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Dyspepsia: An Integrated Review of Diagnosis, Classification, and Mechanisms of Modern and Herbal Medications

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ABSTRACT
Dyspepsia is a common and complex disorder characterized by symptoms such as epigastric pain, bloating, and early satiety, which significantly impact patients' quality of life. The pathophysiology of dyspepsia remains poorly understood, with multiple underlying factors including *Helicobacter pylori* infection, gastric motility disturbances, and visceral hypersensitivity. Modern therapeutic strategies primarily focus on acid suppression and motility enhancement, with Proton Pump Inhibitors (PPIs), H2 blockers, and prokinetic agents as standard treatments. The advent of novel therapies, such as potassium-competitive acid blockers (P-CABs) like Tegoprazan, offers promising alternatives with faster onset and longer-lasting effects. Herbal therapies, including turmeric, ginger, and licorice, have also been explored, showing potential benefits in symptom relief and gastric protection. Despite these advances, the effectiveness of treatment remains variable, and a tailored approach based on patient-specific factors is recommended. This review highlights the current treatment modalities, including both modern and herbal medications, with a focus on pharmacological and non-pharmacological therapies for dyspepsia.
Keywords: Dyspepsia; Functional Dyspepsia; Proton Pump Inhibitors (PPIs); Tegoprazan; Herbal Medicine

INTRODUCTION
The concept of upper gastrointestinal (GI) symptoms has been described for thousands of years. “Stomach disorders” became a significant focus in more developed nations during the eighteenth century, marking the first use of the term dyspepsia. Originally, dyspepsia was defined broadly as any symptoms related to the upper gastrointestinal tract, encompassing a wide range of discomforts in this area. Over time, the definition of dyspepsia has evolved, with the Rome committee playing a key role in refining these definitions through various iterations. This culminated in the Rome IV criteria, which provided a more precise and detailed framework for understanding dyspepsia. Dyspepsia, as defined in modern medical practice, is a common symptom affecting the upper GI tract, typically presenting as pain or discomfort in the upper abdomen. Rather than being a specific disease, dyspepsia is recognized as a complex of symptoms that may arise from a variety of underlying conditions. These can include peptic ulcer disease, infection with *Helicobacter pylori* (H. pylori), and functional dyspepsia (Giri et al., 2023; Drossman & Hasler, 2016).

A previous systematic review revealed that the global prevalence of dyspepsia varies widely between countries, ranging from 1.8% to 57.0%, depending on the diagnostic criteria applied. The overall pooled prevalence of dyspepsia across studies was found to be 20.8%. Various risk factors have been identified, including psychological comorbidities, a history of acute gastroenteritis, female sex, smoking, the use of non-steroidal anti-inflammatory drugs (NSAIDs), and *Helicobacter pylori* infection. Despite extensive research, the precise pathophysiology of dyspepsia remains only partially understood. However, it is believed that the condition is largely due to a disrupted interaction between the gut and the brain, which leads to motility disturbances, visceral hypersensitivity, and changes in gastrointestinal microbiota, as well as alterations in the function of the mucosal and immune systems, and central nervous system (CNS) processing. This disrupted

communication likely contributes to the gastrointestinal discomfort and symptoms associated with dyspepsia (Ford et al., 2015; Ford et al., 2020).

The symptoms associated with dyspepsia can severely affect patients' quality of life. Beyond the physical discomfort, dyspepsia is linked to increased healthcare expenditures, reduced work productivity, and various psychosocial comorbidities, such as anxiety and depression. Due to the severity of their symptoms and the significant impact on their daily lives, patients with dyspepsia are often compelled to seek medical consultation. Dyspepsia places a significant strain on healthcare systems, especially in countries with limited resources. The need for diagnostic tests, treatment options, and healthcare consultations increases healthcare expenditure and demands on healthcare professionals, which can be challenging to manage in both developed and developing countries (Mahadeva et al., 2012; Shetty et al., 2017).

Given the significant burden that dyspepsia places on individuals and healthcare systems, effective treatment is essential. This narrative review offers a comprehensive and timely exploration of dyspepsia management by integrating both conventional pharmacological treatments and complementary herbal remedies. While previous studies usually focused only on modern medical treatments or alternative therapies, this review discusses and compares both approaches together, giving a more complete and balanced understanding. It provides a detailed classification of dyspepsia supported by up-to-date references and highlights recent clinical evidence such as Tegoprazan, and herbal agents like curcumin, ginger, and probiotics. By examining the mechanisms of action, efficacy, and clinical relevance of these treatments, this review contributes novel insights into how dyspepsia can be managed holistically.

