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Review Article

Progress in traditional Chinese medicine for chemotherapy-induced nausea and vomiting, based on the theory of "Fuzheng Quxie" and "Hewei Jiangni"

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Abstract: Chemotherapy-induced nausea and vomiting (CINV) is among the most prevalent adverse reactions in cancer treatment. It significantly diminishes the quality of life of patients and their treatment compliance. Traditional Chinese medicine (TCM) exhibits unique characteristics and potential for the prevention and treatment of CINV. This review summarizes the latest research progress on TCM for CINV, encompassing the theoretical foundation, mechanism of action, and clinical evidence. "Fuzheng Quxie" formulas (reinforcing healthy Qi and eliminating pathogenic factors) and herbs (e.g., Liu-Jun-Zi-Tang, ginseng) enhance the body's tolerance to chemotherapy by enhancing immunity, reducing inflammation and oxidative damage, and promoting tissue repair. "Hewei Jiangni" formulas (harmonizing the stomach and directing rebellious Qi downward), including Xiao-Ban-Xia-Tang, ginger, and external therapies (e.g., acupuncture, moxibustion, acupoint application) directly alleviate nausea and vomiting by regulating gastrointestinal motility, antagonizing emesis-related receptors, and inhibiting inflammatory pathways. Clinical research shows that combining TCM with conventional antiemetic regimens improves the control of delayed CINV and enhances patients' quality of life, while maintaining a favorable safety profile. However, current evidence remains limited by small sample sizes, insufficient mechanistic investigations, and lack of standardized treatment plans. Future research should prioritize high-quality and large-sample clinical trials and clarify its mechanism of action using modern scientific approaches, so as to promote the standardized and efficient application of TCM for the prevention and treatment of CINV.

Keywords: Chemotherapy-induced nausea and vomiting, Fuzheng Quxie, Hewei Jiangni, traditional Chinese medicine, mechanism of action, clinical research

Introduction

Chemotherapy-induced nausea and vomiting (CINV) is one of the most common side effects associated with tumor treatment. It causes substantial physical and psychological distress, seriously affecting patients' quality of life, nutritional status, treatment adherence, and even long-term treatment effect [1]. CINV is classified into three types according to the timing of symptom onset [2, 3]: acute, delayed, and anticipatory CINV. Acute CINV occurs within 24 hours of chemotherapy, whereas delayed CINV may persist for several days and is more difficult to control. Anticipatory CINV is a conditioned response triggered by previous negative chemotherapy experiences, usually appearing before treatment. Guidelines issued by the American Society of Clinical Oncology (ASCO), European Society of Oncology (ESMO), National Comprehensive Cancer Network (NCCN) and other institutions all recommend the combined use of serotonin 3-receptor antagonists (5-HT3RAs), neurokinin-1 receptor antagonists (NK1RAs), and glucocorticoids to improve the prevention and control of CINV [4-6]. However, several clinical challenges remain unresolved. For example, the control of delayed CINV remains suboptimal, and breakthrough symptoms may still occur after preventive treatment. In addition, existing antiemetic drugs often have adverse reactions such as head-

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ache, constipation, and gastrointestinal discomfort [2, 7]. The pathogenesis of CINV involves multiple mechanisms, including direct gastrointestinal mucosal injury, activation of 5-HT3 and NK-1 receptor pathways, inflammatory responses (e.g., NF-κB pathway activation), and gastrointestinal dysmotility [8-12].

Traditional Chinese Medicine (TCM) has a long history in disease prevention and treatment and is characterized by a unique theoretical system. The application of TCM in CINV is not limited to simple suppression of the vomiting reflex. Instead, its therapeutic strategies follow two core principles: one is "Fuzheng Quxie" (reinforcing healthy Qi and eliminating pathogenic factors), which aims to support the body's vital Qi, eliminate pathogenic influences, and enhance resistance to exogenous damage; the other is "Hewei Jiangni" (harmonizing the stomach and directing rebellious Qi downward), which focuses on restoring the physiological function of the spleen and stomach, thereby improving gastrointestinal regulation and descending adverse Qi flow.

In recent years, evidence has demonstrated the efficacy of TCM for preventing and managing CINV. Its underlying mechanisms appear to involve multi-dimensional regulatory effects, including regulating neurotransmitter receptors, inhibiting inflammatory reactions, improving gastrointestinal motility, and regulating intestinal flora [11, 13, 14]. Based on these, this review systematically summarizes recent advances in TCM for CINV. The review discusses the theoretical basis, mechanisms of action, and clinical evidence for TCM therapies. In addition, it also explores the limitations and future research directions of current research, aiming to provide a reference for the application of TCM into oncological supportive care and the uniting of traditional Chinese and western medicine.

Scientific connotation of the Fuzheng Quxie and Hewei Jiangni theories

Fuzheng Quxie theory in the context of CINV prevention and management

The theory of "Fuzheng Quxie" originates from the earliest existing medical classic in China, *the Inner Canon of the Yellow Emperor*, which is one of the basic principles of TCM treatment [15]. In this theory, "Zheng" (healthy Qi) refers to the normal physiologic function, disease resistance, and repair capacity, whereas "Xie" (pathogenic factors) refers to various pathogenic factors [15]. In CINV, chemotherapeutic drugs act as exogenous pathogenic factors that impair spleen and stomach function, thereby causing digestive disorders. Meanwhile, cancer patients often exhibit impaired physical status and decreased resistance due to tumor load, surgical trauma, psychological stress, and other factors. Therefore, the application of Fuzheng and Quxie theory for the prevention and treatment of CINV is reflected in two aspects: enhancing the body's tolerance to chemotherapy-induced injury to promote tissue repair, and counteracting the toxic effects associated with chemotherapeutic drugs.

From the perspective of modern biomedicine, "Fuzheng" corresponds to multiple physiologic processes such as enhancing immune function, improving nutrient metabolism, protecting normal tissues, and promoting damage repair. Previous studies have demonstrated that ginseng, astragalus, and *Atractylodes macrocephala*, possess anti-inflammatory and antioxidant properties that may promote gastrointestinal mucosal repair, reduce gastrointestinal damage, and alleviate gastrointestinal adverse reactions [16-18]. Additionally, these agents can enhance the activity of immune effector cells such as natural killer cells (NK cells) and $CD8^+$T cells, thereby improving the anti-tumor immune surveillance without reducing the anticancer efficacy of chemotherapy [19-21].

"Quxie" may involve directly antagonizing the toxic effect of chemotherapy through mechanisms such as suppression of inflammatory reactions, scavenging of free radicals, and inhibition of emesis-related signaling pathways. For example, astragalus contains multiple bioactive compounds, including flavonoids and alkaloids. Certain flavonoids have been reported to inhibit activation of the NF-κB signaling pathway, thereby reducing the release of inflammatory factors such as tumor necrosis factor-a (TNF-α) and interleukin-6 (IL-6), alleviating oxidative stress and inflammatory reactions, improving intestinal barrier function, and attenuating inflammatory damage to the intestinal mucosa [22, 23]. In addition, some Chinese medicinal agents classified as "Quxie" thera-

pies may directly regulate receptors related to vomiting. For example, alkaloids in *Pinellia ternata* have been reported to antagonize serotonin type 3 (5-HT3) receptors [24], whereas active constituents in ginger can inhibit NK-1 receptor-mediated signaling, thus blocking the vomiting reflex at the receptor level [25].

Hewei Jiangni (harmonizing the stomach and directing rebellious Qi downward) theory in regulating the emetic reflex arc

The treatment principle of "Hewei Jiangni" originates from the discussion of "rebellious stomach Qi causing vomiting" in the Shang Han Lun (*Treatise on Cold Damage Disorders*) and represents a basic principle of TCM in the treatment of vomiting diseases. The stomach is responsible for receiving and digesting food and fluids, and under normal physiologic state, stomach Qi descends harmoniously. Dysfunction of the stomach may cause rebellious Qi movement, manifested as nausea, vomiting, and other related symptoms. Chemotherapeutic drugs can impair spleen and stomach function, resulting in impaired digestive function, abnormal transportation and transformation of food and fluids, thereby inducing rebellious stomach Qi and eventually leading to vomiting. The core concept of "Hewei Jiangni" is to restore the normal physiologic functions of the spleen and stomach and regulate the ascending and descending movement of Qi, thereby promoting the downward flow of stomach Qi and relieving vomiting.

