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## A Review on *Zingiber officinale*

**Jyotsna Dhanik, Neelam Arya and Viveka Nand**

#### Abstract

Spice and medicinal plants gained an important role in agronomy production, pharmacy and exportation because of their increased use as a raw material for the pharmaceutical industry and in the everyday life. 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. The medicinal properties of ginger are due to the presence of gingerol and paradol, shogaols, etc. Currently, there is a renewed interest in ginger, and several scientific investigations aimed at isolation, identification of active constituents, scientific verification of its pharmacological actions for treatment of several diseases and conditions. This article aims at reviewing the most salient recent reports on ethnobotany, pharmacology, phytochemistry and biological activities of *Z. officinale*.

**Keywords:** *Z. officinale*, Pharmacology, Phytochemicals, Nutritional profile, Zingerone

#### 1. 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 [3].

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].

#### Taxonomic position

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 [5]. 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, gingerols, and phytoestrogens [6, 7].

#### Distribution

Ginger is supposed to have originated in South-East Asia. Ginger has been cultivated for thousands of years as a spice and also for its medicinal purposes.

During the medieval years, ginger plants were carried on ships from the Indian subcontinent and were introduced to different parts of the world. Currently, India and China are the dominant suppliers to the world market [8]. Ginger is cultivated in countries like India, China, Nigeria, Indonesia, Bangladesh, Thailand, Philippines, Jamaica etc. It is also grown in Australia, Fiji, Brazil, Sierra Leone and Japan. United Kingdom, United States, Japan and Saudi Arabia. Nigeria ranks first with respect to area under ginger covering about 56.23% of the total global area followed by India (23.6%), China (4.47%), Indonesia (3.37%) and Bangladesh (2.32%). India ranks first with respect to ginger production contributing about 32.75% of the world's production followed by China (21.41%), Nigeria (12.54%) and Bangladesh countries lead in the supply of ginger in the world market. Japan and USA are the major importers. India exports mainly in the form of whole and dry ginger China, Nigeria and Thailand are competing with India in the recent past in the world market. Australia is the world leader in value added products. India has 50% share in oil and oleoresin trade. 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% to the country's total production. In terms of quality, Jamaican and Indian ginger are considered to be superior followed by West African variety. India is biggest producer of *Z. officinale* in the world.

**Table 1:** Top ten Ginger producing country of the world

S. No.	Country	Production(Tonnes)
1.	India	683000
2.	China	425000
3.	Nepal	235033
4.	Indonesia	232669
5.	Nigeria	160000
6.	Thailand	140000
7.	Bangladesh	69000
8.	Japan	57835
9.	Cameroon	46350
10.	Philippines	28216

Food and agricultural Organisation of United Nations: Economic and Social department: The statistical division (2013) [9].

**Table 2:** Top ten Ginger producing states in India

S. No.	State	Production(Tonnes)
1.	Assam	122307
2.	Gujarat	70646
3.	Karnataka	50054.3
4.	Arunachal Pradesh	57000
5.	Meghalaya	62994
6.	Sikkim	52110
7.	Orrisa	35000
8.	Mizoram	28390
9.	West Bengal	25000
10.	Uttarakhand	23440
11.	Kerala	21249
12.	Andhra Pradesh	1369
13.	Telangana	12729

Food and agricultural Organisation of United Nations: Economic and Social department: The statistical division (2013) [9].

## 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. 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 oblong cylindrical 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 [10].

## Agrotechnology

Ginger grows in warm and humid climate. It is mainly cultivated in the tropics from sea level to an altitude of above 1500 MSL and it can be grown both under rainfed and irrigated conditions. For successful cultivation, ginger requires a moderate rainfall at the sowing time till the rhizomes sprout, fairly heavy and well distributed showers during the growing period and dry weather for about a month before harvesting. Ginger thrives the best in well drained soils like sandy or clay loam, red loam or lateritic loam. A friable loam rich in humus is ideal. However, being an exhaustive crop it may not be desirable to grow ginger in the same site year after year. It thrives well under partial shade, though it is also grown on a large scale in open area.

## Varieties of ginger

Several hybrid varieties of ginger are grown in South Asian region. However, the cultivars depends upon the climate, soil and local conditions. The important cultivars are: High Yielding Types: Maran, Karakkal, Rio de Janeiro and Mahim. Less Fiber Content: Jamaica, Bangkok and China Thingpuri. High Oleoresin: Emad Chemed, China, Karuppamadi and Rio de Janeiro.

