



Zinper softgel caps: a natural nutrient helps to ease occasional nausea & promotes healthy GI peristalsis in cancer patients undergoing chemotherapy and radiation therapy

GovindShukla, AnushaPalkamshetti, C.J. Sampath Kumar

Oncowellnessby Lactonova Nutripharm (P) Ltd,(Makers of Zinper softgel caps), 81/3, IDA Mallapur, Hyderabad, Telangana, India-500 076

***Address for correspondence:** GovindShukla

E-mail: lactonovaresearch44@gmail.com

ABSTRACT

Chemotherapy –induced nausea and vomiting (CINV), also known by the term emesis, is one of the most common and dreaded side effects following cancer treatment, and can strongly impact the quality of day –to-day living of cancer patients. Many Chemotherapeutic agents are associated with significant nausea and vomiting which represent a challenge to effective therapy. The active ingredients present in Zinper softgels are terpenes and oleoresin. The major identified components from terpenes are gingerol and shogaols. Zinper softgels has staring potential as anti-tumor, anti-oxidant, anti inflammatory, anti-microbial, anti-emetic effect, Anti-angiogenesis, anti-nausea and an effective adjuvant treatment for chemotherapy-induced nausea and vomiting. The effectiveness of Zinper softgels in preventing or suppressing cancer growth has been examined in a variety of cancer types, including lymphoma, hepatoma, colorectal cancer, breast cancer, skin cancer, liver cancer, and bladder cancer. This article reviews the current available scientific literature regarding the effect of Zinper softgels as A Natural Nutrient to Promote Healthy GI peristalsis in cancer patients.

Keywords: Zinper Soft Gels, Healthy GI Peristalsis

INTRODUCTION

The gastrointestinal (GI) tract is one of the important parts of the body. This tract starts from the mouth, includes esophagus, stomach, small and large intestine, and rectum, and finally ends with anus. The human GI tract is a single tube which is approximately nine meters long in relaxed condition. Disorder in any part of the GI tract results in various malfunctions such as diseases of digestive system and cancer.

GI cancer is defined as the cancer of organs of the digestive system including the esophagus, gallbladder, liver, pancreas, stomach, small intestine, large intestine, rectum, and anus. The common risk factors for GI cancer include infection, smoking, drinking alcohol, high fat diet, age, race, gender, family history, and geographical location.

GI cancer accounts to 20percent of all newly diagnosed cancer cases. Among different GI

cancers, colorectal cancer is the most common cancer and is the second leading cause of death.

Accumulated evidences revealed that changing lifestyle could prevent all these cancers. The major change in lifestyle which proves beneficial includes avoiding tobacco, increase digestion of fruits and vegetables, moderate use of alcohol, caloric restriction, exercise, minimal meat consumption, intake of whole grains, proper vaccinations, and regular health checkups.

Mechanism of action of Ginger Extract in ZINPER softgels

Ginger Extract in ZINPER softgels has shown to have role in cancer prevention by inactivating and activating various molecular pathways. The mechanism of anticancer activity of Ginger Extract in ZINPER includes antioxidant activity and the ability to induce apoptosis, decrease proliferation, cause cell-cycle arrest, and suppress activator protein I (AP-1) and NF- κ B/COX-2 signaling pathways. [4,5]

Gingerol in ZINPER softgels have reported to cause inhibition and proliferation and invasion of ascites hepatoma AH109A cells and appeared to act by causing an S-phase arrest, elongated doubling

time of hepatoma cells, and an increased rate of apoptosis.[22] Gingerol was reported to inhibit both the vascular endothelial growth factor (VEGF)-and basic fibroblast growth factor (bFGF)-induced proliferation of human endothelial cells and cause cell-cycle arrest in the G1 phase proving its anti-angiogenic activity. [6] Gingerol in ZINPER softgels appeared to be most effective in inducing apoptosis in p53-mutant cells and induced arrest, but not apoptosis, in p53-expressing cells.[7]

Gingerol in ZINPER softgels shows a vital role in the suppression in synthesis of pro-inflammatory cytokines such as IL-1, TNF- α and IL-8.[8] studies have proven to show that elevated levels of TNF- α rats was blocked in liver cancer when treated with ginger extract. [9]

Gingerol in ZINPER has proved its anti-oxidant activity by inhibiting ascorbate /ferrous complex induced lipid peroxidation [10] and reported to show its role in scavenging of superoxide anion, hydroxyl radical and H₂O₂, which donates electrons, thus neutralizing it to water [11].

