Therapeutic Role of Ginger (Zingiber officinale) - A Review

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Authors’ contributions
This work was carried out in collaboration among all authors. Author TK designed the study and wrote the first draft of the manuscript. Authors SA, EH and MY performed critical revision of manuscript. Authors SMHA and ZRAAA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Ginger (Zingiber officinale) is a common kitchen spice that belongs to the family Zingiberaceae. It is rich in phytochemistry that is promoting health benefits. It is used as a home remedy to support the common cold, headaches, and pharmacological properties such as anti-inflammatory, antioxidant, antiemetic, antiulcer, and anti-cancer properties, anti-platelet, anti-diabetic and lipid-lowering activities. Gingerols are key ingredients found in ginger that convert into zingerone, shogaol, and parasols, giving flavor and odor. Zingerone and shogaol are present in limited quantities in fresh ginger and more in dried or extracted goods. Especially 6-gingerol and 6-shogaol are pharmacological properties that are effective in antipyretic, analgesic, and hypotensive. The present review is about different therapeutic properties of ginger, including antioxidant properties, anti-diabetic properties, anti-cancer properties etc.

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1. INTRODUCTION

Ginger (Zingiber officinale) rhizome belongs to the family Zingiberaceae widely used as an important cooking spice for various food and beverages around the world, specifically in the Southern Eastern Asian countries, Central, South Africa and United States of America [1]. Ginger rhizome’s flesh can be white, yellow, and red in color, depend upon its variety. It’s cover either be thick or thin brown skin, depending upon the harvesting when it was a young and mature plant. In India and China, fresh ginger use as a flavoring agent in beverages and the preparation of vegetables and meat products [2]. Usually, ginger is consumed as a fresh paste and dried powder. In traditional medicine, the rhizome was used for the treatment of some diseases, including inflammatory disease, and proven various pharmacological activities such as antiemetic, antilucre, anti-inflammatory, antioxidant, antiplatelet, glucose and lipid-lowering, cardiovascular, anti-microbial, gastroprotective, respiratory protection and neuro-protection effects and anti-cancer activities [3-5]. It is also believed to support the common cold, headaches and even helpful in menstrual periods. Ayurveda practitioners commend ginger as a powerful digestive aid; it stimulates the appetite and clears the body’s micro-circulatory channels. It also helps to improve the digestion and transportation of nutrients to targeted body tissues. Furthermore, it is also used as a remedy for joint pain, nausea and motion sickness [6, 7].

The volatile oils and pungent phenol compounds found in ginger rhizome, such as shogaols, zingerone, and gingerols, contribute to the taste and odor of the plant [8]. Volatiles and non-volatiles are two broad categories for fresh ginger. Sesquiterpene and monoterpenoid hydrocarbons, which give ginger its distinct aroma and flavor, were among the volatiles. Gingerols, shogaols, parasols, and zingerone are examples of non-volatile pungent compounds[8]. The major compounds found in ginger are gingerols that are converted into shogaol, zingerone, and parasol and give characteristic flavor and odor. Shogaol and zingerone are found in small quantities in fresh ginger and large quantity in-store products [9]. 6-gingerol and 6-shogaol have pharmacological activities, including antipyretic, analgesic, antitussive and hypotensive effects [10, 11].

Ginger uses for the treatment of many diseases, including degenerative disorders (arthritis and rheumatism), gastrointestinal health (indigestion, constipation, and ulcer), cardiovascular disorders (atherosclerosis and hypertension), vomiting, diabetes mellitus, and cancer [6,12]. It also has the potential for anti-inflammatory and anti-oxidative properties for controlling the ageing process. It has anti-microbial properties that can help treat infectious diseases [10,13-15].

Ginger has remarkable health-promoting properties; therefore, various pharmacological research has been conducted in recent years. Therefore, in this review, we outlined Zinger’s beneficial health properties, as well as the bioactivities of its components and the potential pathways of its key elements.

