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Effects of *Zingiber officinale* in complementary care for postoperative complications: A systematic review

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ABSTRACT

Introduction: Postoperative complications are among the most common complications related to surgery or anesthetics, leading to longer treatment duration and extended hospitalization. So, we decided to explore the clinical outcomes of *Zingiber officinale* or ginger on postoperative complications.
Methods: This study adhered to the PRISMA 2020 guidelines. To find relevant studies published before April 2, 2025, a comprehensive search was done in Scopus, Cochrane Library, Web of Science, and PubMed/MEDLINE. Predefined criteria for including and excluding studies were applied and duplicate entries were eliminated. The data extraction process concentrated on study characteristics, interventions, and key outcomes.
Results: The included studies demonstrated that *Z. officinale* was generally effective in alleviating the severity and frequency of postoperative nausea and vomiting (PONV) compared to standard antiemetics, with several studies reporting a significant decrease in nausea intensity, reduced need for antiemetic medications and improved patient satisfaction. However, the incidence of vomiting was not consistently affected. Moreover, aromatherapy with ginger showed variable effectiveness, with some studies indicating borderline or non-significant effects. Regarding postoperative pain, ginger demonstrated comparable analgesic effects to nonsteroidal anti-inflammatory drugs in several trials, with significant pain reduction observed. Additional benefits included reduced postoperative shivering, anxiety scores, and decreased severity of post-cesarean abdominal distention. However, effects on bowel function and ileus were inconsistent.
Conclusion: *Z. officinale* shows promise as a safe complementary treatment for reducing postoperative complications in various surgical settings. However, additional clinical research is necessary to draw a more definitive conclusion.

Implication for health policy/practice/research/medical education:
Our review indicates that *Zingiber officinale* is a safe and effective complementary therapy for alleviating postoperative nausea, vomiting, and pain. This supports the integration of ginger into perioperative care protocols to improve patient outcomes and satisfaction, while potentially decreasing the dependence on traditional antiemetics and analgesics. Health policymakers should consider endorsing its use to promote a more holistic and cost-effective approach to surgical care. Meanwhile, clinicians are encouraged to thoughtfully incorporate ginger into postoperative management.
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Introduction

Postoperative complications following surgical procedures must be carefully minimized to protect the quality of surgical care. These unintended outcomes can significantly impact patient recovery and overall health, emphasizing the vital need for precise planning and execution in the operating room (1). The most common postoperative complications, such as postoperative nausea and vomiting (PONV), postoperative pain, postoperative fatigue (POF), postoperative cognitive dysfunction (POCD), and postoperative ileus, which are highly prevalent and require prophylactic regimens and

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meticulous anesthesia services according to protocols (2-5). Therefore, surgeons, anesthesiologists, and nurses should be aware of these postoperative complications and methods to reduce them to improve the quality of services provided in the hospital. The preventive strategies for controlling postoperative complications (including pain, PONV, etc.) can reduce additional costs, preserve patients' physiologic baseline, lead to prolonged hospitalization, impaired daily functioning, insomnia, and reduced overall health (6,7). Anesthesiologists and nurses play a crucial role in ensuring compliance with preoperative protocols, including patient preparation and assessment before surgeries, detailed review of the patient's biochemical tests and hemodynamic indicators, perioperative fluid management, considerations for reducing the side effects of anesthetic drugs and pain relief to reduce postoperative complications (8,9).

Medicinal plants and their active compounds can have high potential in complementary therapy due to their fewer side effects and effectiveness in various diseases (10-12). One safe and promising method to reduce postoperative complications is using plants and their derivatives in aromatherapy and extract administration (13,14).

Ginger, or the root of the *Zingiber officinale*, belongs to the *Zingiberaceae* family, which potentially has antioxidant, anti-inflammatory, and antimicrobial activities (15). It is mainly found throughout the subtropical and tropical areas of Asia, Africa, South America, and tropical and subtropical Asia, with India being the largest producer globally (16). The key bioactive components of Zingiber species encompass volatile oils, diarylheptanoids, gingerols, terpenoids, and flavonoids. Notably, gingerols are the primary functional compounds that impart ginger's distinctive pungent and aromatic qualities (16). This group of phenolic compounds, including shogaol, gingerones, gingerdiones, paradol, and zingerone, plays a significant role in the plant's medicinal properties (15,17). The primary active compounds in *Z. officinale* that contribute to its therapeutic and biological effects are illustrated in Figure 1. These active compounds, such as 6-gingerol, 6-shogaol, zingerone, and paradol, have revealed anti-inflammatory, antioxidant, anti-nausea, anticancer and antimicrobial properties in various research (15,18-22).

Numerous studies have been conducted on *Z. officinale* to reduce these adverse effects, revealing a practical impact on attenuating postoperative complications (23-25). However, some studies did not report positive effects, highlighting the need for further research (26-28). Considering the contradictory results in the studies' results and the importance of hospital services, in this systematic review we evaluated clinical outcomes of *Z. officinale* in managing postoperative complications.

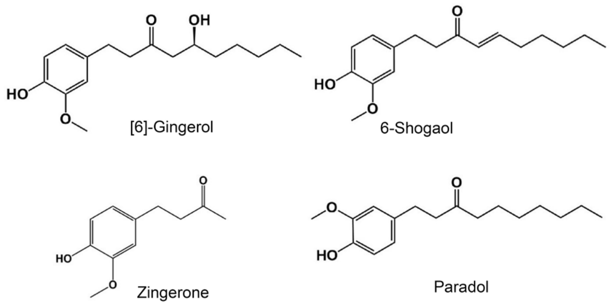

Figure 1. The most active compounds in *Zingiber officinale* responsible for its therapeutic and biological effects.

Materials and Methods

In this study, we followed the suggested protocols in the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (29). So, we followed the guidelines as follows:

Search strategy (database sources and keywords)

An extensive electronic search was performed across multiple high-coverage databases such as the Web of Science, PubMed/MEDLINE, Scopus, Cochrane Library, and the Embase databases on April 2, 2025, to find studies pertinent to our research objectives. In developing our search strategy, we employed Medical Subject Headings (MeSH) terms and common keywords from prior publications. We incorporated keywords extracted from published articles to ensure we included all relevant studies. In this study we used keywords such as: ((“*Zingiber officinale*” OR “Zingiberaceae” OR “Ginger” OR “Gingerol” OR “Shogaol” OR “Zingerone” OR “Paradol”) AND (“Post-surgery” OR “Postoperative” OR “Post-operative” OR “Postoperative complications” OR “Postsurgical” OR “After surgery” OR “Operation” OR “Anesthesia” OR “Isoflurane” OR “Sevoflurane” OR “Ropivacaine” OR “Desflurane” OR “Ketamine” OR “Propofol” OR “Bupivacaine”)).