Ginger extract in ZINPER softgels possesses ant serotoninergic and 5-HT3 receptor antagonism effects which play an important role in the etiology of postoperative nausea and vomiting [12].

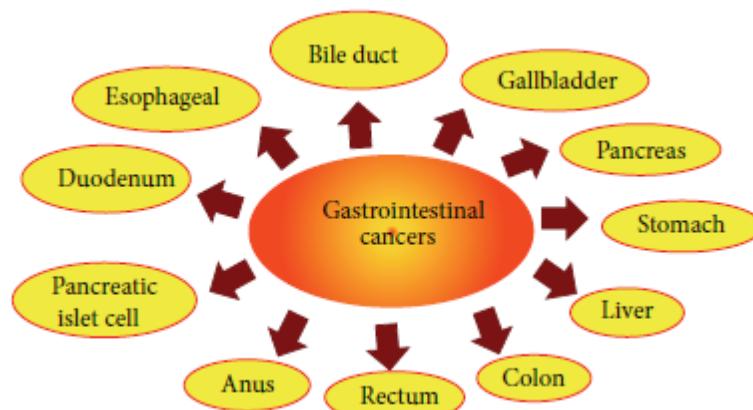


Fig.1 Types of GI Cancer

What is Chemotherapy -Induced Nausea and Vomiting?

Uncontrolled chemotherapy -induced nausea and vomiting (CINV), also known by the term emesis, is one of the most common and dreaded side effects following cancer treatment[3], and can strongly impact the quality of day -to-day living of cancer patients. Many Chemotherapeutic agents are

associated with significant nausea and vomiting which represent a challenge to effective therapy.

Prevalence and diagnosis

Chemotherapy related emesis has been reported in 70% to 80% of cancer patients, effective management of chemotherapy -induced Nausea and vomiting (CINV) is therefore a critical aspect of overall patient care [2].

Patients receiving chemotherapies such as cisplatin –based therapies and women with breast cancer receiving anthracycline plus cyclophosphamide (AC) are at high- risk of

developing CINV. Besides the emetogenicity of the chemotherapeutic agents, other factors such as repeated chemotherapy cycles, and patient risk factors significantly influence CINV [3]

