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Importance and Proven Benefits of Ginger on Molecular Basis Study: Review Article

Upase Amar U[1], Bhusnure Omprakash G[1]*, Gholve Sachin B[1], Giram Padmaja S[2] and Suryawanshi Shivraj V[1]

[1]Channabasweshwar Pharmacy College (Degree), Dept of Quality Assurance, Latur, Maharashtra, India.

[2]Channabasweshwar Pharmacy College (Degree), Dept of Pharmacology, Latur, Maharashtra, India.

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***Corresponding Author Email:** omprakashbhusnure@gmail.com

Abstract

Herbs are now a days widely used because plant herbs provide many benefits of human health another reason is no side effect herbs, synthetic drug have more side effects on the human body. India is popularly known for traditional medicines. Traditional plants have been used from ancient time for the treatment of many diseases like antiemetic, antipyretic, anti-inflammatory, Antioxidant Effects. Zingiber is one of them, the medicinal plants find application in pharmaceutical, cosmetic, agricultural and food industry. The efficacy of some herbal products is beyond doubt, the most recent examples being Silybummarianum (Linn.) Gaertn (Silymarin), Artemisia annua Linn. (artemesinin) and Taxus baccata Linn. (taxol). Randomized, controlled trials have proved the efficacy of some established remedies, for instance Zingier officinaleRosc. Commonly known as ginger. After extensive pharmacological studies, it has been concluded that ginger has significant anti-inflammatory, anti-emetic and chemo-protective effects.

Keywords

Ginger, Anti-Emetic, Gingerol, Shogaol.

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INTRODUCTION

Ginger (Zingiberofficinale Roscoe, Zingiberaceae) is widely used around the world in foods as a spice. Native to tropical Asia, ginger is a perennial cultivated in the tropical climates of Australia, Brazil, China, India, Jamaica, West Africa, and parts of the United States[1].Ginger rhizome has a long history of use in Chinese and Ayurvedic medicine as an antiemetic, antipyretic, and anti-inflammatory agent, Here, the aim was to summarize the more recent and common actions and therapeutic application of ginger and its active constituents.

Ginger is one of the most well-liked spices in the world. From its origin in Southeast Asia it has spread to Europe and has a long tradition within alternative medicine as a cure for diverse diseases. Throughout history ginger has often been used to alleviate vomiting, intestinal disturbances and colds. In more

recent times interest has shifted towards possible effects of ginger on cancer, blood clotting, inflammation and pain. However, little attention has been given to metabolic diseases such as diabetes. Animal studies and human clinical trials have shown promising results. Experimental research in animals both *in vitro* and *in vivo* has shown that ginger can have effects on carbohydrate metabolism, insulin sensitivity and lipids. Moreover, such studies have also been able to show positive results on diabetic complications in the liver, kidneys, nerves and eyes.

The key enzymes controlling carbohydrate metabolism associated with hyperglycemia and type 2 diabetes are α-amylase and α-glucosidase. Ginger extract has *in vitro* been able to inhibit the enzymes α-amylase and α-glucosidase and the inhibiting effect correlated with gingerol and shogaol in the extract. Diabetes mellitus is characterized by defects in insulin release and/or insulin sensitivity. *In vitro* studies have also shown that extract from ginger and gingerol could increase glucose uptake in muscles and fat cells. *In vivo* studies have shown an increase in plasma insulin levels accompanied by reduced glucose levels[2].

Botanical 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[3].

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 sub equal oblong to lanceolate connate greenish segments[4].

Phytoconstituents

The constituents of ginger are numerous and vary depending on the place of origin and whether the rhizomes are fresh or dry but to summarize the major components that have been implicated in the pharmacological activities of the crude drug. The primary pungent agents (phenylalkylketones or vanillyl ketones) of ginger are gingerol, with other gingerol analogues such as the shogoals, paradol and zingerone also found in high levels in rhizome extracts. The major pharmacological activity of ginger appears to be due to gingerol and shogaol. Phenylalkylketones or vanillyl ketones of ginger include 6-gingerol 8- gingerol and 10-gingerol, 6-shogaol, 8- shogaol, 10-shogaol and zingerone. 6-paradol, 6- and 10- dehydrogingerdione and 6- and 10- gingerdione have also been identified[5].

HISTORICAL AND POPULAR USES

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 anti-nausea remedy and to treat bleeding disorders and rheumatism; it was also used to treat baldness, toothache, snakebite, and respiratory conditions[6].