METHODS

This article adopts narrative review approach to examine current treatments for dyspepsia, including pharmacological and non-pharmacological therapies. The studies included in this review were identified through electronic data searches on PubMed, ScienceDirect, and Cochrane Library, using the following keywords: dyspepsia, *Helicobacter pylori*, proton pump inhibitors (PPIs), H2 blockers, prokinetic agents, Tegoprazan, herbal medicine, and gastric motility. Articles were selected based on relevance to the treatment of dyspepsia, with a focus on studies published within the last 15 years. Articles utilized in this study were selected based on inclusion and exclusion criteria. The inclusion criteria set in this study are: 1) articles published between 2010-2025; 2) articles in English or Indonesian. Furthermore, the exclusion criteria included: (1) irrelevant research; (2) articles that were not accessible in full text; and (3) duplicate studies. The data extraction process begins with identifying articles based on keywords and/or titles and abstracts, until the full content of the article is studied to obtain information in accordance with the objectives of this study. After selection based on keywords, titles and abstracts at the initial stage, articles were then screened based on inclusion and exclusion criteria.

RESULTS AND DISCUSSION

Category of Dyspepsia

Dyspepsia can be classified into three main categories: uninvestigated, organic, and functional. Uninvestigated dyspepsia refers to cases where the cause of the symptoms has not yet been explored through diagnostic procedures such as endoscopy. Organic dyspepsia occurs when structural abnormalities or systemic diseases have been identified as the cause of the symptoms. Organic dyspepsia consists of gastric ulcer, gastritis, erosive gastritis, duodenitis, duodenal ulcer and a process of malignancy. In contrast, Functional dyspepsia is diagnosed when no structural abnormalities or diseases are detectable, and the symptoms persist without an identifiable cause. The symptoms should be present for a minimum of three months, with the onset occurring no later than six months prior to the diagnosis. (Mendoza et al., 2022; Syam et al., 2017). The Rome IV criteria classify functional dyspepsia into two subgroups, i.e. the postprandial distress syndrome and epigatric pain syndrome. Postprandial distress syndrome primarily consists of early satiety or a feeling of fullness after eating, while epigastric pain syndrome is primarily characterized by pain or a burning sensation in the epigastric region (Drossman & Hasler, 2016; Francis & Zavala, 2025).

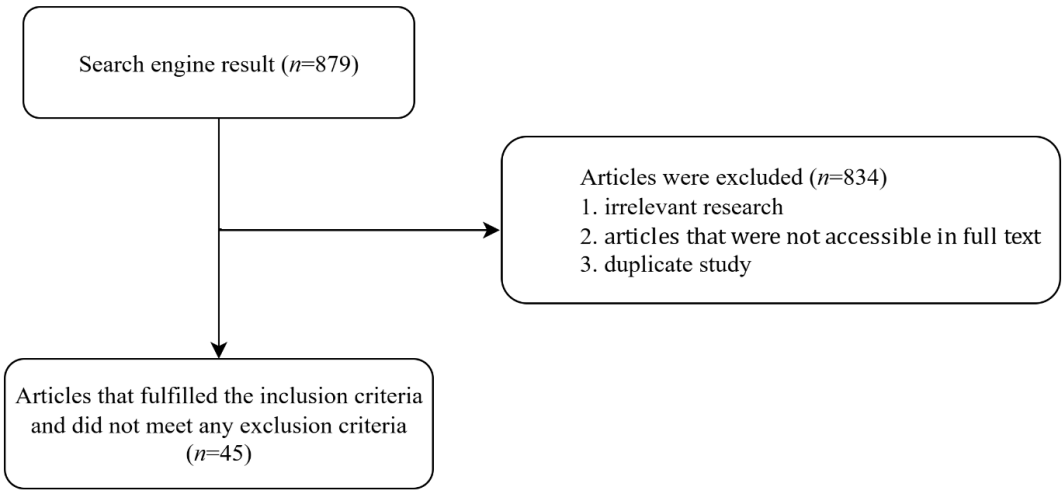

Figure 1. Flowchart of the literature search process

In developing country such as Indonesia, a significant portion of patients in primary care settings are categorized as having uninvestigated dyspepsia, with a reported prevalence of approximately 49.75%. In comparison, the prevalence of dyspepsia in Malaysia has been documented at 24.3%, indicating notable differences in disease burden between neighboring countries. On a global scale, the prevalence of uninvestigated dyspepsia varies significantly across different populations, ranging from 1.8% to 57.0%, with an estimated overall prevalence of 21%. The highest prevalence has been reported in Japan, whereas the lowest prevalence rates have been recorded in Canada and China (Mahadeva et al., 2010; Huang et al., 2021).

