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Phytochemical Analysis of Ginger: Exploring Its Role as a Natural Therapeutic Agent in Pharmaceutical Applications

Research

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مِمَّا يَجْمَعُونَ ﴿٥٨﴾

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Supervisor Certificate

Certify that this Project (Phytochemical Analysis of Ginger: Exploring Its Role as a Natural Therapeutic Agent in Pharmaceutical Applications) was prepared under our supervision at the College of Pharmacy, University of Misan, as graduation research

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Date:

Dedication

**To our parents, without them, we wouldn't be here, our
beloved mother and father**

To everyone whom taught us anything

**To our research supervisor (Dr. Widad Ali Abed
Salman), who supported us all the way**

We dedicate this to you

Acknowledgment

First, a special thanks to "ALLAH " for the guidance, strength, power of mind, protection, and skills and for giving us a healthy life.

we express our deepest gratitude to our supervisors, for their support as with their help we were able to do all the best.

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We really thank them.

Table of contents

Number	Subject	Page No.
	Supervisor Certification	I
	Dedications	II
	Acknowledgment	III
	Table of contents	IV
	List of Figures	V
	Abstract	VI
1.1	Introduction	1-2
2.1	Bioactive Compounds in Ginger	3-4
3.1	Pharmacological Benefits of Ginger	5
3.1.1	Antioxidant	5-6
3.1.2	Anti-hyperglycemic	6-7
3.1.3	Anti-inflammatory	7-8
3.1.3.1	Mechanism of Action of Ginger	8
3.1.4	Antitumor/Anticancer	9
3.1.4.1	Prostate Cancer	9-10
3.1.4.2	Liver Cancer	10
3.1.4.3	Pancreas Cancer	11
3.1.4.4	Colon Cancer	11
3.1.4.5	Gastric Cancer	12
3.1.5	Antihypertention	12-13
3.1.6	Neuroprotective	13
3.1.7	Anticholesterolemic	14
3.1.8	Antibiotic/antimicrobial	15
3.1.9	Antiulcer/gastro protective	15-16
3.1.10	Antiemetic	16-17
3.1.11	Hepatoprotective	17-18
	Conclusion	18
	References	19-27

List of figures

NO.	Title of Figures	Page
1	The medicinal properties of ginger	2
2	Ginger rhizome active compound	4
3	The potential mechanism for the antioxidant action of 6-shogol	6
4	Represents the Anti-inflammatory effect of Ginger	8
5	The antiemetic mechanism of ginger against CINV	17

Abstract

Zingiber officinale, belonging to the Zingiberaceae family, is one of the most widely recognized and utilized spices and herbs worldwide. Known for its versatility, ginger is used both as a flavorful delicacy and as a remedy for numerous ailments in traditional medicine, such as diabetes, hypertension, cancer, ulcers, diarrhea, colds, coughs, spasms, and vomiting. These therapeutic uses have been documented across regions, from China, India, and the Arabian Peninsula to various continents, including Africa (e.g., Nigeria and Egypt).

This review aims to highlight the pharmacological potential of ginger, which is attributed to its bioactive chemical constituents, such as gingerol (including 6-, 8-, and 10-gingerol), 6-shogaol, 6-hydroshogaol, and oleoresin. These compounds exhibit a wide range of therapeutic effects, including antioxidant, antitumor, anti-inflammatory, antihyperglycemic, antihypertensive, anticholesterolemic, antimicrobial, neuroprotective, gastroprotective, antiemetic, hepatoprotective, and Toxicity profiles.

Most of these effects have been validated through in vitro and in vivo studies. However, many therapeutic potentials of ginger remain underexplored, and only a few established effects have undergone clinical trials. This underscores the need for more intensive research to develop preventive and therapeutic drugs derived from ginger.

In conclusion, this review sheds light on the therapeutic significance of ginger and its derivatives in managing a wide range of diseases threatening human health.

1.1 Introduction

Ginger (*Zingiber officinale Roscoe*) belonging to the Zingiberaceae family is a widely recognized herbal spice, believed to have originated from either India [1] or Southeast Asia [2]. Being a sterile plant, it reproduces through rhizomes rather than seeds [3] and thrives in tropical and subtropical regions [4]. Ginger is commonly used for culinary purposes as a seasoning or condiment, and it also holds significant therapeutic value [5]. Known for its potent medicinal properties, ginger exhibits spasmolytic, antipyretic, antiemetic, antioxidant, antiulcer, analgesic, hypotensive, antidiabetic, and anti-inflammatory effects [6, 7]. These benefits are attributed to its content of aromatic essential oils and spicy oleoresins [8].

Therapeutically, ginger has been traditionally used for treating colds [9], sore throats [10], and infections caused by *Staphylococcus aureus* [11]. It has also been tested for its efficacy against cancer cells [12]. Beyond its medicinal applications, ginger serves as a dietary supplement and is widely incorporated as an additive in various snacks and commercial products [13]. Recognized as a safe herbal drug, it has been classified as “Generally Recognized as Safe” (GRAS) [14]. Several studies have demonstrated that treating cells with *Z. officinal* blocks neuronal cell death in vitro and enhances motor neuronal recovery in rats [15, 16]. It has been assiduously asserted that ginger potently enhances cognitive function in several animal models of cognitive disorder, as well as in healthy humans [17]. Moreover, in South Asia, *Z. officinal* has long been used as a type of folk medicine for the treatment of dementia, which is characterized by memory loss as a major clinical symptom [18]. Ginger has been shown to facilitate conditioned inhibitory and spatial learning in adult and aged animals [19,20]. In addition, ginger significantly attenuates scopolamine- and diazepam-induced amnesia in mice [21].