From the perspective of modern medicine, the concept of "Hewei" includes regulating gastrointestinal hormone secretion, improving gastrointestinal motility, restoring the gastric mucosal barrier, and regulating intestinal flora. Certain Chinese medicines, such as ginseng and poria, have been reported to promote the secretion of ghrelin, thereby accelerating gastric emptying, while also regulating the expression of tight junction proteins in the intestine and contributing to intestinal barrier repair. At the same time, these agents can regulate composition of the intestinal flora structure by increasing the abundance of beneficial bacteria [26-29]. Collectively, these effects may help restore normal gastrointestinal function and provide a physiological basis for achieving for "Jiangni" (directing rebellious Qi downward).

"Jiangni" can directly target multiple components of the vomiting reflex arc. First, Jiangni-related TCM age ts can act on peripheral receptors and reduce their sensitivity to chemical stimuli. For example, *Pinellia ternata* and ginger have been reported to stabilize the intestinal pheochromocyte membrane, reduce the abnormal release of neurotransmitters such as 5-HT, attenuating the generation of vomiting signals [14, 24]. Second, these agents can block emetic signal transduction pathways, for instance, by antagonizing receptors like 5-HT3 and NK-1, thus interrupting the transmission of emetic signals at both central and peripheral levels. Third, Jiangni-related compounds can modulate the excitability of the vomiting center. For example, evodiamine from *Evodia rutaecarpa* (*Wu Zhu Yu*), may regulate neuronal activity in the nucleus tractus solitarius of the medulla oblongata, thereby reducing the sensitivity of the vomiting center [30].

Collectively, the theories of Fuzheng Quxie and Hewei Jiangni provide complementary therapeutic strategies for the prevention and management of CINV. Their synergistic mechanisms of action are summarized in **Figure 1**. Representative TCM agents used for CINV management based on these two theories, along with their main active components and mechanisms of action, are summarized in **Table 1**.

Research progress on CINV prevention and treatment based on the Fuzheng Quxie theory

Liu-Jun-Zi-Tang (LJZT)

Liu-Jun-Zi-Tang (LJZT), first recorded in the Ming Dynasty medical text *Yi Xue Zheng Zhuan*, consists of six herbs: ginseng (*Ren Shen*), *Atractylodes macrocephala* (*Bai Zhu*), poria (*Fu Ling*), licorice (*Gan Cao*), aged tangerine peel (*Chen Pi*), and *pinellia ternata* (*Ban Xia*). The formula was developed by adding *Chen Pi* and *Ban Xia* to the foundational Si-Jun-Zi Decoction. LJZT is commonly used for preventing and treating CINV, particularly suitable for patients with spleen-stomach Qi deficiency, and is regarded as a classic Fuzheng Quxie prescription. In Japan, LJZT is known as "Rikkunshito" and has been widely applied in the treatment of functional dyspepsia and chemotherapy-related nausea and vomiting [31].

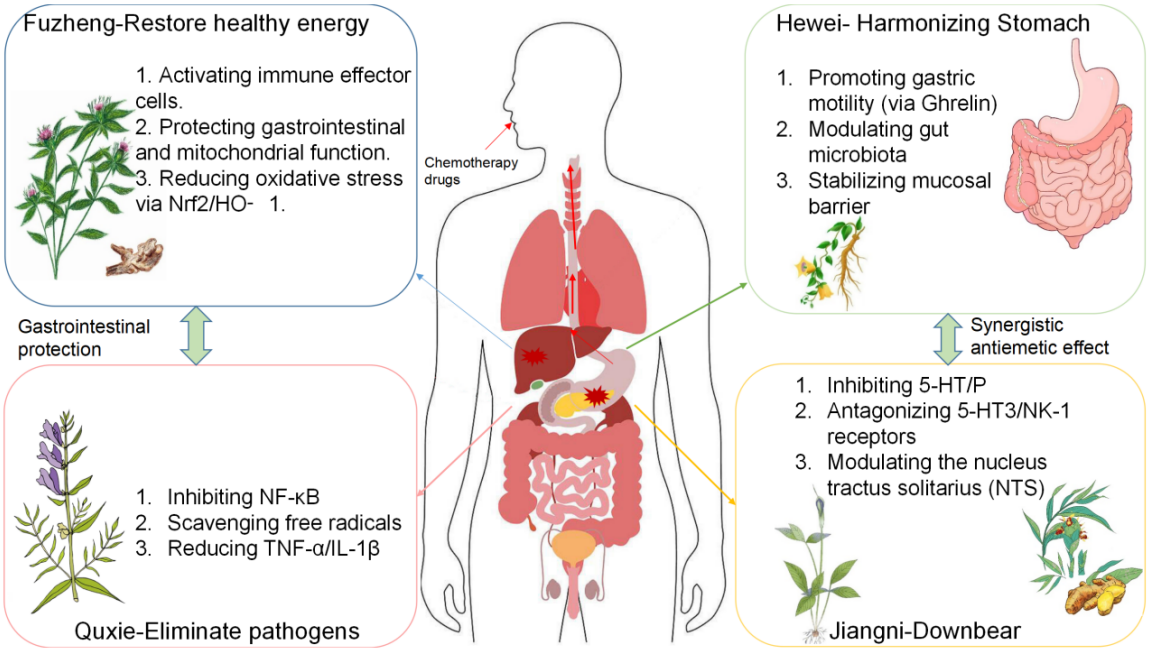

Figure 1. Proposed mechanisms underlying the prevention and treatment of CINV based on the theories of Fuzheng Quxie and Hewei Jiangni. Note: Fuzheng Quxie enhances the body's tolerance to chemotherapy-induced toxicity by boosting immune function, reducing oxidative stress, and suppressing inflammatory responses (e.g., NF-κB pathway). Hewei Jiangni alleviates nausea and vomiting by restoring gastrointestinal function (e.g., improving gastric emptying, regulating gut microbiota composition) and modulating the emetic reflex pathway (antagonizing 5-HT_3/NK-1 receptors, reducing neurotransmitter release). This synergistic interaction may contribute to comprehensive CINV management.

Several clinical studies have evaluated the efficacy of LJZT in CINV management. A large retrospective study based on a Japanese administrative database demonstrated that patients who received LJZT on or before the initiation of cisplatin-based chemotherapy had a significantly lower requirement for intravenous 5-HT3RA administration during days 2-3 after chemotherapy compared to non-users, suggesting that LJZT may alleviate early-phase CINV and reduce the need for rescue antiemetic therapy [32]. Another study based on National Health Insurance Research Database of Taiwan, China reported that gastric cancer patients receiving TCM, including LJZT, during postoperative chemotherapy exhibited higher survival rates. LJZT was the most frequently prescribed formula and was commonly used for treating upper gastrointestinal dysfunction, CINV, and anorexia [33].

However, inconsistent findings have also been reported. A randomized, double-blind, placebo-controlled trial in patients with endometrial or cervical cancer receiving cisplatin-based chemotherapy demonstrated that adding LJZT to a standard triple antiemetic regimen (consisting of granisetron, aprepitant, dexamethasone) did not significantly improve the complete response rate (defined as no vomiting and no rescue medication use) during 24-120 hours post-chemotherapy compared to placebo. Furthermore, other secondary endpoints, such as complete control rate, overall nausea scores, and appetite, also showed no significant improvement [34]. The discrepancies between the studies may be attributable to several factors. First, the patient populations differed substantially. Jo et al. [32] enrolled patients with various cancers including lung and esophageal cancer, resulting in a heterogeneous study population. In contrast, Konno et al. [34] focused exclusively on gynecological tumors, all of whom belonged to the high-risk group for CINV. Second, the background antiemetic regimens differed markedly. The study by Jo et al. [32] did not strictly standardize antiemetic therapy, and many patients did not receive NK1 receptor antagonists (NK1RAs), leading to relatively weak antiemetic coverage. Conversely, all patients in the study

Table 1. Representative herbs based on the theories of Fuzheng Quxie and Hewei Jiangni for the prevention and treatment of CINV

