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**Research Article**

# GINGER: FROM NATURES GARDEN TO MOLECULAR KITCHEN

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**A R T I C L E I N F O**

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**A B S T R A C T**

*Zingiber officinale* is ayurvedic medicinal plant known as ginger belongs to family *Zingibereceae*. From ancient times ginger is consumed as a spice and food additive in the kitchen throughout the world. It has been used as a usual remedy for a range of disease like nausea and vomiting, constipation, fever, jaundice, headache, dementia, pain, arthritis. A long history is available that supports pharmacological role of its compound as anti-cancer, anti-microbial, anti-inflammatory, anti-apoptotic, anti-hyperglycemic, anti-lipidemic, anti-oxidant, anti-diabetic and anti-emetic. This review will assist to expand all information about the earlier period of scientific research and obligatory information about the ginger. It will also explore the medicinal value of ginger in various life-threatening disease. The compounds present in ginger rhizome have major contribution to human health and nutrition. Besides phytochemicals influence on human health, its miRNA might be playing an important role as epigenetic regulator. However, this need to be validated with *insilico* prediction and real lab experimentation. A lot of study is required to rationale its advantageous use.



## INTRODUCTION

Ginger's current name comes from the Middle English *gingivere*, but this spice dates back over 3000 years to the Sanskrit word *srngaveram*, meaning "horn root," based on its appearance. In Greek, it was called *ziggiberis*, and in Latin, *zinziberi*[1]. Ginger (Zingiber officinale Roscoe) is one of the most important medicinal plants which naturally occur in various country including India as well as foreign country like West Indies, Mexico, China, South East Asia, Jamaica, Hawaii, Africa and other parts of the world[2]. The ginger plant has a long history of cultivation known to originate in China and then spread to India, Southeast Asia, West Africa, and the Caribbean. India is a leading producer of ginger in the world. Ginger is cultivated in most of the states in India. Kerala and Meghalaya are major ginger growing states in the country[3]. Ginger has been widely used as a spice to enhance the flavor of food and beverage and for medical purposes in various diseases, particularly to treat ailments such as stomachache, diarrhea and nausea[4]. The consumed portionof the ginger plant is the rhizome, often called "ginger root," although it is not actuallya root[5]. This review covers the articles published between 1997-2017 via Pubmed, Medline and published papers on the Internet from Scientific Information Database.

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***Taxonomy***

| | |
|---|---|
| Kingdom | : Plantae |
| Division | : Angiosperma |
| Class | : Monocotyledoneae |
| Order | : Scitaminaea |
| Family | : Zingiberaceae |
| Genus | : *Zingiber* |
| Species | : *officinale* |

**Fig 1** Ginger rhizome

## METHODS

We conducted a comprehensive search in the following databases: PUBMED, MEDLINE in order to identify relevant studies. The electronic search was conducted using mesh keywords<adverse effects>, <chemistry>, <drug effects>,

<genetics>, <immunology>, <metabolism>, <microbiology>, <parasitology>, <pharmacology>, <physiology>, <therapeutic use>. We used literatures only from English language and studied both human and animal models. Review articles were only included in this review if they offered new insights or opinions.

### *Bioactive Component of Ginger*

Phytochemicals of ginger vary depending on its growing place, freshness and dryness of numerous active ingredients are present in ginger including terpenes and oleoresin which called ginger oil (table 1)[6]. Ginger contains approximately 1.0 to 3.0% volatile oils and a number of pungent compounds[7].