In this systematic review, we also performed comprehensive searches in the specified databases and carefully examined pertinent publications. A concluding search was also conducted in related articles to guarantee that all relevant studies were collected. We transferred the peer-reviewed publications into EndNote 21.0.1 (Thomson Reuters, released July 25, 2023) and systematically eliminated duplicates to remove repeated entries.

Eligibility criteria

We included all types of clinical trials that investigated the effects of *Zingiber officinale* (ginger), administered in any form, on postoperative-associated symptoms in humans. Studies involving various kinds of surgical procedures were eligible. Mixed-intervention studies were included only if the specific effects of ginger could be clearly identified and analyzed separately. We specifically searched for postoperative complications and utilized the PICO framework to ensure focused and relevant

Table 1. PICO elements based on the study aims

Elements		Research aims
P	Population/Patient/Problem	Patients who underwent surgical procedures.
I	Intervention	Any *Zingiber officinale* administration or in combination with other drugs.
C	Comparison/Control	Patients receiving placebo, standard treatment, or no treatment as controls.
O	Outcome	Any effects and adverse events related to surgery and anesthesia were studied.

data collection, effective search strategies, and research questions (30) (Table 1).

We excluded publications such as reviews, letters to editors, case reports, theses, studies that were only available in abstracts or did not have full text accessible. Conference papers, books, and research published in non-English languages were also excluded.

Screening studies and full-text assessment

Two independent reviewers systematically screened the titles and abstracts of all retrieved articles using established inclusion and exclusion criteria. Articles that met the inclusion criteria were selected for full-text retrieval and further assessment. The same reviewers then independently evaluated the full-text records to confirm their eligibility. Any disagreements were addressed and resolved via consultation with a third reviewer.

Data collection and data processing

The data extraction form was used across the studies to collect crucial information, including the author, year of publication, patient population and surgery procedure, and specific parameters related to *Z. officinale* intervention, such as dosage, duration, and route of administration. Outcomes were evaluated through any complication due to surgery or anesthesia agents.

Quality assessment

This systematic review utilized the Cochrane Risk of Bias 2 (RoB 2) tool to evaluate potential bias in randomized controlled trials (RCTs) across critical domains, including the randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and the selection of reported results (31). To visualize these assessments, we used the Robvis package. A Summary Bar Plot illustrated the proportion of studies rated as 'Low risk,' 'Some concerns,' or 'High risk' within each domain. Additionally, a Traffic Light Plot provided a study-level overview of the risk of bias across all assessed domains (32).

Narrative synthesis

Data from the included studies were categorized and summarized based on the type of postoperative complication evaluated, such as PONV, pain, anxiety, gastrointestinal symptoms (including ileus and abdominal distention), and other surgery-related outcomes. The results were synthesized narratively due to the heterogeneity of the interventions (like ginger dosage, formulation, timing, and administration route) and the outcome measures across the studies. This methodology facilitated a structured comparison of findings while considering the variations in study design and clinical context.

Results

Search results

The initial electronic search identified 2,281 titles and abstracts. After removing 812 duplicates, we made additional exclusions: one article was excluded because it was published in a non-English language (33), and two studies were removed due to quasi-experimental design (34,35). Finally, 42 studies were included for final evaluation and review (23-28,36-71) (Figure 2).

Description of the included studies

Research indicated that ginger was effective in minimizing postoperative nausea and decreasing the reliance on antiemetic medications, especially during the initial hours following surgery. While its effects on vomiting are less consistent, some studies have reported reductions at specific intervals. Ginger has been shown to have comparable efficacy to metoclopramide and ondansetron, and when combined with ondansetron. When combined with ondansetron, it further enhanced the PONV. Additionally, oral ginger has demonstrated greater effectiveness than aromatherapy, which has shown limited impact (Table 2).

Studies on ginger's effects on postoperative pain have shown mixed but generally supportive results. In some cases, ginger provided pain relief comparable to standard analgesics such as ibuprofen and diclofenac. Moreover, it also reduced the mean VAS score. However, some findings indicated no significant change in pain scores or outcomes like recovery time, discharge, or need for additional painkillers. Topical applications, such as ginger ointment for episiotomy wounds, did not show significant effects, though some clinical benefits were reported (Table 3).

As Table 4 shows, ginger did not reduce the incidence of abdominal distention following a cesarean section. However, it alleviated the severity by the fourth day and improved appetite. For postoperative anxiety, ginger extract significantly lowered anxiety levels and post-spinal puncture shivering, postoperative ileus.

We utilized the RoB 2 tool to evaluate the risk of bias in RCTs. Figures 3 and 4 present the risk assessment results,

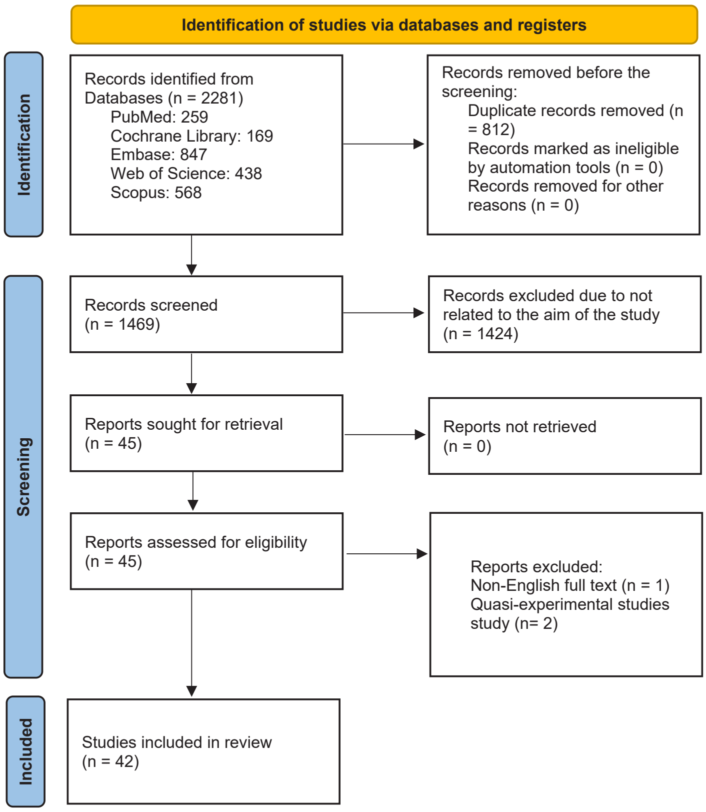

Figure 2. PRISMA flowchart for including studies in the systematic review.

including a traffic light plot and a summary bar plot.

