

A Review on Medicinal Activities of *Zinger Officinale*

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Abstract

Ginger, the rhizome of *Zingiber officinale*, species of the ginger family (Zingiberaceae) has a long history of medicinal use for more than 2000 years as one of the most versatile medicinal plants having a wide spectrum of biological activity and a common condiment for various foods and beverages. Rhizome of *Zingiber officinale* (ginger) is extensively used in medicinal purpose. Ayurveda literatures highlight administration of ginger in both of communicable and non-communicable diseases. Recent advances in analytical chemistry, cytology and microbiology recommend application of ginger in various disease conditions as well as recommendations in Ayurveda literature. The medicinal properties of ginger are due to the presence of gingerol and paradol, shogaols, etc... Currently, there is a renewed interest in ginger. Therefore, in the current study we aimed to describe and delineate on medicinal activities of *Z. officinale* including antiviral, anti-inflammatory, antioxidant, cardiovascular, gastrointestinal, and neuroprotective activities.

Key Words: *Zinger officinale*, Cardioprotective, Anti-Inflammatory, Anticancer, Antioxidant

Introduction

Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources that plays a vital role in treatment of diseases.¹ Traditional knowledge of medicinal plants has always explored the search for new cures. Traditional medicinal plants are often cheaper, locally available and easily consumable, raw or as simple medicinal preparations. These simple medicinal preparations often bring out beneficial responses due to their active chemical constituents.² Medicinal plants are generally known as “Chemical Goldmines” as they contain natural chemicals, which are acceptable to human and animal systems. All these chemicals cannot be synthesised in laboratories. Many secondary metabolites of plant are commercially important and find use in a number of pharmaceutical compounds. Human beings have been dependent on plants for their health care needs since the beginning of civilisation. Of the 2,50,000 higher plant species on earth, more than 80,000 are medicinal in Nature.⁴

Ginger scientifically known as *Zingiber officinale* Roscoe, belonging to family Zingiberaceae is one of 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 viz, nausea, vomiting, asthma, cough, palpitation, inflammation, dyspepsia, loss of appetite,

constipation, indigestion and pain.⁴ Most of traditional and complementary systems of medicine such as Ayurveda, Siddha, Unani, Homeopathy, Tibetan and Chinese etc. prescribe *Z. officinale* individually or as a combination in both of infective and non-communicable diseases.⁴ The plant is mostly investigated for antimicrobial, anticancer, antioxidant, antidiabetic, nephroprotective, hepato-protective, larvicidal, analgesic, antiinflammatory and immunomodulatory activities.⁵⁻¹⁴ In Ayurveda literature ginger is extensively used in loss of appetite (Agnimandya), asthmatic conditions (Svasa), bloated stomach (Adhmana), rheumatoid conditions (Amavata), anemic conditions (Pandu), liver associated conditions and disorders (Udararoga), vomitings (Chardi), swollen joints (Sandhi Shotha), fatigue (Avasada), back pains (Kati Shoola), mal-digestions (Ajeerna), flatulence (Koshta Vata), malabsorption syndrome (Grahani), stomachache (Udara Shoola), piles (Arsha), weakness in heart functions (Hrud Dourbalya), heart disorders (Hrud Roga), elephantiasis (Sleepada), allergies (Sheetapitta), throat associated disorders (Kanta Roga), cough (Kasa), Hiccough (Hikka), common cold (Pratishya), injuries (Kshata), malnutrition (Ksheena), fever due to infections (Vishama Jwara), chronic fever (Jeerna Jwara), lethargy and physical weakness (Samanya Dourbalya), physical weakness due to delivery (Prasavottara Dourbalya), chronic osteoarthritis conditions (Jeerna Sandhi Vata), headaches (Shira Shoola), pain due to nervous disorders (Vata Nadi Shoola), diabetes (Prameha), loss of speech (Swara Bhanga) and otalgia (Karna Shoola).^{15,16}

The current study focuses on describe and delineate on medicinal activities of *Z. officinale* including antiviral, anti-inflammatory, antioxidant, cardiovascular, gastrointestinal, and neuroprotective activities.

