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Herbal Antiemetic Mouth-Dissolving Tablets: A Review of Ginger *(Zingiber officinale)* and Peppermint *(Mentha Piperita L.)*

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Abstract: Nausea and vomiting are prevalent clinical symptoms linked to various conditions, including pregnancy-associated nausea and vomiting (NVP), postoperative nausea and vomiting (PONV), motion sickness, and chemotherapy-induced nausea and vomiting (CINV). While conventional antiemetics, such as 5- HT_3 receptor antagonists, are effective, they often face limitations due to side effects, costs, and adherence issues, particularly among pediatric, geriatric, and dysphagic patients. Herbal Phyto therapeutics, especially ginger *(Zingiber officinale)* and peppermint *(Menthapiperita)*, present safe and effective alternatives. The active components of ginger, including gingerols and shogaols, exhibit antiemetic properties through serotonin (5- HT_3) receptor antagonism, prokinetic effects, and antioxidant activities. Meanwhile, peppermint's volatile oils, predominantly menthol, deliver antispasmodic, anti-serotonergic, and gastrointestinal-soothing benefits. Incorporating these herbs into mouth-dissolving tablets (MDTs) promotes rapid disintegration, enhances patient compliance, and allows for a quicker onset of action without the need for water, making them particularly advantageous for patients experiencing active nausea. Despite encouraging clinical evidence, challenges such as standardization, taste masking, and thorough clinical validation persist. Future research should concentrate on optimizing herbal MDT formulations, standardizing dosages, and aligning with regulatory frameworks to fully exploit their the rapeutic potentialin modern supportive care.

Keywords: *Ginger, Zingiber Officinale, Peppermint, Mentha Piperita, Antiemetic, Nausea, Vomiting, Mouth- Dissolvingtablets, Phytotherapy*

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I. INTRODUCTION

Nausea and vomiting are prevalent clinical symptoms linked to various conditions, including motion sickness, recovery after surgery, pregnancy, and chemotherapy-induced nausea and vomiting (CINV). While traditional antiemetic medications, such as 5-hydroxytryptamine-3 (5-HT_3) receptor antagonists (e.g., ondansetron), are effective, their clinical application is often restricted due to side effects, high costs, and reduced adherence, particularly in pediatric, geriatric, and dysphagic patients [1,2]. These challenges have sparked a growing interest in alternative treatment options, particularly herbal phyto therapeutics, which boast a long-standing history in traditional medicine and are increasingly backed by new pharmacological research.

Among herbal antiemetics, ginger (Zingiber officinale Roscoe) and peppermint (Mentha piperita L.) have garnered significant attention for their well-established gastrointestinal benefits and favorable safety profiles [3,4]. These herbs are especially well-suited for formulation into mouth- dissolving tablets (MDTs), which quickly dissolve in the mouth without requiring water, thus making administration easier and potentially speeding up the onset of therapeutic effects.

- *Ginger (Zingiber officinale)*

Ginger is a perennial herb widely utilized in Ayurvedic, Unani, Traditional Chinese, and Western herbal medicine to treat nausea, vomiting, and other gastrointestinal issues. Its antiemetic properties stem from its bioactive compounds, such as [6]-gingerol, [8]-gingerol, and [6]-shogaol, which exert pharmacological effects through various mechanisms [5].

Preclinical studies have shown that ginger extracts can inhibit chemically induced emesis by influencing gastrointestinal motility and blocking serotonin (5-HT_3) receptors associated with emetic signaling pathways [6]. Clinical research supports these findings; a randomized controlled trial by Lumb et al. demonstrated that ginger's prophylactic effectiveness was comparable to metoclopramide in reducing postoperative nausea and

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vomiting in day-care surgery patients [7].

Multiple systematic reviews and meta-analyses have assessed ginger's antiemetic effectiveness across different conditions. It has shown consistent benefits in pregnancy-induced nausea and vomiting, although evidence for motion sickness, postoperative nausea, and CINV varies due to differences in study design, dosage, and outcome measures [8–10]. Nonetheless, ginger is one of the most extensively researched herbal antiemetics.

➢ *Peppermint (Mentha piperita)*

Peppermint is a hybrid aromatic herb traditionally employed to alleviate gastrointestinal discomfort, including nausea, indigestion, bloating, and gas. Its therapeutic effects are mainly attributed to volatile oils high in menthol and menthone, which possess antispasmodic and carminative qualities [11].

Clinical studies have shown that peppermint oil, when administered orally or through inhalation, can significantly lessen the severity and frequency of nausea and vomiting in postoperative and chemotherapy contexts as a complementary therapy [12,13].

Randomized controlled trials involving cancer patients undergoing chemotherapy have reported a reduction in nausea intensity and vomiting episodes after peppermint extract administration compared to control groups [14]. Systematic reviews further indicate that peppermint aromatherapy may effectively manage nausea across various clinical situations, although inconsistencies in formulation and methodology call for more standardized research [15].

➢ *Herbal Antiemetic Mouth-Dissolving Tablets*

Mouth-dissolving tablets (MDTs), also known as orally disintegrating tablets (ODTs), are solid dosage forms designed to dissolve quickly in saliva without the need for water. MDTs offer notable advantages, including rapid onset of action, enhanced patient compliance, and convenience, particularly for individuals experiencing active nausea or difficulty swallowing regular tablets [16,17].

Integrating herbal antiemetic agents like ginger and peppermint into MDT formulations represents an innovative approach that merges traditional phytotherapy with modern drug- delivery technology. Preliminary formulation studies involving ginger oral thin films and herbal matrix systems have shown the potential for creating stable, patient-friendly, and fast-acting dosage forms for managing nausea [18]. Although commercially available herbal MDT products are currently limited, ongoing research underscores their potential clinical importance.