Herb	Main Active Compounds	Antiemetic Mechanism
Fuzheng Medicine		
Astragalus Membranaceus (Huang Qi)	Astragaloside IV, Astragalus Polysaccharides	Activates Nrf2/HO-1 pathway and reduces oxidative stress
Codonopsis Pilosula/Panax Ginseng (Dangshen/Renshen)	Ginsenosides, Codonopsis Polysaccharides, Ginseng Polysaccharides	Enhances NK, CD3+, CD4+ cell activity and improves immune regulation
Atractylodes Macrocephala (Baizhu)	Atractylenolide, Atractylon, Volatile Oil	Regulates inflammatory cytokines including TNF-α and IL-6
Poria Cocos (Fuling)	Poria Polysaccharides, Pachymic Acid, Triterpenoids	Regulates TLR4/MyD88/NF-κB pathway
Ganoderma Lucidum (Lingzhi)	Ganoderma Polysaccharides, Ganoderma Triterpenoids	Exerts antioxidant, anti-inflammatory effects and protects gastrointestinal mucosa
Dendrobium Officinale (Shihu)	Dendrobium Polysaccharides, Dendrobine, Flavonoids	Protects gastrointestinal mucosal integrity and reduces oxidative injury
Quxie Medicine		
Coptis Chinensis (Huanglian)	Berberine, Coptisine	Inhibits NF-κB signaling pathway
Scutellaria Baicalensis (Huangqin)	Baicalin, Baicalein	Reduces inflammatory responses and modulates VEGF-related pathways
Lonicera Japonica (Jinyinhua)	Chlorogenic Acid, Isochlorogenic Acid	Exerts anti-inflammatory effects
Forsythia Suspensa (Lianqiao)	Forsythin, Volatile Oil	Reduces inflammatory injury and oxidative stress
Hewei Medicine		
Citrus Reticulata (Chenpi)	Naringenin, Hesperidin, Limonene, Volatile Oil	Promotes gastric emptying and gastrointestinal motility
Poria Cocos (Fuling)	Poria Polysaccharides, Pachymic Acid, Triterpenoids	Maintains gastrointestinal barrier function and reduces inflammation
Atractylodes Macrocephala (Baizhu)	Atractylenolide, Atractylon, Volatile Oil	Improves gastrointestinal motility and protects gastric mucosa
Codonopsis Pilosula (Dangshen)	Saponins, Codonopsis Polysaccharides	Exerts antioxidant, anti-inflammatory, and gastric mucosal protective effects
Agastache Rugosa (Huoxiang)	Huoxiang Ketone, Volatile Oil	Exerts anti-inflammatory effects and promotes gastrointestinal motility
Jiangni Medicine		
Pinellia Ternata (Banxia)	Pinellia Alkaloids, Organic Acids	Antagonizes 5-HT3 receptor- mediated emetic signaling
Zingiber Officinale (Shengjiang)	Gingerol, Shogaol, Zingerone	Antagonizes 5-HT3 and NK-1 receptor pathways and alleviates nausea and vomiting
Syzygium Aromaticum (Dingxiang)	Eugenol, Volatile Oil	Regulates gastrointestinal function and alleviates emesis
Evodia Rutaecarpa (Wuzhuyu)	Evodiamine, Rutecarpine	Modulates serotonergic signaling and gastrointestinal motility

by Konno et al. [34] received a contemporary triple antiemetic regimen comprising a 5-HT3RA, an NK1RA (aprepitant), and dexamethasone, resulting in strong antiemetic efficacy, which may have reduced the possibility of observing additional benefits from LJZT. In an earlier phase II study (JORTC KMP-02) conducted in the same patient population, positive results were observed with LJZT administration [35]. These findings indicate that when the baseline antiemetic regimen is insufficiently intensive (without NK1RAs), LJZT can provide additional benefit; and this benefit may become less apparent when LJZT is combined with highly effective modern triple antiemetic therapy containing NK1RAs. Moreover, differences in sample size, chemotherapy protocols, and drug exposure time may also contribute to the heterogeneity of study outcomes. Although current evidence regarding the efficacy of LJZT in CINV remains inconsistent, most observational studies suggest potential clinical benefits. The therapeutic effects of LJZT may vary depending on individual patient characteristics and treatment protocols. A summary of studies investigating LJZT for CINV is presented in **Table 2**.

The antiemetic effects of LJZT may involve multiple targets. Research has shown that LJZT can increase plasma levels of acylated ghrelin, an orexigenic gut hormone, in esophageal cancer patients receiving highly emetogenic chemotherapy (HEC), thereby alleviating CINV and anorexia [36, 37]. Animal studies further demonstrated that LJZT can prevent chemotherapy-induced decline in ghrelin levels through antagonism of 5-HT2B/2C receptors and activation of SIRT1 enzyme (a deacetylase associated with cellular stress resistance and metabolic regulation). In ovarian cancer cell experiments, LJZT was shown to inhibit epithelial-mesenchymal transition, suggesting a role in modulating cancer cachexia- and inflammation-related pathways [36]. However, potential pharmacokinetic interactions between LJZT and certain chemotherapeutic drugs should be considered. Experimental studies have indicated that Xiang-Sha-Liu-Jun-Zi-Tang (a modified form of LJZT) can significantly inhibit the expression and activity of the cytochrome P450 3A (CYP3A), thereby affecting the clearance of CYP3A-dependent chemotherapeutic drugs (e.g., paclitaxel), leading to increased plasma drug concentrations and prolonged half-life [38]. Therefore, careful monitoring of plasma concentrations and appropriate dose adjustments of relevant chemotherapeutic drugs are necessary in clinical application to ensure both efficacy and safety.

Huo Xiang Zheng Qi (HXZQ)

Huo Xiang Zheng Qi Oral Liquid is a commonly used Chinese patent medicine for treating gastrointestinal disorders. Its formula originates from the Song Dynasty medical formulary *Taiping Huimin Heji Jufang* and has traditionally been used to manage symptoms such as vomiting and diarrhea caused by wind-cold and dampness stagnation. Recent studies have suggested its role in preventing and treating CINV, particularly for patients receiving multi-day, highly emetogenic chemotherapy regimens (e.g., cisplatin-based therapy), offering an alternative for patients who are unable to tolerate or receive neurokinin-1 receptor antagonists (NK1RAs). A study evaluating HXZQ Oral Liquid combined with a standard antiemetic regimen (5-HT3 receptor antagonist + dexamethasone) in patients receiving multi-day cisplatin chemotherapy found that the combination improved the complete response rate during the acute phase (days 1-3) and increased the number of CINV-free days [39]. Another multicenter, double-blind, randomized phase III clinical trial involving 166 patients reported that adding HXZQ Oral Liquid to a standard two-drug regimen significantly prolonged the mean duration of CINV-free days throughout the chemotherapy cycle and improved the complete control rate after the high-risk period for CINV [40]. A summary of studies investigating HXZQ for CINV is presented in **Tables 2**, **3**.

The antiemetic mechanism of HXZQ Oral Liquid likely involves its holistic regulatory characteristics of multi-component, multi-target action. Its formulation contains several herbs, including *Pogostemon cablin* (*Guang Huo Xiang*), *Atractylodes macrocephala* (*Bai Zhu*), *Citri Reticulatae Pericarpium* (*Chen Pi*), *Magnolia officinalis* (*Hou Po*), *Poria cocos* (*Fu Ling*), *Pinellia ternata* (*Ban Xia*), and *Glycyrrhiza uralensis* (*Gan Cao*). Potential mechanisms underlying its antiemetic activity may involve: (1) Modulation of neurotransmitter receptors: Alkaloid components derived from *Pinellia terna-*

Table 2. Summary of clinical evidence on TCM for the prevention and treatment of CINV