Sr. No.	Country	Production (Tonnes)
1	India	1109000
2	Nigeria	522964
3	China	463707
4	Indonesia	340341
5	Nepal	271863
6	Thailand	164266

GINGER PRODUCTION, 2016

In Traditional Chinese Medicine (TCM), ginger is considered 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 (i.e. heart disease), reduce cholesterol and fight arthritis. In Malaysia and Indonesia, ginger soup is given to new mothers 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. Some Africans believe that eating ginger regularly will help repel mosquitos.

Ginger migrated westward to Europe by Greek and Roman times. The Greeks wrapped ginger in bread and ate it after meals as a digestive aid. Subsequently, ginger was incorporated directly into bread and confections such as gingerbread. Ginger was so valued by the Spanish that they established ginger plantations in Jamaica in the 1600's. The Eclectic physicians of the 19th century relied on ginger to induce sweating, improve the appetite and curb nausea, and as a topical counterirritant. 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. Ginger is also extensively consumed as a flavoring agent; it is estimated that in India, the average daily consumption is 8 -10 grams of fresh ginger root. The German Commission E approves the use of ginger root as a treatment for dyspepsia and prophylactic against motion sickness[7].

Chemical Structure of Active Constituents

Numerous active ingredients are present in ginger including terpenes and oleoresin which called ginger oil. Gingeral so constitutes volatile oils approximately 1% to 3% and non-volatile pungent components oleoresin[8].The major identified components from terreneare sesquiterpene hydrocarbons and phenolic compounds which are gingerol and shogaol. Pharmaceutical Chemical Composition and Antimicrobial Activity of the Crude Extracts Isolated from *Zingiber officinale* by Different Solvents, lipophilic rhizome extracts, yielded potentially active gingerols, which can be converted to shogaols, zingerone, and paradol[9].

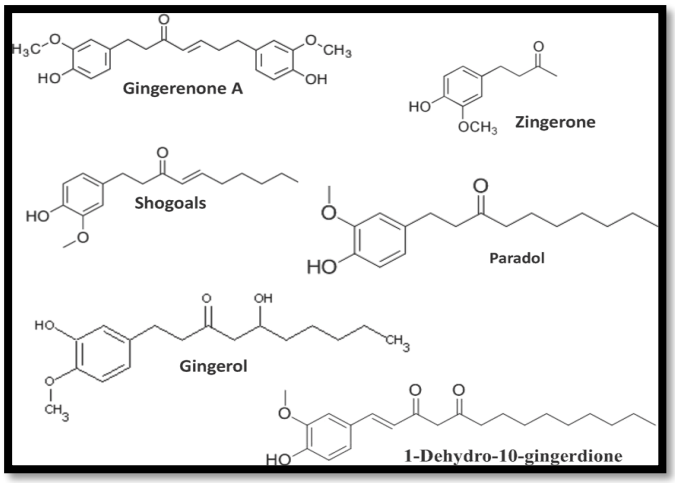
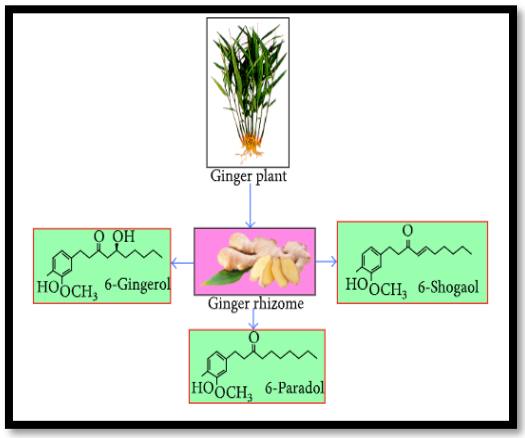


Figure. Chemical of structure of active ingredients of Ginger

Ginger and Its Constituents-



Ginger (Zingiber officinale), a member of the Zingiberaceae family, is a popular spice used globally especially in most of the Asian countries. Chemical analysis of ginger shows that it contains over 400 different compounds. The major constituents in ginger rhizomes are carbohydrates (50–70%), lipids (3–8%), terpenes, and phenolic compounds. Terpene components of ginger include zingiberene, β-bisabolene, α-farnesene, β-sesquiphellandrene, α-curcumene, while phenolic compounds include gingerol, paradols, and shogaol. These gingerols (23–25%) and shogaol (18–25%) are found in higher quantity than others. Besides these, amino acids, raw fiber, ash, protein, phytosterols, vitamins (e.g., nicotinic acid and vitamin A), and minerals are also present.

