

Ginger (*Zingiber officinale*) Compounds Reduces Human Health Risk

Muhammad Arshad Ullah^{1*} , Ali Hassan² , Ameer Hamza³ 

¹ Pakistan Agricultural Research Council, Islamabad, Pakistan

² PMAS- University of Arid Agriculture, Rawalpindi, Pakistan

³ COMSATS- Biosciences Department, Islamabad Campus, Pakistan

*Corresponding Author: Muhammad Arshad Ullah, Pakistan Agricultural Research Council, Islamabad, Pakistan.

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Abstract

Ginger, the root of the plant *Zingiber officinale* roscoe that belongs to the family Zingiberaceae, is globally one of the most commonly used spice and medicinal agent. Chemical analysis of ginger shows that it contains over 400 different compounds. The major constituents in ginger rhizomes are carbohydrates (50-70%), lipids (3-8%), terpenes, and phenolic compounds. Terpene components of ginger include zingiberene, β -bisabolene, α -farnesene, β -sesquiphellandrene, and α -curcumene, while phenolic compounds include gingerol, paradols, and shogaol. These gingerols (23-25%) and shogaol (18-25%) are found in higher quantity than others. Besides these, amino acids, raw fiber, ash, protein, phytosterols, vitamins (e.g., nicotinic acid and vitamin A), and minerals are also present. The characteristic odor and flavor of ginger are due to a mixture of volatile oils like shogaols and gingerols. Active component of ginger is used as alaxative and antacid medication. It is also used to warm the body for boosting the circulation and lowering high blood pressure. Because of its warming effect, ginger acts as antiviral for treatment of cold and flu. Ginger is also used as a flavoring agent in foods and beverages and as a fragrance in soaps and cosmetics. Ginger and its active constituent suppress the growth and induce apoptosis of variety of cancer types including skin, ovarian, colon, breast, cervical, oral, renal, prostate, gastric, pancreatic, liver, and brain cancer. These properties of ginger and its constituents could be associated with antioxidant, anti-inflammatory and antimutagenic properties as well as other biological activities.

Fresh ginger oil was more effective than the dry ginger in inducing the antimicrobial effects. Fresh ginger is more abundant in oxygenated compounds and the observed variance in the antimicrobial effects is possibly due to this. The antibacterial effects of the fresh ginger oil in standardized twenty five bacterial strains (20 serotypes of *Salmonella* and 5 species of other enterobacteria) commonly involved in the spoilage of food and those to be associated with food borne illness and observed the antibacterial effects. Among all spices, it exhibits one of the greatest diversity of uses, such as in dietary supplements, beverages (such as ginger ales), and food products (such as in curry powder, confectionaries, soups, jams, and baked goods).

The extract was observed to scavenge, superoxide, hydroxyl, nitric oxide and ABTS radicals in a dose-dependent manner in vitro. The important constituent 6-gingerol is shown to possess good antioxidant effects, scavenger of peroxy radicals (and cause a dose-dependent inhibition of nitric oxide production). Cell free assays have also shown that the ginger extract prevents enzymatic lipid peroxidation, cumene hydroperoxide and iron/ascorbate-induced oxidation of the membrane lipids. The antioxidant activity of ginger extract was retained even after boiling for 30 min

at 100 degrees $^{\circ}$ C, indicating that the spice constituents were resistant to thermal denaturation and suggesting that in addition to imparting flavor to the food, ginger possess potential health benefits by inhibiting the lipid peroxidation. Ginger oil is also reported to inhibit the H₂O₂-induced oxidative damage.

The extract also showed good thermal stability and exhibited 85.2% inhibition of peroxidation of linoleic acid when heated at 185 $^{\circ}$ C for 120 min indicating its usefulness. The incorporation of ginger rhizome extract in beef patties were effective in controlling lipid oxidation and color changes during cold storage and that the effects were better than that of the commercial antioxidants, sustane 20 and sustane HW-4.

A recent randomized, double-blind, placebo-controlled trial in 162 cancer patients found that ginger provided no additional benefit in reducing prevalence or severity of acute or delayed chemotherapy-induced nausea and vomiting when given with 5-HT₃receptor antagonists and/or aprepitant.