Description

Ginger is herbaceous rhizomatous perennial, reaching up to 90 cm in height under cultivation. Rhizomes are aromatic, thick lobed, pale yellowish, bearing simple alternate distichous narrow oblong lanceolate leaves (Figure 1). The herb develops several lateral shoots in clumps, which begin to dry when the plant matures. Leaves are long and 2 - 3 cm broad with sheathing bases, the blade gradually tapering to a point. Inflorescence solitary, lateral radical pedunculate oblongcylindrical spikes. Flowers are rare, rather small, calyx superior, gamosepalous, three toothed, open splitting on one side, corolla of three subequal oblong to lanceolate connate greenish segments.¹⁷



Figure 1: Showing zinger plant and rhizome

Taxonomy

The family Zingiberaceae is the largest family of Zingiberales and is one of the ten largest monocotyledonous families in India. It occurs chiefly in the tropics with about 52 genera and 1400 species with the greatest concentration in the Indo-Malayan region of Asia and represented by 22 genera and 178 species in India according to Jain and Prakash.¹⁸ Zingiberaceae forms an important group with economic potential and many members of this family yield spices, dyes, perfumes and medicines and some are ornamental. Many of them are

used in ayurvedic and other native systems of medicine. Several reports have been published concerning the biological properties (antimicrobial, antioxidant, anticancer, and a stimulated effect on the immune system) of Zingiberaceae extracts containing many essential oils like terpenes, alcohols, ketones, flavanoids, carotenoids, gingeroles, and phytoestrogens.^{19,20}

Pharmacological Significance

Apart from culinary uses, ginger and its major components, are known to have beneficial medicinal properties. Numerous pre-clinical studies have supported their value in the treatment of diabetes, obesity, diarrhoea, allergies, pain, fever, rheumatoid arthritis, inflammation and various forms of cancer. Tumours induced in the bowel, breast, ovaries, pancreas, Liver, CNS and cardiovascular disorders have been effectively treated in animal models with biologically active constituents of ginger. Ginger and its metabolites have been recognised as potent anti-oxidants due to their ability to inhibit the oxidation of various free

radicals and the production of nitric oxide. The biological activities of several volatile and non-volatile constituents of ginger through selected *in vitro* and *in vivo* models, are discussed in the following sections.

Antiviral

Fresh rhizome of *Z. officinale* has been proven with an antiviral effect against Human Respiratory Syncytial Virus (HRSV) infection via decreasing HRSV- induced plaque formation in respiratory mucosal cell lines. Therefore, high concentration of *Z. officinale* could

stimulate mucosal cells to secrete IFN- β which responsible in counteracting viral infections by reducing viral attachment and internalization.²² This effect is much beneficial in the management of common cold (pratishtya) and fever associated with mucous secretions and management of complications due to cough and asthmatic conditions. The lyophilized juice extract of *Z. officinale* is considered as containing antiviral effect against Hepatitis C viral infection. In the particular study, it has been proven that the *Z. officinale* is effective in inhibiting the viral replication inside the Hepatitis C virus infected Hep G2 cells by affecting viral RNA²³ as well as, another study elaborates that *Z. officinale* is effective in decrease of Hepatitis C virus loads, level of α -fetoprotein and markers relevant to liver functions such as Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) in Egyptian HCV patients.²⁴ Ayurveda recommends administering ginger in udara roga (liver associated diseases conditions), therefore the above finding clarifies the uses of ginger in liver disorders and infective conditions associate the liver. Aqueous extract of *Z. officinale* was proven with antiviral effect against Feline Calcivirus, a surrogate for Human Norovirus when in alimentary channel infections due to foodborne causes.²⁵ Ginger is widely used in alimentary channel disorders under the instructions given in Ayurveda authentic literatures. Especially, in flatulence, constipation, loss of appetite and needs of appetite enhancer, ginger has been recommended. Additionally, ginger is applicable for mal-absorption conditions and digestive diseases. Other than the antiviral effect of ginger in foodborne disorders, Ayurveda elaborates application of ginger in management of complications in foodborne viral infections. Allicin is an active ingredient which contains in *Z. officinale*, consists with anti-influenza cytokines. Hence, *Z. officinale* is effective as an antiviral agent against influenza A (H1N1).²⁶ Macrophage mediated inhibitory effect of *Z. officinale* Rosc on the growth of Influenza A/Aichi/2/68 virus was already studied and which suggests *Z. officinale* is beneficial in macrophage activation leading to production of TNF- α .²⁷ Essential oil of *Z. officinale* is affected genital origin Herpes simplex virus type 2 (HSV-2) mainly before adsorption probably by interacting with the viral envelope.²⁰ In another study, acyclovir-resistant clinical isolates of Herpes simplex virus type 1 (HSV-1) were analyzed *in vitro* for their susceptibility to essential oil of ginger and found high level of virucidal activity against acyclovir sensitive strains and acyclovir resistant HSV-1 clinical isolates and reduced plaque formation significantly.²⁹ Radioprotective effect oral administration of hydroalcoholic extract of *Z. officinale* rhizome for mice are effective in protecting against gamma radiation induced sickness and mortality due to phytochemical actions such as dehydrogingerone and

zingerone. As well, zingerone selectively protects the normal tissues against the tumoricidal effects of radiation in tumor bearing mice.³⁰

