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# A Review of Herbal Treatment for Functional Gastrointestinal Disorders and Infection

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**Abstract:** Functional dyspepsia (FD), a common gastrointestinal condition, poses significant burdens on both individuals and society. In this article, we conducted PubMed searches using specific keywords to review clinical trials focusing on conventional and herbal treatments for dyspepsia as well as the adverse effects of non-herbal treatments. Dyspepsia can be managed using proton pump inhibitors, H2 blockers, and antacids. Additionally, we explore Tegaserod, a partial agonist of the 5-HT4 receptor, in the context of prokinetic medications. We summarise the research supporting the effectiveness of non-herbal dyspepsia treatment, considering factors beyond acid reduction, such as the placebo effect and the variability of dyspepsia symptoms, as discussed in the section on proton pump inhibitor (PPI) medication. Unlike most pharmacotherapies targeting a single mechanism, herbal medications often contain multiple active ingredients that can address several signalling pathways simultaneously. Notable herbs like fennel, cumin, aloe vera, ginger, and licorice have documented uses in the literature. Whether derived from a single plant or a combination,

herbal treatments hold promises for addressing multiple conditions simultaneously. Therefore, evaluating herbal therapy at all stages of development should adhere to the same scientific rigour applied to chemically specific therapies.

**Keywords:** Functional dyspepsia; Herbal treatments; Gastrointestinal disorders; Natural remedies

## 1. Introduction

The term "functional gastrointestinal disorder"[1] (FGID) is used to characterize gastrointestinal (GI) abnormalities and symptoms that are continuous and persistent but have no apparent underlying disease. Dyspepsia[2] is another word for indigestion, which includes feelings of stomach pain, over-fullness, and bloating during and after eating. Other common symptoms include acid reflux, heartburn, and excessive burping. About 80% of dyspepsia sufferers are classified as having functional dyspepsia (FD) because there is no anatomical cause for their symptoms. Functional dyspepsia is associated with a range of hypothesized mechanisms[3], each offering unique opportunities for pharmaceutical intervention aimed at minimizing dyspepsia symptoms. These mechanisms encompass factors such as gastric acid regulation, neurotransmitter modulation, and gastrointestinal motility, which, when dysregulated, can contribute to the manifestation of dyspeptic symptoms.

Recent research has highlighted the pivotal role of the gut microbiota in gastrointestinal conditions like dyspepsia and infections. Dyspepsia's development and persistence can be influenced by gut microbial imbalances. Moreover, maintaining a healthy gut microbiota is crucial for defending against gastrointestinal infections, including those caused by *Helicobacter pylori*. To improve treatment outcomes for dyspepsia and gastrointestinal infections, researchers are exploring strategies to modulate the gut microbiome[4]. Incorporating probiotics or symbiotics into antibiotic therapy has shown promise in enhancing eradication rates and reducing side effects, especially for *H. pylori* infections[5]. Additionally, certain herbs and natural compounds, such as berberine and garlic, exhibit antimicrobial properties against gastrointestinal pathogens, suggesting their potential to promote gastrointestinal health by modulating the gut microbiota[6]. This multifaceted approach, considering the gut microbiota's role and exploring herbal remedies' microbiota-modulating potential, offers a promising avenue for managing these conditions. Further research is needed to understand the mechanisms behind these interactions and their clinical implications.

Potential therapeutic options for dyspepsia, investigated in adult populations with FD, encompass a variety of pharmaceutical and alternative treatments. These treatments can be categorized based on their mechanisms of action and clinical usage includes proton pump inhibitors[7] (PPIs) (e.g., pantoprazole, omeprazole, esomeprazole), H2 receptor antagonists ($H_2$RAs) (e.g. ranitidine, famotidine), 5-HT3 receptor antagonists (e.g. ondansetron), antihistamines (e.g. promethazine), prokinetic agents (e.g. erythromycin, domperidone, metoclopramide), adreno-corticosteroid (e.g. fludrocortisone), antacids (e.g. sucralfate) and neuromodulators/serotonergic drugs (e.g. cyproheptadine, citalopram, paroxetine, fluoxetine, amitriptyline, nortriptyline).

