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Review Article

Ginger (*Zingiber officinale*): A Nobel Herbal Remedy

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A B S T R A C T

Now the trend is reversing towards the traditional medicines i.e. Phytotherapy. Ancient Ayurveda has described about the medicinal plants and their medicinal used in various diseases. Medicinal plants are generally known as "Chemical Goldmines" as they contain natural chemicals, which are acceptable to human and animal systems. Ginger is one which scientifically known as *Zingiber officinale*, belonging to family Zingiberaceae and the most important plant with several medicinal, nutritional and ethnomedical values therefore, used extensively worldwide as a spice, flavouring agent and herbal remedy. Traditionally, *Z. officinale* is used in Ayurveda, Siddha, Chinese, Arabian, Africans, Caribbean and many other medicinal systems to cure a variety of diseases like pain, nausea, vomiting, asthma, cough, inflammation, dyspepsia, loss of appetite, palpitaion, constipation and indigestion. The major phytochemicals of ginger root include gingerols, zingibain, bisabolene, oleoresins, starch, essential oil (zingiberne, zingiberole, camphen, cineole, borneol), mucilage, and proteins which were responsible for the medicinal property of ginger. This study is aimed to review the salient medicinal properties of ginger and is uses in treatment of various diseases.

Introduction

Phytotherapy (herbal medicine or Herbalism) is the study of plant science and use of plants and intended for medicinal purposes or for supplementing a diet. Plants have been the basis for medical treatments through much of human history, and such traditional medicine is still widely practiced today**.** The World Health Organization (WHO) has been promoting a movement for "Saving plants for Saving Lives" This is because of the growing understanding of the pivotal role medicinal plants play in providing herbal remedies to health maladies. India has a rich resource base of medicinal plants, plush with approximately 8,000 different species. According to the Government of India (GOI), traditional medicines are the sole means of health care for about 65 percent of the population. The Knowledge of useful plants must have been the first acquired by man to satisfy his hunger and heal his

wounds (Kshirsagar and Singh 2001). Proven agro-industrial technologies need to be applied to the cultivation and processing of medicinal plants and the manufacture of herbal medicines.

Ginger is a subtropical plant grown for its root (rhizome or underground stem). The root has tan skin, ivory to pale green flesh, peppery, slightly sweet flavor. Ginger has many medicinal uses; the fresh or dried rhizome is used in oral or topical preparations for treatment a variety of ailments, while the essential oil is applied topically as an analgesic. Evidence suggests that ginger is most effective against nausea and vomiting in small animals, associated with surgery, vertigo, travel sickness and morning sickness and pregnancy, and cancer chemotherapy (Bone *et al.*, 1990, Grontved *et al.*, 1988, Sripramote *et al.,* 2003). This study deals to summarized and review upon the use *of Zingiber officinale* by the different ethnic communities of India. This work is also an attempt to present and enlist the use zinger as ethnoveterinary meditational purpose by different communities of India as well as abroad. The authors hope that this review will be helpful in medicinal treatment of animals.

Phytochemical constituents of ginger (*Zingiber officinale*)

Ginger (*Zingiber officinale*) is a flowering plant whose rhizome, ginger root or simply ginger, is widely used as a spice or a folk medicine. The primary known constituents of ginger root include gingerols, zingibain, bisabolene, oleoresins, starch, essential oil (zingiberne, zingiberole, camphen, cineole, borneol), mucilage, and protein. Volatile oils are bisabolene, cineole, phellanadrene, citral, borneol, citronellol, geranial, linalool, limeonene, zingiberol, zingiberene, camphene), oleoresin (gingierol, shogaol), phenol (gingeol, zingerone), proteolytic enzyme (zingibain), vitamin B6, Vitamin C, calcium, magnesium, phosphorus, potassium, linoleic acid, gum, starch, lignin, vegeto matter, asmazone, acetic acid, acetate of potassa, sulphur. The gingerol is the alcohol group of the oleoresin. Ginger owes its aroma to about 1 to 3% of volatile oils, which are bisabolene, zingiberene and zingiberol (Dhanik *et al.,* 2017). The major pharmacological activity of ginger appears to be due to gingerol and shogaol.

