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Herbal remedies for functional dyspepsia: Targeting gut microbiota and motility dysfunction

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Abstract
Functional dyspepsia (FD) is a prevalent functional gastrointestinal disorder characterized by chronic upper abdominal discomfort, early satiety, bloating, and nausea, with complex pathophysiology involving gastric motility dysfunction, visceral hypersensitivity, and gut microbiota dysbiosis. This review evaluates the efficacy and mechanisms of key herbal remedies including *Banha-sasim-tang*, *Foeniculi fructus*, *ginger*, *Zhizhu Kuanzhong*, *Shen-Ling-Bai-Zhu-San*, Kvass, STW 5-II, and Persian-FACT-in managing FD symptoms through gut microbiota modulation, anti-inflammatory effects, and motility regulation. Preclinical and clinical studies demonstrate that these herbal formulations restore gastric emptying, enhance intestinal transit, and rebalance microbial communities. Collectively, these findings highlight the therapeutic potential of herbal medicines as adjunct or alternative treatments for FD, bridging traditional knowledge and modern mechanistic insights. Further large-scale, randomized controlled trials are warranted to validate long-term efficacy and standardization.

Keywords: Functional dyspepsia, gut microbiota, herbal medicine, motility disorders, dysbiosis, phytochemicals

Introduction
Functional dyspepsia (FD) is one of the most prevalent types of functional gastrointestinal diseases (FGIDs), impacting approximately 10% to 30% of adults and 3.5% to 27% of children globally. Symptoms associated with FGIDs encompass abdominal pain or burning sensations, bloating, nausea, feelings of fullness, vomiting, and changes in bowel habits [13]. The underlying mechanisms of FGIDs are complex, but there is growing evidence that gut microbiota plays a crucial role in their development and symptom modulation. Although the precise pathophysiology of FD remains unclear, many patients exhibit gastric hypersensitivity and irregular gastric motility [9]. Gastric hypersensitivity has been linked to symptoms such as postprandial pain, belching, and weight loss in individuals with FD. Additionally, sensitivity in the stomach and duodenum to acid, bile acids, and specific nutrients may trigger abdominal pain in FD patients. Delayed gastric emptying can lead to distal gastric distension, resulting in abdominal pain and feelings of fullness [12]. The gut-brain axis and microbial imbalances in the gut, along with changes in mucosal immune function, visceral hypersensitivity, and abnormal gastrointestinal motility, are also contributing factors. Dietary habits may influence the management of FGIDs. Certain dietary components contribute to the functional food concept and nutraceuticals beyond providing basic nutrition. Among all the most studied dietary bioactive compounds are probiotics and phytochemicals. The beneficial effects of probiotics primarily depend on their ability to alter gut microbiota composition and produce fermentation byproducts (like short-chain fatty acids and enterolactone) that serve various biological functions [3]. Phytochemicals, which are bioactive non-nutrient substances derived from plants, have drawn attention for their potential roles as antioxidants, anti-estrogenics, anti-inflammatories, immunomodulators, and anti-carcinogenics. The pathophysiological mechanisms underlying FGIDs, particularly gut microbiota dysbiosis, are increasingly being studied. The human gut harbors a diverse microbial ecosystem known as the gut microbiome, which facilitates numerous biochemical processes that affect both host physiology and pathophysiology. Alteration in gut microbial balance can cause activation of the mucosal immune system, compromising the epithelial barrier, therefore resulting in visceral hypersensitivity and gastrointestinal motility disorders

