



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**

SJIF Impact Factor: 7.187

<https://zenodo.org/records/11302766><https://www.iajps.com/volumes/volume11-may-2024/22-issue-05-may-24/>Available online at: <http://www.iajps.com>

Research Article

**ROLE OF HERBAL PROKINETICS IN TREATMENT OF
FUNCTIONAL DYSPEPSIA**

Shayestha Nishath, Sameera Taranum, Safoora Naaz, Madiha Naazish, Shaista Tamkanat
Deccan School of Pharmacy, Darrusalam, Nampally, Hyderabad, Telangana, India.
shaistanishat33@gmail.com

Abstract:

Dyspepsia, a common gastrointestinal disorder characterized by upper abdominal discomfort. Its etiology includes gastric predisposition, GERD, peptic ulcer disease, H pylori infection, gastric malignancy, and various physiological and psychological mechanisms such as impaired gastric motility, visceral hypersensitivity, delayed gastric emptying, impaired gastric accommodation, central nervous system dysfunction etc. Although dyspepsia is not related to increased mortality, but it may impact the patient quality of life by causing complications like chronic indigestion, anxiety and depression. The conventional pharmacological treatment includes use of proton pump inhibitors, dopamine-2 receptor antagonists, antidepressants, prokinetic agents etc. But the conventional treatment often come with limitations and potential adverse effects such as nausea, diarrhea etc. Some conventional prokinetic drugs, particularly those like metoclopramide, can aggravate stomach discomfort or cause gastric irritation in some individuals, while herbal prokinetics on the other hand may be kind on the stomach and less likely to exacerbate dyspeptic symptoms.

Hence, the alternative and complementary therapies are considered for the treatment of dyspepsia such as herbal prokinetics, derived from various plants offers promising effects for modulating gastrointestinal motility and reducing symptoms associated with dyspepsia.

The herbal prokinetics may be considered a better choice than conventional prokinetics in the treatment of dyspepsia, because of their minimal side effects, effectiveness in reducing the symptoms such as gastric discomfort and various other advantages over the conventional prokinetic agents.

By exploring various treatment options and comparing the safety and efficacy of herbal prokinetics and conventional prokinetics, this review critically examines the mechanism of action of various herbal prokinetics and evaluates the available clinical evidence supporting their efficacy and safety in dyspepsia management.

This review article aims to show the advantages of using herbal prokinetics over conventional prokinetics and their contribution in improving patient's quality of life without causing serious adverse effects.

While herbal prokinetics offer these potential benefits, it's important to recognize that responses to herbal prokinetics can vary from person to person, and their effectiveness and safety may not be fully confirmed through various clinical trials.

Key Words: *Dyspepsia, Herbal prokinetics, Conventional prokinetics*

Corresponding author:

Shayestha Nishath,
Deccan School of Pharmacy,
Darrusalam, Nampally, Hyderabad, Telangana, India.
shaistanishat33@gmail.com

QR CODE



Please cite this article in press *Shayestha Nishath et al., Role Of Herbal Prokinetics In Treatment Of Functional Dyspepsia., Indo Am. J. P. Sci, 2024; 11 (05).*

INTRODUCTION:

Dyspepsia is condition in which the body does not digested the food or having any trouble in digesting of food. Functional dyspepsia is more common in old age, females, low body mass index, Helicobacter pylori infection and use of non-steroidal noninflammatory or aspirin with symptoms such as pain or burning in stomach, bloating, excessive belching or nausea after eating. It is difficult to diagnosis but can be diagnosed by endoscopy, blood test or bacterium test. These can be treated by the medicine which reduces the acid production, antibiotics, medicines that relive nausea and prokinetics (These are the medicines that help the stomach to empty faster and tighten the valve between the stomach and esophagus. This helps to reduce upper abdominal pain.)

Excluding corrosive inhibitory treatment, prokinetics are the backbone of the therapy of FD. The cost of herbal medicine for FD management is expected to be low, particularly in regions where herbal medicine has been practiced as a tradition.

Prokinetic specialists are of interest in GERD on account of their capacity to upgrade esophageal peristalsis and speed up gastric purging. These specialists incorporate cisapride, metoclopramide, and bethanechol. In pediatric patients whose regurgitation or vomiting is the primary symptom of GERD, cisapride has modestly alleviated symptoms. Because, of cardiac adverse effects, however, cisapride is restricted to a limited access program as previously described.

Prokinetics are the agents that promote the muscle and the nerve movement of gastrointestinal tract, common prokinetic agents are benzamide, cisapride, domperidone, itopride, mosapride etc. The herbs that improve the motility of digestive tract is known as herbal prokinetics such as peppermint oil, ginger, Ashoka leaf, licorice root, amla, etc.

The *Trachyspermum ammi* L. (TA), *Anethum graveolens* L. (AG), and *Zataria multiflora* Boiss

(ZM) are three significant therapeutic spices that are utilized in Iranian and Indian customary medication to regard stomach related messes as a pain relieving, antifatulence, antispasmodic, germ-free, carminative, and anti-diarrheal.

These spices' natural balms contain phenolic monoterpenoids, e.g., carvacrol and thymol; oxygenated monoterpenoids, e.g., D-carvone; and hydrocarbon monoterpenes, e.g., D-limonene. Terpenoids existing in these spices have been as of late drawn in huge consideration because of their antibacterial, cell reinforcement, and mitigating properties. Additionally, both in vivo and in vitro examinations showed the antispasmodic impacts and these plants' capacity to work on Gastrointestinal ulcers. Studies have additionally shown that TA diminishes food travel time through the GI plot, increments stomach related catalysts' movement, and increments pancreatic discharges and bile acids. As per the referenced properties of restorative spices, the current exploration expects to concentrate on the impacts of a combination of ZM, TA, and AG natural ointments on side effects of FD, in a clinical preliminary.

