

REVIEW ON GINGER CONSTITUENTS ROLE IN PREVENTION AND TREATMENT OF GI CANCER

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ABSTRACT

Gastro intestinal tract (GI) cancers are a group of cancers involving the Gastrointestinal and the most commonly affected areas are the stomach, esophagus, liver and pancreas. In Gastrointestinal cancers very high mortality rate and although a large number of chemotherapeutic agents have been introduced in the past few decades to combat GI cancers but very expensive and harm effect on body.

Therefore, there is a need for compound obtained from natural source that are considered safe, cost effective and potential no side. Ginger is natural products used globally has been feel great affection for its culinary, medicinal, and spiritual properties and it consumed as spice and medicine purpose for therapeutic action. In this article, the evidence for the anticancer properties or chemo preventive and therapeutic potential of ginger and its bioactive constituents using in animals and patient have been described.

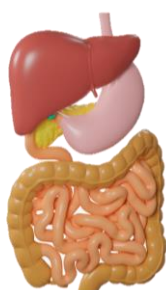
Keywords: Introduction, Main Active Ingredient Of Ginger, Clinical Investigation Of Ginger Constituent Against GI Cancer, Molecular Targets Of Ginger Active Constituents.

I. INTRODUCTION

The gastrointestinal (GI) is a vital part of the body system and it is responsible for processing food, absorbing nutrients, and removing waste from the we consume food. In the body, the GI starts from the mouth, includes the esophagus, stomach, small intestine, large intestine, rectum, and finally the anus. The development of GI cancer is influenced by a combination of genetic factor, lifestyle choices, chronic inflammatory conditions, and environmental factors. But major factors include like smoking, heavy alcohol consumption, age, obesity, poor diet, and infections such as Helicobacter pylori or hepatitis viruses which may cause GI cancer. Common diagnostic tools used for detection of cancer like endoscopy, computed tomography, MRI, PET, biopsy, and genetic testing, etc.

Often, stomach cancer occurs without any symptoms, especially in its early stages. Some symptoms of stomach cancer include feeling full quickly, mild abdominal discomfort, and fatigue, which is common and often confused with another, less serious condition. Some symptoms indicate the severity of the condition. If you have one or more of the symptoms listed below for more than two weeks, see a gastroenterologist.

- Unexplained weight loss
- Abdominal pain
- Vomiting and nausea
- Loss of appetite
- Difficulty or painful swallowing



II. GINGER AND ITS CONSTITUENTS

Ginger are the popular flowering plants, ginger root or ginger which widely used as a spice and in herbal medicine. First time ginger originated in Asia mentioned in Indian texts, such as the Rigveda 1500 BCE and Ayurvedic texts (500 BCE), where it has been used as a cooking spice and it is widely spread from Asia to Africa and the Caribbean and is used worldwide as an anti-nausea medication, anti-spasmodic, and to provide warmth when feeling cold.

- Botanical Name - Zingiber officinale
- Family Name - Zingiberaceae
- Class - Magnoliopsida
- Order - Zingiberales
- Genus - Zingiber Mill.-ginger



Chemical investigation of Ginger that it contain more than 400 different constituents. It contains a many of active chemical components include phenolic compounds, lipids, terpenes, polysaccharides, organic acids, raw fibres, ash, protein, vitamin (e.g., vitamin A) and minerals. Major polyphenols of fresh ginger are the gingerols which include 6-gingerol, 8-gingerol, and 10-gingerol. Gingerols can be converted into the corresponding shogaols with the help of heat treatment or long-time storage in warm place.

III. MAIN ACTIVE INGREDIENT OF GINGER

Gingerol

Gingerol is a phenolic compound found in fresh ginger root and they are bioactive which give different pharmacological effect in disease. Less soluble in water and instability in chemical properties which give to strong biological activity and pharmacological activity, this has been proven to affect against many types of cancers. The main derivatives of gingerols which show therapeutic action, including 6-gingerol, 8-gingerol, and 10-gingerol.

