

Effects of Plant-Derived Active Substances on Quality of Life and Chemotherapy-Induced Nausea and Vomiting in Cancer Patients Receiving Cisplatin-Based Chemotherapy: A Randomized Controlled Trial

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Research Article

Keywords: Cancer, Aromatherapy, Nausea

Posted Date: October 13th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10834191/v1>

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Additional Declarations: No competing interests reported.

Abstract

Objectives

The objective of this trial was to assess the effectiveness of BEO (*Cinnamomum camphora* var. *borneol essential oil*) in reducing the intensity of CINV and enhancing QoL in cancer patients treated with cisplatin-based protocols.

Methods

A randomized, double-blind, controlled trial was conducted involving patients scheduled to receive at least two cycles of high-dose cisplatin chemotherapy ($> 50 \text{ mg/m}^2$). Five minutes prior to the initiation of each chemotherapy session, three drops of the essential oil were applied to a sterile gauze pad ($5 \text{ cm} \times 5 \text{ cm}$), which was secured to the patient's collar at a distance of approximately 20 cm from the nose to facilitate continuous inhalation throughout the treatment. CINV was assessed using the Common Terminology Criteria for Adverse Events (CTCAE v5.0) and the Functional Living Index-Emesis (FLIE).

Results

Baseline characteristics were comparable between the two groups ($P > 0.05$). In the acute period, the two groups showed no significant disparity in nausea or vomiting severity ($P > 0.05$). Nevertheless, during the delayed phase, the intervention group demonstrated a significantly lower severity of vomiting relative to the control group ($P < 0.05$), and a borderline reduction in nausea severity was also observed ($P = 0.053$). FLIE scores indicated significantly better outcomes in the intervention group at both 24 hours and 24–120 hours post-chemotherapy ($P < 0.001$).

Conclusions

Aromatherapy, employed as a complementary intervention, proves beneficial in alleviating delayed emesis and enhancing QoL for patients on chemotherapy. The current findings provide a rationale for integrating aromatherapy into standard practice as a supportive antiemetic modality.

Introduction

Despite advances in cancer treatment that have improved survival, chemotherapy-induced nausea and vomiting (CINV) continues to be a highly distressing side effect. This ongoing issue reflects the considerable global health burden of the disease^[1]. Poorly managed CINV often leads to dose reductions, treatment delays, and alterations in antiemetic regimens, which collectively contribute to suboptimal therapeutic outcomes^[2]. A recent study reported a CINV incidence of 57% in patients receiving highly or moderately emetogenic chemotherapy, consistent with previous data documenting incidences of 60% for nausea and 36% for emesis^[3]. These observations underscore a persistent unmet demand for safer and more broadly effective antiemetic interventions.

Traditional use of plant-based agents for relieving nausea and vomiting is well documented, and their role as adjunctive therapies in oncology is becoming increasingly recognized^[4]. Previous studies have demonstrated the efficacy of aromatic extracts, such as ginger, peppermint oil, and fennel, in alleviating chemotherapy-induced nausea and vomiting (CINV) among cancer patients^[5–7]. The antiemetic properties of these agents are mediated via direct and indirect mechanisms during both acute and delayed phases; these mechanisms include antagonism of 5-HT₃ and NK₁ receptors, antihistaminic activity, anti-inflammatory and antioxidant actions, prokinetic effects, and the reduction of substance P^[4, 8]. *Cinnamomum camphora* var. *borneol*, a chemotype of *Cinnamomum* within the family Lauraceae, is characterized by an essential oil rich in natural borneol and is primarily distributed in South China^[9, 10]. The main component of *Cinnamomum camphora* chvar. *Borneol essential oil* (*BEO*) is D-borneol (D-borneol, C₁₀H₁₈O)^[11]. Owing to its potent pharmacological activity, favorable safety profile, and low potential for drug resistance, *BEO* is extensively utilized as an adjuvant or "guide" drug in traditional Chinese medicine formulations^[12]. Clinical trials have indicated that *BEO* possesses multifaceted biological activities, including anti-inflammatory, analgesic, antibacterial, and antioxidant properties, as well as cognitive benefits^[11, 13, 14]. The therapeutic efficacy of *BEO* is attributed to the synergistic or cumulative effects of its constituents; its clinical value is further underscored by its superior medicinal effects compared to synthetic camphor and L-borneol^[14]. However, limited research has investigated the efficacy of *BEO* in alleviating CINV in cancer patients, and existing studies exhibit heterogeneity regarding dosage, administration timing, routes of delivery, chemotherapy regimens, and cancer types. Consequently, definitive clinical conclusions and recommendations remain elusive.