The evaluation of patients presenting with dyspepsia should always include an assessment of alarm signs. These signs include progressive dysphagia, recurrent or persistent vomiting, unintended weight loss, gastrointestinal bleeding, fever, anemia, a mass in the upper abdomen, a history of gastric cancer within the family, and new-onset dyspepsia in patients over the age of 45. Patients exhibiting any of these symptoms should undergo further investigation, primarily through endoscopy (Syam et al., 2017).

Modern Therapy of Dyspepsia

Helicobacter pylori eradication therapy

For patients with dyspepsia accompanied by *Helicobacter pylori* infection, eradication therapy involving a combination of antibiotics (such as clarithromycin, amoxicillin, or metronidazole) and PPIs is strongly recommended. Studies have shown that *H. pylori* eradication can lead to long-term improvement in dyspepsia symptoms, particularly in patients with positive H. pylori test results. However, the effectiveness of this eradication therapy also depends on the successful elimination of the bacteria, which can be influenced by antibiotic resistance and patient adherence to the treatment regimen (Talley & Ford, 2015).

Proton Pump Inhibitors

As an adjunct to eradication therapy, one of the primary treatments for dyspepsia is Proton Pump Inhibitors (PPIs). PPIs are effective in reducing gastric acid production, particularly in patients who also experience GERD symptoms. PPIs, such as omeprazole and esomeprazole, work by inhibiting the H+/K+ ATPase enzyme in gastric parietal cells, thereby reducing acid secretion. The use of PPIs has been proven effective in alleviating dyspepsia symptoms in patients with or without *Helicobacter pylori* infection. However, the effectiveness of PPIs varies and is generally more effective in patients who also exhibit GERD symptoms (Syam et al., 2023; Moayyedi et al., 2017).