ETIOLOGY:

Functional dyspepsia is a medical condition that arises due to various pathological factors such as:

- Peptic ulcer disease
- Gastrointestinal reflex
- Non-steroidal anti-inflammatory drugs and
- Gastric malignancy.
- Genetic predisposition
- H. pylori infection
- Acute infection and
- Psychological factors by various pathophysiological mechanisms such as

Impair gastric accommodation

Delayed gastric emptying

Visceral hypersensitivity

Duodenal hypersensitivity

Small intestine dysmotility

Central nervous system dysfunction etc.

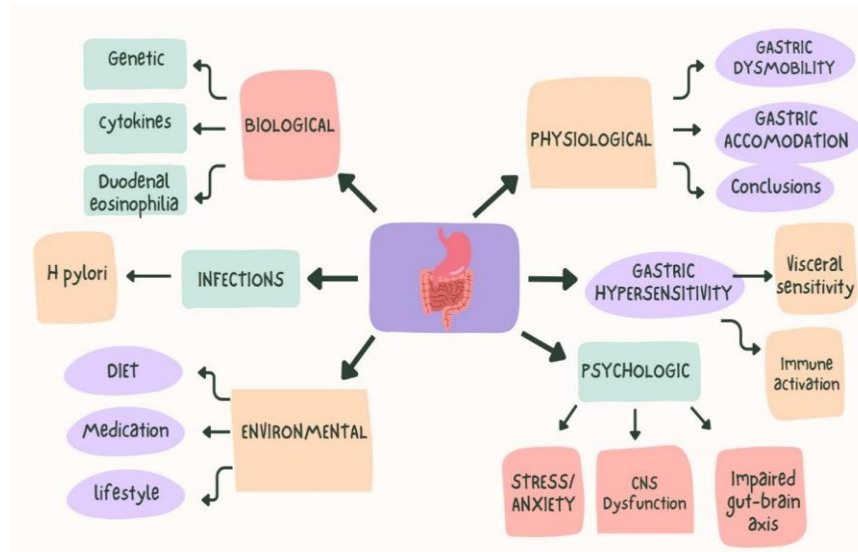


FIGURE-1: Flowchart of various causative agents of dyspepsia.

EPIDEMIOLOGY:

Generally, the epidemiology of functional dyspepsia can be figure out by postprandial pain, epigastric pain and overlapping. Approximately 75% of those with dyspepsia who are investigated have a normal endoscopy, with the majority of the remainder having either peptic ulcer disease or esophagitis.[\[1\]](#)

The global prevalence of dyspepsia is 20-30%. It is barely better in the Western population and occurs more often among girls. While the right prevalence of dyspepsia in India isn't to be had, distinctive research estimate that it affects 7.6-49% of the Indian population.

DIAGNOSIS:

Patients of age 55years or above with dyspepsia are with nausea, vomiting or an elevated platelet count, and the patients of age 60 years or above are with abdominal pain and weight loss.

Dyspepsia is usually diagnosed by the

Physical examination: that includes the signs and symptoms such as pain or burning in stomach, bloating, excessive belching or nausea after eating. The common condition that involves in identification of dyspepsia are gastroesophageal reflux (GERD), Peptic ulcer disease, gastroparesis, irritable bowel syndrome, upper abdominal-related cancer.

Endoscopy: In this procedure at you with a camera lens and a light is passed into the esophagus stomach and the upper part of the small intestine this is known as endoscope which helps to collect the sample for identification of any infection or inflammation.

Blood test: It is one of the examination tests for dyspepsia which includes CBP, electrolytes, GRBS random blood sugar, renal function test, thyroid function test stool test etc.

Radiological method: Gastroparesis can be diagnosed with barium meal method (Gastroparesis is a Condition which effects the muscles of the stomach an improper emptying of the stomach).

Ultrasonography: Functional dyspepsia is associated with delayed gastric emptying. Using ultrasonography to measure the antral area helps us to assess gastric emptying and therefore to assess patients with functional dyspepsia. The antral area was significantly larger in patients with functional dyspepsia compared to healthy subjects after the test meal.

Other examination for diagnosis of functional dyspepsia includes, esophageal pH observing, barium X-beam, blood tests, bacterium tests, either through blood, stool, or breath.

PATHOPHYSIOLOGY:

The exact pathophysiologic mechanism of dyspepsia is not well understood, but several mechanisms are thought to contribute to the development of dyspepsia, some of them are delayed gastric emptying, impaired gastric accommodation to food, hypersensitivity to gastric distention, H pylori infection, altered response to duodenal lipids or acids, abnormal duodenojejunal

motility, gastroduodenal inflammation characterized by altered lymphocytes, increased eosinophils and mast cells or central nervous system dysfunction [2] [3].

Psychological factors like anxiety and depression can cause increased activation of the amygdala, and the dysregulation of the HPA axis suggests that there is central processing of visceral stimuli from sensations in the gastrointestinal tract [4].

Delayed gastric emptying

The symptoms such as fullness, bloating, and belching develops when moves from stomach to small intestine. Many prokinetic agents have been used in the treatment of FD, such as cisapride, domperidone, and itopride[5]. Delayed gastric emptying is considered to be a pathophysiological feature of FD that is closely related to dyspepsia symptoms [6]. The mechanism of gastric emptying delay in relation to the symptoms of dyspepsia is remained unclear. However, A study showed that the prevalence of delayed emptying in FD patients ranges between 20 and 35% [7].

Impaired gastric accommodation

The motor functions of the proximal and distal stomach differ remarkably. Whereas the distal stomach regulates gastric emptying of solids by grinding and sieving the content until the particles are small enough to pass the pylorus, the proximal stomach serves mainly as a reservoir. Accommodation of the stomach to a meal consists of a relaxation of the proximal stomach, providing the meal with a reservoir and enabling an increase in volume without an increase in pressure [2].

Gastric accommodation is mediated by the activation of noncholinergic nerves in the gastric wall that result in the production and diffusion of nitric oxide to gastric smooth muscles [6]. An Antro-fundic reflex, relaxation of the fundus in response to antral distention, also contributes to accommodation [7]. Research has shown that 40% of dyspeptic patients have impaired accommodation, and this is associated with early satiety and weight loss [8].

