

Exploring Herbal Remedies for the Management of Functional Gastrointestinal Disorders and Infections: A Comprehensive Review

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Abstract: *People and society are negatively affected by functional dyspepsia (FD), a prevalent gastrointestinal condition. We searched PubMed using specific keywords for this research to examine clinical papers on conventional and herbal dyspepsia treatments and their adverse effects. Dyspepsia may be treated with H2 blockers, antacids, and PPIs. Tegaserod, a 5-HT4 receptor partial agonist, is also discussed in regard to prokinetic medicines. We review the evidence for non-herbal dyspepsia treatments, taking into consideration factors other than acid reduction, such as the placebo effect and symptom variance, which are discussed in the proton pump inhibitor (PPI) therapy section. Unlike most medications, herbal therapies generally include many active ingredients that target multiple signaling pathways. Literature mentions licorice, ginger, fennel, cumin, and aloe vera. Herbal treatments, whether single-plant or blended, may treat numerous conditions. So, the same scientific criteria used to assess chemically specific drugs should be utilized to evaluate herbal treatment throughout development.*

Keywords: Herbal treatment, Functional gastrointestinal disorders, Infection.

I. INTRODUCTION

Chronic gastrointestinal (GI) abnormalities and symptoms without a reason are termed "functional gastrointestinal disorder" [1]. Indigestion, or dyspepsia [2], causes stomach pain, fullness, and bloating during and after eating. Heartburn, acid reflux, and burping are common. Functional dyspepsia affects 80% of dyspepsia sufferers since their symptoms are not anatomical. Many causes of functional dyspepsia [3] have pharmaceutical treatments. Dysregulated gastric acid, neurotransmitter, and gastrointestinal motility may induce dyspeptic symptoms.

Dyspepsia and infections depend on gut microbiota, according to recent research. Dyspepsia onset and persistence depend on gut microbiomes. Gut microbiota health prevents gastrointestinal diseases like *Helicobacter pylori*. Researchers are researching gut microbiota modification to treat dyspepsia and GI infections [4]. Antibiotics with probiotics or symbiotics may increase *H. pylori* eradication and prevent negative effects [5]. Berberine and garlic may improve gut microbiota [6]. A multimodal approach that incorporates gut microbiota and herbal microbiome-modulating medications may help treat these diseases. Further research is needed to understand these associations' mechanisms and therapeutic implications.

Pharmacological and various treatments for adult FD dyspepsia exist. Pantoprazole, omeprazole, esomeprazole, H2 receptor antagonists, 5-HT3 receptor antagonists, antihistamines, prokinetic agents, and adreno-corticosteroids.

The efficacy and safety of pharmaceutical medications vary between children and adults, which might create unexpected adverse effects. For instance, proton pump inhibitors have no negative effects when taken as directed for a short period but become problematic over time. Parental interest in "safe and natural." therapies is growing. Ancient people employed herbs for wellness. Historically, Egypt, Mesopotamia, Greece, Rome, and Arabia employed plants to prevent and treat illness. Susruta and Charaka [9] commend cardamom, turmeric, ginger, cinnamon, and pepper for their healing powers. Functional gastrointestinal issues are still treated with some of these herbs. Despite extensive use, herb research is sparse. Addressing research gaps and examining herbal medicines as alternative therapies for functional gastrointestinal diseases, notably dyspepsia [10], this review investigates their effectiveness and safety.

Research shows probiotics may prevent chemotherapy-induced intestinal mucositis adverse effects [11]. The gut microbiota is increasingly connected to GI diseases [12]. Herbs with antimicrobial and antioxidant characteristics may help digestion [13]. Traditional medicine anticancer herbs have toxicity studies [14]. Multiple plant saponin extracts have been evaluated for antioxidant and antibacterial properties [15,16]. These studies demonstrate natural substances' therapeutic value. Saponin extracts from *Argania spinosa* L. Skeels [17] are antioxidant and antibacterial, showing that natural chemicals may benefit gastrointestinal health. The examination of herbal medicines for functional gastrointestinal diseases utilizing these investigations may provide new treatments. More preclinical and clinical experiments are required to completely understand these natural medicines' mechanics and therapeutic benefits.

