

A Systematic Review and Meta-Analysis of the Effectiveness of Iranian Herbal Medicines (Ginger, Chamomile, and Mint) in the Management of Chemotherapy-Induced Nausea and Vomiting

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Abstract

Background: Chemotherapy, which is the primary therapeutic approach widely used in cancer treatment, causes various complications, such as diarrhea, nausea, and vomiting. The present study aimed to determine the effects of Iranian herbal medicines (ginger, chamomile, and mint) and phytoestrogens on controlling the side effects of chemotherapy in patients.

Objectives: The present study aimed to determine the effects of Iranian herbal medicines (ginger, chamomile, and mint) and phytoestrogens on controlling the side effects of chemotherapy in patients.

Methods: The search strategy included the use of international electronic sources, such as ISI Web of Science, PubMed, Scopus, and Cochrane Library, and national electronic sources, such as (SID.ir and Magiran) scientific databases, systematically and without a time limit until January 1, 2021. The quality of enrolled articles was assessed using the Jadad Scale. Ginger, chamomile, and mints affecting nausea and vomiting were used as keywords.

Results: Five studies were included in this systematic review. Considering the moderate heterogeneity in the results of studies on the effect of ginger on nausea ($P=0.022$; $I^2=68\%$) and vomiting ($P=0.08$; $I^2=54\%$, 54), a random effects model was employed for data analysis. Based on the results of the meta-analysis, the effect of ginger on the reduction of nausea [standard mean difference=-0.46; (95%CI=-0.91-0.01; $P=0.04$)] and vomiting [standard mean difference= -0.59; (95%CI= -0.96-0.21; $P=0.022$)] was due to effective chemotherapy when comparing with the controls. Moreover, phytoestrogens were more effective in controlling vomiting and nausea in the experimental group [standard mean difference=-0.57; (95%CI: -0.82-0.31; $P<0.001$)]

Results: Five Studies included in this systematic review. Due to the moderate heterogeneity cross the results of ginger studies on nausea ($P = 0.022$; $I^2 = 68\%$) and vomiting ($P = 0.08$; $I^2 = 54\%$), a random effects model was employed for data analysis. Based on results of meta-analysis, the ginger in reducing nausea [standard mean difference =-0.46; (95%CI= -0.91-0.01; $p = 0.04$)] and vomiting [standard mean difference = -0.59; (95%CI= -0.96-0.21; $p = 0.022$)] was due to effective chemotherapy when comparing with the controls. Based on the results of meta-analysis, phytoestrogens were more effective than in the control group [standard mean difference =-0.57; (95%CI: -0.82-0.31; $p <0.001$)] in relief of vomiting and nausea.

Conclusion: As evidenced by the obtained results, ginger and phytoestrogens can improve nausea and vomiting in chemotherapy patients. Phytoestrogens can be a beneficial treatment to relieve nausea and vomiting in patients undergoing chemotherapy.

Keywords: Chamomile, Chemotherapy, Ginger, Mint, Nausea, Systematic review, Vomiting

1. Background

Like other chronic diseases, cancer is regarded as a major challenge in health care (1). According to the World Health Organization (WHO), cancer is considered the second leading cause of death across the globe. Based on statistics, cancer accounted for 9.6 million deaths in 2018 (2). There are several treatments for cancer, including surgery, radiotherapy, and chemotherapy (3). Chemotherapy is the mainstay of systemic cancer treatment, with significant side effects, such as bone marrow depression, mucositis, diarrhea, nausea, and vomiting (4). Chemotherapy-related nausea and vomiting are among the most serious side effects and are a major concern for cancer patients. The prevalence of this problem has been reported to be 96%-54% (5). Despite significant advances in antiemetic drugs, nausea and vomiting are still considered one of the most common and

unpleasant complications of cancer-related chemotherapy (6-7). Patients with cancer may delay chemotherapy out of fear of this undesirable side effect, refuse to complete treatment, be unable to complete treatment, or be dissatisfied if treatment is continued (8).

According to the results of some studies, 48%-67% of patients undergoing chemotherapy do not have reduced nausea and vomiting even if they take large amounts of these drugs. On the other hand, the use of some drugs may lead to drowsiness, extrapyramidal problems, headaches, diarrhea, hypotension, and constipation (9). Due to the limited effect and dangerous side effects of chemical drugs, we are witnessing an increased tendency for non-chemical and non-industrial treatments, such as herbs. One of the low-risk and frontline actions in this field is the use of herbal medicine as the most active part of complementary and alternative medicine, which has attracted much

attention over the past decade (9, 10).

Ginger is obtained from the purple vein-decorated yellow plant called *Zingiber Officinale Roscoe* (11). According to studies, ginger has many beneficial effects in controlling and treating many diseases. Among the beneficial effects attributed to this plant, we can refer to its protective effects on the liver (12), antimicrobial (13), antibacterial (14), and antifungal effects (15), prevention of cell damage (16), headache control (17), control of primary dysmenorrhea and premenstrual syndrome (18), Bronchitis and asthma (19), as well as the treatment of nausea and vomiting (20). Ginger is one of the herbal medicines effective in treating nausea and vomiting, with no known adverse effects (21, 22).