Recent findings indicate that *Z. officinal* can mitigate memory impairment in rats subjected to focal cerebral ischemia [22,23], NMDA administration [24], and amyloid beta (A β) injection [25].

Furthermore, ginger is also a cognitive enhancer in middle-aged women [26]. Very recently, the potential of traditional Chinese medicinal ginger root extract has been assessed in the prevention of behavioral [27].



Fig1: The medicinal properties of ginger

2.1 Bioactive Compounds in Ginger

The nutritional and nutraceutical benefits of ginger are closely associated with the presence of various bioactive compounds. These bioactive compounds, reported in different studies, are classified into three classes: gingerols, volatile oils, and diarylheptanoids [28]. The chemical components of ginger include volatiles (geraniol, borneol, terpineol, zingiberenol, cineole, limonene, camphene, curcumene, zingiberol, geranyl acetate, linalool, α -Farnesene, α -sesquiphellandrene, α -zingiberene, α -bisabolene, elemene, and α -phellandrene) and nonvolatiles (gingerols, shogaols, zingerone, and paradols). These non-volatile phytochemicals, having pungent odors and flavors, are the characteristic bioactive constituents of ginger. The distinctive aroma flavor of ginger is the resultant blend of these three non-volatile active compounds (gingerol, shogaol, and zingerone), which constitute one to three percent of fresh ginger by weight. There are two common components, vanillyl (4-hydroxy-3-methoxyphenyl) and the ketone functional group, that are found in every pungent compound of ginger [29,30].

Gingerol is a pungent oil, yellow in color, that is also found in crystalline solid form with a low melting point. Gingerols are classified into 4-, 6-, 8-, 10-, and 12-gingerol based on the length of the unbranched alkaline chain. 6-Gingerol is the most abundantly available type of gingerol, while considerable amounts of 8-gingerol and 10-gingerol are also found in fresh ginger [31,32]. 6-Gingerol is a moderately pungent and one of the most active phytochemicals in ginger. It has been cited with many health benefits by various researchers [33,34]. More than 400 compounds have been found in the chemical analyses of ginger [35]. These compounds include alkaloids; saponins; flavonoids; steroids; tannins; carbohydrates; glycosides; proteins; amino acids; dietary fiber; ash; phytosterols; vitamins A, B, and C; minerals; and terpenoids, [35,36] while detected to be devoid of acid compounds and reducing sugars [37]. The main components of the ginger rhizome are in the order carbohydrates, lipids, terpenes, and phenolic compounds [38]. The terpenes and the phenolic compounds make up the two foremost classes of phytochemicals in ginger [39].

Phenolic compounds of ginger are also referred to as its nonvolatile components, which have been incriminated in its pharmacological activity.

They consist of gingerols, their 6, 8, and 10 derivatives, and the corresponding series of homologous shogaol and zingerone, obtained from heat or alkali-treated gingerols [39]. Shogaol, paradol and gingerols have been depicted to be responsible for the pungent taste and smell of ginger [40]. The presence of bioactive phytochemicals such as gingerols, shogaols, paradols, gingerdiols, and zingerone is thought to be the cause of ginger's many health benefits (Fig. 3).