TCM Intervention	Study	Study Population	Key Clinical Outcomes
Rikkunshito (Liu-Jun-Zi-Tang)	Jo et al. (2024) [32]	Patients with malignant tumor receiving cisplatin-based chemotherapy	1. Significantly reduced intravenous 5-HT_3RA use on days 2-3 post-chemotherapy; 2. Significantly reduced domperidone use from day 4 onward.
	Konno et al. (2025) [34]	Patients with uterine corpus or cervical cancer receiving cisplatin-based chemotherapy	1. No significant difference in delayed-phase complete response (CR) rate vs. control; 2. No significant improvement in CR, complete control (CC), nausea severity, appetite, or time to treatment failure in acute phase or overall cycle.
Xiang-Sha-Liu-Jun-Zi-Tang	Shih et al. (2021) [33]	Gastric cancer patients undergoing surgery and adjuvant chemotherapy	Alleviated chemotherapy-related gastrointestinal symptoms (dyspepsia, nausea, vomiting, anorexia) and improved postoperative gastrointestinal function.
Huo Xiang Zheng Qi	Wei et al. (2023) [38]	Patients receiving multi-day cisplatin-based chemotherapy without NK1 receptor antagonists (NK1RAs)	1. Significantly improved acute-phase CR rate of CINV; 2. Significantly higher CR rate beyond the risk period; 3. Increased number of CINV-free days in the treatment cycle; 4. Significantly increased Living Index-Emesis (FLIE) scores and quality of life.
	Tong et al. (2025) [39]	Patients undergoing 3-day cisplatin-based highly emetogenic chemotherapy (HEC) without NK1RAs	1. Prolonged mean number of CINV-free days during the treatment cycle; 2. Improved CC rate beyond the risk period; 3. Increased nausea-free days; 4. Improved FLIE scores.
Ginseng	Gao et al. (2025) [50]	Patients with chronic diseases	1. Improved gut microbiota composition; 2. Enhanced intestinal barrier function; 3. Reduced inflammatory signaling pathway activation.
Xiao-Ban-Xia-Tang (XBXT)	Li et al. (2024) [54]	Patients with malignant tumor receiving chemotherapy	1. Improved nausea and vomiting remission rates compared with conventional antiemetic therapy alone; 2. Improved quality of life and dietary intake; 3. Reduced treatment-related adverse events.
Ginger	Silva et al. (2022) [62]	Cervical cancer patients receiving cisplatin + radiotherapy	Improved CINV symptoms, reduced nausea/vomiting severity based on CTCAE grading, and improved nausea-related quality of life.
	Uthaipaisanwong et al. (2019) [64]	Patients with gynecologic malignancies receiving carboplatin + paclitaxel	Daily supplementation with 2 g ginger significantly reduced acute-phase nausea severity and was associated with a low incidence of mild adverse reactions.
	Lin et al. (2025) [63]	Cancer patients receiving chemotherapy (including HEC)	Combined with standard antiemetics, significantly reduced grade ≥ 3 acute nausea and severe overall vomiting, particularly in in HEC regimens.
Hezhong Granules	Wu et al. (2024) [30]	Patients with advanced CRC receiving fluorouracil-based chemotherapy	1. Improved objective response rates (ORR; ~17.5% higher) for acute CINV; 2. Significantly increased CRR and ORR for delayed nausea/vomiting; 3. Reduced daily incidence of CINV (19% lower); 4. Improved quality of life without serious treatment-related adverse events.

CR: complete response, CC: complete control, HEC: highly emetogenic chemotherapy.

Table 3. Summary of experimental pharmacologic evidence for TCM for the prevention and treatment of CINV

TCM Intervention	Study	Model/Cell Line	Key Pharmacologic Mechanisms & Findings
Ginseng	Hu et al. (2021) [45]	Cisplatin-induced intestinal injury in ICR mice	1. Inhibited oxidative stress by increasing superoxide dismutase (SOD) and catalase (CAT) activities and reducing malondialdehyde (MDA) and reactive oxygen species (ROS) levels; 2. Suppressed the NF-κB signaling pathway and reduced TNF-α and IL-1β expression; 3. Inhibited intestinal epithelial apoptosis through regulation of the Bcl-2/Bax/caspase-3/caspase-9 pathway; 4. Upregulated tight junction proteins and improved intestinal barrier integrity.
Xiao-Ban-Xia-Tang (XBXT)	Liang et al. (2024) [58]	Cisplatin-induced rat pica model	1. Reduced kaolin intake and pica behavior; 2. Alleviated gastrointestinal inflammatory injury, and decreased HMGB1, IL-1β, TNF-α expression; 3. Activated Nrf2/SLC7A11/GPX4 pathway and inhibited ferroptosis.
Xiao-Ban-Xia-Tang (XBXT)	Meng et al. (2020) [55]	Cisplatin-induced rat pica model	1. Suppressed both acute and delayed pica behavior and alleviated gastrointestinal pathological injury; 2. Lowered ROS, IL-1β, IL-18 levels; 3. Inhibited activation of the NLRP3 inflammasome in gastric antrum and ileum.
Xiao-Ban-Xia-Tang (XBXT)	Zhao et al. (2024) [60]	Cisplatin-induced rat pica model	1. Reduced kaolin consumption and improved cisplatin-induced weight loss and anorexia; 2. Alleviated gastrointestinal inflammation; 3. Activated AMPK-Nrf2 pathway and restored PINK1/Parkin-mediated mitophagy.
Xiao-Ban-Xia-Tang (XBXT)	Qian et al. (2010) [61]	Cisplatin-induced mink emesis model	Dose-dependently reduced the frequency of retching and vomiting and inhibited NK1 receptor overexpression in ileum and area postrema.
Ginger	Noor et al. (2024) [70]	Solid tumor patients and cancer cell lines	Alleviated CINV, reduced the severity of delayed nausea, and improved nausea-related quality of life.
Ginger	Liang et al. (2025) [69]	Cisplatin-induced rat pica model	Improved pica behavior and gastrointestinal inflammation; inhibited ferroptosis via iron homeostasis regulation (downregulation of TfR1/DMT1 and upregulation of ferritin/Fpn).

ta have been reported to antagonize 5-HT3 and NK-1 receptors [24]; triterpenoids from *Poria cocos,* including Pachymic acid, dehydroeburicoic acid, and 3β-hydroxylanosta-7,9(11),24-trien-21-oic acid, may modulate 5-HT3 receptor-mediated ion currents [41, 42]. (2) Anti-inflammatory and mucosal protective effects: HXZQ has been reported to inhibit the NF-κB signaling pathway, reduce the expression of multiple pro-inflammatory cytokines (e.g., IL-1β and TNF-α), and alleviate intestinal inflammation and oxidative stress, thereby mitigating gastrointestinal dysfunction [43]. (3) Regulation of gastrointestinal motility: HXZQ Oral Liquid promotes the repair of the intestinal mucosal barrier and indirectly improves gastrointestinal dysfunction by modulating gut microbiota and amino acid metabolism [44].

Ginseng and American ginseng

Ginseng primarily exerts a "Fuzheng" effect in the prevention and treatment of CINV. A systematic review and meta-analysis demonstrated that traditional plant medicines containing ginseng can significantly alleviate chemotherapy-related nausea and vomiting when used as adjunctive therapy [45]. Its mechanism of action may involve regulation of gastrointestinal motility and antioxidant activity [45]. Animal studies have shown that Korea red ginseng extract can reduce cisplatin-induced nausea- and vomiting-related behaviors in a dose-dependent manner, suggesting an antiemetic effect [46]. In addition, TCM formulations containing ginseng have been proven to reduce chemotherapy-related adverse reactions, including nausea and vomiting, while improving the quality of life of tumor patients [47].

The main bioactive constituents of ginseng are types of ginsenoside, which are generally divided into two categories: protopanaxadiol-type (PPD-type) and protopanaxatriol-type (PPT-type) ginsenosides. In a rat model of cisplatin-induced pica, total ginsenoside were shown to ameliorate abnormal feeding behavior. Both PPD-type and PPT-type ginsenosides exhibited biological activity, although PPD-type demonstrated stronger effects [48]. In cellular and animal studies, ginsenoside Rh2 (S) and related compounds have been confirmed to exert protective effects against cisplatin-induced toxicity through regulating cytoskeletal homeostasis and inhibiting cell death pathways [49].

The antiemetic mechanism of ginseng also involves modulation of neurotransmitter systems. Previous studies have demonstrated that ginsenoside Rg1 can significantly inhibit 5-HT3A receptor current induced by 5-HT, suggesting that it may alleviate nausea and vomiting symptoms by inhibiting the signal conduction mediated by the 5-HT3 receptor [50].

The anti-inflammatory and immunomodulatory properties of ginseng represent important mechanisms underlying its positive role in CINV treatment. Ginsenoside Rg1 has been shown to inhibit activation of the NF-KB signaling pathway and reduce serum levels of pro-inflammatory cytokines, including TNF-α and IL-1β, thereby attenuating intestinal inflammatory reactions. In addition, ginseng may enhance the activity of NK cells and T cells and promote the secretion of IFN-γ, reducing chemotherapy-induced toxicity without compromising anti-tumor immune effect [51].