Chamomile is another medicinal plant with anti-nausea and vomiting properties. It holds a special place in ancient medical and medicinal texts and Iranian medicine. It has therapeutic effects on diseases of the nervous, gastrointestinal, and respiratory systems (23). Pharmaceutically, different species of this plant and the compounds in its essential oil have been identified and used in treatment. According to studies, chamomile has multiple beneficial effects in controlling and treating fever, migraine, headache, rheumatoid arthritis, as well as stomach and tooth pain (24). Mint, scientifically known as *Mentha piperita* L, is a perennial and fragrant plant used as an antispasmodic, analgesic, antidepressant, and sedative agent with the ability to enhance lactation. Moreover, it can treat urinary tract and respiratory infections, diabetes, varicose veins, diarrhea, and painful menstruation and is used to relieve fever, nausea, and vomiting (25,26). Due to its antagonistic effects against the 5-HT₃ receptor channel, mint can play an essential role in the reduction of nausea and vomiting (27-30).

Multiple clinical trials in Iran examined the performance of chamomile, ginger, and mint herb in alleviating chemotherapy-related nausea and vomiting (31-38). Numerous review and meta-analysis studies have examined the role of chamomile and ginger in reducing the intensity of post-chemotherapy nausea and vomiting. Nevertheless, none of the review studies of Persian articles published in the national database has been included. Furthermore, no study has investigated the effect of phytoestrogens on chemotherapy-induced nausea and vomiting. In light of the aforementioned issues, the present study aimed to assess the impact of the plant collected from Iran on post-chemotherapy nausea and vomiting and an increased tendency to consume herbal medicine.

2. Objectives

The present study aimed to determine the effects of Iranian herbal medicines (ginger, chamomile, and mint) and phytoestrogens on controlling the side effects of chemotherapy in patients.

3. Methods

PRISMA was applied to report a systematic review and meta-analysis. To conduct this review study, we systematically searched the Latin electronic resources of PubMed, ISI Web of Science, Scopus, and Cochrane Library, without a time limit until January 2021. The main keywords for searching the articles evaluating the role of ginger in chemotherapy-related nausea and vomiting were as follows (Figure 1). All studies were included regardless of quality. Language restriction was applied, and only English and Persian articles were included.

Moher D, Liberati A, Tetzlaff J, Altman DG, Group preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 6: e1000097. DOI: 10.1016/j.jclinepi.2009.06.005

In order to complete the study, a query was conducted on the scientific information database (SID) and Magiran database using the keywords of ginger, chamomile, and mints affecting chemotherapy-induced nausea and vomiting. The references listed in the searched articles were included in the search strategy to achieve additional investigations. Two authors independently reviewed the titles and abstracts of extracted papers, and if the subject matter seemed relevant, the article was extracted and thoroughly reviewed by them. Finally, the articles that met the inclusion criteria were evaluated for quality.

The inclusion criteria entailed all randomized clinical trials or quasi-experimental designs searching the effect of herbal medicines on chemotherapy-induced nausea and vomiting. On the other hand, the exclusion criteria were as follows: studies searching the influence of ginger on chemotherapy-induced nausea and vomiting in children, the use of aromatherapy, the use of ginger in combination with other herbal medicines that are completed in countries other than Iran, studies on chemotherapy-related nausea and vomiting in diseases other than breast cancer and review studies.

Measured Outcomes: In these investigations, the influence of ginger was evaluated on acute and delayed nausea and vomiting.

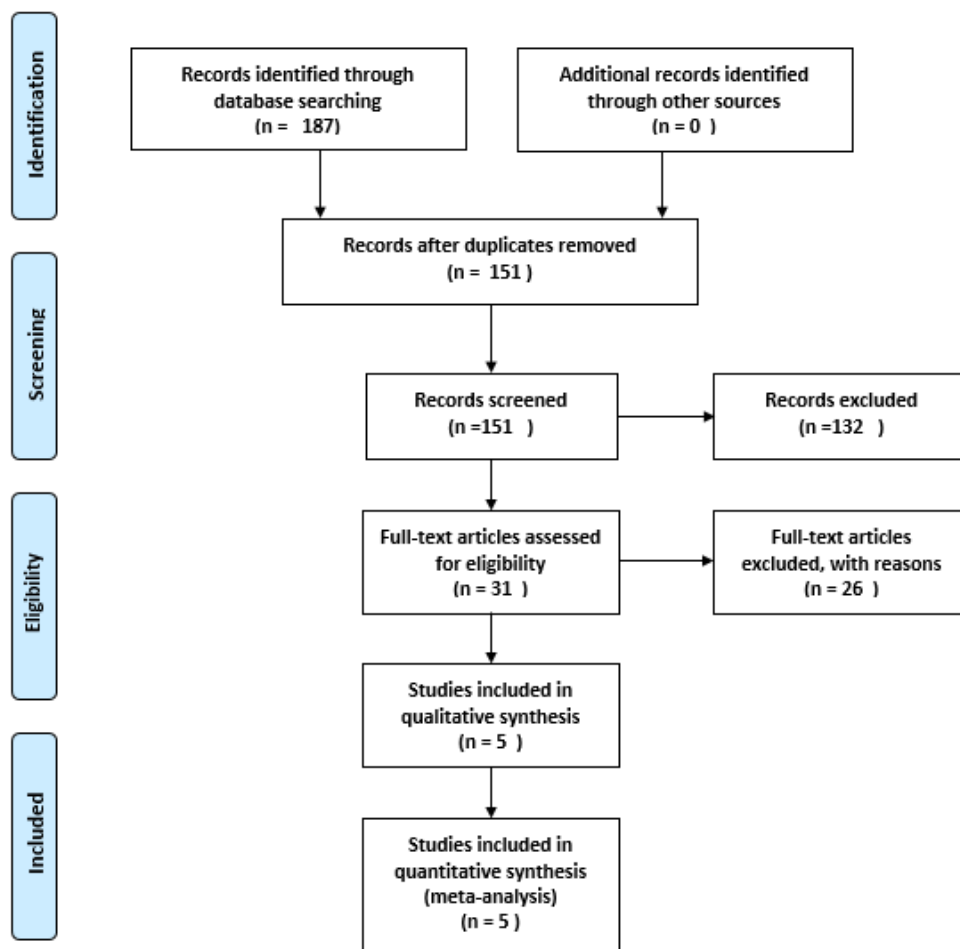


Figure 1. PRISMA statement (2009)

