Ilam University of Medical Sciences

Plant Biotechnology Persa

Online ISSN: 2676-7414

Homepage: https://pbp.medilam.ac.ir

Zingiber officinale (Ginger) properties in clinical trials; a brief review

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Article Info

Article type:
Review Article

Article History:
Received: 01 May 2022
Received in revised form: 03 Oct 2022
Accepted: 20 Oct 2022
Published online: -- Oct 2022

Keywords:
Ginger; Anti-inflammation; Anti-oxidant; Anti-tumor; Anti-diabetic; Anti-lipemic

Abstract

Objective: *Zingiber officinale* (Ginger) is a flowering plant that was once utilized in Chinese medicine, Indian medicine, and Greek herbal therapy to treat many illnesses.

Results: Different parts of this plant, for example, roots and rhizomes, and its extract are widely used as a spice and traditional medicine. It has been shown that ginger has several therapeutic properties, including reducing inflammation, preventing cancer, lowering blood sugar and lipids, regulating the immune system, anti-apoptotic and anti-nausea, and anti-vomiting effects. In addition, nervous diseases, colds, rheumatism, gingivitis, toothaches, asthma, stroke, constipation, and diabetes have been treated with ginger. Ginger is also a powerful antioxidant and can prevent the production and activity of free radicals. Moreover, ginger extract has been utilized as a diaphoretic and anti-flatulent medication for gastrointestinal spasms. It's also used to treat indigestion and colic pain in the intestines.

Conclusion: In this contribution, we provide an overview of various reports of ginger properties in clinical studies and its effects on the treatment of diseases. In addition to summarizing the present literature. This study highlights the potential of this field to open up new avenues for researchers.

*Pl*ant Biotechnology Persa 2022; 4(2): 89-102. DOI: 10.52547/pbp.4.1.3

 Publisher: Ilam University of Medical Sciences

How to cite: Akhzari M, Shabani-Borujeni M, Tavakoli R, Siahkohi HR, Mottaghiyan Z, Fathi J , Mohsenzadeh A, Shafiee SM. *Zingiber officinale* (Ginger) properties in clinical trials; a brief review. Plant Biotechnology Persa 2022; 4(2): 90-103.

Introduction

Zingiber officinale is the scientific name for ginger. This plant was once utilized in Chinese medicine, Indian medicine, and Greek herbal therapy to treat many illnesses. Nervous diseases, Colds, rheumatism, gingivitis, toothaches, asthma, stroke, constipation, and diabetes have been treated with ginger [1]. The Food and Drug Administration has designated ginger as a GRAS (Generally Recognized as Safe) nutritional supplement. The results of human studies show that consuming up to 2 grams per day has the minimum side effects for humans [2]. Due to the existence of numerous chemicals such as gingerol and shogaols, ginger has many medical properties such as regulating immunity, inhibiting tumorigenesis, lowering inflammation, anti-apoptosis, and anti-nausea [1-3]. Shogaols, Zingerone, Gingerols, and paradol, which make up around 3% of the weight of fresh ginger, are responsible for the pungent smell and taste [1, 4-6]. Ginger is high in gingerols and chagavals, according to phytochemical research [7]. 6-gingerol and 6-chagaval are strong 5-lipoxygenase inhibitors [8, 9]. Some proinflammatory cytokines, such as interleukin (IL-1) and (IL-8) and tumor necrosis factor-alpha (TNF), can be inhibited by ginger [10]. Ginger can also inhibit Th1 activity-derived responses [11]. In addition, ginger can suppress Th2-mediated immune responses, which are critical in the development of inflammatory disorders [12].

