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Review Article

Medicinal Plants in Gastroesophageal Reflux Disease (GERD): A Comprehensive Review of Experimental and Clinical Evidence on Esophageal Mucosal Protection

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Abstract

Background: Gastroesophageal reflux disease (GERD) is a chronic digestive disorder that adversely impacts overall well-being, presenting symptoms such as heartburn, regurgitation, and damage to the mucosal lining. The prevalence of GERD has been increasing largely due to dietary habits, obesity, and sedentary lifestyles. Numerous studies have been conducted to evaluate alternative treatments for GERD, particularly with herbal medications. There is limited scientific evidence to support effective treatment of this disease in Sri Lanka.

Objectives: To study the scientific basis of traditional plants that have been known to have mucosal protection properties.

Methodology: A literature review was conducted using multiple sources including databases (PubMed, PubChem, Research4Life), academic search engines (Google Scholar), and publisher platforms (BMC, Springer, PLOS, and ScienceDirect) to provide evidence-based recommendations for these traditional plants, using the keywords "GERD", "Medicinal plants", "Mucosal protection activity", and "Indigenous medicine", from 2015 to 2025.

Results: Plant-derived medicines have several advantages, such as economical value, improved tolerance by the patient, and the lower side effects compared to conventional therapies. Potent esophageal mucosal defense has been demonstrated by various medicinal plants by their anti-inflammatory, antioxidant and mucin–secreting action. Ayurvedic herbs are reported to reduce GERD symptoms in animal and human clinical studies by regulating gastric acid secretion and epithelial healing. In the Unani system, plants have shown the effects to improve mucosal resiliency and relieve dyspeptic symptoms. In the Siddha medicines, plants have shown mucosal protective effect in ethanol induced gastric ulcers. After carefully screening, 30 herbal plants in 19 families from 22 selected articles were shortlisted for this review.

Conclusion: Herbal compounds protect gastric mucosa by reducing inflammation and oxidative stress, increasing mucin secretion, regulating gastric acid, promoting epithelial healing, strengthening mucosal defence, and relieving dyspeptic symptoms.

Keywords: Gastroesophageal Reflux Disease (GERD), Indigenous medicine, Medicinal plants, Mucosal Protection Activity

Introduction

Gastroesophageal reflux disease, commonly referred to as GERD, is a chronic stomach condition. This issue arises when stomach acid flows back into the esophagus. It may also destroy the esophageal lining. What distinguishes GERD, as opposed to reflux, is that it occurs frequently, is very severe and lasts a long time. This may interfere with the life of a person and make it difficult to carry out their day-to-day activities (Bertin et al., 2025; Fass, 2022; Chhabra & Ingole, 2022).

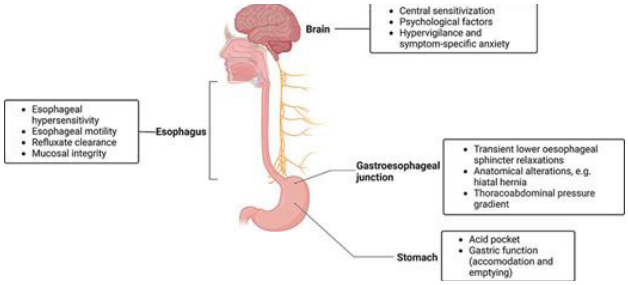

Figure 1 Main mechanisms deriving GERD and its symptoms (Bertin et al., 2025)

The prevalence of GERD is increasing worldwide. Globally, the prevalence of GERD is wide ranging, with ranges documented as 18.1–27.8% in North America, 8.8–25.9% in Europe, 2.5–7.8% in East Asia, 8.7–33.1% in the Middle East, 11.6% in Australia, and 23.0% in South America (Eusebi et al., 2017). In the United States, GERD accounts for about 4% of all primary care visits, with an incidence of 5 per 1,000 person-years (El-Serag et al., 2014). This increased prevalence is due to aging, being overweight, and lack of physical exercise. GERD is also more prevalent among individuals with obesity, unhealthy dietary habits, smoking habits, excessive alcohol consumption, and long-term use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) (Alatawi et al., 2025).

The modern method of managing GERD is with medicines, such as proton pump inhibitors (PPI) and histamine-2 receptor antagonists (H2RA) to ensure that the stomach produces a reduced amount of acid (Chhabra & Ingole, 2022). These drugs are effective for many people. However, some individuals continue to experience the symptoms despite taking the medicine or when they stop taking it, the symptoms often come back. If these medicines are taken long-term, patients may experience severe side effects. They may fail to absorb the nutrients that they require from food. They may even suffer bone fractures (Fass, 2022; Gyawali & Fass, 2018; Świdnicka-Siergiejko et al., 2022).

Table 1: Summary of Conventional Therapeutic Approaches for Gastroesophageal Reflux Disease (GERD)