It is important to note that pharmaceutical medicines' efficacy and safety profiles vary significantly between children and adults, which may lead to unintended consequences. While some therapies, like proton pump inhibitors, show no significant negative effects when taken as directed for a brief period, reports of side effects tend to increase with prolonged use[8].

As a result, parents are becoming more interested in using alternative therapies that are seen as "safe and natural." Since ancient times, herbs have been employed for their health advantages. Herbs were utilized for illness prevention and treatment in Egypt, Mesopotamia, Greece, Rome, and Arabia, according to historical records. Ancient Indian writers Susruta and Charaka[9] highlight the medicinal benefits of cardamom, turmeric, ginger, cinnamon, and pepper in their texts. Some of these plants are still used as natural cures for a variety of illnesses, such as functional gastrointestinal diseases. Herbs are often used, yet there is little supporting research. This review aims to investigate the efficacy and safety of herbal treatments in functional gastrointestinal disorders, particularly dyspepsia[10], with a focus on addressing existing gaps in the literature and exploring the potential of herbal remedies as valuable alternatives in the management of this common condition.

In addition, current research has examined the potential of probiotics to alleviate the adverse effects associated with chemotherapy-induced intestinal mucositis[11]. The gut microbiota has been increasingly recognized as a key player in gastrointestinal conditions[12]. Moreover, some herbs have shown antibacterial and antioxidant activities that may have potential benefits in enhancing gastrointestinal health[13]. In addition, scholarly examinations have been conducted on the toxicological aspects of anticancer plants often used in traditional medicine[14]. Furthermore, assessments have been carried out on the antioxidant and antibacterial properties of saponin extracts derived from several plant sources[15,16]. These investigations have yielded valuable knowledge on the possible therapeutic advantages

offered by natural substances. Furthermore, the assessment of saponin extracts derived from *Argania spinosa* L. Skeels[17] has shown their antioxidative and antibacterial characteristics, hence highlighting the potential of naturally occurring substances in enhancing gastrointestinal well-being. The integration of research results from these studies into the assessment of herbal therapies for functional gastrointestinal diseases has the potential to provide novel approaches for the successful implementation of management methods. Nevertheless, it is vital to do more investigation, including preclinical and clinical studies, in order to comprehensively comprehend the mechanics and clinical ramifications of these natural interventions.

## 2. Methodology

A separate search on both PubMed Central and Scopus to gather relevant literature for this review was conducted. The search was performed using MESH search terms "anti-microbial herbal drugs", "Applications", "conventional medicines", "herbals", "functional gastrointestinal disorder", "gastrointestinal infection", "dyspepsia", and "adverse effects" along with a focus on "human trials summaries". We also reviewed the references of relevant publications to identify additional articles for inclusion. The search was conducted from January 2023 to March 2023, ensuring that the review encompasses recent studies and publications. This review primarily focuses on examining the effectiveness and safety of anti-microbial herbal drugs in treating dyspepsia while also exploring the adverse effects associated with non-herbal drugs. Inclusion criteria encompassed studies published in English, studies published from the past 10 years with the study type including human trials and clinical studies focused on herbal treatments for functional gastrointestinal disorders, dyspepsia, and microbial infections. While exclusion criteria included non-human studies and preclinical research, articles in languages other than English and studies that do not directly address the research objectives of examining herbal treatments' effectiveness, safety, and adverse effects in the context of functional gastrointestinal disorders and microbial infections.

## 3. Discussion

### *3.1. Treatment available for dyspepsia*

In the absence of *Helicobacter pylori* infection, high-quality therapy choices for FD consist of acid-suppressing drugs such as proton pump inhibitors (PPIs) or *H. pylori* antagonists' histamine-2 receptors (H2RAs), central neuromodulators, along with tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin and

norepinephrine reuptake inhibitors (SNRIs), or antipsychotics such as levosulpiride or prokinetics. These later substances include agonists of the 5-hydroxytryptamine (5-HT) receptor, such as tegaserod or buspirone, as well as the inhibitor acetamide acetylcholinesterase. These include medications that act on dopamine receptors, such as domperidone, mosapride, or itopride. The primary reason is that central neuromodulators are used in functional dyspepsia. However, they also have peripheral effects on gastrointestinal motility as a result of their agonism or antagonism with receptors with an affinity for various neurotransmitters, including 5-HT, dopamine D2, histamine, and acetylcholine receptors[7,18].