(Methodological Evaluation of the Quality of Studies)

The quality of enrolled articles was assessed using a Jadad Scale (32). This scale has five items in the following fields: expression of randomization, how to complete randomization, expression of blindness, how to complete blindness, and expression of sample loss and its causes, which is added to the above items

of sample homogeneity at the beginning of the study. In evaluating the quality of studies, scores of 1-2 and 3-5 are ranked as low-quality and high-quality studies, respectively (Table 1). The Oxford quality scoring system (Jadad Scoring) is briefly explained. Please expand on this matter.

Table 1. The quality of enrolled articles was assessed using a Jadad Scale

Study	Randomization			Blinding			Report of dropping out
	Mention randomization	Appropriate Method	Inappropriate Method	Mention blinding	Appropriate method	Inappropriate method	
Panahi 2012	+	+	-	+	+	-	+
Jafarimanesh12020	+	+	-	+	+	-	+
Sanaati 2016	+	+	-	+	+	-	+
Ansari 2016	+	+	-	+	+	-	+
Eghdam-Zamiri 2020	+	+	-	+	+	-	+

Data Extraction

The research team designed the data extraction table, and each of the articles in this study was reviewed by two researchers. Data were tabulated under the following headings: title, author name, year of publication, type of chemotherapy drug, the

chemical drug for nausea and vomiting, side effects of severe nausea and vomiting, age, the sample size in control and intervention group, as well as the length and dose of the drug in intervention and control group. Evaluation tools and overall study results are presented (Table 2).

Statistical Data Analysis

The data were analyzed by comprehensive meta-analysis software. Finally, the heterogeneity between studies was clarified via the Q Cochran test and I2 index. Higgins et al. (33) assigned adjectives of low, moderate, and high to values of <25%, 25%-75%, and >75%. The findings from the heterogeneity test clarified that a fixed-effect model or a random effect was computed to reach the effect size of herbal medicines regarding a 95% confidence interval (95%CI) in forest plots. In this size chart, since the number of articles is less than 10, the publication bias is meaningless, and there is no need to draw a chart (33). Finally, the results from the meta-analysis were illustrated via Forest plot so that the square size means the sample size in each work, and the lines that appeared on both sides signify a 95% CI for the effect size of each study.

4. Results

In a study by Eghdam-Zamiri, the intervention group received 500 mg ginger tablets twice a day for 10 days following chemotherapy (cisplatin) and a week prior to mastectomy. The controls used a placebo. In the intragroup comparison, in the placebo group, the nausea severity (P=0.119) and the vomiting severity (P=0.229) after intervention were not statistically significant. While in the ginger group, the nausea severity (P= 0.001) and the vomiting severity (P=0.004) showed a statistically significant difference after the intervention. Furthermore, within the group, nausea severity (P=0.004) and vomiting severity (P=0.004) were significantly lower in the ginger group than in the placebo (34).

Ansari et al. evaluated the effect of ginger on doxorubicin chemotherapy-induced nausea and vomiting among 150 women with breast cancer.

Table 2. Demographic and clinical variables of the studies included in the review study

The main result	Side effects	Evaluated consequences	questionnaire	Severe nausea and vomiting	age	Length and dose of the drug in the intervention and control groups	Sample size in control and intervention groups	Chemical antiemetics	Drugs used for chemotherapy	Name of authors/ year
Ginger consumption has no effect on reducing nausea and vomiting.	-	nausea and vomiting	Rhodes Index Scores of Nausea, Vomiting, and Retching	Intense	51-83	Ginger 0.5 g per day in the intervention group	Intervention: 50 Controls: 50	Granisetron	docetaxel, epirubicin, and cyclophosphamide	Panahi 2012
Peppermint extract can reduce the severity of nausea, vomiting, and anorexia.	-	Nausea, vomiting, and anorexia	-	-	49/6	Intervention group: 40 drops of peppermint extract mixed in 20 ccs of tap water every 8 hours Control group: every 8 hours 40 drops of distilled water mixed in 20 ccs of water	Intervention: 42 Controller: 42	Granisetron, metoclopramide, dexamethasone, Ondansetron	Trastuzumab, Doxorubicin, Cyclophosphamide, docetaxel	Jafarimane sh 1 2020
Consumption of ginger and chamomile can have a positive effect on reducing nausea and vomiting after chemotherapy.	nausea and vomiting	Generalized Estimating Equations	-	-	20-60	The first group: 500 mg of herbal ginger root powder Group 2: 500 mg capsules of chamomile extract twice a day Control group: Routine drugs	Intervention 1:15 Intervention 2:15 Controls: 15	Metoclopramide and aprepitant	-	Sanaati 2016

Ginger consumption can have a positive effect on reducing nausea and vomiting after chemotherapy	nausea and vomiting	Total Parenteral Nutrition (TPN)	-	48.6	Intervention group: 500 g of ginger powder 2 times a day for 3 days	Intervention: 57 Controls: 62	-	Doxorubicin	Ansari 2016
	nausea and vomiting	Rhodes Index	-	1/47	Intervention group: 2 times a day 500 mg ginger tablets Control group: Plus	Intervention: 30 Controls: 30	-	Cisplatin	Eghdam-Zamiri

These subjects were assigned to intervention (receiving 500-g ginger powder twice daily for three days) and placebo groups. The severity of vomiting was lower in patients receiving ginger than in those receiving placebo and this difference was statistically significant ($P < 0.05$) (28).

