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# The Potential of Phytotherapy In Managing Dyspepsia: A Narrative Review

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## ABSTRACT

Dyspepsia, commonly known as indigestion, is delineated as suffering the manifestations of epigastric pain, nausea, burning, or after-meal fullness. The common therapy for dyspepsia, e.g., proton pump inhibitors or histamine-H2 receptor antagonists, has shown some adverse effects, thus, phytotherapy is currently becoming the drug of interest. Phytotherapy, additionally known as herbal medicine or botanical medicinal drug, includes the use of plant-derived compounds to prevent, alleviate, or therapy for diverse ailments. Most medications commonly used in Chinese traditional medicine or Asian folklore drugs contain mixtures of several plant extracts. Twelve clinical trials reported the effect and safety of phytotherapy on gastrointestinal disorders. Taken together, phytotherapy may be considered safe for the management of dyspepsia with close monitoring of the dose and duration of therapy.

**Keywords:** *dyspepsia; epigastric pain; gastrointestinal disorders; phytotherapy; proton pump inhibitors*

## INTRODUCTION

Dyspepsia, commonly known as indigestion, is delineated as suffering the manifestations of epigastric pain, nausea, burning, bloating, or after-meal fullness, that may alter the daily activities of a patient (Madisch et al., 2018). The pathophysiology of dyspepsia may be multifactorial and remains unclear, with the most related cause being gastric motility and hypersensitivity (Xu et al., 2020), the infection *Helicobacter pylori* (Du et al., 2016), excessive acid secretion, impaired gastric motility and visceral hypersensitivity, microinflammation, gastric acid, psychosocial factors, genetics, and bad lifestyle. There are two types of dyspepsia, the common organic dyspepsia which includes epigastric pain, fullness, discomfort, burning, early satiety, nausea, vomiting, and belching, and functional dyspepsia (FD) which is diagnosed when upper GI endoscopy reveals no organic lesions that might explain the dyspeptic symptoms (Oustamanolakis and Tack, 2012). FD is benign with a prevalence of less than 20% of the population (Francis and Zavala, 2022). It is a condition with a chronic manifestation of many symptoms centered in the upper abdomen. FD is diagnosed based on the Rome IV criteria, which can be divided into two subcategories, (1) postprandial distress syndrome (PDS), characterized by meal-induced dyspeptic

symptoms, and (2) epigastric pain syndrome (EPS) which refers to epigastric pain or epigastric burning that does not occur exclusively postprandially (Stanghellini et al., 2016). PDS patients encounter loss of appetite, early satiation, nausea, retching, vomiting, and bloating. Meanwhile, EPS patients experience stomach cramping and upper abdominal pain (Madisch et al., 2018). *Helicobacter pylori* infection is considered a possible cause of FD symptoms, due to the fact that patients with FD are most likely to get infected with this bacteria (Du et al., 2016). *H. pylori* is a Gram-negative pathogen that selectively occupies the gastric epithelium (Wroblewski et al., 2010). *H. pylori* bacteria alter the production of hydrochloric acid by converting gastrin and somatostatin secretion (Du et al., 2016). FD should be diagnosed based on a comprehensive evaluation of symptoms, age, medical history, the presence of *H. pylori*, and laboratory history. If it is suspected, *H. pylori* eradication is recommended as the first treatment for all patients with FD (Tomita et al., 2018). When the patients show red flag signs or do not respond to treatment, an upper gastrointestinal endoscopy is necessary (Madisch et al., 2018; Miwa et al., 2022).

The goals of pharmacotherapy for dyspepsia are to relieve the pain as well as to increase the quality of life of the patient. The first-line therapy is proton pump inhibitors (PPI) and histamine type 2 receptor antagonists (H2RAs) (Miwa et al., 2022).

The recommended therapy for FD is lifestyle and dietary modification. PPIs and H2RAs are considered effective treatments for FD, based on several controlled trials with a therapeutic gain over placebo, and have been considered as first-line treatment (Madisch et al., 2018).

PPIs are drugs that work by blocking gastric acid production through irreversible binding to the gastric parietal cell H+/K+ ATPase pump. These drugs include omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole, and dexlansoprazole. All PPIs possess a similar basic structure of substituted benzimidazoles, with variations in the type and position of the substituted group (Orel et al., 2021). In patients with FD, PPIs were reported to be more efficient in alleviating pain compared to H2RAs (Dehghani et al., 2011).

The selective H2RAs are less effective in reducing acid production than the PPIs however, these drugs could suppress 24-hour hydrochloric acid secretion in the stomach by approximately 70%. These selective H2Ras are cimetidine (approved in 1977), ranitidine (approved in 1983), famotidine (approved in 1986), and nizatidine (approved in 1988). H2RAs work mainly on basal and nocturnal acid secretion, which is important in peptic ulcer healing (LiverTox, 2018).

