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A REVIEW ON *ZINGIBER OFFICINALE*: A NATURAL GIFT

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ABSTRACT

Ginger is one of the most important natural medicinal plant which is used for the various traditional and medicinal purposes in India as well as china, Caribbean, Africa and African countries this natural gift consumed worldwide as a spice and flavouring agent from the ancient time. Ginger has been used for the centuries to support many various digestive imbalances including, indigestion, nausea, motion sickness, vomiting, diarrhoea, coughing, heartburn and many other uses. Ginger bears an enormous number of pharmacological activities among those, Neuro-protective activity and activity against colon cancer have facilitated the extent of further research for finding out less toxic and more potent drugs for the better treatment of those diseases. This review will facilitate to gain all about the past scientific research and the necessary information about the ginger (*Zingiber officinale* Roscoe).

KEYWORDS: ***Zingiber officinale*, Amaldehyde, Gingerol,Shogaol, etc.**

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INTRODUCTION

Ginger is one of the most important and most power full god gifted natural rhizome which is used in the various purposes in medicinal as well as a home remedy. There is an increasing awareness, both in the medical community and among the public, for the use of unconventional or alternative treatment modalities by patients[1, 2]. Ginger is one of the most important medicinal plants which naturally occur in various country like in India as well as foreign country like West Indies, Mexico, China, South East Asia, Jamaica, Hawaii, Africa and other parts of the world. This natural gift has been consumed worldwide as a spice and flavouring agent from the ancient time[3]. Ginger is used worldwide as a cooking spice, condiment and herbal remedy. The Chinese have used ginger for at least 2500 years as a digestive aid and antinausea remedy and to treat bleeding disorders and rheumatism; it was also used to treat baldness, toothache, snake bite and respiratory conditions[4]. In Traditional Chinese Medicine (TCM), ginger is considered as a pungent, dry, warming, yang herb to be used for ailments triggered by cold, damp weather. Ginger is used extensively in Ayurveda, the traditional medicine of India, to block excessive clotting, reduce cholesterol and fight arthritis. In Malaysia and Indonesia ginger soup is given to new mother for 30 days after their delivery to help warm them and to help them sweat out impurities. In Arabian medicine, ginger is considered an aphrodisiac[5]. Nowadays ginger is extensively cultivated from Asia to Africa and the Caribbean and is used worldwide as a nausea remedy, as an anti-spasmodic and to promote warming in case of chills[6, 7]. The use of plant to treat various diseases in India dates back to the times of Rigveda. Later, the monumental Ayurvedic works like Charaksamhita and Sushrutasamhita followed by other Ayurveda and Siddha treatises have incorporated nearly 700 plant drugs entering in to several medicine preparation used in the management of the health care. In fact this system has been in practice even in remote areas of our country for centuries[8]. The ginger family is a tropical group especially abundant in Indo-Malaysia, consisting of more 1200 plant species in 53 genera. The genus gingiber includes about 85 species of aromatic herbs from East Asia and tropical Australia. The name of the genus, Gingiber, derived from a Sanskrit word denoting “horn-shaped,” in reference to the protrusions on the rhizome[9, 10].

Ginger is a well known herbal medicine, which is usually used in traditional medicine in all over the world. Ginger has many phytonutrients and has aromatic and pungent taste. The rhizome of gingiber is commonly used in herbal prescriptions Ginger contains Essential oils especially gingerol and gingiberene. It also contains pungent principles such as ginger one, gingerol and shogaol[11]. For centuries in alternative and complementary systems of medicine, ginger has been prescribed in the treatment of headache, vomiting, nausea and nervous diseases. Ginger has been noted to treat migraine headaches without side-effects[12].Ginger (*Zingiber officinale* Rosc) (Family: *Zingiberaceae*) is a herbaceous perennial, the rhizomes of which are used as a spice. India is a leading producer of ginger in the world and during 2006-07 the country produced 3.70 lakh tonnes of the spice from an area of 1.06 lakh hectares. Ginger is cultivated in most of the states in India. However, states namely Kerala, Meghalaya, Arunachal Pradesh, Mizoram, Sikkim, Nagaland and Orissa together contribute 70 per cent to the country’s total production. In India the average daily consumption is 8-10 gms of fresh ginger root. Warm and humid and is cultivated from sea level to an altitude of 1500 m about sea level. It can be grown both under rain fed and irrigated conditions[13].

Soil

Ginger thrives best in well drained soils like sandy loam, clay loam, red loam or lateritic loam. A friable loam rich in humus is ideal[13].

Varieties

Some of the prominent indigenous cultivars are Maran, Kuruppampadi, Ernad, Wynad, Himachal and Nadia. Exotic cultivars such as Rio-de-Janeiro had also become very popular among cultivators. The improved varieties of

ginger given in below IISR- Varada, Suprabha, Suruchi, Suravi, Himagiri, IISR Mahima, IISR Rejatha[13].