The overall risk of bias across the included studies was generally acceptable, with the majority (57%) rated as having "some concerns," 34% rated as "low risk," and only 9% classified as having a "high risk" of bias. Most studies demonstrated adequate methodological rigor regarding randomization and handling of outcome data.

Discussion

This systematic review aimed to investigate the effects and mechanisms of *Z. officinale* on postoperative complications. In the following, we examined the possible mechanisms of *Z. officinale* on various side effects explored in the included studies.

Mechanistic effects of *Z. officinale* on PONV

Previous reviews have shown that ginger can reduce the severity of nausea and the need for rescue antiemetics compared to a placebo, and it had no complications in the studied patients. However, its effectiveness in preventing nausea and vomiting may not become apparent until six hours after surgery. Additionally, ginger demonstrated greater efficacy in lowering the incidence of nausea than standard prophylactic antiemetics and can be applied as an alternative therapy for PONV prophylaxis (22,72).
Various factors can affect the effectiveness of *Z. officinale*, including patient gender, age, types of anesthetics (inhalational, sedatives, and opioid analgesics), type of surgery, motion sickness, obesity, previous history, smoking, opioids, race, postoperative pain, ginger dose, and time (statistically significant over 6 h after operation) of drug use (22,72,73). PONV is influenced by various factors, such as patient-related factors, the type of surgery performed, and elements associated with preoperative, intraoperative, and postoperative anesthesia management (74). The most important mechanisms of ginger in attenuating PONV are as follows:

Serotonin or 5-hydroxytryptamine 3 (5-HT3) receptor antagonism

The emetic response is triggered by the release of 5-HT, which sets off a series of neuronal events involving both the central nervous system (CNS) and the gastrointestinal tract (74). Ginger extracts, particularly their pungent arylalkane constituents like [6]-gingerol, have demonstrated a concentration-dependent inhibition of human 5-HT3 receptors. The physiological significance of this inhibitory effect on native 5-HT3 receptors was confirmed using whole-mount preparations of the human submucosal plexus (75). Moreover, Haniadka et al indicated that the most important active compounds of *Z. officinale*, including [6]-Gingerol, [8]-Gingerol, [10]-Gingerol, and 6-shogaol, could act as antagonists of 5-hydroxytryptamine 3 (5-HT3) and neurokinin-1 (NK-1) receptors and exhibit antihistaminic properties. Additionally, these compounds contribute to enhanced

Table 2. Summary of studies on ginger use for postoperative nausea and vomiting (PONV)

Study (First author, year)	Country	Participants	Treatment details (Dosage and duration)	Key findings
Bone (1990) (41)	United Kingdom	Women who underwent major gynecological surgery	Active capsule with ginger root powder at 0.5 g dosage orally administered before the operation	The occurrence of nausea in the groups treated with either ginger root or metoclopramide was similar.
Phillips (1993) (58)	United Kingdom	Women admitted for elective minimally invasive gynecological operation	Two capsules containing 1 g of powdered ginger root were administered 1 h before the induction of anesthesia.	The need for postoperative antiemetics was decreased in patients who were given ginger.
Arfeen (1995) (38)	Australia	Women undergoing gynecological laparoscopic surgery under general anesthesia	500 mg of ginger (2 capsules) was orally administered postoperatively	Decreased the occurrence of PONV
Visalyaputra (1998) (70)	France	Patients listed for cataract surgery under regional anesthesia	Ginger 2 g (four capsules of 0.5 g) was administered orally 1 h prior to the start of anesthesia induction	Not effective in lowering the rate of PONV
Eberhart (2003) (26)	Germany	Women undergoing gynecologic laparoscopies	300 mg (1 capsule containing 100 mg of ginger × 3 times) or 600 mg (2 capsules × 3 times) on the day of surgery preoperatively and at 3 and 6 h postoperatively	Ginger is effective in reducing PONV
Pongrojpaw (2003) (59)	Thailand	Women undergoing gynecologic laparoscopies	2 capsules of ginger, with each capsule containing 0.5 g of ginger powder, 1 h prior to the surgery	The occurrence and rate of vomiting did not show any significant difference. However, the vomiting in the ginger group at 2 and 4 h was reduced.
Apariman (2006) (37)	Thailand	Hospitalized patients who underwent laparoscopic surgery for benign gynecological conditions	Participants took three capsules, each containing 0.5 g of ginger powder, 1 h prior to the procedure	Ginger has demonstrated effectiveness in preventing nausea and has shown borderline significance in reducing vomiting.
Nanthakomon (2006) (56)	Thailand	Women who underwent major gynecologic surgery	The ginger group was given two capsules, each containing 0.5 g of ginger powder, administered 1 h prior to surgery.	The visual analog nausea score and vomiting were reduced in the ginger group.
Tavlan (2006) (67)	Turkey	Patients receiving general anesthesia for thyroidectomy	0.5 g of ginger was administered as premedication 1 h before surgery	The combined use of dexamethasone and ginger did not show greater effectiveness than dexamethasone alone in preventing PONV in patients.
Nale (2007) (55)	India	ASA I and II patients scheduled for non-emergency surgery with a potential risk for PONV	The ginger powder was administered one hour before the operation and thereafter at 8-h intervals for a total of 24 h.	Ginger is effective in reducing PONV.
Hunt (2013) (43)	United States	Patients experiencing PON	Aromatherapy using ginger oil or a blend of ginger, spearmint, peppermint, and cardamom applied after surgery.	Reduced nausea and need for antiemetic medications
Kalava (2013) (27)	United States	Cesarean section patients	One gram of powdered ginger was administered orally 2 h after the surgery.	Decreased the number of periods of intraoperative nausea; however, it did not affect the occurrence of nausea and vomiting
Montazeri (2013) (53)	Iran	Patients undergoing surgical procedures	4 capsules containing 250 mg ginger was applied 1 h before surgery	There were no changes in vomiting at any time; however, it reduced postoperative nausea.
Mandal (2014) (50)	India	Patients undergoing ambulatory surgery	Two capsules containing 0.5 mg of ginger each were administered 1 h before surgery.	Ginger with ondansetron significantly reduced PONV compared to ondansetron alone.
Adib-Hajbaghery (2015) (36)	Iran	Patients undergoing post-nephrectomy	The ginger aroma was applied by inhalation and repeated every 30 min for two subsequent h.	Inhaling ginger aroma significantly reduced post-nephrectomy nausea intensity and the number of vomiting episodes.
Kiberd (2016) (47)	Canada	Children with neurodevelopmental diseases and undergoing elective day surgery	A proprietary aromatherapy blend was applied, including *Z. officinale, Lavandula angustifolia, Mentha Spicata*, and *Mentha xpiperita*.	Aromatherapy demonstrated a minor, non-significant effect size in managing PONV in comparison with the control group.