Function

Anti –inflammation effects

Ginger suppresses arachidonic acid metabolism by inhibiting cyclooxygenase and lipoxygenase enzymes. In reality, ginger's anti-inflammatory properties are attributed to non-volatile chemicals such gingerols, ginger ions, and shogaols, which are potent prostaglandin inhibitors [12, 13]. 158 animals were separated into two treatment and control groups in the Khalili et, al study. The investigation on acute and chronic inflammation included four subgroups and three dosages of 100, 200, and 400 mg/kg ginger extract. The results revealed that at dosages of 200 and 400 mg/kg, the plant extract was able to considerably decrease foot and peritonitis ($p < 0.05$). A dosage of 200 mg/kg of plant extract was also found to considerably reduce acute and chronic pain, as well as chronic inflammation ($p < 0.05$). The plant's anti-inflammatory and analgesic actions have been described as the reduced release of inflammatory mediators and decreased synthesis of analgesics such as serotonin and arachidonic acid [14]. Ginger has been demonstrated to be useful in the treatment of chronic inflammatory illnesses by researchers. Ginger's active components, which include anti-mutagenic, anti-carcinogenic, anti-inflammatory, and antioxidant properties, can help treat inflammatory conditions like cardiovascular disease, diabetes, arthritis, osteoporosis, and malignancies [15]. By suppressing NO generation, its components, such as 6-shogaol and gingerradion, are efficient in preventing macrophage activity and lowering chronic and acute inflammation [16]. In macrophages, 6-shogaol suppresses the generation of NO, IL-1B, and TNF-α [17]. Studies also reveal that 6-shogaol lowers beta-glucuronidase and lactate dehydrogenase levels and has anti-inflammatory properties [18]. Zingerol and 10-gingerol are anti-inflammatory chemicals in ginger that work by boosting PPAR expression and suppressing proinflammatory translation factor (NF-B) [19, 20]. The generation of prostaglandins and leukotrienes, as well as the oxidation of arachidonic acid, increases during inflammation. By inhibiting cyclooxygenases 1 and 2, ginger prevents prostaglandin formation. The extract of this plant also inhibits the production of leukotrienes by inhibiting lipoxygenase 5 [10]. Research shows that ginger extract may have been able to reduce inflammation by inhibiting the release of environmental inflammatory mediators [21]. Ginger as an effective compound of the ginger plant has a strong ability to inhibit the production of prostaglandins, leukotrienes, and canine as the most important inflammatory mediators. In addition, inhibition of the release of cytokines, TNF, and interleukin, which are important mediators of inflammation, has been reported by the ginger extract. It has been shown that the reduction of kappa nuclear factor as a substance-induced in inflammatory processes by interleukins is reduced by the enzyme phosphatase kinase in the plant and inhibits inflammation [21, 22].Ginger extract can reduce inflammation, which is likely owing to the extract's anti-inflammatory impact on cyclooxygenases, particularly cyclooxygenase-2 and prostaglandin E2 in the central nervous system [10]. Flavonoids, which have anti-inflammatory properties, are also found in ginger [gomar A, mirazi N, gomar M. 23Effect of Zingiber officinale on analgesia induced by Morphine in adult male Wistar rats.].

[DOI: 10.52547/pbp.4.2.12]

Flavonoid compounds identified in ginger include quercetin, rutin, catechinepicatechin, and naringenin [24]. Flavonoids lower intracellular calcium via blocking the N-methyl D-aspartate receptor, which in turn lowers the activity of the calcium-dependent nitric oxide synthase enzyme and phospholipase A2. They demonstrate their analgesic and anti-inflammatory actions by decreasing nitric oxide and prostaglandins, particularly prostaglandin E2 and F2 [25]. Flavonoids' anti-inflammatory actions have also been linked to the suppression of inflammatory cytokines such as tumor necrosis factor, which are released by macrophages involved in inflammation and increased prostaglandins [23]. By blocking catechol-O methyltransferase and maintaining catecholamines, certain flavonoids have antioxidant and anti-inflammatory properties [26].