Anti-inflammatory activity

Ginger appears to be promising for safe use in medicine, pharmaceutical and food industries. Ginger is also often used in joint support supplements. Ginger was reported to have effectiveness for relieving joint pain of osteoarthritis (OA) and rheumatoid arthritis probably due to its anti-inflammatory effects. **(**Thomson *et al.*, 2002, Wigler *et al.*, 2003 and Ramadan *et al.*, 2011). Funk *et al.*, (2016) clinically investigated the utility and safety and effectiveness of ginger in dietary supplements to quell joint disease in inflammatory arthritis may be warranted, but should clearly include careful consideration and characterization of the chemical content of the products to be tested. (Rayati *et al.*, 2017) ginger powder is as effective as ibuprofen in the management of postsurgical sequelae. Furthermore, serum C-reactive protein (CRP) levels alone are not suggested for the assessment of anti-inflammatory effects of drugs. Hassan *et al.*, (2017) resulted about the aqueous extracts of *Z. officinale* have significantly decreased the carrageenan-Induced inflammation and related paw edema in our study on Sprague dawley rats. Ginger and coriander contain many chemical constituents which have anti-inflammatory effect against inflammation caused by gamma radiation

(Abd El-Salam and Hassan, 2017). Several research reports have resulted that whole ginger extract have anti-inflammatory effect on the production of NO/iNOS, PGE2/COX-2, TNF-a, IL-1b, and macrophage chemoattractant protein-1 (MCP- 1) in murine macrophages, such as RAW264.7 cells and J774.1 cells, as well as human monocytes, U937 cells.(Imanishi *et al.*, 2004, Lantz *et al.,* 2007 and Chen *et al.*, 2008).

Antioxidant Activity

Antioxidant medicines are molecule that inhibits the oxidation of other molecules. Fuhrman *et al.,* (2000) described about *In vitro*, ginger has been shown to exhibit antioxidant effects. Nunes *et al.,* (2012) reported that Free radical or reactive oxygen species are one of the main culprits in the genesis of various diseases. However, neutralization of free radical activity is one of the important steps in the diseases prevention. Antioxidants stabilize/deactivate free radicals, often before they attack targets in biological cells. Plants fruits, seeds, oil, leaves, bark and roots show an important role in diseases prevention due to the rich source of antioxidant Eleazu *et al.,* (2012) studied antioxidant potentials of six varieties of ginger. All the varieties were observed to possess strong antioxidant activities and had high quantities of phenols, which may be responsible for their antioxidant activities. Correlation analysis in the study revealed that the total phenolic contents of the ginger varieties correlated negatively with their total oleoresin contents. This finding suggested that the oleoresin contents might not have come from their phenolics constituents and that the oleoresins present could have little contribution to the antioxidant activities of the ginger varieties. Jhambh *et al.,* (2015) studied that ethanolic extract of *Zingiber officinale* orally at dosage of 50, 100 and 200 mg/kg b.wt. respectively daily for 30 days which revealed dosage of 50 mg/kg to be safest and protective to rats that may be used in various disease conditions in animals for its antioxidant potential and *In vitro* antioxidant activity of *Zingiber officinale* extracts and its safety study in rats. Danwilai *et al.,* (2017) confirm the antioxidant pharmacological activity of ginger in their study. No serious adverse effects were reported after taking ginger extract as a daily supplement.

Antimicrobial activity

Antibacterial activity

Ginger has strong antibacterial properties. Studies have revealed that a methanol extract of *Z. officinale* rhizomes possesses significant antibacterial activity against *Escherichia coli*, *Salmonella enteriditis and Staphylococcus aureus* (Sunilson *et al.,* 2009). *Escherichia coli* induced diarrhea is the leading cause of death in developing countries and recently it was documented that zingerone exerted protective effect on *E. coli* induced diarrhea (Chen *et al.,* 2008).

Zingerone also showed protective effect in hyper motility mediated diarrhea that was linked to inhibition of gastrointestinal motility (Iwami *et al.,* 2011). A recent study also indicated that zingerone supplemented Pacific white shrimp (*Litopenaeus vannamei*) juveniles showed strengthening of immunity and protection against *V. alginolyticus* challenge (Chang *et al.,* 2012). The essential oil from ginger was studied for antimicrobial activity against *Aspergillus niger, Saccharomyces cerevisiae, Mycoderma sp., Lactobacillus acidophilus and Bacillus cereus*, as determined by paper agar diffusion method (Guptha and Ravishankar, 2005).

Antiviral activity

Among the different viruses which cause the common cold, *Rhinovirus* is one. In plaque reduction test, the dried rhizome of ginger has been investigated for anti-rhino-viral activity. Fractionation by solvent extraction, solvent partition and repeated chromatography guided by bioassay, allowed the isolation of several sesquiterpenes with anti-rhino-viral actiuvity. The most effective activity of these was β- sesquiphellandrene (Denyer *et al.,* 1994).