Table 2. Continued

Study (First author, year)	Country	Participants	Treatment details (Dosage and duration)	Key findings
Zeraati (2016) (71)	Iran	Cesarean section patients	25 drops of ginger extract blended in 30 cc of water were applied one hour before the operation	It reduced nausea and vomiting during cesarean section
Seidi (2017) (62)	Iran	Patients receiving cataract surgery performed under general anesthesia.	The first group received one ginger capsule containing 1 g, while the second group was given two capsules, each with 500 mg.	Nausea and vomiting after the operation were less frequent and intense in the group that took two 500 mg tablets of ginger than in the other two groups.
Bameshki (2018) (39)	Iran	Patients undergoing laparoscopic cholecystectomy	Two capsules containing 250 mg of ginger were administered one hour before surgery.	Reduced severity of PONV in women who were undergoing laparoscopic cholecystectomy
Soltani (2018) (66)	Iran	Patients undergoing laparoscopic cholecystectomy	500 mg of ginger was administered 1 h before surgery.	Reduced severity of PONV in women scheduled for laparoscopic cholecystectomy.
Fearrington (2019) (42)	United States	Surgical patients	Inhalers were used with four drops of peppermint or ginger essential oils or a mix of two drops from each.	Decreased the need for antiemetics to treat PONV
Karaman (2019) (46)	Turkey	PONV patients who underwent general anesthesia	Patients, after undergoing surgery, received two drops of ginger, lavender, or rose oil by aromatherapy, and they inhaled its scent for 5 min	Reduced postoperative nausea scores effectively and reduced the need for vomiting and antiemetic drugs.
Sedigh Maroufi (2019) (61)	Iran	Patients undergoing eye surgery	Patients received capsules of ginger 1 g one h before surgery	Ginger is effective in reducing PONV in 2 h after surgery. No changes in vital signs were seen.
Kamali (2020) (45)	Iran	Patients undergoing abdominal hysterectomy	Patients orally took ginger (1 g) before and after the anesthesia	The impact of ginger on PONV was more significant than that of dexmedetomidine.
Naemi (2020) (54)	Iran	Patients underwent general anesthesia	4 ginger capsules with a hint of lemon were administered 30 min before the operation	No significant difference in PONV was seen between the four drugs (ginger and other antiemetics)
Pakniat (2020) (57)	Iran	Cesarean-section patients under spinal anesthesia	Patients were given 1 gram of oral ginger 30 min prior to undergoing spinal anesthesia.	Reduced PONV similar to metoclopramide.
Beiranvand (2022) (40)	Iran	Patients undergoing upper and lower limb operation	250 mg ginger capsules were administered 2 h before surgery.	Ginger effectively reduces PONV
Sihombing (2022) (65)	Indonesia	Elective surgical procedures patient	Ginger extract with pre-operative high-calorie drink	Reduced nausea and vomiting after the operation
Imani (2023) (44)	Iran	Cesarean-section patients under spinal anesthesia	One ginger capsule containing 1000 mg applied 1 h before surgery	Reduced the severity of PONV and no significant difference between the ginger and ondansetron were seen.
Sforza (2023) (63)	United Kingdom	Women undergoing breast augmentation surgery	3 drops of ginger oil (110 mg) provided on their laryngeal mask before insertion	Reduced the severity of PONV in patients.
Ishikawa (2025) (23)	Japan	Oral surgery under general anesthesia	Essential oils of ginger, peppermint, and lavender (diluted to 1 %) were applied postoperatively.	Aromatherapy significantly enhanced patient satisfaction and reduced the severity of postoperative nausea.

PON: Postoperative nausea.