High Dry Ginger Recovery: Karakkal, Nadia, Maran and Tura. High volatile oil: Sleavea local, Narasapattam and Emad. Chemed.

**Table 3:** Different varieties of ginger

Country	Varieties
India	Varada, Mahima, Rejhata, Suruchi, Suprabha, Himanchal, Maran, Nadia, Karakkal, Mananthody, Sabarimala, Ellakallan, Kakakkalan, Kozhikkalan, Pink ginger, Bhaise, Jolpaiguri
China	China ginger
Nepal	Naval parasi, Bakthapur
Japan	Kintoki
Nigeria	Juggigan
Jamaica	Jamaica
Pakistan	Pakistan
Oman	Oman
Brazil	Brazil

## Nutrient Composition

Ginger is widely used in a variety of foods because of its nutritional composition and flavouring compounds. Ginger rhizomes are rich source of carbohydrates, vitamins, minerals and iron. The different vitamins, minerals and phytochemicals content in present in ginger rhizomes are shown in Table 4, 5 & 6. Ginger possesses a high nutritional value. However,  $\alpha$ -acids, reducing sugars, and vitamin C can give

rise to the Maillard reaction upon heating (similarly as in other foods) with the formation of off-flavors (mainly

heterocyclic compounds) and the formation of melanoidins [11, 12].

**Table 4:** Nutrient composition of Ginger (per 100g 3.5oz) [13]

Constituents	Ginger root (ground)	Ginger root (Raw)
Energy	1404KJ(336Kcal)	333 KJ ( 80 KCal)
Carbohydrates	71.6g	17.7 g
Sugars	3.39g	1.7g
Dietry Fibre	14.1g	2.0g
Fat	4.24g	0.75g
Protein	8.98g	1.82g

**Table 5:** Vitamin content of Ginger (per 100g) [13]

Vitamins	Ginger root(Ground)	Ginger root(Raw)
Thiamine(B1)	0.046mg	0.025mg
Riboflavin(B2)	0.17mg	0.034mg
Niacin(B3)	9.62mg	0.75mg
Panthenic acid(B5)	0.477mg	0.203mg
Vitamin B6	0.626mg	0.16mg
Folate(B9)	13µg	11µg
Vitamin C	0.7mg	5mg
Vitamin E	0.0	0.26mg

**Table 6:** Minerals content of ginger (per 100 g) [13]

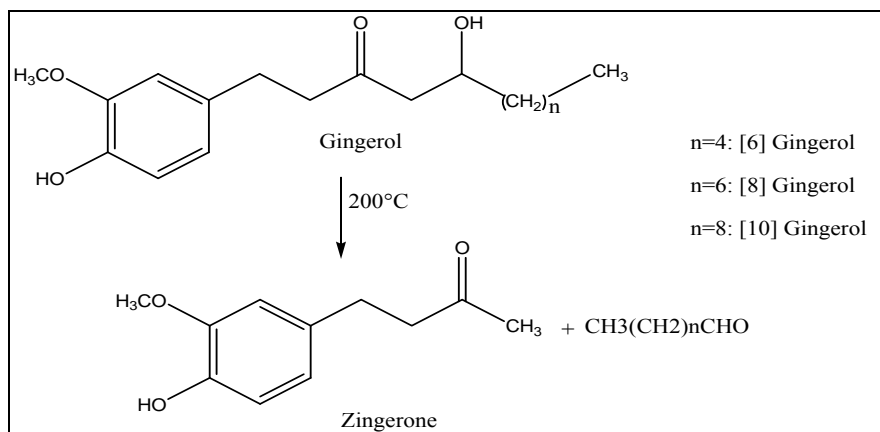
Minerals	Ginger root(Ground)	Ginger root(Raw)
Calcium	114mg	16mg
Iron	19.8mg	0.6mg
Magnesium	214mg	43mg
Manganese	33.3mg	0.229mg
Phosphorus	168mg	34mg
Potassium	1320mg	415mg
Sodium	27mg	13mg
Zinc	3.64mg	0.34mg

