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PHARMACOLOGICAL ACTIVITIES OF GINGER (*ZINGIBER OFFICINALE)*: A REVIW

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ABSTRACT

Zingiber officinale (ginger) has been used for thousands of years as culinary spice and medicinally. It has long been used for the treatment of migraine, bacterial dysentery, toothache, cold and diarrhea. Besides, it also has antibacterial, antifungal, antiparasitic, antiviral, antidiabetic, anti-inflammatory, antioxidant and anti-hypercholesterolaemic properties. It contains a wide variety of biologically active compounds. The major pharmacological activities of ginger appear to be due to gingerols and shogaols. It has not been associated with any significant adverse effects.

Key words: Ginger, antibacterial, antifungal, antiparasitic, gingerols, shogaols.

INTRODUCTION

The rhizome of *Zingiber officinale*, is a common constituent of diet worldwide (Penna *et al.*, 2003). Ginger has a long history of both culinary and medicinal use in Chinese, Japanese and Indian medicinal care with many claims about its usefulness (Leung, 1984). It has been reported that its extracts present many pharmacological activities (Penna *et al.*, 2003; Wang and Wang, 2005).

ACTIVE CONSTITUENTS

Ginger rhizome contains a wide variety of biologically active compounds (Duke and Beckstrom-Sternberg, 1999). The primary pungent agent of ginger is gingerol (Mishra *et al.*, 2004), with other gingerol analogues such as the shogaols (Shadmani *et al.*, 2004). Other constituents include ginger proteases, capsaicin and several sesquiterpenes for example zingiberol and zingiberenol. The major pharmacological activity of ginger appears to be due to the gingerol and shogaols (Suekawa *et al.*, 1984; Wohlmuth *et al.*, 2006).

Gingerols are biologically active compounds of ginger rhizome that make a significant contribution towards medicinal applications of ginger (Wohlmuth *et al.*, 2006). 6-gingerol, 8-gingerol and 10-gingerol are responsible for antifungal activity of ginger (Ficker *et al.*, 2003). Gingerols, however, are thermally labile due to the presence of a β-hydroxyketo group in the structure, and undergo dehydration readily to form the corresponding shogaols (Bhattarai *et al.*, 2001). 6-shogaol is also one of the active constituent of ginger (Hashimoto *et al.*, 2002; Murata *et al.*, 2002). Ginger oil, obtained by steam distillation of the rhizome of ginger, displays considerable compositional diversity, but is typically characterized by a high content of sesquiterpene (Wohlmuth *et al.*, 2006).

ANTIBACTERIAL ACTIVITY

Ginger has been found to be effective against the growth of both Gram-positive and Gram-negative bacteria (Martins *et al.*, 2001), including *Escherichia coli, Salmonella typhimurium* (Jagetia *et al.*, 2003), *Proteus vulgaris, Staphylococcus aureus* (Ekwenye and Elegalarn, 2005) and *Streptococcus viridans* (Schulick, 2001; Mascolo *et al.*, 1989).

Akoachere *et al.*, (2002) investigated the antibacterial activity of ginger on four respiratory tract pathogens viz., *Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae* and *Haemophilus influenzae*. They reported the minimum inhibitory concentration (MIC) of ginger extract as 0.0003-0.7 μg/ml and minimum bactericidal concentration (MBC) from 1.35-2.04 μg/ml. On the other hand, in a study extract of ginger was found only effective against *Bacillus cereus* whereas, *Staphylococcus aureus, Listeria monocytogenes, Escherichia coli* and *Salmonella infantis* were found resistant (Alzoreky and Nakahara, 2002). In contrast in another study ginger was found effective against *Escherichia coli* O157:H7 at 8^{o}C (Gupta and Ravishankar, 2005).