Table 3. Summary of studies on ginger use for postoperative pain management

Study (First author, year)	Country	Participants	Treatment details (Dosage and duration)	Key findings
Phillips (1993) (58)	United Kingdom	Women admitted for elective minimally invasive gynecological operation	Two capsules containing 1 g of powdered ginger root were administered one h before the induction of anesthesia.	The need for painkillers after surgery, recovery duration, and time until discharge was similar across all groups.
Eberhart (2003) (26)	Germany	Women undergoing gynecologic laparoscopy	300–600 mg ginger extract, administered at 3 and 6 h post-operation	No significant effect in women receiving postoperative opioids
Apariman (2006) (37)	Thailand	Hospitalized patients who underwent laparoscopic surgery for benign gynecological conditions	Three ginger capsules containing 0.5 grams of ginger powder were taken one h before the procedure.	Pain decreased at 6 h in the ginger group, no change at 2 h
Kalava (2013) (27)	USA	Elective C-section patients	Two 1 g capsules of powdered ginger, given at 2 h, 2.5 h, and 24 h post-operation	No significant change in pain scores
Rayati (2017) (60)	Iran	Patients after third molar extraction	500 mg ginger capsule daily, for 5 days post-operation	Ginger was as effective as ibuprofen in alleviating pain
Koçak (2018) (48)	Turkey	Post-tonsillectomy patients	500 mg ginger capsule twice daily for 7 days	Pain levels progressively decreased over time
Tianthong (2018) (68)	Thailand	Post-cesarean section patients	2 capsules (500 mg each) three times daily, for 4 days	Significant pain reduction by the fourth day
Mashak (2019) (52)	Iran	Cesarean section patients	One capsule containing 250 mg of ginger every 8 h starting 24 h before the operation	Ginger reduced post-spinal headache at multiple time points
Shabanian (2019) (64)	Iran	Patients post-inguinal hernia repair	250 mg ginger capsule, given at 2, 4, and 6 h post-operation	Ginger was to be equally effective as diclofenac in pain relief.
Vadiati Saberi (2019) (69)	Iran	Periodontal surgery patients	250 mg Zintoma (ginger extract) capsule, at 0, 8, 12, 24, 48 h post-operation	Pain relief was comparable to that of ibuprofen
Menon (2021) (28)	India	Periodontal flap surgery patients	400 mg ginger capsule, taken 3 times daily for 3 days.	No significant difference between ginger and ibuprofen
Cheshfar (2023) (24)	Iran	Nulliparous women with an episiotomy incision	Ginger extract (0.05%) was administered as ointment after the fifth and tenth days of surgery	The ginger ointment did not significantly reduce pain, but it offered some clinical benefit
Sforza (2023) (63)	United Kingdom	Women undergoing breast augmentation surgery	3 drops of ginger oil (110 mg) provided on their laryngeal mask before insertion	Reduced the mean VAS score and decreased the use of postoperative opioids.

VAS: Visual analog scale.

Table 4. Summary of clinical studies on ginger's effects on postoperative ileus, abdominal distention, shivering, and anxiety

Study (First author, year)	Country	Type of complication	Participants	Treatment details (Dosage and duration)	Key findings
Tianthong (2018) (68)	Thailand	Abdominal distension	Women undergoing cesarean section	2 capsules three times (500 mg) after meal for 3 days	Ginger does not reduce the occurrence of abdominal distention after cesarean section but reduces its severity by the fourth day and enhances appetite.
Sihombing (2022) (65)	Indonesia	Postoperative anxiety and metabolic disorder	Elective surgical procedures patient	Ginger extract with pre-operative high-calorie drink	HARS score anxiety level was lowered in the ginger group.
Mashak (2024) (51)	Iran	Post-spinal puncture shivering	Women undergoing cesarean section	25 mg of ginger hydro-alcoholic extract as a suppository immediately after the cesarean section	Reduced shivering after spinal puncture compared to the placebo group
Lorsirirat (2025) (49)	Thailand	Postoperative ileus	Women undergoing benign gynecologic hysterectomy	Two capsules (500 mg) were taken three times daily after meals and continued for three days	Decreased bowel ileus in benign gynecologic abdominal hysterectomy
Pongsupanimit (2025) (25)	Thailand	Postoperative ileus	Women undergoing hysterectomy	1 gram capsule was prescribed after surgery, and the other one at 1 g dosage following each meal (9 doses)	It did not significantly reduce postoperative ileus or enhance bowel function recovery

HARS: Hamilton anxiety rating scale.

gastrointestinal motility through their prokinetic effects (76). In the guinea pig, gingerols and shogaols exert inhibitory effects on muscarinic M3 and 5-HT3 receptors, key mediators in the emetic response. Additionally, while ginger compounds inhibit these pathways, they do not interfere with 5-HT4 receptors, which are known to facilitate gastroduodenal motility, thereby allowing ginger to maintain or enhance gastrointestinal movement (77). Giacosa et al., in their study, reported the same effects. Notably, these compounds have minimal impact on 5-HT4 receptors, crucial for stimulating gastrointestinal motility. This selective action enables ginger to effectively suppress emetic signals while preserving or enhancing normal digestive functions (78).

Modulation of dopaminergic and cholinergic systems

Activation of these afferent pathways can trigger the vomiting reflex via cholinergic (muscarinic), dopaminergic, histaminergic, or serotonergic receptors, potentially causing PONV (79). Extensive cross-interactions of dopamine receptor ligands with a wide range of targets, such as G-protein coupled receptors, enzymes, ion channels, and transporters, further complicate the identification of new therapeutic targets for treating nausea and vomiting (80). Active compounds of *Z. officinale*, including zingerone, 6-shogaol, and 6-gingerol, potentially influence dopaminergic pathways by modulating D2 receptor activity (81,82), another key component of the central emetic pathway. Furthermore, Apfel et al showed that nitrous oxide might cause PONV by influencing dopamine and opioid receptors in the CNS, altering middle ear pressure, and inducing bowel distension as it diffuses into closed body cavities (83). Additionally, the muscarinic actions of acetylcholine (ACh) on the gastrointestinal system can lead to symptoms including nausea, vomiting, and diarrhea (84). Ginger's capacity to interact with both post-synaptic M3 receptors and pre-synaptic muscarinic autoreceptors is noteworthy. Moreover, ginger inhibits pre-synaptic muscarinic autoreceptors, much like standard muscarinic antagonists (85).

Improving gastrointestinal function

Delayed gastric emptying, commonly referred to as gastroparesis, is a well-known contributor to nausea and vomiting. When the stomach takes longer than usual to release its contents into the small intestine, it can result in feelings of fullness, bloating, and discomfort, which can trigger nausea. This delay disrupts the coordinated muscular contractions of the gastrointestinal tract, causing gastric contents to accumulate and leading to increased gastric distension. These factors activate afferent neural pathways involved in the emetic response (86). In the preoperative and postoperative periods, opioids as analgesics and delayed gastric emptying can heighten the risk of PONV (87).

Wu et al, in their study, found that ginger capsules (total 1200 mg) enhance gastric emptying and promote contractions in the antrum of healthy individuals, indicating its potential to improve gastrointestinal motility and alleviate symptoms linked to delayed gastric emptying (88). Another clinical study also revealed that the extract of ginger and artichoke notably enhances gastric emptying in healthy individuals without causing

Figure 3. Summary traffic light plot of the RoB 2 tool.

significant adverse effects (89). Ginger's effects on gastric emptying are primarily linked to the distinctive molecular actions of its bioactive compounds. Gastric hypomotility, commonly associated with delayed gastric emptying, reflects a temporary disruption in the coordinated activity of cholinergic M3 and serotonergic 5-HT3/5-HT4 receptors. Key lipophilic components of ginger root extracts, like [6]-gingerol, [8]-gingerol, and [10]-gingerol have demonstrated the ability to interact with and modulate these receptors, thereby promoting normal gastric motility and enhancing the digestive process (78,89).