2. THERAPEUTIC BENEFITS OF GINGER

The therapeutic effect of Ginger is explained below and summarized in Table 1 and Fig. 1.

2.1 Antioxidant Effect

In rats, ginger consumption reduces lipid peroxidation and restores the activities of superoxide dismutase and catalase, glutathione, and glutathione reductase, and glutathione peroxidase glutathione-S-transferase [16]. Before ischemia, supplementation of ginger resulted in a higher total antioxidant capacity that regularized glutathione peroxidase and superoxide dismutase activities and low total oxidants levels (lower tissue malondialdehyde, NO, and protein carbonyl contents) in comparison to an untreated group of Wistar albino rats. Overall experience fed of ginger (5%) show less kidney damage due to oxidative stress induced by ischemia [17].

The phytochemistry-rich ginger contains scavenges free radicals components that are produced in biological systems. For energy production generated during the process of oxidation, some free radicals are essential [18]. Increases in the production of free radicals show oxidative stress that can lead to damage to DNA [19].

2.2 Anti-Nausea Effect

Throughout history, ginger is commonly utilized for relieving nausea and vomiting. It is also an antiemetic; it is attributed as a carminative effect that helps break up and expel intestinal gas. Researchers compared the effectiveness of
ginger and Vitamin B6 and reported that they were equally effective for reducing nausea and limit vomiting episodes during pregnancy [20,21].

2.3 Anti-Inflammatory Effects

In ancient herbs used to support the body's immune response, ginger has the capacity to reduce inflammation, swelling, and discomfort. Ginger and its derivatives are used in many countries to boost the immune system. Several studies that evaluate the effectiveness of ginger in patients suffering from osteoarthritis have controversial results. The study showed the extract of ginger has a significant effect on dropping osteoarthritis symptoms [22]. 6-Shogaol has potent anti-inflammatory and antioxidant effects used as a therapeutic agent in gout as a rheumatic disease of joints [23]. Several researchers were reported that 6-gingerol extract of dried ginger has exhibit analgesic and potent anti-inflammatory effects [24,25]. Ginger is effective for the treatment of patients suffering from hypoalgesia. These researchers studied 36 participants for curing muscle pain using ginger supplementation for 11 days. They attested that the daily consumption of raw and heat-treated ginger resulted in moderate-to-large declines in muscle pain [26]. In addition, ginger has an antimicrobial quality, which helps in the treatment of infectious diseases. It produces free radicals or reactive oxygen species (ROS) during metabolism further than the antioxidant capacity of a biological system resulting in oxidative stress that plays a vital role in neurodegenerative diseases, cardiac diseases, cancer, and the aging process [27]. Inflammatory disorders like gastritis, esophagitis, and hepatitis, not only caused by infectious agents such as viruses, bacteria, and parasites sometimes affected by physical and chemical agents like heat, acid, cigarette smoke, and foreign bodies, which are recognized as risk factors for human cancer [28,29].

2.4 Cardiovascular Effect

Ginger's antiarrhythmic activity is one of its most significant effects. The studies show the effect of ginger on blood lipids in both animals and humans. The results show that ginger significantly decreases plasma cholesterol in animals, but not in patients who are suffering from any heart disease such as coronary artery disease. Research shows ginger has exhibit antithrombotic activity, in vitro study, its extract inhibits platelet aggregation and thromboxane-B2 (TXB2) production. Furthermore, gingerdione and shogaol also inhibit the formation of 5-hydroxyeicosatetraenoic acid (5-HETE) and prostaglandin-E2 (PGE2) from arachidonic acid, gingerol and dehydroparadol favored the inhibition of cyclooxygenase. Ginger is used as antiplatelet therapy, and it prevents coronary heart disease [30]. In this approach, ginger has less potent than aspirin, but in contrast, it has lesser side effects than aspirin. The function of aspirin is inhibiting arachidonic acid-induced platelet release and aggregation and COX activity; ginger also works as same as the mechanism of action. So suggested that the development of effective gingerol analogs has been used as a substitute for aspirin therapy to prevent ischemic heart disease [31,32].