Shogaol

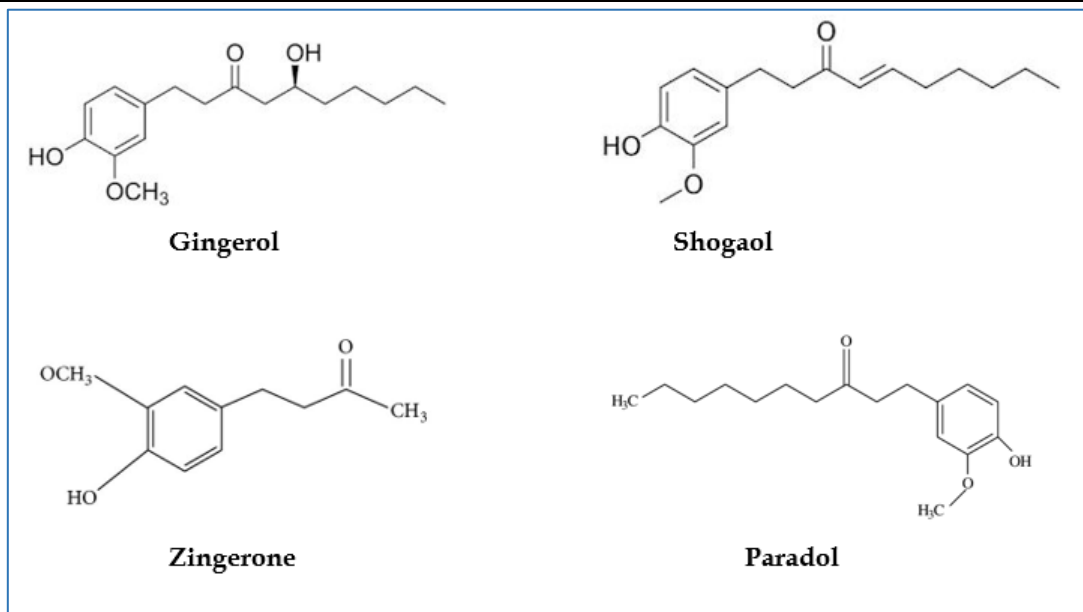
6-shogaol is one of the most important constituents of ginger, which is an alkylphenol compound synthesized by dehydration of 6-gingerol. Scientific research public that 6-shogaol is a signature chemical constituent of ginger, and the quality control index of the ginger. 6-shogaol has been shown to be a therapeutic agent for anticancer, anti-inflammatory, antioxidant, antidepressants and improve neuroprotective activity. Dehydration is produced through the reaction of the active hydrogen on C4 of gingerol with the hydroxyl group of C5 under acidic or heated conditions, which conduct to the formation of shogaol.

Zingerone

Zingerone is a crystalline compound isolated from ginger root originate to 9.2% in ginger and that compound, zingerone, has a basic phenolic ring and has attached methoxy group on the benzene ring and shown strong pharmacological effects including antioxidant, anti-inflammatory, and anticancer activities. It is seen as a yellow to light yellow crystalline powder with a sweet, warm characteristic odor and This is soluble in chloroform, methanol, and ethanol, melts between 40-43°C, and chemically inert during normal operating times. The hydroxyl (-OH), methoxy (-OCH₃), and ketone (-CO-) functional groups of zingerone make it prone to oxidation, reduction, and alkylation reactions.

Paradol

The key bioactive constituent of ginger root has been found to be 6-paradol, synthesized through a biotransformation process from 6-shogaol. It shows many of pharmacological effects and show therapeutic properties like anti- GI Cancer and antioxidant.