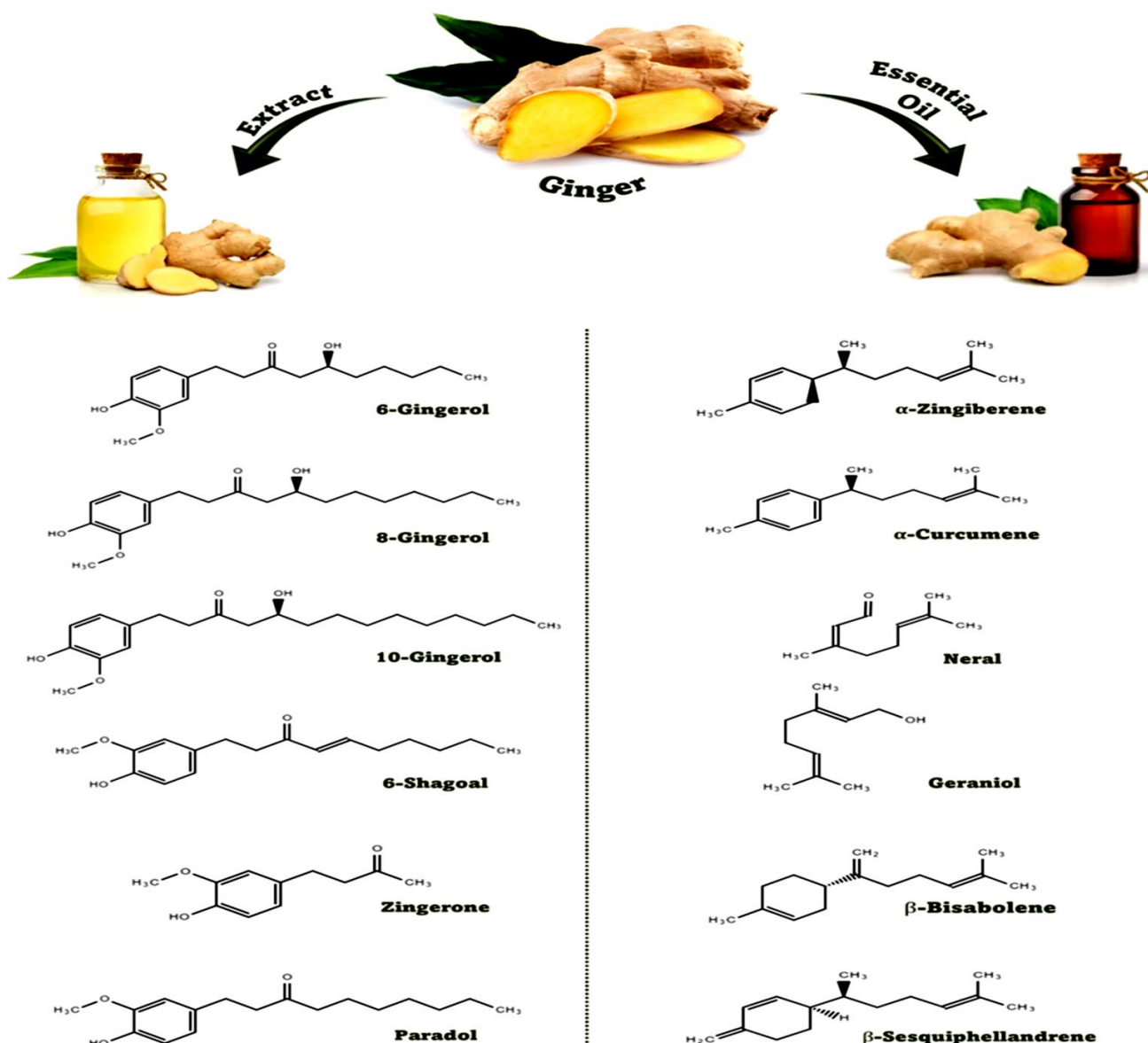


Fig. 2 Ginger rhizome active compound

3.1 Pharmacological Benefits of Ginger:

As mentioned above, ginger's functional and bioactive compounds are associated with multiple health benefits and advantageous characteristics. The exploitation and characterization of the versatile biological and functional competencies of ginger are also crucial for further research. These multifaceted bioactivities of ginger bioactives and their modes of action are discussed here in this section.

3.1.1 Antioxidant

The overproduction of free radicals (ROS) in situations where the antioxidant defense mechanism is compromised leads to oxidative stress. Antioxidants play a vital role in mitigating excessive free radical (FR) generation and reducing oxidative stress. Numerous medicinal plants (MPs) and their constituents have demonstrated their efficacy in preventing diseases, particularly those caused by free radicals.[40]

Ginger is a prominent example of medicinal plants with strong antioxidant properties. It has been shown to reduce lipid peroxidation, such as inhibiting the ascorbate/ferrous complex in rat liver microsomes, as noted by Rahmani *et al.* based on the report by Reddy and Lokesh [41]. Additionally, ginger extracts, active components, and compounds like gingerol exhibit significant scavenging effects against superoxide anion and hydroxyl radicals [39–41]. Notably, these antioxidative properties remain stable even after heating ginger [42].

Furthermore, ginger has been found to reduce intracellular reactive oxygen species (ROS) induced by ultraviolet B (UVB) radiation and decrease cyclooxygenase (COX)-2 activity, as observed in both *in vitro* and *in vivo* studies [42]. Moreover, other derivatives of ginger, such as oleoresin, 6-shogaol, 6-dehydroshogaol, 1-1-dehydro-6-gingerdione, 6-gingerol, 8-gingerol, 10-gingerol, and essential oils, possess pharmacological activities, including antioxidant and antimicrobial effects [43].

They have been shown to be effective against compounds such as 2,2-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS), 1,1-diphenyl-2-picrylhydrazyl (DPPH), hydroxyl radicals, and microbial strains like *Bacillus subtilis*, *Bacillus cereus*, *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans*, *Penicillium* spp., and *Aspergillus niger* [43,44].

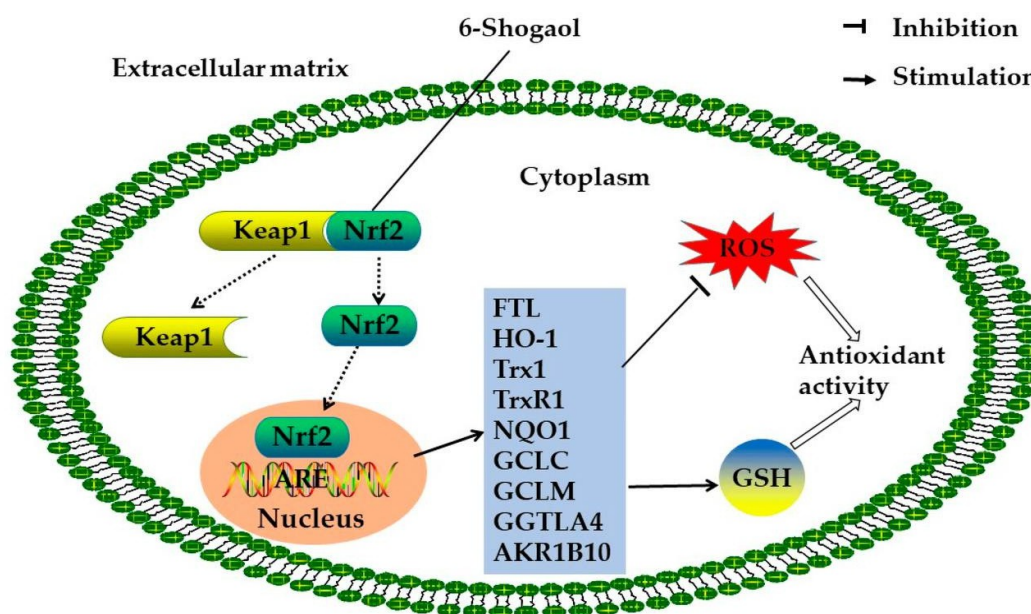


Figure 3: The potential mechanism for the antioxidant action of 6-shogaol

3.1.2 Anti-hyperglycemic

Diabetes mellitus (DM) is one of the noncommunicable diseases with significant global prevalence. It is an endocrine disorder or metabolic derangement characterized by hyperglycemia (elevated blood glucose levels) due to insufficient or ineffective insulin, resulting from abnormalities in the metabolism of carbohydrates, lipids, and proteins. The management or treatment of DM can be achieved through, Non non-pharmacological methods: such as exercise and dietary regimens. Pharmacological methods involving the use of oral hypoglycemic agents (OHAs), such as sulfonylureas, biguanides, etc [45].

