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HERBAL THERAPEUTICS FOR PEPTIC ULCER DISEASE: A PHARMACOLOGICAL AND PATHOPHYSIOLOGICAL REVIEW

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ABSTRACT
Peptic ulcer disease (PUD) is a prevalent gastrointestinal condition marked by mucosal erosion in the stomach or duodenum, often associated with *Helicobacter pylori* infection—affecting up to 81% of those diagnosed. Risk factors include male gender, advanced age, smoking, low socioeconomic status, and familial history. While conventional treatments such as antacids, proton pump inhibitors, and antibiotics are commonly employed, issues like recurrence and adverse effects have spurred interest in alternative therapies. Medicinal plants, known for their multi-targeted actions and low toxicity, are gaining recognition as promising candidates in ulcer management. This review explores the role of phytomedicine in ulcer healing, highlighting herbs such as *Asparagus racemosus*, *Glycyrrhizaglabra*, and *Emblica officinalis* for their mucosal protective, anti-*H. pylori*, antioxidant, and anti-inflammatory properties. Additional botanicals like *Plumbagozeylanica*, *Ocimum sanctum*, and *Solanum nigrum* influence acid secretion and bolster gastric defenses, while *Anacardiumoccidentale*, *Jasminum grandiflorum*, and *Terminalia chebula* exhibit cytoprotective and anti-inflammatory effects. Supported by pharmacological and analytical evidence, these herbs offer a compelling case for integrative approaches in PUD treatment. The review emphasizes the pathophysiological underpinnings of ulcer formation and consolidates scientific insights into plant-based anti-ulcer therapies.

KEYWORDS: Peptic Ulcer Disease (PUD), Herbal therapeutics, Helicobacter pylori, Phytomedicine.

INTRODUCTION
People with peptic ulcer illnesses have a rate of Helicobacter pylori infection as high as 81 percent.[1] According to study, factors like male gender, older age, poorer socioeconomic position, smoking, having a family history of peptic ulcers, and *H. pylori* infection were all linked to an increased chance of developing peptic ulcers. Peptic ulcer disease is a common gastrointestinal disorder characterized by lesions in the stomach or duodenal lining due to an imbalance between aggressive and protective factors. While conventional treatment typically includes antacids, proton pump inhibitors, and antibiotics, the recurrence rate and side effects have led to a growing interest in alternative therapies. Herbal remedies, rooted in traditional medicine, are gaining attention for their multi-targeted mechanisms and lower toxicity. Numerous medicinal plants have demonstrated potential in promoting mucosal defense, reducing gastric acid secretion, and exerting antioxidant and anti-inflammatory effects. Among these, *Asparagus racemosus*, known for its mucosal protective action, shows remarkable healing in stress-induced and drug-induced ulcers. *Glycyrrhiza glabra* offers anti-*Helicobacter pylori* activity and enhances prostaglandin-mediated mucus production. *Emblica officinalis* acts through antioxidant pathways and inhibits microbial growth. Plants like *Plumbago zeylanica*, *Ocimum sanctum*, and *Solanum nigrum* modulate acid secretion and reinforce mucosal integrity. Others such as Anacardiumoccidentale, *Jasminum grandiflorum*, and *Terminalia chebula* exhibit healing through anti-inflammatory and cytoprotective effects. These herbs, supported by analytical and pharmacological studies, hold promise as complementary or alternative anti-ulcer therapies. This review aims to explore the pathophysiological basis of ulcers and highlight herbal interventions validated through scientific evidence.

Pathogenesis: The schematic presentation of Pathogenesis mentioned in below figure-1.

