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The therapeutic effects of ginger extract on gastrointestinal disorders to adults

Rara Poetri Claudya[1], Helga Audelia Sugiaman[2], Salsabil Inas Labiba[3], Margaretha Pramesthi Utari[4], Deni Gunawan[5]

[1,2,3,4,5] Universitas Tarumanagara, Indonesia

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ABSTRACT

Ginger (Zingiber officinale Roscoe) which belongs to the Zingiberaceae and the genus Zingiber families, has active ingredients, such as phenolic compounds and terpenes. Some researchers conducted clinical trials to scientifically assess the effectiveness of ginger as an adjunct therapy as a complementary or alternative drug in several diseases, especially gastrointestinal diseases. This study aims to determine ginger extracts' therapeutic effects on adults' gastrointestinal disorders. The research method used descriptive qualitative through the Literature Review (LR) approach. The data source used a secondary source. Data analysis technique selects literature based on title, year, and indexed articles, then reviews articles that match the subject matter. the articles from those journals are compared to find the differences and similarities. The ginger extracts therapeutic effects are obtained in that these extracts are able to relieve nausea and vomiting due to chemotherapy by suppressing the activation of 5-HT receptors in enteric neurons. In addition, ginger relieves nausea caused by antituberculosis drugs and antiretroviral therapy. Ginger extract and its constituents also have chemopreventive and antineoplastic properties in gastric cancer.

Corresponding Author:

Rara Poetri Claudya,
Universitas Tarumanagara,
Jln. Letjen S. Parman No. 1, Jakarta Barat 11440, Indonesia
Email: rarapoetriclaudya@gmail.com

INTRODUCTION

Ginger (Zingiber officinale), a member of the family Zingiberaceae, is a spice that is popularly used, especially in most Asian countries (G. Demin and Z. Yingying, 2010). In ancient times of India and China, ginger was used as a spice as well as medicine, while in 9th-century in Europe and 10th-century in England, ginger was used only for a medicine (Sasidharan & Menon, 2010). Native Americans also use the rhizomes of wild ginger to regulate menstruation and heart rate. Ginger is assumed to work directly on the digestive system for reducing nausea. Therefore, the drug is used to prevent nausea from chemotherapy, motion sickness, and surgery (Holtmann, 1989).

Chemical analysis of ginger showed that it contains more than 400 different compounds. The main constituents in ginger rhizomes are carbohydrates (50-70%), lipids (3-8%), terpenes, and phenolic compounds (Food, Grzanna, Lindmark, & Frondoza, 2005). The specific aroma of ginger is related to zingiberene and bisabolene, while the spicy taste is caused by the essential oils of gingerol

(23-25%) and shogaol (18-25%). Besides these components, amino acids, raw fiber, ash, proteins, phytosterols, vitamins (e.g. nicotinic acid and vitamin A), and minerals are also contain in ginger. Other gingerol or shogaol-related compounds (1–10%), which have been reported in ginger rhizomes, include 6-paradol, 1-dehydrogingerdione, 6-gingerdione and 10-gingerdione, 4-gingerdiol, 6-gingerdiol, 8-gingerdiol, and 10-gingerdiol, and also diarylheptanoids (Prasad & Tyagi, 2015a).

Ginger has also been found to have biological activities, such as antioxidants (Nile & Park, 2015), anti-inflammatory (Mingzhen Zhang., 2017), antimicrobial, and anticancer activities (Kumar, Murthy, Manjunatha, & Bettadaiah, 2014). The long history of ginger use in humans has prompted clinical trials to scientifically assess the effectiveness of ginger as an adjunct therapy or complementary and alternative drug in a number of diseases, especially gastrointestinal diseases (Lete & Allué, 2016).

Gastrointestinal disorders, such as chronic or acute diarrhea, malabsorption, abdominal pain, and inflammatory bowel disease are very prevalent in the community up to 60% of the adult population which can be classified as having symptoms of gastro-esophageal reflux (GORD), dyspepsia or irritable bowel syndrome (IBS), where about 90% of the symptoms persist for 1-6 months. This study aims to obtain information related to the therapeutic effect of ginger extract on gastrointestinal disorders in adults (SHRADHA AGARWAL, 2014). Based on this, the purpose of this research is to find out therapeutic effects of ginger extract on gastrointestinal disorders to adults.