In a previous study, ginger rhizome only inhibited *Micrococcus luteus* while *Escherichia coli, Salmonalla typhimurium, Vibrio parahaemolyticus, Pseudomonas aeruginosa, Proteus vulgaris, Staphylococcus aureus, Mycobacterium pheli, Streptococcus faecalis* and *Bacillus cereus* were found resistant. It was also reported that its antibacterial activity was heat labile and lost within 20 minutes at 100^{o}C (Chen *et al.*, 1985). Furthermore, the

antimicrobial activity of extracts and essential oil of ginger was evaluated against five strains of *Listeria monocytogenes* and four strains of *Salmonella typhimurium* DT104. it was found that aqueous and ethanolic extracts of ginger had no effect whereas ginger oil only inhibited the strains of *Listeria monocytogenes* while all strains of *Salmonella typhimurium* DT104 were found resistant (Thongson *et al.,* 2005). In another study five *Listeria monocytogenes* isolates were tested against ginger oil, all (100%) isolates were found to be resistant (Byrd *et al.,* 2002).

Ginger oil was tested for antibacterial activity against *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853. It was to be weakly effective against only *Staphylococcus aureus* ATCC 25923 while showed no activity against *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 (Ontengo *et al.,* 1995). The essential oil of ginger was found to be weakly effective against 4 Gram positive bacteria (*Staphylococcus aureus, Bacillus cereus, Enterococcus faecalis, Listeria monocytogenes*) and 4 Gram negative bacteria (*Escherichia coli, Yersinia enterocolitica, Salmonella choleraesuis, Pseudomonas aeruginosa*). It was found that Gram positive strains were more sensitive as compared to Gram negative strains (Lopez *et al.,* 2005). Ginger extract also inhibits the growth of *Helicobacter pylori* which is a primary etiologic factor associated with the development of gastritis and peptic ulcers (Mahady *et al.,* 2003; Mahady *et al.,* 2005; O'Mahony *et al.,* 2005).

ANTIFUNGAL ACTIVITY

Ginger has pronounced antifungal activity against a wide variety of fungi (Martins *et al.,*2001), including strains that were highly resistant to amphotericin B and ketoconazol (Ficker *et al.,* 2003). An antifungal protein, isolated from ginger, exerted antifungal activity towards various fungi including *Botrytis cinerea, Fusarium oxysporum, Mycosphaerella arachidicola,* and *Physalospora piricola* (Wang and Ng, 2005). In another study antifungal activity of ginger oil was investigated against yeast and molds and concluded that ginger oil possesses anti fungal activity against *Candida albicans* (yeast), *Penicillium islandicum* and *Aspergillus flavus* (molds) (Lopez *et al.,* 2005).

ANTIPARASITIC AND ANTIHELMINTIC ACTIVITY

In 1990 a Japanese study showed that the gingerol and shogaol components of ginger could kill Anisakis larvae. Anisakis being one of the principle parasite, which find host in millions of people around the globe (Goto *et al.,* 1990). In a study it was found that ginger possesses *in vitro* antihelmintic activity in sheep, naturally infected with mixed species of gastrointestinal nematodes (Iqbal *et al.,* 2006).

ANTIVIRAL ACTIVITY

The inhibitory effect of ginger on the growth of influenza A/Aichi/2/68 (Aichi) virus was investigated in Madin-Darby Canine kidney (MDCK) cells. Direct addition of ginger to infected cells did not have any inhibitory effect. However, the ginger induced conditioned medium of a murine macrophages (Mphi) cell line exhibited an apparent inhibitory effect on MDCK cells without cytotoxicity. These findings suggested that ginger itself has no inhibitory effect on the growth of influenza virus, but could exert its effect via macrophage activation leading to production of tumor necrosis factor alpha (TNF-α) (Imanishi *et al.,* 2006).

ANTITUMOR ACTIVITY

A few studies have been conducted on the effect of ginger on carcinogenesis. *In vitro* ginger has selective anticancer activity (Surch *et al.,* 1999; Murakami *et al.,* 2003; Leal *et al.,* 2003; Kim *et al.,* 2005; Manju and Nalini, 2005). The results from a study, carried out by Miyoshi *et al.* (2003) provide biological evidence that ginger specific constituents, galanals A and B, are potential anticancer agents. Ginger also improves immunological functiove tumors (Liu and Zhu, 2002).

A study in mice found that orally administered ginger significantly reduced the occurrence of mammary tumors without adverse effects (Nagasawa *et al.,* 2002). Researches have found that extracts of ginger possess anti-skin tumor effects when placed directly on the skin of mice (Katiayar *et al.,* 1996). In addition it has been found that gingerol from ginger inhibits the tumor promotor Epstein-Barr virus (EBV) activation (Ohigashi *et al.,* 1994).