are the key features of FGIDs. To date, most mechanistic studies on gut microbiota related to FGIDs have utilized animal models. Findings from these studies help deepen our understanding of the interactions between gut microbiota and the underlying pathologies associated with FGIDs. Dysbiosis of gut microbiota is an evolving concept in the context of FGIDs, with notable alterations observed in the small intestine and colon of patients. Research has indicated significant differences in the gut microbiota profiles of patients with irritable bowel syndrome (IBS) compared to healthy individuals. Higher levels of pathogenic bacteria like Enterobacter genus and reduced levels of beneficial bacteria like Bifidobacterium and Lactobacillus are seen in IBS patients revealed by a recent meta-analysis study. Patient microbiomes also exhibit decreased microbial diversity, and symptom severity has been associated with specific species within the Clostridiales group and/or certain methanogenic microbes. Furthermore, one study identified an overrepresentation of Methanobrevibacter smithii in fecal samples from patients with functional constipation and constipation-predominant IBS. Another indicated an increased ratio of Firmicutes to Bacteroidetes, with higher counts of Streptococcus and Ruminococcus, combined with lower levels of Lactobacillus and Bifidobacterium in IBS patients. Alterations in the small intestine include the presence of small intestinal bacterial overgrowth (SIBO), characterized by elevated bacterial counts in jejunal aspirates. Recent research on individuals experiencing bloating, abdominal pain, or diarrhea who are suspected to have SIBO has reported changes in the microbial composition balance of their small intestines. Additionally, evidence shows there is a significant reduction in anaerobic genera like Veillonella, Prevotella, and Actinomyces in the duodenal mucosal biopsies of FD individuals compared to healthy individuals [9]. First-line treatment of FD includes regular aerobic exercise, Histamine-2-receptor antagonists, and Proton pump inhibitors (PPIs). These medications are generally well tolerated. Some prokinetic agents might be effective for treating FD, though their efficacy varies by drug class, with many being unavailable outside Asia and the USA. Second-line treatment of FD includes Tricyclic antidepressants (TCAs) utilized as gut-brain neuromodulators, Antipsychotic medications, like sulpiride or levosulpiride, Tandospirone, Pregabalin may provide an effective treatment for FD [2].

Methods

Literature search

I systematically searched Google scholar, ScienceDirect, PubMed and other electronic databases to identify traditional medicine treatment for FD associated gut microbiota alterations. The following search terms were used I combination; 'functional dyspepsia' AND 'gut dysbiosis', 'functional dyspepsia' AND 'gut microbiota', 'herbal medicine' AND 'functional dyspepsia', 'herbal medicine' OR 'natural treatment' OR 'functional dyspepsia'. The electronic searches were supplemented by manual screening of references of included papers and related reviews.

Efficacy of *Banha-sasim-tang* in treating Functional Dyspepsia: BST syrup made by extracting eight herbs with boiling water, then filtering, concentrating, and lyophilizing the extracts. The final syrup included *Pinelliae tuber*, *Scutellariae radix*, *Ginseng radix*, *Glycyrrhizae radix*, *Zingiberis rhizoma recens*, *Coptidis rhizome*, and *Zizyphi frucus*, along with additives such as β-cyclodextrin, apple concentrate, carboxymethyl cellulose, and sodium benzoate. The study investigated loperamide (10 mg/kg), three doses of BST (25, 50, 100 mg/kg), and mosapride (3 mg/kg) in animals. Stomach weight and assessment of gastric emptying utilizing phenol red, intestinal transit rate through a charcoal diet, immunofluorescence staining analysis of stomach tissue, western blot analysis, gene expression analysis using quantitative real-time PCR were carried out [10].

Efficacy of *Foeniculi fructus* in treating Functional Dyspepsia

The study includes loperamide (negative control, 10 mg/kg), three different doses of *Foeniculi fructus* (25, 50, and 100 mg/kg), and mosapride (positive control, 3 mg/kg) in animals. Gastric Weight and gastric emptying, intestinal transit rate by Evans blue, western blot analysis for check of protein level, and quantitative real-time PCR to Evaluate Gene Expression were carried out [5].

Efficacy of ginger in treating Functional Dyspepsia

The research examines three types of ginger juice: dried ginger juice (DGJ), fresh ginger juice (FGJ), and fresh ginger boiled juice (FGBJ). To prepare the boiled ginger juice, 150 grams of fresh ginger and 50 grams of dried ginger are each immersed in one liter of water for one hour. After boiling the mixture for 30 minutes and filtering it, the remaining solids were added back with water and boiled once more for another 30 minutes. The filtered liquids were then combined and concentrated to a final volume of 150 ml, maintaining a dosage ratio of fresh to dried ginger at 3:1. For fresh ginger juice preparation, 150 g of fresh ginger was cleaned and juiced. The juice was then filtered, and the leftover pulp was mixed with an appropriate volume of water and pressed again. The resulting juices were then combined. In the cisplatin group, the animals received cisplatin (5 mg/kg) and normal saline. Parameters like Ethanol-induced gastric mucosal damage, Cisplatin-induced emesis, and Gastrointestinal propulsion were evaluated [4].