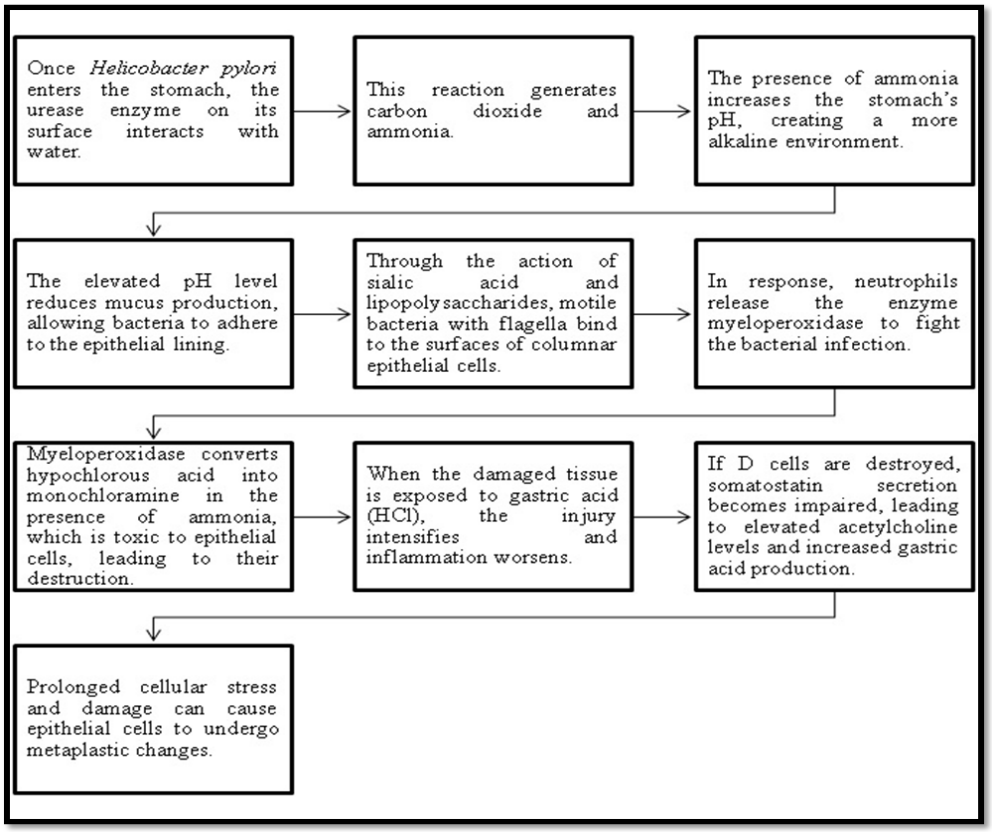

Figure 1: Pathogenesis of Peptic Ulcer.[2]

Herbs exert therapeutic effects on peptic ulcers by modulating key pathogenic factors such as gastric acid secretion, oxidative stress, and inflammation. Integrating these herbs targets multiple pathways involved in ulcer development, promoting mucosal healing and protection mentioned in figure-2.