Other ginger compounds, such as shogaol, have comparable pharmacological actions to NSAIDs in that they block arachidonic acid metabolism and, as a result, prostaglandin synthesis, serving as an anti-inflammatory drug. They are more effective and have fewer adverse effects than traditional anti-inflammatory medicines [27]. 6-shogaols appear to interfere with arachidonic cascade inflammation, resulting in cyclooxygenase inhibition and prostaglandin release suppression. By suppressing the formation of leukotrienes and prostaglandins, ginger is also beneficial in alleviating inflammation and rheumatism [10] . Several genes implicated in inflammatory reactions, including those encoding cytokinin, chemokinin, and cyclooxygenase 2, are inhibited by ginger extract [28, 29]. Shogaol, the main component in dried ginger, can lower TNF levels in macrophages activated by lipopolysaccharide [17]. Research by Li et al. shows that ginger inhibits the activity of the nuclear factor-kappa (NF-κB), reduce TNF-α and IL;-6 levels in hepatitis and reduce liver cytokines and, inflammatory markers [30]. Gingerol has also been found to protect nephrons by lowering inflammation, resulting in a substantial decrease in tumor necrosis factor-alpha, interleukin-2, and interferon-gamma mRNA and transcription [31]. In mouse macrophages, 6. hydrogenerdione, one of the most essential components of ginger, can inhibit the synthesis of IL-6 and TNF-, IL-1B, COX2, and iNOS [32]. Gingerol and shogaol have also been demonstrated to act as serotonin receptor inhibitors, decreasing the release of substance P, which is involved in inflammation and pain [33]. The prostaglandins, IL-6, IL-2, IL-1, and TNF-a are all reduced when serotonin receptors are inhibited [34]. Ginger, interestingly, increases the production of anti-inflammatory genes like IL-10 [35]. By down-regulating antigen-presenting macrophages and decreasing their activity, ginger extract also suppresses the generation of inflammatory cytokines and inflammatory chemokines in activated macrophages and lowers T cell proliferation [33]. Ginger's effect on prostaglandin E2 decrease is most likely due to direct suppression of mRNA expression and cyclooxygenase 2 activity [22]. Because of the anti-inflammatory properties of ginger, some of its active components block nuclear factor (NF-κB) B and TNF-a (gingerols and zerombon). In liver cancer cells, compounds identified in ginger decrease the production of NF-B and TNF-a [36]. Inhibition of TNF-α gene by ginger reduces NF-κB activity, resulting in inhibition of other inflammatory pathways such as cyclooxygenase 2 (COX2) and its derivatives, such as prostaglandin E2. This reduces inflammation and its effects on the body [37].

Anti-oxidant effects

More than 50 antioxidants have been extracted from ginger rhizomes, the most notable of which being 6-gingerol, a spicy compound with high antioxidant activity. By inhibiting the xanthine oxidase system, this chemical reduces the formation of superoxide anions [38]. By lowering malondialdehyde levels and enhancing plasma antioxidant activity, ginger can decrease lipid peroxidation and free radicals [39]. Atashk et al. found that daily ingestion of one gram of ginger capsule for 10 weeks led in a substantial reduction in malondialdehyde concentration, a biomarker of oxidative stress and insulin resistance in 32 obese men with a body mass index more than 30($p < 0.05$). One of the mechanisms of ginger's benefits is the reduction of fats in the liver and blood tissues, as well as enhanced activity of antioxidant enzymes in the blood, as well as the elimination and purification of free radicals and oxidative stress [40]. In the study by Taghizadeh Afshari et al, 18 rats were chosen and separated into three groups of eight after becoming diabetic. For 8 weeks, the diabetic group was given 5% ginger powder daily. In comparison to the control group, the treated group had a significantly lower level of malondialdehyde, a lipid

[DOI: 10.52547/pbp.4.2.12]

peroxidation indicator ($p < 0.01$) and a significantly higher level of antioxidant capacity ($p < 0.05$) [41].