II. DISCOVERY OF MOUTH-DISSOLVING ANTIEMETIC

➢ *Traditional and Early Use (Ancient to Pre-20th Century)*

The therapeutic application of herbal remedies for managing nausea and vomiting boasts a rich history that spans several millennia. Ginger (*Zingiber officinale*) has been widely employed in Ayurvedic, Unani, Traditional Chinese, and Greco-Roman medical traditions to relieve gastrointestinal discomfort, including nausea, vomiting, and dyspepsia [19,20]. Ancient medical texts attribute these effects to ginger's pungent phenolic compounds, thought to enhance digestion and normalize gastric function. Although early ethnomedical records lack controlled clinical validation, the consistent global documentation of ginger as an antiemetic highlights its enduring therapeutic significance.

In a similar vein, peppermint (*Mentha piperita*), recognized for its menthol-rich volatile oils, has been traditionally used in European and Asian medicine to address digestive disturbances such as nausea, flatulence, abdominal pain, and indigestion [21]. Its aromatic, carminative, and spasmolytic properties formed the pharmacological foundation for its widespread application. These traditional uses laid the groundwork for later scientific exploration into the antiemetic potential of both ginger and peppermint.

➢ *Mid-20th Century to Early Modern Scientific Studies*

- *Ginger*

Interest in ginger's antiemetic properties surged during the late 20th century, coinciding with the advent of controlled clinical trials. A groundbreaking randomized controlled study by Lumb et al. compared powdered ginger with metoclopramide and a placebo in women undergoing day-care surgery. The findings revealed that ginger led to a comparable reduction in postoperative nausea and vomiting (PONV) relative to metoclopramide and outperformed the placebo, marking a crucial shift from traditional usage to evidence-based validation [22].

Following this, Chrubasik and Pittler (2005) conducted a systematic review of 24 randomized clinical trials involving approximately 1,073 participants. Their analysis assessed ginger's efficacy in conditions such as kinetosis, PONV, and pregnancy-related nausea and vomiting. While evidence for postoperative and motion-related nausea remained inconclusive, ginger consistently demonstrated benefits in managing pregnancy-associated nausea with minimal adverse effects at doses up to 6 g/day [23].

➢ *Early 21st Century Clinical Evidence*

- *Ginger in Chemotherapy-Induced Nausea and Vomiting (CINV)*

Systematic reviews published in the early 2010s revealed mixed results regarding ginger's effectiveness in managing chemotherapy-induced nausea and vomiting (CINV). Variability in formulation, dosage, study design, and outcome assessments contributed to these inconsistent findings. A comprehensive review published in *Nutrition Reviews* (2013) reported heterogeneous results, stressing the need for well-designed randomized trials [24].

One of the largest randomized, double-blind clinical trials conducted by Schwartzberg et al. evaluated ginger

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supplementation (0.5–1.0 g/day) as an adjunct to standard 5-HT_3 receptor antagonist therapy in adult chemotherapy patients. The study found a significant reduction in acute nausea severity on Day 1 of chemotherapy compared to the placebo; however, its effects on delayed nausea and overall quality of life were limited [25].

A subsequent systematic review and meta-analysis published in 2018 indicated no statistically significant reduction in acute nausea or vomiting with ginger compared to controls in CINV, underscoring the importance of standardized formulations and rigorous trial methodologies [26].

- *Ginger Meta-Analyses on Pregnancy and Other Effects*

Recent meta-analyses up to 2025 consistently affirm ginger's efficacy in decreasing nausea severity during pregnancy (nausea and vomiting of pregnancy, NVP). However, its impact on vomiting frequency remains modest. These analyses also highlight ginger's additional pharmacological activities, including anti-inflammatory and antioxidant properties, which may work in synergy with its antiemetic effects [27,28].

➢ *Peppermint (Mentha piperita) Research*

- *Preclinical and Early Clinical Evidence*

While peppermint's traditional gastrointestinal applications are well-documented, modern pharmacological research has primarily focused on its essential oil components, particularly menthol, and their effects on smooth muscle relaxation and gastrointestinal motility [29].

- *Clinical Trials and Complementary Therapies*

Numerous clinical studies have explored peppermint essential oil administered via inhalation or oral formulations. A quasi-randomized controlled study reported significant reductions in nausea, vomiting, retching, and nausea severity among cancer patients receiving chemotherapy when peppermint oil was used as an adjunct to standard antiemetic therapy [30].

Randomized controlled trials in breast cancer patients further demonstrated significant declines in nausea intensity and vomiting frequency at 24 and 48 hours post-chemotherapy following peppermint extract administration compared to controls [31].

Systematic reviews and meta- analyses suggest that peppermint oil inhalation may effectively reduce nausea and vomiting in postoperative, pregnancy, and chemotherapy contexts, although variability in study quality remains a limitation [32].

Recent randomized trials published in 2025, including studies on rhinoplasty patients, have shown significant reductions in postoperative nausea with peppermint essential oil, indicating renewed clinical interest in peppermint's antiemetic potential across surgical and therapeutic scenarios [33].

- *Emerging Directions: Mouth-Dissolving and Novel Delivery Systems*

Advancements in drug-delivery technology have led to the creation of mouth-dissolving tablets (MDTs) and oral thin films for antiemetic therapy. These systems are designed to dissolve rapidly in saliva without the need for water, enhancing patient compliance and providing a quicker onset of action—crucial benefits during episodes of active nausea [34].

Although commercially available herbal MDTs are still limited, formulation studies involving ginger- and peppermint-based oral thin films and herbal matrix systems demonstrate the feasibility of integrating traditional phototherapeutics' with modern dosage forms. This emerging approach represents a promising strategy for the future management of nausea and vomiting [35].