Season

The best time for planting ginger in the West Coast of India is during the first fortnight of May with the receipt of pre-monsoon showers. Under irrigated conditions, it can be planted well in advance during the middle of February or early March[13].

The ginger plant is an erect perennial growing from one to three feet in height. The stem is surrounded by the sheathing bases of the two-ranked leaves. A cube like spike of yellowish, purple-lipped flowers have showy greenish yellow bracts beneath. The ginger of commerce consists of the thick, scaly rhizomes of the plant. The branch with thick thumb-like protrusions, thus individual divisions of the rhizomes are known as "hands". Rhizomes are 7-15 cm long and 1-1.5 cm broad and laterally compressed.

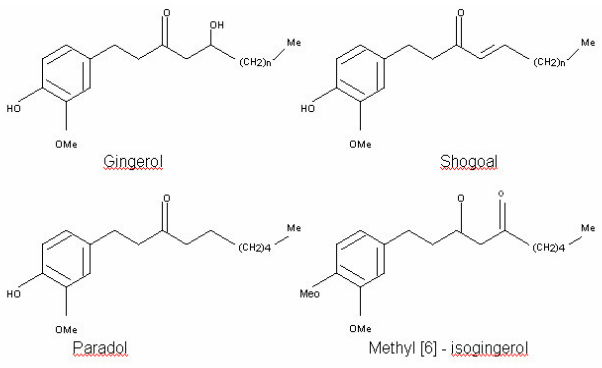
MORPHOLOGY

Appearance profile and physiochemical properties of ginger essential oils from different species[14, 15]

Constituents presents	% of amount
Moisture	80.9
Protein	2.3
Fat	0.9
Mineral	1.2
Fibre	2.5
Carbohydrate	12.3

CHEMISTRY

The pungency of ginger is due to gingerol, an oily liquid consisting of homologous phenols. It is formed in the plant from phenylalanine, malonate and hexonate[16]. In the fresh ginger rhizome, the gingerols were identified as the major active components and gingerol [5-hydroxy-1-(4-hydroxy-3-methoxy phenyl) decane-3-one] is the most abundant constituent in the gingerol series. Powered rhizome contains 3-6% fatty oil, 9% protein, 60-70% carbohydrates, 3-8% crude fibre, about 8% ash, 9-12% water and 2-3% volatile oil. The volatile oil consists of mainly mono and sesqueterpenes; Camphene, betaphellandrene, curcumene, cineole, geranyl acetate, terpheneol, terpenes, borneol, geraniol, limonene, linalool, alpha-gingiberene 30-70%, beta-sesquiphellandrene 10-15% and alpha-farmesene. In dried ginger powder, shagaol a dehydrated product of gengerol is a predominant pungent constituent up to biosynthesis[17, 18,19]. It also contains acrid resinous substances 5-8%[19].



Ginger contains up to 3% of a fragrant essential oil whose main constituents are sesquiterpenoids, with (-)-gingeberene as the main components. Ginger also contains amadaldehyde, paradols, gingerdiols, gingerdiacetates, gingerenones, 6-gingersulfonic acid, diterpenes, gingerglycolipids A, B and C. The other minor compounds are methylegingediol, methylegingediacetates and C_{20}-dialdehyde[16].

STANDARDS AND ADULTERATION

Ginger contains minimum 10% of water soluble extractives, 4.5% Alcohol soluble extractive. It should offer maximum 6% of total ash, 2% Acid insoluble ash and minimum 1.7% water soluble ash[20]. Adulteration can be detected by microscopic examination. Powered ginger may have been prepared from 'wormy' drug and so attention should be paid to the absence of insect fragments. Adulteration can also take the form of addition of 'spent ginger' which has been exhausted in the preparation of essence. This may be detected by the official standards for alcohol-soluble extractive, water soluble extractives, total ash and water soluble ash[16].

PHYTOCHEMICAL SCREENING

Phytochemical screening of ginger ethanolic extract revealed abundant presence of flavonoids and tannins. High concentration of carbohydrates and moderate concentration alkanoids were recorded. Chloroform extract contained moderate concentrations, sterols and terpenes, while petroleum ether one contained moderate lipids content[21]

Table 2
Phytochemical screening of successive ginger

S. No.	Constituents	Petroleum ether	Chloroform	Ethanol
1.	Carbohydrates	×	×	√√
2.	Flavonoids	×	×	√√√
3.	Tannins	×	×	√√√
4.	Sterols	×	√	×
5.	Terpenes	×	√	×
6.	Alkaloids	×	×	×
7.	Oils	√	×	×

×= Not present.
√= Present in moderately high concentration.
√√= Present in very high concentration.
√√√=Abundant present.