Mechanistic effects of *Z. officinale* on postoperative pain

Postoperative pain, which can be moderate to severe, is a common adverse effect after surgery that notably delays recovery, imposes adverse physiologic and psychologic effects, and negatively impacts the overall quality of life (90-93). Afferent neural pathways mediate postoperative pain and can be classified into nociceptive, inflammatory, and neuropathic pain. Nociceptive pain arises from tissue injury and is transmitted through C-fibers, A-delta, and A-beta fibers. In contrast, inflammatory pain occurs due to sensitization of inflammatory mediators such as cytokines, and is generally reversible. Neuropathic pain originates from nerve injury and may persist beyond the acute phase of healing (94,95).

Additionally, pain can be categorized as somatic, sharp, and localized, typically transmitted by A-beta fibers, or visceral, diffuse, and poorly localized, involving C and A-delta fibers and often accompanied by autonomic symptoms. Effective pain management strategies aim to target these pathways by blocking receptor activity or reducing the production of inflammatory mediators (95). The analgesic effects of ginger involve the modulation of thinly myelinated A-delta fibers, unmyelinated C-fibers, and myelinated A-beta fibers, along with the regulation of transient receptor potential vanilloid 1 (TRPV1) receptor. Furthermore, ginger reduces pain by inhibiting inflammatory processes and mitigating oxidative stress (96).

The primary mechanisms by which *Z. officinale* alleviates pain are as follows:

Anti-inflammatory and immunomodulatory properties

Surgical tissue damage triggers a systemic inflammatory response marked by the release of pro-inflammatory cytokines, such as tumor necrosis factor-α (TNF-α), interleukin-1 (IL-1), IL-6, and IL-1β (97,98). These cytokines activate immune cells, including neutrophils, macrophages, and mast cells, resulting in an increased production of reactive oxygen species (ROS) and heightened oxidative stress. IL-1 and IL-6 also play a role in the development of hyperalgesia. Zehsaz et al study showed that the IL-6, IL-1β, and TNF-α concentrations were significantly reduced after six weeks of ginger supplementation. They may effectively attenuate the post-exercise elevation of key pro-inflammatory cytokines, highlighting their potential as an anti-inflammatory

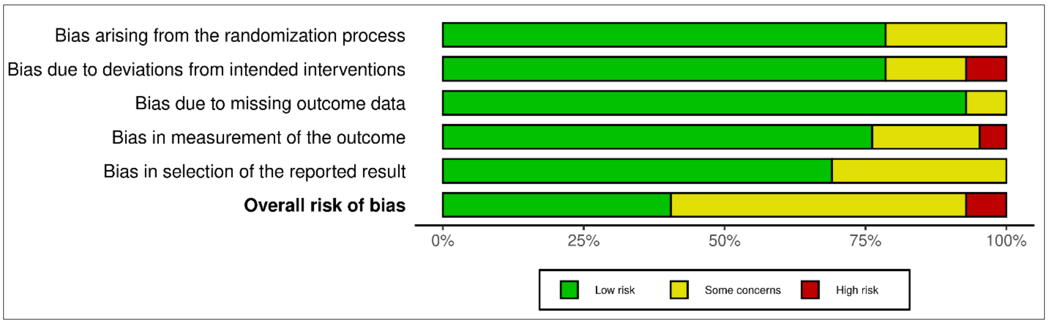

Figure 4. Summary bar plot of the RoB 2 tool.

adjunct in exercise-induced stress (99). *Z. officinale* oil and extract inhibit the release of inflammatory factors and cytokines, including nuclear factor kappa B (NF-κB) signaling, COX-2 expression, IL-1β, IL-6, IL-17, and TNF-α, during neuropathic and chronic pain symptoms (100,101).

Moreover, cyclooxygenase (COX) enzymes are key mediators of pain and inflammation and are central to the analgesic effects of nonsteroidal anti-inflammatory drugs (NSAIDs) and coxibs. Following tissue injury, COX-2 expression is upregulated at the peripheral site, leading to increased prostaglandin E2 (PGE2) production, which sensitizes nociceptors and contributes to the onset and amplification of pain (102). PGE2, a lipid signaling molecule primarily associated with pain and inflammation, is also crucial in promoting tissue regeneration and repair following injury (103).

A clinical trial conducted by Black et al. showed that a short-term intervention lasting less than two weeks using oral raw and heat-treated ginger in osteoarthritis patients showed significant analgesic and anti-inflammatory effects. The study evaluated muscle pain and plasma PGE2 levels, highlighting ginger's targeted inhibition of the COX-2 enzyme (104). In van Breemen et al study, compounds such as 10-gingerol, 8-shogaol, and 10-shogaol have been shown to inhibit cyclooxygenase-2 (COX-2) activity, partly explaining ginger's anti-inflammatory effects. By suppressing COX-2, these bioactive constituents reduce the synthesis of pro-inflammatory prostaglandins, alleviating inflammation and associated pain (105).

T-lymphocytes cells express antigen receptors on their surfaces, enabling them to recognize and respond to invading pathogens. T cells are classified into two subsets based on surface markers, $CD4^+$ and $CD8^+$. $CD4^+$ T cells, also known as helper T cells, can be further divided into Th1 and Th2 subsets, which are characterized by the cytokines they produce, Th1-type and Th2-type cytokines, respectively. Th1-type cytokines play a critical role in the immune defense against intracellular pathogens by promoting a pro-inflammatory response by releasing inflammatory cytokines (106). Conversely, ginger's antioxidant and anti-inflammatory effects may play a key role as an immunomodulator. By neutralizing free radicals, these antioxidants reduce oxidative stress and help maintain immune system balance. These antioxidant effects are closely linked to anti-inflammatory mechanisms, as both work together to regulate free radical production and suppress pro-inflammatory cytokines (107). Phenolic compounds found in ginger have been shown to regulate the activity of essential immune cells including macrophages, neutrophils, dendritic cells, and T-lymphocytes partly by inhibiting key signaling pathways like NF-κB and PI3K/Akt/mTOR. This inhibition ultimately reduces inflammatory responses driven by these immune cells (108).