However, the use of these synthetic agents often comes with drawbacks, including side effects like obesity, limited availability, and high costs. This highlights the urgent need for alternative treatments with minimal or no side effects.

Interestingly, such qualities have been discovered in medicinal plants. Many studies show that ginger and other plants are effective both preventively and therapeutically [45]. For example, research at the University of Sydney in Australia found that ginger was effective in glycemic control for people with type 2 diabetes. One study demonstrated that ginger extracts could increase glucose uptake into muscle cells without relying on insulin, thus helping control high blood sugar levels.

A clinical trial involving diabetic patients who consumed three grams of dry ginger daily for 30 days showed significant reductions in blood glucose, triglycerides, total cholesterol, and LDL cholesterol levels [46–47]. Another study revealed that administering ethanolic extracts of *Z. officinale* orally for 20 days produced a significant antihyperglycemic effect ($P < 0.01$) in diabetic rats. Furthermore, in high-fat diet models, ginger ethanolic extract reduced body weight, total cholesterol, LDL cholesterol, triglycerides, free fatty acids, glucose, insulin, and phospholipids [48].

Overall, ginger combats diabetes by enhancing insulin release and sensitivity, inhibiting carbohydrate metabolism enzymes, and improving lipid profiles. Ginger has a very low glycemic index (GI), meaning it breaks down slowly, regulating blood glucose levels without causing spikes like high-GI foods.

Additionally, studies have shown that ginger has a preventive effect against diabetes complications. It can protect a diabetic's liver, kidneys, and central nervous system, and it reduces the risk of cataracts, a common complication of the disease [46, 49, 50].

3.1.3 Anti-inflammatory

Inflammation is a defensive response experienced by the body against harmful stimuli such as tissue injury or allergens. When these responses exceed normal limits, they can lead to various disorders, including allergies, cancer, autoimmune diseases, metabolic syndrome, and cardiovascular diseases [51]. The Link Between Oxidative Stress and Inflammation Reports indicate a connection between oxidative stress caused by free radicals (FR) and inflammation.

The Use of Nonsteroidal Anti-inflammatory Drugs (NSAIDs). NSAIDs are used to alleviate acute and chronic inflammation by inhibiting the enzymes cyclooxygenase (COX 1 and 2) and/or lipoxygenase [52].

which are involved in breaking down arachidonic acid into prostaglandins. However, the use of NSAIDs is associated with numerous side effects, prompting the search for safer natural alternatives. According to Ojewole [53], ginger extract possesses analgesic, anti-inflammatory, hypoglycemic, and safe effects at doses ranging from 50–800 mg/kg body weight. A dose of 33 mg/kg of ginger oil alleviated acute and chronic arthritis in rats [54]. A study by Rani et al. [55] found that ginger extracted using ethyl acetate exhibited superior anti-inflammatory effects compared to other extracts using water, methanol (polar solvents), or hexane (non-polar solvent). This was due to its ability to inhibit cyclooxygenase and lipoxygenase enzymes.

3.1.3.1 Mechanism of Action of Ginger:

Ginger plays a crucial role in regulating the release of inflammatory mediators such as nitric oxide, prostaglandins, cytokines, tumor necrosis factor (TNF), and interleukins (IL-1 and IL-8) through multiple biochemical pathways [17, 23, 28, 56, 52].