The aromatic constituents include zingiberene and bisabolene, while the pungent constituents are

known as gingerols and shogaols. Other gingerol- or shogaol-related compounds (1–10%), which have been reported in ginger rhizome, include 6-paradol, 1-dehydrogingerdione, 6- gingerdione and 10-gingerdione, 4- gingerdiol, 6-gingerdiol, 8-gingerdiol, 10-gingerdiol, and diarylheptanoids. The characteristic odor and flavor of ginger are due to a mixture of volatile oils like shogaols and gingerols[10].

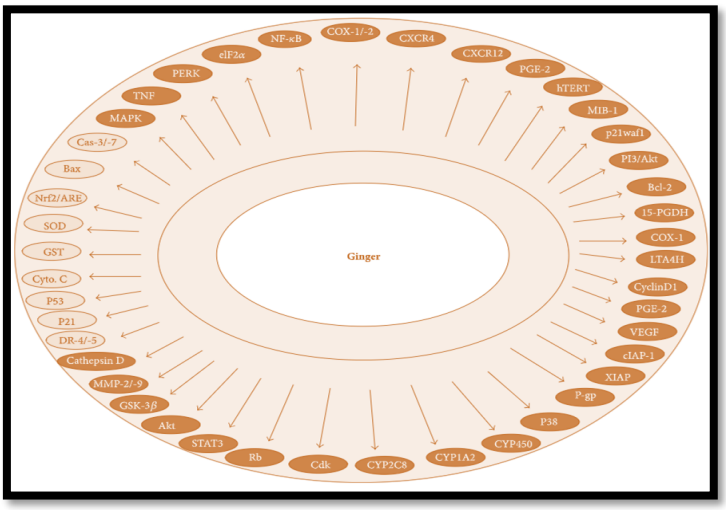
USE OF GINGER AS A TRADITIONAL MEDICINE

Ginger has been used as a spice as well as medicine in India and China since ancient times. It was also known in Europe from the 9th century and in England from the 10th century for its medicinal properties. Native Americans have also used wild ginger rhizome to regulate menstruation and heartbeat. Ginger is thought to act directly on the gastrointestinal system to reduce nausea. Therefore, it is used to prevent nausea resulting from chemotherapy, motion sickness, and surgery. Ginger is known as a popular remedy for nausea during pregnancy. Ginger is also used to treat various types of other GI problems like morning sickness, colic, upset stomach, gas, bloating, heartburn, flatulence, diarrhea, loss of appetite, and dyspepsia (discomfort after eating). According to Indian Ayurvedic medicinal system, ginger is recommended to enhance the digestion of food.

Besides these, ginger has been reported as a pain relief for arthritis, muscle soreness, chest pain, low back pain, stomach pain, and menstrual pain. It can be used for treating upper respiratory tract infections, cough, and bronchitis. As an anti-inflammatory agent, it is recommended for joint problems juice of ginger has been shown to treat skin burns. Active component of ginger is used as a laxative and antacid medication. It is also used to warm the body for boosting the circulation and lowering high blood pressure. Because of its warming effect, ginger acts as antiviral for treatment of cold and flu Ginger is also used as a flavoring agent in foods and beverages and as a fragrance in soaps and cosmetics[10].

MOLECULAR TARGETS

Ginger and its components have been shown to modulate a wide range of signaling molecules. Ginger may upregulate or downregulate the gene expressions, depending on the target and cellular context. Ginger extract increases antioxidant enzymes including GSH, SOD, and glutathione peroxidase. Component of Asian ginger oil also targets to increase the phase II detoxification enzymes as well as nuclear localization of Nrf2/ARE. A number of targets of ginger and its components have been documented in different cancer models. These include transcription factors, enzymes, inflammatory mediators, protein kinases, drug resistance proteins, adhesion molecules, growth factors receptors, cell-cycle regulatory proteins, cell-survival proteins, chemokines, and chemokine receptors. In different GI cancers, ginger extract inhibits transcription factor NF-κB, inflammatory cytokine TNF-α and other enzymes and proteins, which include xanthine oxidase and myeloperoxidase, MDA, HMG CoA reductase, free fatty acids, triglycerides, phospholipase A, and phospholipase C. The active ingredient of ginger, particularly, 6-gingerol and 6-shogaol targets several cellular molecules that contribute to tumorigenesis, cell survival, cell proliferation, invasion, and angiogenesis. 6-Gingerol modulates NF-κB, STAT3, Rb, MAPK, PI3K, Akt, ERK, cIAP1, cyclin A, Cdk, cathepsin D, and caspase-3/7. Similarly, shogaol targets NF-κB, STAT3, MAPK, PI3k/Akt Ca^{2+} signals, COX-2, cyclin D1, survivin, cIAP-1, XIAP, Bcl-2, MMP-9, caspase activation, ER stress, and eIF2α. Besides these, Asian ginger component zerumbone modulates NF-κB, p53 VEGF, p21, and CXCR4 expression. Thus, these molecular targets of ginger components indicate that it may have the potential for preventing and treating the GI cancer[10].



