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Review Article

Ginger: A Potential Neutraceutical, An Updated Review

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ABSTRACT
Ginger **(**rhizome of *Zingiber officinale*) belongs to the Zingiberaceae family, is widely used and is most popular as a culinary spice and in Traditional medicines to add flavor for more than thousands of years. It is also used in pharmaceuticals, nutraceuticals and in cosmetics. Ginger contains a fusion of an aroma oils both volatile (zingiberene) and non-volatile (oleoresin) oils and phenolic compounds (gingerol and shogaol, zingerone and paradol). In ginger rhizomes, also contains starch, saccharides, proteins, colouring matter and trace minerals that plays a huge role as a spice ingredient. In ginger, starch comprises of 40 - 60 % w/w, protein is 6.2 - 19.8 %, wax or lipid is 5.7 - 14.5 % and crude fiber is 1.1 - 7.0 % and oleoresin approximately 4 - 7.5 %. Ginger is available in fresh, dried, pickled, preserved, crystallized, candied and powdered or ground form. It is unstable due to acidic environment or as a result of the increase in temperature; presence of light, air, heat and long term storage but it can be enhanced by Nano emulsion formulation. Ginger has shown various pharmacological effects such antioxidant, anti – inflammatory, gastro protective, anti-bacterial, anti-diabetic etc.

Keywords: Spice, *Zingiber officinale*, Gingerol, Shogaol, Zingerone, Starch, Oleoresin.

INTRODUCTION

Nowadays, many scholars have focused and showed interest on medicinal plants due to swelling of different taste, increase in demand of spice and healthy foods. In ancient time, valuable and multipurpose medicinal plants such as ginger, cumin, caraway, anise, fennel, curcumin, black seed, olive fruits/leaves and dates and their constituents used to cure various diseases via modulation of biological activities[1] but it's also alter the different metabolic and molecular pathways. The plant of ginger has been discovered more than 2500 years back that grown in warm climates of India, China and Jamaica. *Zingiber officinale* (Ginger) is a tropical and subtropical cultivated plant, belongs to Zingiberaceae family and it is closely related to other spicy plants such as turmeric (*Curcuma longa)*, cardamom (*Elettaria cardamomum)*[2]. All of these plants have a spicy aroma property that is mainly due to presence of ketones in there chemical structures. Ginger and it's all useful parts have the numerous properties such as flavoring and carminative, stimulator, digestive aids and antiemetic that can be used as an ingredient in many herbals and cosmetics.

In Chinese and Indian alternative medicines, ginger was used as a dietary supplement as well as a spice and as a flavoring agent for foods and beverages. For centuries, it has been widely used for the treatment of nausea, vomiting, emetic, arthritis, rheumatism, sprains, muscular aches, pains, sore throats, cramps, fever, infectious diseases and helminthiasis[3]. In Chinese medicine, ginger is characterized with warm flavor and aroma hot spice that buildup the body after losing blood, improve the weak and slow pulse by increasing body temperature. Ginger is also well known as a valuable therapeutic and edible plant source. It has been used as an herb in foods and in Traditional medicines for more than thousands of years. Ginger plant or herb can induce perspiration, dispel cold, warm the stomach and arrest vomiting, resolve phlegm and relieve cough, and resolve fish or crab poisoning. As an edible plant source, it can be used to flavor the foods, stimulate the digestion and alter the functional activity of stomach.

Morphology of Ginger

Ginger rhizome is obtained from the underground stems (Fig.1) that surrounded by the sheathing bases of the two-ranked leaves. It is normally an erect perennial growing plant that grown in ground from 1 - 3 feet in height. Rhizomes are 7-15 cm long and 1-1.5 cm broad and laterally compressed. The branches arise obliquely from the rhizome are about 1-3 cm long and terminate in depress scars or in undeveloped buds. The outer surface is buff colored and longitudinally striated or fibrous[4]. Fractured surface shows a narrow cortex, a well-marked endodermis and a wide stele[5].