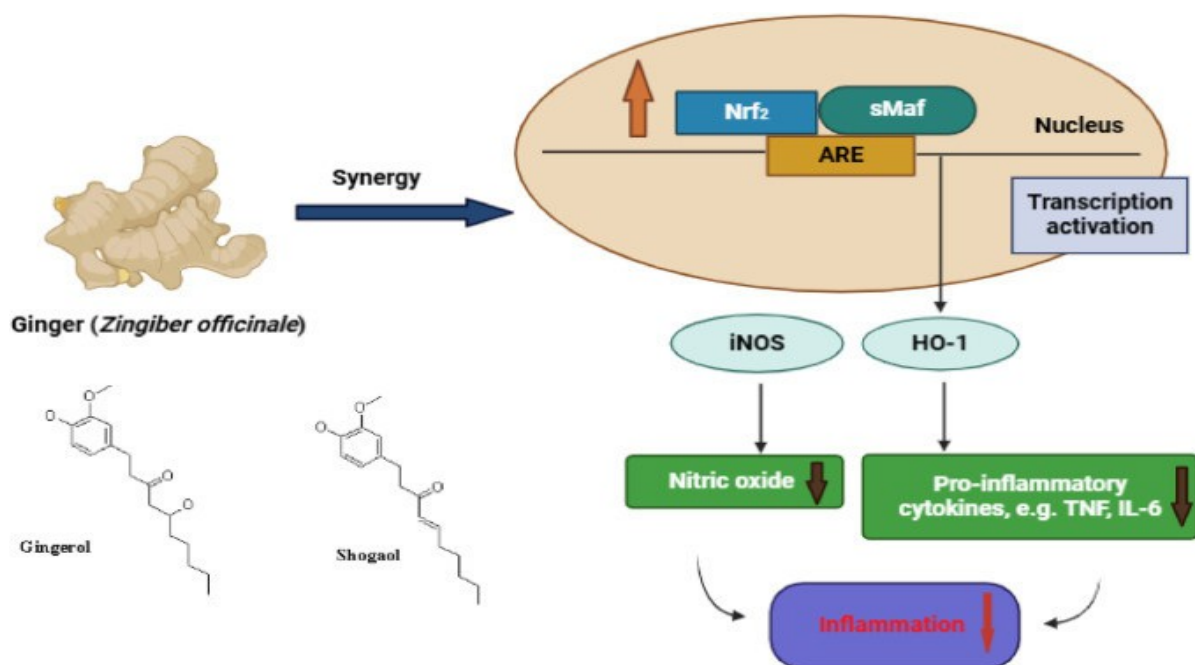


Figure 4 : Represents the Anti-inflammatory effect of Ginger.

3.1.4 Antitumor/Anticancer

There is growing evidence linking diet to cancer prevention and treatment. Cancer is the second leading cause of death in the world after cardiovascular disease. Cancer is one of the noncommunicable diseases with great negative impact on global population. It is caused by a persistent increase in abnormal human body cells leading to the formation of tumors (of malignant cells) with the possibility to be metastatic [57]. The continuous multiplication of these cells is sometimes associated to influence oxidative stress. A number of treatment (chemotherapy, radiotherapy, synthetic drugs, etc.) are currently available; however, they come with one or several side effects (nausea, hair fall), hence, the need for an alternative form of treatment or therapy, particularly from MPs (medicinal plants). In recent times, several plant species have found their relevance in the prevention and treatment of cancer.

Ginger is a great example of such MPs with excellent prophylactic and curative anticancer properties. Ginger and its active compounds have been identified with anti-carcinogenic properties against all stages of cancer development, including cancer initiation, promotion, progression, and drug resistance. Although it must be noted that these effects are not available for all cancer types, several reports on ginger and its derivative (gingerol) have established numerous effects on different types of cancer (lung, colon, ovarian, prostate, etc.) in a study conducted in the United States by Karna *et al.* [58]

3.1.4.1 Prostate Cancer

Daily oral administration of ginger at a concentration of 100 mg/kg body weight (bw) inhibited PC-3 xenograft growth, indicating its effect against prostate cancer in vitro and in vivo. Other studies: In vivo and in vitro studies were carried out to evaluate the action mechanism and cytotoxic effects of ginger against prostate cancer [59]. It was reported that 6-gingerol, 6-shogaol, 10-gingerol, and 10-shogaol showed considerable anti-proliferative effects on prostate cancer cells in humans through the deregulation of the protein expression of MRPI (multi-drug resistance-associated protein 1) and GST (Glutathione-S-transferase).

The proliferation of PC-3 prostate cancer cells was synergistically inhibited through the bifold consolidation of ginger bioactives like 6-gingerol, 8-gingerol, 10-gingerol, and 6-shogaol [60].

3.1.4.2. Liver Cancer

In vitro studies reveal that ginger components are effective against liver cancer. In a study, 6-shogaol has been reported to induce apoptotic cell death of Mahlavu hepatoma cells via an oxidative stress-mediated caspase-dependent mechanism. Glutathione (GSH) depletion is a major contributing factor in arbitrating 6-shogaol-induced apoptosis of Mahlavu cells [61]. Recently Jeena et al. [62] showed that oral administration of ginger oil for one month increases antioxidant enzymes SOD, GSH, and glutathione reductase in blood of mice and glutathione- S-transferase, glutathione peroxidase, and SOD enzymes in liver of mice. Ginger oil also produced significant reduction in acute inflammation produced by carrageenan and dextran and formalin induced chronic inflammation [63], indicating its role in prevention of liver carcinogenesis. Besides glutathione, ROS also been involved in ginger extract-induced apoptosis of HepG2 hepatoma cells. Ginger extract at a dose of 250 $\mu\text{g/mL}$ markedly changes morphology of cells including cell shrinkage and condensation of chromosomes in HepG2 cells [64]. Another study showed that 6-gingerol induced apoptosis of human HepG2 cells through the lysosomal-mitochondrial axis, where cathepsin D played a crucial role in the process of apoptosis. 6-Gingerol induced release of cathepsin D preceded ROS generation and cytochrome c release from mitochondria [65]. It is also reported to protect the lipid peroxidation in liver tissue homogenate/mitochondria. The protective mechanism can be correlated to the radical scavenging property of ginger extract [66]. In an animal model, ginger suppresses ethionine induced liver carcinogenesis by scavenging the free radical formation and by reducing lipid peroxidation. Thus, ginger prevents rat hepatocarcinogenesis [67].