ANTIDIABETIC ACTIVITY

Ginger has been reported to be hypoglycaemic (Srinivasan, 2005). Akhani *et al.* (2004) studied the effect of ginger on streptozotocin-induced type I diabetic rats. They concluded that ginger has anti-diabetic activity. In another study aqueous extract of ginger rhizome was studied in streptozotocin and glucose-induced diabetic rats to evaluate its hypoglycaemic activity and concluded that aqueous extract of ginger rhizome exhibited hypoglycaemic activity in both streptozotocin and glucose-induced diabetic rats (Kalejaiye *et al.,* 2002).

ANTIOXIDANT ACTIVITY

Ginger contains antioxidant properties (Schulick, 2001; Lako *et al.,* 2004; Masuda *et al.,* 2004; Kuo *et al.,* 2005). Ginger has been found to inhibit lipid peroxidation in rat liver microcosms (Reddy and Lokesh, 1992) and successfully scavenge superoxide anions (Krishnakantha and Lokesh, 1993).In an American study 21 compounds were isolated from ginger. It was found that the most of the isolated compounds exhibited stronger antioxidative effect that alpha-tocopherol (Vitamin E) (Kikuzaki and Nakatani, 1994). The antioxidant powers of ginger have been proven in applications where ginger extract was added to meat products. The antioxodative effectiveness of ginger extract was further tested with fresh, frozen and precooked pork patties. The shelf life of all products was improved by the inclusion of ginger extract (Lee *et al.,* 1986).

ANTIEMETIC AND ANTIMOTION SICKNESS ACTIVITY

Ginger is probably most well known for its ability to reduce nausea (Flake *et al.,* 2004). It has been superior to placebo in studies on seasickness, morning sickness, motion sickness, chemotherapy-induced nausea, and pregnancy related nausea (Stewart *et al.,* 1991; Ernst and Pittler, 2000; Keating and Chez, 2002; Pongrojpaw and Chiamchanya, 2003; Lien *et al.,* 2003; Boone and Shields, 2005). Powdered ginger root has been compared to standard drugs used in cambating postoperative nausea and vomiting (Morin *et al.,* 2004; Chaiyakunapruk *et al.,* 2006). Tests have shown that the requirement for postoperative antiemetics was lower in patients receiving ginger. Ginger is an effective and promising prophylactic antiemetic, which may be especially useful for day case surgery (Phillips *et al.,* 1993).

It has been reported that ginger was effective in reducing post-operative nausea and vomiting (Bone *et al.,* 1990; Betz *et al.,* 2005). The ingestion of 1g of ginger in syrup in a divided dose daily may be useful in some patients experiencing nausea and vomiting in the 1st trimester of pregnancy (Keating and Chez, 2002).

A double-blind randomized clinical trial to investigate the effect of ginger on nausea and vomiting following gynaecological laparoscopic surgery was conducted by Arfeen *et al.* (1995). They found that ginger is effective in reducing nausea. Phillips *et al.* (1993) and Bone *et al.* (1990) reported that ginger is effective in reducing post-operative nausea and vomiting. In contrast Visalyaputra *et al.* (1998) found that ginger is ineffective in preventing the post-operative nausea and vomiting associated with diagnostic gynaecological laparoscopy.

Ginger is often advocated as beneficial for nausea and vomiting. Whether the herb is truly efficacious for this condition is, however, still a matter of debate (Ernst and Pittler, 2000). Ginger has long been used as an alternative medicine to prevent and treat motion sickness (Lien *et al.,* 2003; Scurr and Zinopin, 2004). Pharmacological studies of the antimotion sickness of ginger would indicate that ginger is effective in controlling motion sickness by the direct action of ginger's active compounds on the gastric system (Mowrey and Clayson, 1982; Holtmann *et al.,* 1989).

A report on the effects of ginger on motion sickness was reported in the British medical journal-The Lancet. In this clinical trial, 39 men and women who reported very high susceptibility to motion sickness were tested. Motion sickness was induced by being subjected to a rotating, tilted chair while blind folded under controlled conditions. It was found that ginger was significantly effective in reducing motion sickness than the antihistamine dimenhydrinate and a placebo (Grontved *et al.,* 1988). Some studies have, however, failed to show such an effect on either motion or sea sickness (Holtman *et al.,*1989).