This study aims to evaluate the efficacy of *BEO* in mitigating the severity of nausea and/or vomiting in cancer patients undergoing chemotherapy regimens containing cisplatin or carboplatin.

Materials and methods

Study design

The design of this study was a randomized, double-blind, placebo-controlled trial. The protocol was approved by the Ethics Committee of the Drug Clinical Trial Institution at Sun Yat-sen Memorial Hospital, Sun Yat-sen University (Guangzhou, China). The study was conducted in strict accordance with the Declaration of Helsinki, the Belmont Report, the CIOMS guidelines, and the International Conference on Harmonization Good Clinical Practice (ICH-GCP) standards. All study procedures adhered to GCP principles to ensure the protection of the health and rights of the participants. This research project has been registered on the Chinese Clinical Trial Registry with registration number ChiCTR2600129554.

Sample size determination was based on a 2×2 crossover design, assuming a statistical power of 90% and a type I error rate of 5%^[15, 16]. To account for potential attrition, a 20% dropout rate was incorporated, resulting in a requirement of 54 participants per group and a total enrollment of 108 subjects. All patients provided written informed consent prior to study inclusion. The recruitment and follow-up

phases were conducted between April 2025 and January 2026, with a total study duration of 306 days (approximately 10 months).

Study population

Eligibility criteria required that participants be adults with a histologically confirmed malignancy, currently receiving a platinum-based doublet chemotherapy regimen. Candidates were also required to have a projected life expectancy of more than 6 months and an ADL score reflecting either full functional independence or only mild dependency. Those with olfactory dysfunction or respiratory disorders (e.g., asthma, rhinitis) were not eligible. All enrolled individuals provided written informed consent before study entry.

Exclusion criteria: The exclusion criteria encompassed a known allergy to any component of the study product; the administration of other antiemetic agents within 24 hours preceding chemotherapy; and vomiting attributable to opioid use or metabolic imbalances (e.g., electrolyte disorders). Patients with brain metastases, intestinal obstruction, severe cardiovascular disease, hepatic or renal dysfunction, respiratory conditions, active infectious diseases, or other significant gastrointestinal comorbidities were excluded. Additionally, patients receiving concurrent chemoradiotherapy were ineligible for participation.

Procedures

Prior to the formal initiation of the study, a drop of essential oil will be applied to the inner wrist of each patient to screen for potential allergic reactions or headache symptoms; only patients demonstrating no sensitivity to the essential oil will be included. Eligible participants will be randomly assigned to groups using a pre-defined computer-generated list (Power Analysis and Sample Size, PASS). The study cohort will be divided into two groups: an intervention group (n = 54), receiving aromatherapy combined with routine care, and a control group (n = 54), receiving routine care only. Additionally, all enrolled patients will receive standard antiemetic prophylaxis for highly emetogenic chemotherapy (HEC), in accordance with the Multinational Association of Supportive Care in Cancer (MASCC) and the European Society of Medical Oncology (ESMO) guidelines; this regimen consists of an NK-1 receptor antagonist and a 5-HT3 receptor antagonist on day 1, and dexamethasone from day 1 to day 4^[17].

The essential oils will be prepared by the research team prior to each intervention. To ensure a standardized dosage and administration method, three drops of essential oil will be applied to a 5 cm × 5 cm sterile gauze pad using aseptic technique. The gauze will be secured to the patient's collar with a safety pin five minutes prior to the initiation of chemotherapy. This placement ensures a distance of approximately 20 cm from the patient's nose, facilitating continuous inhalation of the aroma throughout the chemotherapy session.

The essential oils utilized in this study will be sourced from certified suppliers and verified to comply with established quality standards. The test formulation comprises *Cinnamomum camphora* var. *borneol*

essential oil, *Oryza sativa* extract, and tocopheryl acetate. Notably, the formulation contains 50% Cinnamomum camphora var. borneol essential oil, which is characterized by a distinct borneol aroma derived from natural plant sources.