PHARMACOKINETICS

The pharmacokinetic property of ginger has been estimated by many studies in both man and animals. Here is some information which reveals some pharmacokinetic properties of ginger. To investigate the pharmacokinetics of [6]-shogaol, a pungent ingredient of *Zingiber officinale* Roscoe, the pharmacokinetic parameters were determined by using (14) C-[6]-shogaol (labelled compound) and [6]-shogaol (non-labeled compound). The maximum plasma concentration [C (max)] and the area under the curve (AUC) of plasma radioactivity concentration increased in a dose-dependent manner for the labelled compound. When the labelled compound was orally administered at a dose of 10 mg/kg, 20.0 + or - 1.8% of the radioactivity administered was excreted in urine, 64.0 + or - 12.9% into feces, and 0.2 + or - 0.1% into breath. On the other hand, when the non-labeled compound [6]-shogaol was orally administered, the plasma concentration and biliary excretion of the unchanged form were extremely low. It would suggest that [6]-shogaol is mostly metabolized in the body and excreted as metabolites[22]. [6]-Gingerol was rapidly cleared from the plasma with a terminal half life of 7.23 min and total body clearance of 16.8 ml/min/kg. Serum protein binding of [6] - gingerol was 92.4%. The renal excretion does not contribute at all to the disappearance of [6] -gingerol from plasma in rats[23]. The extent of [6] -gingerol bound to serum protein was more than 90% and was affected very slightly by the toxicity. This expects indicates that 6- gingerol is eliminated partly by the liver[24]. Nakazwa and Oshawa found that both the gut flora and the enzymes in the liver plays an important role in the metabolism of [6] -gingerol[25].

PHARMACOLOGICAL ACTIVITY

Hypoglycaemic effects

The study showed that the aqueous extract of *Zingiber officinale* at an oral dose of 0.5 ml of extract/rat/day or 500 mg/kg adjusted according to the weight of the rat has a hypoglycemic effect in alloxan induced diabetic rat and maybe help in control of diabetes[26].

Osteoarthritis

A one-month period of therapy with only one dose of ginger extract applied in this study might not have been adequate for all the effects of ginger extract to be detected. Future studies might look in to dose response and duration of therapy of a standardized and highly concentrated ginger extract in patients with osteoarthritis. The result of our study indicated that ginger extract could be used as an alternative to the NSAID and as a supplement drug in patients with osteoarthritis[27].

Gout

The clinical study was conducted on Gouticin that contains different medicinal herbs including *Zingiber officinale*, used as analgesic in Gouty arthritis. Study was conducted in Shifa ul Mulk Memorial Hospital, Hamdard University, Karachi. The drug was prescribed to 50 patients between ages of 35 years to 75 years. The selected drug was administered to attain a successful response to gout. Herbal formulation Gouticine was administered to 50 patients. Clinical study of Gouticin shows that it exhibits the anti-inflammatory effects. It was concluded that Gouticin is remarkably effective for the treatment of acute gout arthritis[28].

Rheumatoid arthritis

An herbal drug arthritin containing different medicinal herbs including *Zingiber officinale* was evaluated in comparison with methotrexate for the treatment of rheumatoid arthritis. Study was conducted in Shifa ul Mulk Memorial Hospital, Hamdard University, Karachi. Herbal formulation Arthritin was administered to 50 patients. Clinical study shows that arthritin exhibits the anti-inflammatory effects. It was concluded that arthritin is effective for the treatment of rheumatoid arthritis[29].

Primary dysmenorrhoea

An herbal drug dysmo off containing different medicinal herbs including *Zingiber officinale* was evaluated in comparison with diclofenic sodium (voren) for the treatment of primary dysmennorrhoea. This comparative study was carried out on 120 patients of ages between 13-30 years in seven consecutive episodes at department of gynaecology and obstetrics in Shifa ul Mulk Memorial Hospital, Hamdard University, Karachi. It was concluded that dysmo off is more effective than voren for treatment of dysmennorrhoea[30].

Effect of Zingiber officinale on hepatic antioxidant levels

CCl_4 group recorded significant decrease in glutathione (63.63%) and total SOD (49.73%) levels, while malondialdehyde showed significant increase by 38.00%. Treatment with ethanol extract improved MDA and SOD levels by 60.56 and 10.70%, respectively. Glutathione enhanced after treatment with chloroform and ethanol extracts by 32.70 and 27.97%. Treatment with silymarin recorded improvement in GSH, MDA and SOD by 40.08, 35.21 and 3.84%, respectively[21].

Potency of Zingiber officinale in improving liver function enzymes and serum protein

CCl_4 group showed significant increase in AST an ALT level by 88.34 and 43.52%, respectively. However, serum total protein insignificantly increased by 8.93, 6.97 and 3.91% after treatment with ethanol, chloroform and petroleum ether extracts, respectively. The observed changes in liver function enzymes showed that ethanol extract recorded the most improvement percentages than the other extracts. AST and ALT were ameliorated by 31.11 and 21.26%, while serum protein was improved by 15.19, 13.24 and 12.39% for the three extracts, respectively. Silymarin enhanced AST, ALT and total protein levels by 36.66, 22.84 and 12.39%, respectively[21].