Patient education and the management of expectations play crucial roles in the comprehensive management of FD[19]. Several studies have emphasized the importance of assuring patients that there is no structural cause for their symptoms, outlining the pathophysiology and course of the disorder, and adopting a realistic approach to treating the predominant symptoms[20,21]. These strategies not only address the physiological aspects of FD but also contribute to improved patient outcomes and satisfaction. While some specific foods have been associated with symptom development, the evidence supporting the effectiveness of lifestyle modifications and exercise in improving dyspepsia symptoms is currently limited or inconclusive[22,23]. Additionally, there are few randomized controlled trials (RCTs) that manipulate nutrition[24]. According to several studies, prokinetic drugs and anti-acid treatments are helpful for some groups of people with functional dyspepsia[25].

### *3.1.1. Anti-acid*

H2 blocker medicine Functional dyspepsia has historically been treated with H2-blockers (histamine H2-receptor antagonists). Although PPIs are frequently used to treat dyspeptic symptoms in functional dyspepsia, RCTs indicate that their efficacy in treating these symptoms is constrained and may only be applicable to individuals who also have reflux symptoms. Compared to individuals treated with the H2 receptor blocker H2RA, PPI therapy has been shown to decrease both basal and gastrin-stimulated stomach acid output. When PPI medication was compared to H2-blocker therapy for non-ulcer dyspepsia, the results were somewhat better overall, but the difference was not statistically significant[24].

### *3.1.2. Prokinetic drugs*

Prokinetics speeds up the emptying of the stomach by inhibiting dopamine and serotonin receptors, which increases gastrointestinal motility. It is advised to accelerate stomach emptying to lessen nausea and other dyspeptic symptoms. Prokinetics are used to

treat FD in children based on this postulated mechanism and effectiveness findings from adults. However, there is inconsistent data about prokinetics' efficacy in people with FD[25].

Tegaserod, a 5-HT4 receptor partial agonist, accelerates gastric emptying and improves gastric accommodation in FD. A report of two large phase 3 studies with tegaserod 6 mg b.i.d. in women with mainly PDS symptoms showed a small benefit of questionable clinical significance[26]. Newer prokinetic agents with 5-HT4 receptor agonist properties have been studied primarily in irritable bowel syndrome with a predominance of constipation (renzapride, prucalopride, ATI-7505, and TD-5108), were studied in healthy volunteer patients with Gastroparesis and patients with FD. Domperidone is a butyrophenone derivative that exerts antidopaminergic effects on peripheral dopamine2 (D2) receptors. A recent study in a Chinese population with nocturnal dyspeptic symptoms showed that domperidone significantly reduced the severity of nocturnal dyspeptic symptoms and this improvement was positively correlated with the reduction in nocturnal bile reflux[25].

### *3.2. The Adverse Effect of Non-Herbal Drugs*

Medical therapy is thus the basis of treatment, even though most therapies have limited effectiveness, and none have been shown to change the long-term natural history of FD. Evidence for the efficacy of various therapies is summarized and presented in a management algorithm in Table 1[27].

There are worries about prokinetics' long-term detrimental impact on children. These worries are mostly based on studies conducted on adults, which indicate an increased risk of diarrhea, drowsiness, cardiac arrhythmia, and extrapyramidal symptoms (such as tardive dyskinesia or dystonic movement) when metoclopramide and domperidone are combined[28]. In long-term open-label research, Tegaserod has shown symptom resolution and a sustained rise in productivity levels in FD, whereas a different study found that those with normal gastric emptying could accommodate their stomachs better. Although the medication was generally well tolerated, it was stopped due to a potential increased risk of cardiovascular ischemic 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 |