II. METHODOLOGY

PubMed Central and Scopus were searched separately for relevant material for this study. MESH search keywords "anti-microbial herbal drugs", "Applications", "conventional medicines", "herbals", "functional gastrointestinal disorder", "gastrointestinal infection", "dyspepsia", and "adverse effects" were used with an emphasis on "human trials summaries". To find further papers, we checked relevant publications' references. The search was undertaken from January to March 2023 to include latest research and publications. This review focuses on the efficacy and safety of anti-microbial herbal dyspepsia treatments and the side effects of non-herbal ones. English-language, 10-year-old human trials and clinical investigations on herbal therapies for functional gastrointestinal problems, dyspepsia, and microbial infections were included. Non-human studies, preclinical research, articles in languages other than English, and studies that did not directly address herbal treatments' effectiveness, safety, and adverse effects in functional gastrointestinal disorders and microbial infections were excluded.

III. DISCUSSION

Treatment available for dyspepsia

Good FD treatments without *Helicobacter pylori* infection include proton pump inhibitors (PPIs) or *H. pylori* antagonists' histamine-2 receptors (H2RAs), central neuromodulators, tricyclic antidepressants (TCAs), SSRIs, SNRIs, or antipsychotics like levosulpiride or prokinetics. Later drugs include acetamide acetylcholinesterase inhibitors and 5-HT receptor agonists like tegaserod or buspirone. Domperidone, mosapride, and itopride are dopamine receptor agonists. Main explanation: central neuromodulators cure functional dyspepsia. They may peripherally impact gastrointestinal motility by acting as antagonists to neurotransmitter receptors such 5-HT, dopamine D2, histamine, and acetylcholine [7,18].

Comprehensive FD therapy needs patient education and expectation management [19]. Many studies emphasize assuring patients that their symptoms have no physical cause, discussing the disorder's genesis and history, and treating the major symptoms realistically [20,21]. Physiologically treating FD improves patient outcomes and satisfaction. Lifestyle and exercise may improve dyspepsia symptoms, although data is scarce [22,23]. Some foods might cause symptoms. Nutrition-manipulated RCTs are uncommon [24]. Several studies demonstrate that prokinetic and anti-acid medicines help functional dyspepsia patients [25].

Anti-acid

Drugs that inhibit H2 H2-blockers have been used to treat functional dyspepsia. RCTs suggest that PPIs are widely used to treat dyspeptic symptoms in functional dyspepsia, however their efficacy may be restricted to individuals with reflux symptoms. Compared to H2RA, PPI reduces baseline and gastrin-stimulated stomach acid production. PPI therapy improved non-ulcer dyspepsia results somewhat compared to H2-blocker treatment, but not significantly [24].

Prokinetic drugs

Inhibiting dopamine and serotonin receptors accelerates stomach emptying and gastrointestinal motility using prokinetics. Accelerating stomach emptying reduces nausea and dyspeptic symptoms. Based on this mechanism and adult efficacy, prokinetics cure FD in children. However, prokinetics' effectiveness in FD patients is variable [25].

Tegaserod, a 5-HT₄ receptor partial agonist, speeds stomach emptying and improves FD gastric accommodation. In women with mostly PDS symptoms, two major phase 3 trials with tegaserod 6 mg b.i.d. indicated a minor effect of

uncertain clinical significance [26]. Newer prokinetic medicines with 5-HT4 receptor agonist characteristics, such as renzapride, prucalopride, ATI-7505, and TD-5108, were examined in healthy volunteer patients with Gastroparesis and FD. Butyrophenone derivative domperidone inhibits peripheral D2 receptors. Domperidone effectively decreased nocturnal dyspeptic symptoms and nocturnal bile reflux in a Chinese population [25].

The adverse effect of non-herbal drugs

Medical therapy is the mainstay of treatment, even though most medications are ineffective and none modify the long-term natural history of FD. Table 1 presents a management plan based on therapy efficacy [27].

Prokinetics' long-term effects on youngsters are feared. Adult studies show that metoclopramide and domperidone increase the risk of diarrhea, sleepiness, cardiac arrhythmia, and extrapyramidal symptoms such tardive dyskinesia and dystonic movement [28]. Tegaserod's long-term open-label research showed symptom relief and a persistent increase in productivity in FD, while another study demonstrated that people with normal gastric emptying could adjust their stomachs better. Although well-tolerated, the medicine was withdrawn owing to a possible increase in cardiovascular ischemia events (Figure 1).

Table 1. Summary of Evidence for Efficacy of Treatment Approaches for Functional Dyspepsia.