3.1.4.3 Pancreas Cancer

Ginger and its constituents are also effective against pancreatic cancer. Park *et al.* [68] have shown that 6-gingerol inhibits the growth of pancreatic cancer HPAC and BxPC-3 cells through cell cycle arrest at G1 phase and independent of p53 status. Further, they found that 6-gingerol decreased both cyclin A and cyclindependent kinase (Cdk) expression followed by a reduction in retinoblastoma (Rb) phosphorylation and blocking of S phase entry [69]. Another study showed that 6-gingerol regulates tight junction-related proteins and suppresses invasion and metastasis of pancreatic cancer cells. These functions of 6-gingerol were mediated through NF- κ B/Snail inhibition via inhibition of the extracellular signal-regulated kinases (ERK) pathway. Thus, 6-gingerol suppresses the invasive activity of PANC-1 cells [70]. Another component of ginger, 6-gingerol, triggers Ca²⁺ signals in the pancreatic β -cells by activating the TRPV1 channels. In fura-2 loaded single rat insulinoma (INS-1E) cells, 6-gingerol increased intracellular Ca²⁺ in a concentration-dependent manner. Intracellular Ca²⁺ increase obtained by 1 μ M 6-gingerol was found to be greater than that obtained by 10mM glucose [71].

3.1.4.4 Colon Cancer

Researchers [72] investigated the effectiveness of ginger against 1, 2-dimethylhydrazine (DMH)-induced colon cancer. They observed that the supplementation of ginger could activate various enzymes such as glutathione peroxidase, glutathione-S-transferase, and glutathione reductase that suppress colon carcinogenesis [73]. Administered ginger orally in mouse models and observed inhibition in the multiplicity of colonic adenocarcinomas through suppression of colonic inflammation in a dose-dependent manner. The mechanism of that includes inhibition of proliferation, induction of apoptosis, and suppression of NF- κ B and hemeoxygenase (HO)-1 expression.

3.1.4.5 Gastric Cancer

Preclinical studies have shown that ginger extract and its constituents possess chemo preventive and antineoplastic properties in gastric cancer. In vitro study showed that 6-gingerol induces apoptosis of gastric cancer cells. It facilitates TNF-related apoptosis-inducing ligand- (TRAIL-) induced apoptosis by increasing caspase3/7 activation. The induction of apoptosis by 6-gingerol was mediated through downregulation of cytosolic inhibitor of apoptosis (cIAP)-1 and inhibiting TRAIL-induced nuclear factor-kappaB (NF- κ B) activation. Besides 6-gingerol, 6-shogaol also reduced the viability of gastric cancer cells by damaging microtubules [128]. When ginger extract was given to Sprague-Dawley rats having acetic acid-induced ulcers, it significantly reduced the gastric ulcer area.[74].

3.1.5 Antihypertention

Hypertension, a silent killer (because it shows no symptoms), is characterized by continuous increase in blood pressure in the arteries of a person. It occurs when the systolic and diastolic blood pressures rise above 140/90 mmHg, respectively. Findings revealed excessive salt intake, smoking, alcohol consumption, narrowing of the kidney, and use of birth control pills as some of the causes of hypertension, a risk factor to many cardiovascular diseases (CVD). Like diabetes, the treatment option may be non-pharmacological (lifestyle modification, etc.) or pharmacological involving the use of synthetic moieties such as diuretics, beta blockers (atenolol), angiotensin-converting enzyme inhibitor (Lisinopril), calcium channel blockers, etc. [75]. However, sadly too, all these antihypertensive agents bring about grievous adverse effects such as angioedema, dry cough, weakness, headaches, etc.; thus, there is need for a substitute form of therapy for sufferers of high blood pressure (HBP). Herbal products from MPs have come very handy in the fight geared toward treating HBP, and a notable example of such plant is ginger. In a study involving rats and guinea pigs, extracts of ginger at concentration range of 0.3-3 mg/kg lower the arterial blood pressure of these animals [76].

Additionally, similar study using ginger aqueous extract and its derivatives revealed similar action [77]. The activity of ginger as anti-hypertensive agent was also corroborated in a study [78] involving human subject when twice daily intake of 10 g of the spice reduced the arterial blood pressure to 94.80 mmHg after 2 months.

3.1.6 Neuroprotective

Neuroprotection refers to the mechanisms by which the central nervous system (CNS) is safeguarded against neuronal damage caused by acute or chronic neurodegenerative disorders, such as stroke, Alzheimer's, Huntington's, and Parkinson's diseases. These conditions result from the breakdown of CNS neurons and the subsequent deterioration of cognitive or intellectual functioning in affected patients [79]. Notably, the onset of neurodegenerative diseases (NDDs) is closely linked to aging, with the likelihood of developing such disorders increasing with age [80].

Medicinal plants, including ginger, have been increasingly utilized in the management and treatment of NDDs, a benefit attributed to their rich phenolic and flavonoid content [80, 81]. Many diseases, including neurodegenerative conditions, are triggered by the excessive production of free radicals (FRs). This connection extends to diabetes, where one of the complications—diabetic neuropathy—further illustrates the relationship between FRs, NDDs, and diabetes. Interestingly, ginger has been reported in various studies to enhance the antioxidant defense mechanisms of the brain in streptozotocin-induced diabetic rats [82–83]. Moreover, the ginger-derived compound 6-shogaol has demonstrated the ability to inhibit microglial activation in cases of transient global ischemia [84]. These findings highlight the potential neuroprotective role of ginger in combating oxidative stress and neuroinflammation associated with neurodegenerative diseases.

3.1.7 Anticholesterolemic

Cholesterol is a vital constituent of the plasma membranes in eukaryotic cells and represents a significant class of sterols [85]. It is essential for the growth and development of higher organisms. However, hypercholesterolemia, characterized by elevated levels of cholesterol, is a known risk factor for various diseases, including cardiovascular disease (CVD), atherosclerosis, and myocardial infarction (MI) [86]. Cholesterol can be classified into good cholesterol (high-density lipoprotein cholesterol, HDL-C) and bad cholesterol (low-density lipoprotein cholesterol, LDL-C). Excessive production of free radicals (FRs) has also been reported to elevate cholesterol levels in the blood [83, 84]. The use of herbal medicines or medicinal plants (MPs) for therapeutic, curative, or preventive purposes against diseases is an age-old tradition [85]. Among these, ginger stands out for its cholesterol-lowering properties.