Liver histopathological analysis

Liver section of control healthy rats were with normal hepatic lobular architecture.The

hepatocytes were within normal limits and arranged in thin plates. The hepatocytes were separated by narrow blood sinusoids lined by endothelial cells. Portal tracts extend with no fibrous tissue or lymphocytes deposition. Healthy rats treated with ethanolic extract showed normal hepatic lobular architecture. The hepatocytes were within normal limits and no hydropic or steatosis changes. Portal tracts were normal and no sign of fibrosis. Treatment with chloroform extract of ginger recorded more or less normal hepatocytes architecture. Petroleum ether extract caused mild hepatocytes aggregation and lymphocytes infiltrations. Injured liver with CCl_4 showed portal loss of hepatic lobular architecture. Ballooning of hepatocytes, deformed cord arrangement and disturbed sinusoids were seen. The hepatocytes showed marked degree of hydropic, steatotic changes and massive necrosis. Portal tracts were extended with marked numbers of chronic inflammatory cells and fibrous tissue[21].

Migraine

500-600mg of ginger powder administration at the onset of migraine for 3-4 days at interval of 4 hours, reported to provide relief from migraine attack[12].

Gastrointestinal tract

The active components of ginger are reported to stimulate digestion, absorption, relieve constipation and flatulence by increasing muscular activity in the digestive tract[31, 32]. It is also significantly reduced the nausea and vomiting[33, 34, 35].

Cardiovascular system

In traditional Chinese medicine, ginger is used to improve the flow of body fluids. It stimulates blood circulation throughout the body by powerful stimulatory effect on the heart muscle and by diluting blood[36]. The improved circulation is believed to increase the cellular metabolic activity, thus contributing to the relief of cramps and tension[37]. A Japanese study showed that the active constituents in ginger reduced the blood pressure and decreased cardiac workload[38]. Ginger reduced the formation of proinflammatory prostaglandins and thromboxane thus lowering the clotting ability of the blood[39]. The inhibition of platelet aggregation by ginger is more than the similar effects observed with garlic and onion[40, 41, 42]. Ginger can prevent the increase in cholesterol levels following intake of cholesterol-rich diet[43]. Ginger is also known to possess antioxidant properties[44, 45, 46].

Anti-oxidant action

The antioxidant properties of [6]-gingerol which is very effective agent for anticipation of ultra violet B (UVB)-induced reactive oxygen species production and COX-2 idiom, and a promising therapeutic agent against UV Binduced skin disorders, has been studied *both in-vitro & in-vivo.* It also has a protective role to toxicity and lethality against some agent like carbon-tetra chloride, cisplatin etc[47, 48].

Analgesic effect

Many studies have been evaluated for the analgesic effect of ginger and its constituents. It has a strong analgesic action which is many cases act by cyclo–oxygenase-1 (COX-1) inhibition. Gingerol and their derivatives, especially [8]-paradol, have been reported to be more potent anti-platelet and cyclo-oxygenase-1 (COX-1) inhibitors than aspirin[49].

Colon cancer

The extract of ginger confined HCT 116 and HT 29 cells at G0/G1 and G2/M phases with consequent decreased in S-phase. This study suggests that ginger extract may bring to bear its antitumor effects on colon cancer cells by suppressing its growth, striking the G0/G1-phase, reducing DNA synthesis and inducing apoptosis[50].

Blood clotting

The effect of an aqueous extract of ginger on platelet thromboxane-B2 (TBX2) and prostaglandin-E2 (PGE2) production was examined after giving rats a raw aqueous extract of ginger daily for a period of 4 weeks, either orally or intraperitoneally (IP). A low dose of ginger (50 mg/kg) administered either orally or IP did not produce any significant reduction in the serum TBX2 levels. However, ginger administered orally caused significant changes in the serum PGE2 at this dose. High doses of ginger (500 mg/kg) were significantly

effective in lowering serum PGE2 when given either orally or IP. However, TXB2 levels were significantly lower in rats given 500 mg/kg ginger orally, but not IP. These results suggest that ginger could be used as an anti-thrombotic and anti-inflammatory agent[51].