III. MOUTH-DISSOLVING ANTIEMETIC TABLETS

Mouth-dissolving tablets (MDTs), commonly referred to as orally disintegrating tablets (ODTs) or fast-dissolving tablets, are solid oral dosage forms designed to dissolve quickly in the mouth without the need for water, typically within seconds to one minute [36]. The United States Food and Drug Administration (FDA) define an orally disintegrating tablet as "a solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue." MDTs effectively combine the stability and dosage accuracy of solid forms with the ease of use associated with liquid formulations, making them an excellent choice for patient-centered drug delivery.

In the realm of antiemetic therapy, MDTs hold particular importance as nausea and vomiting frequently hinder a patient's ability to swallow standard tablets. Their rapid disintegration in saliva facilitates easier administration and may lead to a quicker onset of action, which is essential for providing symptomatic relief in conditions related to nausea, such as motion sickness, postoperative nausea and vomiting (PONV), pregnancy-related nausea, and chemotherapy- induced nausea and vomiting (CINV).

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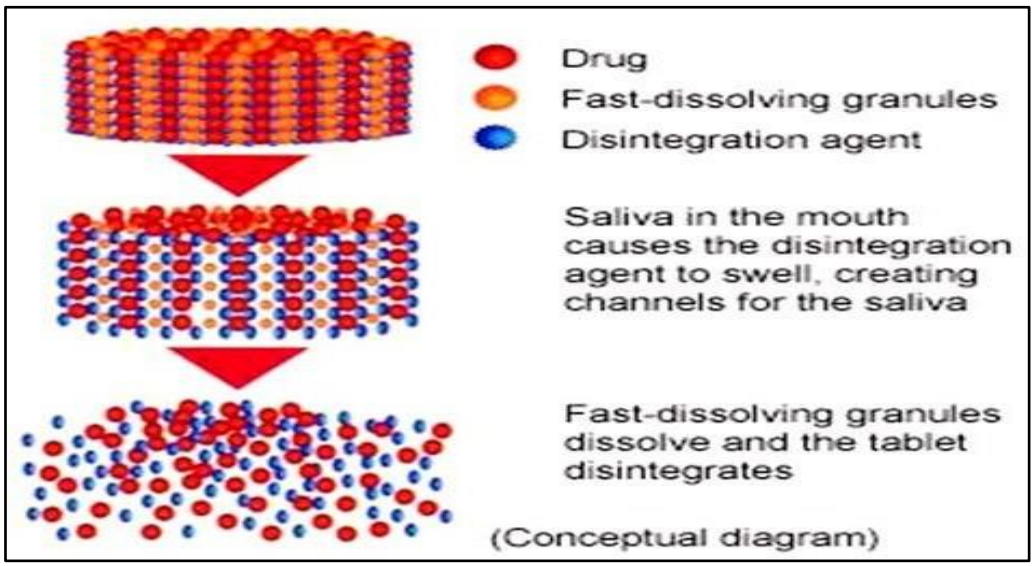

Fig 1 Conceptual Illustration of Saliva-Induced Disintegration and Drug Release from a Fast-Dissolving Tablet.

➢ *The Significance of Mouth-Dissolving Antiemetic Tablets*

Mouth-dissolving antiemetic tablets hold significant clinical importance due to their ability to improve patient compliance, comfort, and treatment effectiveness. Traditional oral antiemetic tablets may be rejected or vomited before they can be absorbed, resulting in therapeutic failure. MDTs address this issue by enabling administration without water, facilitating rapid tablet dissolution, and allowing for potential pre-gastric absorption, ultimately leading to better treatment outcomes.

➢ *Benefits for Diverse Patient Groups*

Moreover, MDTs are particularly advantageous for various patient populations, including:

- Pediatric patients
- Geriatric patients
- Those with psychiatric conditions
- Bedridden individuals
- Patients with swallowing difficulties (dysphagia)
- Individuals experiencing acute nausea who cannot tolerate solid oral forms

From a pharmaceutical standpoint, MDTs signify a crucial advancement in drug delivery technology, prioritizing patient convenience and compliance, and aligning with contemporary regulatory and clinical standards.

➢ *Ideal Characteristics of Mouth-Dissolving Antiemetic Tablets*

- An effective mouth-dissolving antiemetic tablet should have the following properties:
- Rapid disintegration in saliva without the need for water (within 30–60 seconds).
- Pleasant taste and smooth mouthfeel for enhanced patient acceptability.
- Adequate mechanical strength to endure handling and packaging.
- Low sensitivity to moisture and temperature changes.
- Compatibility between the active pharmaceutical ingredient and excipients.
- Sufficient drug release and bioavailability to ensure effective antiemetic action.

➢ *Advantages of Mouth-Dissolving Antiemetic Tablets*

The key benefits of MDTs in antiemetic therapy include:

- *Ease of Administration*

MDTs can be taken without water, making them particularly useful during episodes of nausea when fluid intake may be challenging or not advisable.

- *Improved Patient Compliance*

The quick disintegration and straightforward administration significantly enhance adherence, especially among pediatric and geriatric patients, as well as those who have difficulty swallowing.

- *Rapid Onset of Action*

The fast disintegration facilitates drug dissolution and absorption, which may lead to a quicker therapeutic effect, an essential factor in managing nausea and vomiting.

- *Enhanced Bioavailability*

Certain medications may be absorbed through the oral mucosa before reaching the gastrointestinal tract, partially bypassing first-pass metabolism and thereby improving bioavailability.

- *Accurate Dosing and Stability*

As solid dosage forms, MDTs provide precise dosing and superior chemical stability compared to liquid formulations.

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➢ *Limitations*

While MDTs offer various advantages, they also come with several formulation and practical challenges:

- *Mechanical Fragility*

Due to their porous structure and low compression force, MDTs often demonstrate reduced mechanical strength, making them vulnerable to breakage during handling and transportation [37].