IV. METABOLISM OF GINGER

Although ginger is one of the most widely used spices worldwide for food and medicinal purposes, little is known about its metabolism or metabolites. A complete understanding of the bioactivity of ginger will therefore be essential to fully determine its mechanisms of action and resulting therapeutic effects. Although many food-derived supplements are used today with little information about their activity or safety, these issues are now receiving increased attention. It is may be the most studied bioactive component of ginger, gingerol and The isolation of several metabolites of gingerol after its oral administration to rats at a dose of 50 mg/kg was very carefully reported in study which not give any harm effect.

A one investigation study was supervise on the pharmacokinetics of gingerols and shogaols as well as their combine metabolites that help in the drug formation as well as make them suitable for the human body in absorption, metabolism and elimination. In this investigation human patients were given ginger in doses of 150 mg to 2.0 g and blood samples were taken at intervals ranging from 15 minutes to 70 hours after a single oral dose and the results shown that the free forms of gingerols or shogaols could not be detected and cytochrome P450 and sulfotransferase enzymes help in the metabolism of ginger which is affected by factors such as dose and liver and kidney function and the bioavailability of ginger ranges from 21-30% with a half-life of 2-5 hours and maximum plasma concentrations are reached within 1-2 hours and Understanding in the metabolism of ginger sheds light on its pharmacological effects, potential interactions and optimal dosing formulation.

V. USAGE AND PROCESS OF GINGER

It intake in our body in form of fresh, dried, pickled, crystallized, candied or in powdered forms. Taste and aroma: Tastes like pepper with a hint of sweetness. Ginger is such a versatile and ancient root that you can use it for so many things in life. It always comes in handy. On a culinary level, people know it for its flavor in Asian dishes, Indian foods and baked goods, as well as for tea, beer and of course ginger. Medicinal properties include curing nausea, digestive problems and even inflammation in the body; it is a completely natural remedy for colds, flu and menstrual cramps ginger is used as a traditional Chinese and Ayurvedic medicine to balance energy and therefore treat diseases such as arthritis and diabetes and Along with cosmetic benefits, ginger has antioxidant and anti-inflammatory properties that make it a favorite ingredient in skincare products, as well as its ability to eliminate acne and contribute to hair growth. Industrially, ginger oil is used in perfumes, soaps and even pharmaceuticals. In fact, different cultures have spiritual consideration with various uses of ginger, especially for its purifying and protective reasons seen in rituals and ceremonies. Drawbacks aside, ginger is one of the most versatile roots used for purposes such as insect repellent, fertilizer in gardens and animal feed. Due to this great benefit, ginger has become a part of almost everyday life, from cooking to health and much more.

Ginger inhibit

- oxidative damage
- inflammation
- nausea/vomiting
- cancer
- asthma
- dementia
- diabetes
- ulcerative colitis
- cardiovascular disease
- platelet aggregation
- cholesterol

VI. FUNCTION OF GINGER IN PREVENTION AND TREATMENT OF GASTROINTESTINAL CANCER

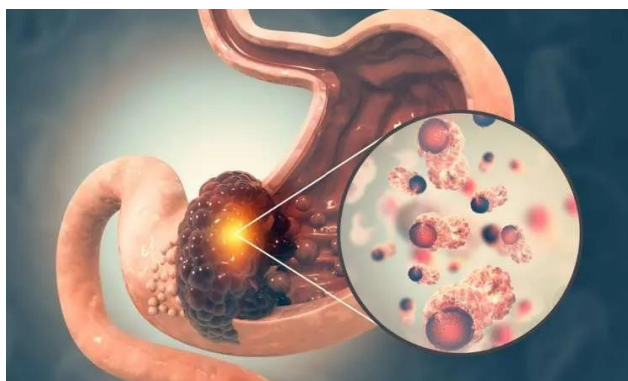
Evidence from experiment studies ginger constituents such as gingerol and shogaol suppress the growth of GI cancer and prevent several types of GI cancer like kidney, colon, prostate, gastric and liver etc.