Blood pressure

Several pieces of evidence, mainly from rat studies, have suggested that ginger exerts many direct and indirect effects on blood pressure and heart rate[52] .More recently the crude extract of ginger induced a dose-dependent (0.3–3 mg/kg) fall in the arterial blood pressure of anesthetized rats. In Guinea pig paired atria, the crude extract exhibited a cardiodepressant activity on the rate and force of spontaneous contractions. In rabbit thoracic aorta preparation, the crude extract relaxed the phenylephrine induced vascular contraction at a dose 10 times higher than that required against K-induced contraction. Ca2+ channel- blocking activity was confirmed when the crude extract shifted the Ca2+ dose–response curves to the right, similar to the effect of verapamil. It also inhibited the phenylephrine control peaks in normal Ca2+-plus and Ca2+-free solutions, indicating that it acts at both the membrane-bound and the intracellular Ca2+ channels. When tested in endothelium- intact rat aorta, it again relaxed the K-induced contraction at a dose 14 times less than that required for relaxing the PE-induced contraction. The vasodilator effect of the crude extract was endothelium-independent because it was not blocked by either L-NAME (a non-selective inhibitor of nitric oxide synthase used experimentally to induce hypertension) or atropine and also was reproduced in the endothelium-denuded preparations in the same dose range. These data indicate that the blood pressure-lowering effect of ginger is mediated through blockade of voltage dependent calcium channels[53]. In another paper, the same group the blood pressure lowering action of aqueous ginger extract was through a dual inhibitory effect mediated via stimulation of both muscarinic receptors and blockade of Ca2+ channels. Interestingly, they also noted that the different constituents of ginger might have opposing actions on the reactivity of blood vessels. For example, an atropine-resistant and LNAME-sensitive vasodilator activity was also noted for the ginger phenolic constituents [6]-, [8]-, and [10]-gingerol, while [6]-shogaol showed a mild vasodilator effect[54].

Immunomodulatory effects

Few studies have examined the potential immunomodulatory activity of ginger. Non-specific immunity was increased in rainbow trout eating a diet containing 1% of a dried aqueous ginger extract for three weeks[55]. Mice fed a 50% ethanolic ginger extract (25 mg/kg) for seven days had higher haemagglutinating antibody titre and plaque-forming cell counts, consistent with improved humoral immunity[56]. One *in vitro* study found that ginger suppressed lymphocyte proliferation; this was mediated by decreases in IL-2 and IL-10 production[57]. Another study found an aqueous ginger extract significantly increased the production of IL-1β, IL-6 and TNF-α in activated peritoneal mouse macrophages[58]. The same study found that splenocyte proliferation and cytokine production were stimulated in a dose-dependent manner when mice were given an aqueous ginger extract for 4 weeks (50-500 mg/kg).

Anti-atherosclerotic effects

A number of animal studies have demonstrated hypocholesterolemic action of ginger and ginger extracts. These studies have shown decreased levels of total cholesterol, low-density lipoprotein (LDL)-, very low-density lipoprotein (VLDL)-cholesterol and triglycerides, and increases in high-density lipoprotein (HDL)-cholesterol[59,60,61,62,63]. In a more recent study, air-dried ginger powder (100 mg/kg orally daily) fed to rabbits with experimentally induced atherosclerosis for 75 days inhibited atherosclerotic changes in the aorta and coronary arteries by about 50%[64]. In this study the ginger treatment did not cause any significant lowering of serum lipids, but lipid peroxidation was decreased and fibrinolytic activity increased. The effects of an aqueous ginger extract, administered orally or intraperitoneally to rats for 4weeks, on serum cholesterol and triglyceride levels and on PGE2 and TxB2 have been reported[51]. At 500 mg/kg both modes of administration led to a

significant reduction in serum cholesterol levels, whereas only intraperitoneal administration led to a reduction with a daily dose of 50 mg/kg. Neither dose caused significant changes to serum triglyceride levels. The higher dose administered orally significantly lowered serum PGE2 and TxB2 levels, and the lower dose also reduced PGE2 levels. It is evident from this that ginger has demonstrated considerable potential as an antiatherosclerotic agent in animal studies, but as yet this promise has not been confirmed in human trials.

Metabolic effects

Significant hypoglycaemic activity in rabbits was produced by an ethanolic extract of ginger[65], and two animal studies have suggested that ginger may improve insulin sensitivity[66,67].

Anti-microbial actions

Ginger extracts have demonstrated antimicrobial activity against a wide range of pathogenic micro-organisms; these include both Gms-positive and Gms-negative bacteria and the yeast *Candida albicans*, but the antimicrobial activity of ginger extracts appears to be moderate in comparison with highly antimicrobial plant extracts of particular interest is an *in vitro* study showing that a crude methanolic extract (MIC 6-50 µg/mL) and a gingerol-containing fraction (MIC 0.8-12.5 µg/mL) significantly inhibited the growth of 19 strains of *Helicobacter pylori,* the micro-organism associated with peptic ulcer disease as well as gastric and colon cancer[68].

Hematologic

Antiplatelet: Some cautious physicians have advised that ginger may alter bleeding time and should not be used concurrently with anticoagulant medications[69].

Human data: In 20 healthy young male volunteers, ginger supplementation (5 gms daily) significantly inhibited the platelet aggregation induced by ADP (adenosine diphosphate) and epinephrine[70]. In human volunteers who took a huge (10 gms) one-time dose of dried ginger, there was a marked inhibition of platelet aggregability[39]. Another study showed no significant impact of fresh or cooked ginger (doses up to 15 gms of fresh ginger or 40 gms of cooked ginger) on thrombotic activity or platelet thromboxane production[71]. There are no reports of bleeding problems in persons consuming up to 5 gms daily of dried ginger[72], however, ginger's effects on platelet activation may have therapeutic implications that bear further investigation for persons with atherosclerotic disease.