Antral and fundic dysfunctions interact to produce the symptoms of functional dyspepsia, and impaired control of fundic accommodation may lead to overload of a hypersensitive antrum [7].

Hypersensitivity to gastric distention

Physiologic stimuli during the stomach related process are not regularly seen yet in certain conditions might actuate conscious sensations. During the previous ten years, it has been proposed that

patients with functional gastrointestinal diseases might have a sensory dysfunction of the stomach, so physiologic stimuli would show side effects [2]

Hypersensitivity to gastric distension is present in a subset of functional dyspepsia patients. It is related with symptoms of postprandial epigastric pain, belching, and weight loss [9]

A systematic analysis showed that the increase of intra-balloon pressure over intra-abdominal pressure needed to induce discomfort or pain is the most appropriate expression of sensitivity to gastric distention [9]

Altered Response to duodenal lipids and acids

The symptoms of dyspepsia are usually seen after the ingestion of meals rich in lipids and fats.

Several studies have shown that lipids causes relaxation of the proximal stomach and improves the sensitivity to proximal stomach distention.[12] These influences of duodenal lipid infusion require lipid digestion and followed by release of cholecystokinin, [11] [12] and they can be blocked by administration of a lipase inhibitor or a cholecystokinin-A receptor antagonist. [10] [11] [12]

Helicobacter pylori infection

One of the most common cause of the dyspepsia is related to H pylori infection. Prevalence of H pylori infection differs greatly in various different parts of the world. It was significantly associated with alcohol consumption. More comprehensive studies are necessary in this region to study the relationship between socio-economic factors, diagnostic methods, premorbid conditions and *H. pylori* infection [13]

The exact mechanism of H pylori infection in the development of symptoms of dyspepsia remains unclear.

The possible mechanisms through which the H pylori infected patients may develop dyspeptic symptoms are

- Inflammation of gastric mucosa
- Abnormal gastric acid secretion
- Post infective changes in gastroduodenal mucosa.

It has been found that the gastrin releasing peptide-stimulated maximal acid output is increased in dyspeptic patients with H pylori infection as that of uninfected patients [14] H pylori alters synthesis of both gastrin(increased) and somatostatin(decreased) in gastric mucosa, as well as ghrelin which is involved in acid secretion, hunger sensations, and gastrointestinal motility. [15]

PHARMACOTHERPY IN FUNCTIONAL DYSEPSIA:

Functional dyspepsia is characterized as something like one month of epigastric uneasiness without proof of natural sickness found during an upper endoscopy, and it represents 70% of dyspepsia. Eight long stretches of corrosive concealment treatment is suggested for patients who test negative for *H. pylori*, or who keep on having side effects after *H. pylori* eradication. On the off chance that corrosive concealment doesn't reduce side effects, patients ought to be treated with tricyclic antidepressants followed by prokinetics and mental treatment.

1. PROTON PUMP INHIBITOR

PPIs are the most broadly involved suppression for the concealment of gastric corrosive. It is used in the treatment of gastroesophageal reflux sickness and peptic ulcers, PPIs have been broadly utilized in the therapy of dyspeptic side effects and in individuals with FD. Monotherapy with a PPI is ineffective in eradicating *H. pylori* infection. However, the addition of a PPI to a combination of antibiotics improves eradication rates compared to those achieved with antibiotics alone.²³ PPIs elevate intragastric pH levels and optimize the antibacterial action of concomitantly administered antibiotics. Furthermore, because PPIs decrease gastric secretory volume, they increase the concentration of antibiotics within the stomach. [17]

2. DOPAMINE-2 RECEPTOR ANTAGONIST

Dopamine-2 antagonist block the dopamine D2-receptor, present in the intestinal sensory system and in the retching focus in the mind. The main D2-receptor adversary utilized for the treatment of motility issues was metoclopramide. This compound is likewise a 5-HT₄-receptor agonist, which might add to its prokinetic activities. Metoclopramide promptly crosses the blood-brain barrier, which underlies the possibly irreversible, neurological incidental effects that might happen with (persistent) metoclopramide consumption. Regarding its mechanism of action, metoclopramide has been shown to improve upper GI symptoms, accelerate gastric emptying rate and increase gastrointestinal motility. Other prokinetic D2-receptor antagonists include cinitapride, clebopride and alizapride, but these are less well-investigated in FD. Studies investigating cinitapride and clebopride reported an improvement of FD symptoms and quality of life. Alizapride is mostly used for its antiemetic properties.

3. ANTIDEPRESSANT

FD is a typical psychosomatic sickness related with various mental problems including nervousness,

despondency, fits of anxiety, and post-horrendous pressure problem. Negative otherworldly, mental and social variables can speed up the beginning of FD side effects and fuel them and in this manner at last influence treatment viability. Weight reduction is a typical side effect of stomach related sicknesses, and may demonstrate a natural illness, yet as of late, certain investigations have discovered that patients with practical gastrointestinal infections frequently showed weight reduction. Antidepressant mirtazapine not only improved patients' conditions concerning indigestive and depressive symptoms, but also increased appetite and body weight (mainly the visceral fat in body fat), much more effectively than either paroxetine or conventional therapy. The clinical efficacy of mirtazapine may be mediated in part through the regulation of brain-gut or gastrointestinal hormones [41]

4. SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS) AND SELECTIVE SEROTONIN AND NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIS)

Clinicians frequently use SSRIs to treat side effects of IBS, a profoundly predominant issue portrayed by lower stomach torment or uneasiness. The reasoning for this is that SSRIs might work on both focal and instinctive agony in certain patients, as well as treating existing together nervousness or despondency. Since IBS regularly coincides with FD, and in light of the fact that FD patients are habitually overly sensitive to gastric distension, utilizing SSRIs to treat the various side effects of FD gives off an impression of being a characteristic expansion of their utilization in IBS. Duloxetine, another selective serotonin and norepinephrine reuptake inhibitor (SNRI), warrants brief mention because a small pilot study suggested that it may be efficacious in IBS patients, and there is considerable symptom overlap between FD and IBS [18]