Anti-tumor effects

Compounds that have anti-inflammatory or antioxidant properties can be considered as anti-cancer agents [42]. The inhibitory impact of 6-gingerol on arachidonic acid, which causes platelet accumulation and the synthesis of thromboxane B2 and prostaglandin D2, was evaluated. By inhibiting the 5-lipoxygenase and prostaglandin synthase pathways, gingerol and shogaol in ginger inhibit the biosynthesis of leukotrienes and prostaglandins [43]. Because of the compounds paradol and 6-gingerol, ginger extract has been shown to be effective in inhibiting skin cancer in mice. Furthermore, in a mouse model of the tumor, these two compounds have been shown to inhibit initial tumor activation [44]. Gingerol has been shown to have anti-carcinogenic properties in the gastrointestinal system, as well as the ability to prevent gastric ulcers and inhibit human colon cancer cells [45, 46]. Gingerol has also been shown to diminish the occurrence of tumors in the early stages of colon carcinogenesis. Oral treatment of aqueous ginger extract to rats inhibited the growth of ovarian tumors, according to the findings [47, 48]. In mice, Gingerol has been demonstrated to have an inhibitory impact on lung cancer metastasis, as well as the capability to enhance the host immune system [49]. Gingerol has also been shown to suppress tumor development and metastasis through having antiangiogenic properties [50]. In mice, ginger triggers apoptosis in Hep2 cells as well as ovarian cancer cells [51]. In another study, it was found that hydroalcoholic extract prepared from ginger rhizome had a lethal effect on C6 glioma cells. This result is in line with previous results which showed that ginger elk extract in a dose and time dependent manner caused cytotoxic effects against liver cancer cell line [52]. Ginger and its 6-gingerol component were reported to trigger apoptosis in endometrial cancer cell lines in one investigation [53]. Ginger extract was discovered to have anti-cancer and anti-inflammatory properties in rats with liver cancer in another research [36]. The cell lethal effects of alcoholic fresh ginger extract on breast cancer cells were examined in a research by Tavakol Afshari et al. In this study, a concentration of 1250 g/ml ginger extract suppressed cancer cell proliferation and morphological alterations after 48 hours ($P < 0.001$). Stimulation of the host immune system, antiangiogenic impacts, suppression of metastasis, and stimulation of apoptosis are some of the mechanisms of anti-cancer properties of ginger, which are mediated by substances like Gingerol and Shogaol [50, 54]. In vitro treatment with ginger in uterine cancer cells effectively inhibits cell growth by 6-shoagol and inhibits NF-κB activity. Also, it can reduces the growth factor and secretion of interleukin 8 [55]. The alcoholic and chloroform extracts of ginger have been shown to have strong cytotoxic effect against the HeLa cell line in the prevention of cervical cancer [56]. Furthermore, 10-gingerol has a greater anti-cancer impact on promyelocytic leukemia cells, lung, ovarian, melanoma, clone, and breast cancer cells than other gingerols. 10-Gingerol inhibits epidermal growth factor receptor expression and promotes apoptosis through inactivating the Akt and p38MAPK cell cycle pathway. Additionally, by inhibiting the metalloproteinase matrix, 10-gingerol prevents cell invasion in response to mitogenic stimuli [57, 58]. Ginger promotes apoptosis by upregulating NAG-1 and halting the G1 cell cycle, which causes cyclin D1 to be downregulated. In these processes, ginger appears to be engaged in a number of mechanisms, including protein degradation and beta-cationin [59]. Moreover, the researchers stated ginger's antiproliferative properties might be related to the induction of apoptosis by elevating the Bax protein to Bcl2 ratio. The down-regulation of important molecules including Bcl-x, Mcl-1-cyclin, D1-survivin (SurviviCDK-4, c-Myc, and hTERT), as well as the regulation of -21 in -k, may be mediated by ginger-dependent growth inhibitory mechanisms. Both c-Myc and hTERT inhibition are regarded particular cancer cell targets during cancer treatment [60].