Antineoplastic

Ginger inhibited Epstein-Barr virus activation[73, 74]. Ginger compounds (6-gingerol and 6-paradol) had inhibitory effects on the viability and DNA synthesis of human promyelocytic leukemia cells[75,76]. Ginger's essential oil significantly suppressed formation of DNA adducts by aflatoxin B1 in a microsomal enzyme-mediated reaction[77].Pre-treatment with an alcoholic extract of ginger provided significant protection against experimentally-induced skin tumors in mice. Other ginger family plants, *Alpinia oxyphylla*, *Zingiber zerumbet* and *Curcuma longa*, also displayed potent anti-tumor effects in mice[78, 79].

Anti-inflammatory activity

In Ayurveda, ginger is reported to be useful in treating inflammation and rheumatism. One of the mechanisms by which ginger exerts its ameliorative effects could be related to inhibition of prostaglandin and leukotriene biosynthesis[80]. Anti- microbial effect: Some constituents of ginger inhibit the growth of some colon bacteria like Escherichia coli, Proteus species, Staphylococci, Streptococci and Salmonella. It has been found that out of 29 plant extracts, ginger extract had the broadest range of anti-fungal activity measured either by the fungi inhibited or as the average diameter of the zones of inhibition[81, 82, 83].

Lipid & glucose concentration in blood

A methanolic extract of dried rhizomes of ginger produced a significant reduction in fructose-induced elevation of lipid levels, be achieved with a dietary supplement of either ginger or its extract containing aldose reductase inhibitors[84].

Effect on Nephrotoxicity

The nephroprotective effect of aqueous ethanol extract of *Zingiber officinale* (200 and 400 mg/kg) was evaluated against doxorubicin-induced (15 mg/kg) acute renal damage in rat. The nephroprotection of ginger is mediated by preventing the Doxorubicininduced decline of renal antioxidant status, and also by increasing the activity by of Glutathione -S- transferse (GST) [85].

Anti-proliferative activity

It has been found that the apoptosis of A549 cells by Ginger aqueous extract is mediated by up regulation of tumor suppressor gene p53 and alteration of the normal Bax/Bcl- 2 ratio followed by down regulation of cellular pro-caspase 3. The morphological change of cells upon Ginger aqueous extract treatment has also been demonstrated. Both the structural and functional properties of tubulin and microtubule were lost, as confirmed by both *ex vivo and in-vitro* experiments[86].

Neuro protective activity

The daily dose (4 mg kg [-1] b.w.) i.p.injection of pure monosodium glutamate (MSG) for 30 days and subsequent withdrawal caused a significant decrease in epinephrine (E), norepinephrine (NE), dopamine (DA) and serotonin (5-HT) content all tested areas (cerebellum, brainstem, striatum, cerebral cortex, hypothalamus and hippocampus) at most of the time intervals studied. The neuroprotective effect is partly attributable to an antagonistic action of ginger root extracts on monosodium glutamate effect, so the monoamines content was increased. From these results, we can say that the ginger extract has a neuroprotective role against monosodium glutamate toxicity effect[87].

Hepatoprotective activity

Ginger is also having significant Hepatoprotective activity. The bromobenzene (BB)-induced hepatotoxicity comes from its reactive metabolites. The efficacy of different doses of ginger (*Zingiber officinale* Rose.) extract in alleviating hepatotoxicity was investigated[88].

Anticoagulant Effects

Ginger has been shown to inhibit platelet aggregation[89, 49, 68] and to decrease platelet thromboxane production *in vitro*[90,91, 49]. (8)-Gingerol, (8)-shogaol, (8)-paradol, and gingerol analogues (1 and 5) exhibited antiplatelet activities[49]. However, its effects *in vivo* have not been well studied. Although ginger to decrease platelet aggregation[92], no effect of ginger on platelet counts, bleeding time, or platelet aggregation[93]. Similarly, ginger to have no effect on platelet aggregation, fibrinolytic activity, or fibrinogen levels[39].

Antiemetic Effects

The mechanism of action of ginger's effect on nausea and vomiting remains uncertain. However, there are several proposed mechanisms. The components in ginger that are responsible for the antiemetic effect are thought to be the gingerols, shogaols, and galanolactone, a diterpenoid of ginger[94, 95, 96].Recent animal models and *in vitro* studies have demonstrated that ginger extract possesses antiserotoninergic and 5- HT3 receptor antagonism effects, which play an important role in the etiology of postoperative nausea and vomiting[97].In a randomized, placebo-controlled, crossover trial of 16 healthy volunteers, ginger (1g orally) had no effect on gastric emptying[98]. It appears unlikely that ginger's anti-emetic or antinausea effects are mediated through increased gastro duodenal motility or through increased gastric emptying. It was demonstrated that oral ginger increases antral motility during phase III of the migrating motor complex (MMC) and increases motor response to a test meal in the corpus[99].However, ginger had no significant effect in the antrum or corpus during other phases, except for a significant decrease in the amplitude of antral contractions during phase II of the MMC. Additionally, there was no effect of ginger on duodenal contractions or on the "motility index."