Participants will be evaluated at three time points: prior to chemotherapy, and at 24 and 120 hours post-chemotherapy. They are required to complete the Common Terminology Criteria for Adverse Events (CTCAE 5.0)^[18] and the Functional Living Index-Emesis (FLIE)^[19] questionnaires. To ensure the accuracy of data recording, all patients were provided with standardized definitions of variables^[18]: nausea was defined as a disorder characterized by a queasy sensation and/or the urge to vomit, while vomiting was defined as a disorder characterized by the reflexive act of ejecting gastric contents through the mouth.

Assessments

To assess nausea and vomiting severity, we utilized the CTCAE v5.0, a system released by the U.S. National Cancer Institute in November 2017 that currently serves as the universal grading tool for AEs in both clinical trials and oncology practice. Its standardized terminology ensures efficient communication of treatment-related safety data and promotes systematic AE management^[18]. Separately, the Functional Living Index-Emesis (FLIE) was employed to evaluate how nausea and vomiting affect patients' daily functioning. Scoring for the FLIE ranges from 18 to 126 overall, with subscale scores of 9 to 63; higher totals reflect better preservation of daily activities, and a score over 108 indicates that daily life is not significantly affected^[19]. Both questionnaires were completed at three predetermined timepoints: prior to chemotherapy, as well as 24 hours and 120 hours after administration.

Throughout the clinical trial, investigators are required to truthfully and comprehensively document all adverse events (AEs) in the case report form, irrespective of their causal relationship to the investigational drug. These records must detail clinical manifestations, onset time, severity, duration, interventions implemented, and outcomes. Furthermore, detailed documentation of concomitant medications is essential to facilitate the analysis of potential correlations between AEs and the investigational product. In the event of a serious adverse event (SAE), investigators must provide immediate medical intervention and submit a written report to the ethics committee within 24 hours, regardless of suspected causality. Concurrently, the SAE Report Form must be completed and submitted to the hospital's adverse reaction monitoring center. SAE records should comprehensively document symptoms, severity, time of onset and treatment, specific measures taken, follow-up details, and the final outcome.

Data Analysis

Data were analyzed using SPSS 25.0. Normality was checked via the Shapiro–Wilk test and Q–Q plots. Normally distributed continuous data are presented as mean $\pm$ SD and were compared using the t-test (paired t-test for paired samples) or one-way ANOVA for multiple groups. Non-normally distributed data

are expressed as median (IQR) and were analyzed using the Mann–Whitney U test, Kruskal–Wallis H test, or Wilcoxon signed-rank test, as appropriate. Categorical variables were compared using the Chi-square or Fisher's exact test. Correlations were assessed by Pearson's or Spearman's rank correlation coefficient. A two-sided $P < 0.05$ was considered statistically significant.

Results

A total of 110 participants were initially recruited. Two subjects withdrew from the study due to cancer progression necessitating a modification of their chemotherapy regimen. Consequently, 108 participants were enrolled and analyzed, with 54 patients assigned to each of the intervention and control groups. Baseline comparability between the two groups was assessed across demographic and clinical variables. The results indicated that the groups were well-balanced, with no statistically significant differences observed in any characteristics (all $P > 0.05$). The demographic and clinical characteristics of the 108 participants are presented in Table 1.

Patient characteristics

The mean age of the participants was comparable between the intervention (54.56 ± 2.13 years) and control (55.78 ± 2.12 years) groups, with no statistically significant difference observed (*Mann-Whitney U* = 1364, $P = 0.563$). Similarly, the mean body mass index (BMI) did not differ significantly between the groups (23.00 ± 0.49 vs. 22.84 ± 0.44 ; $U = 1386$, $P = 0.658$). Regarding gender distribution, the proportion of males and females was balanced across the groups (intervention: 36 males, 18 females; control: 35 males, 19 females), with no significant difference detected ($\chi^2 = 0.041$, $P = 0.839$). In terms of marital status, the vast majority of patients in both groups were married ($n = 48$ in each group). The distribution of educational levels was similar across the two groups ($\chi^2 = 0.631$, $P = 0.427$), with "Junior high school" being the most common category in both (intervention: 21, control: 18).