American ginseng, a closely related species of Asian ginseng, has been widely used in traditional medicine in North America. Studies by Mehendale et al. demonstrated that American ginseng berry extract exhibited antiemetic activity in cisplatin-induced rat models. Ginsenosides such as Re and Rd possess free radical-scavenging properties, which may reduce oxidative stress and protect intestinal tissues from cisplatin-induced oxidative and inflammatory injury [52]. In addition, American ginseng can regulate intestinal flora by increasing the abundance of beneficial bacteria such as *Bifidobacterium* and promoting the production of short-chain fatty acid butyric acid, thereby improving the intestinal microenvironment and maintaining intestinal homeostasis [52]. Clinical observations have further shown that the nausea and vomiting symptoms in patients receiving ginseng preparations during chemotherapy were significantly improved compared to control groups, suggesting that ginseng may serve as a promising adjunctive therapy to alleviate chemotherapy-related adverse reactions [53, 54]. Relevant studies investigating the role of ginseng in the prevention and treatment of CINV are summarized in **Tables 2**, **3**.

Research progress in CINV prevention and treatment based on the Hewei Jiangni theory

Xiao-Ban-Xia decoction (XBXT)

Xiao-Ban-Xia Decoction (XBXT), originating from *Jin Gui Yao Lue* by Zhang Zhongjing in the Eastern Han Dynasty, is composed of two herbal components: *Pinellia ternata* (*Ban Xia*) and ginger (*Sheng Jiang*). This prescription is regarded as a representative TCM formula for the treatment of vomiting-related disorders. Despite its relatively simple composition, XBXT has demonstrated remarkable effects in the prevention and treatment of CINV. Modern research has confirmed its effectiveness and safety, and elucidating several underlying molecular mechanism. Li et al. conducted a meta-analysis integrating data from 16 randomized controlled trials (RCTs) involving a total of 1,246 patients, providing relatively high-level evidence supporting the use of XBXT for CINV management. The analysis results showed that, compared to conventional antiemetic therapy alone, XBXT combined with routine antiemetic scheme significantly improved vomiting and nausea control rates, enhanced patients' quality of life, and reduced the incidence of adverse reactions [55]. Subgroup analysis further suggested that XBXT may exert beneficial effects on both acute and delayed CINV. Inflammatory responses play a critical role in the pathogenesis of CINV. In a cisplatin-induced rat pica model, XBXT was shown to inhibit activation of the NLRP3 inflammasome, accompanied by reductions in the levels of NLRP3, ASC, caspase-1, and IL-1β in the gastric antrum and ileum, as well as decreased serum IL-1β and IL-18 levels [56]. Active ingredients in XBXT (e.g., 6- ginger and shogaol) have also been reported to directly inhibit NLRP3 inflammasome-mediated IL-1β secretion [55, 57]. These findings suggest that XBXT may attenuate chemotherapy-induced intestinal inflammatory injury and subsequently reduce the generation of peripheral vomiting signals through suppression of the NLRP3 inflammasome pathway.

Pyroptosis, a form of pro-inflammatory pathway cell death, has been associated with gastrointestinal injury. Recent studies have shown that XBXT can inhibit cisplatin-induced, gasdermin E (GSDME)-mediated pyroptosis. Mechanistically, XBXT was reported to suppress the activation of the reactive oxygen species (ROS)/c-Jun N-terminal kinase (JNK)/Bax signaling pathway, thereby reducing GSDME cleavage and activation and protecting intestinal epithelial cell (IEC-6) Integrity [58]. The results of this study associate the gastrointestinal protective effects of XBXT with the regulation of emerging cell death pathways and provide a new perspective for explaining its mechanism of alleviating gastrointestinal inflammation and injury.

Oxidative stress represents another core mechanism through which chemotherapeutic drugs induce damage to normal tissues. Previous studies have shown that XBXT can activate the nuclear factor erythroid 2-related factor 2 (Nrf2)/solute carrier family 7 members 11 (SLC7A11)/glutathione peroxidase 4 (GPX4) signaling pathway. In cisplatin-induced injury models, XBXT reduced lipid peroxidation, increased glutathione (GSH) levels, and inhibited ferroptosis through activation of this pathway, thereby improving abnormalities in gastrointestinal mitochondrial ultrastructure and alleviating oxidative damage [59]. These findings suggest that XBXT may exert "Fuzheng"-related protective effects by enhancing endogenous antioxidant defense systems and counteracting chemotherapy-induced oxidative injury.

A recent study using RNA sequencing (RNA-Seq) technology has further clarified the anti-inflammatory regulatory mechanism underlying the protective effects of XBXT against cisplatin-induced vomiting from the perspective of systems biology [60]. In a cisplatin-induced rat pica model, XBXT significantly reduced kaolin consumption and alleviated inflammatory pathologic injury to gastric antral and ileal tissues. RNA sequencing analysis demonstrated that XBXT partially reversed cisplatin-induced dysregulation of ileal gene expression, especially genes related to inflammatory responses, immune regulation, and cytokine generation. Further mechanistic studies showed that XBXT suppressed the overexpression of tryptophan hydroxylase 1 (Tph1), reduced the expression of the macrophage infiltration marker Adgre1 (F4/80), and downregulated key inflammatory mediators, including NLRP3, TNF, IL-1β and IL-6. These regulatory effects were associated with multiple classical inflammatory path-

ways, including the NF-κB, NOD-like receptor, and IL-17 signaling pathways, which is consistent with previous conclusions showing that XBXT inhibits activation of the NLRP3 inflammasome.

Mitochondrial dysfunction also participates in the pathologic process of CINV. XBXT has been reported to restore cisplatin-induced defects in PTEN-induced putative kinase 1 (PINK1)/Parkin-mediated mitophagy. Specifically, XBXT may promote activation of the PINK1/Parkin pathway through modulation of the AMP-activated protein kinase (AMPK)-Nrf2 signaling pathway, thereby facilitating the clearance of damaged mitochondria and alleviating gastrointestinal inflammation [61]. These findings further highlight the role of XBXT in maintaining cellular homeostasis at the organelle level.

In addition to the alkaloid components of *Pinellia ternata* and the bioactive constituents of ginger, which can antagonize the 5-HT3 receptor and the NK-1 receptor respectively [55], animal experiments also confirmed that XBXT can reduce the neurotransmitters associated with vomiting in both central and peripheral systems [62]. These effects suggest that XBXT may directly interfere with signal transmission within the emetic reflex arc. Collectively, these findings support the potential mechanistic overlap between the TCM theory of Hewei Jiangni and modern neuropharmacologic concepts. Relevant studies investigating XBXT in the prevention and treatment of CINV are summarize in **Tables 2** and **3**.

Ginger (Zingiber officinale Roscoe)

In modern clinical management of CINV, ginger represents an important practical application of the Hewei Jiangni theory. Clinical evidence shows that ginger may effectively alleviate CINV symptoms. A clinical trial involving patients with cervical cancer demonstrated that ginger extract improved delayed nausea and retching after cisplatin-based chemotherapy [63]. A meta-analysis showed that supplementation with ginger capsules on the basis of standard antiemetic drugs reduced the incidence of severe acute nausea by 81% and severe vomiting by 53%, with more significant synergistic effects observed in highly emetogenic chemotherapy schemes [64]. Another study involving carboplatin plus paclitaxel chemotherapy showed that daily supplementation of 2 g of ginger significantly reduced acute nausea scores, although no significant improvement was observed for delayed nausea and vomiting [65]. These findings suggest that ginger may exhibit time-dependent therapeutic effects in the prevention and treatment of CINV. Ginger can also be delivered through inhalational aromatherapy, such as ginger essential oil inhalation, to alleviate CINV symptoms. Relevant systematic reviews have reported that adjunctive inhalation of ginger essential oil can effectively alleviate chemotherapy-related nausea [66, 67].