Cancer	Effects
Liver	
HepG2	Promote apoptosis by activation of caspase-3
Liver microsomes	Decrease enzyme like <u>aldo-keto reductase</u> and cytochrome P450 enzymes and stop the formation of M 14 and 15 and 18β - <u>glycyrrhetic acid</u>
SMMC-7721	Inhibit the phosphorylation of eIF2 α and which help as anticancer
<u>hepatoblastoma</u> cell line	Release the <u>cathepsin D</u> and subsequently cytochrome c enhance as anticancer activity and intracellular reactive oxygen genus, reduced the glutathione
Pancreas	
<u>PaCa</u>	Stop the messenger RNA demonstration and protein secretion of <u>angiogenic</u> factors and the NF- κ B activity
PANC-1, <u>BxPC</u>	<u>Respression</u> cell viability regulators and NF- κ B signaling include X-linked inhibitor of apoptosis, cyclooxygenase-2 and matrix <u>metallopeptidase 9</u>
Gastric Cancer	
HUVE-AGS	Stop cell proliferation, NF- κ B activity and vascular endothelial growth factor expression
<u>kBZ Jurkat</u>	Inhibit cyclooxygenase-2 activation and reduce H. pylori which induced inflammation
Colorectal	
Caco-2	Inhibit cytochrome P450 enzymes
HCT116	Give <u>antiproliferative</u> agents and enhance anticancer effect of 5-FU which help in prevention
Cholangiocarcinoma	
CCA (CL-6)	Enhancement of MRP3 and MDR1 genes
KIM-1	Encourage cell death with the help of or through the endonuclease activation and induction of p53

VII. GASTRIC CANCER

In preclinical studies, ginger extract and its components show antineoplastic and anticancer effects against gastric cancer. In in vitro investigation, 6-gingerol ensured apoptosis in gastric cancer cells and facilitated TRAIL-induced apoptosis due to the activation of caspase-3 or 7 protein, which plays a crucial role in cell death and the inhibitory action of TRAIL-induced NF- κ B activation also mediates apoptosis.

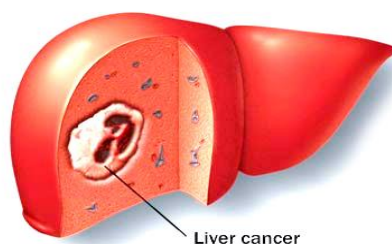
Moreover, 6-shogaol also make less the survival of gastric cancer cells by disrupting microtubules which help to treat GI cancer. Ginger constituent reduces activity of xanthine oxidase and myeloperoxidase as well as malondialdehyde and its extract enhance in anticancer medication by acting as an antioxidant and prevents gastric mucosal damage in body and It is also mentioned that it show the adverse effects of conventional therapeutic medication such as γ -radiation, doxorubicin by modifying P-glycoprotein. Hence, ginger extract shown anticancer activity.



VIII. LIVER CANCER

The bioactive compounds present in ginger, mainly gingerols and shogaols, have been investigated for its potential use in the prevention and treatment of liver cancer and these bioactive compounds show anti-inflammatory, antioxidant, anti-proliferative and immunomodulatory effects which inhibit or stop the growth of liver cancer cells and enhance the apoptosis. Studies conducted so far show that ginger extracts reduce the incidence and size of tumors in animal models related to liver cancer, although there were some human trials that enhance liver function and reduced risk of liver cancer and Some of the active extract isolated in ginger include 6-gingerol and 6-shogaol which have been verify to stop the pathway of cancer cell in Liver.

This modulation effect of ginger on pathways such as NF- κ B, PI3K/Akt and MAPK may explain its potential anticancer effects against liver cancer. While this would not mean that ginger can replace conventional treatments it may emerge as one of the beneficial complementary treatments and 1-3 inches of raw ginger daily 250-500 mg of ginger extract daily, and 1-2 cups of ginger tea daily may be effective for liver which help against cancer However, the reader should consult a physician as ginger may interact with prescription medication, is known to have gastrointestinal harm effect and at this time no conclusions can be drawn about the efficacy and safety of using ginger to prevent or treat liver cancer.