- *Taste-Masking Challenges*

The rapid disintegration of MDTs exposes the drug to taste buds, making effective taste masking crucial, particularly for bitter antiemetic medications [38].

- *Moisture Sensitivity*

Many MDTs are hygroscopic and necessitate specialized moisture-resistant packaging, which can increase both manufacturing and storage costs [39].

- *Limited Drug Loading*

Formulating high-dose drugs and those with poor solubility into MDTs is challenging due to size and palatability limitations [40].

IV. PHARMACEUTICAL AND CLINICAL SIGNIFICANCE

Mouth-dissolving antiemetic tablets mark a crucial progression in oral drug delivery systems, especially for symptomatic treatments that require quick relief and straightforward administration. Their creation highlights the rising focus on patient-centered formulation design, merging pharmacological effectiveness with convenience, safety, and adherence. As research advances, MDTs featuring either synthetic or herbal antiemetic agents are anticipated to take on a more vital role in personalized and supportive care therapies [41].

➢ *Selection of Herbal Antiemetic Agents*

- *Ginger (Zingiber officinale)*

Fig 2 Ginger *(Zingiber Officinale)*

- *Botanical Description and Part Used*

Zingiber officinale Roscoe is a perennial herbaceous plant that belongs to the Zingiberaceae family. It is extensively cultivated in tropical and subtropical areas and has a rich history of medicinal use in traditional practices such as Ayurveda, Unani, Traditional Chinese Medicine, and Western herbal medicine. The rhizome (underground stem) serves as the therapeutically active component of the plant and can be utilized fresh, dried, or in standardized extract form for medicinal purposes, including antiemetic therapy [42].

The ginger rhizome is abundant in volatile oils and non-volatile pungent phenolic compounds, which together contribute to its pharmacological benefits. Due to its stability, safety, and high bioactive content, the rhizome is particularly well-suited for use in oral solid dosage forms, such as mouth-dissolving tablets.

- *Bioactive Constituents and Mechanisms of Antiemetic Action*

The primary bioactive compounds responsible for ginger's antiemetic properties are gingerols ([6]-gingerol, [8]-gingerol, [10]-gingerol) and their dehydrated forms, shogaols, especially [6]- shogaol [43]. These phenolic compounds exert antiemetic effects through multiple complementary mechanisms.

At the molecular level, ginger constituents have been shown to block serotonin (5- hydroxytryptamine, 5-HT_3) receptors found in the gastrointestinal tract and the chemoreceptor trigger zone (CTZ) of the brainstem, which

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are crucial for nausea and vomiting reflexes [44]. This mechanism is particularly relevant for chemotherapy-induced nausea and vomiting (CINV), where excessive serotonin release from enterochromaffin cells stimulates vagal afferents.

Furthermore, ginger displays prokinetic activity, improving gastric emptying and alleviating gastrointestinal stasis, a known contributor to nausea [45]. Its anti-inflammatory and antioxidant properties additionally support gastrointestinal stability by reducing oxidative stress and inflammatory mediators linked to emetic stimuli [2].

Preclinical studies consistently demonstrate that ginger extracts significantly reduce vomiting in cisplatin-induced vomiting models, confirming both peripheral and central antiemetic actions mediated by 5-HT$_3$ receptor antagonism [46].

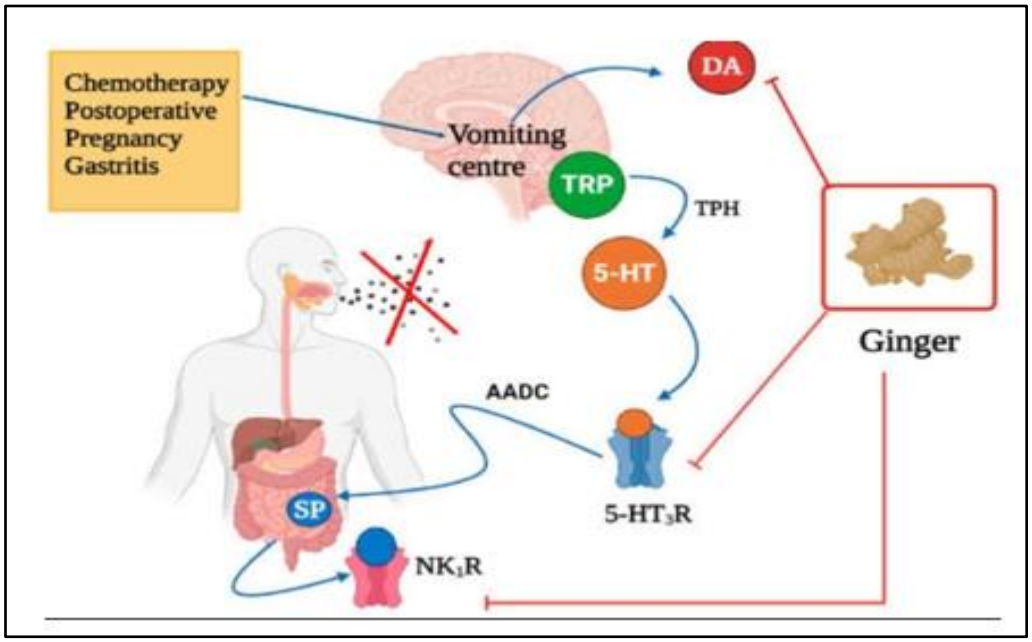

Fig 3 "The Antiemetic Mechanism of Ginger involves Inhibition of Serotonin-Mediated Signaling and Suppression of 5-HT$_3$ Receptor Activation at Both Central and Peripheral Emetic Pathways"

➢ *Clinical Evidence and Therapeutic Efficacy*

Strong clinical evidence endorses ginger as an effective and safe antiemetic across various clinical settings. One of the earliest randomized controlled trials showed that 1 g of powdered ginger was comparable to metoclopramide in alleviating postoperative nausea and vomiting (PONV), while causing fewer adverse effects [47].