Anti-diabetic effects

The anti-diabetic properties of ginger have been proven in several research. A total of 80 individuals with type 2 diabetes were investigated in the Golden Study et al. The patients were given three 1 g capsules of ginger powder daily for eight weeks after being randomly placed to the intervention and control groups. The findings revealed that towards the conclusion of the trial, the intervention group's LDL-C and fasting blood sugar levels had lowered considerably ($p < 0.05$), whereas the levels of APO A1 (a protective apolipoprotein) had increased significantly (p

[DOI: 10.52547/pbp.4.2.12]

<0.05) [61]. In a three-month research by Schidfar et al., type 2 diabetes patients were given three grams of ginger powder daily. At the end of the intervention, serum glucose, HbA1C, insulin resistance, insulin resistance, reactive protein type, C paraoxonase-, 0 total antioxidant capacity, reactive protein type C and malondialdehyde significantly improved in the intervention group compared to the control group(P <0.05) [62]. Mahluji et al. conducted an eight-week study on 94 patients with type 2 diabetes who were given two grams of ginger powder daily. Insulin, LDL-C, triglyceride levels, and insulin resistance indices, HOMA-IR, considerably reduced (p <0.05) at the completion of the intervention, whereas insulin sensitivity index, QUICKI, increased significantly (p <0.05) [63]. 8 randomized controlled clinical trial studies are included in a meta-analysis. When compared to the control group, ginger intake was found to be considerably successful in decreasing total cholesterol, triglyceride, and fasting blood sugar levels while also elevating HDL levels [64]. Arablu et al. studied patients with type 2 diabetes who were randomly assigned to intervention or control groups. For one week, the intervention group took one 800 mg ginger powder capsule every day. The study found that the intervention group had significantly lower fasting blood sugar, triglycerides, total serum cholesterol, and C-reactive protein than the control group (p <0.05) [65]. The effect of ginger on fat metabolism in the liver, which results in a decrease in cholesterol production and conversion of cholesterol to bile acids and their excretion, is one of the proposed mechanisms of ginger's influence on glucose and fat indices [66] . Another process is related to an increase in the levels and activity of vascular lipoproteinlipase, which causes triglycerides in blood vessels to break down and lower the levels of triglycerides in plasma, resulting in a decrease in VLDL[67, 68]. Suppression of hepatic glucose-9-phosphatase activity, resulting in reduced glucose-9-phosphate to glucose conversion, as well as inhibition of hepatic phosphorylase, resulting in reduced glycogen breakdown of liver reserves versus Increased activity of glycogen-synthesizing enzymes are among the mechanisms of lowering blood glucose [69]. Other mechanisms to enhance GLUT-4 and insulin receptors and improve pancreatic beta cell activity have been proposed [70]. Polyphenols in ginger exhibit insulin-like properties. Hepatic gluconeogenesis is inhibited because it enhances uptake of glucose by blocking environmental influences. It also improves residual glucose uptake by stimulating the regeneration process and increasing glucose uptake into muscle and adipose tissue of beta cells [71]. Shanemugam et al. discovered that ginger reduced blood sugar levels significantly in diabetic rats as compared to diabetic control rats [72]. Two research by Nammi et al. and Goyal et al. were performed on healthy rats receiving high-fat diet and obese rats, respectively. Obesity and insulin resistance lower plasma adiponectin levels and mRNA expression, while increasing adiponectin improves insulin sensitivity [73, 74]. By inhibiting the action of the glucosidase and amylase enzymes, ginger may also lower glucose uptake into the blood [75]. In patients with type 2 diabetes and insulin-resistant animals, antioxidant treatment has been found to enhance glucose transport and tolerance. Ginger, sugar cane, paradox, and zinc are some of the antioxidants found in ginger. These compounds' exact mechanism of action is currently unclear. These compounds can work by increasing protein and GLUT4 insulin receptors and improving β-cell function of the pancreas. The impact of ginger on insulin sensitivity appears to be due to its active components' influence on PPAR or adiponectin upregulation. According to Isa et al. study, ginger contains 6-shugaol and 6-gingerol, which enhances adiponectin levels. They claim that 6-shugavel is a PPARγ agonist [76]. Obesity and insulin resistance lower plasma adiponectin levels and mRNA expression, while increasing adiponectin improves insulin sensitivity [73].