In ginger rhizome contains a fusion of aroma oils such as volatile and nonvolatile oils, pungent compounds (gingerols, shogaols), carbohydrates such as starch and saccharides, proteins, coloring matter, trace minerals and etc. Starch is the richest components of ginger, covering of 40 - 60 % w/w of the dry rhizome. The three prominent components viz. crude protein, total lipid and crude fiber

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were compared in different cultivars at different maturity stages of the ginger rhizomes. It was found that the percentage of the crude protein was 6.2 - 19.8 %, lipid was 5.7 - 14.5 % and crude fiber was 1.1 - 7.0 %. Oleoresin (4 - 7.5 %) is a crude extract of ginger rhizome that can obtained by solvent extraction, followed by removal of solvents, while ginger oil can be obtained by water extraction or steam distillation. The composition of the ginger rhizome is summarized in Fig. 2.

Cultivation

Z. officinale also known as ginger belongs to the family Zingiberaceae, is a slender perennial plant firstly cultivated in China and then spread to India, Southeast Asia, West Africa, and the Caribbean. The ginger plant reaches to the height of 2 feet and has greenish yellow flowers resembling orchids with aromatic pungent taste. It is a tropical plant and its underground stem that used for culinary spice and medicinal purposes. The rhizome of *Z. officinale* is one of the most widely used species of the Zingiberaceae family and is a common condiment for various foods and beverages. In history, ginger is characterized as hot aroma flavor spice that is claimed to improve the body and tardy pulse, address a pale complexion, and strengthen the body after blood loss and also it was regarded as a healing gift from God. Ginger has been traditionally used by south eastern countries to treat many ailments including cold and flu symptoms, headaches, high blood pressure and hypercholesterolemia. It has also a potent antiemetic activity.

Active Constituents

The medicinal plants and their constituents cure various diseases such as antioxidant, anti-inflammatory, anticancer, anti-diabetic and anti-tumor effect. The physical properties of active constituents of ginger are given in Table 1.

Gingerol (Fig. 3) is homologues of 1-(3-methoxy-4-hydroxyphenyl)-3-keto-5-hydroxyhexane and include the sub-group methyl gingerols; Gingerol or groups of gingerols (4, 6, 8 and 10 gingerols) are the most active constituent of fresh ginger that are structurally related polyphenolic compounds. Gingerols description is as pungent yellow oil, but it also available in a low melting crystalline solid form. The refreshing pleasant aroma, biting taste and carminative property of ginger makes it as an indispensable ingredient of food processing throughout the world. The Chemical constituents of ginger rhizomes include volatiles (camphene, β-phellandrene, curcumene, cineole, geranyl acetate, terpineol, borneol, geraniol, limonene, β-elemene, zingiberol, linalool, *α*-zingiberene, *α*-sesquiphellandrene, β-bisabolene, zingiberenol and *α*-Farnesene) and non-volatile pungent phytochemicals consisting of the biologically active components viz., gingerols, shogaols, paradols and zingerone that account for the antioxidant, anti-inflammatory, antiemetic and gastro protective activities[6,7]. The characteristic odor and aroma flavor of ginger is caused by a mixture of zingerone, shogaols and gingerols that compose one to three percent of the weight of fresh ginger.

All of the pungent compounds of ginger contains two common moieties i.e. ketone functional group and vanilly (4-hydroxy-3-methoxphenyl). In ginger also contains the organic components such as carbohydrates, fats and proteins [8, 9].

More pungent constituent shogaols formed from the dehydration reaction of ginger during drying. Less pungent and spicy sweet aroma constituent zingerone formed from the cooking ginger.

6-gingerol is a more pungent and major active ingredient of ginger that has anti-bacterial, anti-inflammatory, and anti-tumor-promoting properties. 6-Gingerol positively proven various pharmacological activities such as: analgesic and anti-inflammatory[10], anti-cancer[11, 12], anti-pyretic[13], antioxidant[14], cardiotonic and hypotensive[14], anti-emetic, anti-prostaglandin, anti-rheumatic, anti-ulcer and many others[15-20].

8-Gingerol is one of the active and most pungent constituent of ginger[21]. Many researchers have proved that 8-gingerol had various pharmacological functions, such as anti-platelet aggregation activities[22, 23], spasmolytic activity[24], modulation of macrophage functions[25], inhibiting LPS-induced PGE 2 production and LPS-induced COX-2 expression[26], 5-HT3 receptor blocking activity and immunosuppressive activity[27, 28].