However, due to the side effects of these agents, there is a growing interest in alternative and complementary therapy, using plant-derived products. These products are usually in the form of a mixture of botanical extracts that contain phytochemical components for various medicinal benefits.

This review aims to discover the potential of phytotherapy to control dyspepsia, focusing on the efficacy, safety, and activity of diverse plant-based treatments. By selecting and studying articles about phytotherapy for dyspepsia in humans, we provide a complete evaluation of the advantages and obstacles of phytotherapy as a complementary approach for people stricken by dyspeptic symptoms.

## METHOD

The articles were traced in the PubMed database within 10 years of the publication date from 2013 to 2023 by advanced searches, filtered to free full-text, and simplified using the Boolean operator technique by entering "AND" with the query terms (plant extract) AND (dyspepsia) and resulted in 101 articles. Review articles, nonclinical research, and unrelated studies that do not contain the content information were excluded; thus, only 12 articles were included in this review (depicted in Figure 1).

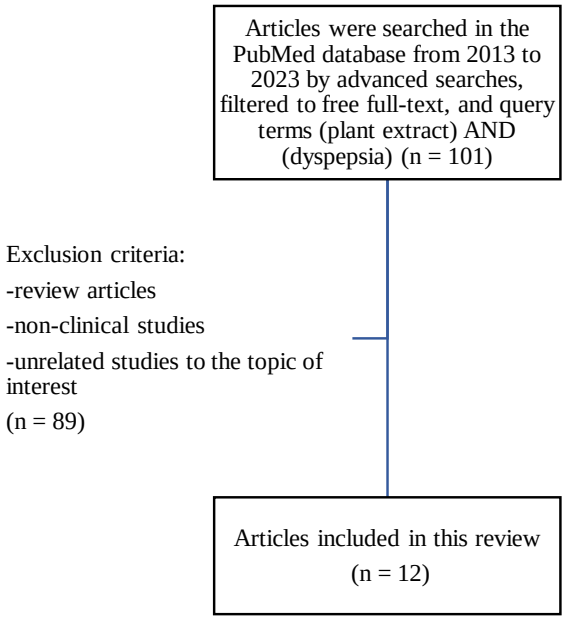


**Figure 1.** The flowchart of the article search

## RESULTS AND DISCUSSION

### Phytotherapy For dyspepsia

Phytotherapy, also called a natural medication or botanical medication, involves using plant-based treatments for health and dealing with various illnesses. The wide range of plant species gives a tremendous array of herbal compounds that possess healing properties for addressing dyspeptic signs and symptoms (Miwa et al., 2022). Natural product extracts have attracted attention in recent years due to their comprehensive therapeutic effects and relative safety. Plant-derived natural products provide a complex, mixed, and diverse array of non-nutritional elements that are the primary basis for drug development. Based on the reviewed studies, most of the drugs that are used as an alternative for dyspepsia are Traditional Chinese Medicine (TCM) tabulated in **Table 1**. These multi-component drugs are considered safe and have a major impact on therapy based on clinical trials. For example, one article announced that a TCM containing curcumin, *Aloe vera*, slippery elm, guar gum, pectin, peppermint oil, and glutamine was effective in improving upper and lower gastrointestinal symptoms (Ried et al., 2020).

**Table 1.** The Efficacy And Safety of Phytotherapy For Dyspepsia In Humans

| Reference | Formulation | Number of Subjects | Dose | Result | Adverse Effects |
|---|---|---|---|---|---|
| Ried et al., 2020 | *Curcuma longa*, *Aloe vera*, *Ulmus rubra*, *Cyamopsis tetragonoloba*, pectin, *Mentha piperita*, and glutamine | 43 patients | 5000 mg/day | Significantly improved upper and lower GI symptoms by 40-60% in 4 weeks | No adverse effects |
| Ha et al., 2023 | Naesohwajung-tang (NHT) | 116 patients with FD | 7000 mg 3 times per day for 4 weeks | A significantly higher reduction in the total dyspepsia symptom ($p < 0.05$) and a higher degree of improvement in the total dyspepsia symptom ($p < 0.01$) than the placebo group. | No adverse effects |