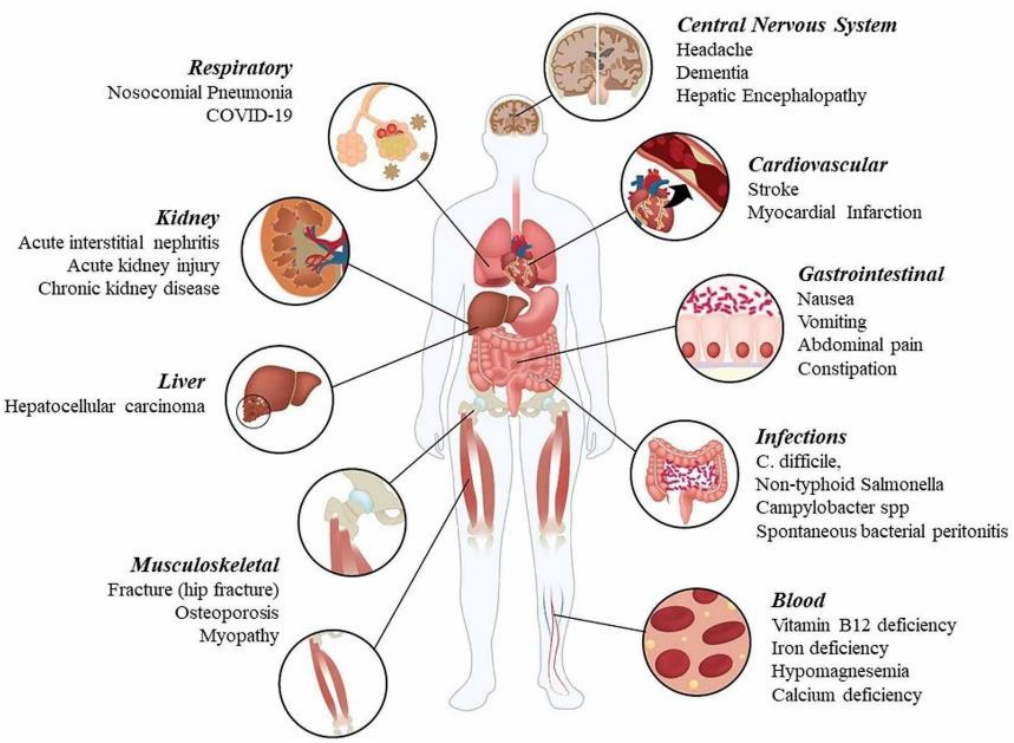


**Figure 1.** Side effects associated with the use of proton pump inhibitors.

Therefore, if a patient has a positive response, medication may be continued, and long-term PPI treatment initiated. Regardless, the good reaction might be attributed to a placebo effect or the variable nature of dyspepsia rather than reduced acid production[29].

### *3.2.1. Gastrointestinal infections*

The incidence of accidental and recurring *Clostridium difficile* infections has been linked to PPI use. Because the production of acid by parietal cells serves as a crucial immunological barrier in the digestive tract, hypochlorhydria brought on by the inhibition of gastric acid secretion raises the risk of bacterial colonization, changes the flora of the gut, and makes people more vulnerable to enteric infections. Strong inhibition of stomach acid output has been linked in studies to a higher risk of *Clostridium difficile* infection[29].

### *3.2.2. Respiratory infections*

PPI usage has frequently been linked to pneumonia, especially in the short term (usually less than 30 to 90 days). A recent meta-analysis, however, revealed that this link could be exaggerated. The PPI-induced hypochlorhydria that promotes micro-aspiration of stomach contents, increasing lung colonization, and the eventual incidence of pneumonia, is

the most plausible reason for the increased risk of respiratory infections associated with PPI usage[29].

### *3.2.3. Gastrointestinal malignancies*

This explains why PPIs are linked to the emergence of neuroendocrine tumours and gastrointestinal tract cancer. Since PPIs reduce stomach acid production, the compensatory rise in gastrin levels in patients has a proliferative effect on the formation of enterochromaffin cells[29].

### *3.2.4. Cardiovascular disease*

PPI usage has been linked to cardiovascular morbidity and death over the past ten years. Acute myocardial infarction and stroke have both been linked to an increased risk of serious acute cardiovascular events when PPI medication is used for an extended period of time or at high doses. By blocking the enzyme activity of dimethylarginine dimethylaminohydrolase, which is in charge of clearing up asymmetric dimethylarginine, PPI use may lower endothelium nitrous oxide levels by lowering nitrous oxide synthase activity. PPIs seem to raise blood levels of chromogranin A, a crucial biomarker for neuroendocrine tumours and a potential indicator of cardiovascular risk[29].