In a study, 65 patients with breast cancer were examined within three groups. The ginger group was treated with herbal ginger root powder (500 mg) along with an anti-nausea diet (aprepitant, metoclopramide, and dexamethasone) two times a day for five consecutive days prior to and five consecutive days following chemotherapy. The chamomile group was treated with chamomile extract capsules (500 mg) twice daily along with the anti-nausea diet. The routine group was treated with the anti-nausea diet. The ginger group exhibited a significant decrease in the incidence of vomiting ($P < 0.0001$) and nausea ($P = 0.006$) compared to the anti-nausea diet alone (31). In the study by Panahi et al., the intervention group was treated with daily 0.5 g ginger concurrent with the anti-nausea diet (dexamethasone + granisetron), and the control group was treated with the anti-nausea diet three times a day for four days immediately after chemotherapy. No significant differences were observed between the prevalence and mean of nausea and vomiting between ginger and placebo between the first six hours, 6-24 hours, the first day, as well as between the second and third day ($P > .05$) (29).

Baboon Sanati et al. studied 65 patients with breast cancer within three groups. The Ginger group was

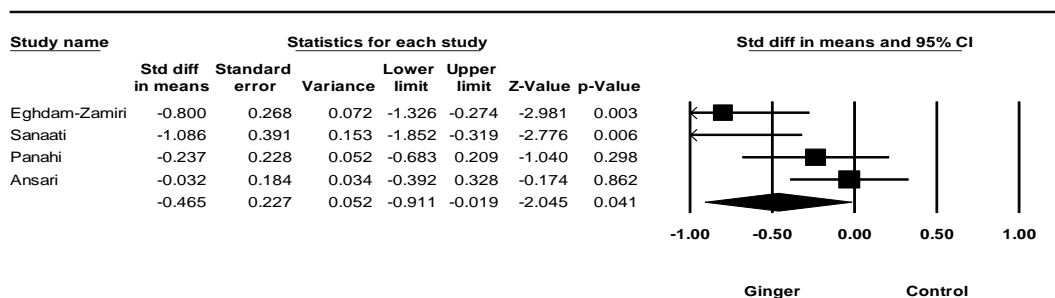
treated with herbal ginger root powder (500 mg) concurrent with an anti-nausea diet (aprepitant + metoclopramide + dexamethasone) twice daily for five consecutive days prior to and five consecutive days following chemotherapy. The chamomile group was treated with chamomile extract capsules (500 mg) twice daily, concurrent with an anti-nausea diet. However, no significant difference was observed ($P = 0.238$). The ginger group displayed a significant decrease in the frequency of vomiting ($P = 0.003$); nonetheless, the ginger had a decreasing effect on the rate of nausea ($P = 0.895$) compared to the anti-nausea diet alone (31).

Peppermint

Jafari Manesh et al. (2020) determined the effect of peppermint (*Mentha piperita*) extract on the severity of anorexia, nausea, and vomiting in breast cancer candidates for chemotherapy. Nausea, and vomiting score were significantly lower in the Peppermint group compared to the controls.

Effect of Ginger on Chemotherapy-induced Nausea

Four studies assessed the effect of ginger on chemotherapy-induced nausea in patients with breast cancer. The result of the Q test demonstrated a discrepancy in the results of the studies ($P = 0.022$; $I^2 = 68\%$). Data were analyzed by meta-analysis using a stochastic effects model. Based on the meta-analysis results, ginger was more effective in controlling mastalgia than the control group -0.46 ; (95% CI: -0.91 - 0.01 ; $P = 0.04$; 4 trials).



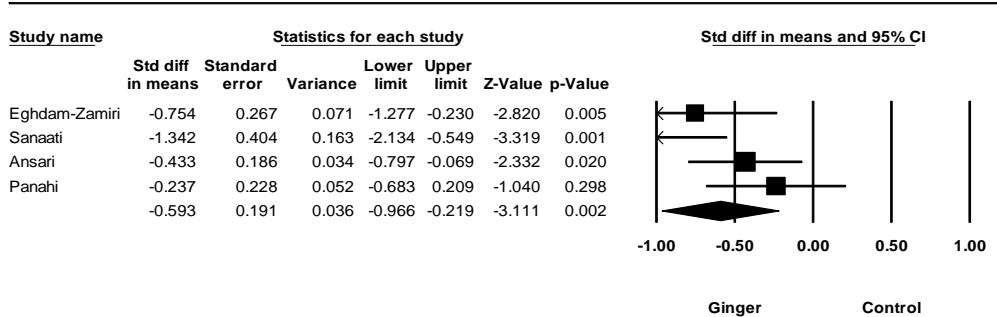
Meta Analysis

Figure 2. Effect size of the averages individually and overall with a 95% confidence interval for studies examining the effect of comparing ginger and controlling nausea

Effect of Ginger on Chemotherapy-induced Vomiting

Four studies assessed the effect of ginger on chemotherapy-induced nausea in patients with breast cancer. The result of the Q test demonstrated a discrepancy in the results of the studies (P= 0.08; I2 =

54%). Data were analyzed by meta-analysis using a stochastic effects model. Based on the meta-analysis results, ginger was more effective in controlling mastalgia compared to the control group -0.59 (95% CI: -0.96-0.21; P= 0.022; P=0.002;4 trials).



