy (Ernst and Pittler, 2004, Ha. *et al.*, 2012; Lantz. *et al.*, 2007).

Ginger has shown good antimicrobial effect against both Gram positive and negative bacteria; however, severally, this effect is reduced due to heating (Jagetia. *et al.*, 2004; Ha. *et al.*, 2012; Tjendraputra. *et al.*, 2001; Kubra. *et al.*, 2013).

Gingerols and Gingerdiol are the main anti-fungal principles and extract of ginger powder is effective against several antifungal diseases (Ernst and Pittler, 2004; Ramkissoon *et al.*, 2012; Mallikarjuna. *et al.*, 2008; Nasri. *et al.*, 2013).

Ginger acts as anti-parasitic; study shows the in vivopotential of methanolic extract of Zingiber officinale in the treatment of trypanosomiasis (Halvorsen. *et al.*, 2002; Jagetia. *et al.*, 2003; Kubra. *et al.*, 2013; Duarte, 2016; Kumar. *et al.*, 2015; Choi. *et al.*, 2013; Saraswat, 2010; Pushpanathan, 2008).

Ginger is a powerful antineoplastic agent. In several studies, extracts of ginger suppress cell proliferation and act against resistance of cancerous cells (Barnes. *et al.*, 2002; Ernst and Pittler, 2000; Nasri. *et al.*, 2013; Kumar. *et al.*, 2015; Saraswat, 2010).

Ginger is having powerful antioxidant activity due to its oil which has protective effect on DNA damage. They have demonstrated this effect in many cell culture (Chaiyakunapruk *et al.*, 2006; Ramkissoon. *et al.*, 2012; Kabuto . *et al.*, 2005; Mahmoud. *et al.*, 2012; Al-Awwadi, 2010; 2013).

Ginger oil has scavenging effects due to volatile oils and same has been proved in many studies (Avato. *et al.*, 2000; Kamtchoung. *et al.*, 2000; Kumar. *et al.*, 2015; Pushpanathan, 2008).

Ginger has preventive effect on lipid peroxidation and it inhibits or breaks its chain (Afzal. *et al.*, 2011).

Studies have suggested that ginger may improve insulin sensitivity in body. The mineral element of ginger is effective for the same (El-Sharaky. *et al.*, 2009; El-Abhar. *et al.*, 2008; Jagetia. *et al.*, 2004; Choi. *et al.*, 2013 ; Pushpanathan, 2008).

Prostaglandin has been shown to have housekeeping and gastro-protective function by maintaining gastric mucosal integrity (El-Sharaky. *et al.*, 2009; Ajith. *et al.*, 2008; Duarte, 2016).

Ginger modulates genetic pathway, acts on tumour suppression of genes and modulates biological Activities (Jagetia. *et al.*, 2004; Ha. *et al.*, 2012; Duarte, 2016).

Ginger has powerful antiviral effect. It is effective in hepatitis C virus (HCV) infection where viral clearance is affected (Chaiyakunapruk. *et al.*, 2006; Kubra. *et al.*, 2013).

The powerful anti-inflammatory action on prostaglandin synthesis help in menstrual cramps (Halvorsen *et al.*, 2002; Mallikarjuna. *et al.*, 2008; Mahmoud. *et al.*, 2012; Kubra. *et al.*, 2013).

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