Anti-inflammatory

Z. officinale is highly effect in inflammations associated with alimentary channel such as colitis. The plant responsible with poshatidylinositol-3-kinase (PI3K), protein kinase B (Akt) and the nuclear factor kappa light chain enhancer of activated B cells (NF- κ B), as well as 6-shogaol responsible in protective effects against tumor necrosis factor α (TNF- α) induced intestinal dysfunction in human intestinal cell models.³¹ In physically, promote attenuate inflammation at post-exercise elevation of cytokines such as plasma IL-1 β , IL-6 and TNF- α .³² In inflammatory bowel disease, *Z. officinale* is highly effective, because of protein kinase B (Akt) and the nuclear factor kappa light chain enhancer of activated B cells (NF- κ B) contains. As a result, an enhancement in anti-inflammatory cytokines and a decline in pro-inflammatory cytokines could be observed. Therefore, an applicable remedy is available at inflammatory bowel disease.³³

Gingerole in *Z. officinale* is containing anti-prostaglandin effects which are beneficial in menstrual pain at dysmenorrhea condition.³⁴ Other than the prostaglandin, ginger inhibits leukotriene biosynthesis through suppression of 5-lipoxygenase synthesis. Rhizome hexane fraction extract of *Z. officinale* inhibit excessive production of Nitric oxide and IL-1 β at allergic reactions. Therefore, management and prevention from allergic conditions are supported by *Z. Officinale*.^{35,36} 6-shagol in *Z. officinale* is highly effective in gout as a rheumatic disease of joints.³⁷ Restoration of heart functions, pain management effect and management of physical weakness and reestablishing of appetite denote anti-inflammatory activity of ginger referring Ayurveda recommendations. Anti-cancer Effect *Z. officinale* exhibits anti-inflammatory and anti-tumorigenic effects due to its bio active molecules such as 6-gingerole, 6-shogaol, 6-paradol and zerumbone, as a result prevention or control from colorectal, gastric ovarian, liver, breast and prostate cancers is possible.³⁸⁻⁴⁵ *Z. officinale* activates enzymes such as glutathione peroxidase, glutathione s transferase and glutathione reductase and suppress colon carcinogenesis.⁴⁶ Oral administration of Zerumbone effects in inhibition of multiplicity of colonic adenocarcinomas through suppression of colonic inflammation due to inhibition of proliferation, induction of apoptosis and suppression of NF- κ B and heme oxygenase (HO)-1 expression.⁴² In gastric carcinomas, gingerol and shogaol effect in TRAIL induced NF- κ B, suppresses cIAP1 expression and increases TRAIL induced caspase-3/7 activation which promotes apoptosis⁴⁴ as well gingerol is effect in liver cancers by arresting cell cycle and induction of apoptosis.⁴⁷ Growth inhibition of human epidermoid carcinoma cells via reactive oxygen species (ROS) induced apoptosis is exhibited by gingerol with considerable amount of toxicity.⁴⁸ Active compounds of *Z. officinale* effect in controlling ovarian cancers via inhibition of NF- κ B activation and diminished the secretion of VEGF and IL-8.⁴⁹ Zerumbone is also effect in controlling pancreatic cancers through p53 signal pathway, formation of apoptotic bodies, condensed nuclei and the increased activity of caspase-3.⁵⁰ Maintaining, proper circulation, nervous conduction, heart functions and balancing

digestive and absorptive disorders through enhancing appetite is beneficial in enhancement of the immunity of the body which supports in alleviate abnormal growths and malfunctions of physiological body.