## *3.3. Treatment of FD with Herbal Medication*

Traditionally, the first step in FD management has been suggested as security. Dietary recommendations (eat more frequently, eat smaller portions, and avoid foods that worsen symptoms) are logical and commonly prescribed to patients with FD, but have not been studied systematically[26]. Some herbal medications may be beneficial because they frequently include a number of active components that can simultaneously target several underlying signalling pathways, in contrast to traditional pharmacotherapies that concentrate on one underlying mechanism (e.g., motility and inflammation). Multitarget therapy may be used as an effective treatment strategy when several factors, either separately or in combination, contribute to the development of symptoms. This is the case until therapies are developed that enable patients to receive individualized care using composite mixtures, particular ingredients, or bioactive ingredients[30]. Herbal medicine's overall therapeutic potential is becoming more widely acknowledged. For the first time, information on traditional Chinese medicine (TCM) is incorporated in the World Health Organization's (WHO) most recent revision of the International Classification of Diseases (ICD-11), which is a component of its Traditional Medicine Strategy (2014–2023). Some herbal preparations have entered the mainstream of complementary and alternative medicine (CAM). As an

illustration, the British National Formulary (BNF) advises using peppermint oil to reduce bloating and gastrointestinal cramps, especially in cases of irritable bowel syndrome. From meditation and colonic irrigation to acupuncture and homoeopathy, CAM therapies are available.

### *3.3.1. STW 5 (Iberogast)*

STW-5 is a liquid formulation of nine herbs that have been used in clinical practice in Germany for over 50 years. Contains bittersweet (*Iberis Amara*), angelica root (*Angelicae radix*), milk thistle fruit (*Silybi Marianifructus*), celandine (*Chelidonii herba*), cumin (*Carvi fructus*), licorice root (*Liquiritiae radix* It), peppermint herb (*Menthae Piperita folium*), balsam leaf (*Melissae folium*). To relieve functional gastrointestinal discomfort, these active ingredients act together. A research study that was only given in abstract form examined STW-5's capacity to reduce FD patients' gastrointestinal problems[31]. Over the course of one week, 918 kids participated in the study. Three times each day, the participants were given 10 to 20 drops of STW-5. Using a 14-item questionnaire, the symptoms of the upper and lower abdomen were evaluated. It is interesting to note that throughout therapy, the school truancy rate decreased from 67.0% to 36.1%. In addition, full symptom alleviation was achieved by 38.6% of kids and/or parents. 94.8% of the children's tolerability was graded as good or outstanding by the doctors[32].

### *3.3.2. Fennel*

Fennel (*Foeniculum vulgare* Mill.) is a well-known aromatic plant that is widely used as a spice and medicinal herb. It has many beneficial effects and is used as a diuretic, an expectorant, and in various dyspeptic disorders[33]. Fennel also has many uses in traditional medicine. Numerous bio-pharmacological investigations have been carried out to assess the traditional usage of *F. vulgare*. Various actions, including anti-aging, anti-allergic, anti-colitis, anti-hirsutism, anti-inflammatory, anti-microbial, anti-viral, antinociceptive, antipyretic, and antispasmodic, have been investigated for certain extracts and isolated components of *F. vulgare*[34]. *F. vulgare* is recommended for the treatment of dyspepsia brought on by gastrointestinal atony, dyspepsia with stomach heaviness, and certain kinds of chronic colitis (which reject conventional therapies). Its entire plant, including the stem, fruit, leaves, seeds, and stem, is used medicinally in a number of ways to treat a wide range of illnesses[34]. In tests, fennel at a concentration of 10% w/v increased gastric acid secretion in rats from 0.12 ml (baseline) to 0.42 ml, although the exact mechanism for this is unknown. Because of this property, fennel infusion is used to stimulate the gastrointestinal effect both nationally and globally[34]. The addition of fennel to preparations containing anthraquinone

ingredients reduces the incidence of abdominal pain commonly associated with this type of laxative[18,35].

### *3.3.3. Cumin*

In Indian Ayurvedic medicine, cumin seeds have tremendous medicinal value, especially for indigestion. Chronic diarrhea and dyspepsia are used[36]. Due to their distinctive aroma, cumin seeds (*Cuminum cyminum* L.) are extensively used as spices, but they are also widely used in traditional medicine to treat a variety of illnesses, including chronic diarrhea and dyspepsia, acute gastritis, diabetes, and cancer. The bioactive components of cumin, including terpenes, phenols, and flavonoids, have been credited with increasing the number of published research studies and providing evidence for its biological and medicinal activity. Another study examined whether the digestive stimulant cumin alters the time that meals stay in rats' gastrointestinal systems after consumption. The time for the meal to move was greatly shortened by 25%. Consuming cumin shortens the time food travels through the stomach roughly in proportion to how well it affects digestive enzymes or bile production[37].