### Chemical composition

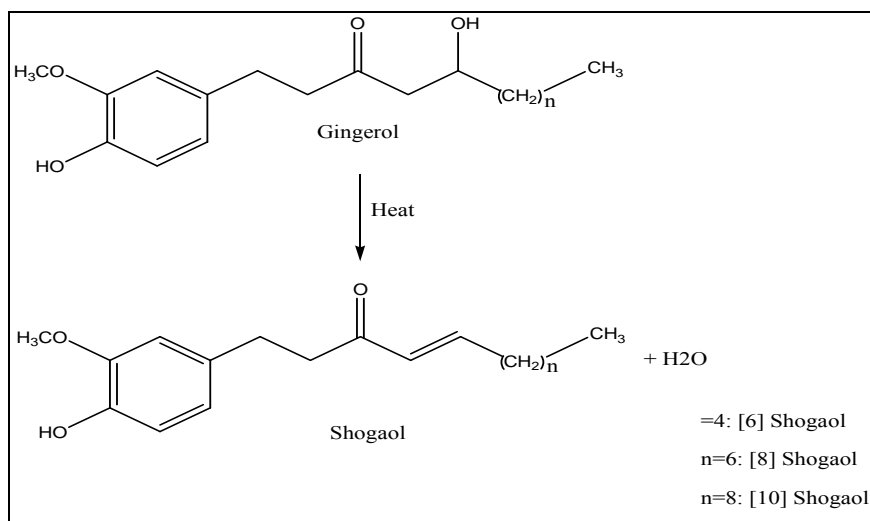
Phytochemical studies show that ginger rhizome contains a wide variety of biologically active compounds which impart medicinal property. *Z. officinale* is reported to possess essential oils, phenolic compounds, flavonoids, carbohydrates, proteins, alkaloids, glycosides, saponins, steroids, terpenoids and tannin as the major phytochemical groups. The chemistry of *Z. officinale* has been the subject of sporadic study since the early 19<sup>th</sup> century. In common with some other pungent spices, considerable advances were made in the early part of the 20<sup>th</sup> century, but it has only been in recent years that a fairly clear understanding of the relationship of its chemical composition to its organoleptic properties has emerged. Ginger, owes its characteristic organoleptic properties to two classes of constituents: the odour and much of the flavour of ginger is determined by the constituents of its steam-volatile oil, while the pungency is produced by nonsteam- volatile components. The aroma and flavour of ginger are determined by the composition of its steam volatile oil, which is comprised mainly of sesquiterpene hydrocarbons, monoterpene hydrocarbons and oxygenated monoterpenes. The monoterpene constituents are believed to be the most important contributors to the aroma of ginger and they tend to be relatively more abundant in the natural oil of the fresh ('green') rhizome than in the essential oil distilled

from dried ginger. Oxygenated sesquiterpenes are relatively minor constituents of the volatile oil but appear to be significant contributors to its flavour properties. The volatile oil consists mainly of the mono- and sesquiterpenes; camphene,  $\beta$ -phellandrene, curcumene, cineole, geranyl acetate, terphineol, terpenes, borneol, geraniol, limonene,  $\beta$ -elemene, zingiberol, linalool,  $\alpha$ -zingiberene,  $\beta$ -sesquiphellandrene,  $\beta$ -bisabolene, zingiberenol and  $\alpha$ -farnesene [14, 15]. Zingiberol is the principal aroma contributing component of ginger rhizome [16].

The species contains biologically active constituents including the non-volatile pungent principles, such as the gingerols, shogaols, paradols and zingerone that produce a "hot" sensation in the mouth. The gingerols, a series of chemical homologs differentiated by the length of their unbranched alkyl chains, were identified as the major active components in the fresh rhizome. The pungency of dry ginger mainly results from shogaols, which are dehydrated forms of gingerols. Gingerols are thermally labile because of the presence of a  $\beta$ -hydroxy keto group and readily undergo dehydration to form the corresponding shogaols. Paradol is similar to gingerol and is formed on hydrogenation of shogaol. Oleoresin, which is isolated by acetone and ethanol extraction, contains 4-7.5% of dried powder, pungent substances namely gingerol, shogaol, zingerone and paradol.