Efficacy of *Zhizhu Kuanzhong* in treating Functional Dyspepsia

The study includes ZZKZ capsules containing Citrus, Aurantium L, Atractylodes Macrocephala Koidz, Bupleurum Chinense DC, and Crataegus Pinnatifida Bunge. The study received 0.1% iodoacetamide, ZZKZ at a low (ZZKZ-L, 0.5 g/kg), medium (ZZKZ-M, 1.0 g/kg), or high dose (ZZKZ-H, 1.5 g/kg). Evaluation parameters Gastric emptying and intestine propulsion test, Gastric smooth muscle activity Recording, Greater splanchnic afferent activity Recording, Enzyme-linked immunosorbent assay, Real-time quantitative PCR analysis [14].

Efficacy of *Shen-Ling-Bai-Zhu-San* in treating Functional Dyspepsia

The study involves SLBZS, composed of ten Chinese medicinal herbs including *Panax ginseng*, *Poria cocos*, *Atractylodes macrocephala*, *Glycyrrhiza uralensis*, *Dioscorea opposite*, *Dolichos lablab*, *Nelumbinis semen*, *Coicis semen*, *Amomi fructus*, *Platycodon grandifl*orum.

The main active components includes ginsenoside Rg1, ginsenoside Re, ginsenoside Rb1, pachymic acid, atractylenolide III and platycodin D in SLBZS extract were determined by the HPLC method. The SLBZS group was given SLBZS suspended in sterile water (1.323 g/kg). Sample collection and biomedical analyses, 16S rRNA gene V4 region sequencing of gut microbiota, Bioinformatics analyses, Whole-metagenome shotgun sequence analyses, and Sequence accession numbers [6].

Efficacy of Kvass in treating Functional Dyspepsia

Kvass is a widely consumed low-alcohol beverage (with an alcohol content of 1%) in Russia, Ukraine, and various Eastern European nations. It is made through the simultaneous fermentation of yeast and lactic acid bacteria, which occur independently. In the study, the model group of animals was given normal saline at a dose of 1 mL/100 g, while the domperidone group received a dose of 2.57 mg/kg. The Kvass groups were administered low (2 g/kg), medium (6 g/kg), and high (18 g/kg) doses. The study measured various outcomes including behavioral observations, changes in weight and food intake, gastric emptying and intestinal propulsion ratios, levels of digestive enzymes in rats, as well as the concentrations of ghrelin, motilin (MTL), gastrin (GAS), and vasoactive intestinal peptide (VIP), and the levels of short-chain fatty acids in the colon [11].

Efficacy of STW 5-II in treating Functional Dyspepsia

The study objective was to evaluate the effectiveness and safety of the herbal formulation STW 5-II, which includes extracts from bitter candy tuft, matricaria flower, peppermint leaves, caraway, licorice root, and lemon balm, for treating individuals with functional dyspepsia. The clinical study was conducted as a randomized, placebo-controlled, double-blind, multicenter trial. Gastroenterologists in private practices or hospitals recruited outpatients experiencing persistent or recurrent dyspepsia for a minimum of 6 months. The age range of the patients varied from 21 to 70 years. To qualify for the trial, participants needed to meet the Rome I criteria for functional dyspepsia. Each participant received treatment over three consecutive 28-day periods either with the herbal preparation (active treatment, AT) or with a placebo. An assessment of Helicobacter pylori status was performed [1].

Efficacy of Persian-FACT in treating Functional Dyspepsia

Persian-FACT is a herbal mixture that has been utilized for centuries in Persian medicine to help reduce the symptoms of dyspepsia, comprising anise, fennel, ajwain, and cumin seeds. The study consists of a single-center, double-arm, parallel-group, double-blind, randomized controlled clinical trial with a 1:1 allocation ratio. We modified the daily dosage of the compound to 14 g, which included 4 g of anise, 4 g of fennel, 2 g of ajwain, and 2 g of cumin. As a result, each sachet contained 7 ± 0.1 g of Persian-FACT, to be taken twice daily. The primary outcome measure was the average severity score of dyspepsia, PDS, and EPS at baseline, as well as during the first and second weeks following the intervention. The assessment of the difference in average severity scores between the Persian-FACT group and the placebo group over the follow-up periods was conducted. The secondary outcome measure involved the mean severity score of bloating, GERD, and constipation at baseline and in the first and second weeks post-intervention. Any unexpected symptoms and complaints reported by participants were recorded to examine potential adverse effects. Systolic and diastolic blood pressure readings were obtained by the physician at the start of the trial and again two weeks after the intervention to monitor for any indications of hypertension. Blood parameters were assessed using photometric methods with standard kits at both the beginning of the trial and four weeks after the intervention to check for potential renal or hepatic issues [8].