5. PHYTOTHERAPY AND COMPLEMENTARY TREATMENT

Phytotherapeutics have for some time been utilized in medication. Various fake treatment-controlled preliminaries have shown a fundamentally beneficial outcome of phytotherapy contrasted and fake treatment in the treatment of utilitarian dyspepsia. Consolidated arrangements are in many cases used to treat utilitarian dyspepsia. For the most part these are fixed blends of peppermint and caraway oil or combinations of severe candytuft (*Iberis amara*), wormwood, gentian, and angelica root, normally in mix with spasmolytic and narcotic concentrates like chamomile, peppermint, caraway, and lemon analgesic. Phytotherapeutics apply a spasmolytic

tension invigorating as well as calming impact on the gastrointestinal tract and this might free the side effects from practical dyspepsia. Treatment of functional dyspepsia with digestive enzymes has also been studied, whereby the clinical action of the fixed combinations of gastric mucous extract and amino acid hydrochloride that are used is exerted not via substitution but by supporting the proteolytic release of amino acids. [40]

6. PROKINETIC AGENTS:

Prokinetics are the therapeutic agents, which are used in the treatment of gastrointestinal disorders such as gastric motility disorder, functional dyspepsia etc. Prokinetic drugs are generally considered as the drug of choice for the treatment of dyspepsia. Currently, many prokinetic drugs have been used to treat functional dyspepsia. Cinitapride, a recently added

drug of choice for the treatment of functional dyspepsia. Cinitapride acts as 5-HT receptor agonist and dopamine receptor antagonist and promotes gastric motility and emptying. Studies showed that cinitapride and metoclopramide were better than other prokinetic drugs for the treatment of functional dyspepsia. Metoclopramide, trimebutine, mosapride, and domperidone showed better efficacy for the treatment of FD than Itopride or acotiamide. [19]

Herbal medicines expand the scope for the treatment of functional dyspepsia, an underserved therapeutic area [20]. The herbal medicines consist of the herbs with desired pharmacological effects on gastrointestinal motility and secretory functions, as well as cytoprotective and psychotropic properties [20]

TABLE-1: List of Prokinetic drugs with their respective mechanism of action, adverse effects and actions.

SI No.	PROKINETIC DRUG	ADVERSE EFFECTS	MECHANISM OF ACTION	ACTION
1.	Prucalopride	Nausea, diarrhea, abdominal pain, headache, dizziness,	5-HT ₄ receptor agonist	Increases peristalsis in colon
2.	Velusetrag	Nausea, diarrhea, abdominal pain, headache	Highly selective 5-HT ₄ receptor agonist	Accelerates the gastric emptying half-time
3.	Felcisetrag	Nausea, diarrhea, abdominal pain, headache	5-HT ₄ receptor agonist	Increases gastric and intestinal motility
4.	Tegaserod	Indigestion, nausea, bloating, diarrhea, bleeding from the rectum, stomach tenderness.	5-HT ₄ receptor agonist	Increases motility of intestine
5.	Trazpiroben	No serious cardiovascular adverse effects,	Dopamine (D ₂ and D ₃) receptor antagonist	Increases motility of stomach and intestine
6.	Domperidone	Cardiovascular events such as QTc prolongation and other endocrine related adverse effects such as hyperprolactinemia. Extrapyramidal symptoms.	Dopamine antagonist	Reduces nausea and vomiting and increases the contractions of stomach and intestine.
7.	Relamorelin	Headache, dizziness and gastrointestinal symptoms.	Ghrelin receptor agonist	Increases growth hormone levels and accelerates gastric emptying
8.	Acotiamide	Nausea, diarrhea, abdominal pain, headache, constipation, rashes.	Muscarinic (M ₁ and M ₂) receptor antagonist	Increase the release of Acetylcholine and restores delayed gastric emptying
9.	Erythromycin	Nausea, vomiting, diarrhea, QT prolongation and pseudomembranous colitis.	Motilin receptor agonist	Stimulates antral and fundic contractions. Enhances gastric emptying and reduces bloating
10.	Azithromycin	Vomiting, diarrhea, headache, loss of taste and smell	Motilin receptor agonist	Stimulates antral and fundic contractions

11.	Clarithromycin	Nausea, vomiting, diarrhea, headache.	Motilin receptor agonist	Antibiotic
12.	Aprepitant	Dizziness, weakness, bloating, diarrhea, constipation, heart burn, stomach pain.	NK1 receptor agonist	Chemotherapy induced nausea and vomiting
13.	Naloxone	Nausea, vomiting, diarrhea, stomach pain, tremors, sweating, fever, weakness, restlessness	Opioid antagonist(non-selective)	Antagonizes the action of opioids
14.	Sildenafil	Dizziness, headache, flushing, blurred vision, rashes, increased sensitivity to light.	Phosphodiesterase-5 Inhibitor	Induces relaxation of smooth muscle cells by blocking PDE5
15.	Cinitapride	Nausea, diarrhea, vomiting, headache	5-HT1 and 5-HT4 receptors agonist and 5-HT2 receptors antagonists.	Increases the levels of acetylcholine
16.	Metoclopramide	Dizziness, trouble sleeping, headache, diarrhea, drowsiness, tiredness, agitation	Dopamine receptor antagonist	Treats nausea and vomiting and increases gastric motility.