Antinociceptive Effects

(6)-shogaol has produced anti-nociception and inhibited the release of substance P in rats, seemingly via the same receptor to which capsaicin binds. However, it was observed to be 100 times less potent and to elicit half the

maximal effect of capsaicin[100] (6)-shogaol, generally more potent than (6)- gingerol, has exhibited antitussive effects[101].

Antigenotoxic Activity

Norethandrolone and oxandrolone were investigated for their genotoxic effect on human lymphocyte chromosomes using chromosomal aberrations and sister chromatid exchanges as parameters and subsequently Genistein and [6]-gingerol were used as antigenotoxic agents to ameliorate the genotoxicity induced by the steroids. Norethandrolone and oxandrolone were studied at 5, 10, 20, 30 and 40 µM, respectively and were found to be significantly genotoxic at 30 and 40 µM. Genistein and [6] - gingerol proved to be equally effective in reducing genotoxic damage at appropriate doses[102].

Mutagenicity

A study was performed to discover the active part in mutagenesis of [6]-gingerol and [6]-shogaol. [6]-Shogoal was much less mutagenic (1 × 103 revertants/108 viable cells/700 µM) than [6]-gingerol (1 × 107 of the same units). Mutation frequencies of their related compounds were 4 × 101 for zingerone, 1 × 107 for 3-hydroxymyristic acid and 3 × 102 for 12-hydroxystearic acid[103].

Growth performance and body weight gain in poultry

The Z. officinale improved body weight gain in broiler chickens at the rate of 120, 240 and 360 ppm[104], however author did not find any significant difference for average daily gain in broilers by feeding ginger at the rate of 5 g/kg[105]. The use of 2% red ginger in the ration of broiler chickens produced higher body weights[106]. The addition of ginger (0.25%) to the basal diet of broiler chicks resulted in higher body weights. In their work[107], the carminative mixture containing ginger at the dose rate of 2 and 4 ml/l of drinking water increased body weight on the 5th week of the experiment[108]. The broiler chicks dosed with aqueous extract of a mixture of plants containing ginger improved body weight gain[109]. A diet containing 1 g/kg of ginger did not affect growth performance[110], whereas supplementation of ginger at the levels of 5, 10, or 15 g/kg slightly improved growth in broilers. In contrast[111], reduced growth rate in starter broilers (1 to 4 wk) when ginger was fed at the rate of 60 g/kg body weight at the 6th week of age[112] which may be due to the toxic effect of this compound[113]. The different results on growth performance of broilers may be ascribed to the different doses used in the experiments.

Carcass traits

The birds fed ginger produced higher carcass weights compared to untreated birds. Dressing percentage, breast weight and leg weights increased significantly in response to an aqueous extract of a plant mixture containing ginger[109]. The improved carcass quality of broilers may be associated with the antioxidant effect of ginger which enhances protein and fat metabolism[105]. Conversely, no effect of ginger supplementation on carcass characteristics including New York dressed percentage, eviscerated weight, ready to cook percentage, abdominal fat pad and giblet weight[113]. The dressing percentage did not differ between control and ginger treated broilers up to sixth week of age[110]. The addition of ginger (0.25%) in the basal diet of broiler chicks did not result in significant differences in carcass characteristics[107].

Egg production and quality

The addition of the essential oil of ginger increased egg shell weight and egg shell thickness in laying hens. However, feeding ginger essential oil did not affect egg index, yolk index and Haugh unit. However, other researchers have not always seen the same benefits[114]. Laying hens fed with ginger at the rates of 5, 10, 15 and 20 g/kg of feed had no effect on laying rate and average egg weight, however egg mass increased significantly in supplemented groups[115]. Feeding ginger at the rates of 0.5 and 0.75% improved egg production although egg weight did not differ between the control and treated groups[116]. Previous work White Leghorn laying hens fed dried fermented ginger (1 and 5%) showed better egg production and mass in comparison to those of control birds. However, there were no significant differences in shell breaking strength, shell thickness, shell ratio, albumin ratio, yolk ratio, yolk colour and Haugh unit

among the dietary treatments. The exact mechanism through which egg laying performance is enhanced is not known[117]. The higher performance of the laying hens may be due to antioxidant, antimicrobial and other activities such as increased blood circulation and secretion of digestive enzymes and reduction in the oxidation of feed[115].