2.5 Anti-Cancer Effect

Ginger act as a chemo-preventive spice, numerous researches focused on the ginger and its various bioactive compound have cancer-preventive and potential cancer therapeutic application [33,34]. Ingredients like 6-gingerol, 6-shogaol, 6-paradol, and zerumbone in ginger reveal anti-inflammatory and anti-tumorigenic activities. The ginger effect in preventing or defeating cancer growth has been studied in a variety of cancer types, including lymphoma, hepatoma, colorectal cancer, breast cancer, skin cancer, liver cancer, and bladder cancer [35]. Researchers believe that ginger's efficacy stems from its ability to suppress prostaglandin and leukotriene biosynthesis by inhibiting the enzyme arachidonate 5-lipoxygenase's biosynthesis. Gingerol inhibits LTA4H activity in HCT116 colorectal cancer cells and suppresses anchorage-independent cancer cell development by binding to LTA4H (leukotriene A4 hydrolase), which has been identified as a promising target therapy for cancer treatment. Gingerol effectivity was found in the experiment to stop the tumor growth, which was done In vivo in nude mice, an effect that was mediated by the inhibition of LTA4H activity. Prevention of colorectal cancer are the first results that identify a direct target of 6-gingerol by inhibiting LTA4H to explain its anti-cancer activity [36]. Extract of ginger has been revealed to have antioxidant, anti-inflammatory, and anti-tumor effects on cells. The researcher examined the anti-cancer effects of a variety of compounds, including 6-gingerol, epigallocatechin gallate (EGCG), asiaticoside (AS), and tocotrienol-rich
fraction (TRF) vitamin E. EGCG+6-gingerol triggered apoptosis synergistically and blocked the development of cancer cells 1321N1 and LN18 glioma [37]. Other researchers [38] 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 [39]. Administered zerumbone 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-κB and hemeoxygenase (HO)-1 expression. In gastric cancer, the Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) plays a major role in promoting apoptosis. The Cascades of caspase proteins activate by ginger and its functional components [40].

Fig. 1. Therapeutic properties of ginger

Table 1. The therapeutic effect of ginger

| Major effect                                                                 | Reference |
|------------------------------------------------------------------------------|-----------|
| Effective treatment in rheumatoid arthritis                                  | [47]      |
| Significantly reduce migraine attacks                                       | [48]      |
| Relieve moderate to mild nausea and vomiting during pregnancy               | [21]      |
| Effective for Chemotherapy-induced vomiting and nausea                      | [49]      |
| Anti-diabetic and Cardiovascular effect                                      | [31]      |
| Effective in knee osteoarthritis patients                                    | [50]      |
| Significantly improves breast milk volume                                  | [51]      |
| Effective for weight loss                                                  | [52]      |
| Helpful to maintain the blood glucose level                                 | [53]      |
| Significantly reduced the frequency of vomiting and nausea during chemotherapy | [54]      |
| Recover the muscle strength after intense exercise, no effect on muscle damage or delayed onset muscle soreness | [55] |
| Significantly reduced menstrual blood loss                                 | [56]      |
2.6 Anti-Diabetic Effect

In diabetes, many studies show that ginger and other plants have effective both preventively and therapeutically [41]. In Australia, the University of Sydney found ginger was effective in glycemic control for people with type 2 diabetes. A study showed that ginger extracts could increase the uptake of glucose into muscle cells without using insulin; hence, it may help control high blood sugar levels. Another clinical trial in diabetic patients that consumed three grams of dry ginger for 30 days shows that blood glucose, triglyceride, and total and LDL cholesterol levels significantly reduced [42-43]. A study of ethanolic extract of *Zingiber officinale* fed orally for 20 days produced a significant anti-hyperglycaemic effect (P < 0.01) in diabetic rats. Furthermore, in high-fat diets, the ethanolic extract of ginger was found to reduce body weights, total cholesterol, LDL cholesterol, triglycerides, free fatty acids, glucose, insulin and phospholipids [44]. Overall, ginger works on diabetes by increasing insulin release and sensitivity, inhibiting carbohydrate metabolism enzymes and improving lipid profiles. Ginger has a very low glycemic index (GI), which means it gradually breaks down to shape glucose and thus does not raise blood sugar levels as high GI foods do. Some other investigations established ginger has a preventive effect against diabetes complications. Ginger can also protect a diabetic’s liver, kidneys, and central nervous system and reduce the risk of cataracts – a common side-effect of the disease [42,45,46].