IX. COLORECTAL CANCER

Ginger is known to have anticancer activity against colorectal cancer, and Radhakrishnan reported that the anticancer activity of 6-gingerol may be related to the inhibition of extracellular signal-regulated kinase 1 and 2, a stress-activated protein kinase.

Based on in vitro studies, certain active principles in ginger inhibit colorectal cancer and prevent any cancerous conditions and a study reported that 6-gingerol restricted the growth of colon cancer hematocrit116 cells, the inhibition of tumor growth is associated with the activity of leukotriene A4 hydrolase, and this was later confirmed by another study conducted with an in silico approach and apart from these, multiple mechanisms have been reported to be involved in 6-gingerol-induced cell growth inhibition in human colorectal cancer and

these include disruption or inactivation of proteins as well as downregulation of cyclin D1, NAG-1 beta-catenin and glycogen synthase kinase 3 beta pathways which help in cancer treatment.



To improve the efficiency of ginger extract in the treatment of colon cancer there was a need to prepare a multiparticulate delivery system, that is ginger extracts contain alginate coated beads and on Dimethylhydrazine induced colon carcinoma in male Wistar rats, preclinical evaluation done on beads showed significantly better reduction of cancer compared to free ginger extract. Use of ginger extract in rats for cancer treatment helped reduce the levels of fecal bile acids, hydroxymethylglutaryl-CoA reductase, free fatty acids, phospholipase A and C with the help of 1,2-dimethylhydrazine. Total ginger extract or active constituent also inhibits the primary levels of colon cancer which ginger supplementation help reduced the risk of colon cancer.