Shogaols (Fig. 4) which are the dehydration products of the gingerols but it's a major constituent of rhizome of ginger. The anti-metastasis activities of 4-shogaol was evaluated[29] and found that its effectively inhibits the metastasis of breast cancer by decreasing NF- kB and Snail, sequentially resulting in the reinforcement of Raf kinase inhibitor protein (RKIP) expression, inhibition of cell migration and invasion.

In a recent study, 6-shogaol was the strongest inhibitor of dibutyl phthalate-induced bronchial smooth muscle cells proliferation and migration[30]. It is also can act as an active anti-prostaglandin compounds and anti-ulcer. Researchers[31] observed that 6-shogaol and 6- gingerol exerted anti-invasive activity against hepatoma cells through regulation of MMP-9 and tissue inhibitor metalloproteinase protein (TIMP-1). 6-shogaol further regulated urokinase-type plasminogen activity. They reported that shogaols of differing side chain lengths had an inhibitory effect on PMA-induced invasion of MDA-MB-231 (ER-negative, p53 mutation, model of more advanced stage breast cancer) breast carcinoma cells, which was associated with a decrease in the extracellular secretion of matrix metalloproteinase-9 (MMP-9). 6-shogaol was found to be potent inhibitor of MDA-MB-231 cell invasion, and the molecular mechanism involves the down-regulation of MMP-9 transcription by targeting the NF-kB activation cascade[32].

6-shogaol inhibited cell proliferation by inducing cells to autophagy cell death through AKT/mTOR inhibition in human non-small cell lung cancer A549 cells and hence can be a promising chemo preventive agent[33]. 6-shogaol was also effective in inducing the apoptotic cell death of Mahlavu cells via an oxidative stress mediated caspase dependent mechanism at >50 µM concentration[34].

Zingerone (Fig. 5) also called as vanillyl acetone, is an active constituent and a crystalline solid content of ginger[35]. It is sparingly soluble in water and freely soluble

Figure 1: Ginger rhizome.

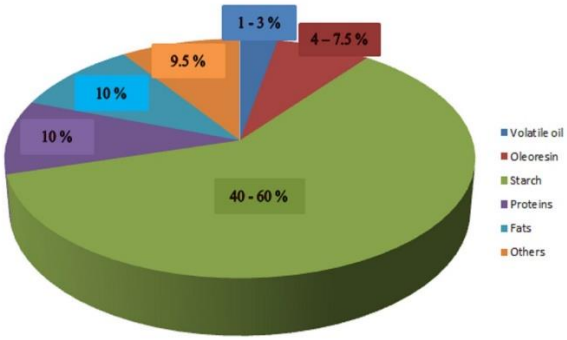

Figure 2: Composition of the ginger rhizome.

in ether. The chemical structure of zingerone is similar to other flavor chemicals such as vanillin and eugenol. It used as additives in spice oils to produce good flavor and in perfumery to introduce spicy aromas. Less pungent and spicy sweet aroma constituent zingerone formed from the cooking ginger through a retro aldol reaction (reversal of aldol addition).

Other constituents of ginger are zingiberene (Fig. 6), paradols, gingerdiones and gingerdiols. Paradols are β-ketone hydroxyl deoxygenation products of gingerols. Gingerdiones, which are β-ketone hydroxyl dehydrogenation products of gingerols and include the sub-group 1-dehydro gingerdiones; and gingerdiols, which are ketone reduction products of gingerols[36-40].

Mechanism of action of Ginger and its constituents

Ginger contains various active phyto-constituents such as [6]-gingerol and [6]-paradol, shogaols, zingerone, and galanals A and B[41-43]. According to the availability of % phyto-content, they play a huge role to prevent and cure various diseases through different mechanisms mentioned below:

Ginger has antioxidant activity through inhibiting free radicals and oxidative stress.

Ginger has anti-inflammatory activity through inhibiting nuclear factor κB and COX[1].

Ginger modulates the genetic pathways such as apoptosis, active the tumor suppressor gene, inhibit VEFG that shows antitumor activity.

Ginger induces apoptosis and activates p53 that are responsible for the cancer prevention[44].

Ginger inhibits the different types of pathogen such as bacteria and microbes that possess the antibacterial and antimicrobial activity [45].