Therapy and Drugs Tested	FD Subgroup Studied	Efficacy	Adverse Events	Limitations of Data
H. pylori eradication therapy (e.g., 1-week course of PPI triple therapy)	Unselected patients, reasonable to use in EPS (epigastric pain syndrome)	Effective	Total adverse events only reported by two trials	None, other than limited reporting of adverse events
H2-RAs (e.g., ranitidine 150mg once daily)	Unselected patients, reasonable to use in EPS (epigastric pain syndrome) or PDS (postprandial distress syndrome)	May be effective	Total adverse events poorly reported	Few trials at low risk of bias; heterogeneity between studies; possible publication bias; some trials included patients with gastro-esophageal reflux symptoms
Prokinetics (e.g., acotiamide 100mg or itopride 50mg three times daily)	Most newer trials recruit patients with PDS (postprandial distress syndrome)	May be effective	Total adverse events no more common with 5-HT1A agonists in a meta-analysis of three RCTs	Only three trials; heterogeneity between studies; effective in unselected patients in one study and significantly improved postprandial symptoms in a second study; imprecision around the estimate of effect
TCAs (tricyclic antidepressant) (e.g., amitriptyline or imipramine started at a dose of 10-25 mg once daily at night and titrated to 50mg once daily at night)	Unselected patients, although seemed to be more effective in EPS (epigastric pain syndrome)	Effective	Total adverse events significantly more common with TCAs in a meta-analysis of two RCTs, Particularly dry mouth and drowsiness	Only four trials; imprecision around the estimate of effect; tolerability may be an issue

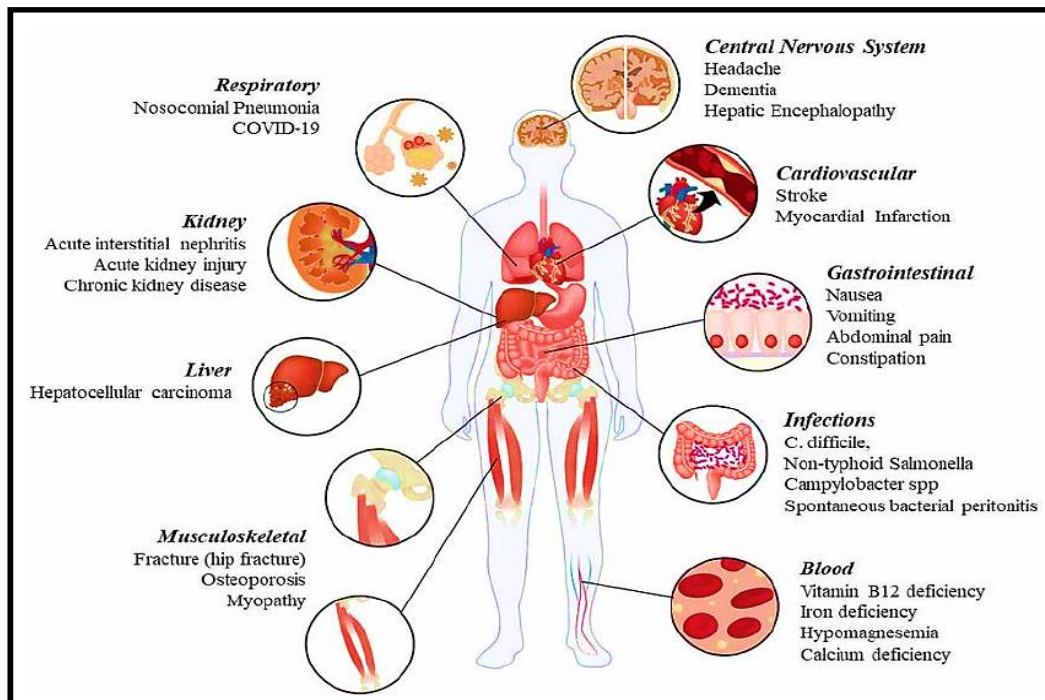


Figure 1. Side effects associated with the use of proton pump inhibitors.

Consequently, long-term PPI treatment may be initiated and medication may be continued if a patient exhibits a favorable response. However, the favorable outcome could potentially be ascribed to the placebo effect or the unpredictable characteristics of dyspepsia, as opposed to a decrease in acid secretion [29].

Gastrointestinal Infections

PPI use has been associated with an increased incidence of accidental and recurrent *Clostridium difficile* infections. As gastric acid secretion is an essential immunological barrier in the digestive tract, hypochlorhydria induced by gastric acid secretion inhibition alters the gut flora, increases the risk of bacterial colonization, and renders individuals more susceptible to enteric infections. A higher risk of *Clostridium difficile* infection has been associated in studies with severe inhibition of gastric acid secretion [29].

