

# The Effect of Peppermint on Chemotherapy Induced Nausea and Vomiting (CINV): A Systematic Review and Meta-Analysis

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## ABSTRACT

**Background & Objective:** Nausea and vomiting induced by chemotherapy represent significant challenges for cancer patients, adversely affecting their quality of life. Aromatherapy, particularly the use of peppermint essential oil, has gained attention as a complementary approach. This study aims to investigate the effects of peppermint essential oil on alleviating these symptoms.

**Materials & Methods:** This meta-analysis was conducted in accordance with the PRISMA-P 2015 guidelines and involved a comprehensive search of reputable databases, including MEDLINE/PubMed and Cochrane, up to August 1, 2023. Only randomized controlled trials (RCTs) that examined the effects of peppermint essential oil on nausea and vomiting in cancer patients were included in the study. The quality of the studies was assessed, and data extraction. Statistical analysis was performed using Stata V.17 software.

**Results:** The conducted meta-analysis demonstrated that the use of peppermint compounds significantly reduces the severity of nausea and vomiting in cancer patients undergoing chemotherapy, because the confidence interval does not include zero, indicating a positive effect (SMD: 0.643, 95% CI: 0.458-0.829). Based on Egger's test and Funnel Plot, no significant publication bias was detected (P=0.125). However, a relatively high level of heterogeneity was observed in the combined studies (P=0.020, I<sup>2</sup>=60.1%), necessitating the use of a random effects model (REM) for data analysis. This heterogeneity could be due to differences in the type of interventions and assessment tools instruments. These results underscore the efficacy of peppermint essential oil in mitigating chemotherapy-induced nausea and vomiting symptoms.

**Conclusion:** Aromatherapy with peppermint essential oil may serve as an effective and cost-efficient treatment for alleviating nausea and vomiting symptoms resulting from chemotherapy. Offering a promising foundation for future research and clinical application.

**Keywords:** Peppermint Oil, Chemotherapy, Nausea, Vomiting, Neoplasms



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## 1. Introduction

The prevalence of cancer as a life-threatening disease, is currently on the rise (1). The global cancer burden is expected to be 28.4 million cases by 2040, a 47% rise from 2020 (2). In Iran, cancer is also a major health concern, as it is the second most common chronic non-communicable disease and the

third leading cause of death (3). Chemotherapy is one of the most common cancer treatments that can affect various body systems, including the digestive system (4), such that Chemotherapy-induced nausea and vomiting (CINV) is one of the most distressing adverse effects among patients undergoing chemotherapy (5).

Approximately 70 to 80 percent of patients experience these symptoms during treatment. The most common cancers include stomach cancer, breast cancer, and colon cancer (6). For patients undergoing moderate to highly emetogenic chemotherapy, the recommended regimen consists of a triple combination of a 5-HT<sub>3</sub> receptor antagonist, a neurokinin-1 (NK-1) receptor antagonist, and dexamethasone. International guidelines recommend the incorporation of olanzapine into treatment as part of quadruple combination therapy. Despite efforts to control CINV using fluorouracil-based treatments, many patients fail to achieve adequate symptomatic relief. Therefore, identifying more effective prophylactic interventions remains an unresolved challenge, despite advancements in combination antiemetic therapy, nausea remains a significant concern, particularly in patients receiving highly emetogenic chemotherapy (7-9). Some patients define it as the biggest problem, even worse than pain (10, 11). It has been reported that chemotherapy-induced nausea and vomiting (CINV) leads to fluid-electrolyte imbalance, dehydration, weight loss, and physiological effects resulting from poor drug absorption and/or reduced excretion by the kidneys. They also have negative impacts on social life, work, daily activities, and mental well-being of patients. In addition, nausea and vomiting cause some patients to refuse chemotherapy or discontinue treatment (12-14). Aromatherapy is an integrative approach for combating CINV, although its effectiveness has not yet been fully proven (15, 16). Aromatherapy is the use of essential oils derived from the fragrant parts of plants for the treatment or relief of physical and emotional symptoms (17, 18). One of the essential oils used in studies to investigate the effect of aromatherapy on CINV is peppermint oil. Peppermint oil is recognized as an effective agent for nausea (19). A study conducted by Zorba and Ozdemir showed that massage and inhalation of an aromatic mixture including peppermint oil significantly reduced CINV (20). Similarly, in other studies conducted using peppermint essential oil, a reduction in the severity of nausea and the frequency of vomiting was observed (21, 22). Considering the lack of a systematic review study that specifically measures the cumulative effect of peppermint essential oil on the severity of nausea and vomiting, this study aims to systematically evaluate the cumulative evidence on the effectiveness of peppermint essential oil in reducing the severity of CINV through a meta-analysis of randomized controlled trials.