EXTRACTION OF CRUDE EXTRACT

One gram of fresh ginger rhizome, *in vitro* root, *in vitro* shoot, callus, *in vitro* micro-rhizome and rhizomes derived from micro propagated plants under greenhouse conditions were dried using oven at 40^{O}C then ground into a fine powder and kept in airtight bags at room temperature in darkness until used.

Samples transferred to a conical flask separately and percolated three times with methanol at room temperature and the methanolic extracts were combined, filtered, evaporated *in vacuo* at 45 ºC and divided into two groups kept with the residue obtained from the solvent extract at 4ºC in sealed brown vials for analysis.

Methanolic residue was dissolved in ethyl acetate, shaked with water several times in a separating funnel and partitioned between water and ethyl acetate and added to 10g sodium sulphate anhydrous to remove water content. The ethyl acetate layer was combined, filtered and concentrated to dryness *in vacuo* at 45 ºC. Residue was re-dissolved in methanol to analysis 6- gingerol by HPLC[10].

NUTRIENT COMPOSITION

Protein (2.3%), Fat (0.9%), carbohydrates (12.3%), mineral (1.2%), fiber (2.4%) and moisture (80.9%) are the main constituents of fresh ginger. Minerals like phosphorous, calcium, and iron present in ginger are iron, calcium and phosphorous. It also contains vitamins such as thiamine, riboflavin, niacin and vitamin C. The composition varies with the type, variety, agronomic conditions, curing methods, drying and storage conditions[11].

INTERNATIONALLY ACCEPTED PRODUCTS OF GINGER

1. Dried Ginger

Dried ginger is the most important product in terms of trade after fresh ginger. Dried ginger is the raw material to make ginger powder and also for ginger oil and oleoresin extraction. It is obtained by drying of fully matured rhizomes, harvested at an age of 8 to 9 month. At this age the rhizomes have fully developed flavour, aroma and pungency. By converting in to dried form, ginger can be preserved for longer time. Dried ginger can be exported in two different forms, one is as whole peeled and other one is as sliced unpeeled. Chinese dried ginger has more export potential than Indian ginger because of its bright color and more fibrous characteristics[12].

The volatile oil and fiber content, the pungency level, aroma and flavour are need to be assessed for quality assurance of the dried form of ginger. Lower grades of coated whole, clean peeled, split and sliced types are used for blending in the preparation of powdered mixed spices. Varieties with high dry recovery percentage (>20 %), bold fingers and low fiber content (<4 %) are required for dry ginger production. Cochin and Calicut dry ginger exported from Kerala are two popular variety of India, produced from local cultivars, i.e. Kuruppampady, Cheranad, Erenad and Wayand local. Dried ginger can be used directly as a spice after grinding and also used for the extraction of ginger oleoresin and ginger oil.

The yield of dry ginger is 16–25% of the green ginger. Dried ginger is available in different forms like the whole dried ginger, splits or slices and its quality greatly depends on the method of drying[13].

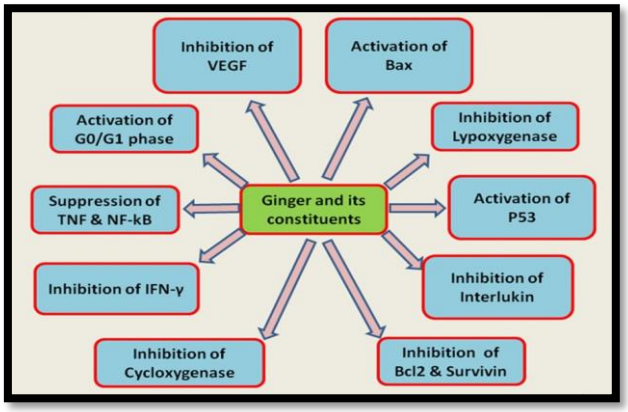
2. Ginger Powder

Ginger powder is rarely used in its pure form, but it is an important ingredient of curry powder. It is also used in ginger wine, ginger beer and baked goods. Ginger powder can be found after grinding the dry ginger. So, for ginger powder the main raw material is dry ginger. Ginger powder can be used as pharmaceuticals and used for the production of

herbal medicines. It also used as food additive. Ginger powder also has a very good export market[14].