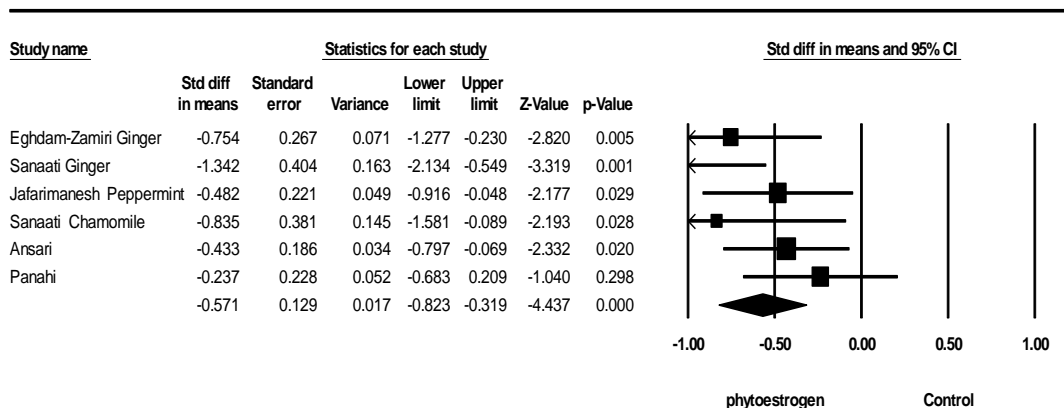
Meta Analysis

Figure 3. Size of the effect of the averages individually and overall with a 95% confidence interval for the study of the effect of comparing ginger and control on vomiting

Phytoestrogens on Chemotherapy-induced Vomiting

Six studies assessed the effect of phytoestrogens on chemotherapy-induced vomiting in patients with breast cancer compared to that in the control group. The result of the Q test showed heterogeneity between study results (P = 0.196; I2 =31%). Data

were analyzed by meta-analysis using a stochastic effects model. According to the meta-analysis results, ginger was more effective in controlling mastalgia compared to the control group -0.57; (95% CI: -0.82-0.31; P<0.001;6 trials).



Meta Analysis

Figure 4. Measurement of the effect of the averages individually and overall with a 95% confidence interval for studies examining the effect of comparing phytoestrogens on vomiting

Sensitivity Analyses

Sensitivity analyses were performed to detect heterogeneity when I2 was high or moderate. Studies one by one were extracted using sensitivity analyses that could not determine the resource of heterogeneity.

5. Discussion

Nausea and vomiting occur more frequently in the acute phase (first 24 hours of chemotherapy) and have a negative effect on patients' lives (35). The

widespread use of anti-nausea drugs has been associated with significant side effects, such as hypotension, headache, diarrhea, drowsiness, and constipation (36). According to the results of the present study, studies evaluated the effectiveness of Iranian herbal medicines (ginger, chamomile, and mint) in controlling nausea and vomiting following chemotherapy in patients with breast cancer. According to the present review study, ginger and mint can improve nausea and vomiting in chemotherapy patients. The ginger significantly reduced the frequency of vomiting; nonetheless, it

had a less marked effect on the frequency of nausea compared to the anti-nausea diet alone (31).

The findings of two studies conducted abroad on the effect of ginger on nausea and vomiting in patients undergoing chemotherapy align with the present meta-analysis. The study by Luke Samon et al. in 2016, entitled "Effectiveness of ginger in the prophylaxis of chemotherapy-induced nausea-vomiting in breast cancer patients receiving adriamycin and cyclophosphamide." In this study, 34 patients received 500 mg of ginger capsule for five days and a placebo twice daily in the control group. All patients receive ondansetron and dexamethasone prophylaxis. According to the results, ginger is a safe drug; however, to reduce nausea, it did not affect breast cancer patients receiving adriamycin and cyclophosphamide along with ondansetron and dexamethasone ($P=0.3$) (37). The inhalation effect of ginger was investigated. In a study by Lane et al. (2014) entitled "The effect of ginger inhalation on chemotherapy-induced nausea and vomiting, as well as the quality of life, in breast cancer patients," patients in the intervention group received (30 people) for five days of aromatherapy with ginger oil and control group (30 people) received placebo. The nausea score was lower in the intervention group than in the control group ($P=0.04$). However, no significant difference was observed regarding vomiting in both groups ($P=0.5$). Nevertheless, there was a significant change from baseline to global health status in the intervention group ($P<0.001$). In the intervention group, an improvement was detected in function and appetite ($P=0.002$, $P<0.001$), respectively.

A recent systematic review of nine clinical trials published around the world reported that ginger might be effective in reducing nausea in the acute phase of chemotherapy in patients with breast cancer. Consistent with the present meta-analysis, the authors concluded that the study of the effect of ginger on nausea and vomiting requires a high-quality clinical trial (38). A recently published systematic review and meta-analysis of nine clinical trials on Chinese herbal remedies suggested that adjuvant use of Chinese herbal remedies with chemotherapy may reduce side effects associated with chemical agents, including nausea and vomiting, diarrhea, alopecia, myelosuppression, and impaired immune function. Most of the studies included in this meta-analysis were of poor quality (39).

Mechanism of the Possible Effect of Ginger

Ginger products exert an antiemetic effect using various mechanisms. Gingerol and Shogavels could decrease gastric contractions but increase gastrointestinal activity. Moreover, treatments have an anti-serotonin effect and exert destructive effects against free radicals that cause vomiting (40). A study assessed the possible mechanism of ginger in

inhibiting cisplatin-induced vomiting and nausea. The findings of this study on mice and minks indicated that ginger reduced cisplatin-induced nausea by regulating the central and peripheral systems 5-Hydroxytryptamine, the Substance P system, and the Dopamine system (41).