Results

***Banha-sasim-tang* (BST) showed significant prokinetic effects in a loperamide-induced functional dyspepsia model by restoring gastric motility through multiple mechanisms**

Loperamide injection induced delayed gastric emptying, evidenced by forestomach fullness, increased stomach weight, and elevated phenol red retention, all of which were significantly reduced by BST pretreatment ($p< 0.05$ or $p< 0.01$) to a similar effect as the prokinetic drug mosapride. At the cellular level, BST preserved c-kit protein expression ($p< 0.01$) by reversing loperamide's 50% reduction, while also restoring smooth muscle function through upregulation of neuronal nitric oxide synthase (nNOS) and smooth muscle contractile genes (5HT4R, ANO1, RYR3, and smMLCK). Notably, BST completely reversed loperamide's inhibition of small intestinal motility ($p< 0.01$), matching mosapride's efficacy. The therapeutic effects appear mediated through ICC protection (via c-kit maintenance), smooth muscle regulation (via nNOS and contractile protein restoration), and potential modulation of gut motility hormones. These findings prove that BST ameliorates impaired smooth muscle motility, relieves early satiety, and improves GI motility. The study highlights BST's potential as a comprehensive prokinetic therapy for patients with PDS-type FD [10].

***Foeniculi fructus* has established pharmacological effect in animal models for the treatment of functional dyspepsia**

This study goal is to identify the bioactive factors and remedial mechanisms of *F. fructus* by a network pharmacological analysis with experiments. The study discovered 45 different composites, of which 9 were linked as active. also, target information was available for 41 of the 45 composites, leading to the identification of 260 target genes. Genes associated with FD and *F. fructus* include nascence- 2A adrenergic receptor (ADRA2A), brain-deduced neurotrophic factor (BDNF), cholecystokinin (CCK), C- reactive protein (CRP), glucagon (GCG), recap factor Jun (JUN), hERG (Kcnh2), cyclooxygenase 1 (PTGS1), cyclooxygenase 2 (PTGS2), peptide YY (Pyy), flash receptor eventuality cation channel subfamily V member 1 (TRPV1), and serotonin transporter (SLC6A4). The injection of loperamide, which induces gastric food retention, was vindicated through macroscopic observation and redounded in increased phenol red retention in the stomach. In discrepancy, pretreatment with *F. fructus* eased this outgrowth and significantly reduced phenol red retention. This result was verified through quantitative analysis. The group entering *F. fructus* treatment showed a markedly lower gastric weight compared to the loperamide

group ($p< 0.05$). The treatment with *F. fructus* demonstrated goods similar to those of the pretreatment medicine mosapride. Loperamide injection drastically dropped the expression of nNOS, TEME16A, and TRPM7 proteins in gastric towel, while pretreatment with *F. fructus* significantly enhanced the expression of these proteins ($p< 0.01$). likewise, loperamide injection reduced the expression of smooth muscle compression related genes like 5HT4R, RYR3, ANO1, and smMLCK. These differences were canceled by pretreatment with *F. fructus* ($p< 0.05$, $p< 0.01$). The administration of loperamide specially lowered small intestine motility compared to the control group. still, this subduing of small intestine motility was significantly restored by pretreatment with *F. fructus* ($p< 0.01$). Pretreatment with mosapride also greatly restored small intestine motility similarly as *F. fructus*. Postprandial malnutrition is a common issue faced by cases with IBS and FD, particularly those with predominant constipation. The detention in gastrointestinal mobility caused by loperamide was significantly relieved by pretreatment with *F. fructus* excerpt. These study findings suggest that *F. fructus* holds outcome for managing functional dyspepsia [5].