**Table 1** The ginger oil from different places

| Extraction (medium) | Bioactive compound reported | Geographic location | Ref |
|---|---|---|---|
| Hydrodistilled and dried over anhydrous Sodium Sulphate | ar-curcumene (22.1%), zingiberene (11.7%), β-bisabolene (11.2%) and cadina-1,4-diene (12.5%) | Cuba | 12 |
| Hydrodistilled and dried over anhydrous Sodium Sulphate | Organic ginger oil contain zingiberene (29.8%),geranial (10.5%), β-bisabolene (6.1%) and ar-curcumene (5.8%) and normal ginger oil contain zingiberene (28.6%),geranial (9.2%), β-bisabolene (5.8%) and ar-curcumene (5.6%) | Guwahati | 13 |
| Water and steam distilled | ar-cucumene(11.7 %) and β-bisabolene(4.1 %), by water distillation and by steam distillation were ar-curcumene(12.6 %), α-zingiberene(10.3 %), β-bisabolene(8.1 %) and β-sesquiphellandrene(7.4 %) | Vietnam | 14 |
| Hydrodistilled and dried over anhydrous Sodium Sulphate | In all the four oils, zingiberene (10.5% - 16.6%) was the major constituent. Majhauley variety from sikkim had higher content of zingiberene (16.6%) followed by e-citral (12.0%), z-citral (8.8%), camphene (7.6%) and ocimene (6.5%) | Mizoram, Chennai and Sikkim | 15 |
| Hydrodistilled and dried over anhydrous Sodium Sulphate | In Indian species a-Zingiberene(28.25%) b-Sesquiphellandrene(15.65%),a-Curcumene(15.23%) and trans-g-Cadinene (11.88%).In Chinese species a-Zingiberene (35.67%) b- Sesquiphellandrene (15.27%), trans-g-Cadinene (9.25%) and E-Citral (6.0%) were main components | Indian and Chinese species | 16 |
| Hydrodistilled and dried over anhydrous Sodium Sulphate | monoterpenes (47.8 %) and sesquiterpenes (51.8%) with germacrene-D (20.9 %), linalool (11.8 %) and camphene (9.4 %) | New delhi | 17 |
| Methanol | Zingiberene (23.69), followed by AR-curcumene (23.69), α-Bergamotene (23.69), Gingerol (14.31), Zingerone (10.07), β-esquiphellandrene (9.94), (Z)-β-Farnesene (9.94), Caryophyllene (9.94) and c-Elemene (0.72) | Maharashtra | 18 |
| Ethanol Extract | α Gingiberene(20.57%) and β Seiquphellandrene (12.71%), α Curcumen (11,27%), Cyclo Hexane(10.61%), α Fernesene (9.77%) others were Cis-6-Shagole (7.45%), Gingerol (4.46%) | Rajasthan | 19 |
| Hydrodistilled | Zingiberene(29.5%) andsesquiphellandrene (18.4%) | Nigeria | 20 |
| Hydrodistilled and dried over anhydrous Sodium Sulphate | Nedumangadu variety zingiberene (30.3%),ar-curcumene(11%),β-bisabolene(7.2%), sesquiphellandrene(6.6%) and δ-cadinene (3.5%) | Trivendrum | 21 |
| Hydrodistilled and dried over anhydrous Sodium Sulphate | Gorubathane oil were beta sequiphellandrene (10.9%), thingria oil were zingiberene (12.58%) and ar-curcumene (9.89%) and of shingboi oil were geranial (20.07%) and neral (9.44%) | Sub Himalayan Region | 22 |

**Table 2** Role of various extract of ginger in different types of cancer

| Extract medium | Compound | Cell line Type | Target | Ref |
|---|---|---|---|---|
| Ethanol | 6-shogaol and 6-gingerol | pancreatic cancer cellsPanc-1 | Increase the ratio of LC3-II/LC3-I and caused loss of SQSTM1/p62 | 23 |
| Ethanol | Ginger extract | liver cancer in the DEN-initiated and CCl | VEGF FGF, and TGFb1 | 24 |
| Methanol and ethanol | 6- shogoal 6-dehydrogingerdione | Breast cancer cell lines MCF-7 and MDA-MB-231 | NF-κB, Bcl-X, Mcl-1, and Survivin, cyclin D1 and CDK-4 and also increased expression of CDK inhibitor, p21 and inhibit c-Myc,reduction of matrix metalloproteinase-9 expression | 25-27 |
| Ethanol | [6]-gingerol | colon cancer cell SW480 | Inhibition of ERK1/2/JNK/AP-1 pathway | 28 |
| Not Specified | Zerumbone | NSCLC A549 cells | Inhibition of FAK/AKT/ROCK pathway | 29 |
| Ethanol | 6-gingerol | H-1299 human lung cancer cells, CL-13 mouse lung cancer cells, HCT-116 and HT-29 human colon cancer cells, | Inhibitionof 12-O-tetradecanoylphorbol 13-acetate (TPA)-induced tumor promotion | 30 |
| Ethionine | Ginger extract | liver cancer | NFkappaB and TNF-alpha | 31 |
| Methanol | 6-Shogoal | Human LNCaP, DU145, and PC3 and mouse HMVP2 prostate cancer cells | Decreased the level STAT3 and NF-κB-regulated target genes survivin, and cMyc and modulated mRNA levels of chemokine, cytokine, cell cycle, and IL-7, CCL5, BAX, BCL2, p21, and p27 | 32 |
| Ethanol | 6-shogoal | Ovarian cancer cells SKOV3 | VEGF and IL-8 | 33 |