The study by Borhan et al. (2017), which investigated the effect of chamomile extract on the severity of chemotherapy-dependent nausea and vomiting, was performed quasi-experimentally on 60 patients undergoing chemotherapy. In the mentioned study, two hours before chemotherapy, the intervention group used chamomile extract, and the control group used distilled water. At the beginning of the study, there was no statistically significant difference between the two groups in terms of mean nausea and vomiting scores ($P=0.4$). In all these times, the nausea score in the control group was significantly higher than that in the intervention group. No statistically significant difference was noted when comparing the two groups regarding the prevalence of vomiting ($P=0.05$) (42). In contrast to the aforementioned research, in a study, treatment with ginger significantly reduced the incidence of nausea ($P=0.006$) and vomiting ($P<0.0001$) compared to the anti-nausea diet alone (31).

Study Limits and Suggestions for Future Studies

Among the notable limitations, we can refer to the degree of heterogeneity which could be due to different sample sizes, hours of giving herbal medicines, types of chemotherapy, control groups, and anti-chemical decomposition regimes. The methodological quality of some of the studies reviewed in this systematic review was low. Heterogeneity may be due to the type of extract (Estonian, ethanolic, and fruit juices). Ginger extract types models had a beneficial effect on reducing nausea induced by cisplatin.

Nevertheless, acetone extract and fruit juice had more effectiveness in decreasing nausea in comparison with 50% ethanolic ginger extract (43). In another study, acetone extract showed more beneficial effects in comparison with ethanolic extract (44).

Almost don't have an intention to treat analysis, and don't performed inadequate reporting of random allocation. It is suggested that future studies be designed and reported on a consortium basis. The small number of included studies is the second limitation of this review. The last limitation is the small sample size, indicating a need for more studies with a larger sample size in this field.

6. Conclusion

Based on the results, ginger and mint can improve nausea and vomiting in chemotherapy patients.

Contradictory findings have been reported with chamomile. Therefore, due to the high prevalence of nausea and vomiting in chemotherapy patients, patients' interest in complementary medicine, and the low cost of this treatment, this method can help improve nausea and vomiting in chemotherapy patients.

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Conflicts of interest

The authors declare no conflict of interest.