| Reference | Formulation | Number of Subjects | Dose | Result | Adverse Effects |
|---|---|---|---|---|---|
| Choi et al., 2020 | *Flos Lonicera* extract (GCWB104) | 92 patients with FD | 300 mg of GCWB104 containing 125 mg of *Flos Lonicera* extr act, twice daily for 8 weeks | Improvements in mild to moderate FD and irritable bowel syndrome symptoms | No adverse effects |
| Wang et al., 2021 | Combination of *Panax notoginseng* saponins (PNS) and acetylsalicylic acid (ASA) | 42 patients (35–75 years) with stable coronary heart disease (SCHD) and chronic gastritis | 60 mg of PNS twice daily in addition to 100 mg of ASA for 2 months | The combination of PNS and ASA potentiated the antiplatelet effect of ASA via AA/COX-1/$TXB_2$ pathway in platelets and mitigated ASA-related gastric injury via the AA/PG pathway in gastric mucosa compared with ASA alone. | No adverse effects |
| Lv et al., 2017 | Xiangsha Liujunzi granules containing *Astragalus mongholicus*, *Codonopsis pilosula*, rhizoma *Atractylodis*, *Macrocephalae* rhizome, *Poria cocos*, Fructus *Aurantia*, *Amomum villosum*, *Ligusticum chuanxiong*, rhizoma *Corydalis*; medicated Leaven and *Glycyrrhiza uralensis* | 216 patients with FD | 14 g granules in 130 ml | Effective in the management of FD, especially in patients with postprandial fullness and bloating, early satiety, and epigastric pain | No adverse effects |
| Lazzini et al., 2016 | Prodigest capsules containing *Zingiber officinalis* 20 mg and artichoke (*Cynara cardunculus*) 100 mg | 11 healthy volunteers | 1-2 capsules per day for 7 days | Prodigest capsules facilitate gastric emptying in a dose-dependent manner | No adverse effects |
| Du, 2014 | Xiaoyao pill, consisting of Radix *bupleuri*, *Angelica sinensis*, radix *Paeoniae alba*, rhizoma *Atractylodis macrocephalae*, *Wolfiporia extensa*, radix *Glycyrrhizae*, mint, rhizoma *Zinjiberis recens* | 180 female patients with FD accompani ed by depression | 3 g per day | Improve the symptoms in patients with perimenopausal FD | No adverse effects |

| Reference | Formulation | Number of Subjects | Dose | Result | Adverse Effects |
|---|---|---|---|---|---|
| Xu et al., 2020 | QZWTG containing radix *Bupleuri*, rhizoma *Corydalis*, Fructus *Aurantii*, Nutgrass *Galingale* rhizome, radix *Paeoniae alba*, radix *Glycyrrhizae preparata* | 384 patients with FD | 2.5 g per day for 4 weeks | Effective in improving clinical symptoms | No adverse effects |
| Hajiaghamohammadi et al., 2016 | Licorice herb (*Glycyrrhiza glabra*) | 120 patients with positive rapid urease test | Addition of licorice 380 mg twice per day to the triple clarithromycin-based regimen | The addition of licorice to the triple clarithromycin-based regimen increases *H. pylori* eradication, especially in the presence of peptic ulcer disease | Not evaluated |
| Zhang et al., 2021 | Liujunzi decoction containing radix *Codonopsis*, rhizoma *Atractylodis macrocephalae*, Fu Ling (Poria), rhizoma *Pinelliae*, pericarpium *Citri reticulatae*, radix *Glycyrrhizae* | 220 patients with FD | Liujunzi decoction was decocted in water for an oral dose twice a day for 6 days | Not yet reported | Not yet reported |
| Su et al., 2018 | Radix *Bupleuri*, *Corydalis* rhizoma, fructus *Aurantii*, Nutgrass *Galingale* rhizome, white Peony root, *Glycyrrhizae* radix et rhizoma praeparata cum melle | 197 patients with PDS (postprandial distress syndrome) | 2.5 g per day | Shows effects on the main gastrointestinal symptoms and psychological disorders in PDS | 2 patients reported side effects: mild constipation and moderate elevation of urinary protein |
| Du, 2014 | JX pills containing *Paeonia lactiflora*, *Atractylodes macrocephala*, Mentha canadensis, Bupleurum falcatum L; Angelica sinensis (Oliv.) Diels; Thespesia populnea L.; Glycyrrhiza inflata; Batalin; suffruticosa Andrews; Gardenia jasminoides J.Ellis | 144 women with FD | 12 g per day | The JX pills were superior to the placebo in terms of improving the GIS in patients with FD | 3 patients reported side effects |

## CONCLUSIONS

Dyspepsia is a condition with a chronic manifestation of many symptoms that are centered in the upper abdomen. The first-line therapy is PPIs or H2Ras. However, these drugs may cause side effects and complications. Most of the phytopharmaceuticals that are used as an alternative for dyspepsia are Traditional Chinese Medicines (TCM) which consist of more than one plant. Of the twelve clinical trials, eight studies reported no adverse effects, and two studies reported mild side effects (1.01% and 2.08% of the patients, respectively), therefore, phytotherapy can be considered a safe and effective alternative therapy for dyspepsia.

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