A large multicenter, double-blind, placebo-controlled trial involving cancer patients undergoing chemotherapy indicated that ginger supplementation (0.5–1.0 g/day) significantly mitigated the severity of acute nausea when used alongside standard 5-HT$_3$ receptor antagonists [48]. However, its effects on delayed nausea and vomiting were variable, illustrating the complexity of CINV management.

Systematic reviews and meta-analyses have highlighted consistent benefits of ginger for nausea and vomiting of pregnancy (NVP), with effective doses ranging from 500 to 1,500 mg/day, and an excellent safety profile [49]. While reductions in vomiting frequency are less consistent, overall improvements in nausea scores are significant.

Importantly, long-term safety data reveal that ginger is well tolerated at doses up to 6 g/day, with minimal gastrointestinal or systemic side effects, making it suitable for repeated use in chronic nausea conditions [50].

➢ *Justification and Appropriateness for Mouth-Dissolving Tablet Formulation*

Ginger boasts several attributes that render it highly suitable for incorporation into mouth- dissolving tablets (MDTs):

- *Rapid Onset of Action*

MDTs allow for partial absorption of active constituents through the oral mucosa, bypassing first- pass metabolism and facilitating a quicker onset of antiemetic action—an essential advantage during acute nausea episodes when rapid relief is needed.

- *Improved Patient Compliance*

Patients dealing with nausea, vomiting, or dysphagia often struggle to swallow traditional tablets. Ginger-based MDTs dissolve swiftly in saliva without requiring water, enhancing compliance among pediatric, geriatric, pregnant, and chemotherapy patients.

- *Safety and Natural Origin*

As a commonly consumed dietary spice with extensive clinical safety data, ginger is regarded as a natural and patient-friendly alternative to synthetic antiemetics, which frequently come with side effects like sedation, extrapyramidal effects, or constipation.

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- *Formulation Feasibility*

Although ginger has a pungent and bitter flavor, modern pharmaceutical technologies—like taste-masking polymers, sweeteners, and flavoring agents—can effectively address palatability concerns. Standardized ginger extracts with controlled gingerol content further ensure consistent dosing and reproducibility in MDT formulations [51].

➢ *Benefits of Using Ginger as a Herbal Antiemetic in MDTs*

- Broad-spectrum antiemetic activity (PONV, NVP, motion sickness, CINV)
- Multiple mechanisms of action (5-HT_3 antagonism, prokinetic effect, antioxidant action)
- Excellent safety and tolerability profile
- High patient acceptability due to natural origin
- Compatibility with fast-dissolving oral delivery systems

Table 1 Pharmacognostic , Phytochemical, Mechanistic, and Clinical Profile of Ginger (*Zingiber officinale*)

Parameter	Details	Reference
Botanical Description	*Zingiber officinale* *Common Name: Ginger* Family**:** Zingiberaceae Type: Perennial herb Medicinal Part: Rhizome	Ali et al., *Food Chem Toxicol*. 2008; 46(2): 409–420. [1]
Key Bioactive Components	Phenolic Compounds: [6]-gingerol [8]-gingerol [10]-gingerol [6]-shogaol	Semwal et al., *Phytochemistry*, 2015; 117: 554–568. [2]
Mechanism of Antiemetic Action	Key Effects of 5-HT_3 Receptor Antagonism Prokinetic Effects Anti-inflammatory Actions Antioxidant Properties	Ernst & Pittler, *Br J Anaesth*. 2000; 84(3): 367–371. [3]
Preclinical Evidence: Utilizing Model Systems	Notable Decrease in Cisplatin- Induced Emesis in Animal Models	Sharma & Gupta, *Pharmacological Research*. 1998; 38(3): 195–199. [4]
Clinical Efficacy: Postoperative Nausea and Vomiting (PONV)	Ginger (e.g., 1 g) has been found to be comparable to metoclopramide in alleviating postoperative nausea.	Lumb, *Anaesthesia*. 1993; 48(8): 715–717. [5]
Clinical Efficacy: Chemotherapy-Induced Nausea and Vomiting (CINV)	Ginger supplementation (0.5– 1.0 g/day) has been shown to alleviate the severity of acute nausea.	Ryan et al., *Journal of Clinical Oncology*. 2012; 30(36): 4819–4826. [6]
Clinical Effectiveness: Managing Pregnancy Nausea	Significant decrease in nausea scores observed at dosages of 500–1,500 mg per day.	Viljoen et al., *Nutr J*. 2014; 13: 20–30. [7]
Safety Profile	Well, tolerated; doses of up to 6 g per day exhibited minimal adverse effects.	Chrubasik et al., *Phytomedicine*. 2005; 12(9): 684–701. [8]
Flavor and Organoleptic Challenges	Bitter and pungent flavor; necessitates taste-masking in oral multi-drug therapy formulations.	Fu et al., *Crit Rev Ther Drug Carrier Syst*, 2004; 21(6): 433–476. [9]
Rationale for MDT Development	Rapid absorption through the oral mucosa; enhanced adherence; effective for nausea and vomiting.	Fu et al., *Critical Reviews in Therapeutic Drug Carrier Systems*. 2004; 21(6): 433–476. [9]

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➢ *Peppermint (Mentha piperita L.)*

Fig 4 Peppermint (Mentha Piperita L.)