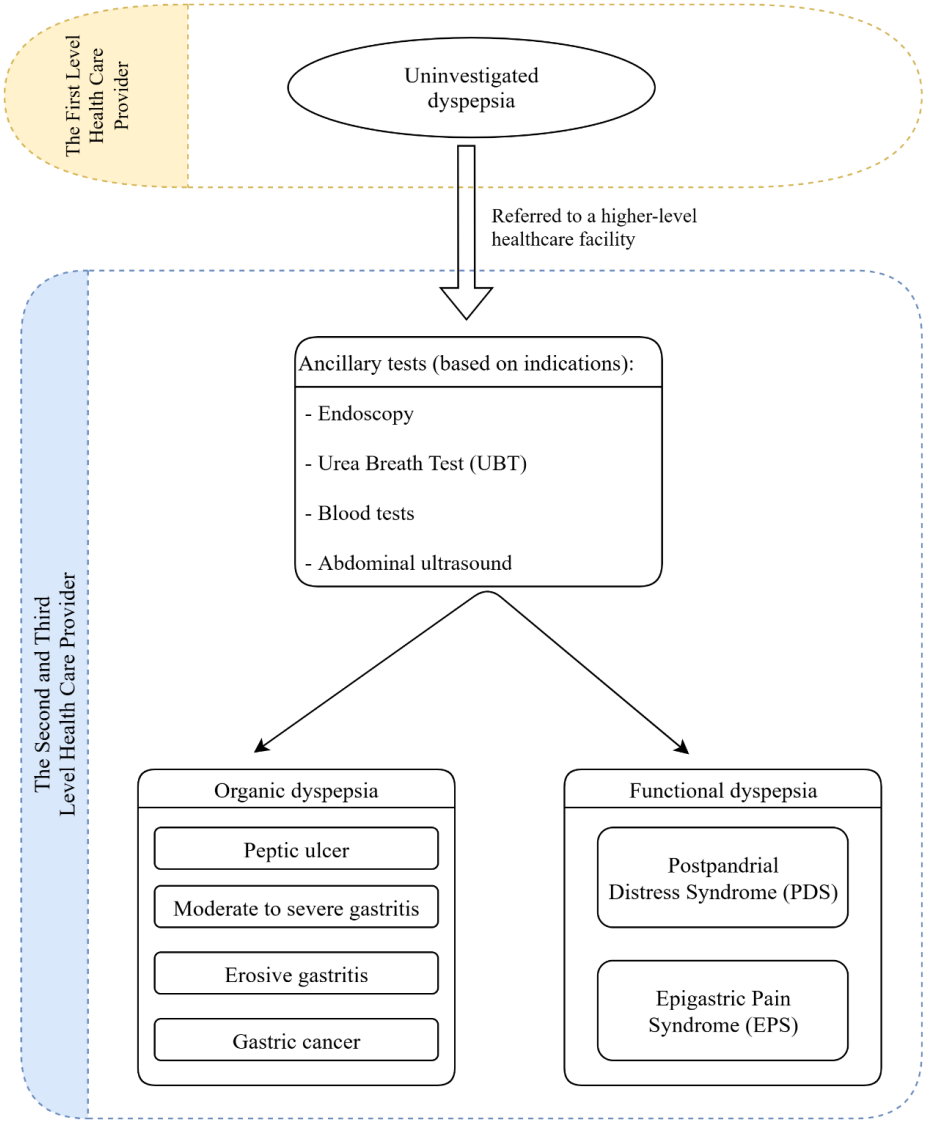

Figure 2. Algorithm for diagnosis of uninvestigated dyspepsia

H2 blockers or histamine-2 receptor antagonists

In addition to eradication therapy, another primary treatment for dyspepsia is H2 blockers or histamine-2 receptor antagonists (H2RAs). These drugs primarily target the reduction of gastric acid secretion by inhibiting histamine at the H2 receptors on the parietal cells of the stomach, which results in decreased production of stomach acid. This mechanism proves beneficial not only in conditions like GERD and peptic ulcers, but also in functional dyspepsia. In functional dyspepsia, where gastrointestinal motility and sensitivity are often disrupted, the reduction of stomach acid can help alleviate troublesome symptoms such as epigastric pain, postprandial fullness, and bloating, offering symptomatic relief for individuals affected by this condition (Li et al., 2019; Nugent et al., 2025).

Potassium-competitive acid blocker

In addition to H2 blockers, Tegoprazan, a novel potassium-competitive acid blocker, offers another potential therapy in the treatment of acid-related gastrointestinal disorders. Unlike PPIs, which irreversibly inhibit the H+/K+-ATPase enzyme in parietal cells, Tegoprazan provides rapid

and reversible inhibition of gastric acid secretion. This leads to a faster onset of action and longer duration of acid suppression, making it effective in alleviating common dyspepsia symptoms such as epigastric pain, bloating, early satiety, and heartburn. As a new class of acid-suppressive drugs, Tegoprazan is emerging as a promising treatment, offering potential benefits over traditional PPIs. A clinical study has demonstrated that Tegoprazan significantly reduces gastric acid secretion and improves gastric accommodation, providing substantial relief from gastrointestinal symptoms. It has been shown to have comparable or superior efficacy compared to conventional PPIs in the treatment of functional dyspepsia and GERD. These findings highlight the potential of Tegoprazan as an effective and safer alternative in the management of acid-related disorders, marking it as an important advancement in acid-suppressive therapy (Kim et al., 2019; Huh et al., 2024).

Prokinetic agents

Further enhancing gastric motility, prokinetic agents like domperidone and metoclopramide are commonly used to enhance gastric motility in patients with functional dyspepsia, particularly for those experiencing postprandial fullness, bloating, and nausea. These medications work by stimulating dopamine D2 receptors, which help accelerate gastric emptying, thus reducing these symptoms. However, their use requires careful monitoring due to potential side effects, such as extrapyramidal disorders (movement disorders) and hyperprolactinemia (elevated levels of prolactin). These side effects are significant enough to warrant careful observation during treatment (Camilleri et al., 2018; Talley, 2017).

Additionally, acotiamide, a novel prokinetic agent, offers a unique approach to treating functional dyspepsia. Unlike conventional prokinetic drugs, acotiamide primarily works by inhibiting acetylcholinesterase, which enhances acetylcholine activity and improves gastric motility. Acotiamide has low affinity for serotonin receptors (5-HT2, 5-HT3, and 5-HT4) and dopamine D2 receptors, distinguishing it from other prokinetic agents. This mechanism improves gastric emptying and gastric accommodation, helping to alleviate symptoms like postprandial fullness, early satiety, and epigastric pain in patients with functional dyspepsia. By improving gastric motility, acotiamide effectively reduces discomfort associated with dyspepsia, providing a safer alternative with fewer side effects than traditional prokinetics (Shrestha et al., 2021).

Antidepressants

Finally, low-dose tricyclic antidepressants can also be considered for patients with dyspepsia, particularly when visceral sensitivity is one of the primary causes of pain. These medications work by modulating neurotransmitters in the central nervous system, which helps decrease the perception of visceral pain—often a major contributor to discomfort in dyspepsia. The effectiveness of these antidepressants is particularly evident in patients who do not respond to other conventional therapies and who have significant psychological components, such as depression or anxiety, that exacerbate dyspepsia symptoms (Talley, 2017; Ford et al., 2020).