Key words: ginger; zingiberaceae; bacterial; brain cancer

Introduction:

Ginger (*Zingiber officinale*), a member of the Zingiberaceae family, is a popular spice used globally especially in most of the Asian countries (Demin and Yingying, 2010). Chemical analysis of ginger shows that it contains over 400 different compounds. The major constituents in ginger rhizomes are carbohydrates (50-70%), lipids (3-8%), terpenes, and phenolic compounds (Grzanna et al., 2005). Terpene components of ginger include zingiberene, β -bisabolene, α -farnesene, β -sesquiphellandrene, and α -curcumene, while phenolic compounds include gingerol, paradols, and shogaol. These gingerols (23-25%) and shogaol (18-25%) are found in higher quantity than others. Besides these, amino acids, raw fiber, ash, protein, phytosterols, vitamins (e.g., nicotinic acid and vitamin A), and minerals are also present (Shukla and Singh, 2007).

Other gingerol- or shogaol-related compounds (1-10%), which have been reported in ginger rhizome, include 6-paradol, 1-dehydrogingerdione, 6- gingerdione and 10-gingerdione, 4-gingerdiol, 6-gingerdiol, 8-gingerdiol, and 10-gingerdiol, and diarylheptanoids (Ali et al., 2008). The characteristic odor and flavor of ginger are due to a mixture of volatile oils like shogaols and gingerols (Sasidharan and Nirmala Menon, 2010). It was also known in Europe from the 9th century and in England from the 10th century for its medicinal properties (Harold, 2004). Active component of ginger is used as a laxative and antacid medication. It is also used to warm the body for boosting the circulation and lowering high blood pressure. Because of its warming effect, ginger acts as an antiviral for treatment of cold and flu (Qidwai et al., 2003). Ginger is also used as a flavoring agent in foods and beverages and as a fragrance in soaps and cosmetics (Alam, 2013).

Evidences from in vitro, animal, and epidemiological studies suggest that ginger and its active constituent suppress the growth and induce apoptosis of variety of cancer types including skin, ovarian, colon, breast, cervical, oral, renal, prostate, gastric, pancreatic, liver, and brain cancer. These properties of ginger and its constituents could be associated with antioxidant, anti-inflammatory, and antimutagenic properties as well as other biological activities (Srinivasan,

2014).

Thus, ginger extract promotes ulcer healing by acting as an antioxidant and prevents gastricmucosal damage (Ko and Leung, 2010).

It is also reported to be effective in ameliorating the side effects of conventional therapeutic agents including γ -radiation, doxorubicin, and cisplatin by regulating P-glycoprotein (Pereira et al., 2011). Thus ginger extract exhibits chemosensitizing effects in certain neoplastic cells in vitro and in vivo.

In gastric cancer cell lines, zerumbone inhibited cell proliferation, VEGF expression, and NF- κ Bactivation (Tsuboi et al., 2014).

Park et al. (2006) have shown that 6-gingerol inhibits the growth of pancreatic cancer HPAC and BxPC-3 cells through cell cycle arrest at G1 phase and independent of p53 status. Ginger, the root of the plant *Zingiber officinale* roscoe that belongs to the family Zingiberaceae, is globally one of the most commonly used spice and medicinal agent. The plant is known as Sringavera in Sanskrit and it is speculated that this term may have given way to Zingiberi in Greek and then to the Latin term Zingiber (Vasala, 2004).

Ginger has been cultivated for thousands of years as a spice. It is an important cash crop in India and is grown primarily in the states of Kerala, Karnataka and Northeast India (Vasala, 2004). Of the Indian varieties, the Cochin and Calicut ginger, have a lemon-like bite note and are popular (Vasala, 2004). When compared to the Indian varieties, the Chinese ginger is low in pungency and is principally exported as preserves in sugar syrup or as sugar candy (Vasala, 2004). The yield and oil characteristic and content vary with cultivar and environmental factors. There are many local varieties grown over the world. More than 400 accessions of ginger are maintained at the Indian Institute for Spice Research in Calicut, Kerala, India (Vasala, 2004). The following Indian cultivars are results of selection by the Indian Institute for Spice Research with high yield and high oil content (Vasala, 2004). With respect to the African varieties, the Jamaican ginger is highly popular basically due to its delicate aroma and fine-textured powder, while the Nigerian and Sierra Leone

dried ginger possess camphoraceous and coarser odor and are rich in both aroma and pungency factors (Vasala, 2004). The composition of fresh ginger oil shows that it contains more of oxygenated compounds (29%) compared to dry ginger oil (14%) (Sasidharan and Menon, 2010). The higher content of geranal and other oxygenated compounds makes fresh ginger oil more potent than dry ginger oil (Sasidharan and Menon, 2010). The content of hydrocarbon compounds are more in dry ginger oil compared to fresh ginger oil (Sasidharan and Menon, 2010). Additionally, zingiberol is also another predominant aromatic component of the rhizome (Vasala, 2004).