RESEARCH METHOD

The research method used descriptive qualitative through the Literature Review (LR) approach. A literature review was conducted to reveal in-depth information regarding ginger extracts' therapeutic effects on adults' gastrointestinal disorders. This type of review article aims to provide information about ginger extracts on gastrointestinal disorders. The data source used a secondary source (Lenis *et al.*, 2020).The sources used secondary data from journals and books (Y. B. Lee, E. J. Byun, 2019). The data collection method was through collecting data from articles related to ginger extracts and gastrointestinal disorders. Data analysis used bibliographic annotation analysis (Mudavanhu, 2017). Data analysis technique selects literature based on title, year, and indexed articles, then reviews articles that match the subject matter. the articles from those journals are compared to find the differences and similarities.

RESULTS AND DISCUSSION

Ginger (Zingiber officinale Roscoe) which belongs to the family Zingiberaceae and the genus Zingiber has long been consumed as a kitchen spice and herbal medicine (Cells *et al.,* 2013). The long history of ginger use in humans has prompted clinical trials to scientifically assess the effectiveness of ginger as an adjunct therapy or as a complementary and alternative drug in a number of major gastrointestinal diseases (Lete & Allué, 2016). The anti-inflammatory, antioxidant, antitumor, and antiulceral effects of ginger have been proven in several studies. However, some results are still controversial, perhaps due to the chemical instability of gingerol (the most active ingredient of ginger), which is an easily oxidized substance (Giacosa, Bombardelli, Riva, Porro, & Rondanelli, 2015)

Ginger Biology

*Zingiber officinale (*Roscoe), a Curcuma or *temulawak* of the family Zingiberaceae, is a herbaceous perennial plant (available in the form of rhizomes) that grows up to 90 cm in height. The leaves are lanceolate, seemingly simple, crisscrossed, distichous, narrow, and long with a sheathed base of 2–3 cm, while the rhizome (7–15 cm long and 1–1.5 cm wide) is aromatic, thick-cupped with a pale tint, and yellow coloring. The flowers are small, have high petals, strongly fused sepals, are three-toothed, and split on one side with three unequal corollas forming oblong to lanceolate segments

with a green tint. Ginger causes many lateral clump shoots that are on dry ripening. Ginger originated from Southeast Asia, mainly in India but is now well-spread or cultivated in China, Bangladesh, Australia, and Nigeria (Mele MA, 2019).

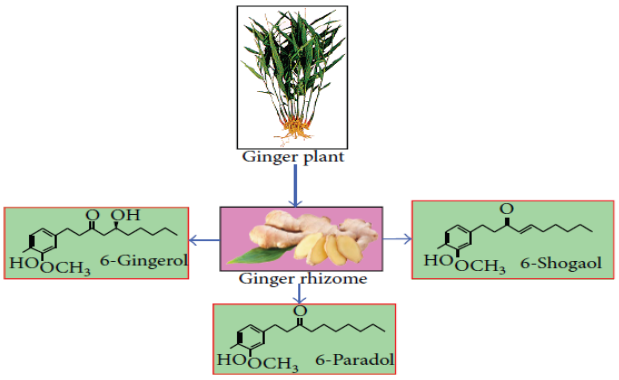

Figure 1. Ginger, ginger rhizome, and main active components: 6-gingerol, 6-shogaol, and 6-paradol
Source: Prasad, S and Amit K. Tyagi (2015)

Bioactive Content of Ginger

More than 400 compounds have been found in the chemical analysis of ginger [21]. These compounds include alkaloids; saponins; flavonoids; Steroids; Tannins; carbohydrates; glycosides; protein; amino acids; dietary fiber; ash; phytosterols; vitamins A, B, and C; minerals; and terpenoids (Dhanik J, Arya N, 2017). The main components of ginger rhizomes are carbohydrates, lipids, terpenes, and phenolic compounds (Grzanna R & CG., 2005). **Qian** ginger has rich active constituents, such as phenolic compounds and terpenes (Prasad & Tyagi, 2015). The phenolic compounds in ginger are mainly gingerol, shogaol, and paradol. In fresh ginger, gingerol is the main polyphenol, such as 6-gingerol, 8-gingerol, and 10-gingerol. By heat treatment or long storage, gingerol can be turned into shogaol. After hydrogenation, shogaol can be converted into paradol (Stoner, 2013). There are also many other phenolic compounds in ginger, such as quercetin, zingerone, gingerenone-A, and 6-dehydrogingerdione (Ji, K.; Fang, L.; Zhao, H.; Li, Q.; Shi, n.d.) . In addition, there are several terpene components in ginger, such as β-bisabolene, α-curcumene, zingiberene, α-farnesene, and β-sesquiphellandrene, which are considered the main constituents of ginger essential oil. In addition, there are polysaccharides, lipids, organic acids, and raw fiber (Hsiang *et al.,* 2013).