3. CONCLUSION

Ginger is well known as a condiment and spices used for flavoring food and also its use as a therapeutic purpose from a thousand years ago. Ginger and its bioactive components include gingerols, shogaol, and paradols are active/valuable ingredients which use as a novel therapeutic strategy against various degenerative diseases. This review appreciated natural products drugs (ginger), have beneficial effects for cardiovascular disorders, diabetes mellitus, and gastrointestinal health, and have anti-inflammatory and antibacterial effects. The application of ginger is safe and promising health benefits in the past as well as the future.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Sabulal B, Dan M, Kurup R, Pradeep NS, Valsamma RK, George V. Caryophyllene-rich rhizome oil of *Zingiber nimmonii* from South India: Chemical characterization and antimicrobial activity. Phytochemistry. 2006;67(22):2469-73.
2. Kausar T, Kausar MA, Khan S, Haque S, Azad ZRAA. Optimum additive composition to minimize fat in functional goat meat nuggets: A healthy red meat functional food. Processes. 2021;9(3).
3. Jafarzadeh A, Nemati M. Therapeutic potentials of ginger for treatment of multiple sclerosis: A review with emphasis on its immunomodulatory, anti-inflammatory and anti-oxidative properties. Journal of Neuroimmunology. 2018;324:54-75.
4. Ali BH, Blunden G, Tanira MO, Nemmar A. Some phytochemical, pharmacological and toxicological properties of ginger (*Zingiber officinale* Roscoe): A review of recent research. Food and Chemical Toxicology. 2008;46(2):409-20.
5. Sharma PK, Singh V, Ali M. Chemical composition and antimicrobial activity of fresh rhizome essential oil of *Zingiber officinale* Roscoe. Pharmacognosy Journal. 2016;8(3).
6. Kumeshini S, Kumar G, Kumar P, Banu G. Ethnobotanical survey of anti-diabetic medicinal plant s used by the native people of Palayapalayam, Namakkal I District, Tamilnadu, India. Inter J Pharma Sci Res. 2013;1(5):448-55.
7. Anh NH, Kim SJ, Long NP, Min JE, Yoon YC, Lee EG, et al. Ginger on Human Health: A Comprehensive Systematic Review of 109 Randomized Controlled Trials. Nutrients. 2020;12(1):157.
8. Semwal RB, Semwal DK, Combrinck S, Viljoen AM. Gingerols and shogaols: Important nutraceutical principles from ginger. Phytochemistry. 2015;117:554-68.
9. Jolad SD, Lantz RC, Solyom AM, Chen GJ, Bates RB, Timmermann BN. Fresh organically grown ginger (Zingiber officinale): composition and effects on LPS-induced PGE2 production. Phytochemistry. 2004;65(13):1937-54.

10. Sivasothy Y, Chong WK, Hamid A, Eldeen IM, Sulaiman SF, Awang K. Essential oils of Zingiber officinale var. rubrum Thiebade and their antibacterial activities. Food chemistry. 2011;124(2):514-7.

11. Ashutosh Kumar Y, Reetu, Arun G. Antidiabetic Effects of Zingiber officinale Rosc. on Streptozotocin- and High-Fat Diet-Induced Diabetic Rats. Asian Journal of Pharmaceutical and Clinical Research. 2019:77-80.