Regarding disease and treatment characteristics, the distribution of tumor stages was comparable between the two groups ($\chi^2 = 0.138$, $P = 0.710$), with Stage IV being the most prevalent in both the intervention ($n = 36$, 66.7%) and control ($n = 29$, 53.7%) cohorts. The proportion of patients with comorbidities showed no significant difference ($\chi^2 = 0.333$, $P = 0.564$). Functional independence in basic activities of daily living was predominant, with 41 patients (75.9%) in the intervention group and 39 (72.2%) in the control group classified as having "no dependency" ($\chi^2 = 1.087$, $P = 0.581$). Chemotherapy duration was also comparable between groups ($\chi^2 = 4.317$, $P = 0.115$), with the majority of patients receiving infusions for more than 4 hours (intervention: $n = 38$, 70.4%; control: $n = 42$, 77.8%). Finally, patients' expectations regarding post-chemotherapy nausea were similarly distributed across both groups ($\chi^2 = 1.125$, $P = 0.771$).

The intervention and control groups exhibited statistical equivalence across all baseline characteristics, confirming the validity of the randomization process and suggesting that subsequent disparities in outcomes are attributable to the intervention. None of the patients presented with bowel obstruction,

vestibulopathy, clinically significant electrolyte abnormalities, uremia, gastric atony, or severe psychiatric disorders, all of which have been identified as potential risk factors for CINV^[20].

Table 1
General information about patients in the two groups

Item	Intervention Group(n = 54)	Control Group(n = 54)	Statistic value	P value
Age (years, mean ± SD)	54.56 ± 2.13	55.78 ± 2.12	1364 ^U	0.563
BMI (mean ± SD)	23.00 ± 0.49	22.84 ± 0.44	1386 ^U	0.658
Gender (n, %)				
Male	36(66.7)	35(64.8)	0.041	0.839
Female	18(33.3)	19(35.2)		
Marital Status (n, %)				
Unmarried	6(11.1)	5(9.3)	0.358	0.550
Married	48(88.9)	48(88.8)		
Divorced	0(0)	1(1.9)		
Education Level (n, %)				
Primary school or below	7(12.9)	13(24.1)	0.631	0.427
Junior high school	21(38.9)	18(33.3)		
Senior high school	9(16.7)	10(18.5)		
Technical secondary school	4(7.4)	2(3.7)		
Junior college	4(7.4)	7(12.9)		
Undergraduate	9(16.7)	3(5.6)		
Postgraduate or above	0(0)	1(1.9)		
History of Nausea and Vomiting (non-chemotherapy related) (n, %)				
no	30(55.6)	32(59.3)	0.151	0.697
yes	24(44.4)	22(40.7)		
Tumor Stage (n, %)				
Stage I	5(9.3)	3(5.6)	0.138	0.710
Stage II	5(9.3)	8(14.8)		
Stage III	7(12.9)	8(14.8)		
Note: U = Mann-Whitney U test; χ^2 = Chi-square test.				

Item	Intervention Group(n = 54)	Control Group(n = 54)	Statistic value	P value
Stage IV	36(66.6)	29(53.7)	0.333	0.564
Unknown	1(1.9)	6(11.1)		
Comorbidities (n, %)				
no	26(48.1)	29(53.7)		
yes	28(51.9)	25(46.3)		
Activities of Daily Living (BADL) Assessment (n, %)			1.087	0.581
Independent	41(75.9)	39(72.2)		
Mildly dependent	13(24.1)	14(25.9)		
Moderately dependent	0(0)	1(1.9)		
Duration of Chemotherapy (n, %)			4.317	0.115
< 2 hours	6(11.1)	1(1.9)		
2–4 hours	10(18.5)	11(20.3)		
> 4 hours	38(70.4)	42(77.8)		
Expectation of Nausea (Anticipated post-chemotherapy nausea) (n, %)			1.125	0.771
Mild	31(57.4)	35(64.8)		
Moderate	12(22.2)	9(16.7)		
Severe	2(3.7)	3(5.6)		
No	9(16.7)	7(12.9)		
Note: U = Mann-Whitney U test; χ^2 = Chi-square test.				