Antioxidant and free radical scavenging activities

Postoperative tissue injury leads to oxidative stress, contributing to inflammation and pain. A significant positive correlation was observed between surgical complications and the preoperative levels of glutathione peroxidase (GPX) and malondialdehyde (MDA). However, by the seventh postoperative day, the most significant predictors of complications were the levels of superoxide dismutase (SOD) and MDA, indicating a shift in oxidative stress markers associated with surgical outcomes (97). *Z. officinale* and its active compounds, [6]-gingerol and [6]-shogaol, are effective in alleviating mechanical, spontaneous, and thermal (cold and heat) pain by alleviating inflammation and oxidative stress in the tissue (109). Ginger has high levels of phenolic compounds like shogaols, gingerols, paradols, and zingerone with antioxidant properties (15). *Z. officinale* and its active constituents enhance both the concentration and activity of key antioxidant defense markers, including total antioxidant capacity (TAC), glutathione (GSH), SOD, catalase (CAT), GPX, and oxidized glutathione (GSSG) (110).

Inhibition of nociceptive signal transduction

Transient receptor potential vanilloid receptor subtype 1 (TRPV1) is a crucial receptor expressed in nociceptive neurons that mediates the detection and transmission of pain signals in response to thermal, chemical, mechanical, and osmotic stimuli (111). The TRPA1 channel plays a vital role in detecting harmful chemical signals, as it is activated by both external irritants and endogenous compounds generated during tissue injury or neurogenic inflammation (112). Similar capsaicin, compounds in ginger, including shogaols, gingerols, and zingerone, evoke a pungent sensation akin to activating the TRPV1 ion channel. This channel is found in pain-transmitting primary afferent nerve fibers and reacts to harmful stimuli, essential in mediating pain perception (113). The antioxidant and analgesic properties of ginger extract and its aromatic and pungent compounds exert their effects through the intricate pathways of TRPC5 and TRPA1 channels. Among these compounds, [6]-shogaol stands out as the key player, intricately modulating the activity of TRPC5 and TRPA1 and revealing the spice's powerful health benefits (114). It is plausible that ginger, due to its pungent compounds, affects TRPV1 like capsaicin. TRPV1 features two gating mechanisms, a selectivity filter and an S6 activation gate, through which it regulates ion flow in response to noxious stimuli, including those triggered by spicy substances (115).

Moreover, 5-HT in the CNS modulates pain perception. 5-HT influences synaptic transmission and plasticity through its diverse receptors, particularly in key pain-related regions such as anterior cingulate cortex (ACC), insular cortex (IC), and spinal cord (116). Alterations in 5-HT signaling are closely linked to chronic pain, with serotonin capable of enhancing and inhibiting pain signals depending on the receptor subtype and neural context. These findings highlight the potential of targeting specific 5-HT receptors as a promising approach for managing chronic pain (116).

Ginger may alleviate postoperative pain by modulating the 5-HT pathways essential for pain perception and central sensitization. Bioactive compounds found in ginger, such as [6]-gingerol and [6]-shogaol, are believed to influence serotonergic signaling through their interaction with specific 5-HT receptors, notably 5-HT1A and 5-HT3, which are involved in both the facilitation and inhibition of nociceptive transmission. By enhancing the activity of inhibitory serotonin receptors and diminishing excessive excitatory signaling in critical regions like the spinal cord and brainstem, ginger may help restore the balance in pain pathways disrupted by surgical trauma (117).

Additionally, N-methyl-D-aspartate (NMDA) is a glutamate receptor crucial for amplifying and modulating pain signals within the CNS. Therefore, it is a key component of nociceptive signal transduction, particularly in the central sensitization phase of pain processing (118).

Peripheral inflammation activates N-methyl-D-aspartate receptors (NMDARs) in the spinal cord, contributing to the onset of allodynia, hyperalgesia, and central sensitization. This activation increases intracellular calcium levels, which subsequently triggers the phosphorylation of key signaling molecules, including protein kinase C (PKC) and extracellular signal-regulated kinase 2 (ERK2). As a result, neuronal excitability is heightened, further amplifying pain signaling (119). In contrast, the same dose increased the expression of NMDAR2A, a subtype linked to neuroprotection and synaptic stability. This differential regulation suggests that RGO may help modulate pain by shifting NMDA receptor activity toward a more protective and less sensitizing profile (120). Chia et al, in their *in vitro* study on SH-SY5Y neuroblastoma cells, revealed that Zerumbone could decrease the expression of both NMDA receptor subtype NR2B and TRPV1 receptors. This downregulation contrasts with findings in brain tissue samples (121).

Activation of various potassium (K^+) channels, such as voltage-dependent, ATP-sensitive, small-conductance calcium-activated (SK), and large-conductance calcium-activated (BK) channels, plays a crucial role in regulating neuronal excitability. When these channels open, they allow the efflux of K^+ ions from the neuron, causing membrane hyperpolarization. This hyperpolarized state makes it more difficult for the neuron to attain the threshold level needed to fire an action potential, dampening neuronal responsiveness and reducing pain signal transmission (122). Furthermore, 8-gingerol has been recognized as the most potent inhibitor of the human ether-à-go-go-related gene (hERG) K^+ channel among the gingerol compounds (123).

Therefore, according to the mentioned studies, the most important mechanisms effective in reducing postoperative complications such as PONV and pain are shown in Figure 5.

Side effects

The studies included found that there were no serious adverse effects from ginger extract or oil. One study noted minimal adverse effects from 1 g of powdered ginger root in women presenting for elective laparoscopic gynacologica1 surgery, which were not significantly different from the control group (58). In another study, two participants received 0.5 g of ginger. One reported experiencing flatulence and bloating, while the other reported heartburn. The remaining three participants each received 1 g of ginger. One experienced severe heartburn after ingesting the capsules, another felt nauseous, and the third reported frequent burping (38). Adverse events were generally infrequent across all treatment groups, with reported side effects including isolated cases of flu-like symptoms, heartburn, cardiovascular and respiratory symptoms, infections requiring antibiotics, and allergic reactions; the overall incidence was comparable between the placebo group (n=11), the ginger 3 × 100 mg (n=8), and the Ginger 3 × 200 mg group (n=13) (26). Another study by et al. reported that side effects such as heartburn, abdominal discomfort, flu-like symptoms, and insomnia were reported in 16.7% and 6.7% of patients in the ginger group. However, the differences were not statistically significant between placebo and ginger groups (37).