Treatment	Mechanism of Action	Indications	Limitations / Side Effects	Source
Proton Pump Inhibitors (PPIs)	Irreversibly inhibit H^+/K^+-ATPase in gastric parietal cells, reducing acid secretion	First-line therapy for erosive esophagitis and severe NERD	Long-term use associated with infections (e.g., *Clostridioides difficile*), kidney disease, Nutrient malabsorption	Fass (2022)
H2-Receptor Antagonists (H2RAs)	Block H2 receptors on parietal cells, decreasing acid production	Mild to moderate GERD, especially nocturnal reflux	Tachyphylaxis with long-term use; less effective than PPIs for healing	Pish-Kenari et al. (2018)
Antacids	Neutralize existing gastric acid	Immediate relief for occasional symptoms	Short duration of action; ineffective for mucosal healing	Argyrou et al. (2018)
Alginate-based therapy	Forms a mechanical foam/gel barrier at the gastric cardia to reduce reflux	Adjunct therapy for postprandial and nocturnal symptoms	Short-lived effect; does not inhibit acid production	Fass (2022)
LINX device (Magnetic Augmentation)	Magnetic ring reinforces the lower esophageal sphincter (LES) while allowing food passage	Moderate GERD; alternative to surgery	Not suitable for metal allergies or large hernias; postoperative dysphagia	Świdnicka-Siergiejko et al. (2022); Leowattana & Leowattana (2022)
Endoscopic therapies (TIF, Stretta)	TIF recreates the anti-reflux valve; Stretta uses radiofrequency to tighten LES	Mild to moderate GERD unresponsive to PPIs	Limited long-term outcome data; availability issues	Argyrou et al. (2018)
Lifestyle and dietary modification	Weight loss, meal timing, head elevation, and avoidance of triggers	Recommended for all GERD patients	Requires patient adherence; variable effectiveness	Fass (2022)
Baclofen (GABA-B agonist)	Inhibits transient LES relaxations (TLESRs)	Refractory GERD not responsive to acid suppression	CNS adverse effects (e.g., sedation, dizziness); poor tolerability	Gyawali & Fass (2018); Pish-Kenari et al. (2018)
Prokinetics (e.g., metoclopramide)	Improve gastric emptying and esophageal motility	Refractory GERD with delayed gastric emptying	CNS effects (e.g., fatigue, extrapyramidal symptoms)	Pish-Kenari et al. (2018)
Surgical fundoplication (Nissen)	Reinforces LES by wrapping stomach around lower esophagus	Severe or refractory GERD; large hiatal hernia	Dysphagia, gas-bloat syndrome; invasive procedure	Fass (2022)

Note. *NERD* = non-erosive reflux disease; *LES* = lower esophageal sphincter; *TIF* = transoral incisionless fundoplication.

The cost of taking these medicines for the rest of one's life is also remarkably high. People are interested in utilizing alternative treatments to improve their well-being, such as medicinal herbs (Hershcovici & Fass, 2011; Ansong et al., 2025). Medicinal plants are quite beneficial as they can assist the body in numerous ways, including decreasing inflammation, combating harmful agents, and safeguarding internal organs (Al-Sulivany et al., 2024). Medicinal plants are often easier for people to use. Plant-based therapies are generally associated with fewer side effects than conventional pharmacotherapy. Medical use of plant-based medicines has been proven to improve the defense mechanisms of the esophageal mucosa; however, a comprehensive review of such evidence is needed to inform clinical practice. Therefore, the objectives of this review are to critically assess the evidence of experiments and clinical trials on the effectiveness and mucosal protective effects of traditional medicinal plants in the treatment of GERD (Alecci et al., 2016; Zohalinezhad et al., 2015).

METHODOLOGY

A comprehensive literature review on medicinal plants in the management of Gastroesophageal Reflux Disease (GERD) was conducted using PubMed (US National Library of Medicine, USA), Research4Life and PubChem databases, Google Scholar academic search engines, BMC, Springer, PLOS, and ScienceDirect publisher platforms. The keywords used in the search included GERD, "medicinal plants", "mucosal protection activity", and "indigenous medicine". The review considered studies that had appeared between the year 2015 and 2025 and employed a two-stage methodology of evaluation and screening. Over 454 articles were identified by the initial search.

Duplicates were removed, and titles and abstracts screened, followed by relevant full texts being critically reviewed, resulting in 22 eligible studies being screened for inclusion. Articles that appeared only in English were included, and conference communications and abstracts were excluded.

RESULTS

Medicinal Plants

Throughout the review, the following medicinal plants, which are used in indigenous medicine, were identified.

Table 2

Medicinal Plants Classified by Order and Family

Class	Order	Family	Example species
Liliopsida	Poales	Poaceae	*Bambusa arundinacea*
Liliopsida	Asparagales	Asparagaceae/ Amaryllidaceae	*Asparagus racemosus; Allium sativum; Allium hookeri*
Liliopsida	Zingiberales	Zingiberaceae	*Zingiber officinale; Elettaria cardamomum; Curcuma spp.*
Magnoliopsida	Malvales	Malvaceae	*Malva parviflora*
Magnoliopsida	Piperales	Piperaceae	*Piper nigrum*
Magnoliopsida	Sapindales	Rutaceae	*Aegle marmelos*
Magnoliopsida	Caryophyllales	Cactaceae	*Opuntia ficus-indica*
Magnoliopsida	Brassicales	Brassicaceae	*Brassica oleracea*
Magnoliopsida	Rosales	Rosaceae	*Rubus spp.*
Magnoliopsida	Myrtales	Combretaceae/ Myrtaceae	*Terminalia chebula; Terminalia bellirica; Myrtus communis*
Magnoliopsida	Cucurbitales	Cucurbitaceae	*Benincasa hispida*
Magnoliopsida	Fabales	Fabaceae	*Glycyrrhiza glabra; Glycine max*
Magnoliopsida	Asterales	Asteraceae	*Artemisia campestris; Artemisia absinthium; Sonchus oleraceus L.*
Magnoliopsida	Apiales	Apiaceae	*Coriandrum sativum; Cuminum cyminum;*
			Foeniculum vulgare; Centella asiatica
Magnoliopsida	Lamiales	Lamiaceae / Oleaceae / Plantaginaceae	*Salvia officinalis; Satureja hortensis; Olea europaea; Plantago ovata*

From the above plants, 30 herbal plants from 19 Families are discussed in this review. Medicinal plants with potential Anti-GERD activity

1. Order: Poales (Family: Poaceae ex; *Bambusa arundinacea*)

'Safoof-i-Tabkheer', an Unani formulation containing *Bambusa arundinacea*, showed significant efficacy in reducing GERD symptoms (40.65–53.89%) in 30 patients without side effects, likely due to its carminative, analgesic, and anti-inflammatory properties (Sehar et al., 2021).