Blood biochemistry

Serum glucose, total cholesterol, LDL-cholesterol and VLDL cholesterol decreased significantly in broilers fed with 0.4 and 0.6% aqueous ginger extract, however, HDL-cholesterol concentration increased in these birds[118]. Supplementation of ginger (0.25%) in the basal diet of broiler chicks did not result in any significance difference in terms of total protein, albumin, globulin, urea and creatine[107]. The effect of dosing broilers (10 ml/l of drinking water) with an aqueous extract of a mixture of medicinal plants (garlic, berberine and aloe vera) along with ginger, which resulted in a significant decrease in serum glucose, ALT (alanine aminotransferase), AST (aspartate aminotransferase) and ALP (alkaline phosphatase) concentration, however, serum protein increased significantly in the treated group. In the same experiment, the cholesterol profile including total cholesterol, triglyceride, LDL, VLDL decreased significantly in the treated group, while HDL cholesterol concentration increased[119]. The total protein concentration was higher at 21 day and 42 days of sampling in broilers treated with ginger powder but cholesterol concentration was reduced at these intervals[105]. The carminative mixture containing ginger at the dose rate of 2 and 4 ml/L of drinking water did not affect serum albumin, globulin and total protein in broilers[108]. Reduced total protein and globulin in the plasma from broiler chicks were due to dietary supplementation of 60 g/kg this may be due to a toxic effect of the ginger[109]. Supplementation of ginger at the rate of 5, 10 and 15 g/kg did not affect total protein and albumin in the serum of broiler chickens[111]. The discrepancies in these results may be due to the difference in doses used as well as experimental conditions. The exact mechanisms through which blood metabolites are altered are not known. It was postulated that (E)-8 beta, 17-epoxyllabed-12-ene-15, 16-dial, a compound isolated from ginger, interferes with cholesterol biosynthesis in liver homogenates of hypercholesterolaemic mice causing its reduction[120]. Feeding rats with ginger significantly elevated the activity of hepatic cholesterol 7-alpha-hydroxylase which is a rate limiting enzyme in the biosynthesis of bile acids and stimulates the conversion of cholesterol to bile acids leading to the excretion of cholesterol from the body[121].

DOSES

Adult doses: There is disagreement on the optimal form and dose of ginger. Reputable Physicians and herbalists recommend a range of doses: Dried ginger: 250 milligmss four times daily by mouth[122]. Some German herbalists Recommend up to four times this amount[123]. Chinese herbalists may use up to 10 times this amount.

Tea: 1 tsp of fresh ginger root boiled in 1 –2 cups of water for 10 –20 minutes. Cool for 5 minutes and sweeten as desired. It may be mixed with peppermint or chamomile.

Ginger tincture: 1.5 – 3.0 ml per dose[122]

Candied ginger: A 1 inch square piece is presumably equivalent to 500 – 1000 of dried ginger[124, 125].

Multi-ingredient preparations containing ginger: Adenas, Adrenas, Cura, Digestive Aide, Donalg, Ginger syrup, Ginkgo plus herbal formula, Herbal Booster, Herbal Cleansee, Herbal digestive aide, Strong ginger tincture, Unex amarum, Vitaglow Herbal Laxative, Weak Ginger Tincture.

DRUG INTERACTIONS

No drug interactions are known; however, due to ginger's apparent effect on platelets, it should be used cautiously in individuals using anticoagulants[126].

Interactions with other herbs or pharmaceuticals: Unknown; none reported. Some herbalists recommend avoiding use by patients taking anticoagulant medications; no adverse interactions have been reported[127].

Safety during pregnancy, lactation and/or childhood: Unknown. Presumed safe based on its long history of use as food. Because of the reported uterotonic activity of a related species,

Zingiber cassumunar, some herbalists recommend avoiding ginger during pregnancy[122, 128, 129]. No adverse effects in pregnancy have been reported.

ADVERSE EFFECTS

Orally, ginger is usually well tolerated when used in typical doses. However, higher doses of 5 gms per day increase the risk of side effects and decrease tolerability. Common side effects of ginger include abdominal discomfort, heartburn, diarrhea and a pepper-like irritant effect in the mouth and throat. Topically, ginger can cause dermatitis in sensitive individuals[130].

CONCLUSION

Ginger has versatile nature in medicinal and traditional field. Ginger is a aromatic stimulant carminative and flavouring agent. It is prescribed in dyspepsia flatulent colic, nausea, vomiting, cold, cough and asthma. Ginger has the ability to down regulate free radicals elevation, improve liver and cholesterol, biomarkers, ameliorate hepatic marker enzymes, reduce collagen deposition, fibrosis severity and normalize the hepatic cells architecture. Phytoconstituents are rich of different pharmacological activity. Spices and condiments are common part of human diet obtained from plant kingdom. Because of its flavor, color, food preservation and enhance palatability, they have been extensively used in view of their health. The ginger bears an enormous number of pharmacological activities such as Cardio protective activity, Anti-inflammatory activity, Anti-microbial activity, Antioxidant property, Anti-proliferative activity, Neuro-protective activity and Hepato-protective activities which have been proved. Among those, Neuro-protective activity as well as effect of ginger in colon cancer has facilitated the extent of the further research with a positive outcome.

Ginger rhizome and Ginger plant

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