Ginger reduces the prostaglandins production by enzyme inhibition. 6-shogaol has a strong anti-tissue or expectorant effect and could help reduce blood pressure. It has also shown anti-allergic effects, inhibit the release of histamine from mast cells and inhibit cancer growth in ovarian cancer.

Stability

Ginger is widely used in pharmaceuticals, nutraceuticals and cosmetics. 6-gingerol, a major constituent of oleoresin in ginger extract, is used as microcirculation stimulating agent and natural dietary component for antioxidation. However, 6-gingerol is unstable due to acidic environment or as a result of the increase in temperature, presence of light, air, heat and long term storage. The stability of 6-gingerol can be enhanced by Nano emulsion formulation[46].

Nutritional Profile

Fresh ginger contains numerous phytochemicals that are known to have antioxidant, antimicrobial, gastro protective and anti-inflammatory properties. The rhizome of ginger is an excellent source of dietary fibers that contain certain health benefits, essential oils, moisture, protein, fat, minerals, vitamins and carbohydrates. The composition and nutritional profile of ginger are varies with the type, variety, extraction & curing methods, drying and storage conditions[47]. As per USFDA, the nutritional profile of ginger is given in Table 2.

Uses

General uses

Ginger is used in cooking to flavor foods and also as a spice. It is also used to lower blood sugar, reduce seizures, strengthen bones, and treat the eye, cough, colic, heart palpitation, swellings, dyspepsia, loss of appetite, and rheumatism[48,49].

Folklore medicine

Ginger is using traditionally as a stimulant and carminative. It also used frequently for the treatment of dyspepsia, gastro paresis, slow motility symptoms, constipation or colic. It is also frequently employed to disguise the taste of medicines.

Pharmacological uses

Ginger and its constituent showed the various pharmacological and biological activities such as antipyretic, anti-nausea, anti-inflammatory, anthelmintic, fungicidal, antibacterial, antitussive, cardiotonic, sedative activities, hypoglycemic and positive cardiac inotropic activities. Ginger improves appetite and digestion, increase bile and reduce gastric secretions, stimulate vasomotor and respiratory centers that described below:

Antioxidant activity

Antioxidants are the neutralizer substances that can neutral the oxidative stress and free radicals. Oxidative stress is an alteration of reactive oxygen species (ROS) generation and neutralizer defense body system[50, 51]. In our body, the production of free radicals can be balanced by intake of various antioxidants or by body defense system[52]. Various medicinal plants and their constituents are currently available that are a rich source of antioxidant and also played a significant role in prevention of disease. Ginger is a good example of antioxidant that reduces the level of oxidative stress and free hydroxyl radical production[53].

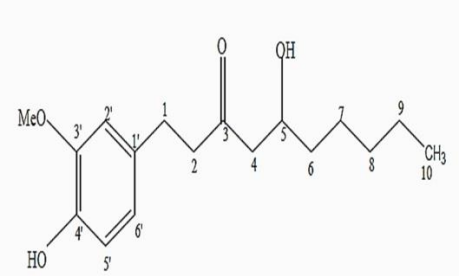

Figure 3: Structure of gingerol.

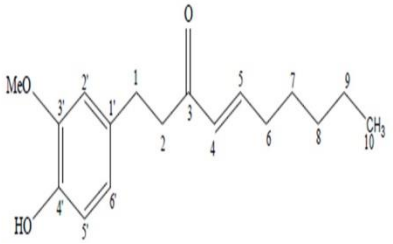

Figure 4: Structure of Shogaol.

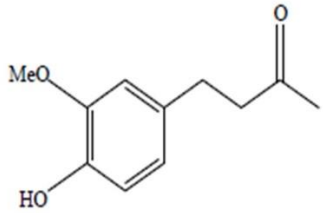

Figure 5: Structure of zingerone.

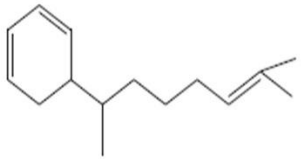
Figure 6: Structure of zingiberene.