Anti-lipemic effects

Ginger has the ability to modify fat metabolism by inhibiting cellular cholesterol production, elevating bile acid production to remove cholesterol from the body, increasing cholesterol removal from the body, and raising fecal cholesterol excretion [77]. By suppressing intestinal lipase, enhancing bowel movements, and limiting intestinal fat absorption, ginger can help decrease triglycerides [78]. It is also possible to lower fat serum by increasing the quantity and activity of the enzyme vascular lipoprotein lipase [79]. Furthermore, in rat liver, the major components of ginger have been demonstrated to decrease cholesterol production [80]. In diabetic rats, Abdul Rahim et al. investigated the effects of ginger on glucose, blood lipid pattern, and kidney function. The researchers discovered that diabetic rats that ate ginger had lower levels of low-density lipoprotein cholesterol [81]. Al-Amin and Akhani, also found

[DOI: 10.52547/pbp.4.2.12]

comparable results in their studies on the efficacy of ginger on decreasing triglycerides in diabetic rats [82, 83].

Respiratory diseases

In asthma patients, 6-gingerol and 6-shogaol in ginger rhizome are potent inhibitors of 5 lipoxygenase and leukotrienes, which create inflammatory mediators [9, 84]. Ginger's effect in lowering the formation of nitric oxide (NO) via gingerols in asthma sufferers is another protective mechanism. The nitric oxide synthase enzyme is inhibited by these substances. Nitric oxide is implicated in the dilatation of bronchial arteries in asthma patients, and studies show that the amount of nitric oxide in exhaled air is greater in asthma patients than in healthy individuals, and is linked to eosinophils inflammation [85, 86]. Farzin et al. conducted a trial on 32 asthmatic patients who were given 250 mg ginger powder capsules three times a day for four weeks. The study found that the volume of active exhalation in the first second (Forced Expiratory Flow 1), maximum expiratory flow (peak expiratory flow), and asthma control test scores (Asthma Control Test) all improved significantly ($P < 0.05$) [86]. The findings of a psychiatric research on 60 patients with acute bronchitis indicated that taking a hydroalcoholic extract of ginger root (40 mg) and marshmallow (300 mg) in drops (every 6 hours) for 10 days significantly decreased cough and chest pain in the case group compared to the control group. The anti-inflammatory characteristics of this extract, as well as its mucilage properties and prevention of platelet aggregation, were considered as mechanisms of action [87]. Another research found that giving asthmatics 150 mg/ml ginger drops three times a day alleviated chest tingling, decreased chest pain, and lowered asthma, shortness of breath, and nocturnal cough [77]. Ahui et al. demonstrated a reduction in the number of eosinophils in the fluid (BAL) of bronchoalveolar lavage fluid and lung tissue of mice given ginger, as well as a substantial reduction in interleukin-5 and eutoxin levels [12]. In addition, ginger has the capacity to prevent neutrophil and macrophage recruitment and it impacts macrophage responses and proinflammatory cytokines by inhibiting the synthesis of Th1 cytokines such interleukin-1, interleukin-8, and TNF- α [10, 88]. As a result, ginger can be used to treat asthma by decreasing Th2-mediated immune responses.