Ginger oil has been reported to possess antimicrobial effects and studies by, Natta and co workers (2008) have shown that the essential oil of ginger extracted by hydro distillation possess high antibacterial effects on food pathogens (*S. aureus*, *B. cereus* and *L. monocytogenes*), with a minimum concentration to inhibit *B. cereus* and *L. monocytogenes* of 6.25 µg/ml (Natta et al., 2008). Subsequent studies have shown that the oil extracted from the leaf and rhizome were moderately active against the Gram-positive bacteria *Bacillus licheni formis*, *Bacillus spizizenii* and *Staphylococcus aureus*, and the Gram-negative bacteria *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas stutzeri* (Sivosathy et al., 2011).

Studies with the gram-positive bacteria, *Bacillus subtilis* (NCIM 2162), *Staphylococcus aureus* (NCIM 2602), *Micrococcus luteus* (NCIM, 2704), and gram-negative bacteria, *Escherichia coli* (NCIM 2576), *Pseudomonas aeruginosa* (NCIM, 2200), *Proteus vulgaris* (NCIM, 2813), *Klebsiella pneumoniae* (NCIM, 2957) have also shown ginger oil to be effective (Sayyad and Chaudhari, 2010). The results indicate that the antibacterial effects were as follows *Bacillus subtilis* > *Staphylococcus aureus* > *Escherichia coli* = *Proteus vulgaris* > *Pseudomonas aeruginosa* > *Micrococcus luteus* > *Klebsiella pneumoniae* (Sayyad and Chaudhari, 2010). Ginger oil has also been shown to possess antibacterial effects on the growth of psychrotrophic food-borne bacteria (Fabio et al., 2003).

On a comparative note, recent studies by Sasidharan and Menon, (2010) have shown that the fresh ginger oil was more effective than the dry ginger in inducing the antimicrobial effects. Fresh ginger is more abundant in oxygenated compounds and the observed variance in the antimicrobial effects is possibly due to this (Sasidharan and Menon, 2010). Nanasombat and Lohasupthawee (2005) studied the antibacterial effects of the fresh ginger oil in standardized twenty five bacterial strains (20 serotypes of *Salmonella* and 5 species of other enterobacteria) commonly involved in the spoilage of food and those to be associated with food borne illness and observed the antibacterial effects.

The extract was observed to scavenge, superoxide, hydroxyl, nitric oxide and ABTS radicals in a dose-dependent manner in vitro (Baliga et al., 2003; Jagetia et al., 2004). The important constituent 6-gingerol is shown to possess good antioxidant

effects (Masuda et al., 2004), scavenger of peroxy radicals (and cause a dose-dependent inhibition of nitric oxide production (Ippoushi et al., 2003).

Cell free assays have also shown that the ginger extract prevents enzymatic lipid peroxidation, cumene hydroperoxide and iron/ascorbate-induced oxidation of the membrane lipids (Shobana and Naidu, 2000).

The antioxidant activity of ginger extract was retained even after boiling for 30 min at 100 degrees o C, indicating that the spice constituents were resistant to thermal denaturation and suggesting that in addition to imparting flavor to the food, ginger possess potential health benefits by inhibiting the lipid peroxidation (Shobana and Naidu, 2000). Ginger oil is also reported to inhibit the H2O2-induced oxidative damage (Lu et al., 2003).

The extract also showed good thermal stability and exhibited 85.2% inhibition of peroxidation of linoleic acid when heated at 185°C for 120 min indicating its usefulness (Zia-ur-Rehman et al., 2003). Subsequent studies have also shown that the incorporation of ginger rhizome extract in beef patties were effective in controlling lipid oxidation and color changes during cold storage and that the effects were better than that of the commercial antioxidants, sustane 20 and sustane HW-4 (Mansour and Khalil, 2010).

Discussion:

Among all spices, it exhibits one of the greatest diversity of uses, such as in dietary supplements, beverages (such as ginger ales), and food products (such as in curry powder, confectionaries, soups, jams, and baked goods) (Schwertner and Rios, 2008).

It has been a part of healing strategies in Asia, India, Europe, and the Middle East for centuries for treatment of such disorders as arthritis, stomach upset, asthma, diabetes, and menstrual irregularities, to name a few (Tapsell and Hemphill, 2006; Wang and Wang, 2005 and Ali et al., 2008). Ginger also contains about 1% to 3% volatile oil that imparts a distinctive odor to ginger and which is composed mainly of monoterpenoids and sesquiterpenoids, including camphene, borneol, zingiberene, sesquiphellandrene, and bisabolene (Chubrasik et al., 2005).