Anti-inflammatory activity

Inflammation is an immune process which involves the different types of mediators such as interleukin1 (IL1), tumour necrosis factor (TNF) and anti-inflammatory cytokines. NSAID drugs are generally used to treat the acute and chronic type of inflammations. Ginger and its constituents are classical and traditional agents and come under the classification of non-steroidal anti-inflammatory drug. Ginger shows significant anti-inflammatory effect but it also shows adverse and side effects such as gastric ulcer. Ginger inhibits COX and 5 lipoxygenase that are essential for arachidonate metabolism[54], the synthesis of pro-inflammatory cytokines such as IL1, TNFα and IL8[1, 55, 56] and blocked the elevated expression of TNFα in liver cancer rats[57]. It regulates the induction of inflammatory genes[58, 59] and production of NFκB gene, involved in cellular proliferation and angiogenesis[60].

Antitumor activity

Tumour is a multi-step process of genetic and metabolic changes[61, 62]. The various medicinal plants and their constituents including ginger used to cure tumor via modulation of biological activities[63, 64]. Ginger plays a vital role to control tumor through different steps such as regulation of tumor suppressor gene, induction of apoptosis and inactivation of VEGF pathways.

6-gingerol is an important constituent of ginger that play a specific role to suppress the transformation of tumor, hyper proliferation, and inflammatory processes that involve in various steps of carcinogenesis, angiogenesis and metastasis[65-68]. Ginger induces apoptosis in prostate cancer cell line-LnCaP by increasing the expression of p53 and Bax and also decreasing the expression of Bcl2[69-71]. 6-gingerol stimulates apoptosis through regulation of NAG1 and G cell cycle arrest through down regulation of cyclin D1[72] and inhibited pulmonary metastasis in mice bearing B16F10 melanoma cells through the activation of CD8+ T cells[73].

6-shogaol is also a very common and important constituent of ginger that shows anticancer activities against breast cancer via inhibition of cell invasion reduction of matrix metallo proteinase 9 expressions[74].

Antimicrobial activity

Ginger and its constituents prevented the growth of bacteria and fungi and have both cidal and static activity. Ginger showed antimicrobial activity against *E coli*, *Salmonella typhi* and *Bacillus subtilis*[75]. Ginger and its important constituent's gingerol and shogalol are identified antibacterial agent against periodontal bacteria[76], *Candida albicans*[77-80] *M. avium* and *M. tuberculosis*[81]. Ginger extract and gingerol also showed antifungal properties[82].

Anti-diabetic activity

Diabetes is disorder of carbohydrate metabolism that leads to low blood insulin level[83-85]. Ginger and its constituents significantly controlled diabetes through decreasing blood glucose level[86] and inhibition of oxidative stress and anti-inflammatory process.

Neuroprotective effect

Ginger and its constituents showed neuroprotective effect through the inhibition of microglia by accelerating brain antioxidant defense mechanisms and decreasing the MDA levels to the normal levels in the diabetic rats[87, 88]. Ginger also decreased the LPO and increased GSH, SOD, CAT, GPx, GST, GR and QR and protein level in treated rats[89] and confirmed the protective effect.

Gastro protective effect

Gastric ulcer is a major problem and various factors such as food ingredients, stress, Helicobacter pylori and drugs are responsible for this. Ginger and its constituent's 6-gingerol and 6-shogaol controlled the gastric related problems via increase mucin secretion[90-92].

Antiemetic effect

Ginger and its constituents such as gingerols, shogaols, galanolactone and diterpenoid illustrate a significant effect on nausea and vomiting[93, 94]. The extract of ginger also possessed 5HT3 receptor antagonism and anti-serotoninergic effect on animal model[95-97].

Hepatoprotective effect

Based on experiment, the extract of ginger and other constituents shown a significant effect against CCl_4 induced hepatic disorder[98]. The single dose administration of aqueous extract of ginger (200, 400 mg/kg) shown to reduce acetaminophen induced hepatotoxicity and

Table 1: Physical property of active constituents of ginger.