Antifungal activity

Extract of ginger powder is effective against several antifungal diseases. The principle antifungals in the ginger are the gingerols and gingerdiol. (Ramkissoon *et al.,* 2012, Nasri *et al.,* 2013).

Anthelmintic activity

The rhizome of *Z. officinale* aqueous extracts was show antihelmintic activity against the earthworm *Pheretima posthuma*. The result showed that the test extract (100mg/ml) possess significant antihelmintic activity (Dubey *et al.,* 2010). Methanol extracts of *Z. officinale* was screened for their in vitro anthelmintic activity. Results revealed that *Zingiber officinale* killed all the test worms (*Haemonchus contortus*) within two hours post exposure being 100% effective (Iqbal *et al.,* 2001).

Anti-diabetic activity

Diabetes is a major global health problem worldwide. Diabetes is a metabolic disorder, caused by abnormality of carbohydrate metabolism and is a major health problem. The major cause of diabetes is low blood insulin or insensitivity of target organ for insulin (Maiti *et al.,* 2004). Severe tissue and vascular damages occur if animal is untreated which is followed by serious complications such as neuropathy, retinopathy, nephropathy, ulceration and cardiovascular complications. An important finding based on in STZ treated-type 1 diabetic rat model reported that, oral administration of ethanolic extract of ginger significantly decrease fasting blood glucose level (Ojewolew *et al.,* 2006). Earlier study reported that significant blood glucose lowering effect of ginger juice in diabetic and nondiabetic animals (Sharma *et al.,* 1977). In the presence of 0.11M- 6GN and 30mM 2-deoxy-D-ribose, the growth of osteoblastic Mc3T3 –E1 cells was increased, as a result of elevating the alkaline phosphatase activity, collagen content and osteocalcin secretion of the cells. At concentrations of 1 and 100 nM, 6- GN increased the osteoprotegerin secretion in osteoblastic cells and decreased the protein carbonyl contents of osteoblastic cells, which is of importance in bone diseases related to diabetes (Choi *et al.,* 2007). The antidiabetic activity of fresh juice of *Z. officinale* was proposed to be correlated through 5-HT receptor antagonism. Since 6-gingerol the chemical and biological marker substance present in *Z. officinale* is reported to possess 5-HT antagonistic activity the present investigation was undertaken to study the effect of methanolic extract and its fractions in STZ-induced NIDDM rats and to correlate with concentrations of 6-gingerol present therein (Yamahara *et al.,* 1989). Recent studies showed that gingerol, its chief active constituent, enhanced cell-mediated glucose uptake via increasing insulin-sensitivity, thus improving chronic disease, as diabetes (Akhani *et al.,* 2004). The main component 6-gingerol also exhibited hypoglycemic property when administered to diabetic mice and improved

impaired insulin signaling in arsenic intoxicated mice (Singh *et al.,* 2009, Chakraborty *et al.,* 2012).

Anti-obesity activity

Okamoto *et al.,* 2011 reported that 6-GN counteracts body weight gain and fat accumulation in mice. A study conducted by Tzeng and Liu (2013) revealed that 6-GN inhibits rosiglitazone-induced adipogenesis by suppressing oil droplet accumulation and by decreasing the droplet size in 3T3-L1 cells (Tzeng *et al.,* 2011). Histochemical staining also permitted the detection of oil droplets in adipocytes at concentrations ranging from 5 to15 lg/mL. A reduction in the levels of fatty acid synthase and adipocyte-specific fatty acid binding protein was also reported.

Anti-atherosclerotic activity

Rabbits with experimentally induced atherosclerosis for 75 days, when fed air dried ginger powder (100 mg/kg orally daily) inhibited atherosclerotic changes in the aorta and coronary arteries by about 50% (Verma *et al.,* 2004). Ginger treatment did not cause any significant lowering of serum lipids in the study but fibrinolytic activity increased and lipid peroxidation was decreased.

Antiemetic Activity

Ginger is most commonly used to treat nausea and vomiting in early pregnancy which is either provided by doctor or used as self-treatment by women (Allaire *et al.,* 2000).

It would be more effective than vit-B6 to overcome the severity of nausea and is also effective in decreasing the frequency of vomiting episodes in early pregnancy (Ensiyeh *et al.,* 2009). Studies based on animal model revealed that, ginger extract possesses antiserotoninergic and 5-HT3 receptor antagonism effects which play an important role in the etiology of postoperative nausea and vomiting (Bhattarai *et al.,* 2001). A study in the favors of ginger role in nausea and vomiting indicating its effect and provide relief in severity in nausea and vomiting (Vutyavanich *et al.,* 2001).