Herbal and Complementary Medication of Dyspepsia

Herbal medicine has long been used to treat dyspepsia, particularly in cultures where plant-based therapies and holistic approaches are integrated into everyday healthcare practices. These remedies are often favored for their natural properties and are commonly sought as alternatives or adjuncts to conventional pharmaceutical treatments. While herbal remedies are widely used and appreciated in many cultures, it is crucial to evaluate their effectiveness through scientific research and to use them under the guidance of healthcare professionals to ensure both safety and efficacy (Xiao et al., 2012; Franco et al., 2019; Gwee et al., 2021). Therefore, the following section will review several herbal and complementary medicines that have undergone clinical trials, providing evidence of their potential benefits and effectiveness in managing dyspepsia symptoms.

Turmeric *(Curcuma longa)*

Turmeric, obtained from the rhizomes of *Curcuma longa*, has been used for centuries in the prevention and treatment of various diseases. The active compound in turmeric, curcumin, a natural phenolic ingredient, has recently attracted significant attention for its potential therapeutic effects in

managing dyspepsia. Curcumin is known for its anti-inflammatory and antioxidant properties, which may help mitigate inflammation within the gastrointestinal tract, thereby reducing symptoms associated with dyspepsia. Moreover, curcumin has been shown to improve gastric motility and reduce visceral hypersensitivity, further supporting its effectiveness in managing digestive discomfort. Additionally, curcumin is generally regarded as safe when used appropriately, with minimal adverse effects reported in clinical trials (Dulbecco & Savarino, 2013; Thavorn et al., 2024).

A randomized controlled trial comparing curcumin with omeprazole, a commonly prescribed PPI, found that curcumin exhibited similar efficacy in improving dyspepsia symptoms. Both treatments led to significant reductions in pain, bloating, and discomfort, demonstrating that curcumin may serve as an effective alternative to PPIs in managing functional dyspepsia. The mechanism behind curcumin's efficacy is thought to be its ability to modulate the gut-brain axis, reduce visceral hypersensitivity, and improve gastric motility, thus addressing the underlying factors contributing to dyspepsia (Kongkam et al., 2023). Additionally, a study conducted between November 2017 and November 2018 compared the effects of *Curcuma longa* to omeprazole and placebo in patients diagnosed with functional dyspepsia. The results showed that curcumin significantly reduced both pain and non-pain symptoms in the Severity of Dyspepsia Assessment (SODA) compared to the placebo group after 4 weeks. While there were no significant differences between curcumin and omeprazole groups, curcumin was found to improve health-related quality of life and patient satisfaction to a level comparable to omeprazole, with curcumin also yielding the highest improvement in the EuroQol-5 Dimension (EQ-5D) index. These findings support curcumin's role as a promising alternative treatment for functional dyspepsia, providing a similar level of efficacy and safety as conventional therapies like omeprazole, while improving patient satisfaction and quality of life (Yongwatana et al., 2022).

Ginger *(Zingiber officinale)*

Ginger has long been utilized for its therapeutic benefits in gastrointestinal disorders, including dyspepsia. The primary mechanism of action of ginger in dyspepsia is attributed to its bioactive compounds, particularly gingerol and shogaol, which exhibit anti-inflammatory, antioxidant, and muscle relaxant properties. These compounds help enhance gastric motility, reduce gastric mucosal irritation, and improve gastric emptying time, all of which are crucial for alleviating symptoms such as bloating, early satiety, and postprandial fullness, commonly associated with dyspepsia (Nikkhah Bodagh et al., 2018). Additionally, ginger has been shown to modulate the gut-brain axis, influencing the communication between the gastrointestinal tract and the central nervous system, which can help reduce visceral hypersensitivity—a significant factor in the pathophysiology of dyspepsia (Aregawi et al., 2024).

Several RCTs have evaluated the efficacy of ginger in treating dyspepsia. In a clinical trial by Aregawi et al. (2023), ginger supplementation was shown to significantly reduce symptoms of functional dyspepsia, including nausea and gastric discomfort, compared to placebo. Similarly, Nikkhah Bodagh et al. (2018) found that ginger supplementation improved gastrointestinal motility and provided symptom relief in patients with dyspepsia, with effects comparable to conventional pharmacological treatments such as prokinetics. Moreover, some findings support ginger's efficacy in enhancing gastric function, which helps in improving the overall digestive process and relieving postprandial distress. These studies indicate that ginger can be a valuable adjunctive treatment for dyspepsia, especially in managing symptoms related to delayed gastric emptying and bloating (Aregawi et al., 2024; Aregawi & Zoltan, 2025).