The most commonly used parts of the ginger plant are rhizomes and horizontal stems on which the roots grow. Oleoresins extracted from ginger rhizomes contain bioactive compounds categorized as essential oils and nonvolatile spicy compounds that include gingerol, shogaol, paradol, and zingerone (Badoni *et al.,* 2015). Gingerol is a spicy phenolic compound identified as the main source of pharmacological and physiological properties attributed to ginger, [6-gingerol being a bioactive compound found in higher concentrations in oleoresin sample studies and most investigated in preclinical settings (Koh *et al.,* n.d.)

Ginger Extract Pharmacology

Reviews are from most of the world's countries, such as Egypt, Korea, Pakistan, India, Oman, Brazil, and Canada etc. (Mingzhen Zhang., 2017), have established the pharmacological potential of the official Zinger plant (Roscoe) on the effects of active components that can target certain diseases (Food *et al.,* 2005), inflammation, cancer, emetic, nausea, and vomiting. Thus, pharmacological potential include antioxidant, anticancer, antitumor, anti-inflammatory, antihyperglycemic, antihypertensive, anti-neurodegenerative and anticardiovascular (Chaiyakunapruk N, Nathisuwan S, & C., 2006).

Antioxidant, Antioxidants play an important role in reducing free radicals and oxidative stress. Many Medical Plants (MP) and/or their constituents have shown their superiority in preventing the onset of diseases, especially those triggered by free radicals. Ginger, a good example of MP with excellent antioxidant effects can decrease lipid peroxidation, such as inhibition of ascorbic/ferrous complexes in rat liver microsomes as cited by Rahmani *et al.,* (Rahmani AH, Shabrmi FM, 2014) and Mele (Mele MA, 2019) in the Reddy and Lokesh report (Reddy AA, 1992) using a concentration of 150 mM. Ginger or its derivatives (extracts, compounds, or active components) and gingerol were found to have a good cleansing effect on superoxide anions and hydroxyl radicals (Stoilova I, Krastanov A & Denev P, 2007). Other ginger derivatives, such as oleoresin, 6-shogaol, 6 dehydroshogaol, 1-dehydro-6-gingerdione, 6-gingerol, 8-gingerol, 10-gingerol, and essential oils have pharmacological activities of antioxidant, antimicrobial, etc., on 2,2-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS), 1,1-diphenyl-2-picrylhydrazyl (DPPH), hydroxyl radicals, and microbial strains, such as Bacillus subtilis, Bacillus cereus, Staphylococcus aureus, Escherichia coli, Candida albicans, Penicillium spp., and Aspergillus niger (Bellik Y, 2014).

Anti-tumor/Anti-cancer, Cancer is one of the non-communicable diseases with a large negative impact on the global population. This is due to the continuous increase in the cells of the human body leads to the formation of tumors (malignant cells) by metastasizing (Greenwell M, 2015). Continuous multiplication of cells is associated with the influence of oxidative stress. A number of treatments (chemotherapy, radiotherapy, synthetic drugs, etc.) are currently available. However, having one or several side effects (nausea, hair loss) requires an alternative form of treatment or therapy, especially of MP. In recent times, quite a number of plant species have found their relevance in the prevention and treatment of cancer, and the efforts of researchers to continue to develop new sections. Ginger is a great example as an excellent prophylactic and curative anticancer. Although it must be known that this effect is not available for all types of cancer. Some reports of ginger and its derivatives (gingerol) have established many effects on different types of cancer (lung, colon, ovarian, prostration, etc.). In a study conducted by Karna *et al.* (Karna P, Chagani S & Rida PC, Asif G, Sharma V, 2012) in the United States, oral administration of ginger showed a concentration of 100 mg/kg body weight (bb) inhibits the growth of PC-3 xenographt, showing its effect on the prostate cancer in vitro and in vivo. In addition, similar concentrations were found in other studies (Habib SHM, Hamid NAA, Das S, & YAM., 2008) which reduced the increased activity of tumor necrosis factor-alpha (TNF-α) due to blockage of rat liver cancer. In addition, ginger derivatives, e.g. 6-shogaol, 8-shogaol, 10-shogaol, 6-gingerol, 6-paradol, and zingerone in several studies have also shown activity on various forms of cancer including lung, colon, colorectal, ovarian cancers (Rahmani AH, Shabrmi FM, 2014) and Gunathilake and Rupasinghe (Gunathilake KDPP & HP., 2015). Besides, ginger has also been reported to inhibit tumor growth achieved through different molecular mechanisms, such as increased regulation of suppressive genes, apoptosis, induction, and inactivation of vascular endothelial growth factor (VEGF) (molecular pathways) (Rahmani AH, Shabrmi FM, 2014).