Antipyretic activity

Yeast induced fever in rats is reduced when soxhlet extract of ginger in 80% ethanol is administered at 38% (100mg/kg) (Sacchetti *et al.,* 2005). Antipyretic effect of acetylsalicylic acid is same as at same dose of extract of ginger. The ginger extract did not affect the temperature of normothermic rats. This antipyretic activity may be mediated by COX inhibition.

Anti-hypercholesterolemic activity

Ginger decrease the cholesterol levels by interferes with cholesterol biosynthesis. Anti-lipidemic effect of ginger is done by reducing thermogenesis and high lipids levels. Ginger also helps to increase serum HDL- cholesterol (Ozgoli and Goli, 2009; Vutyavanich *et al.,* 2001; Al- Awwadi, 2010).

Anti-neoplastic activity

Ginger is considered as a powerful neoplastic agent.

Extracts of ginger suppress cell proliferation and act against resistance of cancerous cells, found in several studies. (Barnes *et al.,* 2002; Newall *et al.,* 1996; Ernst and Pittler, 2000; Nasri *et al.,* 2013; Kumar *et al.,* 2015; Saraswat, 2010).

Biological activity

Active compound of ginger	Biological activities
Gingerol and gingerol related compound	The antioxidant activity. Anti-tumour activity via induction of apoptosis, modulation of genetic and other biological activity. Anti-inflammatory and anti-analgesic activity. Anti-microbial activity. Hepato-protective activity.
Paradol	Anti-oxidant and anti-cancerous activity. Anti-microbial activity.
Shogoal	Anti-oxidant and anti-inflammatory activity. 6- shogaol showed anticancer activities through the inhibition of cell invasion reduction of matrix metalloproteinase-9 expression, anti-proliferation activity and anti-invasion.
Zingerone	Antioxidant activity. Anti-inflammatory action. Anti-bacterial activity
Zerumbone	Anti-tumour activity. Anti-microbial activity.
1-Dehydro-(10) gingerdione	Regulation of inflammatory genes.
Terpenoids	Induce Apoptosis by activation of p53.
Ginger flavonoids	Antioxidant activity.

(Rahmani *et al.,* 2014)

Anti-ulcerogenic activity

This has both many benefits and drawbacks. In albino rats ginger cytoprotective and gastric anti-ulcerstudies have been carried out. 80% ethanol, 0.6M HCl, 0.2M NaOH and 25% NaCl cause cytodestruction, whereas Indomethacin, aspirin, and reserpine like ulcerogenic agents produce gastric ulcers, beside hypothermic restraint stress and by pylorus ligated shay rat technique. The result demonstrate that the extract in the dose of 500 mg/kg orally exert highly significant cytoprotection against 80% ethanol, 0.6M HCl, 0.2M NaOH and 25% NaCl induced gastric lesions and also prevent gastric ulcer induced by the anti-inflannatory drugs and hypothermic rerestraint stress. These observations suggest cytoprotective and anti-ulcerogenic effect of the ginger (Al-Yahya *et al.,* 1989). A new anti-ulcer principle named 6-gingesulfonic acid was isolated from the dried rhizome of ginger together with three new monoacyldigalactosylglycerols named gingerglycolipids A, B and C, by monitoring the effects on HCl/ethanol-induced gastric lesions in rats. 6- gingesulfonic acid showed more potent anti-ulcer activity than 6-gingerol and 6-shogaol (Yoshkawa *et al.,* 1992).

Immuno-modulatory activity

Probably the immune-boosting properties of the ginger have the beneficial effects in the treating coughs, colds and flu (Khaki *et al.,* 2004). Immunomodulatory activity of ginger have examined in few studies. Non-specific immunity was increased in rainbow trout eating a diet containing 1% of a dried aqueous ginger extract for three weeks

(Dugenci *et al.,* 2003). Higher haemagglutinating antibody titre and plaque forming cell counts, consistent with improved humoral immunity, found in mice fed a 50% ethanolic ginger extract (25 mg/kg) for seven days (Puri *et al.,* 2004). Ginger suppressed lymphocyte proliferation, found in in-vitro study which was mediated by decrease in IL-2 and IL-10 production (Wilasrusmee *et al.,* 2000).