## 2. Materials and Methods

This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-P) 2015 guidelines (23).

### 2.1 Data source and search strategy

A comprehensive search of the literature from MEDLINE/PubMed, Embase, Web of Science, Cochrane, and Google Scholar was conducted by two authors (from the beginning until August 1, 2023) (Appendix ). Various combinations of relevant keywords

and Mesh terms were used for each database search. Articles related to the use of the following phrases were retrieved: (peppermint oil, nausea, vomiting, cancer patients, chemotherapy, and randomized controlled trials). (Drug Therapy [mh] OR Chemotherapy [tiab] OR Pharmacotherapy [tiab] OR Drug Therapies [tiab]) AND (Neoplasms[mh] OR Neoplasia[tiab] OR Neoplasm[tiab] OR Tumor[tiab] OR Cancer[tiab] OR Malignant Neoplasm[tiab] OR Malignancy[tiab] OR Malignancies[tiab] OR Malignant Neoplasms[tiab] OR Benign Neoplasm[tiab])) AND (Vomiting[mh] OR Emesis[tiab])) AND (Nausea[mh])) AND (Mentha piperita[mh] OR Mentha x piperita[tiab] OR Peppermint[tiab] OR Peppermints[tiab] OR mint oil[tiab]). To review the gray literature, both domestic and foreign theses were accessed through ProQuest. Additionally, the website <http://www.greyliit.org> was used to find relevant articles. Furthermore, an extensive manual search was conducted in the reference lists of the included articles to identify any missing studies. All duplicates were removed, and each study source was manually screened to identify eligible studies.

### 2.2 Qualified studies

We included all relevant studies that met our predefined PICO criteria (1). The randomized controlled trials (RCTs) included in the study were registered (2). The participants were cancer patients undergoing chemotherapy who experienced symptoms of nausea and vomiting (4). To reduce the severity of nausea and vomiting in patients, these studies used compounds from peppermint (peppermint essence, peppermint oil, etc.) It was used.

### 2.3 Qualitative assessment

The quality of the included studies was independently assessed by two authors (HE, MH) based on factors such as study design, number of sites, blinding of results, and follow-up completion rates. The quality of studies was assessed using the Cochrane Risk of Bias 2.0 (Rob 2) tool (24).

### 2.4 Data extraction

All relevant studies were independently extracted by the first two authors (HE, MH) following the PRISMA guidelines (23). The third author (AS) reviewed and confirmed the results of the first two authors' assessment of study quality, noting any discrepancies. Complete versions of all relevant articles were obtained and reviewed. The extracted data included the lead authors, year of publication, country of the trial, demographic characteristics of the patients, and key outcomes.

### 2.5 Statistical analysis

A meta-analysis was conducted to compare the effects of mint and placebo on the severity of nausea and vomiting using Stata software version 17. Statistical heterogeneity was assessed using the I<sup>2</sup> statistic and the chi-square test. I<sup>2</sup> values above 50% were considered to indicate high heterogeneity. In cases of significant heterogeneity, a sensitivity analysis was conducted to assess the impact of

each study on the overall effect estimate. A random effects model (REM) was used in the analysis. The assessment of publication bias for each outcome was conducted using the Egger test, with a significance level set at 0.05.