- *Botanical Description and Part Used*

Mentha piperita L., widely known as peppermint, is a perennial aromatic herb that belongs to the Lamiaceae family. It is a natural hybrid of Mentha aquatica and Mentha spicata and is cultivated extensively across Europe, Asia, and North America. Peppermint has long been utilized in various traditional medicinal systems, including Ayurveda, Traditional Chinese Medicine, Unani medicine, and European herbal practices, primarily to address gastrointestinal issues such as nausea, vomiting, indigestion, and abdominal spasms [52].

The primary medicinal components of peppermint are its leaves and flowering aerial parts. These parts are rich in essential oils and are typically used in forms such as dried leaf powder, hydroalcoholic extracts, or standardized peppermint oil preparations. Due to their high essential oil content, stability, and patient acceptability, peppermint leaf extracts are particularly well- suited for oral solid dosage forms, including mouth-dissolving tablets.

- *Bioactive Constituents and Mechanisms of Antiemetic Action*

The pharmacological effects of peppermint are largely attributed to its volatile oil constituents, including menthol, menthone, methyl acetate, limonene, and 1,8-cineole [53]. Among these, menthol stands out as the key bioactive compound responsible for peppermint's antiemetic and antispasmodic properties.

Peppermint's antiemetic action operates through several mechanisms. Menthol has been shown to modulate calcium channels in gastrointestinal smooth muscle, resulting in relaxation and a reduction in gastrointestinal spasms, which are significant contributors to nausea and vomiting [54]. Furthermore, peppermint oil exhibits anti-serotonergic activity, particularly through the inhibition of 5-HT_3 receptors, which are crucial in the emetic reflex pathway [55].

Additionally, peppermint influences the chemoreceptor trigger zone (CTZ) and vagal afferent signaling, thus diminishing the perception of nausea. Its carminative, cholagogue, and mild local anesthetic properties further enhance gastrointestinal comfort and mitigate emetic stimuli [56]. The antioxidant and anti-inflammatory properties of peppermint polyphenols also contribute to

its protective role against chemically or surgically induced nausea [2].

Preclinical studies have shown that peppermint oil significantly decreases the frequency of emesis in experimentally induced nausea models, supporting both central and peripheral mechanisms of its antiemetic action [57].

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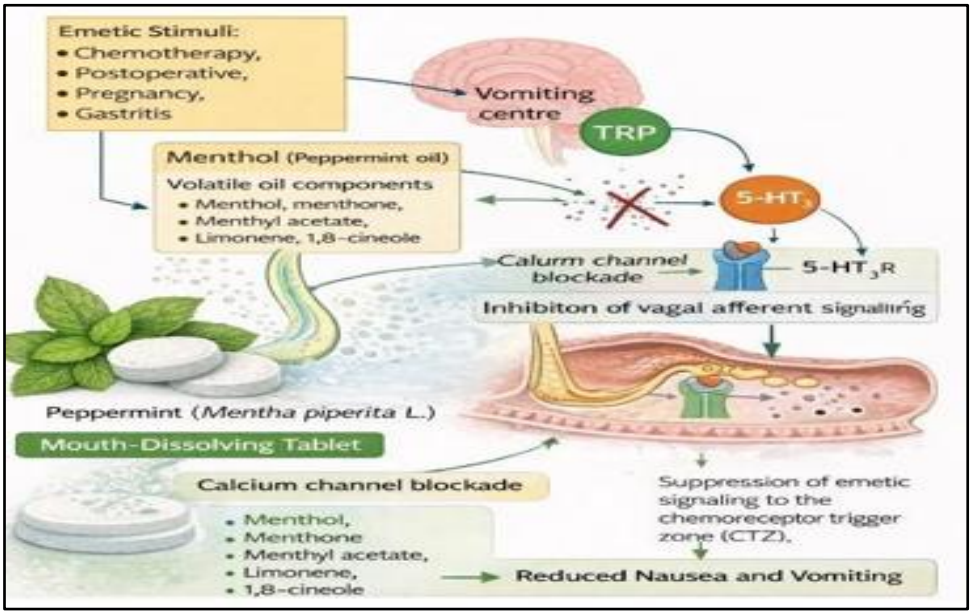

Fig 5 Proposed Antiemetic Mechanism of Peppermint (Mentha piperita L.) in Mouth- Dissolving Tablet

- *Clinical Evidence and Therapeutic Efficacy*

Clinical research is accumulating evidence that supports the antiemetic potential of peppermint across various contexts. Early randomized controlled trials indicated that inhaling or orally administering peppermint oil significantly reduced postoperative nausea and vomiting (PONV) when compared to a placebo [58].

Several studies involving oncology patients found that peppermint oil, when used alongside standard antiemetic treatments, greatly reduced the severity and frequency of chemotherapy- induced nausea and vomiting (CINV) [59]. A randomized controlled trial involving breast cancer patients undergoing chemotherapy reported significant reductions in nausea intensity within 24– 48 hours following peppermint oil treatment [60].

Systematic reviews and meta-analyses have further emphasized peppermint's effectiveness in managing nausea during pregnancy, postoperative recovery, and motion sickness, although variations in study designs and dosage forms indicate a need for further standardization [61].

Peppermint is generally recognized as safe, with minimal adverse effects noted at therapeutic doses. Both oral and inhalational formulations have shown excellent tolerability, making peppermint a viable option for repeated use in both acute and chronic nausea scenarios [62].

- *Rationale and Suitability for Mouth-Dissolving Tablet Formulation*

✓ *Rapid Onset of Action*

Mouth-dissolving tablets facilitate quick disintegration in the oral cavity, enabling faster absorption of peppermint's volatile constituents and providing immediate relief from nausea without requiring water.

✓ *Improved Patient Compliance*

Peppermint-based mouth-dissolving tablets are particularly beneficial for patients experiencing active nausea, vomiting, or dysphagia. The pleasant cooling sensation and refreshing flavor of peppermint enhance patient acceptance, especially among pediatric, geriatric, and oncology populations.