**Fig 1:** Conversion of Gingerols to Zingerone & aliphatic aldehyde at high temperature

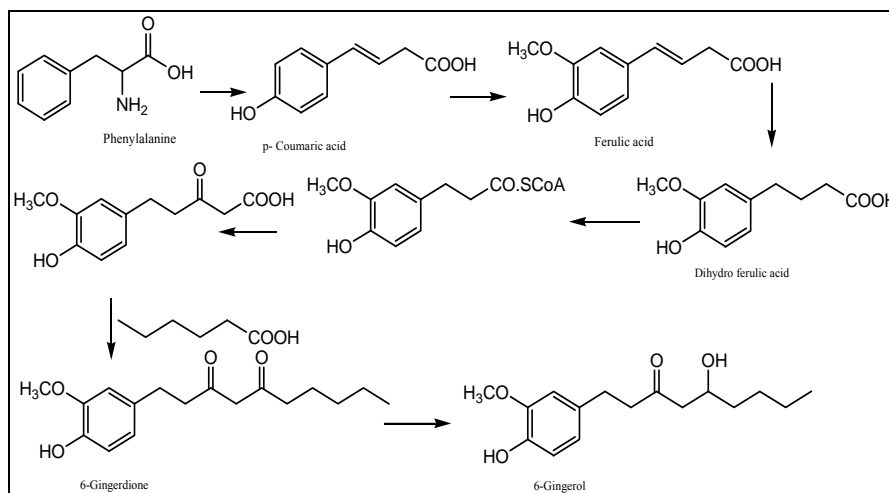


**Fig 2:** Dehydration of Gingerols to Shogaols at high temperature

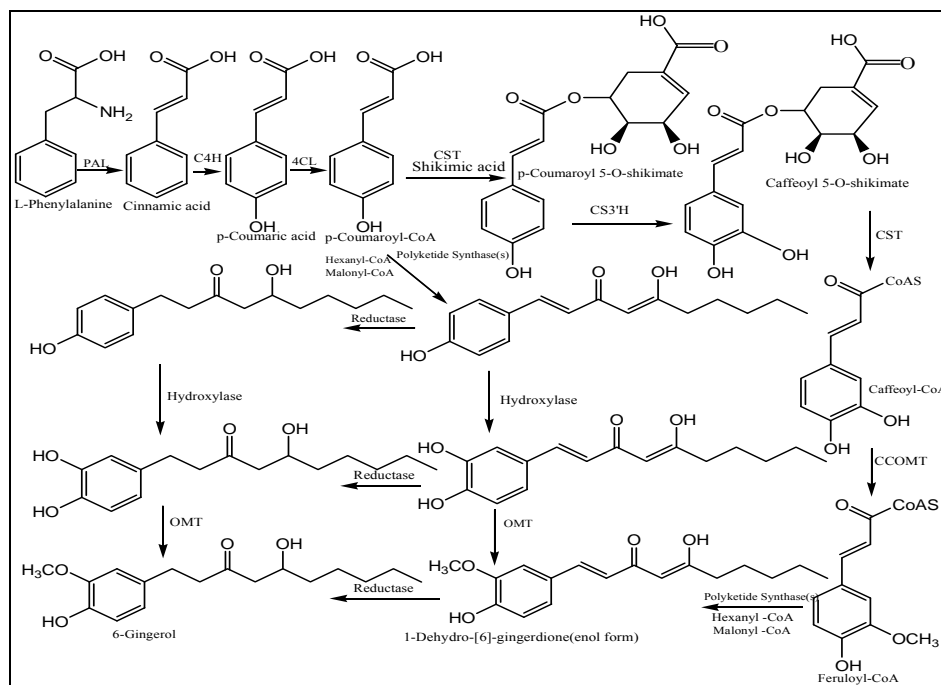
### Biosynthesis

Macleod and Whiting (1979) stressed the importance of dihydroferulic acid and hexanoic acid in the biosynthesis of (S)-6-GN in ginger [17]. The roles of these compounds were further elucidated when the complete route of biosynthesis of (S)-(+)-6-GN in ginger was proposed by Denniff and Whiting (1976a) and (Denniff *et al.*, 1980) [18, 19]. According to these researchers, phenylalanine is converted to dihydroferulic acid, which subsequently participates in a biological Claisen

reaction with malonate and hexanoate to form 6-dehydrogingerdione, which is finally converted to 6-GN (Scheme 1). Ramirez-Ahumada *et al.*, 2006 suggested an alternative pathway for 6-GN biosynthesis in ginger, in which particular enzymes, including phenylalanine ammonia lyase, p-coumaroyl shikimate transferase, p-coumaroyl quinate transferase, caffeic acid O-methyltransferase and caffeoyl-CoA-O-methyltransferase, play key roles in the process (Scheme 2) [20].