### 3. Results

#### 3.1 Selection and explanation of studies

Based on the search strategies, we initially identified a total of 396 references through both electronic and manual searches. After screening the titles and abstracts, we selected 311 references, excluding irrelevant and review articles. After reading the complete article, 297 trials were excluded: 203 were not randomized controlled trials (RCTs), 12 trials had unclear outcomes, 3 trials were duplicates, the intervention measures in 6 trials regarding mint were not compared to another substance, and follow-ups were incomplete in 4 trials. Ultimately seven eligible RCTs were included in the meta-analysis. The PRISMA flow chart is summarized ([Figure 1](#)). Two authors (HE, MH) independently reviewed each eligible study and extracted data, including the title, publication date, country, demographic characteristics (such as number of patients, average age), and assessment tools for nausea and

vomiting, the characteristics of the reviewed articles are summarized ([Table 1](#)). In total, there were 286 patients in the peppermint essential oil group and 277 patients in the control group. According to the diagnostic standard all patients had a diagnosis of cancer (mostly breast cancer) and were undergoing chemotherapy. The results of the meta-analysis comparing the effectiveness of mint compounds on the severity of nausea and vomiting, as well as publication bias and heterogeneity, are presented.

#### 3.3 The results of the effectiveness of mint compounds on the severity of nausea and vomiting.

The meta-analysis found a significant reduction in the severity of nausea and vomiting among participants using peppermint products compared to those who did not use these substances. The standardized mean difference (SMD) was 0.643, with a 95% confidence interval (CI) of 0.458–0.829, indicating a moderate effect size ([Table 2](#)). In this study, a funnel Plot ([Figure 2](#)) and Egger's test ([Table 3](#)) were used to examine publication bias, which was not significant ( $P = 0.125$ ). Thus, no significant publication bias was observed for this finding. However, the integrated studies showed a relatively high heterogeneity ( $I^2=60.1\%$ ,  $P=0.020$ ), so in these circumstances, REM was applied for data analysis.

**Table 1.** Overview of study characteristics

Study, country	Design	Study size	Age, mean (SD)	Duration of cancer (years)	Intervention	Control	Procedure	Nausea assessing tools (range)
<b>Eghbali et al (34)</b>	RCT	100	46.8±9.72	6.56±12.93	PEO (n= 50)	NS (n=50)	Intervention: 20 min breaths of a 100% PEO swab Control: 20 min breaths of a 100% NS swab	Rhodes Index of Nausea and Vomiting (0-32)
<b>Jafarimanesh et al (27)</b>	RCT	84	50.75±10.56	2.24	PEO (42)	W (42)	Intervention: 40 drops of peppermint extract mixed in 20 cc water Control: 40 drops of distilled water mixed in 20 cc water	Visual Analogue Scale (VAS) (0-10)
<b>Tayarani-Najaran et al (28)</b>	RCT	100	44±11	Na	PEO (50)	W (50)	Intervention: received peppermint capsules every four h Control: received placebo capsules every four h	Check list (0-100)
<b>Haddadi et al (25)</b>	RCT	60	39.85±7.99	Na	ICM (30)	W (30)	Intervention: 30 cc Bits of Ice containing mint	Visual Analogue Scale

Study, country	Design	Study size	Age, mean (SD)	Duration of cancer (years)	Intervention	Control	Procedure	Nausea assessing tools (range)
							Control: 30 cc of tap water	(VAS) (0-10)
<b>Mapp et al (22)</b>	RCT	79	52.7± 14.5	Na	37 (CW/PO)	42 (CW)	Intervention: cool damp washcloth to apply to the neck area with two drops of peppermint oil added. Control: a cool damp washcloth to apply to the neck area with no scent	Baxter Retching Faces (BARF) (0-10)
<b>Ertürk and Taşçı (18)</b>	RCT	80	52.28±10.31	Na	PEO (36)	W (44)	Intervention: 2 drops of 100% PEO upper lip Control: 2 drop of water upper lip	Visual Analogue Scale (VAS) (0-10)
<b>Demont et al (26)</b>	RCT	60	59.67±	Na	PEO (41)	W (19)	Intervention: 1-2 drop of 100% PEO upper lip Control: 1- 2 drop of water upper lip	Criteria for Adverse Events (CTCAE) (0-10)