COMPOSITION OF ZINPER SOFT GELS

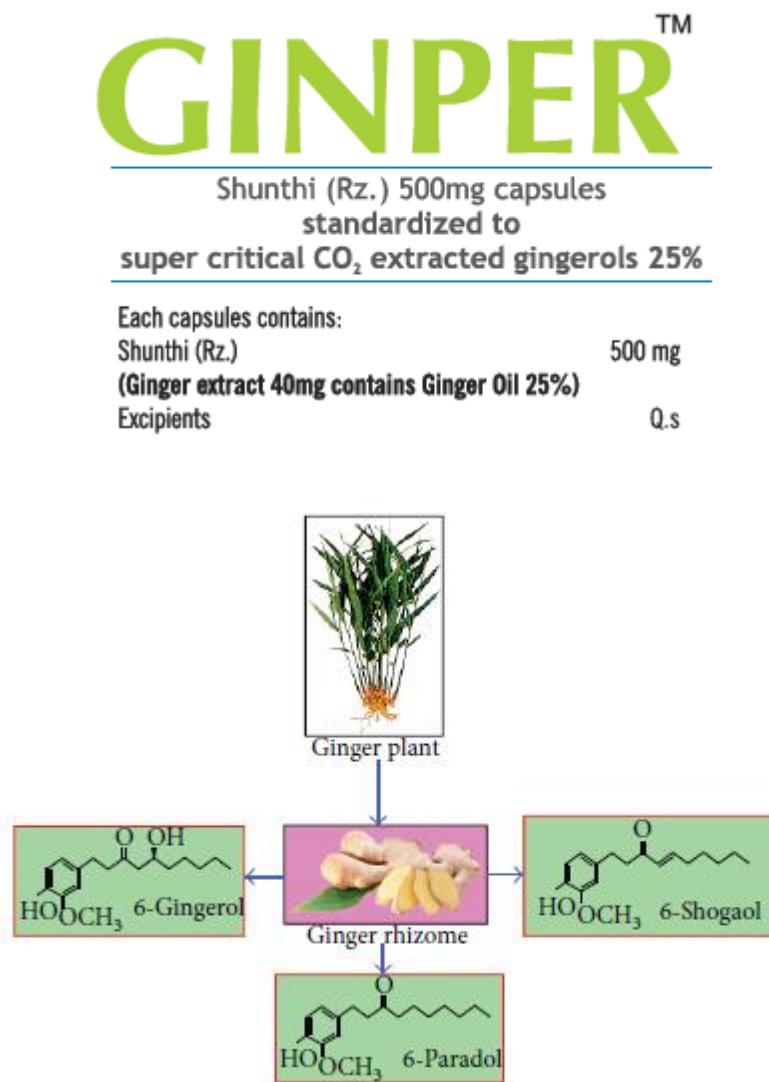


Fig.2 Active constituents of Ginger

Clinical study Reports on Ginger extract in ZINPER soft gel caps

Ginger in zinper softgels has been recommended to combat nausea associated with chemotherapy. Gingerol in Zinper softgels was reported to reduce cisplatin (a platinum-based chemotherapy drug)-induced emesis in a vomiting model of mink possibly by inhibiting the central or

peripheral increase of 5-hydroxytryptamine, dopamine, and substance P [14].

Gingerol in zinper softgels were reported to effectively decrease proliferation of YYT colon cancer cells and the angiogenic potential of endothelial cell tubule formation in immortalized MS1 endothelial cells [16].

Gingerol in zinper softgels was reported to inhibit both proliferation and invasion of ascites

hepatoma AH109A cells and appeared to act by causing an S-phase arrest, elongated doubling time of hepatoma cells, and an increased rate of apoptosis [17].

Ginger in Gingerol induced cell-cycle arrest and suppressed the growth of human pancreatic cancer cell lines, human pancreatic adenocarcinoma (HPAC) cells, which express wild-type p53 and BxPC-3 cells that express a mutant p53 protein [18].

A double-blind randomized clinical trial was conducted to investigate the effect of ginger on the

nausea and vomiting following gynaecological laparoscopic surgery. Both 0.5 and 1.0 g ginger were effective in reducing nausea, with only the higher dose being effective at reducing vomiting [19].

In a double blind study, a group of 80 naval cadets were recruited, each of who was given either 1 gram of powdered ginger or a placebo while at sea. Symptoms of nausea were recorded once an hour during 4 hours following treatment administration. Symptoms in the ginger group were 38% less than in the placebo group [21].