**Scheme 1:** Biosynthetic pathway for 6-gingerol [19].



**Scheme 2:** Biosynthesis of 6-gingerol [20]. Enzymes: PAL= phenylalanine ammoniylase; C4H= cinnamate 4-hydroxylase; 4CL= 4-coumarate: CoA ligase; CST= p-coumaroyl shikimate transferase; CS3H= p-coumaroyl 5-O-shikimate 3'-hydroxylase; OMT= O-methyltransferase; CCOMT= caffeoyl-CoA O-methyltransferase

### 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.

### Antioxidant activity

Antioxidants are compounds or systems that can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. They can use several mechanisms: (i) scavenging species that initiate peroxidation, (ii) chelating metal ions so that they are unable to generate reactive species or decompose peroxides, (iii) quenching  $\cdot\text{O}_2^-$  preventing formation of peroxides, (iv) breaking the auto-oxidative chain reaction, and/or (v) reducing localized  $\text{O}_2$  concentrations [33]. Ginger can be regarded as the storehouse of antioxidants. It has an extraordinary property of scavenging reactive oxygen species (ROS), free radicals, peroxides, and various other damaging oxidants. The active ingredients like gingerols, shogaols, zingerone, and so forth present in ginger exhibit antioxidant activity. It inhibits an enzyme, namely, xanthine oxidase, which is mainly involved in the generation of reactive oxygen species. Zingerone has been reported to protect *in vitro* DNA against stannous chloride induced ROS oxidative damage [34]. Zingerone provides direct adaptogenic effect by preventing oxidative stress on smooth muscles of intestine [35]. These findings lead to a conclusion that

zingerone is a potent antioxidant.

Geraniol is an important chemopreventive agent and various studies have demonstrated that geraniol has a potent antioxidant effect by scavenging oxygen-free radicals and increasing the level of total glutathione content (GSH) in murine skin [36]. Gingerol analogues, 6-, 8-, 10-GN, as well as 6-SG, displayed anti-oxidant activities with  $\text{IC}_{50}$  values ranging from 8.05 to 26.3  $\mu\text{M}$  for the DPPH radical, 0.85–4.05  $\mu\text{M}$  for the superoxide and 0.72–4.62  $\mu\text{M}$  for the hydroxyl radical [21].

Eleazu and Eleazu (2012) studied antioxidant potentials of six varieties of ginger [37]. 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. Masuda *et al.*, 2004 analyzed an antioxidant activity of gingerol-related compounds isolated from the dichloromethane extract of the ginger rhizomes. Gingerols, shogaols, gingerdiols, gingerdiones, and dehydrogingerdiones (with an alkyl group bearing 10-, 12-, or 14-carbon chain length) showed antioxidant activity [38]. Their results suggested that the substituents on the alkyl chain might contribute to both radical scavenging effect and inhibitory effect of autoxidation of oils. Stoilova *et al.*, 2007 evaluated the antioxidant effect of ginger and its  $\text{CO}_2$  extract [39].

### Antimicrobial activity

Foodborne illnesses are a major concern for consumers, the food industry, and food safety authorities. In recent years, considerable effort has been made to find natural antimicrobials that can inhibit bacterial and fungal growth in foods in order to improve quality and shelf-life. Natural extracts of plants have been used for many years for different

purposes and recently they have been screened for their potential use as alternative remedies and food preservatives [40]. The antibacterial activities of plant extracts and oils can be useful for the preservation of raw and processed food, in the pharmaceutical industry and as alternative medicines and natural therapies [41].

Ginger has strong antibacterial and to some extent antifungal properties. Studies have revealed that a methanol extract of *Z. officinale* rhizomes possesses significant antibacterial activity against *Escherichia coli*, *Salmonella enteritidis* and *Staphylococcus aureus* [42]. *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 [43]. Zingerone also showed protective effect in hyper motility mediated diarrhea that was linked to inhibition of gastrointestinal motility [31]. A recent study also indicated that zingerone supplemented Pacific white shrimp (*Litopenaeus vannamei*) juveniles showed strengthening of immunity and protection against *V. alginolyticus* challenge [44].