Different types of ginger juices showed pharmacological effects on the associated symptoms in animal models of functional dyspepsia

In this investigation, the model group that received normal saline exhibited gastric mucosal damage, which was mitigated in the FGJ, FGBJ, and DGJ groups in a dose-dependent manner. Additionally, the gastric mucosa appeared lighter and showed reduced infiltration of inflammatory cells in both the ginger-boiled juice group and the ginger juice group in comparison to the model group. The findings suggest that ginger juice can inhibit gastric mucosa inflammation and consequently aid in the repair process of the gastric mucosa. The ulcer index (UI) for treatment groups was significantly lower than that of the model group ($p< 0.01$). The FGJ and DGJ groups showed a notable reduction in the rate compared to the FGBJ group ($p< 0.05$). The significant reductions imply that administering ginger juice resulted in a decreased intestinal propulsive rate ($p< 0.05$). The intestinal propulsive rate is lowered in FGJ group when compared to the FGBJ group. On the other hand, boiled ginger juice and ginger juice exhibited effects on gastrointestinal propulsion. Among these, FGBJ displayed the most powerful effect on intestinal propulsion. A total of eight gingerols were identified in DGJ, FGJ, and FGBJ, with three particularly correlating positively with the protective effects against gastric mucosal damage: 6-paradol, 10-gingerol, and 12-shogaol. Both DGJ and FGJ contained 10-gingerol. DGJ, FGJ, and FGBJ all contained 6-shogaol. In summary, the primary conclusion of the study is that ginger juice FGJ or DGJ could be effective in preventing gastric mucosal injury, while FGBJ may be the optimal choice for enhancing gastrointestinal propulsion [4].

A traditional Chinese medicine, *Zhizhu Kuanzhong* (ZZKZ), has been found to reduce gastric hypersensitivity and motor dysfunction associated with functional dyspepsia in a rat model

The extract of ZZKZ is absorbed through the intestinal mucosa, indicating it acts directly on gastric motility. It exhibited a dual effect on the contraction of gastric smooth muscle strips: a mild facilitatory effect at lower doses (0.2–0.6 ml) and a significant inhibitory effect at higher doses (1.2–1.6 ml). Compared to healthy controls in adult rats with functional dyspepsia induced by indomethacin, body weight was notably lower, but those treated with ZZKZ or domperidone showed significant weight gain. Functional dyspepsia rats exhibited reduced food intake, which improved significantly with domperidone, ZZKZ-M, and ZZKZ-H treatment. Delayed gastric emptying and slower intestinal propulsion are seen in FD rats; however, treatment with domperidone and ZZKZ effectively upregulated gastric motility by normalizing gastric emptying and intestinal movement. Gastric smooth muscle strips contractile activity was decreased in the dyspeptic rats, which was prevented by domperidone, ZZKZ-M, or ZZKZ-H. ZZKZ stimulated both spontaneous and acetylcholine-induced contractions in the gastric smooth muscle strips of these rats and alleviated the spontaneous activity as well as chemical (acid perfusion) and mechanical (intragastric distension) stimulation of gastric sensory neuron firing. Additionally, serotonin (5-HT) induced gastric smooth muscle contraction and gastric sensory neuron firing is improved by ZZKZ. There were evidencees that the treatment also enhanced the release of serum 5-HT, leading to reduced 5-HT3 receptor and increased 5-HT4 receptor mRNA expression in the intestines of the dyspeptic rats. The study concludes that ZZKZ positively influences gastric hypersensitivity and motor dysfunction related to functional dyspepsia, involving alterations in the gastric 5-HT system characterized by lower 5-HT3 activity and enhanced 5-HT4 distribution. These findings shows that ZZKZ may be a promising option for relieving symptoms of functional dyspepsia and suggest the need for further research into its molecular mechanisms [14].

***Shen-Ling-Bai-Zhu-San* (SLBZS), a traditional chinese herbal medicine, used in the treatment of FD, and appears to influence the gut microbiota**