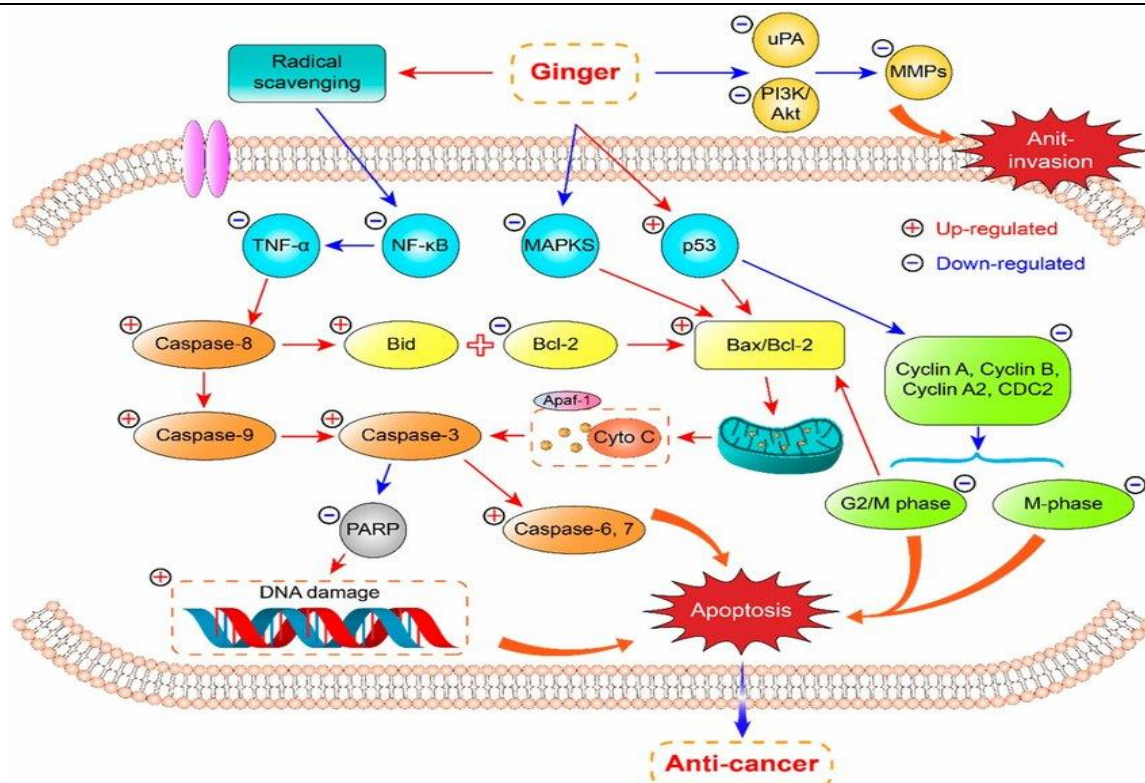
X. CLINICAL INVESTIGATION OF GINGER CONSTITUENT AGAINST GI CANCER

In addition to preclinical studies, clinical studies demonstrated that ginger has potential in the prevention and treatment of various GI disorders. A systematic review that ginger constituents, particularly 6-gingerol and 6-shogaol which show antioxidant and anti-inflammatory properties, which may contribute to their preventive effects against various GI cancer. In this clinical study cancer patients receiving chemotherapy were given a normal diet, a protein drink with ginger, and an additional high protein with ginger two time in one day and they found that food with ginger decrease and chemotherapy nausea and reduced antiemetic drugs for therapy and clinical investigation on 30 patients at colorectal cancer and patients were given 2g par day ginger which help in prevention of cancer.

A study review on 66 patients with colorectal cancer who had received chemotherapy treatment reported that massage with ginger and coconut oil increased cellular immunity in these patients and they demonstrated that this aromatherapy along with massage increased lymphocyte numbers by 11% and it also relieved fatigue, symptoms, pain, and stress in cancer patients. In randomized control trial of 20 patients at increased risk for colorectal cancer, ginger (2 g for 28 days) also reduced the growth of normal colorectal epithelium, and increased apoptosis and help as anticancer activity and this beneficial activity of ginger was shown to be decrease expression of Bax, human telomerase reverse transcriptase, and MIB-1. However, there was a negligible change in the levels of p21 and Bcl-2 and ginger has shown anti-inflammatory activities evident in a study conducted using 30 normal subjects and 20 subjects at increased risk for colorectal cancer and these results prove anticancer potential of ginger against colorectal cancer.

XI. MOLECULAR TARGETS OF GINGER ACTIVE CONSTITUENTS

Ginger bioactive compounds include 6-gingerol, 6-shogaol and etc. target many molecular pathways involved in GI cancer and its compounds inhibit the NF- κ B pathway which monitor inflammation and cell survival, reduce cancer growth and they also reduce or stop the levels of cyclooxygenase-2 and Prostaglandin E2, which are analogous inflammation-induced cancer progression in colorectal cancer. Ginger compounds inhibit pathways such as mitogen-activated protein kinase (MAPK), which are important in cell proliferation and survival, making them important targets in cancer therapy and Experimental Investigation of Ginger bioactive constituents like 6-gingerol, 6-shogaol show anti-cancer activities against the GI cancer and the anti-cancer activity of ginger and its bioactive compounds give its ability to modulate many targeting molecules and pathways like cyclooxygenase-2, Mitogen-Activated Protein Kinase or MAPK, cyclin D1, Metalloproteinases, and growth protein.



XII. CONCLUSION

The medicinal properties of ginger have been known for thousands of years, and in preclinical and clinical studies provide evidence of the efficacy of ginger and its active compounds against a wide range of human diseases including GI cancers and ginger has been proven to be effective against various cancers of the GI system such as gastric cancer, pancreatic cancer, liver cancer, colorectal cancer. The efficacy of such potent agents on these cancers remains to be guaranteed and ginger and its polyphenols have been shown to target several signaling molecules providing a basis for its use against multifactorial human diseases and Ginger shows potential in the prevention and treatment of gastrointestinal cancers with further research is essential to establish its effectiveness and to determine appropriate dosages and formulations for clinical use in cancer or other pharmacological activity.

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