Active constituents	Description/ Organoleptic properties	Molecular formula	Molecular weight (g/mol)	Melting point (^{0}C)	Boiling point	UV maximum (λ_{max})	Refractive index
6-Gingerol	Yellow oil, Pungent taste, 50% soluble in alcohol, ether, chloroform and benzene	$C_7H_{26}O_4$	294	29	bp_{18} 235 – 240 bp_6 227 - 229	282 - 284	ηD^{20} 1.5224
6-Shogaol	Pale yellow oil, Pungent taste, dehydrate product of gingerol	$C_7H_{24}O_3$	276	25.2 – 26.2	$bp_{2\text{-}2.5}$ 201.3	---	ηD^{25} 1.5212
Zingerone	Less pungent and has a spicy sweet aroma, Formed from cooking ginger, slowly volatile in steam, sparingly soluble in water and Polyethylene	$C_{11}H_{14}O_3$	194	40 - 41	bp_{14} 187 - 188	---	---
Zingiberene	Constituents of ginger oil, nature oil	$C_{15}H_{24}$	204	---	bp_{14} 134	---	ηD^{20} 1.4959

increased the antioxidant enzymes activity levels in the liver and also decreased ALT, AST and ALP levels[99]. The active constituents of ginger are also helpful in controlling the lead induced reduction in the liver weight, to increase plasma SOD and CAT activity, decrease LPx[100] and mancozeb induced hepatotoxicity[101].

Effect on migraine

Ginger showed relief from migraine attack after administration of dose of 500-600 mg for 3-4 days with gap of 4 hours[102].

Effect of ginger on eye

Ginger and its constituents play an important role in preventing of diabetes and retinopathy. 0.1 and 1.0 mg/ml dose of ginger extract reduced CMLKLH and MGO derived advanced glycation end (AGE) products. Ginger also controlled the various types of diseases including diabetic liver, kidney, eye and neural system complications[103].

In Beverage, Soup and Condiments

Beverage formulation

Fermentation of fine ginger grains with yeasts resulted in the beverage having health promoting effects. An acidic beverage was formulated for pregnant women containing carbohydrates, essential vitamins (B6, C & folic acid) and minerals (ammonium iron, citrate, calcium gluconate, calcium lactate, and magnesium carbonate) along with ginger juice so as to maintain the good nutritional state of foetus. Archer formulated an organic, ergogenic and energy enhancing drink with a soothing effect. The isotonic soft drink comprised of extract from ginger, leaves of *Cymbopogon citratus*, peppermint along with sugar or other sweeteners dissolved in purified water. A process for the manufacture of an improved herbal beverage prepared from mixture of extracts of ginger root (*Z. officinale*) along with China Root (*Smilax domingensis* Willd), Bejuco Indio (*Gouania polygama*) and Pimento leaves (*Pimenta dioica* Merr) was described. The beverage was both stable, relatively free from undesirable fermenting complexes. Original beverage formulation without ginger possessed sedative effect due to china root. Improved beverage with inclusion of ginger reduced sedative effect. A process for producing the fermented milk drinks as well as foods involved culturing of animal milk using lactic acid bacteria in a medium containing its growth promoter (viz., selected from ginger extract, tea extract, green onion extract, oleic acid and derivatives) was reported. These fermented milk drinks and foods can contain a large number of viable cells of lactic acid bacteria and sustain the activity (acid producing ability) at a high level.

Bakery products

Ginger used to increase and maintain the long shelf life of bread through moisture adsorption characteristics of ginger that keeps bread below 12- 15% dry basis (60-64% of RH) at room temperature[104]. Ginger have also used for the composition of ginger pudding, contains ginger powder (1.6-4 % w/w), milk protein (31-62 % w/w), wheat protein (7-15 % w/w), calcium lactate (1.6-5.5 % w/w), carrageenan (0. 8-2. 4 % w/w) and lactic acid bacteria (0.4-1.6 % w/w) and these all ingredients mixed with cow milk and heated in a microwave oven. Powdered and dry form

Table 2: Nutritional profile of Ginger (100 g).

Types of nutrient	Examples of nutrient	Amount
Protein	-----	1.8 g
Water	-----	78.9 g
Phyto-sterols	-----	15 mg
	Total Carbohydrates	18 g
Carbohydrates	Dietary Fiber	2 g
	Sugar	1.7 g
	Total Fat	750 mg
	Saturated Fat	203 mg
Fats and Fatty acids	Monounsaturated Fat	154 mg
	Polyunsaturated Fat	154 mg
	Omega-3 Fatty Acids	34 mg
	Omega-6 Fatty Acids	120 mg
	Vitamin C	5 mg
	Vitamin E	260 mcg
	Vitamin K	0.1 mcg
	Thiamin	25 mcg
Vitamins	Riboflavin	34 mcg
	Niacin	750 mcg
	Vitamin B6	160 mcg
	Folic acid	11 mcg
	Pantothenic Acid	203 mcg
	Choline	28.8 mg
	Calcium	16 mg
	Iron	600 mcg
	Magnesium	43 mg
	Phosphorous	34 mg
Minerals	Potassium	415 mg
	Sodium	13 mg
	Zinc	340 mcg
	Copper	226 mcg
	Manganese	229 mcg
	Selenium	0.7 mcg

of ginger is classically used as a flavor for gingerbread, cookies, crackers and cakes, ginger ale, and ginger beer.