7. HERBAL PROKINETIC DRUGS:

Herbal medicines expand the scope for the treatment of functional dyspepsia, an underserved therapeutic area [20]. The herbal medicines consist of the herbs with desired pharmacological effects on gastrointestinal motility and secretory functions, as well as cytoprotective and psychotropic properties [20]

Peppermint oil-caraway oil (POCP)

Peppermint oil is extracted from the leaves of *Mentha piperita* L. The combination of peppermint oil and caraway oil is available as proprietary formulation known as Menthacarin. Peppermint oil induces relaxation of smooth muscles leading to increased gastric accommodation and antispasmodic action in intestine. It is also reported to modulate visceral hypersensitivity [42]

Peppermint and caraway oil probably result in a large improvement in global symptoms of dyspepsia compared to placebo at four weeks and increase the improvement rate of global symptoms of dyspepsia. There may be little to no difference in the rate of adverse events between this intervention and placebo. The intervention probably improves the quality of life [27]

Rikkunshito

Rikkunshito is an Herbal medicine, used in the treatment of upper gastrointestinal disorders, gastric motility disorders and conditions like dyspepsia. In China, it is known as Liu-Jun-Zi Tang, and it is originally described as Chinese herbal formula in the Chinese classic medical book. Rikkunshito is

composed of beta-eudesmol derived from the *Atractylodes lancea rhizoma*, ginsenosides derived from *Ginseng radix*, hesperidin derived from the *Citri unshiu pericarpium* Peel, glycyrrhizin derived from the *Glycyrrhizae radix*, *Pinelliae tuber*, *poria*, *Zizyphi fructus*, and shogaol derived from the *Zingiberis rhizoma*. [28]

The mechanism of action of Rikkunshito broadly include actions such as promoting ghrelin secretion, mediating gastric adaptive relaxation and stimulating gastric emptying [29]

Side effects include hepatic dysfunction or pseudoaldosteronism due to glycyrrhizin present in *Glycyrrhiza* [30]

The studies being conducted to know the clinical effects of Rikkunshito on patients with functional dyspepsia, concluded that gastrointestinal symptoms were significantly improved and gastric emptying was enhanced and also improvement of epigastric pain and postprandial fullness were observed in the group treated with rikkunshito, and this suggested that the efficacy may be lower in *H pylori* uninfected individuals [28]

STW-5 (Iberogast)

The herbal formulation called as STW-5(Iberogast) is combination of 9 different herbs, *Iberis amara totalis recens*, *Angelicae radix*, *Cardui mariae fructus*, *Chelidonii herba*, *Liquiritiae radix*, *Martricaridae flos*, *Melissae folium*, *Carvi fructus*, and *Menthae piperitae folium*. This formulation is known to produce relaxation if gastric muscles particularly those of fundus region and hence can improve fundus

accommodation. The *Iberis amara*, or bitter candy tuft, is proposed to have multiple effects such as stimulatory effect on smooth muscles of stomach and small intestine, decreases leukotriene concentration and acid secretion, and dose-dependent anti-ulcerogenic effect, while *Matricariae flos*, known as chamomile flower shows anti-depressant and anxiolytic effects. [42]

Zhizhu Kuanzhong (ZZKZ)

Zhizhu Kuanzhong is available as proprietary fixed combination formulation in China. It consists of four herbs namely *Atractylodes macrocephala* (Bai Zhu), *Citrus aurantium* (Zhi Shi), *Bupleurum* (Chai Hu), and *Crataegus pinnatifida* or Hawthorn (Shan Zha). The *Shan Zha* and *Bai Zhu* have been studied and were reported to promote gastric emptying and intestinal propulsion. The *Chai Hu* enhance gastric

fluid emptying and small intestine transit speed, with anti-anxiety and anti-depressant effect. The *Zhi Shi* exhibited inhibitory action on the spontaneous contraction of pyloric circular smooth muscle strip. [42]

Artichoke leaf extract (ALE)

Artichoke (*Cynara acolymus*) leaf extract is used in the treatment of functional dyspepsia because it gives inhibitory action to vigorous contractions and the compound cyanopictin, shows effects such as increase bile flow, lipid lowering, antioxidant, and anti-spasmodic actions. [42]

However, several species of medicinal plants show gastroprotective actions such as anti-oxidant, anti-inflammatory, anti-apoptotic, anti-helicobacter pylori and prokinetic effects [17] some of them are shown below in the table 2.

TABLE-2: LIST OF HERBAL PROKINETIC AGENTS AND THEIR RESPECTIVE MECHANISM OF ACTION AND INDICATIONA.

SI No.	NAME OF HERBS	PART OF PLANT USED	MECHANISM OF ACTION	INDICATION OR USES	REFERENCE
1.	Methanol Extract of <i>Chasmanthera dependens</i> (Hochst)(Menispermaceae)	Stem	Enhance the Antioxidant system, decrease acid output, lipid peroxidation, and improve the architecture of gastric mucosa	Gastroprotective effects, antioxidant properties and Anti-ulcerogenic effects.	[30]
2.	<i>Olea europaea</i> (Oleaceae)	leaves	It shows anti-inflammatory action by decreasing NF-KB, COX-2, and TNF-alpha expressions and down regulating iNOS and IL-1beta in the gastric mucosa. The gastroprotective mechanism involves antioxidant activity, through NF-KB inhibition and increased Nrf2 mRNA expression.	Anti-inflammatory, Anti-oxidant, and gastroprotective effect.	[31]
3.	<i>Artemisia capillaris</i> (Compositae)	Aqueous extract	It reduces the gastric damage by inducing SOD activation and decreasing inflammatory cytokines such as IL-1beta and IL-6, through down-regulation	Anti-inflammatory and Gastroprotective effects.	[32]
4.	<i>Persea americana</i> Mill; avocado (Lauraceae)	Seeds	It shows gastroprotective activity by increasing endogenous antioxidant enzyme activity and	Gastroprotective, Anti-oxidant, Anti-inflammatory and Antimicrobial	[33]