The antiemetic benefits of ginger are not limited to adults; pediatric patients may also benefit from ginger supplementation. A systematic review focusing on children undergoing chemotherapy included 4 clinical trials with a total of 189 pediatric patients. The results showed that oral ginger supplements combined with a standard antiemetic regimen significantly reduced the incidence of both acute and delayed CINV without reported severe adverse reactions [68]. Furthermore, a multicenter, double-blind, placebo-controlled randomized trial (the SPICE trial) used a standardized ginger root extract providing 60 mg of gingerols daily in four divided doses. The results demonstrated that this regimen significantly improved nausea-related quality of life in chemotherapy patients while maintaining stable peak serum concentrations of active ginger components, thereby providing relatively high-quality evidence supporting a standardized dosing strategy for adults [69]. A summary of research on ginger for CINV is presented in **Tables 2** and **3**.

Ginger exerts antiemetic effects through multiple pathways. Its main active ingredients, 6-gingerin and 6-shogaol, have been reported to regulate iron homeostasis by downregulating the expression level of transferrin receptor 1 (TFR1) and divalent metal ion transporter 1 (DMT1), while upregulating the expression level of ferritin and iron transporter (Fpn). Through these mechanisms, ginger may reduce ferroptosis-associated gastrointestinal injury due to iron metabolism dysregulation, thereby attenuating cisplatin-induced intestinal inflammation and mucosal damage [70]. Additionally, these compounds have been reported to antagonize 5-HT3 and NK-1 receptor-mediated signaling

pathways, suppress the release of serotonin, and inhibit substance P-mediated vomiting reflex [25]. In addition, 6-shogaol has been shown to upregulate the expression of 8-hydroxyguanine DNA glycosylase 1 (OGG1) and down-regulate flap endonuclease 1 (FEN1), thereby suppressing activation of the mitochondrial DNA-cyclic GMP-AMP synthase-stimulator of interferon genes (mtDNA-cGAS-STING) signaling pathway. Through this, 6-shogaol reduces the gastrointestinal inflammatory response and further suppresses the generation of emetic signals [71]. The above findings have deepened current understanding of the anti-inflammatory and antiemetic mechanisms underlying ginger activity.

In terms of combination therapy, ginger combined with Neiguan acupoint (P6) compression has been reported to exert synergistic effects, enhancing the relief of delayed CINV symptoms [72]. Ginger can also be combined with 5-HT3RAs and dexamethasone to improve antiemetic efficacy in highly emetogenic chemotherapy regimens [73]. In terms of safety, ginger is generally well tolerated. The reported incidence of adverse reactions in adults range from 2.8% to 8.5%, with most events consisting of mild gastrointestinal symptoms, such as heartburn and diarrhea, and no significant differences compared to placebo groups [64, 65]. Similarly, no obvious adverse reactions were observed in pediatric studies, further supporting its favorable safety profile [68]. Nevertheless, caution may be warranted in patients receiving anticoagulant treatment or those with gallstones due to potential safety concerns [74].

In summary, ginger has shown promising therapeutic effect in the prevention and treatment of CINV. It can be used in combination with conventional antiemetic regimens or nonpharmacological interventions to optimize the treatment effect. Moreover, its favorable tolerability supports its use in combination with traditional Chinese and western medicine for CINV management. However, the benefit of ginger for delayed CINV requires further validation through large-scale clinical studies. In particular, stratified investigations across different chemotherapy regimens and age groups are needed to define its optimal clinical indications and target populations.

Hezhong Granules

Hezhong Granules consist of several herbs, including *Pinellia ternata (Ban Xia), Evodia rutaecarpa (Wu Zhu Yu), and ginger (Zingiber officinale, Sheng Jiang).* This formula represents a TCM prescription developed based on the Hewei Jiangni theory. Recent studies have suggested the potential of Hezhong Granules in preventing and treating CINV. Wu et al. [30] demonstrated that the addition of Hezhong Granules to a standard antiemetic regimen significantly improved the complete response and objective response rates for both nausea and vomiting during the delayed phase (24-120 hours) in patients with advanced colorectal cancer. Moreover, the combination therapy reduced the daily incidence of CINV events post-chemotherapy and effectively enhanced patients' quality of life. These results indicate that Hezhong Granules can synergistically enhance the management of delayed CINV when combined with standard antiemetic therapy. Relevant studies investigating Hezhong Granules for CINV are presented in **Table 2**.

The therapeutic effects of Hezhong Granules are likely mediated through the synergistic action of multiple bioactive components. Beyond the established antiemetic activities of *Pinellia ternata* and ginger, previous studies have suggested that this compound formula may inhibit the vomiting center and alleviate gastrointestinal reactions by suppressing the release of serotonin (5-HT) and substance P from gastrointestinal enterochromaffin cells, as well as by reducing tryptophan hydroxylase levels and NK-1 receptor expression [30]. These pharmacologic findings are broadly consistent with the TCM concept of Hewei Jiangni.

However, current evidence regarding the use of Hezhong Granules for CINV remains limited and is still at a preliminary exploration stage. Notably, an ongoing study evaluating the effects of this prescription on progression-free survival in patients with metastatic colorectal cancer has included CINV control as one of its secondary endpoints [75]. Future research may produce higher-level evidence to clarify the comprehensive value of Hezhong granules in improving symptom control, quality of life, and long-term outcomes in improving symptom con-

trol, quality of life, and long-term outcomes in patients receiving chemotherapy.

Research on acupuncture and external TCM therapies for CINV prevention and treatment

Body acupuncture

Body acupuncture is an important non-drug treatment for CINV. Guided by the TCM principles of Fuzheng Quxie and Hewei Jiangni, acupuncture is believed to regulate the neuro-immune-endocrine network and enhance the body's resistance to chemotherapy-induced toxicity, harmonize gastrointestinal function, and alleviate nausea and vomiting symptoms [76]. A systematic review and meta-analysis verified that acupuncture combined with routine nursing was superior to routine nursing alone in improving the complete control rates of both acute and delayed vomiting. This supports its use in CINV [77].

In clinical application, acupoint selection is generally based on syndrome differentiation and meridian theory. Commonly used acupoints include Neiguan (PC6), Zusanli (ST36), and Zhongwan (CV12) [77, 78]. From perspective of meridian distribution, the gastric meridians, Ren meridian, and pericardium meridian are among the most commonly selected meridians in clinical practice, which reflects the TCM principle of combining proximal and distal acupoints according to meridian pathways. Local acupoints located in the thoracoabdominal region (e.g., CV12, the Tianshu [ST25]) are often used in combination with distal limb acupoints (e.g., ST36, PC6). Mechanistically, PC6 has been reported to improve gastrointestinal dynamics through modulation of vagal pathways, ST36 can regulate the brain-gut axis, and CV12 contributes to normalization of spleen-stomach function [79].

Previous studies showed that body acupuncture combined with conventional antiemetic drugs significantly improved delayed vomiting remission rate and delayed nausea control, compared to conventional drug treatment alone [80]. Subgroup analyses further demonstrated that body acupuncture may enhance antiemetic effect regardless of whether serotonin 5-HT3RAs were included in the antiemetic regimen. The therapeutic benefits appeared to be especially pronounced in patients receiving highly emetic chemotherapy or in those with inadequate symptom control despite a standard antiemetic regimen [78, 80]. Furthermore, a meta-analysis including 10 RCTs confirmed that stimulation of the PC6 acupoint alone significantly reduced the severity of both acute and delayed nausea and exerted beneficial effects on acute vomiting [81]. A summary of research on body acupuncture for CINV is presented in **Table 4**.

The therapeutic mechanisms of body acupuncture mainly involve both immune regulation and neuroendocrine modulation. At the immunoregulatory level, body acupuncture has been reported to modulate multiple pathways such as the cholinergic anti-inflammatory pathway (CAIP) and the vagal-adrenal pathway. Stimulation of core acupoints such as ST36 can activate the CAIP, inhibit activation of the nuclear factors, promote the polarization of macrophages to anti-inflammatory M2 phenotype, while suppressing M1 polarization, and reducing the release of pro-inflammatory cytokines (e.g., TNF-α and IL-1β). In addition, acupuncture may enhance the activity of NK cells and regulate the balance between regulatory T cells/auxiliary T cells 17 (Treg/Th17), thereby alleviating intestinal mucosal inflammation and maintaining immune homeostasis [82]. At the neuro-endocrine level, body acupuncture can regulate central and peripheral neurotransmitters (e.g., serotonin, dopamine, acetylcholine) and neuropeptides (e.g., β-endorphin, substance P). Acupuncture has also been reported to modulate stress responses through the hypothalamic-pituitary-adrenal (HPA) axis and promote the secretion of gastrointestinal hormones, including ghrelin and gastrin, thereby improving delayed gastric emptying and gastrointestinal dysmotility [83].