Respiratory Infections

PPI use has been linked to pneumonia on numerous occasions, particularly when administered for a brief duration of time (typically less than 30 to 90 days). However, a recent meta-analysis has indicated that this association may be overstated. Hypochlorhydria elicited by PPIs, which increases lung colonization and the eventual incidence of pneumonia by promoting micro-aspiration of gastric contents, is the most plausible explanation for the increased risk of respiratory infections associated with PPI use [29].

Gastrointestinal malignancies

This explains the association between PPI use and the development of neuroendocrine tumors and cancer of the gastrointestinal tract. The compensatory increase in gastrin levels among patients has a proliferative impact on the development of enterochromaffin cells [29], due to the fact that PPIs inhibit gastric acid production.

Cardiovascular disease

PPIs have been related to cardiovascular disease and mortality for 10 years. PPI usage at high dosages or for a long time increases the risk of acute myocardial infarction and stroke. Since dimethylarginine dimethylaminohydrolase clears asymmetric dimethylarginine, PPIs may reduce endothelial nitrous oxide levels by reducing nitrous oxide synthase activity. PPIs increase blood chromogranin A, a biomarker for neuroendocrine tumors and cardiovascular risk [29].

Treatment of FD with Herbal Medication

Tradition advises FD management begin with security. FD patients are encouraged to eat more frequently, eat less, and avoid symptoms-escalating foods, however these recommendations have not been tested [26]. Instead of targeting one

mechanism like motility and inflammation, herbal medications may work because they include various active components that target many signaling pathways. Multitarget treatment may help when numerous factors produce symptoms. Until composite mixtures, particular compounds, or bioactive molecules may modify therapy [30]. Herbal medicine is getting more accepted. The WHO's recent ICD-11 contains TCM information for the first time as part of its Traditional Medicine Strategy (2014–2023). These plants are popular in complementary and alternative medicine. Peppermint oil is recommended by the British National Formulary (BNF) for bloating and gastrointestinal symptoms, especially in IBS. Meditation, colonic irrigation, acupuncture, and homoeopathy are CAMs.

STW 5 (Iberogast)

The liquid blend of nine herbs STW-5 has been utilized in German medicine for over 50 years. Bittersweet, angelica root, milk thistle fruit, celandine, cumin, licorice root, peppermint, and balsam leaf. Together, these potent ingredients alleviate functional gastrointestinal discomfort. An abstract research examined STW-5's gastrointestinal benefits for FD patients. In one week, 918 kids participated in the study. Participants got 10–20 STW-5 drops three times daily. A 14-item questionnaire measured upper and lower abdominal discomfort. During therapy, school absenteeism reduced from 67.0% to 36.1%. Additionally, 38.6% of children and parents saw total symptom alleviation. Doctors assessed 94.8% of children's tolerability as great.

Fennel

A popular spice and medicine, fennel (*Foeniculum vulgare* Mill.) is fragrant. A diuretic, expectorant, and dyspeptic treatment, it has several benefits. Fennel has several traditional medical applications. Numerous bio-pharmacological studies have examined *F. vulgare*'s traditional use. *F. vulgare* extracts and isolated components have been studied for anti-aging, anti-allergic, anti-colitis, anti-hirsutism, anti-inflammatory, anti-microbial, anti-viral, antinociceptive, antipyretic, and antispasmodic properties. *F. vulgare* treats dyspepsia caused by gastrointestinal atony, stomach heaviness, and persistent colitis that rejects traditional treatments. Its stem, fruit, leaves, seeds, and stem are used medicinally to cure several diseases. Fennel at 10% w/v increased stomach acid output in rats from 0.12 to 0.42 ml, however the mechanism is uncertain. Fennel infusion stimulates the gastrointestinal action domestically and worldwide due to its feature. Fennel lowers stomach discomfort in anthraquinone laxatives [18].

Cumin

Cumin seeds are useful in Indian Ayurvedic medicine, particularly for dyspepsia. We utilize chronic diarrhea and dyspepsia. Cumin seeds (*Cuminum cyminum* L.) are used as spices and in traditional medicine to cure chronic diarrhea, indigestion, acute gastritis, diabetes, and cancer due to their characteristic scent. Terpenes, phenols, and flavonoids in cumin have increased study and shown its biological and therapeutic properties. Cumin's effect on rats' gastrointestinal transit duration was studied in another investigation. A 25% reduction in food movement time. Cumin shortens stomach transit time in proportion to its effect on digestive enzymes or bile production.