References

- Barandeh M, Babaei M, Mehdizadeh Toorzani Z, Sharifiyan Rjtjnmf. Effect Of Self-Care On Quality Of Life In Women With Breast Cancer Undergoing Chemotherapy. *Nurs Midwifery J*. 2017;**15**(3):199-207.
- WHO.Cancer.<https://www.who.int/news-room/fact-sheets/detail/cancer>. 2018
- Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin*. 2016;**66**(4):271-89. doi: [10.3322/caac.21349](https://doi.org/10.3322/caac.21349). [PubMed: [27253694](https://pubmed.ncbi.nlm.nih.gov/27253694/)].
- Oun R, Moussa YE, Wheate NJ. The side effects of platinum-based chemotherapy drugs: a review for chemists. *Dalton trans*. 2018;**47**(19):7848. doi: [10.1039/c8dt90088d](https://doi.org/10.1039/c8dt90088d). [PubMed: [29808879](https://pubmed.ncbi.nlm.nih.gov/29808879/)].
- Klein J, Griffiths P. Acupressure for nausea and vomiting in cancer patients receiving chemotherapy. *Br J commu Nurs*. 2004;**9**(9):383-8. doi: [10.12968/bjcn.2004.9.9.15936](https://doi.org/10.12968/bjcn.2004.9.9.15936). [PubMed: [15389150](https://pubmed.ncbi.nlm.nih.gov/15389150/)].
- Dranitsaris G, Molassiotis A, Clemons M, Roeland E, Schwartzberg L, Dielenseger P, et al. The development of a prediction tool to identify cancer patients at high risk for chemotherapy-induced nausea and vomiting. *Ann Oncol*. 2017;**28**(6):1260-7. doi: [10.1093/annonc/mdx100](https://doi.org/10.1093/annonc/mdx100). [PubMed: [28398530](https://pubmed.ncbi.nlm.nih.gov/28398530/)].
- Shinomiya K, Inoue T, Utsu Y, Tokunaga S, Masuoka T, Ohmori A, et al. Hypnotic activities of chamomile and passiflora extracts in sleep-disturbed rats. *Biol Pharm Bull*. 2005;**28**(5):808-10. doi: [10.1248/bpb.28.808](https://doi.org/10.1248/bpb.28.808). [PubMed: [15863883](https://pubmed.ncbi.nlm.nih.gov/15863883/)].
- Gholamy R, Dehghan M, Vanaki Z, Ghaedi F, Soheili M, Mosarezaee A. Efficacy of complementary therapies in reduction of chemotherapy induced nausea and vomiting in breast cancer patients: Systematic review. *Cmj*. 2014;**4**(2):831-44.
- Hickok JT, Roscoe JA, Morrow GR, Ryan JL. A phase II/III randomized, placebo-controlled, double-blind clinical trial of ginger (*Zingiber officinale*) for nausea caused by chemotherapy for cancer: a currently accruing URCC CCOP Cancer Control Study. *Support Cancer Ther*. 2007;**4**(4):247-50. doi: [10.3816/SCT.2007.n.022](https://doi.org/10.3816/SCT.2007.n.022). [PubMed: [18632524](https://pubmed.ncbi.nlm.nih.gov/18632524/)].
- Joyce M, Hawks J. Heart disorders: Medical-surgical nursing: Clinical Management for positive outcomes. Translated By: Nikravanemofrad M, Barahimi N First edition Tehran: Jameenegar-Salemi publications. 2009;**184**:92-4.
- Dissanayake KG, Waliwita WA, Liyanage RP. A review on medicinal uses of *Zingiber officinale* (ginger). *Int J Health Sci Res*. 2020;**10**(6):142-8.
- Rahimlou M, Yari Z, Hekmatdoost A, Alavian Z, Keshavarz A. Effect of ginger supplementation on liver enzymes, hepatic fibrosis and steatosis in nonalcoholic fatty liver disease: a double blind randomized-controlled clinical trial. *Iranian J Nutr Sci Food Technol*. 2016;**11**(2):1-8.
- Zamanzad B. The antibacterial properties of *Allium cepa* (onion) and *Zingiber officinale* (ginger) extracts on *Staphylococcus aureus* *Pseudomonas aeruginosa* *Escherichia coli* and *Candida albicans* isolated from vaginal specimens. *Journal of Shahrekord Uuniversity of Medical Sciences*. 2010;**11**.
- Gupta S, Ravishankar S. A comparison of the antimicrobial activity of garlic, ginger, carrot, and turmeric pastes against *Escherichia coli* O157: H7 in laboratory buffer and ground beef. *Foodborne Pathog Dis*. 2005;**2**(4):330-40. doi: [10.1089/fpd.2005.2.330](https://doi.org/10.1089/fpd.2005.2.330). [PubMed: [16366855](https://pubmed.ncbi.nlm.nih.gov/16366855/)].
- Shoaei N, Mohammadi P, Roudbar Mohammadi S. Antifungal Effect of *Teucrium polium* and *Zingiber officinale* extracts on Clinical isolates of *Candida* Species. *Armaghane Danesh*. 2012;**17**(5):416-22.
- Padervand S, Hassani A, Kalalian MH, Donyaei A. The effect of taking ginger supplement and progressive endurance training on cellular damage in non-athlete men.
- Prasad S, Pathak R, Desai A, Vajpeyee S, Bhavsar V. The Analgesic Effects Of Ginger-Juice (*Zingiber Officinale* Roscoe) On Wistar Albino Rat. *National Journal of Integrated Research in Medicine*. 2015;**6**(6).
- Fanaei H, Behboodi Moghadam Z, Kasaeiyan A. Comparison the effects of ginger and curcumin in treatment of premenstrual syndrome. *Iran South Med J*. 2015;**18**(3):575-86.
- Roohi Broujeni H, Ganji F, Roohi Broujeni P. The effect of combination of Zingiber and *Althea officinalis* extracts in acute bronchitis-induced cough. *J Shahrekord Uni Med Sci*. 2009;**10**(4).
- Basirat Z, Moghadamnia A, Kashifard M, Sarifi-Razavi A. The effect of ginger biscuit on nausea and vomiting in early pregnancy. *Acta Medica Iranica*. 2009:51-6.
- Abolghasmi S. The Effect of Ginger on nausea and vomiting during pregnancy. *Babol Med sci J*. 2004;**6**(3):17-20.
- Feyer P, Kleeberg UR, Steingraber M, Günther W, Behrens M. Frequency of side effects in outpatient cancer care and their influence on patient satisfaction a prospective survey using the PASQOC® questionnaire. *Support Care Cancer*. 2008;**16**(6):567-75. doi: [10.1007/s00520-008-0422-4](https://doi.org/10.1007/s00520-008-0422-4). [PubMed: [18322707](https://pubmed.ncbi.nlm.nih.gov/18322707/)].
- Zarezadeh S, Riahi H, Shariatmadari Z, Sonboli A. Effects of cyanobacterial suspensions as bio-fertilizers on growth factors and the essential oil composition of chamomile, *Matricaria chamomilla* L. *J Appl Phycol*. 2020;**32**(2):1231-41. doi: [10.1007/s10811-019-02028-9](https://doi.org/10.1007/s10811-019-02028-9).
- Pareek A, Suthar M, Rathore GS, Bansal V. Feverfew (*Tanacetum parthenium* L.): A systematic review. *Pharmacogn Rev*. 2011;**5**(9):103-10. doi: [10.4103/0973-7847.79105](https://doi.org/10.4103/0973-7847.79105). [PubMed: [22096324](https://pubmed.ncbi.nlm.nih.gov/22096324/)].
- Gruenwald J, Brendler T, Jaenicke C. PDR for herbal medicines: Thomson, Reuters; 2007.
- Joulaeeraad N, Ozgoli G, Hajimehdipoor H, Ghasemi E, Salehimoghaddam F. Effect of aromatherapy with peppermint oil on the severity of nausea and vomiting in pregnancy: a single-blind, randomized, placebo-controlled trial. *J Reprod Infertil*. 2018;**19**(1):32-8. [PubMed: [29850445](https://pubmed.ncbi.nlm.nih.gov/29850445/)].
- Heimes K, Hauk F, Verspohl EJ. Mode of action of peppermint oil and (-)-menthol with respect to 5-HT₃ receptor subtypes: binding studies, cation uptake by receptor channels and contraction of isolated rat ileum. *Phytother Res*. 2011;**25**(5):702-8. doi: [10.1002/ptr.3316](https://doi.org/10.1002/ptr.3316). [PubMed: [21077259](https://pubmed.ncbi.nlm.nih.gov/21077259/)].
- Ansari M, Mohammadianpanah M, Omidvari S, Mosalaei A, Ahmadloo N, Nasrollahi H, et al. Efficacy of ginger in control of chemotherapy induced nausea and vomiting (CINV) in breast cancer patients (BCPs) receiving doxorubicin-based chemotherapy (DBCT). *Annals of Oncology*. 2015;**26**:111.
- Panahi Y, Saadat A, Sahebkar A, Hashemian F, Taghikhani M, Abolhasani E. Effect of ginger on acute and delayed chemotherapy-induced nausea and vomiting: a pilot, randomized, open-label clinical trial. *Integr Cancer Ther*. 2012;**11**(3):204-11. doi: [10.1177/1534735411433201](https://doi.org/10.1177/1534735411433201). [PubMed: [22313739](https://pubmed.ncbi.nlm.nih.gov/22313739/)].
- Jafarimanesh H, Akbari M, Hoseinian R, Zarei M, Harorani M. The Effect of Peppermint (*Mentha piperita*) Extract on the Severity of Nausea, Vomiting and Anorexia in Patients with Breast Cancer Undergoing Chemotherapy: A Randomized