Anti-nausea and vomiting effects

The anti-nausea and anti-emetic properties of ginger have been shown in various studies. It can also prevent dyspepsia produced by planes, ships, cars, and other vehicles rotating and moving abnormally. Other research on the efficacy of ginger root in preventing seasickness have found that taking one gram of ginger can lower the intensity of seasickness in naval expeditions [42]. The anti-nausea action of ginger has been related to its influence on intestinal gas in several studies. In mice, ginger sulfonic acid, which is derived from ginger root, is beneficial in treating stomach ulcers caused by Hcl/ethanol induction [89]. One study found that ginger in biscuit form is effective for relieving the severity of nausea and, to some extent, of vomiting in pregnancy [90]. Ginger has also been demonstrated to be safe and beneficial for nausea and vomiting during pregnancy in other placebo-controlled studies [91]. Although the efficacy of ginger in the treatment of nausea is not particularly substantial compared to other therapies, other studies have found that its administration is relatively low and without adverse effects [92]. In another study, it was discovered that individuals who got 250 mg of ginger experienced less nausea and vomiting than those who received placebo [93]. Other studies have compared ginger's anti-nausea and vomiting properties with vitamin B6, and both are similarly beneficial [94]. Pregnant women were randomly allocated into two groups in a double-blind control trial. For three days, one group received 650 mg of ginger while the other received 25 mg of vitamin B6 three times a day. Ginger was quite effective and had little negative side effects [95]. Another trial that was done at random between two groups that received ginger at a dose of 1 g per day and vitamin B6 at a dose of 40 mg per day found that nausea and vomiting were much lower in the ginger group than in the vitamin B6 group [96]. Ginger's anti-nausea and anti-vomiting properties in chemotherapy have also been reduced in other trials [97, 98]. According to a research, ginger's anti-nausea and anti-vomiting properties might be utilized as a pre-surgery prophylaxis [99]. The usefulness of ginger in laparoscopic gynecological procedures has been studied extensively. Patients who took one gram of ginger before this procedure, especially 2-4 hours earlier, had reduced nausea and vomiting [100]. Another study involved 60 patients who were randomly assigned to one of two groups: those who received 3 grams of ginger and those who

[DOI: 10.52547/pbp.4.2.12]

received a placebo one hour before the therapy. Although the ginger group experienced less nausea than the placebo group, there was no difference in the rate of vomiting In the investigation by Hemmatzadeh et al., the intervention group received four 250 mg capsules of ginger rhizome powder each day, whereas the control group received three 10 mg tablets of metoclopramide. There was a significant difference in the severity of nausea and the frequency of vomiting in both groups after taking the medicine compared to before treatment among pregnant women under 20 weeks ($p = 0.01$). In pregnant women under 20 weeks, there was a significant difference in the severity of nausea and the frequency of vomiting in both groups after taking the medicine compared to before therapy ($p = 0.01$). In terms of symptom reduction, there was a significant difference between the two groups in favor of ginger ($P = 0.04$) [101]. Ozgoli et al. conducted a study on 67 women with nausea (35 in the control group and 32 in the experimental group) who were given 250 mg ginger four times a day for four days and a lactose-containing placebo in the control group. The results showed that severe nausea in the case group improved significantly before treatment ($p = 0.05$) when compared to the control group. In addition, the case group experienced fewer vomiting episodes than the control group [102].

Bleeding and blood clotting effects

Antiplatelet and antihypertensive effects were discovered in animal specimens in a research [44]. According to certain investigations, caution should be considered while taking ginger and other similar herbal remedies after surgery due to increased bleeding [103]. Especially when used with anticoagulants like warfarin [100]. In one research, however, ginger had no effect on blood pressure, heart rate, or coagulation factors, and had no effect on anticoagulants like warfarin [104]. When ginger is taken with certain medications, such as nifedipine, the coagulation rate decreases and the risk of bleeding increases. According to one study, taking ginger and nifedipine combined had a worsening effect on platelet aggregation prevention [105]. In healthy individuals, several investigations have demonstrated that ginger has no effect on the anticoagulant effects of warfarin [106]. Ginger extract was found to lower dose-dependent blood pressure in an animal research [107]. Taking ginger with a variety of drugs, including verapamil, nifedipine, fludipine, amlodipine, and isradipine, has been shown to reduce blood pressure and produce irregular heartbeats in studies [108]. Ginger has components known as a platelet-activating inhibitor, without the potential side effects of aspirin. However, it has less antiplatelet effect than aspirin. This effect is used in the treatment of coronary heart disease [109]. Ginger has been shown to have an anti-fibrin effect in subsequent researches [110]. A calcium channel blocker with a synergistic impact on platelet aggregation has been discovered in ginger anipine. These effects were examined on two different groups of people: healthy volunteers and hypertension patients [111].