Acute Phase Nausea and Vomiting Symptoms

The severity of acute nausea and vomiting (occurring within 24 hours of chemotherapy) was compared between groups and is presented in Table 2. For nausea, Grade I was observed in 79.6% (n = 43) of the intervention group, Grade II in 16.7% (n = 9), and Grade III in 3.7% (n = 2); in the control group, the corresponding rates were 63.0% (n = 34), 31.5% (n = 17), and 5.6% (n = 3). Vomiting was absent (Grade 0) in 92.6% (n = 50) of intervention patients and 88.9% (n = 48) of controls. No statistically significant differences were detected between the groups for acute nausea ($\chi^2 = 3.713$, $P = 0.156$) or vomiting ($\chi^2 = 0.541$, $P = 0.763$), suggesting that the two arms were well matched in terms of acute CINV severity.

Table 2
Comparison of acute-phase CINV severity between the two groups

Group	n	Acute-phase nausea grading				Acute-phase vomiting grading			
		0	I	II	III	0	I	II	III
Intervention Group	54	0	43	9	2	0	50	3	1
Control Group	54	0	34	17	3	0	48	5	1
Statistic value	3.713	0.541							
P value	0.156	0.763							

Delayed-phase Nausea and Vomiting Symptoms

A comparison of delayed-phase CINV severity (24–120 hours post-chemotherapy) between the two groups is presented in Table 3. For delayed nausea, Grade I was noted in 92.6% (n = 50) of the intervention group and 75.9% (n = 41) of the control group; Grade II in 7.4% (n = 4) versus 22.2% (n = 12); and Grade III in none of the intervention patients versus 1.9% (n = 1) of controls. The observed difference approached but did not attain statistical significance ($\chi^2 = 5.890$, $P = 0.053$). With respect to delayed vomiting, complete absence (Grade 0) was recorded in all 54 intervention patients (100%) and in 51 control patients (94.4%), while Grade I vomiting occurred in 3 controls (5.6%). This between-group difference was statistically significant ($\chi^2 = 6.464$, $P = 0.039$), indicating that the intervention was effective in lessening delayed-phase vomiting.

Table 3
Comparison of delayed-phase CINV severity between the two groups

Group	n	Delayed-phase nausea grading				Delayed-phase vomiting grading			
		0	I	II	III	0	I	II	III
Intervention Group	54	0	50	4	0	0	54	0	0
Control Group	54	0	41	12	1	0	51	3	0
Statistic value	5.890	6.464							
P value	0.053	0.039							

Comparison of quality of life between the two groups

A comparison of quality-of-life scores, assessed using the FLIE at three predefined timepoints, is shown in Table 4. No significant baseline difference was detected between the intervention (124.31 ± 5.32) and control (121.53 ± 11.56) groups ($U = 1294.50$, $P = 0.138$), indicating comparable initial QoL. At 24 hours following chemotherapy, significantly higher FLIE scores were observed in the intervention group (119.35 ± 10.77) relative to controls (110.46 ± 10.08 ; $U = 761.00$, $P < 0.001$). In the delayed phase (24–

120 hours post-treatment), the intervention arm continued to exhibit superior scores (123.26 ± 5.59 vs. 110.19 ± 12.50 ; $U = 492.50$, $P < 0.001$).

Table 4
Functional Living Index - Emesis (FLIE)

Item(mean ± SD)	Intervention Group (n = 54)	Control Group(n = 54)	Statistic	P
Pre-chemotherapy	124.31 ± 5.32	121.53 ± 11.56	1294.50 ^U	0.138
Within 24 hours post-chemotherapy	119.35 ± 10.77	110.46 ± 10.08	761.00 ^U	<0.001
24–120 hours post-chemotherapy	123.26 ± 5.59	110.19 ± 12.50	492.50 ^U	<0.001
Note: U = Mann-Whitney U test.				

