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Bioactive compounds and biological activity of ginger

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Abstract. Ginger has an abundant amount of biological compounds. Both fresh and dried gingers have a beneficial effect. It has popularity as spices all over the world. However, for the last century, ginger and ginger extracts have been interested in their medicinal properties. Ginger is being used for medical care and avoidance of diseases in the past. Now it is considered a medicinal plant. Ginger has been showing to contribute as anti-carcinogenic, anti-diabetic, anti-tumor activity. It is also effective against pregnancy-induced nausea and vomiting and has proved to treat motion sickness and arthritis. Numerous studies have taken place by an animal model for confirmation of ginger pharmacological activity. In this review, we focused on ginger and its constituents and the therapeutic activity of ginger extracts.

Keywords*: ginger extracts, biological component, shogaol, gingerol, therapeutic activity*

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1. Introduction

Ginger (*Zingiber officinale)* is prominent as species globally, especially in Southeast Asian countries. It is a perennial plant, and mainly ginger rhizome is used and functional food due to its potentiality in health [1]. These are now cultivated prominently in India, Bangladesh, China, Australia, and Nigeria. In the southeast Asian region, fresh ginger is used for the flavor of cooked curry and meat. However, nowadays, ginger is used to flavor bakery products, condiments, beverages, desserts, and various sauces. Also, the roots are peeled, sometimes eaten raw, pickled, candy, or dipped in chocolate. Moreover, it has been used in soaps and cosmetics worldwide.

For medicinal purposes, ginger is being used since ancient years. For instance, it is well documented in Sanskrit, Chinese and Greek history, and Arabic and Roman literature [2]. For the treatment of diarrhea, stomach aches, and nausea the ginger has been used, according to Asian practitioners. It was also recognized in Europe from the 9th century and in England from the 10th century for its medicinal use. Both conventional and traditional medicine is convinced of the therapeutic activity of ginger.

Ginger is preventive for digestive problems like indigestion, intestinal infections, and different types of food poisoning. It has been seen to be active against vomiting related to pregnancy and arthritis treatment and prevent travel sickness. Furthermore, fresh ginger is known to ubiquitous with digestive enzymes. It has also been applied for the remedy of skin burns. Moreover, boosting circulation and lowering high blood pressure by warming the body is another usage of fresh ginger. From ancient times, it also has famous for its healing properties. So, this review focused on the active component of ginger extracts and the potential activity against harmful diseases.

2. Bioactive compounds of ginger

The chemical studied of ginger found that it has over 400 different constituents. The major pungent compounds from the lipophilic rhizome extract have yielded potentially active gingerols, converted to shogaols, zingerone, and paradol (Figure 1). Dried or extracted products have a high amount of zingerone and shogaols compared with fresh ginger.

The crucial compounds are carbohydrates (50–70%), lipids (3–8%), phenolic acids, and terpenes in ginger rhizomes [3]. In addition, phytosterols, amino acids, raw fiber, ash, protein, vitamins (vitamin A and nicotinic acid), and minerals also exist [4].

The primary bioactive compounds of gingers are 6-gingerol, 6-shogaol, zingerone with phenolics and flavonoids. 4-, 6-, 8-, and 10-gingerdiols, 6- and 10-gingerdiones, 6-methylgingerdiol, 6-hydroxyshogaol, 6-, 8-, 10-dehydroshogaols, diarylheptanoids, and zingerone have also been investigated as gingerol and shogaol related compounds. These minor constituents only contribute from one to 10% of the overall gingerols and shogaols [5].