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 [46]. Another study reports on the bioassay-guided isolation of antifungal compounds from an African land race of ginger, *Zingiber officinale* Roscoe, and the identification of 6, 8 and 10-gingerols and 6-gingerdiol as the main antifungal principles.

**Anti-diabetic activity** Diabetes is a metabolic disorder and major global health problem worldwide. It is caused by abnormality of carbohydrate metabolism which is related to low blood insulin level or insensitivity of target organs to insulin [47]. Untreated cases show severe tissue and vascular damage leading to serious complications such as retinopathy, neuropathy, nephropathy, cardiovascular complications and ulceration. 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 [48]. Earlier study reported that significant blood glucose lowering effect of ginger juice in diabetic and non-diabetic animals [49]. The growth of osteoblastic MC3T3-E1 cells was increased in the presence of 0.1 mM 6-GN and 30 mM 2-deoxy-D-ribose, 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 [50]. 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 [51].

Recent studies showed that gingerol, its chief active constituent, enhanced cell-mediated glucose uptake via increasing insulin-sensitivity, thus improving chronic disease, as diabetes [52]. The main component 6-gingerol also exhibited hypoglycemic property when administered to diabetic mice and improved impaired insulin signaling in arsenic intoxicated mice [53, 54].

### Anti-cancer activity

A continued increase in the incidence of cancer has alerted consumers to the use of functional foods that protect against, and reduce the acceleration of the disease. The beneficial effects of ginger and its metabolites against a variety of carcinomas and cell lines of the lung, colon, skin, pancreas, prostate, liver, ovary, colon, breast, kidney, etc. have been recognised by many researchers over the past 20 years.

An ethanolic ginger extract applied topically to mouse skin provided a highly significant protective effect against the development of skin tumours, and this was associated with the inhibition of 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-caused induction of epidermal ornithine decarboxylase, cyclooxygenase and lipoxygenase activities [55]. A subsequent study showed [6]-gingerol to have similar activity [56].

A more recent study showed that topical application of [6]-gingerol inhibited COX-2 expression in mouse skin stimulated with the tumour promoter TPA [27]. Results from this study suggested that the inhibition of COX-2 expression was the result of the blocking of the p38 MAP kinase- NFκB signalling pathway. A cytotoxic or cytostatic effect mediated by apoptosis was found for [6]-gingerol and [6]-paradol in human promyelocytic leukaemia HL-60 cells, and also for four diarylheptanoids and two shogaols [57, 58].

Recent studies have shown that zingerone contains anticancer potential. It has been proved that supplementation with zingerone in DMH (dimethyl hydrazine) treated rats led to a significant decrease in tumor incidence and aberrant crypt foci formation with simultaneous modulation in the levels of tissue lipid peroxidation and antioxidant status [32].

Another important study has shown that 6-shogaol show anticancer activities against breast cancer via inhibition of cell invasion reduction of matrix metalloproteinase-9 expression [59]. Another important finding suggest that 6-gingerol stimulates apoptosis through upregulation of NAG-1 and G1 cell cycle arrest through downregulation of cyclin D1 [60]. An important study reported that ginger root extracts and gingerol play a significant role in inhibition of the growth of *Helicobacter pylori* CagA<sup>+</sup> strains, which has a specific gene linked to the development of gastric premalignant and malignant lesions [45]. Previous findings described the potent anti-tumor activity of geraniol against different types of malignancies, including carcinomas of the prostate, the liver, the colon and the oral cavity [61, 62, 63, 64].

### Antiinflammatory activity

Inflammation is a host defence mechanism of the body and it's an essential immune response that enables the body to survival during infection or injury and maintains tissue homeostasis in noxious conditions. Inflammation is a localized protective reaction of cells tissues of the body to allergic or chemical irritation, injury or infections.

Recent study documented the ability of a hexane fraction of dried ginger methanolic extract to suppress proinflammatory gene expression in LPS-activated BV2 microglial cells, thus displaying anti-neuroinflammatory activity [65].

Gingerol and structurally related pungent principles of ginger including shogaol exert inhibitory effects on biosynthesis of prostaglandins and leukotrienes through suppression of prostaglandin synthase or 5-lipoxygenase [66, 67]. Several reports have addressed the anti-inflammatory effects of whole ginger extract on the production of NO/iNOS, PGE2/COX-2, TNF-α, IL-1β, 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 [30].