Peppermint essential oil (PEO), Normal Saline (NS), Ice containing mint (ICM),

**Table 2.** Forest plot of the nausea severity score. CI: Confidence interval

Name/year	SMD	[95%Conf.Interval]	% Weight	Forest plot
<b>Eghbali et al (34)</b>	0.591	(0.190-0.991)	21.41	
<b>Jafarimanesh et al (27)</b>	0.843	(0.396-1.289)	17.22	
<b>Tayarani-Najaran et al (28)</b>	0.493	(0.095-0.891)	21.69	
<b>Haddadi et al (25)</b>	0.613	(0.095-1.131)	12.80	
<b>Mapp et al (22)</b>	0.434	(-0.022-0.889)	16.55	
<b>Ertürk and Taşçı (18)</b>	2.331	(1.389-3.273)	3.87	
<b>Demont et al (26)</b>	0.379	(-0.350-1.108)	6.46	
<b>I-V pooled SMD</b>	0.643	(0.458-0.829)	100.00	

Heterogeneity chi-squared = 15.04 (d.f = 6) p = 0.020

I-squared (variation in SMD attributable to heterogeneity) = 60.1%

Test of SMD=0: z= -6.80 p = 0.000

Table 3. Egger test

Parameter	Description
Data Input Format	theta, se_theta assumed
Test Type	Egger's test for small-study effects
Number of Studies	7
Root MSE	1.339

Note: data input format theta se\_theta assumed.  
Regress standard normal deviate of intervention  
Effect estimate against its standard error  
| Std\_Eff | Coefficient | Std. Err. | t | P>|t| | 95 %Conf. Interval |  
-----|-----|-----|-----|-----|-----|  
| Slope | -0.2444188 | 0.4984119 | -0.49 | 0.645 | [-1.525627, 1.03679] |  
| Bias | 3.668179 | 1.991821 | 1.84 | 0.125 | [-1.451959, 8.788318] |  
Test of H0: no small-study effects      P = 0.125