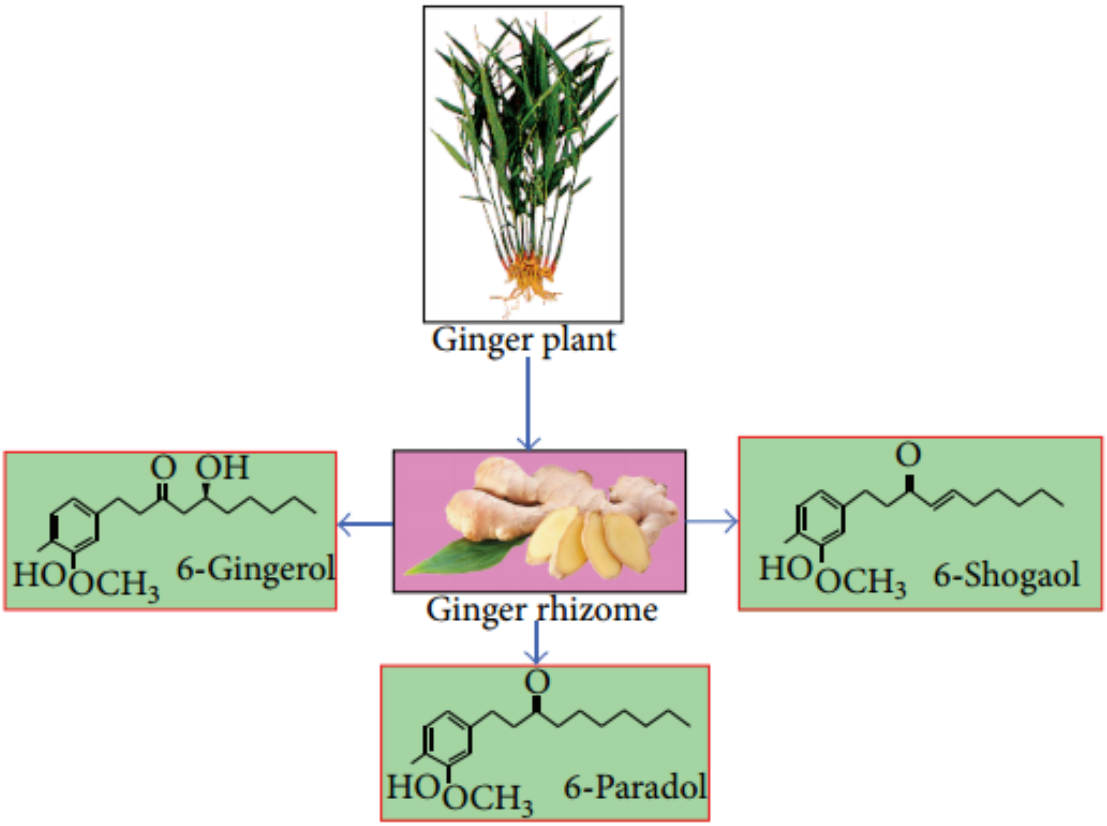

Figure 1. Ginger plant, rhizome, and active components (6-gingerol, 6-paradol, and 6-shogaol) [6].

The aromatic properties include zingiberene and bisabolene; however, the pungent contents are known as gingerols and shogaols. The potential essential flavor of gingers is due to the mixture of volatile oils like shogaols and gingerols. *Z. officinale* has various antioxidants such as ascorbic acid, alkaloids, beta-carotene, polyphenols, and terpenoids. It also has vital volatile oils such as oleoresins, bisabolene, cineol, phellandrene, citral, borneol, and citronellol. For instance, the essential oil of ginger was investigated for testing the anti-inflammatory effect in rats. Moreover, proteolytic enzymes (zingibain), vitamin B6, vitamin C, and linoleic acid also have been investigated in ginger.

2.1. 6-gingerol

[6]-Gingerol is responsible for its characteristic aroma and taste. It was the most prominent active component, such as antioxidant, anti-inflammatory, analgesic, and antipyretic properties in ginger with various pharmacological effects [7]. It has been investigated that 6-gingerol induced apoptosis through the upregulation of the G1 cell cycle and NAG-1 arrest by down-regulation of cyclin D1 [8]. 6-gingerol has been identified as having anti-cancerous effects [9]. It has a potential role in suppressing the hyperproliferation, inflammatory processes, and transformation that engaged in various steps of angiogenesis and metastasis. For instance, the activation of CD8+ T cells inhibited B16F10 melanoma cells of pulmonary metastasis in mice [10]. The anti-tumoral activity showed by 6-gingerol through induction of reactive oxygen species (ROS) triggers p53 activation, apoptosis, and arrest of the cell cycle [11].

2.2. 8-, 10-gingerols

There are gingerols constituent such as 8-and 10-gingerols. Sodium-induced acute ulcerative colitis in rats affects ginger extracts mainly by 8-and 10-gingerols [12]. Moreover, *in vitro* and *in vivo* analysis of [10]-gingerol has been reported against metastatic triple-negative breast cancer (TNBC) [13]. In addition, it has experimented that 10-gingerol inhibits cervical cancer in "Tongling White Ginger" [9].10-gingerols have also shown the effect of anti-neuroinflammatory capacity on the form of fresh ginger [14].

2.3. 6-shogaol

Shogaol, which is the dehydration product of gingerols content (6-gingerol to 6-shogaol) caused the pungency of dried ginger (Figure 2). 6-shogaol has antioxidant properties that can be ascribed to the persistence of unsaturated ketone moiety [7]. Inactivated macrophages, 6-dehydroshogaol, 1-dehydro-6-gingerdione, and 6-shogaol has experimented for the potent inhibitors of nitric oxide synthesis [15]. In addition, matrix metalloproteinase-9 expression inhibits cell invasion reduction, 6-shogaol show anti-cancer activity against breast cancer [16]. Moreover, 6-shogaol used to human colorectal carcinoma cells to induce apoptosis through the production of ROS [17].