✓ *Safety and Natural Origin*

Peppermint's extensive history of dietary and medicinal use, combined with robust safety data, positions it as a natural and well-tolerated alternative or complement to synthetic antiemetics, which are often linked to sedation and extrapyramidal side effects.

✓ *Formulation Feasibility*

Peppermint's natural flavor and aroma minimize the need for extensive taste-masking strategies in mouth-dissolving tablet formulations. Standardized peppermint oil or dry extracts can be easily incorporated into fast-dissolving matrices using conventional excipients [63].

- *Benefits of Using Peppermint as a Herbal Antiemetic in Mouth-Dissolving Tablets*

✓ Effective against PONV, CINV, pregnancy-related nausea, and motion sickness
✓ Multiple mechanisms of action (5-HT$_3$ modulation, antispasmodic, antioxidant)
✓ Excellent safety and tolerability profile
✓ Pleasant organoleptic properties that enhance patient compliance
✓ High compatibility with fast-dissolving oral drug delivery systems

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Table 2 Pharmacogenetic, Phytochemical, Mechanistic, and Clinical Profile of Peppermint (Mentha piperita L.)

Parameter	Details	Reference
Botanical Description	*Mentha piperita* L.; Family: Lamiaceae; Medicinal part: Leaves and aerial parts	McKay & Blumberg, *Phytother Res*. 2006; 20(8): 619–633. [1]
Key Bioactive Components	Menthol, menthone, methyl acetate, limonene, 1,8-cineole	Kamatou et al., *Phytochemistry*. 2013; 96: 15–27. [2]
Mechanism of Antiemetic Action	5-HT_3 receptor modulation, calcium channel blockade, antispasmodic action	Hawthorn et al., *Aliment Pharmacol Ther*. 1988; 2(2):101–118. [3]
Preclinical Evidence	Reduced emesis in chemically induced nausea models	Hills & Aaronson, *J Pharm Pharmacol*. 1991; 43(12): 891–895. [6]
Clinical Efficacy (PONV)	Significant reduction in postoperative nausea	Tate, *J Adv Nurs*. 1997; 26(3):543–549. [7]
Clinical Efficacy (CINV)	Decreased nausea severity in cancer patients	Lua & Zakaria, *Complement Ther Clin Pract*. 2012; 18(4): 226–230.[8]
Safety Profile	Well, tolerated; minimal adverse effects	EMA, *Herbal Monograph*. 2013; 1–8. [11]
Suitability for MDT	Pleasant taste, rapid action, high patient compliance	Fu et al., *Crit Rev Ther Drug Carrier Syst*. 2004; 21(6): 433–476. [12]

➢ *Formulation Approaches for Herbal Mouth-Dissolving Tablets (MDTs)*

Herbal mouth-dissolving tablets (MDTs) are crafted to dissolve quickly in the mouth without the need for water, providing a user-friendly dosage form for managing nausea and vomiting. In the realm of herbal antiemetic therapy, MDTs that include plant-derived active ingredients such as *Zingiber officinale* and *Mentha piperita* merge the advantages of phytotherapy with contemporary oral drug-delivery technology. Various formulation strategies have been documented to achieve rapid disintegration, adequate mechanical strength, and optimal bioavailability.

➢ *Direct Compression Method*

Direct compression is the most commonly used technique for creating herbal MDTs due to its simplicity, cost-effectiveness, and compatibility with moisture- and heat-sensitive herbal extracts. This method involves blending the active herbal extract with directly compressible excipients, which include:

- Diluents (mannitol, lactose)
- Super disintegrants (Crosspointe, croscarmellose sodium, sodium starch glycolate)
- Sweeteners
- Flavoring agents
- Lubricants

The mixture is then compressed into tablets. This approach is particularly beneficial for herbal formulations as it reduces processing steps and helps maintain the stability of phytoconstituents.

➢ *Freeze-Drying (Lyophilization)*

Freeze-drying is a specialized method used to create highly porous MDTs that disintegrate extremely quickly. The formulation is prepared as a solution or suspension, filled into blister cavities, frozen, and then lyophilized to eliminate water through sublimation. Although freeze- dried tablets offer excellent mouthfeel and dissolve within seconds, this technique can be costly, has limited drug loading capacity, and results in fragile tablets. Thus, its application in herbal MDTs is mainly reserved for low-dose phytoconstituents.

➢ *Molding Technique*

The molding technique entails creating a moist mixture of the drug and excipients using hydroalcoholic solvents, followed by molding and drying at low temperatures. Molded MDTs show rapid dissolution due to their porous nature; however, they often exhibit poor mechanical strength and necessitate careful handling.

➢ *Sublimation Technique*

In the sublimation method, volatile substances like camphor, ammonium bicarbonate, or urea are included in the tablet blend and subsequently removed by sublimation to create a porous matrix. This enhances water penetration and accelerates tablet disintegration. This technique has been effectively utilized in fast-dissolving formulations that include herbal actives.

Overall, direct compression stands out as the most practical and scalable method for formulating herbal antiemetic MDTs, owing to its industrial applicability, reproducibility, and compatibility with standardized herbal extracts.

➢ *Evaluation Parameters of Herbal Mouth-Dissolving Tablets*

Assessing herbal mouth-dissolving tablets (MDTs) is vital to guarantee their quality, safety, effectiveness, and patient acceptance. Since these herbal MDTs are solid oral dosage forms, they are evaluated using pharmacopeial standards and parameters reported in literature, similar to those for conventional MDTs.

- *Weight Variation*

Weight variation testing is crucial for ensuring uniform dosing across tablets. In line with pharmacopeial standards, tablets must adhere to specified weight limits to maintain consistent drug content and therapeutic effectiveness.