Gastro-protective activity

Peptic ulcer is a major threat in both male and female. Several factors including stress food ingredients, drugs and helicobacter pyloric are responsible for gastric ulcer. There are lots of medicinal plants and constituents so antiulcer effects in various ways but the exact mechanism are not known. Ginger plays a vital role in ulcer prevention via increasing mucin secretion. Earlier findings showed anti-ulcerative effect of ginger in experimental gastric ulcer model (Yamahara *et al.,* 1988). The major constituents of ginger such as 6- gingerol and 6- shogaol suppress gastric secretion in-situ, 6- shogaol was more intensive (Suekawa *et al.,* 1984).

Cardiovascular activity

Ginger has been described as great heart tonic. It has a great importance in the ayurvedic medicine. It protect the heart by different way, by reducing blood clotting that can lead to plaque formation or thrombosis, by open the blockage in blood vessels these decreasing peripheral vascular resistance and hence blood pressure, by lower the high blood cholesterol level making the heart healthy (Akoachere *et al.,* 2002). Ginger extracts as well as 6-and 8-gingerol have been shown to modulate eicosanoid responses in smooth vascular muscles ex vivo (Hata *et al.,* 1998). An early study found a dose-dependent positive inotropic action of 6-, 8- and 10- gingerol on isolated guinea pig left atria, and 'gingerol' stimulated the Ca2+- pumping ATPase activity of fragmented sarcoplasmic reticulum prepared from mammalian skeletal and cardiac muscle (Kabayashi *et al.,* 1987, Shoji *et al.,* 1982).

In a recent study a crude extract (70% aqueous methanol) of fresh ginger induced a dose dependent fall in arterial blood pressure of anaesthetised rats; this effect was shown to be mediated through blockade of voltage-dependent calcium channels (Ghayur *et al.,* 2005).

Effect on female reproductivity

Labania, (2005) and Abu Baker (2013) conformed the ability of ginger to improve the functional efficiency of the uterus and ovary. Ghusoon and Al-Neamah (2016) investigated that cadmium chloride induce toxic pathological changes in uterus and ovaries of rats and these changes were improved after giving ginger extract, which provide a strong evidence for the beneficial role of antioxidants plants in improving the effect of cadmium chloride toxicity in rat's female.

Effect on male reproductivity

Morakinyo, (2008) studied about using doses of 500 mg/kg and 1000 mg/kg and find that extract of *Zingiber officinale* possesses pro-fertility properties**.** Ginger administration significantly increased serum testosterone levels if given at 100 mg/kg b.wt, in rats (Khaki *et al.,* 2009)**.** Aleissa M.S. (2014) evaluated protective effect of ginger against cisplatin-induced reproductive toxicity and resulted that therapeutic efficacy of ginger increased the activities of testicular antioxidant

enzymes and restored sperm motility of cisplatin-treated in rats.

Toxicity of ginger

The use of *Zingiber offficinale* has been listed in "Generally Recognized as Safe" (GRAS) document of the US FDA. A dose of 0.5 – 1.0 g of ginger powder ingested 2-3 times for periods ranging from 3 months to 2.5 years did not cause any adverse effects in Rats. The British Herbal Compendium documents no adverse effects of ginger. The acute oral LD_{50} in rats of roasted ginger is 170 g/kg body weight and for dry ginger is more than 250 g/kg body weight. (Langner *et al.,* 1998 and Wu *et al.,* 1990). Awwad and Elkhishin (2009) studied that high dose of ginger can be toxic by causing severe hypotension and bradycardia with induction of hyaline changes and fainting of some nuclei in cardiac myocyte fibers of a pre-necrotic stage. Administration of ginger to rats for 28 days in the low dose (50 mg/ kg) produced bradycardia with waviness of some cardiac muscle fibers. Ginger in a high dose (500 mg/ kg) for 28 days, produced both hypotension and bradycardia with degenerative changes in cardiac myocyte fibers. The hypotensive and bradycardic effects of ginger may partially, be due to induction of vasodilatation by increasing nitric oxide release or synthesis and partially due to a calcium channel blocking effect.

The current trend of use of chemical drugs for the treatment of various diseases is very costly and most of them have sever adverse effects on treated animals at prolonged consumption. On comparison, the herbals are easily available and cheap. Their regular use or consumption had no side effects and generally considered as safe on therapeutic level. Ginger is a common most herb available all over world and have many medicinal properties like anti-inflammatory, anti-oxidant, antimicrobial, antipyretic, anti-diabetic, anti-emetic etc. Ginger shows an important effect in the suppression of NFkB, COX_2, and LOX, induction of apoptosis, activation of tumor suppressor gene and also modulates various biological activities. Ultimately it can be concluded that ginger can helps to prevent various diseases effectively at lower price without any adverse effect.

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