Figure 2 Bambusa arundinacea (Gaikwad et al., 2024)

2. Order: Asparagales (Family: Asparagaceae ex; *Asparagus racemosus* (Shatavari), Family: Amaryllidaceae ex; *Allium sativum* (Garlic), *Allium hookeri*)

Shatavari *(Asparagus racemosus)* has been traditionally utilized for urinary tract infections, kidney stones, cardiovascular disease, rheumatism, jaundice, diabetes, brain and reproductive problems, as well as respiratory conditions. In a case study, a 33-year-old man with chronic GERD received treatment with Shatavari root extract, combined with lifestyle and dietary changes, leading to total symptom relief (acidity, bleeding, epigastric pain, and sleep issues) in 45 days, with no side effects (Amarprakash et al., 2021).

Figure 3 Asparagus racemosus (Alok et al., 2013)

Figure 4 Allium hookeri plant and root (Pandey et al., 2018)

Figure 5 Allium sativum (Garlic) bulbs (Choudhary et al., 2022)

Garlic *(Allium sativum)* and *Allium hookeri* roots have antibacterial, antiviral, antifungal, anti-inflammatory, anti-diabetic, anticoagulant, and anti-obesity effects due to bioactive compounds like S-allyl cysteine and organosulfur compounds (Nan et al., 2018; Kim et al., 2019). In rat models of reflux esophagitis, black garlic extract diminished mucosal injury and inflammation by inhibiting the NF-κB pathway, highlighting its gastroprotective properties (Nan et al., 2018; Kim et al., 2019).

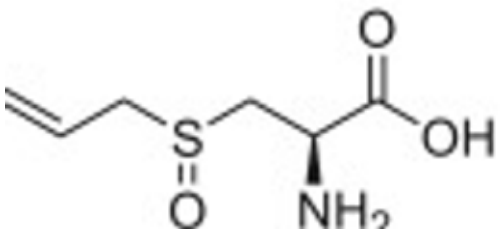

Figure 6 Chemical structure of Alliin (Kuete, 2017)

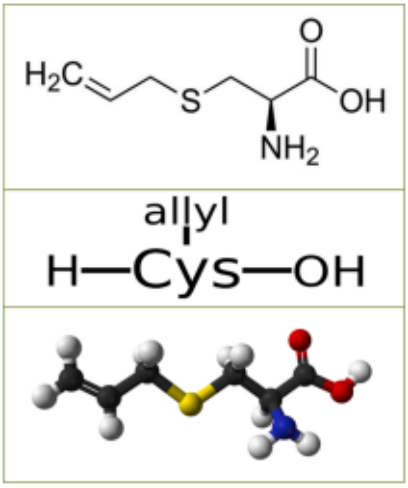

Figure 7 Chemical structure of S-Allyl cysteine (Rais et al., 2023)

3. **Order: Zingiberales (Family: Zingiberaceae ex; *Zingiber officinale* (Ginger), *Elettaria cardamomum* (Cardamom), *Curcuma* spp. (Turmeric)**

Figure 8 Zingiber officinale (Verma & Meshram, 2024)

Ginger has been traditionally utilized for digestive issues, high blood pressure, diabetes, vomiting, and nausea. It includes phenolic compounds, tannins, gingerols, shogaols, and flavonoids, which provide gastroprotective benefits by boosting mucosal protection, neutralizing acid, lowering inflammation (through arachidonate cascade inhibition), reducing acid production, enhancing digestion, and preventing ulcer formation. Its effectiveness was shown in Siddha polyherbal formulation (Yamuna et al., 2019), in Unani polyherbal formulation (Zafar et al., 2019), PEA-blended (Spigarelli et al., 2024), and monotherapy (Sharma et al., 2025) formulations, utilizing models like aspirin/alcohol-induced gastric ulcers in rats, GERD sufferers (n=10), and in-vitro esophageal cellular lines. Findings indicated decreased reflux, heartburn, and enhanced digestion without any cytotoxic effects or negative reactions.

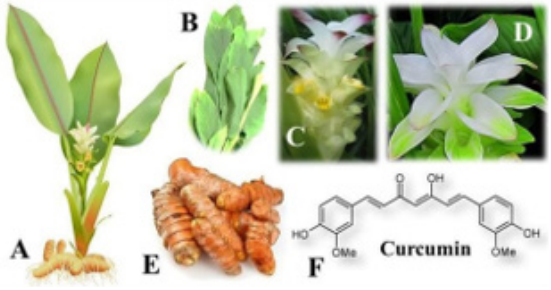

Figure 9 A. Curcuma longa plant; B. Leaves of Curcuma longa; C & D. Flower of Curcuma longa; E. Root of Curcuma longa; F. Chemical structure of curcumin phytochemical (Tripathy et al., 2021)

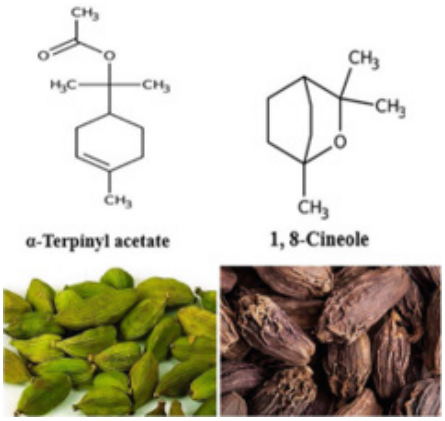

Figure 10 A. Chemical structure of α-Terpinyl acetate; B. Raw Elettaria cardamomum; C. Chemical structure of 1,8-Cineole; D. Dried Elettaria cardamomum (Cheikhyoussef et al., 2023)

Figure 11 A. Cuminum cyminum plant; B. Seeds of Cuminum cyminum (Parajapti et al., 2019)

Elettaria cardamomum showed carminative, analgesic, and anti-inflammatory actions. In 30 GERD patients, significant symptom relief was observed without side effects, confirming its safety and efficacy (Sehar et al., 2021).