### *3.3.4. Aloe Vera*

The plant aloe vera is used in both allopathic and Ayurvedic medicine, as well as in homeopathy. According to research, it has the ability to treat acne, prevent damage to epithelial cells, repair sunburns, and function as a very effective laxative. Various pharmacological benefits, including antioxidant, anti-inflammatory, analgesic, antiproliferative, and anti-diabetic capabilities, are also thought to exist, according to the data. In adult research, its use in the treatment of FD has been investigated[38].

### *3.3.5. Ginger*

Ginger, usually referred to as ginger root or Zingiber officinale, is a widely used spice. It was one of the earliest spices to be transported for the spice trade and is a native of the Indian subcontinent and South Asia. Early research from the 1990s discovered that dogs' stomach motility was enhanced by the herbal remedy dai-ketchup-to, which is based on ginger. In some pro-inflammatory diseases, ginger can also lessen subjective pain perception. Nutraceuticals like ginger have been researched in cases of FAPD, which has been linked to stomach hypersensitivity and aberrant central nervous system processing of gastrointestinal stimuli[38].

### *3.3.6. Licorice*

Few research studies investigate the mechanism of actions that contribute to licorice's efficacy in FD. According to animal research, its antiulcer effect is attributed to mucus formation, free radical scavenging, and prostaglandin inhibition. Commonly cited as the active substances in charge of the effects are glycyrrhizin and licorice flavonoids. There were clinical investigations that looked at how licorice affected upper gastrointestinal symptoms. One of the trials indicated that licorice root powder and a licorice substitute (*T. numularia*) greatly reduced indigestion symptoms such as sour belching, nausea, and a burning feeling in the chest and throat. However, the trial lacked a placebo, did not specify if it was blinded, and appeared solely focused on evaluating the efficacy of the substitute[38].

In accordance with the findings of various human trials investigating the effects of herbal ingredients on upper gastrointestinal conditions, a comprehensive summary is provided in Table 2. Specifically, we highlight the individual impacts of ingredients such as aloe vera, ginger, and licorice on upper GI conditions, elucidating their respective contributions to the field.

**Table 2.** Summary of human trials on herbal ingredients and upper GI conditions.

| **Ingredients** | **Characteristics** | **Duration** | **Intervention** | **Outcome Measured** | **Results** | **Reference** |
|---|---|---|---|---|---|---|
| Aloe Vera | Age: 18–65; 45 females and 34 males; GERD patients | 4 weeks | 10 mL 1x/day A. vera syrup (Standardized to 5.0 mg polysaccharide per mL of syrup) (10 mL total) | GERD | Aloe vera effectively reduced the frequencies of all GERD symptoms except vomiting at weeks 2 and 4 | [39] |
| Ginger | Age: 18–65; 5 males and 10 females' patients with *H. pylori-positive* FD | 4 weeks | 3 g, 1x/day ginger powder tablets (3 g total) | *H. pylori* positive FD and FD | Ginger supplementation resulted in significant improvement of all dyspepsia symptoms including fullness, early satiety, nausea, belching, gastric pain, and gastric burn, but not vomiting | [40] |
| Licorice | Age: 18–65; 31 males and 19 females patients with FD as | 30 days | 75 mg, 2×/day of flavonoid-rich extract of licorice (150 mg total) | Functional dyspepsia | As compared to CG, IG showed a significant decrease in total symptom scores ($p \leq 0.05$), and a significant improvement in | [41] |

| | | | | | | |
|---|---|---|---|---|---|---|
| | diagnosed by Rome III criteria | | | | quality of life ($p \leq 0.05$) as well as overall treatment efficacy. | |