MECHANISM OF ACTION OF GINGER IN DISEASES MANAGEMENT Ginger, the rhizome of the *Zingiberofficinale*, plays an important role in prevention of diseases. But the exact mechanism of action in diseases management is not understood fully. It is thought that ginger act as anticancer due to various constituents such as vallinoids, viz. gingerol and paradol, shogaols, zingerone and galanals A and B and constituents show a therapeutics role in diseases control via modulation of various biological activities as describe as following[15,16]**:**

1. Ginger and its constituents show antioxidant activity and prevent the damage of macro-molecules, caused by the free radicals/oxidative stress.
2. Ginger and its constituents also show a vital role as anti-inflammatory processes. Earlier studies on in *vitro* investigations of ginger preparations and some isolated gingerol related compounds showed that anti-inflammatory effects of ginger such as inhibition of COX and inhibition of nuclear factor $^{\kappa B}$[17,18].
3. Ginger also acts as antitumor via modulation of genetic pathways such as activation tumour suppressor gene, modulation of apoptosis and inhibition of VEGF. Earlier study has shown that terpenoids, constituents of ginger induce apoptosis in endometrial cancer cells through the activation of p53[19].
4. Ginger also shows antimicrobial and other biological activities due gingerol and paradol, shogaols and zinger one. An important finding showed that 10% ethanolic ginger extract was found to possess antimicrobial potential against pathogens[20].



TOTAL PHENOLIC COMPOUND ANALYSIS[21,22]

Total polyphenol content was estimated using Folin-Ciocalteu (FC) as

Antioxidant components estimation

A known amount of extract (10 mg/ml) was mixed with 1.0 ml of FC reagent and 0.8 ml of 2% Na2Co3 was added and the volume was made up to 10 ml using water- methanol (4:6) as diluting fluid. Absorbance was read at 740 nm after 30 min using spectrophotometer. Tannic acid (0 - 800 mg/L) was used to produce standard calibration curve. The total phenolic content was expressed in mg of Tannic acid equivalents (TAE) /100 g of sample[21,22].

DETERMINATION OF ANTIOXIDANT ACTIVITY OF DIFFERENT EXTRACT

Radical scavengingactivitybyDPPH (2,2-diphenyl-1-picrylhydrazyl)

Effect of different extracts on DPPH free radical was measured. Positive control (standard) was prepared by mixing 4.0 ml of ascorbic acid (0.05 mg/ml) and 1.0 ml of DPPH (0.4 mg/ml) for water extract, and negative control (blank) was prepared by mixing extract base (water/methanol/ethanol/acetone) with1.0 ml of DPPH. Four different concentrations of extract was mixedwith4.0 ml of DPPH, the volume made up to known volume, mixed well and left to stand at room temperature in a dark place for 30 min. Absorbance was read using a spectrophotometer at 520 nm. The ability of extract to scavenge DPPH was calculated using the following equation:

$$\text{Radical scavenging activity \%} = \frac{\text{Control OD} - \text{Sample OD}}{}$$

Control OD

Total Antioxidant Activity by Phosphomolybdenum Method-

The extract (0.1 ml) (10 mg/ml) was mixed with reagent solution (0.6 M sulphuric acid, 28 mM sodium phosphate and 4 mM ammonium molybdate in 100 ml). The tubes were capped and incubated in boiling water bath at 95°C for 90 min, then cooled to room temperature and absorbance was read at 695 nm with spectrophotometer against blank. Water soluble antioxidant capacity expressed as equivalent of ascorbic acid (µmol/g of sample) [21,22].

MOLECULAR BASIS

Nutritional composition

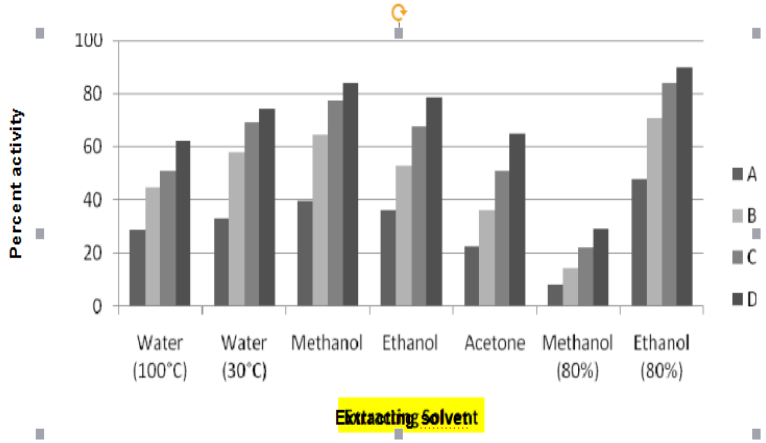
The nutritional composition of dry ginger was determined with standard techniques. Protein and fat content were found to be 5.98 and 4.37 g /100 g DW. The reported values for composition of ginger by various authors are in the following range; for protein, 7.2 to 8.7, fat, 5.5 to 7.3 and ash, 2.5 to 5.7 g/100 g DW. In our study, ash, iron, calcium and phosphorous contents were 4.53 g, 9.41 mg, 104.02 mg, 204.75 mg/100 g DW, respectively. Ash content was in the range of reported values and calcium content, that, 104.02 mg/100 g DW was very close to the value reported for Indian foods.