HAGE-101912, a polyherbal drug with *Cuminum cyminum* (Azeemuddin et al., 2023), and turmeric (*Curcuma longa*) extract (Kong et al., 2025) showed anti-reflux, gastroprotective, anti-inflammatory, and antioxidant properties. In rat models, they diminished gastric acid and ulcer index, enhanced lower esophageal sphincter contraction, safeguarded mucosa, and decreased TNF-α, IL-1β, IL-8, and NF-κB activation. The therapy combining quercetin and curcumin outperformed each compound used separately (Azeemuddin et al., 2023; Kong et al., 2025).

4. Order: Malvales (Family: Malvaceae ex; *Malva parviflora*)

A comparative investigation demonstrated that the leaf mucilage and fruit extract of *Malva parviflora* exhibit anti-inflammatory (carrageenan-triggered paw edema), antitussive (SO_2-induced coughing), and gastroprotective (ethanol-induced gastric ulcer) properties, with leaf mucilage displaying more significant therapeutic efficacy for inflammatory and gastrointestinal conditions (Altyar et al., 2022).

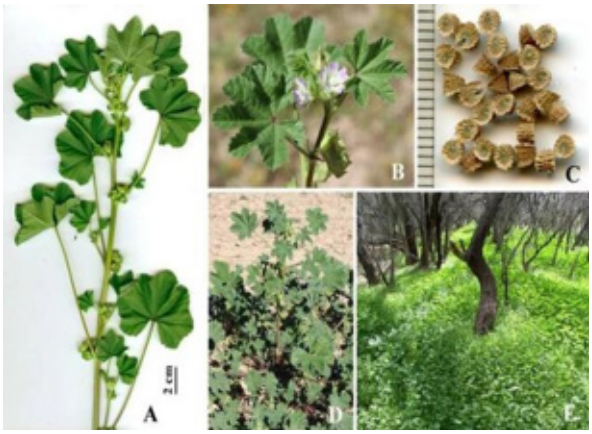

Figure 12 A. Malva parviflora plant (Early vegetative stage); B & C. Flowering and fruiting stage; D. Seeds; E. Mature plant in habitat (Felger et al., 2015)

5. Order: Piperales (Family: Piperaceae ex; *Piper nigrum* (Black pepper)

Shanmuga Chooranam, which has *Piper nigrum* (black pepper), has been traditionally utilized for digestive, respiratory, and neurological issues, and it showed gastroprotective capabilities by diminishing aspirin-induced gastric ulcers and maintaining mucosal integrity in Wistar rats (Yamuna et al., 2019).

Figure 13 Piper nigrum (Wulandari, 2021)

6. Order: Sapindales (Family: Rutaceae ex; *Aegle marmelos*)

The pulp of *Aegle marmelos*, commonly utilized for numerous conditions such as digestive issues and inflammation, displayed notable anti-ulcer properties in male Wistar rats (0.19-0.20 kg) with ethanol-induced gastric ulcers. The high-dose extract was more effective than omeprazole in minimizing ulceration and enhancing gastric mucosa, with no side effects or deaths reported (Sharma et al., 2025).

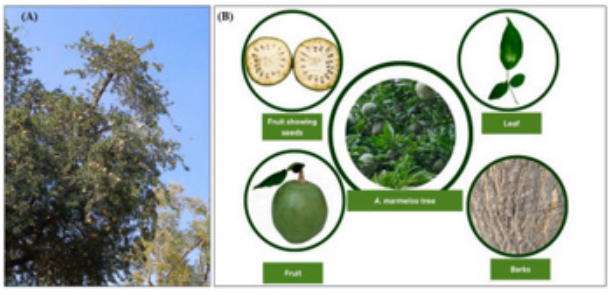

Figure 14 A. Aegle marmelos B. Parts of plant (Yadav & Rana, 2025)

7. Order: Caryophyllales (Family: Cactaceae ex; *Opuntia ficus-indica)*

Opuntia ficus-indica, rich in polyphenols and mucilage, acts as a gastric mucosal protector with anti-inflammatory and anti-ulcer properties (Alecci et al., 2016). Its flavonoid and polyphenol-rich extracts reduce reactive oxygen species and inflammation (Spigarelli et al., 2024). Clinical trials showed significant improvements in GERD symptoms and quality of life, with reductions in heartburn, acid regurgitation, and pro-inflammatory cytokines, and no adverse effects reported (Alecci et al., 2016; Spigarelli et al., 2024). The extract combined with Palmitoylethanolamide (PEA) was more effective than extract alone (Spigarelli et al., 2024).

Figure 15 Opuntia ficus-indica Fruit photographs of Opuntia ficus-indica; A. Yellow Tuna; B. Saltena Tuna; C. Cordobesa Orange Tuna; D. White Tuna; E. Reddish Tuna; F. Amyclaea. (Ahumada et al., 2019)

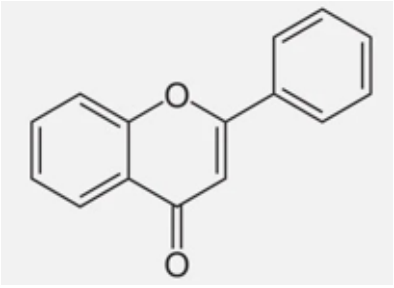

Figure 16 Flavonoids (Patel et al., 2013)

8. Order: Brassicales (Family: Brassicaceae ex; *Brassica oleracea*)

Brassica oleracea shows various pharmacological effects including anti-diabetic, anti-cancer, anti-hypertensive, anti-cholesterolemic, antioxidant, anti-inflammatory, antibacterial, anti-obesity, anticoagulant, and hepatoprotective properties. The entire plant extract consists of flavonoids, tannins, phenolics, and various compounds, while the juice of the fruit is abundant in mucilage, fiber, and glucosinolates that have cytoprotective and alkaline properties. Clinical studies involving GERD patients demonstrated complete immediate relief from heartburn and discomfort, due to mucosal coating, acid neutralization, and esophageal healing, with no side effects reported (Noah, 2022).