Anti-Inflammatory, Inflammation is the response (defense) perceived by the body to harmful stimuli, such as wounds on tissues or allergens. There have been reports of a link between free radicals triggered by oxidative stress and inflammation. The use of non-steroidal anti-inflammatory drugs (NSAIDs) is used to correct acute and chronic types of inflammation. NSAIDs demonstrate this action by inhibiting enzymes (cyclooxygenase, COX 1 and 2, and/or lipoxygenase, 5, 10, 15) involved in the breakdown of arachidonic acid into prostaglandins. Unfortunately, there are many side effects arising from the use of NSAIDs, so the search for alternative forms of treatment with minimal or no side effects in natural products. Ginger, an example of such MP including its derivatives, has been reported to have anti-inflammatory potential in vitro and in vivo studies of 33 mg/kg bb of ginger oil given to rats also relieves acute and chronic arthritis (Mele MA, 2019). In addition, ginger and zingerone extracts may inhibit the activation of NF-κB and lower IL-1β levels

in the mice colon, which relieves colitis induced by sulfonic acid 2, 4, 6-trinitrobenzene (Hsiang *et al.,* 2013).

Anti-Hyperglycemic, Diabetes mellitus (DM) is one of the global non-communicable diseases with a major prevalence. Endocrine disorders or metabolic disorders characterized by hyperglycemia (increased levels of glucose in the blood) due to insufficient or ineffective insulin arising from abnormalities in carbohydrates, lipids, and proteins. Treatment or management of DM can be non-pharmacological (exercise, dietary) or pharmacological which requires the use of oral hypoglycemic agents (OHA), such as sulphonyl ureas, biguanides, and so on. However, the use of such chemicals or synthetic substances have the side effects (obesity), unavailable, and unaffordable. So, it is required for alternative forms of treatment with little or no side effects. Many reports are available in the literature on ginger that establish the potential of this spice in in vitro and in vivo studies (Roufogalis BD, 2014). A similar example is the report of Ojewole 500 mg/kg bb of ginger extract lowering plasma sugar levels after induction of streptozotocin in animal model and in vitro because there are reports of a correlation between oxidative stress and DM [20] as well as other DM complications, such as hyperlipidemia, hypercholesterolerolemia, retinopathy, and neuropathy (Ojewole JA, 2006) (Ojewole JA, 2006)

Anti-Neurodegenerative, Some individuals, especially elderly people, have a high risk for neurodegenerative diseases, such as Alzheimer's disease (AD) and Parkinson's disease (PD) (Lim *et al.,* 2014). Many investigations have revealed that ginger positively affects memory function and shows anti-neuroinflammatory activity, which may contribute to the management and prevention of neurodegenerative diseases (Park *et al.,* 2013). Results from a culture model of lipopolysaccharide-activated BV2 microglia (LPS) revealed that 10-gingerol is responsible for the strong anti-neuroinflammatory capacity of fresh ginger. It inhibits the expression of proinflammatory genes by blocking the activation of NF-κB, which causes a decrease in levels of NO, IL-1β, IL-6, and TNF-α (Ho et al., 2013). In addition, ginger extract had a protective effect on AD in rats and high-dose ginger extract lowered latency in showing significant memory deficits, as well as levels of NF-κB, IL-1β, and MDA (Dysfunction *et al.,* 2013).