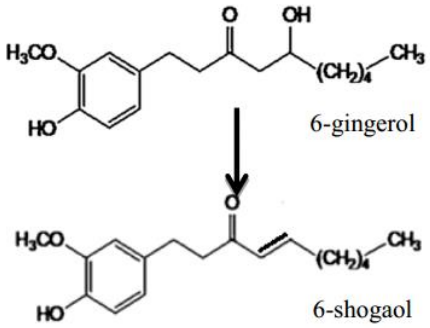

Figure 2. Schematic diagram of degradation 6-gingerol to 6-shogaol [18].

2.4. Terpenoid compounds

Ginger has a rich source of terpene compounds. It has terpenes (monoterpenes, sesquiterpenes, and sesquiterpene alcohols) composed of 20%–25% [19]. Terpene compounds of ginger such as zingiberene, β-bisabolene, α-farnesene, β-sesquiphellandrene, and α-curcumene [6]. It has been identified that ginger has monoterpenes (such as α-pinene, camphene, myrcene, and α-phellandrene) and oxygenated monoterpenes (geranial, citronellal, neral, linalool, borneol, and alpha-terpineol). Ginger oil has a high amount of sesquiterpene hydrocarbons as well as sesquiterpene alcohols, primarily zingiberene (30%) and β-bisabolene (10-15%) [20]. In addition, ginger possesses sesquiterpenes (α-farnesene, ar-curcumene, cadinene, copaene, zingiberene, and zingiberenol) in the extract [19].

3. Biological activities of ginger compounds

Ginger has been used as an herbal remedy, as described before. It is essential herbal medicine. From the last century, ginger extracts have performed more research from producing new avenues for identifying the treatment of harmful diseases. Ginger and its pungent isolated compounds are known to have many potent biological activities. It has the potentiality to modulate the enzymatic profile and act as the prevention of diseases. It possesses various medicinal activities, including anti-inflammation, anti-tumor, insect repellent, antibacterial, anti-mutagen, anti-carcinogenic and antioxidant properties.

3.1. Antioxidant activity

Ginger has potent antioxidant activity. It has been believed that ginger is a plant with a potent antioxidant compound that prevents various diseases. It also has an essential role in the decrement of lipid oxidation. For instance, inhibition of ascorbate/ferrous complex about rat liver microsomes generated lipid peroxidation [21]. In addition, scavenging superoxide anion

and hydroxyl radicals have been shown by ginger extract and gingerol; moreover, after heating treatment, ginger antioxidant activity unchanged [22].

It has been documented that the prevention of damaged macromolecules due to oxidative stress could be cured by ginger extracts and their derivatives [23]. 6-gingerol is a powerful antioxidant compound combined with anti-inflammatory and anti-apoptotic action by *in vivo* and *in vitro* studies [24].

3.2. Neuroprotective activity

Ginger has neuroprotective activity owing to the phenolic and flavonoids compounds. Ginger extracts have been studied as a neuroprotective effect on monosodium glutamate-induced toxicity in the rat's brain. This article showed that the ginger roots extract has a significant role in neuroprotective role in this toxicity [25]. It has experimented that transient global ischemia through microglia inhibition by 6-shogaol showed the neuroprotective outcome [26]. Sometimes the brain damage has been occurred, particularly for diabetic patients. It has been identified that ginger might be a therapeutic alternative to diabetic-induced damage in the brain [27]. This finding has also been proved in the streptozotocin-induced diabetic brain of rats. In addition, ginger extracts pre-treatment decreased the seizures' behavior in pentylenetetrazol receiving mice [28].

3.3. Anti-emetic activity

As earlier mentioned, ginger juice is used for motion sickness because of its central and peripheral anticholinergic and antihistaminic effects. Gingerols, shogaols, and galanolactone, and diterpenoid of ginger extract may reduce nausea and vomiting [29]. For example, it has been proved by the animal model that it has anti-serotoninergic and 5- HT3 receptor antagonism, which showed an essential function in the etiology of postoperative vomiting and nausea [30]. Ginger has been tested for a double-blind, placebo-controlled trial to manage nausea and vomiting in cancer patients [31].