<sup>43, 68]</sup>. The proposed mechanism behind 6-shogaol inhibition of NO evolution in stimulated macrophages involves down-regulation of inflammatory iNOS and COX-2 gene expression by inhibition of the activation of NF- $\kappa$ B, because NF- $\kappa$ B plays a critical role in the coordination of the expressions of pro-inflammatory enzymes <sup>[69]</sup>. For the human being, the consumption of fresh ginger demonstrated promising results for the decrease of arthritis-induced <sup>[70]</sup>. These results show that ginger could be used as anti-inflammatory agent and thus as anti-pain <sup>[71]</sup>.

#### Analgesic activity

[6]-shogaol has also been shown to inhibit acetic acid-induced writhing in mice and to elevate the nociceptive threshold of the yeast-inflamed paw <sup>[22]</sup>. Experiments carried out by Onogi and co-workers suggested that [6]-shogaol inhibits the release of Substance P by stimulation of the primary afferents from their central terminal and hence shares this site of action with capsaicin <sup>[72]</sup>.

#### Antipyretic activity

A Soxhlet extract of ginger in 80% ethanol reduced yeast-induced fever in rats by 38% when administered orally (100 mg/kg) <sup>[73]</sup>. This was comparable to the antipyretic effect of acetylsalicylic acid at the same dose. The ginger extract did not affect the temperature of normothermic rats. This antipyretic activity may be mediated by COX inhibition.

#### Immunomodulatory activity

The beneficial effects of ginger in treating coughs, colds and flu is probably linked to immune-boosting properties of the plant <sup>[74]</sup>. 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 <sup>[75]</sup>. 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 <sup>[76]</sup>. One *in vitro* study found that ginger suppressed lymphocyte proliferation; this was mediated by decreases in IL-2 and IL-10 production <sup>[77]</sup>.

#### Anti-atherosclerotic activity

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% <sup>[78]</sup>. In this study the ginger treatment did not cause any significant lowering of serum lipids, but lipid peroxidation was decreased and fibrinolytic activity increased.

#### Anti-obesity activity

Okamoto *et al.*, 2011 reported that 6-GN counteracts body weight gain and fat accumulation in mice <sup>[24]</sup>. 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 <sup>[23]</sup>. Histochemical staining also permitted the detection of oil droplets in adipocytes at concentrations ranging from 5 to 15  $\mu$ g/mL. A reduction in the levels of fatty acid synthase and adipocyte-specific fatty acid binding protein was also reported.

#### Renoprotective activity

6-Gingerol displays renoprotective activity to alleviate cisplatin-induced oxidative stress and renal dysfunction in

rats. The compound aids in restoring renal functions, reducing lipid peroxidation and enhancing the levels of reduced glutathione, superoxide dismutase and catalase activities at doses of 12.5, 25, and 50 mg/kg, respectively <sup>[25]</sup>.

#### Anti-platelet aggregation activity

Significant anti-platelet aggregation activity was displayed by 6-GN and 6-SG, while 10-GN inhibited  $\text{Ca}^{2+}$ -dependent contractions in media high in  $\text{K}^{+}$  <sup>[79]</sup>. The aggregation and release reaction of arachidonic acid and collagen-induced rabbit platelets were inhibited by 6-GN at 0.5–20  $\mu$ M. It also inhibited thromboxane B2 and PG D2 formation, caused by arachidonic acid, at 0.5–10  $\mu$ M 6-GN <sup>[28]</sup>.

**Antiangiogenic activity** Kim *et al.*, 2005a has performed that [6]-Gingerol has anti-tumor-promoting activities. They reported its novel anti-angiogenic activity *in vitro* and *in vivo*. *In vitro*, [6]-gingerol inhibited both the VEGF- and bFGF-induced proliferation of human endothelial cells and caused cell cycle arrest in the G1 phase <sup>[26]</sup>. It also blocked capillary-like tube formation by endothelial cells in response to VEGF, and strongly inhibited sprouting of endothelial cells in the rat aorta and formation of new blood vessel in the mouse cornea in response to VEGF. The results demonstrate that [6]-gingerol inhibits angiogenesis and may be useful in the treatment of tumors and other angiogenesis-dependent.