Figure 17 Botanical parts of Brassica oleracea (Quizhpe et al., 2024)

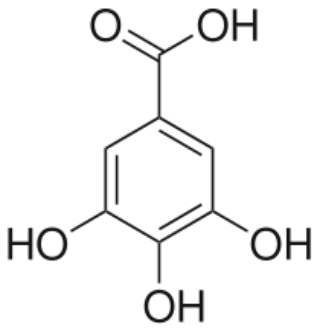

Figure 18
Tannin (Lozada-Ramírez et al., 2021)

9. Order: Rosales (Family: Rosaceae ex; *Rubus* spp.)

Extracts from Rubus spp. leaves, recognized for their antioxidant and anti-inflammatory effects, are utilized to treat GERD along with other issues such as fever, diarrhea, skin infections, joint pain, and wound healing. A randomized, double-blind, non-inferiority clinical trial involving 86 GERD patients demonstrated efficacy, with adverse effects such as gas bloat and dysphagia (Al-Sulivany et al., 2024).

Figure 19 Rubus spp.; A: Floral buds; B: Detail of flower petals, stamens, and carpels; C: In vitro germinated pollen grains; D: Fruiting; E: Ripe fruit; F. Seedling emergence (Figueiredo et al., 2013)

10. Order: Myrtales (Family Combretaceae ex; *Terminalia chebula, Terminalia bellirica,* Family Myrtaceae ex; *Myrtus communis*)

Extracts of *Terminalia chebula* and *Terminalia bellirica*, abundant in phenolics, tannins, and flavonoids, are essential components of Shanmuga Chooranam. They provide gastroprotective, antioxidant, anti-inflammatory, and acid-neutralizing benefits, safeguarding gastric mucosa and preventing ulcers without adverse effects (Yamuna et al., 2019).

Figure 20 A. Terminalia chebula B. Fruit C. Seeds (Pradeep et al., 2022)

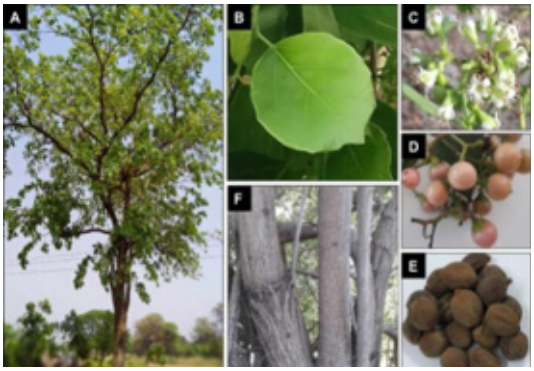

Figure 21 A. Terminalia bellirica B. Leaves C. Flower D. Fruit E. Seeds F. Bark (Gupta et al., 2020)

Myrtus communis fruit, abundant in tannins and polyphenols, demonstrates anti-inflammatory, antioxidant, anti-*Helicobacter pylori*, gastric acid-inhibiting, and mucosal protective properties. Its extract successfully alleviates GERD symptoms by minimizing reflux and dyspepsia, demonstrating similar efficacy and safety to omeprazole, with minor side effects such as dysphagia and gas bloating noted (Zohalinezhad et al., 2015; Al-Sulivany et al., 2024).

Figure 22 Myrtus communis and berries (Al-Snafi et al., 2024)

11. Order: Cucurbitales (Family: Cucurbitaceae ex; *Benincasa hispida*)

Benincasa hispida extract, derived from aerial parts, fruit juice, seed, and root, demonstrates anti-reflux, prokinetic, and gastroprotective effects in female Wistar rats, including gastric acid reduction, esophageal ulcer healing, improved lower esophageal sphincter contraction, and mucosal protection, without side effects (Azeemuddin et al., 2023).

Figure 23 Benincasa hispida (Raj et al., 1993)

12. Order: Fabales (Family: Fabaceae ex; *Glycyrrhiza glabra, Glycine max* (soybeans)

Glycyrrhiza glabra root extract exhibits anti-inflammatory, anti-reflux, prokinetic, and gastroprotective properties in Wistar rats, alleviating gastric acid and esophageal ulcers, enhancing lower esophageal sphincter contraction, and safeguarding gastric mucosa without adverse effects. Elevated doses of the extract reduced ulceration and protected the gastric mucosa more effectively than omeprazole, with no mortality or behavioural alterations (Azeemuddin et al., 2023; Sharma et al., 2025).

Figure 24 Glycyrrhiza glabra plant and its root (Abraham & Florentine, 2021)

Figure 25 Glycine max (soybeans) (Edde, 2022)

Lactobacillus delbrueckii-fermented soybeans influence gut microbiota, strengthen the intestinal barrier, reduce pro-inflammatory cytokines (IL-4, IL-6, IL-8), and alleviate GERD symptoms. A 12-week study involving 110 adults demonstrated considerable improvement in heartburn and regurgitation, along with decreased inflammation, establishing the safety and effectiveness of fermented soybeans as an adjunct treatment for GERD (Tan et al., 2024).