- Controlled Trial. *Integr Cancer Ther.* 2020;**19**:1534735420967084. doi: [10.1177/1534735420967084](https://doi.org/10.1177/1534735420967084). [PubMed:33118401].
31. 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 Pac J Cancer Prev.* 2016;**17**(8):4125-9. [PubMed: 27644672].
 32. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJM, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary?. *Control Clin Trials.* 1996;**17**(1):1-2. doi: [10.1016/0197-2456\(95\)00134-4](https://doi.org/10.1016/0197-2456(95)00134-4). [PubMed: 8721797].
 33. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002;**21**(11):1539-58. doi: [10.1002/sim.1186](https://doi.org/10.1002/sim.1186). [PubMed: 12111919].
 34. Eghdam-Zamiri R, Khanbabayi Gol M. Effects of ginger capsule on treatment of nausea and vomiting in patients receiving cisplatin undergoing mastectomy: a randomized clinical trial. *Iran J Obstet Gynecol Infertil.* 2020;**22**(11):15-21. doi: [10.22038/IJOGI.2020.14949](https://doi.org/10.22038/IJOGI.2020.14949).
 35. Najafi S. Ginger effects on control of chemotherapy induced nausea and vomiting. *IJBD.* 2014;**7**(1):7-14.
 36. Ebrahimi SM, Parsa-Yekta Z, Nikbakht-Nasrabadi A, Hosseini SM, Sedighi S, Salehi-Surmaghi MH. Ginger effects on control of chemotherapy induced nausea and vomiting. *Tehran Uni Med J.* 2013;**71**(6):395-403.
 37. Thamlikitkul L, Srimuninnimit V, Akewanlop C, Ithimakin S, Techawathanawanna S, Korphaisarn K, et al. Efficacy of ginger for prophylaxis of chemotherapy-induced nausea and vomiting in breast cancer patients receiving adriamycin-cyclophosphamide regimen: a randomized, double-blind, placebo-controlled crossover study. *Support Care Cancer.* 2017;**25**(2):459-64. doi: [10.1007/s00520-016-3423-8](https://doi.org/10.1007/s00520-016-3423-8). [PubMed : 27714530].
 38. Saneei Totmaj A, Emamat H, Jarrahi F, Zarrati M. The effect of ginger (*Zingiber officinale*) on chemotherapy-induced nausea and vomiting in breast cancer patients: A systematic literature review of randomized controlled trials. *Phytother Res.* 2019;**33**(8):1957-65. doi: [10.1002/ptr.6377](https://doi.org/10.1002/ptr.6377). [PubMed: 31225678].
 39. Li S, So TH, Tang G, Tan HY, Wang N, Ng BFL, et al. Chinese Herbal Medicine for Reducing Chemotherapy-Associated Side-Effects in Breast Cancer Patients: A Systematic Review and Meta-Analysis. *Front Oncol.* 2020;**10**: 599073. doi: [10.3389/fonc.2020.599073](https://doi.org/10.3389/fonc.2020.599073). [PubMed: 33363030].
 40. Ghanbari A, Montazeri A, Niknami M, AtrkarRoshan Z, Sobhani A, Najafi B. Effect of adding ginger to routine treatment on the intensity of chemotherapy-induced nausea and vomiting in cancer patients who referred to Razi Hospital, Rasht. *J Ardabil Univ Med Sci.* 2010;**10**(4):352-61.
 41. Tian L, Qian W, Qian Q, Zhang W, Cai X. Gingerol inhibits cisplatin-induced acute and delayed emesis in rats and minks by regulating the central and peripheral 5-HT, SP, and DA systems. *J Nat Med.* 2020;**74**(2):353-70. doi: [10.1007/s11418-019-01372](https://doi.org/10.1007/s11418-019-01372). [PubMed: 31768887].
 42. Burhan Naji, Vardanjani M, Sassani L. Investigating the effect of chamomile plant extract on chemotherapy-related nausea and vomiting. *Ibn Sina J Nurs Midwifery Care.* 2017;**25**(4):6-140
 43. Sharma SS, Gupta YK. Reversal of cisplatin-induced delay in gastric emptying in rats by ginger (*Zingiber officinale*). *J Ethnopharmacol.* 1998;**62**(1):49-55. doi: [10.1016/s0378-8741\(98\)00053-1](https://doi.org/10.1016/s0378-8741(98)00053-1). [PubMed: 9720611].
 44. Sharma S, Kochupillai V, Gupta S, Seth S, Gupta Y. Antiemetic efficacy of ginger (*Zingiber officinale*) against cisplatin-induced emesis in dogs. *J ethnopharmacol.* 1997;**57**(2):93-6. doi: [10.1016/s0378-8741\(97\)00054-8](https://doi.org/10.1016/s0378-8741(97)00054-8). [PubMed: 9254112].