From the perspective of brain-gut axis regulation, stimulating CV12 has been associated with activation of the brain default mode network, while ST36 mainly regulates sensorimotor networks and brain-gut axis-related pathways. Experimental studies further suggest that acupuncture may suppress overactivation of neurons in the nucleus tractus solitarius and inhibit activation of the NLRP3 inflammasome, thereby reducing transmission of peripheral vomiting signals to the central nervous system and decreasing the sensitivity of the vomiting

Table 4. Summary of research on acupuncture and external TCM therapy for the prevention and treatment of CINV

Method	Study	Core Mechanism	Results
Acupuncture Therapy	Yan Y, et al. 2023 [77]; Wang et al. 2025 [78]	1. Stimulation of acupoints such as Neiguan (PC6) and Zusanli (ST36) regulates gastrointestinal autonomic function and modulates the emetic reflex pathway; 2. Suppresses inflammatory signaling pathways, including NF-κB and NLRP3, reducing the release of TNF-α and IL-1β; 3. Downregulates tryptophan hydroxylase 1 (Tph1) expression and reduces serotonin overproduction; 4. Regulates central neurotransmitters including dopamine and substance P (SP).	1. Significantly reduces the incidence and severity of cisplatin-induced nausea and vomiting (CINV), with a particularly prominent improvement effect on delayed emesis; 2. Alleviate the chemotherapy-induced gastrointestinal mucosal injury; 3. Demonstrates favorable safety and tolerability and improves quality of life.
Auricular Acupuncture/ Auricular Acupressure (AA)	Chen et al. 2021 [88]; Tan et al. 2022 [89]	1. Stimulation of auricular acupoints including Shenmen, Stomach, Spleen, and Sympathetic modulates autonomic nervous system activity; 2. Exert antiemetic effects through the synergy of specific acupoint stimulation effects and non-specific placebo effects; 3. Regulate central and peripheral emesis-related neurotransmitter pathways, including 5-HT; 4. Alleviates chemotherapy-induced gastrointestinal inflammation.	1. Combined with conventional antiemetics, it significantly improves the complete response rate (CRR) for CINV; 2. Reduces the incidence and severity of acute nausea; 3. May improve delayed CINV, although the difference did not reach statistical significance.
Moxibustion	Yao et al. 2022 [90]	1. Thermal stimulation on acupoints inhibits the release of 5-HT3 from enterochromaffin cells and promotes the production of G-CSF, blocking the transmission of emetic signals to the vomiting center and inhibiting its abnormal discharge; 2. Two-way regulation of gastrointestinal motility and secretory function, by upregulating the messenger ribonucleic acid expression of nitric oxide synzyme in gastrointestinal tissue and downregulating the messenger ribonucleic acid expression of angiotensin II, the gastric emptying function is regulated; 3. Activate mast cells and phagocytes, promote antibody production, enhance the body's immunity, and inhibit the release of inflammatory cytokines such as interleukin 1B and interleukin 6, so as to alleviate intestinal mucosal inflammation; 4. Modulates the neuroendocrine network related to gastrointestinal motility through acupoint stimulation.	1. Significantly reduces the incidences of post-chemotherapy nausea and vomiting when used alone or in combination with conventional therapy; 2. May improve additional gastrointestinal symptoms such as bloating and abdominal discomfort; 3. Generally demonstrates good safety and tolerability.
Acupoint Application	Chen et al. 2024 [91]; Wang et al. 2025 [81]	1. Herbal paste application to acupoints including Shenque (CV8), Zusanli (ST36), and Neiguan (PC6) regulates gastrointestinal function and downward movement of stomach Qi; 2. Bioactive compounds such as gingerols may antagonize 5-HT3 receptors and inhibit emetic signal transmission; 3. Modulates brain-gut peptide hormones (e.g., Cholecystokinin [CCK], Ghrelin) to improve gastric emptying and reduce intestinal mucosal inflammation.	1. Combined with conventional antiemetic medicine, significantly improves delayed CINV control; 2. Ranked among the most effective non-pharmacological interventions in network meta-analysis; 3. Associated mainly with mild local adverse reactions and improved quality of life.

PC6: Pericardium 6, ST36: Stomach 36, CV8: Conception Vessel 8, CV12: Conception Vessel 12, 5-HT: 5-hydroxytryptamine, G-CSF: granulocyte colony-stimulating factor, CCK: cholecystokinin.

center [84]. Several RCTs have confirmed that body acupuncture can effectively reduce the incidence of delayed nausea. Subgroup analysis further shows that treatment duration of at least 5 days may provide greater benefits for delayed vomiting, highlighting the importance of adequate treatment duration for achieving sustained therapeutic effects [85].

Ear acupuncture and auricular acupressure

Ear acupuncture and auricular acupressure are important nonpharmacological interventions for CINV management. Guided by the TCM principle of Fuzheng Quxie, these therapies stimulate auricular points corresponding to the internal organs to regulate the flow of Qi and blood, support spleen-stomach function, and alleviate chemotherapy-induced gastrointestinal dysfunction and inflammatory reactions [86].

A meta-analysis including 19 RCTs reported that auricular therapies combined with conventional antiemetic drugs significantly improved the overall remission rate of CINV (RR=1.31, 95% CI 1.22-1.41) and reduced delayed nausea (SMD=-0.68) and vomiting (SMD=-0.91). Additionally, the combined therapy reduced the incidence of antiemetic drug-related adverse reactions, such as constipation and fatigue [87]. An RCT involving breast cancer patients demonstrated that the complete remission rate of acute CINV in the ear acupuncture group was significantly higher than that in the conventional care group (52.6% vs. 23.7%) [88]. This antiemetic effect may stem from both specific therapeutic effects and placebo-related responses.

Mechanistic studies suggest that ear acupuncture and auricular acupressure may exert multitarget regulatory effects. Stimulation of auricular acupoints such as Shenmen and sympathetic points may modulate vagal activity and the release of central neurotransmitters (e.g., 5-HT, substance P) thus interfering with transmission of the emetic reflex arc. In addition, these therapies can inhibit activation of the NF-κB pathway and reduce the levels of pro-inflammatory cytokines (e.g., TNF-α), and protect the intestinal mucosal barrier [89].

In recent years, research on ear acupuncture for CINV has increasingly focused on the establishment of standardized treatment protocols. One auricular acupressure protocol developed based on the STRICTA selected seven auricular acupoints, including Shenmen, stomach, and sympathetic points, and applied *Vaccariae Semen* (Wang Bu Liu Xing) seeds for acupressure stimulation three times daily for 30 s per session over a 5-week intervention period. Validation by 14 experts demonstrated a content validity index ranging from 85.7% to 100%, and subsequent clinical application suggested that the protocol significantly reduced both the incidence and severity of CINV [89]. Another evidence-based study further clarified key intervention parameters for auricular acupuncture and auricular acupressure, including continuous treatment duration for 5 days after chemotherapy and stimulation intensity, thereby providing a basis for standardized application of these therapies [90]. A summary of relevant research on ear acupuncture and auricular acupressure for CINV is shown in **Table 4**.

Despite these promising findings, current studies on auricular therapies for CINV remain limited by relatively small sample sizes and difficulties associated with blinding design. Future multi-center, large-scale RCTs are warranted to further define the optimal clinical indications of these therapies across different chemotherapy regimens and to evaluate their long-term safety.

Moxibustion and other external therapies

Moxibustion is a traditional Chinese external therapy that involves the combustion of moxa to produce thermal stimulation at specific acupoints. It is considered particularly suitable for patients with spleen-stomach deficiency-cold patterns. Its therapeutic principles are closely associated with the theories of “Fuzheng Quxie” and “Hewei Jiangni”. On the one hand, moxibustion is believed to warm and tonify spleen-stomach function, thereby enhancing the body’s tolerance to chemotherapy-related toxicity; on the other hand, it may regulate Qi movement and promote the downward flow of stomach Qi to alleviate vomiting symptoms.

In recent years, high-quality evidence has supported the application of moxibustion for CINV. A systematic review involving 2,990 patients indicated that, compared to control groups,

moxibustion significantly reduced the incidence and severity of nausea and vomiting, while also improving functional status and quality-of-life outcomes [91]. In addition, moxibustion was reported to alleviate other chemotherapy-related gastrointestinal symptoms, such as bloating, diarrhea, and constipation, highlighting its advantages in overall regulation.