			mucus production, and decreased oxidant factors and inflammatory cytokines	activities	
5.	<i>Aloe vera</i> (Xanthorrhoeaceae)	Leaves	It shows Anti-inflammatory action by inhibiting mRNA and protein expression levels of matrix MMP-9, iNOS, and nNOS in the gastric mucosa.	Anti-inflammatory and Gastroprotective action	[34]
6.	<i>Aronia melanocarpa</i> (Michx.) Elliot. (Black Chokeberry)	Fruit	It shows anti-inflammatory properties by reducing MCP-1, MDA, NF- κ B and TNF-alpha levels, and increasing SOD, CAT, and GPX activity and upregulation of the IL-4, HSP-70, NO, and PGE ₂ expressions. The gastroprotective effect is might be due to the downregulation of TNF-alpha-based NF-KB, MCP-1 signaling, and its anti-oxidant properties.	Anti-inflammatory, Anti-oxidant, and gastroprotective effects	[35]
7.	<i>Caryocar coriaceum</i> Wittm. (Caryocaraceae)	leaves	The capsaicin sensitive receptors such as opioid receptors, alpha-2 adrenergic receptor, and primary afferent neurons are involved in the mechanism of gastric protection.	Gastroprotective effect	[36]
8.	<i>Prunus armeniaca</i> L. (Rosaceae)(apricot)	Kernel oil	It shows gastroprotective effects by decreasing number of iNOS and TUNEL positive cells and MDA and IL-6 levels in the gastric mucosa.	Gastroprotective, anti-inflammatory, anti-oxidant, and anti-apoptotic effects.	[37]
9.	<i>Plinia edulis</i> (Vell) Sorbal (Myrtaceae) (Cambuca)	fruit	It shows gastroprotective effects by inhibiting H ⁺ . K ⁺ -ATPase activity	Gastroprotective effect	[39]
10.	<i>Sphenodesme involucrate</i> var. <i>paniculate</i> (C. B. Clarke) Munir (lamiaceae)	Leaves	Prevents gastric ulcers and eradicate <i>H. pylori</i> infections	Anti-ulcer and Anti- <i>H. pylori</i> activities.	[38]

PROGNOSIS:

There is no cure for functional dyspepsia. Most people manage their symptoms wellwith lifestyle changes and medications. Treating *Helicobacter pylori* (if present in the stomach) may significantly

reduce the symptoms. The symptoms of the condition can be variable, and may eventually occur much less frequently or go away completely. There is no cure for functional dyspepsia. Most people manage their symptoms wellwith lifestyle changes and

medications. Treating *Helicobacter pylori* (if present in the stomach) may significantly reduce the symptoms. The symptoms of the condition can be variable, and may eventually occur much less frequently or go away completely. If the condition is left untreated for too long you may be at increased risk of stomach cancer. Chronic indigestion can be caused by physiological problems as well. In the case of a hiatal hernia, part of the stomach can escape upward through your diaphragm, causing it to bulge into the chest cavity. This condition is closely related to [acid reflux](#) and typically requires careful dietary and lifestyle changes to relieve symptoms.

- Eat more modest, more-successive dinners. Having an unfilled stomach now and again adds to practical dyspepsia. Only corrosive in your stomach might cause you to feel debilitated. Have a go at eating a little nibble like a wafer or a piece of natural product.
- Do whatever it takes not to skip dinners. Keep away from huge dinners and indulging. Eat more modest dinners more regularly.
- Avoid trigger food varieties. A few food varieties might set off utilitarian dyspepsia. These may incorporate greasy and zesty food sources, carbonated refreshments, caffeine, and liquor.
- Bite your food gradually and totally. Permit time to partake in your dinners.

CONCLUSION:

In summary, herbal prokinetics demonstrate considerable promise in the management of dyspepsia. Natural agents like ginger, peppermint, and artichoke extract offers diverse mechanism of actions, including modulation of gastrointestinal motility and reduction of visceral hypersensitivity. Their generally favorable safety profiles and reduced risk of adverse effects compared to conventional medications, such as metoclopramide and domperidone, make them appealing options for patients seeking natural remedies.

Moreover, herbal prokinetics often provide additional health benefits beyond their prokinetics effects. For instance, ginger exhibits anti-inflammatory properties, while peppermint can alleviate symptoms of irritable bowel syndrome, enhancing overall symptom management and patient satisfaction.

Furthermore, the accessibility and affordability of many herbal prokinetics contribute to their attractiveness, particularly in regions where conventional medications may be less accessible or

costly. This accessibility can empower patients to take a more self-management of symptoms.

However, despite the growing evidence supporting the efficacy and safety of herbal prokinetics, further well-designed clinical trials are necessary to establish their effectiveness, optimal dosing regimens, and long-term safety profiles. Efforts to standardize herbal preparations and ensure quality control are vital for ensuring consistency and reliability in their therapeutic effects.

In conclusion, while herbal prokinetics offer significant advantages over conventional treatments for dyspepsia, including reduced risk of adverse effects and additional health benefits, ongoing research and clinical validation are essential to fully realize their potential and integrate them effectively into clinical practice.

ABBREVIATIONS:

GERD; gastroesophageal reflux disease
 FD; Functional dyspepsia
 COX-2; Cyclooxygenase-2
 iNOS; Inducible nitric oxide synthase
 IL; interleukin
 MCP-1; monocyte chemoattractant protein 1
 NF- κ B; Nuclear factor kappa B
 n-NOS; neuronal nitric oxide synthase
 TNF- α ; Tumor necrotic factor -alpha
 TGF- β 1; transforming growth factor -beta 1

REFERENCES:

1. Alexander C. Ford, Nicholas J. Talley 10 January 2014 *Epidemiology of Dyspepsia* wiley online library[1]
2. JAN TACK, RAF BISSCHOPS, and GIOVANNI SARNELLI October 2004 *Pathophysiology and Treatment of Functional Dyspepsia GASTROENTEROLOGY* [1]
3. Francis P 1, Zavala SR 1 StatPearls Publishing, Treasure Island (FL), 03 Mar 2020 *Functional Dyspepsia Europe PMC plus*. [2][5]
4. *Journal of Neurogastroenterology and Motility*. 2022[3]
5. S Kindt, J Tack 19 July 2006 *Impaired gastric accommodation and its role in dyspepsia BMJ JOURNALS*[7]
6. MARIA PI'A CALDARELLA, FERNANDO AZPIROZ, and JUAN-R. MALAGELADA May 2003 *Antro-Fundic Dysfunctions in Functional Dyspepsia GASTROENTEROLOGY*[8]
7. JAN TACK, HUBERT PIESSEVAUX, BERNARD COULIE, PHILIP CAENEPEEL, and JOZEF JANSSENS DECEMBER 1998