Discussion

A randomized, double-blind, placebo-controlled design was employed to test the efficacy of *BEO* aromatherapy for preventing CINV and improving QoL in patients on platinum-based regimens. While no significant acute-phase CINV reduction was achieved, the intervention showed promising effects on delayed vomiting and produced significant QoL gains during both phases. Associations with better vomiting-specific QoL and fewer delayed episodes were also observed, but these were not judged clinically relevant. Because MCID values for nausea/vomiting incidence, vomiting frequency, and malnutrition have not been established, clinical significance was determined through professional judgment. The null hypothesis—that *BEO* is ineffective for anticipatory or acute CINV and HRQoL—cannot be rejected based on current evidence, and potential confounders were not found to have a meaningful impact. Further well-powered investigations that assess both CINV and HRQoL are warranted to confirm these results and to clarify how improved CINV control might affect everyday activities. *BEO* proved safe, with no serious adverse events reported in relation to the intervention.

The chemical composition of *BEO* closely resembles that of peppermint oil, being primarily characterized by monoterpenes and sesquiterpenes known to facilitate digestion and exert antioxidant and antibacterial activities^[4, 14]. The observed reduction in nausea and vomiting scores in this study may be attributed to the multifaceted pharmacological properties of *BEO*, including analgesic, anti-inflammatory, and antioxidant effects, as well as the amelioration of cognitive dysfunction. These findings align with prior in vitro investigations regarding the regulatory effects of these constituents on gastrointestinal motility^[4, 14].

During the acute phase (within 24 hours post-chemotherapy), no statistically significant differences were observed between the intervention and control groups regarding the severity of nausea ($P = 0.156$) or vomiting ($P = 0.763$). All participants in both groups received standard antiemetic prophylaxis in

accordance with MASCC/ESMO guidelines, comprising NK-1 receptor antagonists, 5-HT3 receptor antagonists, and dexamethasone^[22, 23]. This potent regimen likely achieved high efficacy in controlling chemotherapy-induced nausea and vomiting (CINV), thereby limiting the potential for additional improvement from complementary interventions. Indeed, 92.6% of patients in the intervention group and 88.9% in the control group did not experience acute vomiting, underscoring the effectiveness of standard pharmacologic prophylaxis.

In contrast to the acute phase, the intervention showed marked efficacy during the delayed phase (24–120 hours post-chemotherapy). Complete prevention of delayed vomiting was achieved in all 54 patients (100%) in the intervention group, versus 51 patients (94.4%) in the control group, a difference that was statistically significant ($P = 0.039$). Regarding delayed nausea, although the between-group difference did not reach statistical significance ($P = 0.053$), a favorable trend was observed in the intervention group: grade I nausea occurred in 92.6% of patients, compared with 75.9% in the control group, and no grade III nausea was reported in the intervention group. This phase-specific efficacy may be attributed to the pharmacological properties of the active components within the essential oil. Consistent with prior findings, aromatherapy appears to be more effective in alleviating delayed chemotherapy-induced nausea and vomiting, whereas its impact on the acute phase is relatively limited^[5, 24, 25].

A principal finding of this study was the significant improvement in quality of life, as quantified by the Functional Living Index-Emesis (FLIE). Although baseline FLIE scores were comparable between the groups ($P = 0.138$), the intervention group exhibited significantly higher scores both within the first 24 hours (119.35 ± 10.77 vs. 110.46 ± 10.08 , $P < 0.001$) and during the 24–120 hour interval following chemotherapy (123.26 ± 5.59 vs. 110.19 ± 12.50 , $P < 0.001$). Notably, mean FLIE scores in the intervention group consistently exceeded the established threshold of 108, indicating that chemotherapy-induced nausea and vomiting (CINV) did not substantially impact patients' daily functioning. Conversely, scores in the control group remained below this threshold during both post-chemotherapy assessments, suggesting clinically meaningful functional impairment. The observed enhancement in quality of life surpassed the magnitude expected based solely on the reduction in CINV severity. This discrepancy implies that aromatherapy may confer benefits extending beyond direct antiemetic effects, potentially mediated through anxiolytic and mood-enhancing properties. Specifically, the olfactory stimulation provided by borneol may alleviate anxiety and improve psychological well-being, factors known to modulate symptom perception and overall quality of life. These observations align with prior research on aromatherapy in oncology populations, wherein improvements in emotional well-being frequently exceed symptom-specific outcomes^[26].

Study Strengths and Limitations

The present study possesses several notable methodological strengths. The randomized, double-blind design minimized potential bias and bolstered internal validity. Furthermore, the utilization of standardized, validated instruments—specifically CTCAE 5.0 and FLIE—ensured reliable and comparable outcome assessment. The intervention protocol was rigorously standardized regarding dosage,

application method, and timing, thereby enhancing reproducibility. Additionally, the comprehensive collection of baseline characteristics facilitated the confirmation of group comparability across multiple demographic and clinical variables.