12. Y.A. MY. Gingerol and Its Role in Chronic Diseases. Adv Exp Med Biol 2016(929):177-207.

13. Jiang H, Xie Z, Koo HJ, McLaughlin SP, Timmermann BN, Gang DR. Metabolic profiling and phylogenetic analysis of medicinal Zingiber species: Tools for authentication of ginger (Zingiber officinale Rosc.). Phytochemistry. 2006;67(15):1673-85.

14. Nicoll R, Henein MY. Ginger (Zingiber officinale Roscoe): a hot remedy for cardiovascular disease?. International Journal of Cardiology. 2009;131(3):408-9.

15. Li H, Liu Y, Luo D, Ma Y, Zhang J, Li M, et al. Ginger for health care: An overview of systematic reviews. Complementary therapies in medicine. 2019;45:114-23.

16. Ahmed RS, Suke SG, Seth V, Chakraborti A, Tripathi AK, Banerjee BD. Protective effects of dietary ginger (Zingiber officinale Rosc.) on lindane-induced oxidative stress in rats. Phytotherapy Research. 2008;22(7):902-6.

17. Uz E, Karatas OF, Mete E, Bayrak R, Bayrak O, Atmaca AF, et al. The effect of dietary ginger (Zingiber officinale Rosc) on renal ischemia/reperfusion injury in rat kidneys. Renal failure. 2009;31(4):251-60.

18. Ramaa CS, Shirole AR, Mundada AS, Kadam VJ. Nutraceuticals-an emerging era in the treatment and prevention of cardiovascular diseases. Current Pharmaceutical Biotechnology. 2006;7(1):15-23.

19. Hussein MR, Abu Dief, E. E., Abou El Ghait, A. T., Adly, M. A., & Abdelraheem, M. H. (2006). Morphological evaluation of the radioprotective effects of melatonin against X-ray induced early and acute testis damage in Albino rats: an animal model. International Journal of Experimental Pathology. 2006;87(3):237-50.

20. Viljoen E, Visser J, Koen N, Musekiwa A. A systematic review and meta-analysis of the effect and safety of ginger in the treatment of pregnancy-associated nausea and vomiting. Nutrition Journal. 2014;13(1):20.

21. Sharifzadeh F, Kashanian M, Koohpayehzadeh J, Rezaian F, Sheikhansari N, Eshraghi N. A comparison between the effects of ginger, pyridoxine (vitamin B6) and placebo for the treatment of the first trimester nausea and vomiting of pregnancy (NVP). The Journal of Maternal-Fetal & Neonatal Medicine. 2018;31(19):2509-14.

22. Grzanna R, Lindmark L, Frondoza CG. Ginger - an herbal medicinal product with broad anti-inflammatory actions. Journal of Medicinal Food. 2005;8(2):125-32.

23. Grzanna R, Lindmark L, Frondoza CG. Ginger - an herbal medicinal product with broad anti-inflammatory actions. Journal of Medicinal Food. 2005;8(2):125-32.

24. Young H-Y, Luo Y-L, Cheng H-Y, Hsieh W-C, Liao J-C, Peng W-H. Analgesic and anti-inflammatory activities of [6]-gingerol. Journal of Ethnopharmacology. 2005;96(1-2):207-10.

25. Minghetti P, Sosa S, Cilurzo F, Casiraghi A, Alberti E, Tubaro A, et al. Evaluation of the topical anti-inflammatory activity of ginger dry extracts from solutions and plasters. Planta Medica. 2007;73(15):1525-30.

26. Black CD, Herring MP, Hurley DJ, O’Connor PJ. Ginger (Zingiber officinale) reduces muscle pain caused by eccentric exercise. The Journal of Pain. 2010;11(9):894-903.

27. Sharifi-Rad M, Varoni EM, Salehi B, Sharifi-Rad J, Matthews KR, Ayatollahi SA, et al. Plants of the genus Zingiber as source of antimicrobial agents: From Tradition to Pharmacy; 2017.