Antioxidant

Z. officinale is effective in Parkinson's disease because zingerone, an active ingredient in ginger scavenged peroxide and hydroxyl ions as well as suppress lipid peroxidation.⁵¹ Ginger consists with renoprotective effect in renal failures because of anti-inflammatory properties by attenuating serum C-reactive protein levels and antioxidant effects by reducing lipid peroxidase marker, malondialdehyde levels and increasing renal superoxide dismutase activity.⁵² Carbon tetra chloride and acetaminophen induced liver damages in acute liver injuries are preventing.⁵³ Through proper digestion and absorptions, as well as maintaining proper circulations ginger supports elevation of waste productions while physiological functions. Hence accumulation of physical excretions evacuates from the body and immune-enhancement is occurred.

Cardiovascular

Ginger, in traditional Chinese medicine, is used to monitor the movement of body fluids. It exhibited a dominant stimulatory effect on the heart muscles by diluting blood and thereby exciting blood circulation all over the body.⁵⁵ Enhanced circulation improved the cellular meta-bolic activity thereby relieving cramps and tension.⁵⁶ Besides, reports from Japanese group have shown that the blood pressure and cardiac workload could be declined due to certain active constituents in ginger. Additionally, ginger reduced the formation of pro-inflammatory prostaglandins and thromboxane thereby lowering the clotting ability of the blood.⁵⁷ The inhibition of platelet aggregation by ginger is more than the alike effects studied with garlic and onion.⁵⁸ One of the most important properties of ginger is that it be capable of averting increased cholesterol levels, following intake of cholesterol-rich diet.⁵⁹ The ginger extracts as well as 6- and 8-gingerols have been shown to modulate eicosanoid responses in smooth vascular muscles *ex-vivo*.⁶⁰ These analogues were found to inhibit AA-induced serotonin release by human platelets in a dose range similar to the effective dose of aspirin and their aggregation. Importantly, 6-gingerol and 6-shogaol, at the doses of 10–100 µg/kg, not only lowered systemic blood pressure in anesthetized rats but also caused 537Gastrointestinal effects bradycardia when administered intravenously.⁶¹ Several evidences, mostly from experiments performed on rats, have suggested that ginger exerts many direct and indirect effects on blood pressure and heart rate⁶² showing a dose-dependent (0.3–3 mg/kg) fall in the arterial blood pressure of anesthetized rats. The Ca²⁺ channel blocking activity of gingerols was found to be similar to the effect of verapamil, indicating that it acts at both the membrane-bound and the intracellular Ca²⁺ channels. Recent study has also confirmed the blood pressure lowering effect of ginger is mediated through blockade of voltage dependent calcium channels⁶³ through a dual inhibitory effect mediated via stimulation of both muscarinic receptors and blockade of Ca²⁺ channels. This group noted that the different constituents of ginger might have opposing actions on the reactivity of blood vessels. For example, an atropine-resistant and L-NAME (NG-nitro-L-arginine methyl

ester)-sensitive vasodilator activity was also noted for the ginger phenolic constituents 6-, 8-, and 10-gingerols, while 6-shogaol showed a mild vasodilator effect.⁶³ Experiments have shown inconclusive and contradictory results in anticoagulating potential of ginger. Lumb and Bordia et al. found no effect of ginger on platelet count, bleeding time, platelet aggregation, fibrinolytic activity, or fibrinogen levels.^{64,65} Ginger has been shown to inhibit platelet aggregation⁶⁶ and to decrease platelet thromboxane production in vitro.⁶⁷ 8-Gingerol, 8-shogaol, 8-paradol, and gingerol analogues exhibited antiplatelet activities, but Verma et al. found ginger to decrease platelet aggregation.⁶⁸ Similarly, Janssen et al.⁶⁹ showed no effect of oral ginger on platelet thromboxane B2 production, while Srivastava found thromboxane levels to be decreased by ginger ingestion in a small study.⁷⁰ These studies demand a thorough evaluation of activity with respect to anticoagulant effect