Other uses of ginger and their dosage

Ginger has been utilized as a diaphoretic and anti-flatulent medication for gastrointestinal spasms. It's also used to treat indigestion and colic pain in the intestines. Rhizome should be taken at a dose of 1-2 grams 30 minutes before travel or 0.5 grams two or four times a day for anti-nausea effect [112, 113]. The root of Zingiber Officinale stimulates the immune system [114]. Its rhizome possesses antimicrobial, antioxidant, anti-cancer, and anti-diabetic properties, as well as reducing platelet aggregation [115]. The suggested oral dose for anti-nausea effect (particularly Shagol and Gingerol) is 100 mg/kg. For anti-nausea effects, ethanol or acetone extract of ginger at dosages of 100, 50, 25, and 200 mg / kg is suggested. The effects of ginger juice at 2 and 4 mg/kg are the same [116]. Ginger oil contains anti-inflammatory properties. Swelling produced by injection of dead Mycobacterium TB is greatly reduced after taking 33 mg/kg for 26 days [117]. Oral ingestion of 1.8 grams of powdered ginger root was shown to be more efficacious than 100 mg of dimenhydrinate in one investigation [118]. It has been reported that ginger can be used as a migraine headache prophylactic. This impact might be due to prevention of thromboxane formation or inhibition of free radicals produced during arachidonic acid generation [119-125].

Safety and side effects of ginger

Ginger is a well-known spice. It is recognized by the US Food and Drug Administration as a safe and dependable food additive [58]. Ginger has also been designated by the European Health Council as a food flavoring source that may be used in low quantities in meals. Ginger extract has been

[DOI: 10.52547/pbp.4.2.12]

shown to contain neurotoxic components in a number of exploratory researches [59]. Some Ginger has also been reported to possess mutagenic substances in other investigations [60]. Pregnant mice tolerated the 1000 mg per kilogram dosage adequately. In other studies, this substance was administered to male and female mice as a gavage with varied dosages of 1000, 500 mg/kg, and 2000 mg/kg for 35 days, and the results revealed that no behavioral or growth abnormalities were observed in these animals [61]. Overall, studies demonstrate that taking ginger orally is generally safe, with just minor negative effects in rare circumstances.

Conclusion

Due to the fact that ginger has many applications in the treatment of diseases and on the other hand, modern science confirms this by discovering the mechanisms related to the useful components of this plant in the control of various disorders and diseases. Therefore, the use of this plant as a medicinal plant is recommended with due regard to the recommended dosage and duration of use. However, future clinical trials are needed to further confirm this claim.

Abbreviations

GRAS: Generally Recognized as Safe, IL: interleukin, TNF: tumor necrosis factor-alpha, NF-κB: nuclear factor-kappa, NO: nitric oxide.

Acknowledgment

Not applicable.

Funding

Not applicable.

Availability of data and materials

The data that support the findings of this study are available on request from the corresponding author.

Authors' contributions

J.F, R. T, M. Sh, S.SH and M.A: study design, acquisition of data, analysis and interpretation of data. Drafting of manuscript. J. F, R. T, Z M, M. Sh, S.SH and R.T. All authors read and approved the final manuscript

Ethical principles

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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