28. Nile SH, Park SW. Chromatographic analysis, antioxidant, anti-inflammatory,
and xanthine oxidase inhibitory activities of ginger extracts and its reference compounds. Industrial Crops and Products. 2015;70:238-44.

29. Gupta R, Singh PK, Singh R, Singh RL. Pharmacological activities of Zingiber officinale (ginger) and its active ingredients: A review. International Journal of Innovation Science and Research. 2016;4:1-18.

30. Tabibi H, Imani H, Atabak S, Najafi I, Hedayati M, Rahmani L. Effects of ginger on serum lipids and lipoproteins in peritoneal dialysis patients: a randomized controlled trial. Peritoneal Dialysis International. 2016;36(2):140-5.

31. Arzati MM, Honarvar NM, Saedisomeolia A, Anvari S, Effatpanah M, Arzati RM, et al. The effects of ginger on fasting blood sugar, hemoglobin A1c, and lipid profiles in patients with type 2 diabetes. International journal of endocrinology and metabolism. 2017;15(4).

32. Koo KLK, Ammit AJ, Tran VH, Duke CC, Roufogalis BD. Gingerols and related analogues inhibit arachidonic acid-induced human platelet serotonin release and aggregation. Thrombosis Research. 2001;103(5):387-97.

33. Ryan JL, Heckler CE, Roscoe JA, Dakhil SR, Kirshner J, Flynn PJ, et al. Ginger (Zingiber officinale) reduces acute chemotherapy-induced nausea: A URCC CCOP study of 576 patients. Supportive care in cancer. 2012;20(7):1479-89.

34. Zick SM, Ruffin MT, Lee J, Normolle DP, Siden R, Arawi S, et al. Phase II trial of encapsulated ginger as a treatment for chemotherapy-induced nausea and vomiting. Supportive Care in Cancer. 2009;17(5):563-72.

35. Mahomoodally MF, Aumeeruddy MZ, Rengasamy KRR, Roshan S, Hammad S, Pandoohee J, et al., editors. Ginger and its active compounds in cancer therapy: From folk uses to nano-therapeutic applications. Seminars in Cancer Biology; 2019: Elsevier.

36. Jeong C-H, Bode AM, Pugliese A, Cho Y-Y, Kim H-G, Shim J-H, et al. [6]-Gingerol suppresses colon cancer growth by targeting leukotriene A4 hydrolase. Cancer Research. 2009;69(13):5584-91.

37. Rahman AA, Makpol S, Jamal R, Harun R, Mokhtar N, Ngah WZW. Tocotrienol-rich fraction,[6]-gingerol and epigallocatechin gallate inhibit proliferation and induce apoptosis of glioma cancer cells. Molecules. 2014;19(9):14528-41.

38. Manju V, Nalini N. Chemopreventive efficacy of ginger, a naturally occurring anticarcinogen during the initiation, post-initiation stages of 1, 2 dimethylhydrazine-induced colon cancer. Clinica Chimica Acta. 2005;358(1-2):60-7.

39. Kim M, Miyamoto S, Yasui Y, Oyama T, Murakami A, Tanaka T. Zerumbone, a tropical ginger sesquiterpene, inhibits colon and lung carcinogenesis in mice. International Journal of Cancer. 2009;124(2):264-71.

40. Yodkeeree S, Sung B, Limtrakul P, Aggarwal BB. Zerumbone enhances TRAIL-induced apoptosis through the induction of death receptors in human colon cancer cells: Evidence for an essential role of reactive oxygen species. Cancer Research. 2009;69(16):6581-9.

41. Parveen K, Siddiqui WA, Arif JM, Kuddus M, Shahid SMA, Kausar MA. Evaluation of vegetables and fish oils for the attenuation of diabetes complications. Cellular and Molecular Biology. 2019;65(7).

42. Shidfar F, Rajab A, Rahideh T, Khandouzi N, Hosseini S, Shidfar S. The effect of ginger (Zingiber officinale) on glycemic markers in patients with type 2 diabetes. Journal of Complementary and Integrative Medicine. 2015;12(2):165-70.