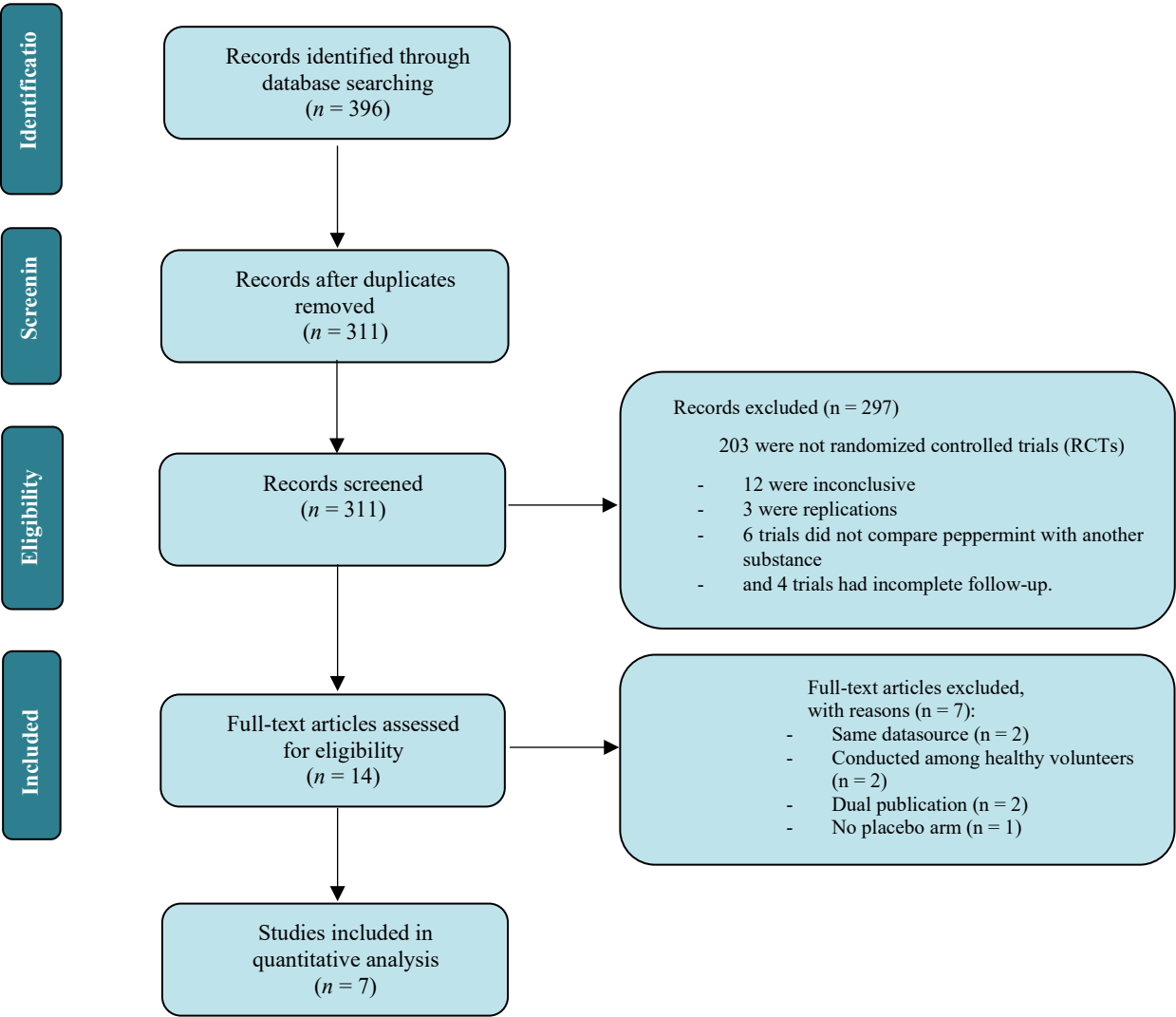
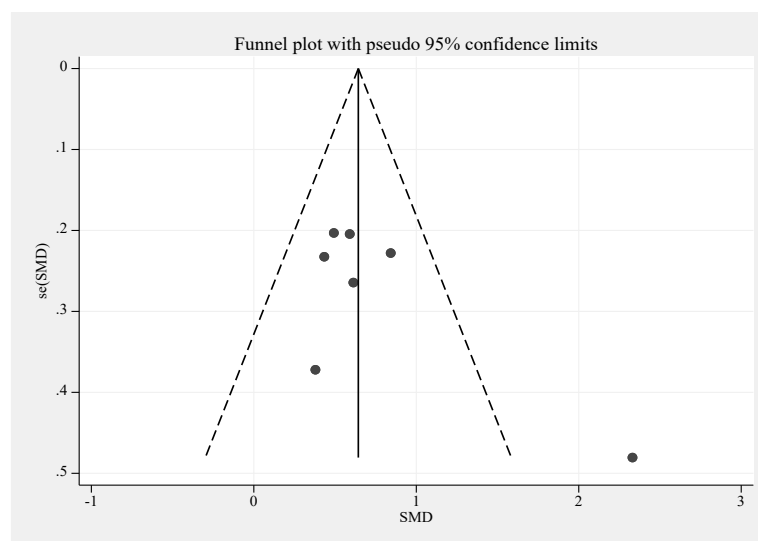


Figure 1. PRISMA flow chart of included studies (Designed by Authors, 2025).