### *3.4. Treatment of Microbial Infection with Herbal Medication*

Gastrointestinal (GI) infections constitute a significant burden on public health worldwide. Characterized by symptoms such as diarrhea, vomiting, abdominal pain, and cramps, these infections can range from mild, self-limiting conditions to life-threatening diseases, especially in immunocompromised individuals or those with comorbid conditions. Conventionally, gastrointestinal infections are treated with antibiotics, but the increasing prevalence of antibiotic-resistant pathogens is posing an immense challenge. In this light, herbal remedies, which have been employed since ancient times, are being revisited for their potential efficacy and safety in the treatment of GI infections. This review also examines the current evidence-based literature on herbal treatment modalities for GI infections, focusing on their efficacy, mechanism of action, and safety profile[39]. To elucidate the bioactivities and potential therapeutic applications of herbal antimicrobial agents, Table 3 has been compiled to present a comprehensive overview of the bioactivities of these herbs, including clove, cinnamon, turmeric, ginger, fennel, and eucalyptus.

One of the most studied herbal remedies for GI infections is berberine, an alkaloid extracted from plants like Barberry (*Berberis vulgaris*) and Goldenseal (*Hydrastis Canadensis*). Berberine has demonstrated potent antimicrobial activity against a wide range of organisms, including *Helicobacter pylori*, a leading cause of peptic ulcers and gastric cancer [40]. It has also exhibited beneficial effects in alleviating intestinal inflammation and modulating gut microbiota, thus showing promise in managing inflammatory bowel diseases[41–44].

**Table 3**. 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 |

Another promising herb is thyme (*Thymus vulgaris*), whose essential oil has been shown to possess potent antimicrobial properties against several GI pathogens, including *Escherichia coli* and *Staphylococcus aureus* [42]. Garlic (*Allium sativum*) is another widely used herb that has been reported to exhibit substantial antimicrobial activity against various GI pathogens. Allicin, the main bioactive compound of garlic, has demonstrated significant activity against pathogenic strains of *Escherichia coli*, *Salmonella*, and *Helicobacter pylori*[45–48].

Probiotics, such as *Lactobacillus* and *Bifidobacterium*, although not traditionally categorized as herbal remedies, are naturally occurring bacteria in fermented foods. They have shown effectiveness in managing several GI conditions including antibiotic-associated diarrhea and inflammatory bowel disease[18,24,49,50]. While these remedies show promise, it is essential to note that they may interact with conventional medications, leading to adverse events or altered drug efficacy. Furthermore, the lack of standardization in herbal preparations poses challenges in establishing the dosage, quality, and safety of these remedies.

As the global burden of antibiotic resistance grows, the exploration of herbal remedies for the treatment of GI infections could provide promising alternatives or adjuncts to conventional treatments[51–54]. The antimicrobial efficacy of compounds like berberine[43,55,56], thymol, and allicin, and the beneficial effects of probiotics, hold significant potential. However, more rigorous clinical trials are required to determine the optimal dosage, safety, and efficacy of these remedies, especially those suffering from COVID-19 or long COVID[57–59]. Concurrently, efforts should be made to standardize herbal preparations to ensure consistent quality[60,61].

## 4. Conclusion

Non-pharmacological therapy for FD is receiving more attention from families and medical experts to treat dyspepsia symptoms. Patients with FD are expected to benefit from the non-invasive nature and probable low adverse effects of these non-addictive, non-pharmacological treatments, especially those who have tried and failed traditional

medications. Even though some FD patients respond well to non-pharmacological treatment, the data currently available is insufficient to support its routine usage in the treatment of FD patients. To truly harness the potential of herbal remedies and optimize their therapeutic outcomes, it is essential to recognize the importance of individualized treatment approaches. Variability in patient characteristics, preferences, and responses to herbal remedies underscores the need for tailored treatment plans. Therefore, further well-conducted, large-scale clinical trials are warranted to determine the effectiveness and potential variations in response to these remedies. Additionally, as we explore the multifaceted benefits of herbal treatments, it is imperative to maintain the same level of scientific rigor and dedication to research as we do for treatments with a chemical focus. We recommend considering herbal remedies as a viable treatment option for functional dyspepsia, keeping in mind the significance of individualized care in optimizing patient outcomes.

**Author Contributions:** KV-GS performed the literature search and manuscript writing. TAN-BM and SM provided critical editing and proofreading. SM created the illustrative Figures for the manuscript. AKB conceptualized this review writing project.WHC and LCM edited the manuscript and all authors approved the final manuscript.

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