Antihypertensive, Hypertension, a silent killer (due to asymptomatic appearance) characterized by a continuous, increase in blood pressure in a person's arteries, occurs when systolic and diastolic blood pressure rises above 140/90 mmHg, respectively. The findings revealed excessive salt intake, smoking, alcohol consumption, kidney narrowing, and birth control pill use become some of the causes of hypertension, risk factors for many cardiovascular diseases. Such as diabetes, non-pharmacological (lifestyle modification, etc.) or pharmacological treatment options involve the use of synthetic parts, such as diuretics, beta inhibitors (atenolol), angiotensin modifier enzyme inhibitors (Lisinopril), calcium channel inhibitors, etc. (Balogun FO, 2019). However, all these antihypertensive drugs cause severe side effects, such as angioedema, dry cough, headache, etc. Thus, it is necessary to have a form of replacement therapy for people with high blood pressure. An example of a herbal product is ginger. In a study involving rats and guinea pigs, ginger extract in the concentration range of 0.3-3 mg/kg lowered the arterial blood pressure of the animal (Gunathilake KDPP & HP., 2015). In addition, similar studies using ginger extract and its derivatives revealed the similar actions. The activity of ginger as an antihypertensive agent was also found in studies involving human subjects when the intake of 10 g of ginger twice a day reduced arterial blood pressure to 94,80 mmHg after two months. It is worth mentioning that the mechanism of action of this spice is through the stimulation of muscarinic receptors and the blockage of calcium channels. (Aming SN, 2006)

Anti-Cardiovascular, Cardiovascular disease has been considered the leading cause of early mortality and 17,9 million people die per year (Du *et al.,* 2016). Dyslipidemia and hypertension are known to be risk factors for cardiovascular diseases, including stroke and coronary heart disease (Khosravani *et al.,* 2016). A series of studies have shown that ginger can lower blood fat levels and blood pressure (Ho *et al.,* 2013), contributing to protection from cardiovascular diseases. Ginger

extract reduced the weight of rats fed a high-fat diet and also increased serum high-density lipoprotein cholesterol levels (HDL-C), a protective factor on coronary heart disease. In addition, ginger extract increases levels of apolipoprotein A-1 and lecithin-cholesterol acyltransferase mRNA in the liver, which is associated with the formation of high-density lipoprotein (HDL) (Oh et al., 2017).

Gastrointestinal Disorders

The digestive system consists of the gastrointestinal tract and accessory organs. The digestive tract consists of the oral cavity, pharynx, esophagus, stomach, small intestine, and colon. Accessory organs are teeth, tongue, and gland organs, such as salivary glands, liver, gallbladder, and pancreas. The digestive system serves to provide mechanical processing, digestion, food absorption, water secretion, acids, enzymes, buffers, salts, and excretion of waste products (Ogobuiro I, Gonzales J, 2022). Diseases of the digestive system can be one of the many causes, affecting anywhere from the mouth to the opening. There are several disorders of the gastrointestinal system, including:

Nausea and Vomiting weixia, Nausea and vomiting are common gastrointestinal complaints that can be triggered by various emetic stimuli through the central and/or peripheral nervous system. Both nausea and vomiting are considered as defense mechanisms when threatening toxins/drugs/bacteria/viruses/fungi which enter the body either through the enteral (e.g. gastrointestinal tract) or parenteral routes, including blood, skin, and respiratory systems. Meanwhile, vomiting is the act of forcibly expelling gastrointestinal contents, nausea is believed to be a subjective sensation that is more difficult to study in non-human species (Zhong *et al.,* 2021).

Nausea and vomiting can be triggered by several mechanisms, such as (i) toxins/drugs/bacteria/viruses/fungi that enter the gastrointestinal lumen and subsequently, indirectly stimulate the emetic nuclei of the brainstem located in the dorsal vagal complex through the release of local emetic neurotransmitters in the upper gastrointestinal tract and the subsequent activation of the corresponding receptors present on the vagus nerve and/or splanchnic nerve; (ii) toxic agents/drugs or infectious organisms that enter the body systemically and can act directly on the emetic nuclei of the dorsal vagal complex in the brainstem; (iii) pathologies of the gastrointestinal tract, which stimulate vagal afferents or other visceral organs (e.g., the heart), and stimulate visceral afferent; (iv) emotional and cognitive stimuli within the central nervous system (CNS), including the cerebral text cord and the limbic system. The process of nausea and vomiting results from continuous interaction between the gastrointestinal tract, including the enteric nervous system, CNS, and autonomic nervous system (McKenzie, E.; Chan, D.; Parsafar, S.; Razvi, Y.; McFarlane, T.; Rico, V.; Pasetka, M.; DeAngelis, C.; Chow, 2019).