The study investigate the impact of SLBZS on FD, we monitored the body weight and biochemical markers of rats across all groups. The control group rats showed a noticeable reduction in body weight, food and water intake, but the SLBZS group had gained more weight than the FD group. Gut hormones that regulate digestive tract movements and secretions are MTL and GAS, Theses hormone levels reduction shows decline in gastrointestinal motility and gastric emptying in FD group. Concurrently, SLBZS significantly elevated these hormone levels. The urinary D-xylose excretion rate, indicates intestinal absorption capacity, was considerably higher in the SLBZS group compared to the FD group. For the assessment the impact on gut microbiota, the overall gut microbiota structure across all groups using 16S rRNA gene sequencing were analysed. The UniFrac distance between the control and FD groups was higher than that between the control and SLBZS groups, suggesting that FD altered the original microbiota while SLBZS positively influenced its modulation. Additionally, the FD group exhibited overgrowth of Akkermansia and Mucispirillum. Mucispirillum has been associated with inflammation, while Akkermansia has demonstrated an inverse correlation with body weight. Notably, FD rats also showed an increase in Helicobacteriaceae and Prevotellaceae, Lactobacillaceae. Conversely, the levels of short-chain fatty acid (SCFA)-

producing bacteria (which include Allobaculum, Clostridium, and Adlercreutzia) and the sulfate-reducing bacteria were also altered. These overgrowth of microbes are decreased in SLBZS groups. Therefore, SLBZS could be the treatment of dyspepsia, and regulate the dysregulated composition and function of the gut microbial diversity [6].

Kvass is a popular low-alcohol beverage, its effect on Improving Functional Dyspepsia in Rats

The body weight of the rats in the treatment group was notably greater compared to the normal group ($P< 0.05$). Additionally, compared to the normal group, the treatment group's food intake was significantly higher ($P< 0.05$). The study's findings illustrated that the stomach residual rate was significantly higher ($P< 0.05$) in the normal control group and significantly lower ($P< 0.05$) in the high-dose, medium-dose, and low-dose Kvass groups compared to the model group. The intestinal propulsive ratio in the was significantly lower ($P< 0.01$) in model group comparing to the normal group. While, the intestinal propulsive rate in comparison to the model group, it was considerably greater in the high-dose, medium-dose, and low-dose Kvass groups ($P< 0.05$) respectively. In comparison to the normal control group, the volumes of gastric juice, pepsin activity, and pepsin excretion over an hour period in the model group were significantly reduced ($P< 0.05$), while pepsin excretion in both the positive group and high-dose Kvass group was significantly greater ($P< 0.05$) than the model group. The plasma levels of ghrelin, MTL, and GAS in the model group were significantly reduced ($P< 0.05$) comapred to normal control group. In contrast, the plasma GAS content rose, albeit not significantly, whereas the levels of ghrelin and MTL in the rats in the Kvass dosage group were significantly higher ($P< 0.05$) than in the model group. Both the medium-dose and high-dose groups experienced a significant ($P< 0.05$) drop in VIP levels. The concentrations of MTL and GAS in the model group's gastric antrum were significantly lower ($P< 0.05$) than those in the normal control group. VIP levels in the medium- and low-dose groups did not change substantially from the model group, while ghrelin levels in the positive group and high-dose group were significantly elevated ($P< 0.05$), and the GAS content in the high-dose group was significantly greater. In comparison to the blank group, the model group's colon had reduced amounts of total short-chain fatty acids. In the positive group, levels of SCFA and total SCFA were significantly higher ($P< 0.05$) relative to the model group, apart from valeric acid and isovaleric acid. Butyric acid and valeric acid levels were greater in the medium-dose group than in the low- and high-dose groups. As a result, Kvass drinks can significantly improve rat gastrointestinal function and possibly reduce functional dyspepsia symptoms [11].

Herbal preparation STW 5-II, for the treatment of patients with functional dyspepsia