Gastrointestinal

Peptic ulcer is a major health problem worldwide in both males and females having several factors triggering its effect including food ingredients, stress, *H. pylori*, and drugs. In traditional system of medicine, medicinal plants and its constituents have shown antiulcer effect in various ways, but their exact mechanism is not fully understood.⁷¹ Ginger and its constituents show a vital role in ulcer prevention via increasing mucin secretion. Earlier findings have shown antiulcerative effects of ginger in experimental gastric ulcer models.⁷² Studies have demonstrated 6-gingerol and 6-shogaol suppressed gastric contraction in situ, with 6-shogaol having more intensive effect.⁷³ It was found that acetone, 50% ethanolic extracts (100–500 mg/kg), and ginger juice (2–4 mL/kg) reversed cisplatin induced delay in gastric emptying in rats when given orally.⁷⁴ The effect on gastric motility may be partially explained by the antiemetic properties of ginger. Several experiments on the effect of ginger on gastric motility have supported this observation. Ginger is found to stimulate bile secretion, intestinal lipase, trypsin, chymotrypsin, amylase, sucrase, and maltase activities in rats, with 6- and 10-gingerols being chiefly responsible for this activity. These findings support the traditional use of ginger as a digestive stimulant. Traditionally, ginger is probably best utilized in alleviating symptoms of nausea and vomiting, and several controlled studies have reported that ginger is generally effective as an antiemetic.⁷⁵ But its mechanism of action 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.⁷⁶ Animal models and in vitro studies have demonstrated that ginger extract possesses antiserotonergic and 5-HT₃ receptor antagonism effects, which play an important role in postoperative nausea and vomiting.⁶⁴ The effectiveness of ginger as an antiemetic has been attributed to its carminative effect, which helps to break up and expel intestinal gas. This idea was supported by the results of a randomized, double-blind trial in which healthy volunteers reported ginger effectively accelerated gastric emptying and stimulated antral contractions.⁷⁷ Contrary to this in another randomized, placebo-controlled, crossover trial of 16 healthy volunteers, ginger (1 g orally) had no effect on gastric emptying.⁷⁸ However, this is also true that nausea and vomiting during pregnancy affects most pregnant women, and over the years, ginger has been used to alleviate the condition.⁷⁹ At least one survey indicated that the overall use of dietary

supplements in pregnant women appears to be low, but ginger is commonly recommended and used to prevent nausea.⁷⁹ Several double-blind, randomized, placebo-controlled clinical trials have indicated that ginger consumption is effective and safe in helping to prevent nausea and vomiting during pregnancy.^{80,81}

Ginger may also increase the conversion of cholesterol into bile acids by increasing the activity of hepatic cholesterol-7- α -hydroxylase, the rate limiting enzyme of bile acid biosynthesis.⁸² There is evidence that ginger rhizome (root) increases stomach acid production thereby interfering with antacids, sucralfate (Carafate), H₂ antagonists, or proton pump inhibitors. Interestingly,⁸³ shogaol, generally being more potent than (6)-gingerol, has shown inhibitory intestinal motility in intravenous preparations and facilitatory gastrointestinal motility in oral preparations. A number of animal studies have demonstrated hypocholesterolemic action of ginger and ginger extracts by decreased lipid peroxidation and increased fibrinolytic activity. These studies have shown decreased levels of total cholesterol, LDL-cholesterol, very low-density-lipoprotein-cholesterol and triglycerides, and increased levels in high-density-lipoprotein-cholesterol.⁸⁴ 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%. It is evident from these findings that ginger has demonstrated potential of being an antiatherosclerotic agent in animal studies, but as yet this promise has not been confirmed in human trials. Experimentally, it has found that ethanolic extract of ginger show antipyretic effect comparable to that of acetylsalicylic acid at the same dose.⁷¹ This antipyretic activity may be mediated by COX inhibition. Furthermore, studies have shown that the ginger crude extract and the paracetamol drug have the same level of efficacy in lowering body temperature. Further studies on this aspect will be a welcome step.

Neuroprotective

Ginger and their constituents play a vital role as a neuroprotector. The exact mechanism of action of ginger in this vista is not known fully. But it is thought ginger shows neuroprotector effect due to the phenolic and flavonoids compounds. An important study has shown that 6-shogaol has neuroprotective effects in transient global ischemia via the inhibition of microglia.⁸⁵ Another finding in the support of ginger as neuroprotector suggests that it exhibit neuroprotective effect by accelerating brain anti-oxidant defense mechanisms and down regulating the MDA levels to the normal levels in the diabetic rats.⁸⁶

Conclusion

Ayurveda recommends *Zingiber officinale* (ginger) to manage various disease conditions in spite of mentioning modern perspectives on antiviral, anti-inflammatory, and anticancer and antioxidant effects. *Zingiber officinale* has been subjected to many extensive clinical investigations. Comparing recommendations of ginger for medicinal purpose according to the Ayurveda literatures could be applied in modern scenarios in disease prevention and health promotion.

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