In terms of safety, ginger is generally well-tolerated with few adverse effects. According to Nikkhah Bodagh et al. (2018) and Aregawi et al. (2024), ginger supplementation was associated with minimal side effects, which were mostly mild and transient, such as gastrointestinal irritation or heartburn. Despite this consideration, ginger remains a safe and effective natural remedy for managing dyspepsia symptoms, particularly when used under proper guidance and within recommended dosages.

Licorice (*Glycyrrhiza glabra*)

Licorice *(Glycyrrhiza glabra)* has long been used for its therapeutic effects on gastrointestinal disorders, including dyspepsia. The primary bioactive compound in licorice, glycyrrhizin, along with flavonoids and saponins, contributes to its anti-inflammatory, antioxidant, and gastric-protective properties. These active ingredients help to reduce gastric inflammation, promote mucosal healing, and enhance gastric motility. Licorice has also been shown to inhibit *Helicobacter pylori* growth, which is often associated with gastritis and peptic ulcers, further contributing to its efficacy in managing dyspepsia symptoms (Chandrasekaran et al., 2011; Raveendra et al., 2012).

In a clinical trial, licorice has been found to be effective in alleviating dyspepsia symptoms, such as bloating, indigestion, and abdominal discomfort. Additionally, licorice is believed to help balance gastric acid levels, which may contribute to its efficacy in managing symptoms related to acid reflux and gastritis. Two studies, conducted by Puram et al. (2013) and Raveendra et al. (2012), indicate that licorice, particularly in its deglycyrrhizinated form, is generally safe with minimal side effects when used under recommended guidelines. In one RCT, licorice, particularly in its deglycyrrhizinated form, demonstrated similar effectiveness to omeprazole in treating functional dyspepsia, with no significant differences in outcomes between the two treatments. The trial observed improvements in both pain and non-pain symptoms following treatment with licorice. Furthermore, licorice exhibited comparable satisfaction levels to omeprazole, suggesting it could be an effective and well-tolerated alternative for managing dyspepsia (Raveendra et al., 2012; Puram et al., 2013).

Cinnamon *(Cinnamomum zeylanicum)*

Cinnamomum zeylanicum, also known as Ceylon cinnamon (the source of its Latin name, zeylanicum) or 'true cinnamon', contains cinnamaldehyde as its primary bioactive compound, which is responsible for its therapeutic effects in gastrointestinal disorders, including dyspepsia. The mechanism of action involves anti-inflammatory, antioxidant, and antimicrobial properties, which contribute to gastric protection and improvement in gastric motility. Cinnamaldehyde has been shown to reduce gastric mucosal inflammation and improve gastric emptying, which alleviates symptoms like bloating, early satiety, and postprandial fullness. Additionally, cinnamon's active components may help reduce visceral hypersensitivity, which is a key factor in functional dyspepsia and related conditions like gastritis and acid reflux. This makes *Cinnamomum zeylanicum* a potential natural remedy for managing dyspepsia, especially in patients experiencing discomfort due to impaired gastric function or sensitivity (Alqasoumi, 2012; Ranasinghe et al., 2013; Zobeiri et al., 2021).

In a randomized, double-blind, placebo-controlled clinical trial, *Cinnamomum zeylanicum* (cinnamon oil) was evaluated for its efficacy in managing functional dyspepsia. Patients received either cinnamon oil or a placebo (sesame oil) over a six-week period, with symptom severity assessed using the Total Dyspepsia Score (TDS) and the Gastrointestinal Symptom Rating Scale (GSRS). While both groups showed significant improvements from baseline ($P < 0.001$), there was no significant difference between the two at the endpoint ($P = 0.317$ and 0.174, respectively), suggesting that cinnamon oil did not perform better than placebo. While these results suggest that cinnamon oil did not outperform placebo in this trial, several factors may have influenced the outcome. The study was limited by a relatively small sample size, a short duration of follow-up, and a lack of deeper statistical or subgroup analysis. Moreover, the choice of sesame oil as a placebo may not have been entirely inert, potentially confounding the results (Zobeiri et al., 2021).

The choice of placebo (sesame oil) may have introduced confounding effects, as sesame oil is not entirely inert and may possess mild gastroprotective properties (Singletary, 2022). The absence of a more inert placebo might have diminished the contrast between groups. Despite these limitations, the study is valuable as one of the first to explore cinnamon oil specifically in the context of functional dyspepsia. Preclinical evidence has shown that cinnamaldehyde, the main bioactive compound in cinnamon oil, may exert antispasmodic, anti-inflammatory, and prokinetic effects. These findings support the rationale for further well-designed clinical studies to better assess the therapeutic potential of cinnamon oil in gastrointestinal disorders. (Alqasoumi, 2012; Ranasinghe et al., 2013).