Commonly used acupoints in clinical practice include Zusanli (ST36), Zhongwan (CV12), Shenque (CV8), and Neiguan (PC6). The combination of these acupuncture points reflects the TCM principle of integrating proximal and distal acupoint selection according to meridian theory. Through coordinated stimulation of these acupoints, moxibustion may strengthen spleen-stomach function, reduce reflux and stop vomiting. Mechanistically, the thermal stimulation by moxibustion may exert therapeutic effects through multiple pathways, including modulation of autonomic nerve system activity, suppression of neurotransmitter release such as 5-HT, and attenuation of intestinal inflammatory reactions [91]. In terms of safety, adverse reactions associated with moxibustion are relatively mild, mainly manifested as transient local warmth sensations or skin erythema, suggesting that moxibustion is relatively safe under standardized operation. Relevant studies investigating moxibustion for CINV are summarized in **Table 4**.

Acupoint application therapy (acupoint herbal patching therapy) is an external treatment method in which herbal preparations are applied to specific acupoints. Therapeutic effects are achieved through transdermal absorption and acupoint-mediated stimulation, representing a practical application of the Hewei Jiangni theory in TCM. Compared with oral administration, this therapy can avoid gastrointestinal irritation, provide sustained stimulation, and achieve relatively high patient compliance.

Recent studies have confirmed that acupoint patching therapy combined with routine antiemetic scheme has a significant advantage in preventing and treating delayed CINV. A Bayesian network meta-analysis of 4,081 patients compared 14 non-drug interventions and reported that acupoint patching therapy ranked first for improving delayed vomiting and delayed nausea, with superior efficacy than conventional antiemetic treatment alone [80]. Another clinical study described a treatment protocol using Shenque (CV8), Zusanli (ST36), and Neiguan (PC6) as the primary acupoints, combined with herbal patches containing ginger, clove, and other ingredients, together with acupressure stimulation. The combined therapy significantly improved the response rate of delayed CINV and reduced the severity score of delayed nausea [92]. Mechanistically, the therapeutic effect of acupoint application therapy may involve multiple pathways. Bioactive ingredients absorbed transdermally may modulate emesis-related receptors such as 5-HT3 and NK-1 receptors; In addition, acupoint stimulation itself can regulate brain-gut axis function and promote the secretion of gastrointestinal hormones, including ghrelin and gastrin, thereby contributing to improvements in gastrointestinal motility and emesis control [92].

In summary, external TCM methods, including moxibustion and acupoint application therapy, have demonstrated good therapeutic efficacy and favorable safety profiles for the prevention and treatment of CINV through multi-target and multi-pathway regulatory effects. These therapies represent important practical applications of the TCM theories of Fuzheng Quxie and Hewei Jiangni. Future research should focus on further standardizing treatment protocols, conducting more high-quality, large-sample randomized controlled trials, and clarifying the optimal integration strategies between these therapies and conventional antiemetic regimens, as well as their underlying biological mechanisms.

Clinical compatibility strategy of “Fuzheng” and “Jiangni” at different stages of CINV

In the clinical management of CINV, the application of Fuzheng Quxie and Hewei Jiangni should not be regarded as a simple combination. Instead, the compatibility and therapeutic emphasis of these approaches should be dynamically adjusted according to patient’s physical status and their stage of chemotherapy treatment.

Continuous administration of Fuzheng-related herbs before chemotherapy and throughout the treatment course may enhance patients’ tolerance to chemotherapy and reduce treatment-related toxicities. A systematic review and meta-analysis in patients with advanced

gastric cancer showed that Shenqi Fuzheng Injection combined with chemotherapy reduced the incidence of grade 3-4 nausea and vomiting, and myelosuppression, while significantly improving patients' quality of life [93]. Similarly, in patients with non-small cell lung cancer, Shenfu Injection combined with chemotherapy significantly reduced the risk of grade 3/4 nausea and vomiting (RR=0.29) and improved Karnofsky Performance Status (KPS) scores, suggesting that Fuzheng-based holistic regulation may alleviate the severity of CINV [94]. For acute CINV, therapeutic strategies prioritizing Hewei Jiangni interventions combined with 5-HT_3RAs may improve symptom control, appetite, and quality of life, while reducing adverse reactions [24]. Modern studies further suggest that Hewei Jiangni formulations, such as Xiao-Ban-Xia-Tang, may enhance antiemetic efficacy and reduce adverse events [55]. Commonly used antiemetic herbs including ginger and *Pinellia ternata* (Ban Xia) have been extensively investigated and demonstrated benefits in CINV management. Furthermore, non-pharmacologic interventions also play an important role in CINV management. Evidence suggests that approaches such as acupressure and transcutaneous electrical acupoint stimulation may improve both acute and delayed CINV symptoms, while auricular acupressure appears to show a particularly favorable effect on delayed nausea and vomiting [81, 87].

Limitations

1. Variability in study design and methodologic quality: Most available clinical studies are limited by relatively small sample sizes. In many RCTs, challenges in implementing adequate blinding procedures may increase the risk of selection bias and execution bias.

2. Mechanism research is still in the exploration stage: Although several TCM formulas or isolated active ingredients have shown anti-inflammatory, antioxidant, neurotransmitter-regulating effects in experimental models, their specific targets, signaling pathways, and pharmacologically active constituents have not been fully clarified. Most mechanistic studies remain descriptive in nature and lack systematic and translational investigation.

3. Insufficient long-term follow-Up data: Existing studies have mainly focused on short-term efficacy evaluation. Evidence regarding the long-term safety of TCM interventions and their effect on long-term clinical outcomes remains limited.

4. Challenges in standardizing individualized treatment plans: TCM emphasizes syndrome differentiation and individualized treatment, resulting in variability in herbal prescriptions and therapeutic protocols across clinical studies. Although this individualized approach reflects an important characteristic of TCM, it also poses challenges for protocol standardization, reproducibility, and generalizability of study findings.

5. Lack of consensus on combined treatment model: At present, there is a lack of high-quality evidence supporting the optimal combination of TCM interventions with conventional antiemetic regimens. Clinical TCM practice largely relies on experience and lacks standardized guidance, which hinders the process of incorporating TCM intervention into international evidence-based clinical guidelines.

Conclusion and future perspectives

Guided by the TCM theories of Fuzheng Quxie and Hewei Jiangni, TCM-based interventions for CINV management represent a holistic and multi-target therapeutic strategy. Existing evidence suggests Fuzheng-oriented formulas and medicinal herbs, such as Bai-Zhu-San, ginseng, and related compounds, may enhance immune function, reduce inflammation and oxidative stress, promote tissue repair, and improve patients' tolerance to chemotherapy-induced toxicity. In contrast, Hewei Jiangni-based therapies, including XBXT, ginger, and external interventions (e.g., acupuncture, Moxibustion), primarily focus on regulating gastrointestinal function and suppressing abnormal activation of the emetic reflex pathways, thereby alleviating nausea and vomiting. Clinical studies have shown that the combination of TCM interventions and conventional antiemetic regimens can produce synergistic effects, particularly in the control of delayed CINV, while maintaining favorable overall safety profiles and improving patients' quality of life and treatment adherence.

To further advance this field and promote clinical transformation, several directions warrant

particular attention. First, future studies should strictly follow the international reporting standards and carry out rigorously designed, large-scale, multicenter, randomized double-blind placebo-controlled trials to provide more reliable medical evidence. Second, modern technologies, such as systematic biology, metabolomics, microbiome analysis, and molecular imaging, should be integrated to further elucidate the biological mechanisms underlying TCM interventions for CINV and to clarify key bioactive compounds and molecular targets. Third, while preserving the TCM principle of syndrome differentiation and individualized treatment, efforts should be made to establish standardized diagnostic criteria, treatment protocols, and efficacy evaluation systems for common CINV-related syndromes, thereby balancing individualized treatment strategies with reproducibility and comparability of clinical studies. Furthermore, the optimal integration models between TCM interventions and conventional antiemetic therapies should be systematically investigated. Through continuous high-quality research, TCM may provide evidence-based complementary therapeutic options for the comprehensive management of CINV.

Disclosure of conflict of interest

None.

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