N.J. Talley's Functional Dyspepsia and Delayed Gastric Discharge, A common clinical syndrome in practice is functional dyspepsia, which is defined as chronic or recurrent epigastric pain or discomfort. In this syndrome, no cause can be identified using conventional diagnostic tests. Many of these patients complain about food-related symptoms even though the physiology is still unclear (Castillo EJ, Camilleri M, Locke GR, 2004). Delayed gastric emptying has been reported to occur in a subset of patients with dyspepsia functiononal, ranging from 25% to 50%. Delayed gastric emptying correlates with the presence of antral hypomotility although the underlying cause of antral hypomotility has not yet been determined. Other important potential abnormalities identified in functional dyspepsia include impaired fundus accommodation, hypersensitivityof gastric to distension and Helicobacter pylori infection (Moayyedi P, Deeks J, Talley NJ, 2003)

The controversy continuing is the correlation between gastric emptying and symptoms of functional dyspepsia. Studies from Europe, in particular, have reported that delayed gastric emptying is associated with a certain pattern of symptoms, namely relevant postprandial fullness and vomiting, especially in women. Other studies, especially from the United States, have failed to identify a typical symptom profile in patients with delayed gastric emptying compared to those who

have normal emptying. This problem has clinical importance because can identify those who are likely to experience delayed gastric emptying and can help to target an investigation and treatment (Camilleri M, 2004).

Irritable Bowel Syndrome (IBS), Irritable bowel syndrome (IBS) is a chronic disorder of the gastrointestinal tract, characterized by abdominal pain and habitual bowel movements. IBS is the most frequently diagnosed disorder by gastroenterologists and diagnoses are made based on a symptom-based classification system (Halmos EP, Power VA, Shepherd SJ, Gibson PR, 2014)

IBS is a multifactorial disorder, contributing to symptomatology: gastrointestinal dysmotility, inflammation, visceral hypersensitivity, and changes in the gut microbiota. Diet and exposure to stress (including early life events) become the causative factors of heterogeneous disorders. Stress has been identified as a mechanism in the IBS development. A major component of the stress response system include the autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenal axis (HPA) that has been the subject of numerous studies on IBS. Lastly, genetic predispositions and environmental interactions, such as family susceptibility and psychosocial stressors, have been involved in multifactorial IBS atogenesis (Fukudo S, 2011).

IBS increases with post-traumatic stress disorder (PTSD), an increased number of life stressors, anxiety, and depression. These findings describe the interdependence or cross-talk between the brain and intestine or gut in IBS, a connection commonly known as the Brain-Gut Axis (BGA). BGA refers to pathways among physiological systems, including the Central Nervous System (CNS), Enteric Nervous System (ENS), and Autonomic Nervous System (ANS). The endocrine, nervous, and neuroimmune pathways facilitate bidirectional communication between the CNS and the intestines. The patients with IBS have been known to exhibit disorders in BGA, including central and autonomic functions, facsor peripherals, peptides, and hormones. Differences in the central processing mechanisms of BGA have also been evidenced in IBS patients compared to healthy controls, through the use of neuroimaging techniques (Stasi C, Rosselli M, Bellini M, Laffi G, 2012).

Abnormalities of the Oral Cavity, Oral cavity abnormalities include salivary gland tumors, such as pleomorphic adenoma, mucoepidermoid carcinoma, and Warthin tumors. All of which affect the proper saliva content and production. Inside the esophagus, there are various pathologies of scleroderma, dysmotility of the esophagus, strictures of the esophagus, esophagitis, akalasia, and varicose veins of the esophagus. The disease can affect the food movement into the stomach. Further along the gastrointestinal tract, gastritis involves inflammation of the stomach. This condition may vary, depending on the duration of symptoms. Gastritis may have an acute onset caused by NSAIDs or mucosal ischemia. The effects of chronic gastritis is usually caused by Helicobacter pylori or an autoimmune disease (Mohamed, Thio, Thomas, & Phillips, 2020).

Effects of Ginger Extract on Gastrointestinal Diseases

The gastrointestinal tract is one of the important parts of the body. This tract starts from the mouth, covering the esophagus, stomach, small and large intestines, as well as the rectum, and finally ends with the anus. The human gastrointestinal tract is a single tube about nine meters long under relaxed conditions (E. N. Marieb, 2005). Disorders in any part of the GI tract result in various malfunctions, such as diseases of the digestive system and cancer.