13. Order: Asterales (Family: Asteraceae ex; *Artemisia campestris, Artemisia absinthium, Sonchus oleraceus* L.)

Artemisia campestris, rich in antioxidants, restores antioxidant enzyme activity and protects the esophageal mucosa. Traditionally, it treats digestive issues, skin conditions, diabetes, hypertension, and venom effects (Jabri et al., 2018). *Sonchus oleraceus* L. contains flavonoids and phenolic compounds with gastroprotective, antioxidant, anti-inflammatory, antisecretory, and anti-ulcer properties, used for gastrointestinal diseases and inflammation (Vecchia et al., 2022). *Artemisia absinthium* L. (wormwood) has bioactive compounds that provide gastroprotection, anti-ulcer, anti-inflammatory, and antioxidant effects (Boeing et al., 2023). Studies on gastric ulcer and GERD models show these plants reduce ulcer indices, oxidative stress, inflammatory cytokines (TNF-α, IL-1β, IL-6), Myeloperoxidase (MPO) activity, gastric acid secretion, and restore mucus content

without harmful side effects (Jabri et al., 2018; Vecchia et al., 2022; Boeing et al., 2023).

Figure 26 Sonchus oleraceus L. (Puri et al., 2018)

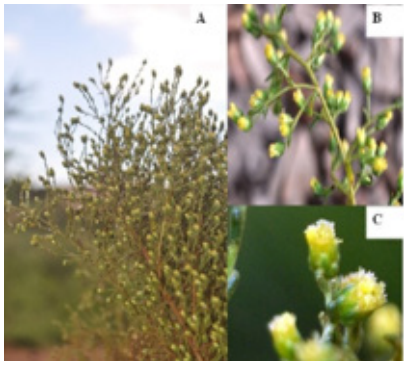

Figure 27 Artemisia campestris; A. General plant; B. Flower heads; C. Inflorescence (Dib et al., 2017)

Figure 28 Artemisia absinthium L. (Tobyn et al., 2011)

14. Order: Apiales (Family: Apiaceae ex; *Coriandrum sativum, Cuminum cyminum, Foeniculum vulgare, Centella asiatica*)

Figure 29 Foeniculum vulgare; A. In its natural habitat; B. Stem; C. Leaves; D. inflorescences and flowers; E. Fruits; and F. Population of F. vulgare (Badgujar et al., 2014)

Figure 30 Coriandrum sativum (Arituluk, 2022)

Centella asiatica and *Cuminum cyminum*, extracted from various plant parts, are key in the HAGE-101912 polyherbal formulation, showing anti-reflux, prokinetic, and gastroprotective effects (Azeemuddin et al., 2023). *Foeniculum vulgare* and *Coriandrum sativum*, used in Unani formulations, primarily utilize seed extracts and roots for treating gastrointestinal, respiratory, skin diseases, asthma, arthritis, and wounds (Sehar et al., 2021; Sharma et al., 2025). Their efficacy is supported by animal studies, clinical trials, and antioxidant assays (DPPH, ABTS, FRAP), showing reduced ulceration, increased gastric mucosa, decreased gastric acid, improved esophageal sphincter function, and symptom relief comparable or superior to omeprazole (Azeemuddin et al., 2023; Sehar et al., 2021; Sharma et al., 2025).

Figure 31 Centella asiatica (Azerad, 2016)

15. Order: Lamiales (Family: Plantaginaceae ex; *Plantago ovata*, Oleaceae ex; *Olea europaea,* Lamiaceae ex; *Salvia officinalis, Satureja hortensis*)

Figure 32 Olea europaea (Calabriso et al., 2015)

Olea europaea oil extract is utilized to treat GERD owing to its antioxidant and anti-inflammatory properties. It addresses fever, diarrhea, skin infections, joint discomfort, and healing of wounds. The leaf extract, abundant in oleuropein and antioxidant, minimizes gastric mucosal harm by decreasing oxidative stress and boosting enzyme activity. Clinical trials indicated a notable decrease in pro-inflammatory cytokines, and the combination with PEA enhanced GERD treatment, although gas bloating and dysphagia were noted as side effects (Al-Sulivany et al., 2024; Alecci et al., 2016).

Figure 33 Plantago ovata; A. Vegetative; B. Reproductive phase; C. P. ovata ovaries. (Kotwal et al., 2016)

Psyllium seed (*Plantago ovata*) extract, rich in soluble fiber and mucilage, is effective and safe for managing functional constipation in GERD patients. It reduces GERD recurrence risk better than omeprazole and elimination of clinical symptoms was observed in studies (Hosseini et al., 2018).

Satureja hortensis L., with carminative, antispasmodic, and anti-inflammatory properties, was tested in a double-blind trial in GERD patients. However, 500 mg thrice daily did not improve symptoms compared to placebo; improvements were likely due to lifestyle changes in both groups (Kashani et al., 2018).

Figure 34 Satureja hortensis L. (Kazempour et al., 2021)

Salvia officinalis (sage) leaf extract contains terpenoids, phenolic acids, flavonoids, and other active compounds with strong antioxidant, antimicrobial, and anti-inflammatory activities. It scavenges free radicals, modulates oxidative stress by boosting enzymes like Superoxide Dismutase (SOD) and catalase, inhibits NF-κB, and suppresses bacterial growth. Multiple assays confirm its potency, but further clinical studies are needed to confirm its benefits in humans (Brindisi et al., 2021; Šobot et al., 2024).

Figure 35 Salvia officinalis ("Salvia Officinalis (Common Sage)," 2022)

A total of 22 studies were included, consisting of 12 animal experiments, 7 human clinical trials, and 3 in-vitro studies. For this review, no statistical analysis was performed. Quantitative data such as percentage changes, mean differences, sample size, and P-value from the included studies were extracted and synthesized descriptively. It describes the efficacy and the safety of medicinal plants used in the management of GERD.