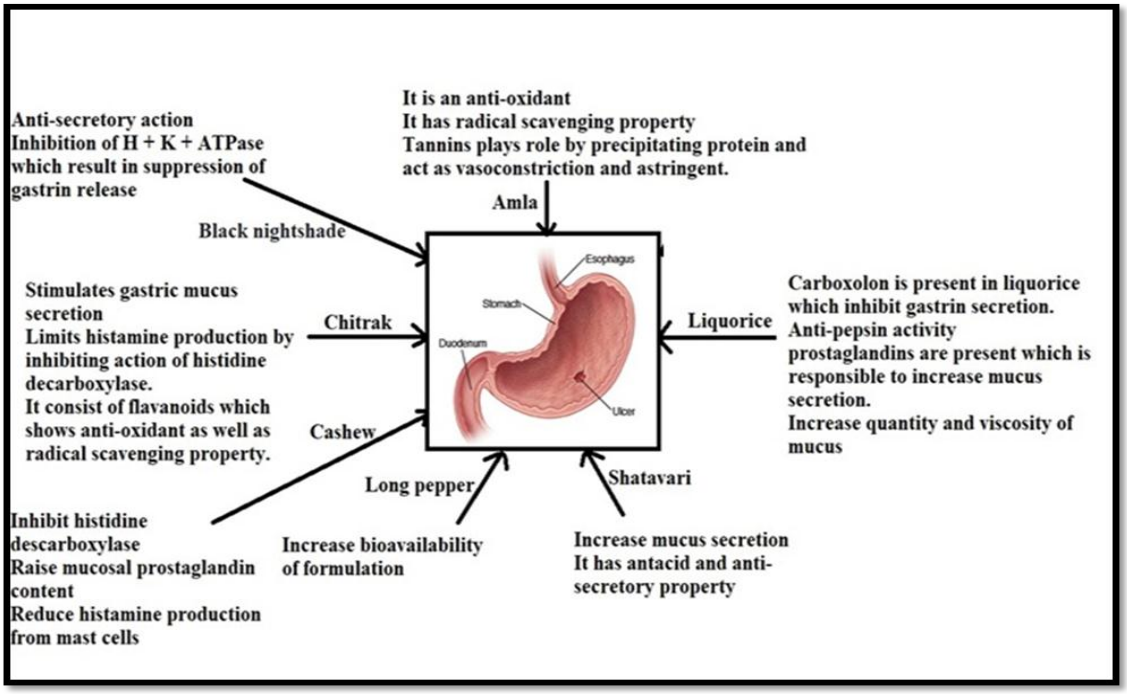

Figure 2: Possible herbs as anti-ulcer with its analytical approach.

Asparagus racemosus **(Shatavari)** is recognized in classical Ayurvedic texts such as the *Charaka* and *Susrutha Samhitas* as an important *sitavirya* herb used in the management of peptic ulcer disease. Experimental studies have demonstrated the anti-ulcerogenic potential of fresh root juice of A. racemosus against various ulcer

models, including pylorus ligation and cold-restraint stress-induced gastric ulcers. Clinical administration of Ayurvedic formulations containing A. racemosus twice daily over a month has resulted in significant symptom relief and endoscopic evidence of ulcer healing.

Mechanistically, A. racemosus enhances mucosal defense by reducing epithelial cell shedding and increasing mucin secretion, thereby strengthening the gastric mucosal barrier. In indomethacin-induced ulcer models, crude extracts of A. racemosus significantly lowered the ulcer index and decreased gastric secretion volume, primarily through inhibition of gastric hydrochloric acid release, which protects the mucosa from acid-related injury. The powdered root also supports healing by promoting the longevity of gastric mucosal epithelial cells and increasing both the secretion and viscosity of gastric mucus.

Clinical observations further confirm the efficacy of fresh root juice in patients with duodenal ulcers, with marked symptomatic improvement. Moreover, combinations of A. racemosus with other herbs like Terminalia chebula have shown synergistic effects, reducing ulcer severity and protecting against ulcerogenic agents such as pentagastrin and carbachol. Studies indicate that A. racemosus may reduce the responsiveness of gastric parietal cells to secretagogues and narcotic agents, reflected by decreased gastric secretion volume and elevated gastric pH. However, its lack of direct antacid or strong antisecretory activity suggests that its protective effects are largely mediated via enhancement of mucosal defense rather than acid suppression.[3-12]

Plumbago zeylanica (Chitrak) exhibits significant anti-ulcer potential, attributed to its ability to reinforce the gastric mucosal barrier, suppress excessive acid secretion, and mitigate oxidative stress-induced mucosal injury. Its bioactive constituents contribute to the prevention of ulcer formation and promote gastrointestinal healing in experimental studies. Phytochemical analyses reveal that the roots contain flavonoids, which possess potent antioxidant properties and act as free radical scavengers. These compounds contribute to strengthening the gastric mucosal defense by stimulating mucus secretion, thereby protecting the lining of the stomach. Experimental studies demonstrate that Plumbago zeylanica effectively prevents ulcer formation and reduces gastric acid secretion. One mechanism involves the inhibition of histidine decarboxylase, the enzyme responsible for histamine synthesis in the gastric mucosa, thus limiting histamine-induced acid release. Its strong anti-ulcer potential is supported by multiple investigations showing reduced ulcer indices in animal models. Additionally, tannins present in the root may confer protection by forming a protective proteinaceous layer over the inflamed mucous membranes of the gastrointestinal tract, reducing irritation and promoting healing. Notably, Plumbago zeylanica exhibits inhibitory activity against *Helicobacter pylori*, a key bacterium implicated in the pathogenesis of gastric ulcers, further underscoring its therapeutic value in ulcer management.[13-21]

Solanum nigrum **(Black nightshade)** extract has demonstrated significant anti-ulcer activity in experimental models. In pylorus-ligated animals, the extract reduces pepsin concentration and secretion, as well as the volume, concentration, and overall output of gastric acid. In ethanol-induced ulcer models, treatment resulted in elevated plasma gastrin levels alongside increased gastric mucosal H^+/K^+-ATPase activity, a key enzyme involved in acid secretion. The anti-secretory effect of Solanum nigrum is primarily attributed to inhibition of H^+/K^+-ATPase and suppression of gastrin release, contributing to reduced acid secretion. Additionally, its ulcer-protective and healing properties are likely linked to both antisecretory and antioxidant mechanisms. Pretreatment with Solanum nigrum extract effectively modulates gastric acid secretion, inhibits histamine release, and suppresses gastric endocrine cell proliferation, leading to a marked decrease in gastrin hormone levels, thereby protecting the gastric mucosa from ulceration.[22]