**Figure 2.** Funnel plot of the nausea severity score (Designed by Authors, 2025).

## 4. Discussion

The results of the meta-analysis indicated that the consumption of peppermint reduces the severity of both nausea and vomiting (24). The results of the meta-analysis indicated that the consumption of peppermint reduces the severity of nausea and vomiting. Accordingly, 7 randomized controlled trials (RCTs) were included in the meta-analysis. All the reviewed articles highlighted the effectiveness of peppermint in reducing the severity of nausea. Additionally, five of the studies reported the impact of peppermint consumption on vomiting. In one study by Haddadi et al (25), peppermint had no effect on vomiting, whereas in the study by Mapp et al (22), only nausea was assessed and vomiting was not evaluated, and vomiting was not evaluated. The lack of impact of peppermint on vomiting may be attributed to the shorter duration of the intervention in some studies, as most selected studies involved a longer duration of peppermint use (18, 26-28). Therefore, it is important to note that peppermint has a positive effect on reducing nausea in chemotherapy patients, and further research is needed to assess its impact on vomiting.

Mint can play a crucial role in reducing nausea and vomiting due to its antagonist effects on the 5-HT3 receptor channel (29, 30). 5-HT3 receptors are found in both the central and peripheral nervous systems. Drugs that selectively block 5-HT3 receptors are currently the gold standard in treating nausea and vomiting caused by chemotherapy and post-surgery (31). The method of consuming mint varied in the studies examined, such that in three of the selected studies in this systematic review, the way this herbal remedy was consumed was orally (sucking on ice, capsules, and mint extract) (25, 27, 28).

In this regard, Abdolhosseini et al (32) acknowledged that according to traditional Iranian medicine, mint can reduce nausea and vomiting by strengthening the stomach and cardia, alleviating and

drying excess moisture in the stomach, and improving appetite, as well as reducing phlegm. Furthermore, mint, considering its warm nature, is effective for cold stomachs (32). The cold temperature causes the blood vessels in the peripheral areas of the digestive system [esophagus and stomach] to constrict, reducing the entry of chemotherapy agents into these regions and decreasing nausea and vomiting (25). Holding ice chips in the mouth and drinking cold water helps patients keep their mouths cool and moist. By preventing dry mouth and increasing saliva production, nausea and vomiting can be managed (33).

Four other articles also mentioned aromatherapy, with two studies referring to placing a drop between the upper lip and the nose (18, 22, 34). Aromatherapy has been widely used in three countries: Indonesia, Iran, and Turkey, all of which are Muslim countries that have a tradition of using herbal remedies as a non-pharmaceutical treatment to create a sense of calm and comfort (35). During inhalation, volatile particles bring the fragrant elements present in the oil to the top of the nose. The vibration of nasal hair sends electrochemical information to the emotional center, and then this information is transmitted to other parts of the body through the circulatory system by releasing neurotransmitters. The scent produced by aromatherapy stimulates the activity of chemical nerve cells in the brain (34). Aromatherapy stimulates the hypothalamus to release enkephalins, which can be used as a natural painkiller and provide a soothing flavor. The pituitary gland releases chemicals into the bloodstream to regulate the function of other glands. The soothing aroma of the Raffa core stimulates the brain to release serotonin, reduces cortisol secretion, and activates the 5HT3 receptor, which can block the vomiting center to prevent nausea after inhaling the therapeutic scent (35, 36).



On the one hand, menthol in mint acts as a stomach relaxant when inhaled, reducing nausea and vomiting by relaxing the stomach muscles and numbing the stomach lining (19, 37, 38). Additionally, inhaling mint has a calming effect on the individual. Aromatherapy with mint has a psychological effect, and this effect will reduce personal anxiety. Reducing anxiety decreases the likelihood of nausea and vomiting (18, 37). Peppermint oil and menthol have calcium channel blocking activity and reduce muscle spasms by preventing the entry of calcium (39).

Arafa Badr conducted a study on 50 children diagnosed with leukemia. In the intervention group, two drops (0.2 milliliters) of 2% peppermint essential oil were placed on a piece of cotton, and the child was instructed to breathe it in for three minutes before the start of the chemotherapy session. Inhalation of peppermint essential oil was carried out during three consecutive chemotherapy sessions. The control group of children received standard hospital care. The results showed that the percentage of children with leukemia who inhaled peppermint essence in three sessions gradually reduced the occurrence of delayed nausea and vomiting in children. These findings can be explained by the belief that menthol reduces nausea and vomiting by relaxing the smooth muscles of the gastrointestinal tract (40). Of course, this study was conducted on a small number of children, so the results may not be generalizable to other age groups.