Volatile compounds were mainly alpha zingiberene (22.29%), beta-sesquiphellandrene (8.58%), alpha-farnesene (3.93%), beta bisabolene (3.87%), alpha-curcumene (2.63%), which was mostly consisted of sesquiterpene hydrocarbons. The pungent compounds of ginger were mainly 6-gingerol(9.38%), 6-shogaol(7.59%), zingerone(9.24%) produced by the thermal degradation of gingerols or shogaols[8].The pungency of fresh ginger is primarily due to the gingerols. The pungency of dry ginger mainly results from shogaols which are the dehydrated forms of gingerols. Minor pungent phenolic compounds of this medicinal plant are paradols or 5-deoxygingerols, Isogingerol, isoshogaol, gingerdiones, 3-dihydroshogaols, dihydroparadols, acetyl gingerols, gingerdiols, mono- and di-acetyl gingerdiols, dehydrogingerdiones, diarylheptanoids, beta-sesquiphellandrene, beta-bisabolene, ar-curcumene and diarylheptanoids[9].

In addition to [6]-gingerol, [4]-, [7]-, [8]-, and [10]-gingerol were identified, as well as methyl [4]-gingerol and methyl [8]-

gingerol. [4]-, [6]-, [8]-, [10]- and [12]-shogaol were characterized, as were methyl [4]-, methyl [6]- and methyl [8]-shogaol identified by Jolad *et al*. (2004)[10]. Fresh ginger contains 80.9% moisture, 2.3% protein, 0.9% fat, 1.2% minerals, 2.4% fibre and 12.3% carbohydrates. The minerals present in ginger are iron, calcium and phosphorous. It also contains vitamins such as thiamine, riboflavin, niacin and vitamin C[11].

***Pharmacological Role***

***In Cancer***

Several studies have been conducted on the medicinal properties of ginger against various disorders, including cancer. Evidence that ginger-derived compounds have inhibitory effects on various cancer cell types is increasingly being reported in the scientific literature (in table 2).

***Anti-microbial***

Natural spices ginger possess effective anti-bacterial activity against multi-drug clinical pathogens *Pseudomonas aeruginosa*[34].[10]-gingerol and [12]-gingerol effectively inhibited the growth of these oral pathogens anaerobic Gram-negative bacteria, *Porphyromonasgingivalis* ATCC 53978, *Porphyromonasendodontalis* ATCC 35406 and *Prevotella intermedia* ATCC 25611, causing periodontal diseases[35]. Dehydrozingerone efficacy against *Aspergillus oryzae*, *Aspergillus flavus, Aspergillus niger, Aspergillus ochraceus, Fusarium oxysporum* and *Penicilliumchrysogenum* shows it is a potential antifungal agent[36]. In an in vitro study 10% ethanolic ginger extract was found to possess antimicrobial potential against all the three pathogens *Streptococcus mutans, Candida albicans*, and *Enterococcus faecalis*[37].

***Anti-oxidant***

Ginger is a source of a large number of antioxidants and also plays an important role in the reduction of the lipid oxidation and inhibits the pathogenesis of diseases[38,39]. Phenolic bioactives of ginger-6-gingerols, 8-gingerols, 10-gingerols, and 6-shogaol-seem to be strong inhibitors of Cu (+2)-induced LDL oxidation showing antioxidant activities[40].

***Anti-diabetic***

The mechanistic rationale for anti- diabetic effects of *Zingiber officinale* includes the inhibition of several transcriptional pathways, lipid peroxidation, carbohydrate-metabolizing enzymes, and HMG-CoA reductase and the activation of antioxidant enzyme capacity and low-density lipoprotein receptors[41]. One report shows that the 3 months supplementation of ginger improved glycemic indices, TAC and PON-1 activity in patients with type 2 diabetes[42]. An study demonstrated that daily consumption of 3 one-gram capsules of ginger powder for 8 weeks is useful for patients with type 2 diabetes due to FBS and HbA1c reduction and improvement of insulin resistance indices such as QUICKI index[43].