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- *Hardness and Friability*

Tablet hardness indicates mechanical strength, while friability measures resistance to wear during handling and transport. Typically, MDTs exhibit lower hardness values (2–4 kg/cm²) to promote rapid disintegration, and friability should remain under 1% to guarantee adequate tablet integrity.

- *Wetting Time and Water Absorption Ratio*

Wetting time signifies the duration needed for saliva to infiltrate the tablet matrix, while the water absorption ratio reflects the tablet's ability to absorb moisture. Optimal characteristics for MDTs include short wetting times and high water absorption ratios, which are associated with quicker disintegration.

- *Disintegration Time*

Disintegration time is a key quality attribute for MDTs. Most studies indicate that acceptable disintegration times range from 30 to 60 seconds. Quick disintegration is crucial for immediate drug release and a faster onset of antiemetic action, particularly during acute episodes of nausea.

- *Drug Content Uniformity*

Ensuring uniform distribution of herbal active ingredients within MDTs is essential for accurate dosing. Drug content is typically analyzed through validated methods such as UV-visible spectrophotometry or high-performance liquid chromatography (HPLC).

- *In-Vitro Dissolution Studies*

In-vitro dissolution testing assesses the rate and extent of drug release from MDTs. These studies are generally conducted using phosphate buffer (pH 6.8) to mimic salivary conditions. Rapid dissolution profiles for herbal MDTs support their effectiveness for swift therapeutic action.

Table 3 Evaluation Parameters for Herbal Mouth-Dissolving Tablets (Reported in Literature)

Parameter	Standard Acceptance Criteria	Reference
Weight Variation	In accordance with pharmacopeial standards.	Seager, 1998 [4]
Hardness	2 to 4 kg/cm²	Bandari et al., 2008 [8]
Friability	Less than 1%	Fu et al., 2004 [1]
Wetting Time	Under 60 seconds	Gohel et al., 2004 [9]
Disintegration Time	60 seconds or less	Fu et al., 2004 [1]
Drug Content	85% to 115% of the label claim	Bandari et al., 2008 [8]
In-vitro Dissolution	Instantaneous Release in Just Minutes	Mohana chandran et al., 2011 [12]

➢ *Future Prospects of Herbal Mouth-Dissolving Antiemetic Tablets*

The outlook for mouth-dissolving antiemetic tablets (MDTs) that contain ginger (*Zingiber officinale*) and peppermint (*Mentha piperita*) is very promising. This is largely due to the growing demand for rapid-acting, user-friendly, and safer alternatives to traditional antiemetic treatments. Continuous advancements in herbal standardization, formulation techniques, and regulatory guidelines are expected to greatly enhance both the clinical and commercial potential of these dosage forms.

Enhanced standardization of herbal extracts, with specific levels of bioactive components such as gingerols, shogaols, and menthol, will be vital for ensuring dosage accuracy, consistency across batches, and regulatory approval for herbal MDTs. Such improvements are likely to boost reproducibility in clinical results and encourage broader pharmaceutical acceptance.

Innovative formulation techniques, including nanotechnology-based carriers, solid lipid formulations, and advanced taste-masking polymers, are anticipated to enhance the dissolution rate, oral mucosal absorption, and bioavailability of herbal active ingredients. These advancements could prove particularly useful in addressing acute conditions such as chemotherapy-induced and postoperative nausea, where a quick onset of action is critical.

Future clinical studies are expected to broaden the therapeutic uses of ginger- and peppermint- based MDTs and investigate their role in personalized antiemetic therapy. Combining herbal MDTs with lower doses of conventional antiemetics may offer synergistic effects while reducing side effects.

The growing regulatory acknowledgment of evidence-based herbal medicines, along with the inclusion of ginger and peppermint in pharmacopeial monographs, further reinforces their integration into standardized oral drug-delivery systems. Additionally, the sustainability, cost-effectiveness, and appealing sensory properties of these herbs align well with patient-centered and environmentally conscious healthcare approaches.

In conclusion, with ongoing technological advancements, thorough clinical validation, and regulatory alignment, herbal antiemetic MDTs are set to become a significant element of contemporary supportive care therapy.

V. CONCLUSION

Herbal antiemetic mouth-dissolving tablets (MDTs) offer a promising integration of traditional herbal medicine and modern oral drug delivery systems. Among these, ginger (*Zingiber officinale*) and peppermint (*Mentha piperita*) stand out as the most scientifically validated herbal antiemetic agents, supported by a wealth of pharmacological, preclinical, and clinical research. Their diverse mechanisms of action—including 5-HT_3 receptor antagonism, modulation of gastrointestinal motility, antispasmodic properties, and antioxidant effects—make them effective for managing nausea and vomiting related to pregnancy, postoperative

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recovery, motion sickness, and chemotherapy-induced nausea and vomiting (CINV) [64-68].

Formulating these herbal extracts into mouth-dissolving tablets provides significant patient- centered benefits, such as rapid disintegration without the need for water, enhanced compliance, and a quicker onset of action, especially in pediatric, geriatric, dysphagic, and actively nauseous patients [69,70]. Among the various formulation strategies, direct compression is the most feasible and scalable method for developing herbal MDTs. Evaluation parameters like disintegration time, wetting time, mechanical strength, drug content uniformity, and dissolution behavior are crucial to ensure quality and consistency [71,72].

Despite the positive results, challenges remain regarding herbal extract standardization, taste masking, dose uniformity, and regulatory alignment. Overcoming these obstacles through standardized phytochemical profiling, innovative formulation technologies, and well-structured clinical trials will be essential for broader clinical acceptance. In summary, ginger- and peppermint-based MDTs show significant promise as safe, effective, and patient-friendly alternatives or complements to traditional antiemetic therapies in contemporary pharmaceutical practice.

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