Compared to standard proton pump inhibitor therapy, clinical studies demonstrate that symptoms improve effectively from 40% to 100% with multiple herbal formulations. Experimental animal studies demonstrated a significant reduction in ulcer index, gastric acid secretion, and inflammatory cytokine levels ($p < 0.05$), along with improvements in gastric mucosal protective mechanisms. Overall, these findings highlight the important therapeutic value of medicinal plants in the management of GERD.

The following bar chart exhibits the percentages of symptom reduction across the families of medicinal plants which are included in the study.

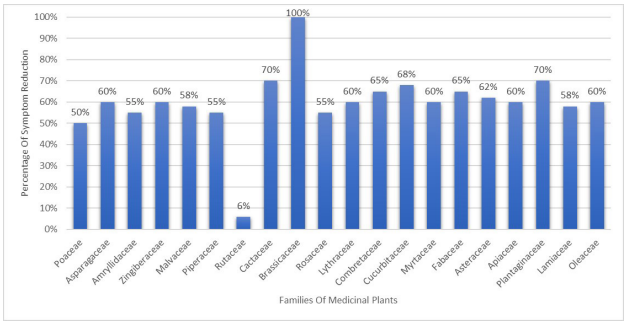

Figure 36 Percentage of symptom reduction across the families of medicinal plants

Identified side effects

Most of the clinical trials conducted on herbal formulations for the management of GERD showed a good safety profile. In preclinical studies, the herbal extracts showed no significant toxicity and mortality when tested on animals. In fact, some of the extracts showed non-cytotoxic activity. Further, clinical trials have given promising results where herbal interventions have been found to be generally well tolerated, with mild and self-limiting side effects. For example, a randomized trial of a comparison of Ayurvedic Ayucid capsules and omeprazole was conducted, and although mild side effects were noted in the herbal and omeprazole groups, respectively, there were no treatment withdrawals. In this trial, there were 26 side effects in the herbal group and 13 in the omeprazole group were identified (Tamoli et al., 2018). The reported symptoms of gas bloating, dysphagia, and constipation were found to be infrequent and mild in nature (Zohalinezhad et al., 2015; Al-Sulivany et al., 2024). Thus, it can be concluded that, according to the available evidence, herbal therapy appears to have good safety, although long-term safety and pharmacovigilance studies are limited in scale.

Linked Interactions with Medication for GERD

Herbal drugs employed in the management of GERD may be expected to produce pharmacokinetic interactions with conventional pharmacotherapy; however, evidence on the occurrence of such interactions with GERD drugs is limited. Therefore, knowledge on the safety profile of conventional GERD drugs is essential.

Antacids, proton pump inhibitors, and histamine-2 receptor antagonists are commonly used drugs for GERD. Antacids with aluminium content may cause constipation. Additionally, prolonged antacid use may cause renal problems. Diarrhoea is a possible side effect of magnesium and calcium antacids. Excessive use of calcium antacids may cause constipation, hypercalcemia, and nephrolithiasis (Hershcovici & Fass, 2011).

Long-term use of antacids and proton pump inhibitors may cause electrolyte imbalance and renal toxicity (Ansong et al., 2025). Proton pump inhibitors (PPIs) and histamine 2 receptor antagonists are highly effective at inhibiting acid secretion. But their long-term use has been associated with several potential concerns. These concerns include rebound acid hypersecretion, relapses of symptoms after the termination of the treatment, nutrient malabsorption, increased risk of infections, gastric mucosal effects, and bone mineral density loss (Zhang et al., 2021). The safety profile of the histamine-2 receptor antagonists, such as ranitidine, was generally considered satisfactory during the clinical trials. The safety considerations included the use of drug during pregnancy and regulatory issues, which need to be evaluated with caution (Zhang et al., 2021).

With the above considerations in mind, more clinical studies need to be conducted on the possible pharmacodynamic and pharmacokinetic interactions between herbal therapies and proton pump inhibitors, H2 receptor antagonists, and prokinetics. Such studies will help monitor the safety and therapeutic effects.

DISCUSSION

This comprehensive review brings forward experimental and clinical evidence with respect to the role of medicinal plants in the management of gastroesophageal reflux disease (GERD), where a particular focus has been given on esophageal mucosal protection. The reliability of the available evidence with respect to the strength and translational value has shown variability across the studies.

The preclinical evidence reviewed in this paper has revealed some notable patterns. The majority of the studies have shown supportive evidence that shows a reduction in esophageal lesion scores, oxidative stress markers, gastric acidity, and pro-inflammatory mediators after administration of these herbal extracts. On a more technical note, antioxidant activity levels may play a vital role in the protection of the gastric mucosa. The majority of the investigated plants have demonstrated a decrease in oxidation activity and an enhancement of antioxidant enzymes namely, superoxide dismutase and glutathione peroxidase. In addition, these plants have demonstrated a reduction of inflammatory pathway activity, especially NF-κB and cytokines such as TNF-α, IL-1β, and IL-6. These mechanisms support the basis of how these potential treatments may protect against GERD-related damage.

Strength of available evidence

Herbal therapies for gastroesophageal reflux disease (GERD) and related gastric disorders show valuable therapeutic potential across preclinical, animal, and limited clinical investigations. Several plant-derived compounds and polyherbal formulations appear to exert protective effects on the esophageal and gastric mucosa through multiple biological mechanisms. For example, the Ayurvedic polyherbal formulation HAGE-101912 has been reported to reduce esophageal

injury through antacid activity, proton pump inhibition, lower esophageal sphincter (LES) modulation, and prokinetic effects that improve gastric emptying (Azeemuddin et al., 2023).