A meta-analysis conducted by Thomson *et al.* [86] evaluated randomized controlled trials on the effect of ginger intake on lipid concentrations in hyperlipidemia subjects. The analysis calculated the weighted mean difference (WMD) and 95% confidence intervals (CI) for lipid concentrations, including total cholesterol (TC), triglycerides (TG), LDL-C, and HDL-C. Ginger supplementation was found to significantly reduce TG concentrations (WMD: -8.84; 95% CI) and showed similar effects on TC and HDL-C. Ginger in various forms (tablets, capsules, powder, or rhizomes) significantly reduced TG levels and increased HDL-C, with the results varying according to the clinical condition of the subjects [87]. Studies on both animals and humans demonstrated that ginger effectively decreased plasma cholesterol levels in animals. However, it showed limited efficacy in patients already suffering from heart diseases, such as coronary artery disease. A curcumin extract was also reported to lower LDL and oxidized LDL (ox-LDL) levels while increasing HDL levels by reducing oxidative stress and attenuating the development of aortic fatty streaks in rabbits fed a high-cholesterol-diet.[88]

3.1.8 Antibiotic/antimicrobial

Infectious diseases are rapidly becoming one of the leading causes of death worldwide. Various bacterial pathogens are responsible for these infections, and antibiotics have long been the primary treatment to counter their devastating effects. However, the growing resistance of microorganisms to antibiotics is rendering these treatments increasingly ineffective, despite their significant side effects [89]. This alarming trend has prompted researchers to explore alternative approaches, including the use of medicinal plants (MPs) for treating infectious diseases.

Among these plants, ginger has garnered significant attention due to its well-documented antimicrobial properties. Studies conducted both *in vitro* and *in vivo*, as well as preclinical investigations, have demonstrated the efficacy of ginger extracts—obtained using solvents such as ethanol, ethyl acetate, and hexane—in inhibiting microbial growth. Research by Rahmani *et al.* [90] and Gunathilake and Rupasinghe [91] highlights the antimicrobial activity of ginger derivatives, such as 6-dehydrogingerdione, 6-gingerol, 10-gingerol, and 6-shogaol. These compounds have been shown to exhibit antibacterial effects against several bacterial strains, including *Acinetobacter baumannii*, *Helicobacter pylori*, *Mycobacterium avium*, and *Mycobacterium tuberculosis* [92-94].

Remarkably, evidence suggests that ginger and its derivatives may surpass certain synthetic antibiotics in potency when combating infectious diseases [94]. This further underscores the potential of ginger as a natural and effective alternative in addressing the growing challenge of antibiotic resistance.

3.1.9 Antiulcer/gastroprotective

Ulcers, whether gastric or duodenal, have been a prevalent disease affecting a significant portion of the global population for over a century [95,96]. They are caused by an imbalance between protective factors (such as bicarbonates, prostaglandins, mucin, and nitric oxide) and aggressive factors (such as acid and pepsin), resulting in considerable mortality and morbidity.

Various factors contribute to the onset and progression of ulcers, including etiological agents like *Helicobacter pylori* as well as sedentary lifestyles, poor diet, NSAID usage, smoking, bacterial infections, and oxidative stress caused by free radicals.

Treatment typically involves antimicrobial agents (e.g., metronidazole, tetracycline, and amoxicillin) to eradicate *H. pylori*, antisecretory agents like omeprazole, H₂ receptor antagonists (e.g., cimetidine, ranitidine), and agents that disrupt the bacterial cell wall or membrane, such as bismuth salts. However, these therapies often come with toxic side effects, prompting the search for alternative treatments with fewer adverse effects.

Medicinal plants, such as ginger, have gained attention for their antiulcer and gastroprotective properties. Ginger's antiulcer effects are primarily achieved through increased mucin production [97], a protective factor that safeguards the stomach lining and reduces the risk of ulcers, and the inhibition of thromboxane synthetase [98]. Overactivity of this enzyme weakens the stomach's defense against ulcers by reducing blood flow to affected areas and promoting inflammation.

Several studies, have confirmed the gastroprotective properties of ginger and its active constituents, such as 6-gingerol and 6-shogaol. These findings highlight ginger's potential as a safer and effective alternative for ulcer prevention and treatment. [99]

3.1.10 Antiemetic

Ginger is a Natural Remedy for Nausea. Numerous studies have explored the mechanisms behind ginger's anti-nausea effects and its applications in various medical conditions. [100] The exact mechanisms by which ginger reduces nausea are not fully understood, but several factors are believed to contribute. Ginger is thought to inhibit the activity of serotonin, a neurotransmitter that plays a role in nausea and vomiting. Ginger can help regulate gastrointestinal motility, reducing the frequency and intensity of contractions that can lead to nausea. Also Ginger in a study using rodents was found to possess anti-serotonin and 5-HT₃ receptor antagonism effect in inducing nausea and vomiting during post-surgery [101].