However, several limitations warrant acknowledgement. First, the absence of a placebo control utilizing an inert aromatic substance precludes the definitive distinction between the specific pharmacological effects of borneol and the non-sensory effects of aromatherapy. Future investigations should consider employing an odorless placebo or an alternative essential oil devoid of known antiemetic properties. Second, the single-center design and a relatively homogeneous population—predominantly Han Chinese patients with advanced solid tumors—may constrain the generalizability of the findings to broader populations and diverse healthcare settings. Third, the study duration was restricted to the initial chemotherapy cycle; thus, the persistence of therapeutic benefits across multiple cycles remains undetermined. Fourth, although patients with known olfactory abnormalities were excluded, the lack of formal olfactory function testing or verification of aroma perception may have implications for treatment fidelity. Finally, while the sample size was adequate for detecting differences in vomiting outcomes, it may have been underpowered to detect modest yet clinically significant differences in nausea severity, as suggested by the borderline P-value observed for delayed nausea ($P = 0.053$).

Clinical Implications and Future Directions

The findings of this study hold significant clinical implications. Aromatherapy utilizing *Bergamot Essential Oil (BEO)* constitutes a safe, cost-effective, and non-invasive complementary intervention readily integrable into standard oncology care. Its demonstrated efficacy in mitigating delayed-phase vomiting—a clinically refractory condition frequently unresponsive to conventional antiemetics—establishes its value as an adjunct to pharmacologic prophylaxis. Furthermore, the observed enhancement in quality of life, even within the context of contemporary antiemetic regimens, suggests that aromatherapy fulfills critical patient needs extending beyond mere symptom management.

Future investigations should prioritize several key domains. First, multicenter trials encompassing diverse patient populations are warranted to validate the generalizability of these results. Second, studies aimed at determining the optimal concentration, frequency, and duration of exposure are essential to refine clinical protocols. Third, elucidation of the underlying neurobiological mechanisms, potentially via functional neuroimaging, could provide critical insights into how olfactory stimulation modulates emetic pathways. Fourth, longitudinal follow-up across multiple chemotherapy cycles is necessary to establish the sustainability of therapeutic benefits. Finally, comparative effectiveness analyses against other complementary modalities (e.g., acupuncture, ginger, psychological interventions) are required to inform evidence-based clinical decision-making.

Conclusions

This randomized controlled trial demonstrates that aromatherapy utilizing *Cinnamomum camphora* *chvar. borneol essential oil (BEO)*, as an adjunct to standard antiemetic prophylaxis, significantly mitigates

delayed-phase vomiting and enhances quality of life in patients undergoing platinum-based chemotherapy. Although acute-phase chemotherapy-induced nausea and vomiting (CINV) was not significantly altered—likely attributable to the efficacy of standard pharmacologic prophylaxis—the intervention yielded significant benefits during the delayed phase. The complete remission of delayed vomiting and the substantial improvements in FLIE scores within the intervention group represent clinically meaningful outcomes, supporting the integration of aromatherapy into comprehensive CINV management strategies. Consequently, as a safe, well-tolerated, and patient-centered intervention, borneol-based aromatherapy constitutes a valuable complementary approach to optimizing supportive care in oncology.

Declarations

Funding:

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Ethics approval:

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University Sun Yat-sen Memorial Hospital, Sun Yat-sen University (March 27, 2025/SYSKY-2025-201-01)

This research project has been registered on the Chinese Clinical Trial Registry with registration number ChiCTR2600129554.(ChiCTR2600129554||<http://www.chictr.org.cn/>, August 6th, 2026)

Author Contribution

All authors contributed to the study conception and design. Jie Chen is responsible for the quality control of project implementation. Material preparation, data collection and analysis were performed by Jinmei Chen, Jinmei Liang, Yanhui Zhang and Jie Yang. The first draft of the manuscript was written by Ying Chen and all authors commented on previous versions of the manuscript. Xinxin Xie is responsible for the original text revision and proofreading. All authors read and approved the final manuscript.

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