Several phytochemicals with strong antioxidant and anti-inflammatory activity also play a vital role in mucosal protection. Black garlic (*Allium sativum*) has been shown to exert antioxidant and anti-inflammatory effects in reflux models by enhancing endogenous antioxidant enzymes and suppressing inflammatory cytokine (NF-κB) signaling pathways (Nan et al., 2018). Combinations of bioactive compounds such as curcumin and quercetin have demonstrated synergistic inhibition of inflammatory mediators, suggesting that polyphenolic interactions may enhance therapeutic efficacy compared with single compounds alone (Azeemuddin et al., 2023). Oxidative stress and inflammatory signaling pathways play an essential role in esophageal mucosal injury. Therefore, these mechanisms are biologically plausible in GERD pathophysiology.

Although most available evidence is derived from experimental models, several clinical investigations have reported symptomatic improvement with herbal therapies. Certain Ayurvedic formulations have shown valuable clinical outcomes compared to antacids in relieving GERD-related symptoms with favorable safety profiles (Azeemuddin et al., 2023). Similarly, some studies show psyllium seeds, mastic gum, and coriander-based triphala formulations have been reported to provide symptom relief compared to proton pump inhibitors (PPIs), with improved safety and tolerability profiles (Hosseini et al., 2018). Furthermore, meta-analytical evidence suggests that combining herbal therapies with PPIs may enhance clinical outcomes in GERD management compared with conventional therapy alone (Zhang et al., 2021).

The overall strength of the above evidence is limited. Many studies involve small sample sizes, short follow-up periods, and heterogeneous herbal formulations. Several trials focus primarily on symptom-based assessment rather than objective diagnostic assessment such as endoscopic healing or ambulatory pH monitoring. Most of the research has also been conducted in Asian populations, which may limit the generalizability of the findings to other regions because the dietary habits and lifestyle of other regional populations are different compared to Asian population. Standardization of herbal preparations and consistent pharmacological characterization remain major challenges, and potential herb–drug interactions with conventional GERD medications have not been extensively investigated. Therefore, large multicenter randomized clinical trials with standardized formulations and longer follow-up periods are required to establish reliable clinical efficacy (Zhang et al., 2021).

Cultural and Regional Use of Medicinal Plants

The use of medicinal plants for gastric disorders has deep historical roots in multiple traditional medical systems. Traditional Chinese medicine (TCM) incorporates herbal formulations such as Jianpi and Ligan Hewei therapy, often combined with acupuncture, to improve gastrointestinal motility and protect mucosal integrity (Zhang et al., 2021).

Ayurvedic and Persian medical traditions aim to restore physiological balance through herbal preparations that reduce inflammation and regulate gastric acidity; for example, Ayucid capsules are used to alleviate reflux symptoms and mucosal irritation (Tamoli et al., 2018). Polyherbal formulations such as coriander-based triphala, containing *Coriandrum sativum* and related ingredients, have demonstrated antioxidant activity and anti-*Helicobacter pylori* effects (Sharma et al., 2025).

Ethnobotanical evidence highlights the extensive use of medicinal plants in indigenous medicines. For example, the Adi tribal community has been reported to use more than 54 plant species for digestive disorders, preparing herbal pastes,

decoctions, and extracts from locally available plants (Chetry et al., 2018). Even though these medicinal plants have been used since ancient times, many of them still have not been scientifically standardized and approved by the regulatory authorities.

Integration with Conventional Therapy

Herbal medicine also shows potential as an adjunctive therapy to conventional GERD therapy. Some studies suggest that combining herbal formulations with PPIs may enhance therapeutic outcomes. For example, the combination of Jianpi therapy with PPI treatment has been reported to improve clinical outcomes, while Ligan Hewei therapy combined with PPIs demonstrated improved mucosal healing compared with PPI monotherapy (Zhang et al., 2021). Certain phytochemicals such as curcumin and quercetin exert anti-inflammatory effects through inhibition of NF-κB signaling, which may complement acid suppression mechanisms of PPIs (Azeemuddin et al., 2023).

Some herbal therapies target physiological mechanisms beyond acid suppression. The polyherbal formulation HAGE-101912 has been shown to enhance LES tone and improve gastric emptying (Azeemuddin et al., 2023), while psyllium seeds have been reported to alleviate GERD symptoms in patients with constipation and reduce relapse rates compared with omeprazole therapy (Hosseini et al., 2018). Safety profiles of most herbal therapies appear favorable, although mild adverse effects such as allergic dermatitis associated with mastic gum, gas bloating, and dysphagia have occasionally been reported (Zohalinezhad et al., 2015; Al-Sulivany et al., 2024). These treatments can be used with standard medicines like PPI as a long-term therapy to keep symptoms away.

A successful integration of herbal medicine into conventional GERD management requires standardized formulations, controlled dosing, and comprehensive evaluation of potential herb–drug interactions. Detailed pharmacological studies and well-designed clinical trials are essential to ensure both efficacy and safety before widespread clinical implementation.

CONCLUSION

This review reveals that 30 medicinal plants from 19 families have significant therapeutic potential for treating Gastroesophageal Reflux Disease (GERD), primarily due to their mucoprotective, anti-inflammatory, and gastric acid-regulating effects. The findings suggest that this herbal treatment can effectively treat heartburn and regurgitation symptoms by enhancing esophageal mucosal resistance and improving lower esophageal sphincter function, serving as a cost-effective and well-accepted therapy compared to conventional Proton Pump Inhibitors (PPIs) and Histamine-2 Receptor Antagonists (H2RAs). The existing evidence is limited by small sample sizes, short trial durations, and varied preparations, although these medicines show favourable safety profiles and have a long history of traditional use. Herbal drugs play a vital role as alternative or primary treatment, but the interaction with conventional therapy should be evaluated carefully. Standardizing herbal therapy and conducting clinical trials to ensure safety and efficacy are important to integrate them into modern conventional therapy. Herbal drugs show considerable potential as an adjunctive therapy or primary therapy, particularly in regions like Sri Lanka with robust traditional medical systems.

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