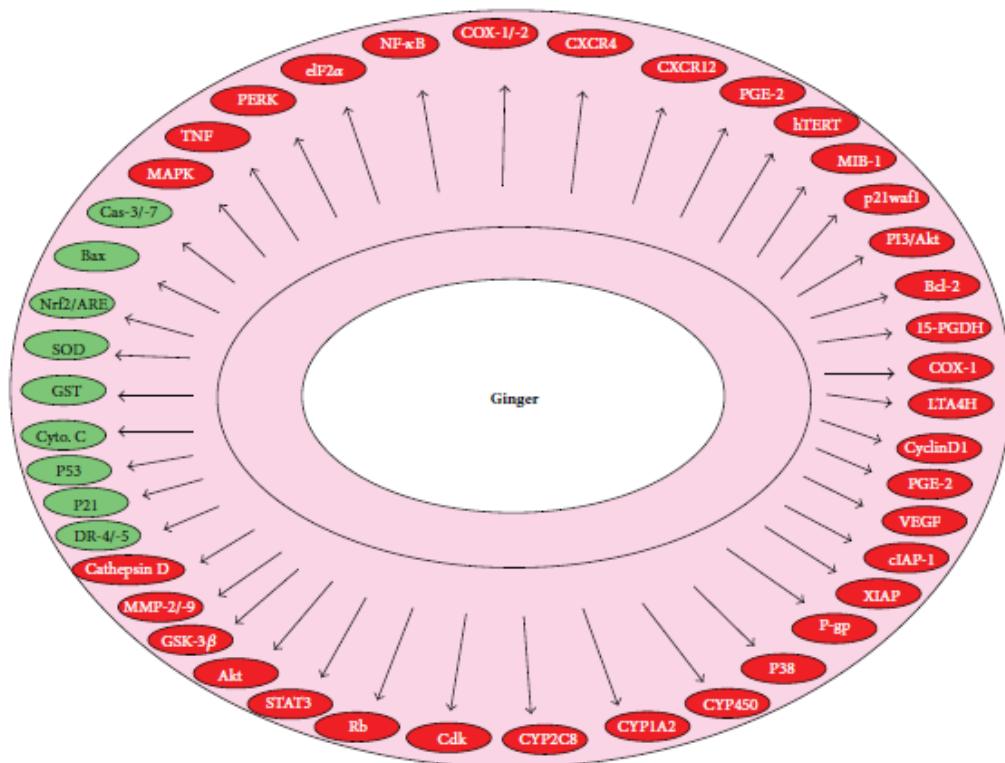


Fig.3; Molecular targets of ginger against GI cancer

Pre Clinical study of Ginger in ZINPER Soft Gel caps

A study investigated the effect of ginger in Zinper on colon carcinogenesis in rats. The rats received weekly injections of a carcinogen for 15 weeks and 50mg/kg of ginger daily by mouth. In the presence of cancer carcinogen plasma lipids were oxidized and cancer incidences were significantly increased, while anti-oxidants were significantly decreased. Ginger extract in ZINPER supplemented rats had a significantly smaller number of tumors and cancer incidence, in addition

supplemented rats has significantly less lipid oxidation and higher level of enzymatic and non-enzymatic antioxidants. [13]

The component gingerol in Zinper Soft Gels, was tested for effectiveness in preventing new vessel formation. In cell cultures, gingerol inhibited both the VEGF- and bFGF-induced growth of human skin cells. The ginger component actually stopped the cell from reproducing. In addition, gingerol also blocked capillary-like tube formation by endothelial cells, strongly inhibited sprouting of endothelial cells in the rat aorta, and inhibited the

formation of new blood vessels in the mouse cornea.

When mice were injected with gingerol in Zinper, the growth of cancerous melanoma cells was reduced [6].

Cisplatin can cause renal oxidative and nitrosative stress and dysfunction. However, rats that were administered cisplatin and gingerolin zinper exhibited lower lipid peroxidation and conservation of GSH coupled with enhanced superoxide dismutase and catalase, which resulted in a restoration of normal renal function [15].

The carcinogenesis-inhibiting activity of ginger in zinper softgels was studied in a skin tumorigenesis model in mice. Topical application of the extract on the skin of mice subsequently exposed to the tumour inducer TPA (12-*O*-tetradecanoyl-phorbol-13-acetate) resulted in significant inhibition of tumour development and multiplication. TPA-induced tumorigenesis was significantly inhibited ($p<0.0005$) by the ginger extract (2 mg/mouse; 56% inhibition). The same dose significantly inhibited TPA-induced cyclooxygenase ($p<0.0005$) and lipoxygenase activity (38-72% inhibition) [20].

Recommended Usage of Zinper softgels caps

- One softgel cap per day or As Directed by Healthcare Practitioner.
- Do not exceed the recommended daily dose.

SUMMARY & CONCLUSION

The medicinal properties of ginger in zinper softgels caps have been known for thousands of years, a significant number of *invitro*, *in vivo*, and epidemiological studies further provide substantial evidence that ginger in zinper softgels caps and its active compounds are effective against wide variety of human diseases including GI cancer. Ginger in zinper softgels caps has been found to be effective against various GI cancers such as gastric cancer, pancreatic cancer, liver cancer, colorectal cancer, and cholangiocarcinoma.

Therefore, efficacy of such potent agents on these cancers is warranted. Ginger and its polyphenols in zinper softgels caps have been shown to target multiple signaling molecules that provide a basis for its use against multifactorial human diseases including cancer.