Ginger (Zingiber officinale Roscoe) is a traditional remedy used to treat gastrointestinal symptoms. Recent studies have shown that ginger can effectively relieve nausea and vomiting (Bossi *et al.,* 2017). In clinical trials, inhalation of ginger juice may reduce the intensity of nausea and the incidence of emesis after nephrectomy in patients (Adib-hajbaghery & Hosseini, 2015). In addition, ginger extract can also relieve nausea and vomiting due to chemotherapy by suppressing the activation of 5-HT receptors in enteric neurons (Science & Isar, 2013). In a double-blind, randomized, and placebo-controlled trial, supplementation with ginger may improve nausea-related quality of life in patients after chemotherapy. The dose administered was 500 mg (×2) (~1 g/day) ginger extract + routine antiemetic regimen. The results were obtained that ginger and chamomile were

equally effective for reducing the frequency of vomiting. Ginger significantly affects the frequency of nausea (Marx, Wolfgang, Mccarthy et al., 2017). In addition, ginger relieves nausea caused by antituberculosis drugs and antiretroviral therapy (Emrani, Shojaei, & Khalili, 2016).

The most common cause of nausea and vomiting is pregnancy. Nausea and vomiting affect up to 80% of women during the first trimester of pregnancy that range from morning sickness to hyperemesis gravidarum (HG) (Fergus P McCarthy, Jennifer e Lutomski, 2014). The impact of ginger consumption as an antiemetic on pregnancy nausea and vomiting has been widely studied in clinical studies for at least 30 years (Giacosa *et al.,* 2015). Studies have shown that ginger in doses of 1 g/day is effective in pregnancy nausea and vomiting without significant side effects (Firouzbakht, Nikpour, Jamali, & Omidvar, 2014). The American College of Obstetricians and Gynecologists (ACOG) and also the National Institute for Health and Clinical Excellence have accepted ginger as a cure for nausea and vomiting during early pregnancy (Giacosa *et al.,* 2015).

Evidence from in vitro, animal, and epidemiological studies suggests that ginger and its active components suppress growth and induce apoptosis of various types of cancer including skin, ovaries, colon, breast, cervix, mouth, kidneys, prostate, stomach, pancreas, liver, and brain cancer. The properties of ginger and its constituents can be attributed to its antioxidant, anti-inflammatory, and antimutagenic properties as well as other biological activities (Srinivasan, 2014).

Preclinical studies show that ginger extract and its constituents have chemopreventive and antineoplastic properties in gastric cancer. In vitro studies show that 6-gingerol induces apoptosis of gastric cancer cells. It facilitates apoptosis-inducing of TNF-related ligand-inducing (TRAIL-) by increasing activation of caspase-3/7. Induction of apoptosis by 6-gingerol was mediated through downregulation of cytosolic inhibitors of apoptosis (cIAP)-1. Then, the inhibition of wavering-inhibition of TRAIL-induced was mediated of factor-cappaB (NF-κB). Besides 6-gingerol, 6-shogaol also reduces the viability of gastric cancer cells by damaging microtubules (Ishiguro *et al.,* 2007).

The anticancer activity of ginger on colorectal cancer has been well documented. Numerous in vitro studies have shown that ginger and its active components inhibit the growth and proliferation of colorectal cancer cells. In one study, 6-gingerol inhibited the growth of HCT116 cells in colon cancer. Suppression of tumor growth was found to be associated with inhibition of leukotriene A4 hydrolase activity, which was further confirmed by an in silico approach (Jeong *et al.,* 2009).

CONCLUSION

Ginger (Zingiber *officinale* Roscoe) which belongs to the family of Zingiberaceae and the genus Zingiber, has long been consumed as herbs and herbal medicine. Chemical analysis showed that ginger contains more than 400 different compounds. The main constituents in ginger rhizomes are carbohydrates (50-70%), lipids (3-8%), terpenes, and phenolic compounds. Ginger has many advantages for the body, namely as an antioxidant, anti-inflammatory, antimicrobial, and anticancer activity. In addition, ginger or ginger extracts are also beneficial for the gastrointestinal system that ginger can relieve nausea and vomiting due to chemotherapy by suppressing the activation of 5-HT receptors in enteric neurons. Ginger extracts and their constituents also have chemopreventive and antineoplastic properties in gastric cancer. The long history of ginger use in humans has prompted clinical trials to scientifically assess the effectiveness of ginger as an adjunct therapy or complementary and alternative drug in a number of diseases, especially gastrointestinal diseases. It is advisable for further research to conduct experimental research to determine therapeutic effects of ginger extract on gastrointestinal disorders to adults.

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