Baby foods

Ginger used for the composition of infant food products such as ginger puree (0.1-0.5%) with one or more fruits or vegetables to reduce gastrointestinal reflux.

Soup mix

Ginger used as a spice ingredient for the preparation of ready to use chicken soup mix. In dehydrated chicken soup mix involved ingredients are extracted liquid of cooked meat with ginger, garlic and onion which blended with starch to find powder. Then this powder mixed with milk powder, salt, monosodium glutamate (MSG), ascorbic acid, pepper powder and sugar.

Condiment

Ginger and its constituents used for the manufacture for ginger condiment. Ginger extract or granules are cooked in vegetable oils to find golden color granules that are useful for long time purpose.

In Pharmaceutical Compositions

Pharmaceutical Compositions for Anti-inflammation

Ginger and its constituents used to inhibit or eliminate the inflammation in various cases which reported in Table 3. The compositions of ginger are prepared by different methods either in such as or in combined form with other herbs or chemical agents.

Pharmaceutical Compositions for Treatment of Ulcer

The incorporation of honey with ginger and its constituents in toothpaste was said to useful to prevent oral ulceration, remove the malodor and decrease inflammation[116]. Ginger extract is also useful and helpful in the treatment of gastric cancer caused by stress or acid, or *Helicobacter pylori* induced ulcer etc.

Pharmaceutical Compositions for Treatment of Cancer

Ginger and its constituents used for the treatment of prostate as well as oral cancer in the synergistic form or in mixture composition such as ginger, boswellia extract, salts of glucosamine, and curcuminoids, extracts of white willow and quercetin[117]. Another mixture composition is ginger with rosemary, turmeric, oregano, holy basil, *Scutellaria baicalensis*, rosemary, green tea, Chinese goldthread and bearberry used in the treatment of tumor genesis of glioblastoma[118, 119].

Pharmaceutical Compositions for Treatment of Diseases of Skin and Appendages

A synergistic formulation of ginger and bisabolol used to reduce skin irritation[120]. Another mixture composition of herbal formulation is ginger with black walnut, wormwood, turmeric, garlic, licorice, chamomile, clove, nutmeg, aloe vera and niacin also used for the treatment of dys-hidrosis and dry skin disorders[121]. A mixture of herb extracts such as licorice, ginger, kudzu, sophora and thyme used in skin care products preparation for synergistic antioxidant effect[122].

Safety, Efficacy and Toxicity of Ginger

Ginger is recognized by the United States Food and Drug Administration (FDA) "Generally Recognized as Safe" GRAS food additive. The dose of ginger is safe when 250 mg – 1gm, 3 times a day used for nausea treatment and 250 mg, 4 times a day for morning sickness. By several investigators, numerous acute toxicity and dose studies of ginger were performed to check the safe dose in animal model study. They have reported that the dose of 0.5 to 1.0 g of ginger powder ingested 23 times for periods of 3 months to 2.5 years did not cause any adverse effects[123]. Another study on animals[124] showed that the doses of 2.5 g/kg body weight were tolerated without any mortality. But, when the dose was increased to 33.5 g/kg body weight then there was 10-30% mortality.

An another important study reported[125] and showed that ginger extract with different dosages such as 100, 333 and 1000 mg/kg administered to pregnant rats for 10 days during the period of organogenesis caused neither maternal nor developmental toxicity. Other study was reported[126] and conducted in both male and female rats at the dosages of 500, 1000 and 2000 mg/kg body weight for 35 days and results proved that chronic administration of ginger was not associated with any mortalities and abnormalities in general conditions, behavior, growth and food and water consumption

Adverse Effects and Contraindications

Ginger has shown possible CNS depression, arrhythmias, bleeding abnormalities with large overdoses. A pregnant female should use ginger with cautions when taking

Table 3: Pharmaceutical Compositions of ginger for Anti-inflammatory.