The effect of mint on nausea and vomiting has also been observed in other patient groups, such as those undergoing open-heart surgery and pregnant women. In a preliminary study by Maghami *et al* (41), the intervention group received aromatherapy with peppermint essential oil through a nebulizer before extubation following surgery. The results showed that inhaling peppermint essential oil has beneficial effects in reducing nausea and vomiting after open-heart surgery (41). A limitation of this study is the short-term effect of mint, and it is unclear whether the long-term effects persist. In the studies by IGAR Agustini *et al* (42) and Amzajerdi *et al* (43), which examined the effect of peppermint aromatherapy on the incidence of nausea and vomiting during pregnancy in pregnant women, the results showed a statistically significant difference in the average nausea and vomiting after the peppermint aromatherapy intervention. However, it should be kept in mind that there may be a risk of subjective bias given that patients self-report the severity of nausea and vomiting. Other studies have also compared the effects of peppermint on nausea and vomiting with other herbal medications, emphasizing the greater impact of peppermint. For instance, in the review study by Palatty *et al* (44), the results showed that among four plants (Indian milk thistle, sea buckthorn, peppermint oil, and ginger), peppermint oil was more effective in reducing nausea and vomiting caused by radiotherapy (44). The study by Amzajerdi *et al* (45), which aimed to compare the temporal effects of peppermint and lavender aromas on nausea and

vomiting during pregnancy over a period of 7 days based on the Rhodes index, showed that the aroma of peppermint demonstrated its effects on nausea and vomiting in pregnant women earlier than the aroma of lavender (45). In the study by Joulaeeraad *et al* (46), after 4 days of using peppermint aroma, no significant effect on reducing the intensity of nausea was reported compared to the control group. In the clinical study by Pasha *et al* (47), that examined the effect of peppermint essential oil aromatherapy on nausea and vomiting in pregnant women, it was found that nausea did not significantly decrease with peppermint oil (47). One of the reasons for the inconsistency between the two studies mentioned above could be the duration of the interventions, which was less than a week. Our results suggest that peppermint essential oil may be a useful adjunctive therapy for the management of CINV. However, further large-scale trials are needed to confirm its long-term efficacy and optimal administration protocols.

### Limitations

The number of clinical trials investigating the effects of peppermint on the severity of nausea and vomiting is limited. Studies on delayed nausea and vomiting have been fewer. The duration and frequency of peppermint use varied across studies. The severity of nausea and vomiting was self-reported, which may be a subjective bias. The only methods of consuming peppermint were capsules and sweat, and the infusion method was not studied.

## 5. Conclusion

Chemotherapy-induced nausea and vomiting (CINV) is a significant issue that often impacts patients' quality of life and adherence to treatment. The widespread use of anti-nausea drugs is also linked to notable side effects. Given the high prevalence of nausea and vomiting in chemotherapy patients, the side effects of conventional treatments, and the low cost of medicinal plants, mint may offer an effective solution to alleviate these symptoms. The most effective method of using mint to reduce nausea and vomiting in cancer patients undergoing chemotherapy is through mint aromatherapy.

## 6. Declarations

### 6.1 Acknowledgments

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### 6.2 Ethical Considerations

Not applicable.

### 6.3 Authors' Contributions

Hassan Eslami Aliabadi conceptualized and designed this study. Hassan Eslami Aliabadi and Mohaddeseh Hosseinzadeh carried out the work of entering data into the software as well as analyzing and finally interpreting the data. Azam Saedikia and Mohaddeseh Hosseinzadeh contributed to writing and improving the manuscript. Finally, all authors read and approved the final version of the manuscript.

### 6.4 Conflict of Interest

The authors declare that there are no conflicts of interest.

### 6.5 Fund or Financial Support

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### 6.6 Using Artificial Intelligence Tools (AI Tools)

The authors were not utilized AI Tools.

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