REFERENCES

- [1]. Arshad H Rahmani₁, Fahad M Al shabrm₂, et.al. Active ingredients of ginger as potential candidates in the prevention and treatment of diseases via modulation of biological activities. *Int J Physiol Pathophysiol Pharmacol* 6(2), 2014, 125-136.
- [2]. Morran C, Smith DC, Anderson DA, Mc Ardle CS. Incidence of nausea and vomiting with cytotoxic chemotherapy: a prospective randomized trial of antiemetic. *Br Med J* 1, 1979, 1323-1324. (445053).
- [3]. Navari RM *Drugs* 73, 2013, 249-262.
- [4]. Ann M. Bode and Zigang Dong. Chapter 7 *The Amazing and Mighty Ginger: Biomolecular and Clinical Aspects*. 2nd edition. Boca Raton (FL): CRC Press/Taylor & Francis; 2011.
- [5]. Lee E, Surh Y. J. Induction of apoptosis in HL-60 cells by pungent vanilloids, [6]-gingerol and [6]-paradol. *Cancer Lett.* 134(2), 1998, 163-8. Thatte U, Bagadey S, Dahanukar S. Modulation of programmed cell death by medicinal plants. *Cell Mol Biol (Noisy-le-grand)* 46(1), 2000, 199-214.
- [6]. Kim E. C, Min J. K, Kim T. Y, editors. et al. [6]-gingerol, a pungent ingredient of ginger, inhibits angiogenesis in vitro and in vivo. *Biochem Biophys Res Commun.* 335(2), 2005, 300-8
- [7]. Park Y. J, Wen J, Bang S, Park S. W, Song S. Y. [6]-gingerol induces cell cycle arrest and cell death of mutant p53-expressing pancreatic cancer cells. *Yonsei Med J.* 47(5), 2006, 688-97.
- [8]. Tjendraputra E, Tran VH, Biu-Brennan D, Roufogalis BD, Duke CC. Effect of ginger constituents and synthetic analogues on cyclooxygenase-2 enzyme in intact cells. *Bioorg Chem* 29, 2001, 156-163.
- [9]. Habib SH, Makpol S, Abdul Hamid NA, Das S, Ngah WZ, Yusof YA. Ginger Extract (*Zingiber Officinale*) has Anti-Cancer and Anti-Inflammatory Effects on Ethionine-Induced Hepatoma Rats. *Clinics* 63, 2008, 807-813.
- [10]. Reddy AA, Lokesh BR. Studies on spice principles as antioxidants in the inhibition of lipid peroxidation of rat liver microsomes. *Mol Cell Biochem* 111, 1992, 117-124.

- [11]. Halliwell B, Gutteridge JMC. Free Radical in Biology and Medicine. Oxford, UK: Oxford University Press; 1985.
- [12]. Lumb AB. Mechanism of antiemetic effect of ginger. *Anaesthesia* 48, 1993, 1118.
- [13]. Thomson M¹, Al-Qattan KK, The use of ginger (*Zingiber officinale Rosc.*) as a potential anti-inflammatory and antithrombotic agent. *Prostaglandins Leukot Essent Fatty Acids.* 67(6), 2002 , 475-8.
- [14]. Qian Q. H, Yue W, Wang Y. X, Yang Z. H, Liu Z. T, Chen W. H. Gingerol inhibits cisplatin- induced vomiting by down regulating 5-hydroxytryptamine, dopamine and substance P expression in minks. *Arch Pharm Res.* 32(4), 2009, 565–73
- [15]. Kuhad A, et.al. [6]-gingerol prevents cisplatin-induced acute renal failure in rats. *Biofactors.* 26(3), 2006, 189–200.
- [16]. Brown A. C, et.al Ginger's (*Zingiber officinale Roscoe*) inhibition of rat colonic adenocarcinoma cellsproliferation and angiogenesis in vitro. *Phytother Res.* 23(5), 2009, 640–5
- [17]. Yagihashi S, Miura Y, Yagasaki K. Inhibitory effect of gingerol on the proliferation and invasion of hepatoma cells in culture. *Cytotechnology.* 57(2), 2008, 129–36
- [18]. Park Y. J, Wen J, Bang S, Park S. W, Song S. Y. [6]-gingerol induces cell cycle arrest and cell death of mutant p53-expressing pancreatic cancer cells. *Yonsei Med J.* 47(5), 2006, 688–97.
- [19]. Yagihashi S, Miura Y, Yagasaki K. Inhibitory effect of gingerol on the proliferation and invasion of hepatoma cells in culture. *Cytotechnology.* 57(2), 2008, 129-36.
- [20]. Katiyar S K, Agarwal R & Mukhtar H, Inhibition of tumor formation in SENCAR mouse skin by ethanol extract of *Zingiber officinale* rhizome, *Cancer Res.* 56, 1996, 1023.
- [21]. Grontved A, Brask T, Kambskard J & Hentzer E, Ginger root against seasickness: a controlled trial on the open sea, *Acta Otolaryngologica*, 105, 1988, 45.