Compositions	Method of preparations	Evaluation by	Effects	References
Ginger rhizomes with an organic solvent (such as ethyl ether, acetone, methanol and ethanol)	Organic solvent or Steam distillation or Supercritical CO_2	RP-HPLC	Anti-inflammation or anti-platelet aggregation	105
Ginger, Fructus jujubae, Radix astragali, Radix glycyrrhizae, Ramulus cinnamomi, and green tea	---	---	Anti-allergic for Type I	106
A dietary supplement composition comprising water/alcohol extract of ginger, *Strobilanthes cusia*, *Panax pseudo-ginseng*, *Eucommia ulmoides*, *Momordicae grosvenori*, licorice root, and *Allium fistulosum*	---	---	Ameliorating inflammatory	107
Ginger as such or combined with drugs	---	---	Human cytochrome inhibitor P450 (CYP) enzymes (cytochrome P450 3A4, CYP3A4) and increase the oral bioavailability	108-111
Turmeric, gingko and ginger, and synthetic chemical	---	---	Treatment of a beta amyloid protein-induced disease	112
Ginger extract	---	---	Human drug transporter inhibitor) and increase the oral bioavailability	113
Ginger extract and bisabolol	---	---	Eliminate the irritation and/or inflammation on endodermal tissue of the respiratory as well as gastrointestinal tract	114
Gingerol and anthocyanidin	---	---	Inhibiting of inflammation	115

Table 4: Difference between properties of ginger and cumin spice.

Properties	Ginger	Cumin
In volatile (% Yield)	0.31 (0.08%)	2.52 (0.11%)
In nonvolatile (% Yield)	0.52 (0.03% w/w) in n-hexane extract	4.08 (0.17% w/w) in methanol extract
Phenolic content	95.2 mg/g dry extract in methanol extract 87.5 mg/g dry extract in hexane extract	--- 10.6 mg/g dry extract) in hexane extract
Antioxidant activity	83.87 (0.50%)	85.44 (0.50%)
Components	Camphene, p-cineole, R-terpineol, zingiberene and pentadecanoic acid	Cuminal, γ-terpinene and pinocarveol
Uses	Antioxidant, anti – inflammatory, gastro protective, anti-bacterial, antidiabetic	Antioxidant, anti-platelet, antibacterial, antifungal, anti-diabetic, anti- Parkinson's
Active constituents	Gingerol, shogaol, zingerone, paradol, zingiberene and ginger oil (oleoresin)	b-pinene, p-cymene, g-terpinene, cumin aldehyde and cumin oils (oleoresin)

anticoagulant therapies. If a patient is suffering from heart diseases and gallstones and exercise on regular caution should be followed due to ginger's cardio tonic effects. It might be increased or decreased blood pressure and cause hypoglycemia.

Difference between Properties of Ginger and Cumin Spice

Ginger and cumin both has been recognized as the building blocks of the flavor of foods. The % yield, phenolic content, chemical composition and antioxidant properties of ginger (*Zingiber officinale*) and cumin (*Cuminum cyminum*) were evaluated and shown the difference between them in Table 4[127-129]. After the differentiating of

ginger and cumin, both can be used as a potential source of natural antioxidants in foods.

CONCLUSION

The rhizome of *Zingiber officinale* (Ginger), Zingiberaceae family, is widely used and most popular as a culinary spice in cooking to add flavor and color in Traditional medicines for more than thousands of years. It is also used in pharmaceutics, nutraceuticals and in cosmetics. Ginger contains a number of chemical constituents such as gingerol, shogaol, paradol, oleoresins which are responsible to provide different pharmacological actions. Ginger used in beverage formulations, condiments, baby foods and in bakery products to enhance and create a spicy and crunch flavor. Many researchers have lot of interest in developing ginger as a less toxic and effective therapy for diseases and they have been proven about ginger's pharmacological activities such as cardio-protective activity, anti-inflammatory activity, anti-microbial activity, antioxidant property, anti-proliferative activity, neuro-protective activity and hepato protective activities. Even though from these activites of ginger, respiratory tract infection, cancer and tumor treatments are still remaining to be prove that extending the further and future research with a positive outcome.

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