43. Bandari U, Pillai KK. Effect of ethanolic extract of Zingiber officinale on dyslipidaemia in diabetic rats. Journal of Ethnopharmacology. 2005;97(2):227-30.

44. Nammi S, Sreemantula S, Roufogalis BD. Protective effects of ethanolic extract of Zingiber officinale rhizome on the development of metabolic syndrome in high-fat diet-fed rats. Basic & Clinical Pharmacology & Toxicology. 2009;104(5):366-73.

45. Arャblou T, Arャaeian N, Valizadeh M, Sharifi F, Hosseini A, Djالali M. The effect of ginger consumption on glycemic status, lipid profile and some inflammatory markers in patients with type 2 diabetes mellitus. International Journal of Food Sciences and Nutrition. 2014;65(4):515-20.
with type 2 diabetes: a randomized, double-blind, placebo-controlled trial. Complementary Therapies in Medicine. 2014;22(1):9-16.

47. Aryaeian N, Shahram F, Mahmoudi M, Tavakoli H, Yousefi B, Arablou T, et al. The effect of ginger supplementation on some immunity and inflammation intermediate genes expression in patients with active rheumatoid arthritis. Gene. 2019;698:179-85.

48. Martins LB, Rodrigues AMdS, Rodrigues DbF, dos Santos LC, Teixeira AnLc, Ferreira AVM. Double-blind placebo-controlled randomized clinical trial of ginger (Zingiber officinale Rosc.) addition in migraine acute treatment. Cephalalgia. 2019;39(1):68-76.

49. Marx W, McCarthy AL, Ried K, McKavanagh D, Vitetta L, Sali A, et al. The effect of a standardized ginger extract on chemotherapy-induced nausea-related quality of life in patients undergoing moderately or highly emetogenic chemotherapy: A double blind, randomized, placebo controlled trial. Nutrients. 2017;9(8):867.

50. Mozaffari-Khosravi H, Naderi Z, Dehghan A, Nadjarzadeh A, Fallah Huseini H. Effect of ginger supplementation on proinflammatory cytokines in older patients with osteoarthritis: outcomes of a randomized controlled clinical trial. Journal of nutrition in gerontology and geriatrics. 2016;35(3):209-18.

51. Paritakul P, Ruangrongmorakot K, Laosooksathit W, Suksamarnwong M, Puapornpong P. The effect of ginger on breast milk volume in the early postpartum period: A randomized, double-blind controlled trial. Breastfeeding Medicine. 2016;11(7):361-5.

52. Attari VE, Ostadrahimi A, Jafarabadi MA, Mehralizadeh S, Mahluji S. Changes of serum adipocytokines and body weight following Zingiber officinale supplementation in obese women: A RCT. European Journal of Nutrition. 2016;55(6):2129-36.

53. Khandouzi N, Shidfar F, Rajab A, Rahideh T, Hosseini P, Taheri MM. The effects of ginger on fasting blood sugar, hemoglobin A1c, apolipoprotein B, apolipoprotein Al and malondialdehyde in type 2 diabetic patients. Iranian Journal of Pharmaceutical Research: IJPR. 2015;14(1):131.

54. Sanaati F, Najafi S, Kashaninia Z, Sadeghi M. Effect of ginger and chamomile on nausea and vomiting caused by chemotherapy in iranian women with breast cancer. Asian Pacific Journal of Cancer Prevention. 2016;17(8):4125-9.

55. Matsumura MD, Zavorsky GS, Smolina JM. The effects of pre-exercise ginger supplementation on muscle damage and delayed onset muscle soreness. Phytotherapy Research. 2015;29(6):887-93.

56. Kashefi F, Khajehei M, Alavinia M, Golmakani E, Asili J. Effect of Ginger (Zingiber officinale) on heavy menstrual bleeding: A placebo-controlled, randomized clinical trial. Phytotherapy Research.2015;29(1):114-9.