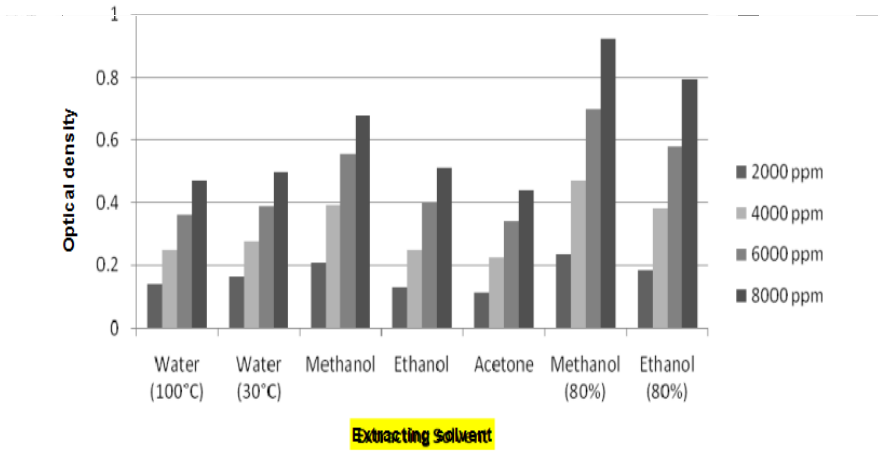
Trace minerals namely zinc, copper, manganese and total chromium were estimated with atomic absorption spectrophotometer and found to be 1.08mg, 0.641mg, 10.74 mg and total chromium was 83.37 µg/100g DW, respectively. Vitamin C and total carotenoids content were found to be 10.97 and 92.96 mg/100 g, respectively. Soluble and insoluble fibre of sample was determined, soluble fibre was slightly higher than insoluble fibre. Antioxidant components were estimated in seven extracting media. Total polyphenols, tannin and flavonoids were found to be more in 100°C water extract than other extracts. It can be because of more solubility of these components in hot water than othersolvents.[21,22] Antioxidant components and total antioxidant activity of ginger in different solvent extracts.

Estimation of antioxidant activity

Antioxidant activity of dry ginger was estimated with three different methods.

1. **Total antioxidant activity**
   Total antioxidant activity was highest in methanolic extract at 98822 µmol/g followed by ethanolic extract at 91176 µmol/g. Least total antioxidant activity was found in acetonic extract[21,22].
2. **Free radical scavenging activity**





Reducing power of Ginger in different solvent extracts

DPPH is a stable free radical in methanol or aqueous solution and accepts an electron or hydrogen radical to turn into stable diamagnetic molecule. It is usually used as a substrate to evaluate the antioxidative activity of antioxidants, thus we have estimated the antioxidant activity through free radical scavenging of ginger. Free radical scavenging potency of sample which showed the highest DPPH radical scavenging activity in 80% methanolic extract followed by 80% ethanolic extract. DPPH radical scavenging activity of methanolic extract was found to be in a range of 32 to 90.1% in 100 mg of 18 different ginger species. In the present study, DPPH free radical scavenging activity of methanolic extract was 39.6, 64.7, 77.6 and 84.4% in 0.25, 0.5, 0.75 and 1.0 mg of sample, respectively, which is higher than the reported values[21,22].

Molecular marker analysis of *Z. officinale*

DNA fingerprinting/profiling is a technique in which combined use of several single locus detection systems used as versatile tools for investigating various aspects of plant genomes. Molecular profiling of ginger revealed different DNA pattern which depends on ecological conditions of environments. Ginger is found to have high medicinal value and India is the place where largest diversity is found. In India, most of the popular commercial varieties are clonal selections from traditional cultivars. Breeding in ginger is seriously handicapped by poor flowering and seed set. Most of the crop improvement programs of these species are confined to evaluation and selection of naturally occurring clonal variations. In such species, the extent of genetic diversity is low, unless samples are drawn from diverse agro-ecological conditions. Therefore, diversity analysis and identification of genetically distant clones or genotypes are vital to the ginger improvement program. Recently have carried out RAPD analysis of 12 accessions of ginger collected from the Indian subcontinent. Ginger undergone genetic diversity due to wide variations in ecological conditions. Thirteen out of twenty primers screened were informative and produced 275 amplification products, among which 261 products (94.90%) were