**Hepato-protective activity** Earlier investigators based on experimental findings have shown that, ginger and its constituents play a significant role in hepato-protection. An important study on ginger showed its protective effect against the  $\text{CCl}_4$ -induced hepatotoxicity <sup>[80]</sup>. Another report has shown that, administration of single dose of aqueous extract of ginger (200, 400 mg/kg prior to acetaminophen) was effective in preventing the acetaminophen-induced hepatotoxicity and also decreased ALT, AST and ALP levels and increased the activities of antioxidant enzymes levels in the liver <sup>[81]</sup>. A recent report showed that, ginger is effective in reversing lead induced reduction in the liver weight, to increase plasma SOD and CAT activity, decrease LPx <sup>[82]</sup>.

#### Larvicidal activity

Larvicidal activity of *Z. officinale* was reported against *Angiostrongylus cantonensis* a round worm. *A. cantonensis* is a parasitic nematode which causes angiostrongyliasis, the most common cause of eosinophilic meningitis in Southeast Asia and the Pacific Basin. In the study, [6]-gingerol, [10]-shogaol, [10]-gingerol, [6]-shogaol and hexahydrocurcumin were isolated from the roots of *Z. officinale* and screened for larvicidal activity against the larvae of *A. cantonensis*. Among all, [10]-gingerol showed higher larvicidal than hexahydrocurcumin, mebendazole and albendazole <sup>[83]</sup>.

#### Anti-emetic activity

Ginger is the herb most commonly used to treat nausea and vomiting in pregnancy, either recommended by providers or used as self-treatment by women <sup>[84]</sup>. It would be even more effective than vitamin B6 for relieving the severity of nausea and is equally effective for decreasing the number of vomiting episodes in early pregnancy <sup>[85]</sup>. Studies based on animal model revealed that, ginger extract possesses antiserotonergic and 5-HT<sub>3</sub> receptor antagonism effects which play an important role in the etiology of postoperative nausea and vomiting <sup>[86, 87, 88]</sup>. A study in the favors of ginger role in nausea and vomiting indicating its effect and provide relief in severity in nausea and vomiting <sup>[89]</sup>.

### Neuroprotective activity

Ginger and their constituents play a vital role as 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<sup>[90]</sup>. Another finding in the support of ginger as neuroprotector suggests that, it exhibit neuroprotective effect by accelerating brain anti-oxidant defence mechanisms and down regulating the MDA levels to the normal levels in the diabetic rats<sup>[91]</sup>. A recent report on ginger juice showed that, ginger has protective effect by decreasing the LPO and increasing GSH, SOD, CAT, GPx, GST, GR and QR and protein level in treated rats<sup>[92]</sup>.

### Anthelmintic activity

Aqueous extracts of rhizome of *Z. officinale* was investigated for their anthelmintic activity against the earthworm *Pheretima posthuma*. The result revealed that the test extract (100mg/ml) possess significant anthelmintic activity<sup>[93]</sup>. 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<sup>[94]</sup>.

### Gastroprotective activity

Peptic ulcer is a major problem worldwide in both sexes. Various factors including food ingredients, stress, *Helicobacter pylori* and drugs are responsible of gastric ulcer. Several medicinal plants and its constituents show anti-ulcer effect in various ways but the exact mechanism is not understood fully. Ginger and its constituents show a vital role in ulcer prevention via increasing mucin secretion. Earlier findings have shown anti-ulcerative effects of ginger in experimental gastric ulcer models<sup>[95]</sup>. Chief constituents of ginger such as [6]-gingerol and [6]-shogaol suppressed gastric contraction *in situ* and suppression by the [6]-shogaol was more intensive<sup>[22]</sup>.

### Cardiovascular activity

Including in Ayurvedic science, ginger has been described as great heart tonic. It helps in preventing various heart diseases by reducing blood clotting that can lead to plaque formation or thrombosis. It can also open the blockage in the blood vessels thus decreasing peripheral vascular resistance and hence blood pressure. Ginger also may help to lower high cholesterol making the heart healthy<sup>[96]</sup>. Ginger extracts as well as [6]- and [8]-gingerol have been shown to modulate eicosanoid responses in smooth vascular muscles *ex vivo*<sup>[97, 98, 99]</sup>. 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 Ca<sup>2+</sup>-pumping ATPase activity of fragmented sarcoplasmic reticulum prepared from mammalian skeletal and cardiac muscle<sup>[29, 100]</sup>. 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<sup>[101]</sup>.

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