Table I. Summary of herbal and complementary medication research of dyspepsia

Interventions	Duration	Study Country	Study Design	Outcome	Main Results
Turmeric *(Curcuma longa)*					
- Curcumin capsule 250 mg orally QID (2 capsule/dose) (2 g per day) - Omeprazole capsule 20 mg orally SID - Curcumin capsule 250 mg orally QID (2 capsule/dose) (2 g per day) + Omeprazole capsule 20 mg orally SID	4 weeks	Kongkam et al. (2023) Thailand	RCT *n* = 206 49.7 years	RTT: SODA	Curcumin and omeprazole had comparable efficacy for functional dyspepsia with no obvious synergistic effect.
- *Curcuma longa* Linn capsule 500 mg orally QID (2 g per day) - Omeprazole 20 mg SID - Placebo	4 weeks	Yongwatana et al. (2022) Thailand	RCT *n* = 132 56.4 years	RTT: SODA QoL: EQ-5D index	*Curcuma longa* can improve dyspeptic symptoms, improve quality of life, and provide satisfaction equivalent to omeprazole in treatment of functional dyspepsia.
Ginger *(Zingiber officinale)*					
Swanson Ginger Root Capsule 540 mg BID (1.08 g per day)	4 weeks	Aregawi et al. (2023) Hungary	Before and after clinical study *n* = 51 49.7 years	RTT: Rome IV questionnaire	Ginger supplementation significantly reduced most symptoms of functional dyspepsia, such as postprandial fullness, early satiety, epigastric pain, epigastric burning, and heartburn.
Swanson Ginger Root Capsule 540 mg BID (1.08 g per day)	8 weeks	Aregawi & Zoltan (2025) Hungary	open-label clinical trial *n* = 51 49.7 years	QoL: SF-NDI	After eight weeks of ginger supplementation, there was a significant improvement in QoL, as indicated by a decrease in SF-NDI scores.
Licorice *(Glycyrrhiza glabra)*					
- GutGard (root extract of *Glycyrrhiza glabra) Capsule* 75 mg BID (150 mg per day) - Placebo	30 days	Raveendra et al. (2012) India	RCT *n* = 50 45.2 years	RTT: the severity symptoms (as measured by 7-point Likert scale), the global assessment of efficacy QoL: SF-NDI	The root extract of *Glycyrrhiza glabra* (GutGard) at 75 mg twice daily for 30 days significantly improved dyspepsia symptoms and quality of life, showing superiority over placebo.

Table I. (Continued)

Interventions	Duration	Study Country	Study Design	Outcome	Main Results
Cinnamon *(Cinnamomum zeylanicum)* - Cinnamon oil soft capsule orally TID - Placebo (sesame oil soft capsule) orally TID	6 weeks	Zobeiri et al. (2021) Iran	RCT *n* = 64 41.9 years	RTT: GIS	Both cinnamon oil and placebo significantly reduced dyspepsia scores from baseline, but showed no significant difference between them at the endpoint.
Probiotics - *L. gasseri* OLL2716-containing yogurt (85 g/day) - Placebo yogurt (85 g/day)	12 weeks	Ohtsu et al. (2017) Japan	RCT *n* = 116 42.8 years	RTT: The global assessment	*L. gasseri* OLL2716 has beneficial effects on functional dyspepsia without *Helicobacter pylori* involvement.
- The probiotic treatment consisted of a 1:1 combination of spray-dried *Bacillus coagulans* MY01 and *Bacillus subtilis* MY02 endospores (total of 2.5 × 10^9 colony-forming units per capsule) in a mixture of 50 mg with 300 mg maltodextrin per capsule, orally BID - Placebo contained 350 mg maltodextrin per capsule orally BID - Probiotic + PPI - Placebo + PPI	8 weeks	Wauters et al. (2021) Belgium	RCT *n* = 68 40.1 years	RTT: LPDS, PAGISYM QoL: PAGI–QOL	The combination of *Bacillus coagulans* MY01 and *Bacillus subtilis* MY02 was effective and safe for functional dyspepsia, showing benefits over placebo, including reduced small intestinal bacterial overgrowth in patients using proton pump inhibitors.