3.4. Anti-inflammatory activity

Ginger and its components show a prominent role as anti-inflammatory processes. For instance, it has experimented that ginger oil (33 mg/kg), oral administration to rats for 26 days which reduced the paw and joint swelling related to acute, chronic adjuvant arthritis [32]. For investigating the anti-inflammatory effect in the cell wall of streptococcal induced rheumatoid arthritis model in female Lewis arthritis ginger essential oil has been applied by oral dose. It has been shown that it inhibited acute joint pain [33]. Moreover, inhibition of cyclooxygenase (COX) and inhibition of nuclear cause NF-kappaB (κB) has been studied *in vitro,* which is shown to have anti-inflammatory effects [3]. In addition, ginger extracts have shown that they can help relieve osteoarthritis pain in the knee [34]. It is also reduced the pain of rheumatoid arthritis by improving joint movement as well.

3.5. Hepatoprotective activity

Ginger extracts have a significant hepatoprotective effect. Alcoholic liver disease is expected due to heavy alcohol intake, and alcoholism ranks as a significant health problem. It has been investigated that ginger has a protective effect on rats against carbon tetrachloride-induced hepatotoxicity. Furthermore, liver cirrhosis induced by carbon tetrachloride in rats has been identified to have protective effects on ginger [35]. Ginger extracts also increased the antioxidant enzyme in the liver. For instance, for preventing acetaminophen-induced hepatotoxicity, an aqueous extract of ginger (200, 400 mg/kg before acetaminophen) can be used [23].

3.6. Anti-ulcer activity

Anti-ulcer compounds have been found from the ginger. Anti-ulcer activity of 6-gingesulfonic acid and three mono acyldigalactosylglycerols, ginger glycolipids A, B, and C, has been proved. In other words, the effect of anti-ulcer activity has been identified by experiment gastric ulcer animal models [36]. In addition, the potential thromboxane synthetase inhibition is the main reason for the anti-ulcer activity of ginger [37]. The main part of ginger, such as [6]-shogaol and [6]-gingerol helps to the suppressed gastric contraction *in situ;* doing this [6]-shogaol was more intensive than other compounds. Further, chronic myeloid leukemia cell line K562 has been suppressed by ginger whole extracts [38].

3.7. Anti-biotic activity

Together with the leaf and root extract of ginger showed antibacterial activity. In addition, it can be used as conventional antibiotics to fight against infections. For instance, more antibacterial activity against *Staphylococcus aureus* and *Streptococcus pyogenes* has been seen in ginger extracts [39]. In addition, 10% of ethanol ginger extract was investigated to have antimicrobial action against microorganisms [40]. Ginger extracted essential oil and oleoresin showed potential antimicrobial activity [41].

3.8. Anti-mutagenic and anti-cancer activity

Ginger also worked as an anti-tumor activity by modulating genetic pathways. It helps for the activation of the suppressing gene of the tumor. Furthermore, inhibition of vascular endothelial growth factor and modulation of apoptosis can be done by ginger. For instance, it has been identified that ginger's terpenoid compound has been induced apoptosis in endometrial cancer cells via the activation of tumor protein p53 [42]. It has been discovered that for the treatment of prostate cancer, whole ginger extract has been proved *in vitro* and *in vivo* experiments [43]. On the other hand, ginger extract (100 mg/kg body weight) treatment expressed the highest performance of TNF-α in rats' liver cancer blockage [44]. Moreover, ginger has an anti-cancer effect against pancreatic cancer [45]. It has experimented with the anti-carcinogenic effect of breast cancer [46].

3.9. Anti-diabetic activity

Diabetes endocrine dysfunctions are characterized by defects in insulin secretion or action of a human. The prevalence of diabetes is on the inflation following the World Health Organization. Ginger is recommended as a potential drug in the treatment of diabetes. Ginger and its components showed a crucial role in the control of diabetes and its complications to the antihyperglycemic effect. Ginger also reduces the sugar level for diabetic patients and reduces the cholesterol levels in the blood. For instance, an ethanol extract from ginger reduced the blood glucose level [47]. The antihyperglycemic effects of ginger have been experimented *with in vitro* and *in vivo* on cells successfully.

4. Conclusion

Ginger is known as species in different communities throughout the world. Ginger rhizome and extracts have a huge source of pharmacological values. It has been discussed that ginger has various biological compounds, but the effects of 6-gingerol and 6-shogaol compounds have more essential than other compounds. However, other compounds should be elucidated over that compound, like terpenoids and phenolic content. The majority of experiments have been focused on analgesic effects, anti-vomiting, and anti-emetic of ginger extracts. It has been paved the way for the researcher to find herbal medicine, which has fewer side effects than other medicine. Therefore, future research should be based on other types of therapeutic activity of ginger extracts.

Conflicts of interest. There is no conflict of interest.

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