found to be polymorphic. The percentage polymorphism of all 12 accessions ranged from 88.23% to 100%. Out of 275 amplification products 261 was found to be polymorphic 94.90%. In another study have screened 60 RAPD primers, out of this; the 30 which gave reliable pattern were used for amplification. A total of 269 scorable bands were produced, out of which 126 were polymorphic. Seventeen ISSR primers produced 160 scorable bands out of which 76 were polymorphic. The genetic similarity by the RAPD and ISSR markers were in the range of 0.76–0.97. Though good morphological genetic variability was reported in ginger. But the present molecular diversity study revealed a rather low genetic variability as reported earlier using isozyme markers. In a study used rice SSR markers as RAPD markers to assess the relationship among the *Zingiber* species and genetic variability in ginger (*Z. officinale*) accessions from Asian countries. Among all molecular plant markers, RAPD is best, suitable tool for poorly studied species such as ginger, because it requires no prior information on the genome and is also cost-effective. Several studies have reported the successful use of RAPD markers to assess genetic diversity and phylogenetic relationship in different crop species. Being a poorly studied genome, little information is available on the molecular characterization of gingers investigated the diversity within and among *Zingiber* species and found that *Z. officinale* from different geographical origin were identical in phylogenetic analysis and metabolic profiling[32].

There were significant variations reported in 16 elite cultivars of ginger by using cytological and RAPD marker. In Malaysian region were carried out an experiment in three varieties of ginger by RAPD marker and reported variations among samples. have carried out an assessment of genetic diversity by AFLP in morphologically distinct Indonesian gingers and found out no clear genetic differentiation between small and big type (morphological variants) gingers. In addition, higher genetic variability was detected in collections from small-scale local farms in comparison to genebank accessions and market collections[32].

Cultivation of traditional as well as improved clones is common in India. RAPD variation from 44.95 to 72.48 in species of ginger. In another study were also observed 40% variations in *Z. officinale* by AFLP marker[32].

MOLECULAR MARKER STUDIES OF GINGER

S. No.	Plant	Markers
1	*Z. officinale*	AFLP
2	*Z. officinale*	RAPD
3	*Z. officinale*	IRAP and REMAP
4	*Z. officinale*	Isoenzymes
6	*Z. officinale*	SSR
7	*Z. officinale*	ISSR, SSR
8	*Z. officinale*	RAPD and ISSR
9	*Zingiber officinale*	SCAR
10	*Zingiber officinale*	SNP
11	*Zingiber officinale, Z. barbatum and Z. mioga*	RSB-RAPD
12	*Zingiber barbatum*	PBA

IMPORTANCE AND BENEFITS[33]

1. Prevention cancer
2. Enhances sexual activity
3. Provides relief from menstrual cramps
4. Cures nausea and removes excess gas from body
5. Regulates sugar levels
6. Facilitates digestion and cures diarrhea
7. Boost's bone health and relieve joint pain
8. Cures nausea and removes excess gas from body
9. Maintain normal blood circulation
10. Reduce pain and inflammation
11. Combats morning sickness
12. Ovarian cancer treatment
13. Migraine relief

USES

PHARMACOLOGY

1. Anti-cancer effects:

The anticancer effects of ginger are thought to be attributed to various constituents including vallinoids, viz. (6)-gingerol and (6)-paradol, shogaols, zingerone and Galanals A and B[15]. Galanals A and Bhave been found to be potent apoptosis inducers of human T lymphoma Jurkat cells[23].

2. Anticoagulant Effects

Ginger has been shown to inhibit platelet aggregation and to decrease platelet thromboxane production *in vitro*.Gingerol, (8)-shogaol, (8)-

paradol, and gingerol analogues (1 and 5) exhibited anti-platelet activities.However, its effects *in vivo* have not been well studied. Although ginger to decrease platelet aggregation, Lumb found no effect of ginger on platelet count, bleeding time, or platelet aggregation. Similarly, ginger to have no effect on platelet aggregation, fibrinolytic activity, or fibrinogen levels. no effect oforal ginger on platelet thromboxane B2 production, while Srivastava found thromboxane levels to be decreased by ginger ingestion in a small study[24].