A total of 126 patients were involved in the study. The dyspepsia and GIS scores for the different treatment groups were recorded at baseline, as well as after 4 and 8 weeks of treatment. A marked reduction in symptom scores was observed in the active treatment group when compared to both the baseline and placebo groups ($p< 0.001$). After 4 weeks, 20.3% (n = 12) of those receiving active treatment and 10.2% (n = 6) of those on placebo experienced complete symptom relief ($p > 0.05$ vs. placebo), while after 8 weeks, 43.3% (n = 26) and 3.3% (n = 2) reported complete relief, respectively ($p< 0.001$ vs. placebo). According to diary records, stable treatment success was achieved in 62.5% of patients receiving active treatment during the first 4 weeks, compared to 33.3% of those on placebo ($p = 0.002$). After 8 weeks, these rates were 82.8% (group I) and 44% (group IV), respectively ($p = 0.003$). Patients receiving active treatment for 4–8 weeks reported significantly fewer days with limitations in daily activities related to their condition and lower absenteeism from work compared to those on placebo ($p = 0.01$). Symptoms were alleviated in 43 out of 45 patients (95.6%) and they were continued with the active treatment, having responded positively to the initial active treatment. Among patients assigned to placebo, 20 out of 26 (76.9%) had adequately controlled symptoms. Of those who responded to active treatment and continued on it, 71.1% achieved complete remission. Among the 41 patients who did not respond to placebo, 32 (78%) experienced improvement during active treatment, and 12 patients (29.3%) were entirely symptom-free. During a subsequent follow-up period of another 12 weeks without a set treatment, 57.3% of all patients experienced relapses. No differences were noted regardless of whether patients had been on placebo or active treatment in the last 4 weeks of the treatment, and serious side effects were reported. Eleven patients during the active treatment phase and 9 during the placebo phase reported adverse effects such as headaches, periorbital edema, sweating, and feeling faint. Additional patients noted occurrences of the common cold, headaches, and taste disturbances. Blood tests before and after treatment revealed no abnormal results. The tolerability assessment conducted by investigators and patients indicated that it was rated as very good and good, respectively [1].

The effectiveness of Persian-FACT, a traditional herbal medicine, as a treatment for functional dyspepsia (FD) was investigated

Our initial goal was to collect data from 150 patients experiencing dyspepsia. Out of the 70 functional dyspepsia patients evaluated for eligibility, 67 were randomly assigned to either the Persian-FACT group (n = 34) or the placebo group (n = 33). Of these, 32 participants in the Persian-FACT group and 23 in the placebo group completed assessments at baseline, one week, and two weeks and there is no significant difference was noted between the Persian-FACT and placebo groups. Four patients (17.4%) in the Persian-FACT group and four patients (22.2%) in the placebo group were also taking pantoprazole during the study, with no statistically significant difference ($P = 0.713$). According to Generalized Estimating Equations (GEE) analysis, dyspeptic symptoms decreased in both groups, but the improvement was significantly greater in the Persian-FACT group during the first and second weeks (mean difference = 3.36, 95% CI = 0.55 to 6.17, $P = 0.019$). Postprandial distress syndrome (PDS) symptoms was significantly lower severity in the Persian-FACT group of in the second week than the placebo group. The severity of epigastric pain syndrome (EPS) symptoms was significantly reduced in the Persian-FACT group compared to the placebo group starting from the first week (mean difference = 2.74, 95% CI = 1.09 to 4.40, $P = 0.001$). Additionally, the Persian-FACT group exhibited significantly decreased postprandial fullness two weeks post-intervention compared

to the placebo group (mean difference = 1.23, 95% CI = 0.11 to 2.35, P-value = 0.031), although this reduction was not significant during the first week (P-value = 0.097). One week after treatment, significant reductions in bloating (mean difference = 3.367, 95% CI = 0.313 to 6.421, P = 0.031) and constipation (mean difference = 3.238, 95% CI = 0.030 to 6.507, P = 0.049) were observed in the Persian-FACT group compared to the placebo group, although no significant differences were found in the second follow-up for either symptoms (bloating: P = 0.072; constipation: P = 0.152). Additionally, symptoms of gastroesophageal reflux disease were significantly lower in the Persian-FACT group than in the placebo group during both weeks of treatment (mean difference = 1.238, 95% CI = 0.084 to 2.392, P = 0.036). Both groups reported three mild adverse events that resolved within a few hours: dry mouth (9% in Persian-FACT vs. 4% in placebo), headache (3% in each group), and transient abdominal pain (6% in Persian-FACT vs. 4% in placebo). No significant changes were noted in blood pressure (systolic: P = 0.383; diastolic: P = 0.266) or liver enzyme levels (AST: P = 0.862; ALT: P = 0.505; alkaline phosphatase: P = 0.926), nor in renal function tests (BUN: P = 0.685; creatinine: P = 0.383) among participants [8].

Conclusion

The results of this review show that herbal remedies can reduce FD symptoms by altering gut health. However, further studies are needed to clarify the mechanistic effect of these herbals on FD outcomes.

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Conflicts of interest

The authors declare no conflicts of interest. All of the authors have approved the final article.

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