ANTI-NFLAMMATORY ACTIVITY

Ginger possesses anti-inflammatory properties (Sharma *et al.,* 1994; Raji *et al.,* 2002; Thomson *et al.,* 2002; Grzanna *et al.,* 2005; Vendruscolo *et al.,* 2006; Zhou *et al.,* 2006). More than 200 drugs have been tested through the 1990's in order to find a cure for rheumatism and musculoskeletal ailments. These have included non-steroidal anti-inflammatory drugs, corticosteroids, gold salt, anti-rheumatic drugs, methorexate and cyclosporin. None of these is

found to be safe (Srivastava and Mustafa, 1992). A common side effect of treating inflammation with modern drugs is that ulcers in digestive system can be created or their condition made worse. Ginger cannot only relieve the symptoms of inflammation, it also protects the creation of digestive ulcers (Schulick, 1993).

GINGER AND THE CIRCULATORY SYSTEM

Ginger also stimulates the immune system (Tan and Vanitha, 2004). Ginger has been found to be beneficial in reducing platelets aggregation, which leads to coronary artery disease (Bordla *et al.,* 1997), therefore, decreases the risk of clotting, which may lead to either heart attack or stroke (Srivastava, 1964; Tognolini *et al.,* 2006), while having no effect on blood lipids and blood sugar (Bordla *et al.,* 1997). In other studies ginger was shown to be anti-hypercholestrolaemic (Giri *et al.,* 1984; Bhandari *et al.,* 2005). Similarly, Akhani *et al.* (2004) reported that treatment with ginger caused a decrease in serum cholestrol, serum triglyceride and blood pressure in diabetic rats.
The effect of an aqueous extract of ginger on serum cholesterol and triglyceride levels as well as platelet thromboxane-B2 and prostaglandin-E2 production was examined. The result of this study concluded that ginger has cholesterol-lowering and antithrombic activities (Thomson *et al.,* 2002).

OTHER ACTIVITIES

Fresh ginger has been used in eastern countries for many complains including rheumatism, bacterial dysentery, toothache, malaria and for cold and moist conditions such as excess mucus and diarrhea. In the west it is better known as digestive aid and for flatulence and colic (Geck, 2000). Respiratory disorders indicating ginger as a remedy are: asthama, chest trouble, pulmonary and catarrhal diseases, throat diseases and cold (Zaman and Khan, 1970). Ginger treatment has also been found to be useful in treatment of migrain, where it is proposed that pain relief from ginger may occur without any of the side effects that occur with standard treatments (Mustafa and Srivastava, 1990; Cady *et al.,* 2005).

Ginger is eminently useful in habitual flatulency, atonic dyspepsia, hysteria and enfeebled and relaxed habits, especially for old individuals (Ghayur and Gilani, 2005). It is excellent to relieve nausea, pain and cramps of stomach and bowels, and to obviate tenesmus. Ginger is occasionally of value in fever, particularly pain and movement of gases within the intestine (Felter and Lloyd, 1898). Apart from these, it also finds use in piles and gout and used as diuretic, sedative to pain, in urinary incontinence, cholera and pneumoniae (Nadkerni, 1976). Ginger oil obtained by steam distillation of the rhizome of ginger is also used in the beverages (Campanella *et al.,* 2003) and fragrance industries (Wohlmuth *et al.,* 2006).

Chinese medicine has incorporated ginger in remedies for the digestive system for centuries and it is regularly used as a calmative for stomach upsets. Other digestive benefits from ginger are the natural enzyme action on protein digestion (Thompson *et al.,* 1973), stimulation of digestion, pro-biotic support of the natural gut flora, anti-diarreal properties and liver protection (Schulick, 1993).

CONTRAINDICATIONS

Ginger has not been associated with any significant adverse effects in trials which are associated with other antiemetic medication (Holtmann *et al.,* 1989), except for some degree of heart burn sensation and rare cases of allergic reaction (Meyer *et al.,* 1995; O'Hera *et al.,* 1998). In some cases gastrointestinal upset is reported (Weidner and Sigwart, 2001). 6-gingerol is a potent mutagen, however, ginger juice also contains antimutagenic compounds that suppress 6-gingerol (Nakamura, 1982).

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