Abbreviations: SID, once daily; QID, four times a day; BID, twice a day; TID, three times a day; QoL, quality of life; RCT, randomized controlled trial; RTT, response to treatment; EQ-5D, EuroQol- 5 Dimension; SODA, Severity of Dyspepsia Assessment; SF-NDI; Short-form Nepean Dyspepsia Index; GIS, Gastrointestinal Symptom Score; *L. gasseri, Lactobacillus gasseri OLL2716;* PPI, Proton pump inhibitors; LPDS, Leuven Postprandial Distress Scale; PAGISYM, Patient Assessment of Upper Gastrointestinal Disorders Symptom Severity Index; PAGI–QOL, Patient Assessment of Upper Gastrointestinal Disorders Quality of Life.

Probiotics

From the perspective of complementary medicine, probiotics have shown promising potential as a non-pharmacological treatment for dyspepsia, especially in improving gastrointestinal symptoms such as bloating, early satiety, and postprandial fullness. Mechanistically, probiotics may benefit dyspepsia patients by restoring microbial balance in the gut, enhancing intestinal motility, and modulating immune responses. For instance, probiotics help in correcting the duodenal microbiota dysbiosis, which is common in dyspepsia, by increasing beneficial bacteria and reducing the abundance of harmful pathogens. The beneficial effects are also associated with the production of short-chain fatty acids (SCFAs), which can influence gut-brain communication and reduce visceral hypersensitivity—a key factor in dyspepsia pathophysiology. RCTs support their efficacy, with studies showing symptom improvement in dyspepsia patients. For example, *Lactobacillus gasseri* OLL2716 reduced gastric symptoms, particularly in postprandial distress syndrome patients, while *Bacillus coagulans* MY01 and *Bacillus subtilis* MY02 demonstrated significant symptom relief after 8 weeks of treatment. Combining probiotics with conventional therapies, such as PPIs, further enhanced clinical outcomes, suggesting that probiotics can be a promising adjunct in managing dyspepsia (Ohtsu et al., 2017; Wauters et al., 202; Zhang et al., 2020; Tziatzios et al., 2023).

Non-pharmacological Approaches for Dyspepsia

Non-pharmacological interventions for dyspepsia are particularly beneficial as part of a holistic treatment approach. While medications such as PPIs and prokinetics target the physical symptoms of dyspepsia, non-pharmacological strategies address the underlying lifestyle and psychological factors that contribute to the condition. The key interventions include dietary changes, lifestyle modifications, stress management, and psychological therapy.

Dietary and lifestyle modifications are critical in managing dyspepsia symptoms. Patients are advised to avoid foods that may trigger symptoms, such as spicy, fatty, or acidic foods, and to adopt a pattern of eating smaller, more frequent meals throughout the day. This helps prevent the overloading of the stomach and reduces discomfort associated with dyspepsia. In addition, avoiding smoking and limiting alcohol consumption are essential recommendations. Smoking can weaken the lower esophageal sphincter and promote acid reflux, while alcohol can irritate the stomach lining and increase acid production, both of which may exacerbate symptoms. Other important lifestyle changes include maintaining an ideal body weight and avoiding late-night meals, which can help prevent acid reflux and worsen dyspepsia symptoms (Talley & Ford, 2015; Moayyedi et al., 2017).

Given the strong link between dyspepsia and psychological factors, stress management techniques, such as meditation, yoga, and cognitive-behavioral therapy (CBT), have been found to be effective in reducing symptoms. These methods help improve communication between the brain and the gut, often referred to as the gut-brain axis. By stabilizing visceral responses and reducing pain perception, these techniques can significantly alleviate the discomfort associated with dyspepsia. Stress reduction therapies help patients manage the psychological factors contributing to their gastrointestinal symptoms, addressing both the physical and emotional components of the condition (Ford et al., 2020; Dehghanizade et al., 2015; Mukhtar et al., 2019).

CONCLUSION

Dyspepsia remains a prevalent and challenging condition with multifactorial origins, including both gastrointestinal and psychological components. Although several pharmacological treatments, including PPIs, H2 blockers, and prokinetic agents, are commonly used, their effectiveness varies among individuals, highlighting the need for a more personalized approach. The introduction of novel therapies such as Tegoprazan (a potassium-competitive acid blocker) represents a promising advancement, offering rapid and reversible acid suppression with a favorable safety profile. Additionally, the potential of herbal therapies, such as turmeric, ginger, and licorice, in managing dyspepsia symptoms suggests that complementary medicine could play a significant role in treatment strategies. Future research is needed to further validate the long-term efficacy and safety of both modern and herbal approaches. Overall, a multidisciplinary approach that combines pharmacological treatment with lifestyle modifications and psychological support is essential for managing dyspepsia effectively and improving patients' quality of life.

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