- Role of Impaired Gastric Accommodation to a Meal in Functional Dyspepsia GASTROENTEROLOGY[9]
8. JAN TACK, PHILIP CAENEPEEL, BENJAMIN FISCHLER, HUBERT PIESSEVAUX, and JOZEF JANSSENS SEPTEMBER 2001 Symptoms Associated With Hypersensitivity to Gastric Distention in Functional Dyspepsia GASTROENTEROLOGY[10]
 9. Feinle†,a, O Meiera, B Ottob, M D'Amatoc, M FriedaMarch 1, 2001. Role of duodenal lipid and cholecystokinin A receptors in the pathophysiology of functional dyspepsia BMJ JOURNAL [11]
 10. CHRISTINE FEINLE,* THOMAS RADES,‡ BA'RBEL OTTO,§ and MICHAEL FRIED* APRIL 2001 Fat digestion modulates gastrointestinal sensations induced by gastric distention and duodenal lipid in humans.GASTROENTEROLOGY[12]
 11. CHRISTINE FEINLE,* MASSIMO D'AMATO,‡ and NICHOLAS W. READ* MAY 1996 Cholecystokinin-A Receptors Modulate Gastric Sensory and Motor Responses to Gastric Distention and Duodenal Lipid.GASTROENTEROLOGY[13]
 12. Ram Chandra Subedi, Binit Upadhaya Regmi, Bishnu Deep Pathak, Bishal Dhakal, Deekshanta Sitaula4, Ujjawal Paudel2, Prabal KC4, Srijana Maharjan5, Anurag Karki, Sunil Baniya, Sushil Joshi, Chiranjibi Pant3, Kumar Roka 2023 RESEARCH ARTICLE Prevalence of Helicobacter pylori infection in dyspeptic patients presenting to a tertiary care center of a developing country: a cross-sectional study F1000Research[14]
 13. Emad M. El-Omar *, Ian D. Penman *, Joy E.S. Ardill ‡, Ravi S. Chittajallu *, Catherine Howie *, Kenneth E.L. McColl *September 1995, Pages 681-691 Helicobacter pylori infection and abnormalities of acid secretion in patients with duodenal ulcer disease.Gastroenterology[15]
 14. Muhammad Ali Khan, MD, and Colin W. Howden, MD March 2018 - Volume 14, Issue 3 The Role of Proton Pump Inhibitors in the Management of Upper Gastrointestinal Disorders Gastroenterology & Hepatology[17]
 15. Thaise Boeing1, Priscila de Souza 1 , Luisa Mota da Silva1, Arquimedes Gasparotto Junior September 2, 2021 Herbal Medicines in the Treatment of Dyspepsia: An Overview, Thieme [18]
 16. B. E. Lacy*, N. J. Talley†, G. R. Locke III‡, E. P. Bouras§, J. K. DiBaise¶, H. B. El-Serag**, B. P. Abraham**,C. W. Howden††, P. Moayyedi‡‡& C. Prather§Review article: current treatment options and management of functional dyspepsia 7 February 2012 Alimentary Pharmacology & Therapeutics Volume 36, Issue 1[19]
 17. Young Joo Yang, Chang Seok Bang, Gwang Ho Baik,Tae Young Park,Suk Pyo Shin, Ki Tae Suk & Dong Joon Kim 26 June 2017 volume 17, Article number: 83 Prokinetics for the treatment of functional dyspepsia: Bayesian network meta-analysisBMC Gastroenterology [20][27]
 18. Pittayanon R, Yuan Y, Bollegala NP, Khanna R, Leontiadis GI, Moayyedi P 18 October 2018 Prokinetics for functional dyspepsiaCochrane Library[21][25]
 19. A. O. Quartero, M. E. Numans, R. A. De Melker, A. W. Hoes, N. J. De Wit 08 Jul 2009Research ArticleDyspepsia in Primary Care: Acid Suppression as Effective as Prokinetic Therapy. A Randomized Clinical Trial Scandinavian Journal of Gastroenterology Volume 36, 2001 - Issue 9[22]
 20. Michael Camilleri*Jessica Atieh 24 August 2021New Developments in Prokinetic Therapy for Gastric Motility Disorders Frontiers in Pharmacology Sec.Gastrointestinal and Hepatic PharmacologyVolume 12 - 2021 [23]
 21. Lorenzo Drago1, 1, Luigi Pasquale2, Giuseppe Milazzo3, Fabio Monica4, Salvatore Aragona5, Leonardo Ficano6, Roberto Vassallo7, and Gastrobiota Group Journal of International Medical ResearchVolume 49, Issue 1, January 2021Evaluation of main functional dyspepsia symptoms after probiotic administration in patients receiving conventional pharmacological therapies.[24]
 22. Leonard Ho1 , Claire C. W. Zhong2 , Charlene H. L. Wong2 , Justin C. Y. Wu3 , Karina K. H. Chan4 , Irene X. Y. Wu5*, Ting Hung Leung1 and Vincent C. H. Chung1,2 20 December 2021 Chinese herbal medicine for functional dyspepsia: a network meta-analysis of prokinetic-controlled randomised trials Chinese Medicine[26]
 23. Germán Báez Camila Vargas,Marcelo Arancibia,Cristian Papuzinski15 June 2023 Non-Chinese herbal medicines for functional dyspepsia cochrane library[28]
 24. Kazumi Inokuchi,Tatsuhiko Masaoka*,Takanori Kanai 08 June 2021
 25. Sec. Gastrointestinal and Hepatic Pharmacology Volume 12 - 2021 Rikkunshito as a