3. Emetic

Emetic is a substance causing vomiting.Vomiting (synonyms: emesis, puking, barfing, heaving, throwing up, etc.) is the involuntary, forceful expulsion of the contents of one's stomach through the mouth and sometimes the nose**.**

Common causes of emetics:

- Chemotherapy
- Gastroparesis (This condition in which occurs the muscles of the stomach wall don't function properly, interfering with digestion).
- General anesthesia
- Intestinal obstruction
- Motion sickness: First aid
- Morning sickness etc[24].

4. Anti-emetics

An antiemetic is a drug that is effective against vomiting and nausea. Antiemetic's are typically used to treat motion sickness and the side effects of opioid analgesics, general anaesthetics, and chemotherapy directed against cancer. They may be used for severe cases of gastroenteritis, especially if the patient is dehydrated.

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[25].

5. Anti-Inflammatory Effects

Ginger has a long history of use as an anti-inflammatory and many of its constituents have been identified as having anti- inflammatory properties.

Ginger has been found to inhibit prostaglandin biosynthesis and interfere with the inflammatory cascade and the vanilloid nociceptor. Ginger has been shown to share pharmacological properties with non-steroidal anti-inflammatory drugs (NSAIDs) because it suppresses prostaglandin synthesis through the inhibition of cyclooxygenase-1 and cyclooxygenase-2. However, ginger can be distinguished from NSAIDs based on its ability to suppress leukotriene biosynthesis by inhibiting 5-lipoxygenase. This discovery preceded the observation that dual inhibitors of cyclooxygenase and 5-lipoxygenase may have a better therapeutic profile and have fewer side effects than NSAIDs.

It was also discovered that a ginger extract derived from *Zingiber officinale* (and *Alpinagalanga*) inhibits the induction of several genes involved in the inflammatory response, including genes encoding cytokines, chemokines, and the inducible enzyme cyclooxygenase 2. This discovery provided the first evidence that ginger modulates biochemical pathways activated in chronic inflammation. Identification of the molecular targets of individual ginger constituents provides an opportunity to optimize and standardize ginger products with respect to their effects on specific biomarkers of inflammation[26].

6. 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[27].

7. Antioxidant Effects

In vitro, ginger has been shown to exhibit antioxidant effects (6)-gingerol appears to be the antioxidant constituent present in ginger, as it was shown to protect HL-60 cells from oxidative stress. Ginger oil has dominative protective effects on DNA damage induced by H_2O_2. Ginger oil might act as a scavenger of oxygen radical and might be used as an antioxidant[28].

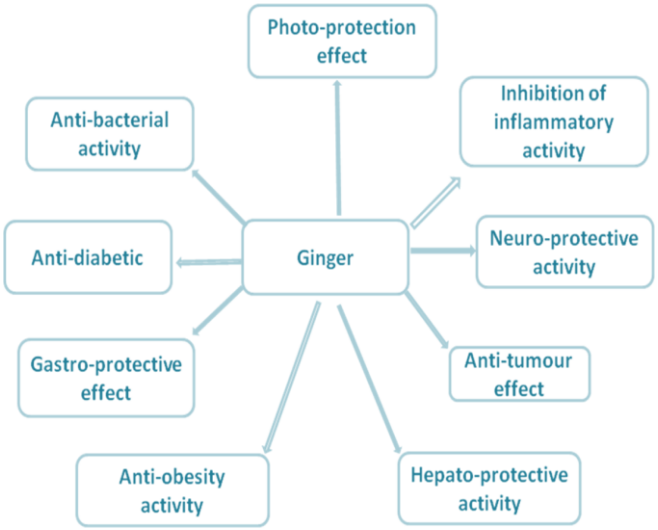
8. Cardiovascular Effects

In vitro research indicates that gingerols and the related shogaols exhibit cardio depressant activity at low doses and cardiotonic propertiesat higher doses Both (6)-shogaol and (6)- gingerol and the gingerdiones, are reportedly potent enzymatic inhibitors of prostaglandin, thromboxane, and leukotriene biosynthesis[29].

9. Gastrointestinal Effects

There is evidence that ginger rhizome (root) increases stomach acid production. If so, it may interfere with antacids, sucralfate (Carafate), H2 antagonists, or proton pump inhibitors. In contrast, other *in vitro* and animal studies have revealed gastro protective properties. in addition, (6) shogaol, generally more potent than (6)-gingerol, has inhibited intestinal motility in intravenous preparations and facilitated gastrointestinal motility in oral preparations as a potential anti-inflammatory and antithrombotic agent. Ginger extract has also been reported to inhibit the growth of *Helicobacter*

pylori in vitro. However, a significant increase in the exfoliation of gastric surface epithelial cells following the consumption of 6g or more of ginger (after examining gastric aspirates in 10 healthy volunteers).[30]



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