***Radioprotective effect***

Radioprotective effects of ginger essential oil (GEO) on mortality, body weight alteration, hematological parameters, antioxidant status and chromosomal damage were studied in irradiated mice and found GEO as a potential radioprotective compound44.

***Antileishmanial activity***

The antileishmanial activity of a water extract from ginger was investigated and it was found that a purified fraction from ginger could be evaluated in future works as a therapeutic alternative, on its own or in association with other drugs, to treat disease caused by *L. amazonensis*[45].

***Osteoartheritis and Ostioporosis***

6-shogaol reduced the inflammatory response and protected the femoral cartilage from damage produced in a CFA monoarthritic model of the knee joint of rats[46]. An important study on osteoarthritis patients of knee has revealed that, highly purified and standardized ginger extract had significant effect on reducing symptoms of OA of the knee[47]. Ginger hexane extract may be used to prevent and treat osteoporosis by inhibiting osteoclast differentiation[48].

***Anti-emetic effect***

Various studies have evaluated effects of ginger in prevention and management of nausea and vomiting in different conditions such as pregnancy, chemotherapy, and post-operation[49]. Meta-analysis demonstrates that a fixed dose at least 1 g of ginger is more effective than placebo for the prevention of postoperative nausea and vomiting and postoperative vomiting[50]. Addition of ginger (1.5 g/d) to standard antiemetic therapy in patients with advanced breast cancer effectively reduces the prevalence of nausea 6 to 24 hours postchemotherapy[51].

***Anti-inflammatory***

12-dehydrogingerdione is a potent inhibitor of proinflammatory mediator production in Raw 264.7 macrophage cells[52].Another finding suggested that ginger and zingerone were likely tosuppress the activation of NF-κB, the production of IL-1β, and the infiltration of inflammatory cells in mice[53].Zingerone exerts its potent anti-inflammatory action by increasing hepatic nuclear factor-4 and Peroxisome proliferator-activated receptors activities, while suppressing NF-kappaB activity[54].

***Anti-platelet activity***

[8]-Gingerol, [8]-shogaol, [6]-paradol,[8]-paradol and gingerol derivatives are more potent anti-platelet agents. [8]-Paradol, was found to be the most potent COX-1 inhibitor and anti-platelet aggregation agent[55,56]. [6]-gingerol and [6]-shogaol exhibited potent anti-platelet aggregation bioactivity. In addition, [10]-gingerol inhibited the $Ca^{2+}$-dependent contractions in high $K^+$ medium[57].

***Cardiovascular disease***

Daily administration of 1,000 mg ginger reduces serum triglyceride concentration, which is a risk factor for cardiovascular disease, in peritoneal dialysis (PD) patients[58]. Dietary supplementation with rhizomes of ginger inhibited arginase activity and prevented hypercholesterolemia in rats that received a high-cholesterol diet[59]. One record suggests that [6]-shogaol exerts its antiproliferative effect through accumulation of cells in the G0 /G1 cell-cycle phase associatedwith activation of the Nrf2/HO-1 pathway[6]

***Dysmenorrhea***

An important study provides suggestive evidence for the effectiveness of 750-2000 mg ginger powder during the first 3-4 days of menstrual cycle for primary dysmenorrheal[61].

***Migraine***

500-600mg of ginger powder administration at the onset of migraine for 3-4 days at interval of4 hours, reported to provide relief from migraine attack[62].

***Gastroprotective***

Histopathological examination showed Ginger essential oil (GEO) could reduce the gastric ulcer in rat stomach as seen from the ulcer index and histopathology of the stomach. Moreover, oxidative stress produced by ethanol was found to be significantly reduced by GEO[63].

***Hepatoprotective***

Ethanolic extract of rhizomes of ginger against thioacetamide-induced hepatotoxicity in rats showed hepatoprotective effect[64]. Coadministration of 6-Gingerol-rich fraction (6-GRF) exhibited chemoprotection against fungicide carbendazim (CBZ)-mediated hematotoxicity, augmented antioxidant status, and prevented oxidative damage in the kidney and liver of rats[65]. Oral administration of aqueous extract of *Zingiber officinale* along with paraben significantly ameliorates paraben-induced lipid peroxidation in the liver of mice[66].