- Therapeutic Agent for Functional Dyspepsia and its Prokinetic and Non-Prokinetic Effects *Frontiers in Pharmacology*[29]
26. Toshitaka Kido^{1,2,*}, Yoichiro Nakai², Yoshio Kase², Iwao Sakakibara², Masaaki Nomura³, Shuichi Takeda², and Masaki Aburada^{2,4} April 20, 2005 Effects of Rikkunshi-to, a Traditional Japanese Medicine, on the Delay of Gastric Emptying Induced by NG-Nitro-L-arginine *Journal of Pharmacological Sciences*[30]
 27. Stephanie Abiola Tijani, Samuel B. Olaleye and Ebenezer O. Farombi April 19, 2018 Anti-ulcerogenic effect of the methanol extract of *Chasmanthera dependens* (Hochst) stem on male Wistar rats *Journal of Basic and Clinical Physiology and Pharmacology*[31]
 28. Muhammad Ali Hashmi, I Afsar Khan, Muhammad Hanif, Umar Farooq, and Shagufta Perveen February 23, 2015 Traditional Uses, Phytochemistry, and Pharmacology of *Olea europaea* (Olive) *Evidence-Based Complementary and Alternative Medicine*[32]
 29. Dahee Yeo^{a 1}, Su Jung Hwang^{a b 1}, Woo Jean Kim^{c 1}, Hyun-Joo Youn^a, Hyo-Jong Lee *Biomedicine & Pharmacotherapy* Volume 99, March 2018, Pages 681-687 The aqueous extract from *Artemisia capillaris* inhibits acute gastric mucosal injury by inhibition of ROS and NF-κB *Journals & Books*[33]
 30. Brenna Ramos Athaydes^a, Gisele Maziero Alves^b, Arícia Leone Evangelista Monteiro de Assis^c, João Victor Dutra Gomes^d, Ricardo Pereira Rodrigues^a, Bianca Prandi Campagnaro^b, Breno Valentim Nogueira^c, Dâmaris Silveira^d, Ricardo Machado Kuster^e, Thiago Melo Costa Pereira^{b f}, Rodrigo Rezende Kitagawa^a, Rita de Cássia Ribeiro Gonçalves *Food Research International* Volume 119, May 2019, Pages 751-760 Avocado seeds (*Persea americana* Mill.) prevents indomethacin-induced gastric ulcer in mice *Journals & Books*[34]
 31. Chul-Hong Park, Hyeong-U Son, Chi-Yeol Yoo & Sang-Han Lee Pages 2110-2115 05 Sep 2017 Research Article Low molecular-weight gel fraction of *Aloe vera* exhibits gastroprotection by inducing matrix metalloproteinase-9 inhibitory activity in alcohol-induced acute gastric lesion tissues *taylor& francis online*[35]
 32. Antonisamy Paulrayer^{1,†}, Aravinthan Adithan^{1,†}, Jeong Ho Lee^{2,†}, Kwang Hyun Moon², DaeGeun Kim², SoYeon Im², Chang-Won Kang¹, Nam Soo Kim¹ and Jong-Hoon Kim^{1,*} 17 May 2017 *Aronia melanocarpa* (Black Chokeberry) Reduces Ethanol-Induced Gastric Damage via Regulation of HSP-70, NF-κB, and MCP-1 Signaling *International journals of molecular sciences*[36]
 33. Luis Jardelino de Lacerda Neto^a, Andreza Guedes Barbosa Ramos^a, Valterlucio Santos Sales^a, Severino Denicio Gonçalves de Souza^a, Antonia Thassya Lucas dos Santos^a, Larissa Rolim de Oliveira^a, Marta Regina Kerntopf^a, Thais Rodrigues de Albuquerque^a, Henrique Douglas Melo Coutinho^a, Lucindo Jose Quintans-Júnior^c, Almir Gonçalves Wanderley^b, Irwin Rose Alencar de Menezes^a *Chemico-Biological Interactions* Volume 261, 5 January 2017, Pages 56-62 Gastroprotective and ulcer healing effects of hydroethanolic extract of leaves of *Caryocar coriaceum*: Mechanisms involved in the gastroprotective activity *Journals & Books*[37]
 34. M. A. Ovali, A. Yılmaz & M. Alpaslan Published online: 20 Sep 2018 Gastroprotective effect of apricot kernel oil in ethanol-induced gastric mucosal injury in rats *taylor& francis online*[38]
 35. Puthanpura Sasidharan Sreeja^a, Karuppusamy Arunachalam^b, Sathyanarayanan Saikumar^a, Muniyandi Kasipandi^a, Sivaraj Dhivya^a, Rajan Murugan^a, Thangaraj Parimelazhagan *Biomedicine & Pharmacotherapy* Volume 97, January 2018, Pages 1109-1118 Gastroprotective effect and mode of action of methanol extract of *Sphenodesme involucrata* var. *paniculata* (C.B. Clarke) Munir (Lamiaceae) leaves on experimental gastric ulcer models *Journals & Books*[39]
 36. Tati Ishikawa^a, Raquel dos Santos Donatini^a, Ingrid Elida Collantes Diaz^b, Massayoshi Yoshida^{b c}, Elfriede Marianne Bacchi^a, Edna Tomiko Myiake Kato *Journal of Ethnopharmacology* Volume 118, Issue 3, 13 August 2008, Pages 527-529 Evaluation of gastroprotective activity of *Plinia edulis* (Vell.) Sobral (Myrtaceae) leaves in rats *Journals & Books*[40]
 37. Madisch, A; Andresen, V; Enck, P; Labenz, J; Frieling, T; Schemann, M 2018 The Diagnosis and Treatment of Functional Dyspepsia *aerzteblatt.de*[41]
 38. Jiang SM, Jia L, Liu J, Shi MM, Xu MZ. Beneficial effects of antidepressant mirtazapine in functional dyspepsia patients with weight loss. *World J Gastroenterol* 2016; 22(22): 5260-5266 [42]

39. Kok-Ann Gwee, Gerald Holtmann, Jan Tack, Hidekazu Suzuki, Jinsong Liu, Yinglian Xiao, Min-Hu Chen, Xiaohua Hou, Deng-Chyang Wu, Clarissa Toh, Fang Lu, Xu-Dong

Tang
30 November 2020 Neurogastroenterology & Motility
Volume 33, Issue 2
Herbal medicines in functional dyspepsia—Untapped opportunities not without risks[43]