Sesquiterpenoids have a 15-carbon skeleton. Besides the pungent phenolic compounds (gingerols and shogaols), there are also bioactive diarylheptanoids and zingerone that are believed to contribute to its purported health benefits (Jiang et al., 2006).

Despite the widespread use of ginger and the numerous studies into its actions, there is limited information on bioavailability of the ginger components ginger oleoresin (Wang et al., 2009).

Furthermore, at 30 minutes after dosing, tissue levels were maximum and generally were greater than those levels in blood (Jiang et al., 2008).

A recent report, in which healthy humans received oral doses of ginger ranging from 100 mg to 2g, showed that major gingerol and shogaol constituents were readily absorbed and

appeared in the serum predominantly as glucuronide conjugates. Importantly, no free forms were detectable (Zick et al., 2008).

In another study, the degradation kinetics and products of [6]-gingerol and [6]-shogaol under varying physiological conditions were characterized in a model of stomach and intestine environments (Bhattaraj et al., 2007).

In vitro experiments using microsomal preparations from both humans and rodents confirm that [6]-gingerol is metabolized to a complex mixture of glucuronidated polar metabolites (Pfeifer et al., 2006).

There is also evidence that metabolism of [6]-gingerol, most notably by enzymes in rat liver but also by those of gut microorganisms, may affect the disposition of this ginger constituent (Nakazawa and Ohsawa, 2002).

The scientific literature provides evidence that ginger has a number of potential health benefits (Ernst and Pittler, 2006). This evidence suggests that ginger may help alleviate nausea, both during pregnancy and from other causes. Some research suggests positive benefits of ginger in alleviating inflammation, especially that contributing to osteoarthritis (Grzanna et al., 2005). Preliminary evidence is also available on ginger and relief of hypertension¹⁸ and that ginger intake may have a role in cancer prevention (Shukla and Singh, 2007). Finally, initial preclinical research demonstrates that ginger lowers blood cholesterol and blood glucose levels. Evidence for the benefit of ginger as an antiemetic in pregnancy is some of the strongest (Chubrasik and Pittler, 2005; Bryer, 2005; Sonkusare, 2008; Ozgoli et al., 2009 and Smith et al., 2004).

Yet, using higher doses of ginger (91 g/d) during pregnancy has been discouraged because of concerns about potential teratogenicity (Friedman, 2000 and Marcus and Snodgrass, 2005).

Nonetheless, there is, as yet, no direct clinical evidence that consumption of ginger by pregnant women is harmful (Westfall, 2004).

Conclusion:

Furthermore, the quality and integrity of ginger preparations manufactured for use by women during pregnancy need to be carefully established (Schwertner et al., 2006). There is a lack of consistent beneficial effect of ginger for use on motion sickness or kinetosis (White, 2007 and Cohen, 2007).

Findings from human studies are mixed (Manusirivithaya et al., 2004; Levine et al., 2008 and Hickok et al., 2007).

In this regard, a recent randomized, double-blind, placebo-controlled trial in 162 cancer patients found that ginger provided no additional benefit in reducing prevalence or severity of acute or delayed chemotherapy-induced nausea and vomiting when given with 5-HT₃receptor antagonists and/or aprepitant (Zick et al., 2009).

The findings from human studies examining ginger for amelioration of nausea and vomiting after surgery (mostly gynecological and lower extremity surgeries) are not consistent (Morin et al., 2004; Chaiyakunapruk et al., 2006;

Thompson and Potter, 2006 and Tavlan et al., 2006). The possible mechanisms behind any antiemetic action of ginger are not well characterized. In rats and humans, ginger constituents appear to have differing effects on gastrointestinal motility and transit times, which in part may be due to differences in experimental conditions and dosages used (Wu et al., 2008 and Ghayur and Gilani, 2006).

In rodents, ginger extracts have been demonstrated to possess cholinergic agonist actions, muscarinic antagonist-like effects, and antiserotonin actions. Ginger also may act on the 5-HT₃receptor ion-channel complex in the gastrointestinal tract (Abdel-Aziz et al., 2006 and Riyazi et al., 2007). In humans, ginger intake (1Y2 g) may block production of gastric prostaglandins and decrease plasma vasopressin release induced by circularvection (Lien et al., 2003 and Gonlachanvit et al., 2003).

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