***Miscellaneous Effect***

Ginger extract has a neuroprotective role against monosodium glutamate toxicity effect[67]. Considering the significance of appropriate and timely treatment ginger may be considered as an effective therapeutic option for heavy menstrual bleeding and blastocystosis[68,69]. It may be alternative treatment against monogenean parasite *Gyrodactylusturnbulli* in the guppy and nematode *Ascaridia galli*[70,71] and Ginger-partition moxibustion combined with glucocorticoid achieves better effect forthyreoitis at subacute stage[72]. Other Pharmacological actions of ginger include antischistosomal, and anti-Alzheimeractivities[73,74]. Ginger may blarvicidal against A. simplex and parasite *Angiostrongylus cantonensis*[75,76]. Numerous studies showed ginger as antinociceptive, renal protective and anti-obesity agent[77-79]. Ginger can suppress Th2-mediated immune responses and might thus provide a possible therapeutic application in allergic asthma[80]. Hydroethanolic extract of ginger has anticonvulsant effects in seizure[81]. One data suggest that dried ginger extract has a synaptogenic in memory enhancement[82]. 4 g of ginger supplementation may be used to accelerate recovery of muscle strength following intense exercise[83]. 6-gingerol is a potential hair growth suppressive drug[84]. 6-dehydrogingerdione is presented as a novel biofunctional healing agent for human skin wound repair[85].

***Genetics Research***

Despite the medicinal values of *Zingiber officinale*, information regarding its genome and transcriptome is limited. The transcriptome of Ginger was analyzed using expressed sequence tag (EST) dataset (38, 169 total). ESTs were clustered and assembled, resulting in 8624 contigs and 8821 singletons (17,441 unigenes). Out of the 8624 assembled contigs, 11 contigs were involved particularly in gingerol biosynthesis. The analytical results on ginger ESTs are integrated into a user friendly freely available web based database to share the transcriptomic data, "GINGEREST"[86].*De novo* assembly on the *Z. officinale* chloroplast genome using DNA sequences from a shotgun library of total cell DNA were performed which resulted in two major contigs of 87,626 and 45,356. A final plastome with 162,598 bp was produced. YCF1 and YCF2 gene are the longest proteins encoded by known plastomes and appear to be indispensable to plant survival[87]. First transcriptome data of *de novo* transcriptome assembly of an elite ginger cultivar "Suruchi" from Odisha were identified 41,969 transcripts. The transcript length varied from 300 bp to 8404 bp with a total length of 3,96,40,526 bp and N50 of 1251 bp[88]. After mining EST from dbEST of NCBI 64026 SNP sites and 7034 indel polymorphisms with frequency of 0.84 SNPs / 100 bp were found[89]. Fujisawa M *et al*. isolated a cDNA that codes for a sesquiterpene synthase from young rhizomes of ginger Japanese cultivar "Kintoki". The cDNA, designated ZoTps1, the (S)-beta-bisabolene synthase gene in ginger[90]. A novel promoter, named GVDE promoter, was first isolated and analyzed which contained the circadian box, I-box, G-box and GT-1 motif[91]. A total of 16 potential miRNA families were predicted by using homology search based computational approach in ginger. Thirteen miRNA families were found to regulate 300 target transcripts and play an important role in cell signaling, reproduction, metabolic process and stress. miR5015 was observed to regulate the biosynthesis of gingerol by inhibiting phenyl ammonia lyase (PAL). miR5021, miR854 and miR838 were identified to regulate the rhizome development and the essential oil biosynthesis in ginger[92]. However, role of these miRNA on human genome as epigenetic regulator have not been tested by anyone. Releases of plant miRNA in human blood have been reported earlier (Zhang *et al*.). Therefore, a systematic study on this aspect is wanted with real wet lab data.

## CONCLUSION

Data collected in this review showed that ginger is under investigation in recent years and considered to be a safe herbal medicine and also used in various types of ayurvedic formulations with only few and irrelevant adverse/side effects. Over the years, many investigations have been reported that ginger and many of its phytoconstituents are rich of different pharmacological actions which have been proved. It is easily available, consumed worldwide as a spice and flavoring agent and more beneficial for human health, other than there were limited researches about major diseases. More studies are required for the validation of the advantageous medicinal uses as epigenetic regulator and perhaps the development and formulation of pharmaceutical products for their better economic and therapeutic utilization for the assistance of mankind may appear in the years to come.

***Conflicts of Interests***

All authors have declared that no competing interests exist.

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