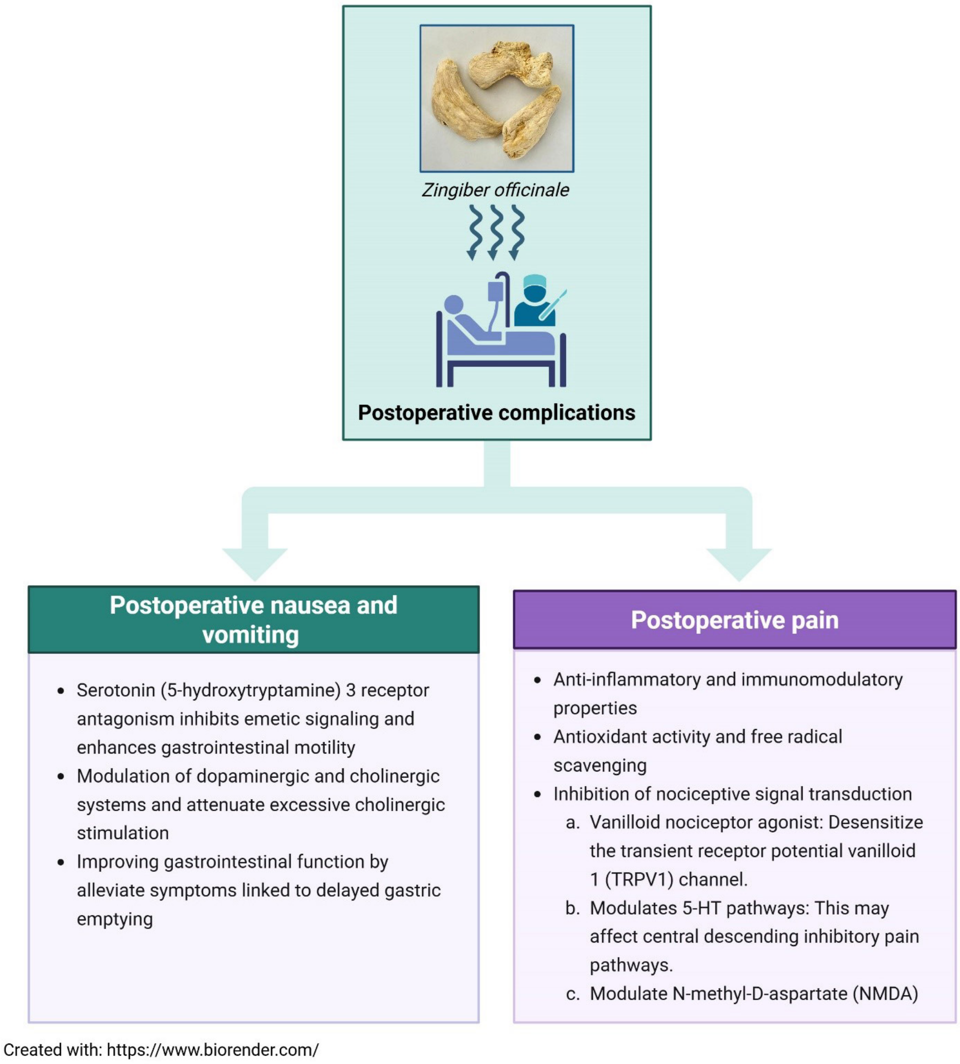

Figure 5. Gingers' mechanisms on reducing PONV and pain.

Limitations

A limitation of this study was the heterogeneity among the included studies in terms of ginger dosage, formulation and type of administration (oral capsule, extract, essential oil, ointment), timing and frequency of administration, surgical procedures, and measured outcomes (Different measuring tools). On the other hand, in some studies, the drug was administered as combination therapy with other chemical or herbal drugs. This could affect the outcome and comparison of studies. Different dosages could affect the bioavailability of ginger's active compounds, and this was another limitation of the present study. Additionally, the limited number of studies addressing other postoperative complications may reduce the statistical power and precision of the analysis, while increasing the potential for bias. Due to high heterogeneity, a quantitative synthesis (meta-analysis) was not feasible.

Conclusion

Current evidence suggests that ginger shows promise as a safe complementary treatment for managing postoperative complications, particularly PONV. It consistently reduces nausea in the early postoperative period. It lowers the need for antiemetic medications, showing comparable efficacy to standard drugs like metoclopramide and ondansetron, with enhanced effects when combined with the latter. While its impact on vomiting is less consistent, some studies report significant reductions at specific intervals. Oral ginger proves more effective than aromatherapy, which offers limited benefits. Findings regarding postoperative pain are mixed; some studies indicate that ginger provides relief comparable to ibuprofen and diclofenac and reduces VAS scores, though others report no significant effects. Additionally, ginger may help alleviate other postoperative issues such as anxiety, post-spinal shivering, and abdominal distention, though its benefits in preventing postoperative ileus remain inconclusive. So, ginger is a promising adjunctive therapy, warranting further standardized research to confirm its optimal use and broader clinical application.

Further well-designed, standardized clinical trials are needed to establish optimal dosing strategies, treatment durations, and broader applicability across different surgical contexts.

Authors' contribution

Conceptualization: Hedayatallah Lalehgani.
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Formal analysis: Hedayatallah Lalehgani.
Investigation: Hedayatallah Lalehgani.
Methodology: Ali Amini.
Project administration: Hedayatallah Lalehgani.
Resources: Hedayatallah Lalehgani.
Software: Ali Amini.
Supervision: Hedayatallah Lalehgani.
Validation: Ali Amini.
Visualization: Ali Amini and Hadi Shakerin.
Writing–original draft: Ali Amini and Hedayatallah Lalehgani.
Writing–review & editing: Hedayatallah Lalehgani, Hadi Shakerin, and Ali Amini .

Conflict of interests

The authors declared no conflict of interest, financial or otherwise.

Ethical considerations

Nil.

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