Aloe Vera

Aloe vera is utilized in homeopathy, Ayurveda, and allopathy. Research shows it may heal acne, reduce epithelial cell damage, restore sunburns, and be an efficient laxative. The research suggests antioxidant, anti-inflammatory, analgesic, antiproliferative, and anti-diabetic properties. Its application in treating FD in adults has been studied.

Ginger

Ginger root (*Zingiber officinale*) is a popular spice. It originated in India and South Asia and was one among the first spices traded. Ginger-based dai-ketchup-to improved dogs' gastrointestinal motility in 1990s study. Ginger reduces subjective pain in various pro-inflammatory disorders. Ginger has been studied for FAPD, which is connected to stomach hypersensitivity and abnormal central nervous system processing of gastrointestinal stimuli.

Treatment of Microbial Infection with Herbal Medication

GI infections are a global health hazard. Immunocompromised or comorbid individuals may die from these infections, which include diarrhea, vomiting, stomach pain, and cramping. Although antibiotics heal most gastrointestinal illnesses, antibiotic-resistant organisms are becoming a big issue. Ancient herbal remedies are being retested for GI illness treatment efficacy and safety. Herbal GI infection therapy evidence-based literature is also reviewed for efficacy, mechanism of action, and safety. Bioactivities and therapeutic applications of herbal antibacterial substances including clove, cinnamon, turmeric, ginger, fennel, and eucalyptus are listed in Table 2. Barberry (*Berberis vulgaris*) and Goldenseal (*Hydrastis Canadensis*) contain berberine, a well-studied GI herb. Berberine is effective against various

species, including *Helicobacter pylori*, which causes peptic ulcers and stomach cancer. It modifies gut flora and lowers intestinal inflammation, suggesting therapy for inflammatory bowel diseases.

Table 2 Herbal antimicrobial agents and their bioactivities [31].

Herbal drug	Bioactivities
Clove	Antioxidant, antimicrobial, anti-inflammatory, anti-mutagenic, anti- allergic and anti-cancer
Cinnamon	Antioxidant, antimicrobial, anti-inflammatory, anticancer, cholesterol- lowering, immunomodulatory and cardiovascular
Turmeric	Antioxidant, antimicrobial, anti-inflammatory, anticancer, hypoglycaemia, and anticoagulant
Ginger	Antioxidant, antimicrobial, anti-diabetic, neuro-protective, analgesic, cardiovascular, gastrointestinal, anti-inflammatory, anticancer, and antihypertensive
Fennel	Antioxidant, antimicrobial, and anti-inflammatory
Eucalyptus	Antioxidant, antimicrobial anti-inflammatory, and antipyretic

Thyme (*Thymus vulgaris*) essential oil kills GI pathogens including *Escherichia coli* and *Staphylococcus aureus*. Another common antibacterial herb for GI illnesses is garlic (*Allium sativum*). Its main bioactive element, allicin, fights pathogenic *Escherichia coli*, *Salmonella*, and *Helicobacter pylori* strains.

Fermented foods include non-herbal probiotics like *Lactobacillus* and *Bifidobacterium*. They control antibiotic-associated diarrhea and inflammatory bowel disease successfully [18,24]. These medicines have promise, but they may interfere with conventional drugs and cause adverse effects or inefficiency. Unstandardized herbal medications make dosage, quality, and safety difficult to assess.

In the face of antibiotic resistance, herbal GI remedies may be effective options or adjuncts. Allicin, berberine, and thymol are antimicrobials; probiotics are helpful. These medicines, especially for COVID-19 or prolonged COVID, require further clinical trials to determine the appropriate dosage, safety, and efficacy. Standardizing herbal remedies maintains quality.

IV. CONCLUSION

Families and doctors are increasingly using non-pharmacological FD treatment to manage dyspepsia. These non-addictive, non-pharmacological therapies could assist FD patients who have tried and failed standard drugs because to their non-invasiveness and minimal side effects. Some FD patients react well to non-pharmacological therapy, but the evidence is inadequate to recommend its frequent use. Individualized therapy is important to maximize herbal medicines' therapeutic benefits. Customized treatment regimens are needed due to patient traits, preferences, and herbal remedy reactions. Therefore, more well-conducted, large-scale clinical studies are needed to assess the efficacy and possible variations of these therapies. As we study herbal medicines' many advantages, we must apply the same scientific rigor and attention to research as for pharmaceutical treatments. We offer herbal medicines for functional dyspepsia, bearing in mind that customized therapy improves patient results.

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