Derivatives of ginger such as gingerol, shogaols, galanolactone, and diterpenoid were also established to reduce nausea and vomiting [102-104]. Others revealed that the reports of management of nausea and vomiting in cancer patients are also available in the literature [105]

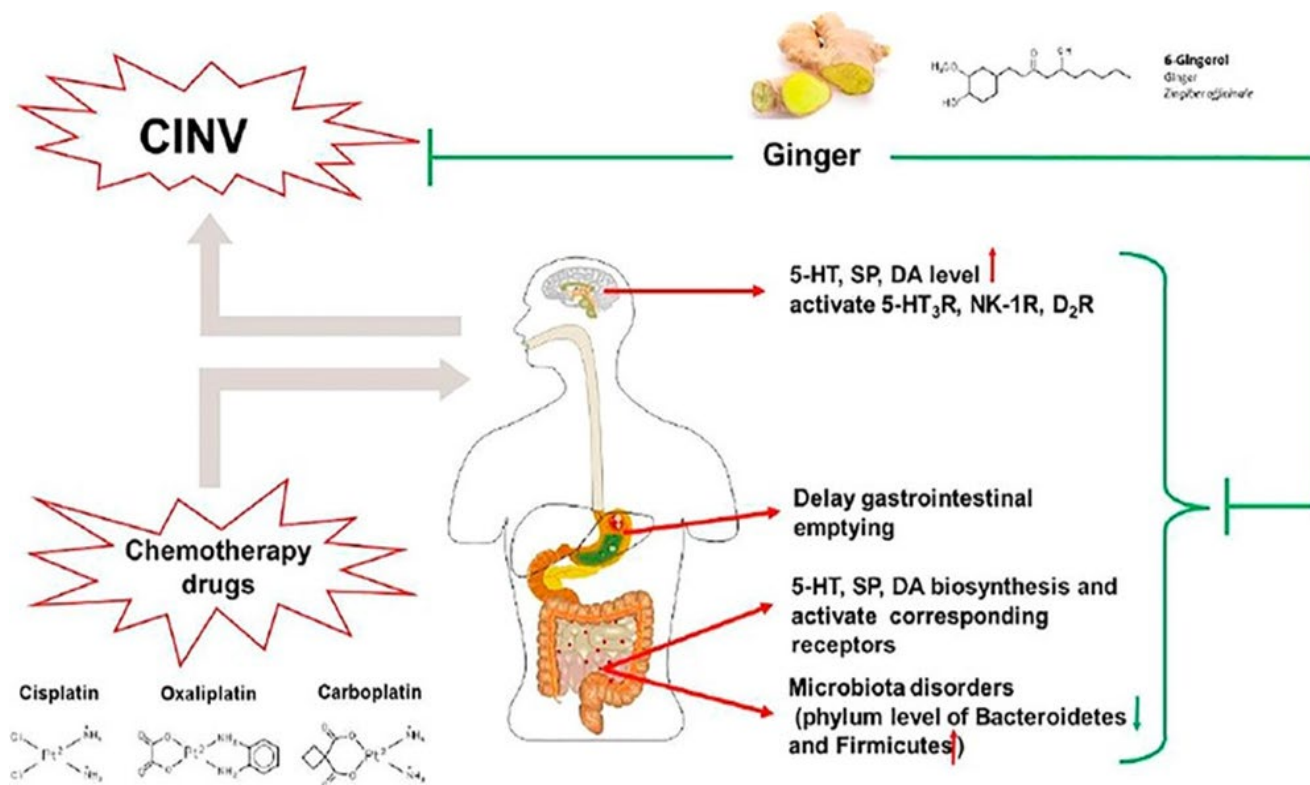


Figure 5 : The antiemetic mechanism of ginger against CINV. In the central nervous system, ginger markedly reduces levels of 5-HT, SP, and DA and blocks 5-HT₃R, NK-1R, and D₂R. In the peripheral nervous system, ginger inhibits the biosynthesis of 5-HT, SP, and DA, blocking their respective receptors. Also, ginger ameliorated microbiota disorders and delayed gastric emptying induced by chemotherapeutic agents.

1.3.11 Hepatoprotective

The liver, being the second largest organ in the body (after the skin), plays a crucial role in the metabolism of drugs and other chemical substances. Consequently, maintaining liver health is essential for overall well-being. [106] Liver ailments represent a significant global health challenge, often caused by exposure to toxic chemicals such as carbon tetrachloride, thioacetamide, certain antibiotics, and excessive alcohol consumption. [107]

Unfortunately, conventional drugs used to treat liver diseases are often ineffective and come with undesirable side effects.

In this context, medicinal plants (MPs) like ginger have emerged as promising alternatives for treating liver-related ailments. For instance, a study reported significant relief from liver cirrhosis in rats with carbon tetrachloride-induced liver toxicity when ginger was administered, either alone or in combination with curcumin, at a dosage of 100 mg/kg body weight, showing an amelioration of liver injury [108,109].

Additionally, another study demonstrated that ginger, at doses of 200 and 400 mg/kg body weight, enhanced the activity of antioxidant enzymes (such as superoxide dismutase, catalase, and glutathione peroxidase) while reducing the levels of liver function enzymes (alanine transaminase and aspartate aminotransferase) in acetaminophen-induced hepatic injury [110].

Conclusion

The world today is plagued by a multitude of diseases that continue to pose significant challenges to the health and well-being of humanity. Unfortunately, synthetic drugs, despite their widespread use in therapy and prevention, often come with adverse side effects, diminishing their effectiveness and acceptability. This has led to a growing embrace of medicinal plants, such as ginger, as alternative solutions for combating a wide range of ailments, whether minor or life-threatening.

Extensive research has highlighted the remarkable therapeutic potential of ginger and its derivatives in addressing numerous health issues. While clinical evidence remains limited, these findings provide a glimmer of hope for the future. It is envisioned that ginger, with its natural healing properties, could play a pivotal role in rescuing humanity from the ever-evolving health challenges that threaten their quality of life and survival.

6. References

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