Anacardium occidentale **(Cashew)** leaves have demonstrated notable antiulcerogenic activity, particularly a 70% ethanolic extract which dose-dependently inhibited gastric lesions induced by HCl/ethanol in experimental models. Phytochemical analysis of this extract reveals a rich presence of flavonoids, including saponins and quercetin glycosides, compounds known for their potent antioxidant properties. Flavonoids contribute to ulcer prevention by inhibiting histidine decarboxylase, thereby reducing histamine release from mast cells and increasing mucosal prostaglandin levels, which enhance gastric mucosal defense. Additionally, quercetin itself has been identified as an effective agent in protecting against gastric mucosal damage. Several saponins isolated from cashew leaves also exhibit anti-ulcer activity, further contributing to the gastroprotective effects of the extract.[23-27]

Jasminum grandiflorum leaf extract has shown notable ulcer healing effects, with studies demonstrating its capacity to elevate gastric juice pH and decrease stomach volume, free acidity, and total acidity, thereby contributing to mucosal protection and ulcer resolution. The anti-ulcer activity may be attributed to the soothing effects of essential oils and the protein-precipitating ability of tannins present in the leaves. Pretreatment with the extract has been shown to restore mucosal glandular structures fully, suggesting potent anti-secretory and antioxidant effects. Reactive nitrogen species (RNS) are known contributors to gastric mucosal damage, and the leaf extract exhibits dose-dependent inhibition of nitric oxide radicals. This antioxidant capacity is likely due to phenolic compounds identified via the Folin-Ciocalteu

method. Superoxide dismutase (SOD) and catalase (CAT), key antioxidant enzymes that neutralize harmful free radicals by converting superoxide anions into hydrogen peroxide and then into water, respectively, are crucial in gastroprotection. Depletion of these enzymes increases susceptibility to oxidative damage via lipid peroxidation. Treatment with *Jasminum grandiflorum* ethanolic leaf extract has been found to restore SOD and CAT levels close to normal, supporting its role in mitigating oxidative stress and promoting gastric mucosal healing.[28-32]

Anogeissus latifolia bark extract exhibits protective effects on the gastric mucosa, potentially through the inhibition of the enzyme 5-lipoxygenase, which plays a role in inflammatory pathways. Phytochemical analysis reveals that the extract contains substantial amounts of gallic acid (0.95% w/w) and ellagic acid (0.25% w/w). These phenolic compounds contribute to the extract's potent antioxidant activity, which is likely, a key mechanism underlying its anti-ulcer properties.[33]

Willow-Leaved/ *Utleria salicifolia*: The 50% ethanolic extract of *Utleria salicifolia* rhizome demonstrates dose-dependent anti-ulcer efficacy. Administration of the extract at doses of 100 and 200 mg/kg provided 68% and 90% protection, respectively, against cysteamine-induced duodenal ulcers in rats. The anti-ulcer effect is attributed to enhanced free radical scavenging by the body's primary defense systems, which correlates strongly with endocrinological responses, particularly plasma corticosterone levels. Additionally, the protective mechanism involves an increase in gastric prostaglandin synthesis and sulfhydryl compounds, both of which play critical roles in mitigating ethanol-induced gastric mucosal injury. During superficial mucosal damage, increased secretion of gastric mucus creates a favorable microenvironment that supports restitution and mucosal repair.[34-37]

Hemidesmus indicus root extract demonstrates significant gastroprotective activity by enhancing gastric mucosal defense mechanisms. Treatment with the extract results in increased levels of protective factors such as gastric pH, hexose, hexosamine, fucose, and sialic acid, whereas the extract simultaneously reducing harmful factors like pepsin and total protein content. The elevated carbohydrate-to-protein ratio suggests enhanced mucin production, contributing to the strengthening of the mucosal barrier. Additionally, a rise in sodium and potassium ion concentrations in the treated group implies an associated increase in bicarbonate ion secretion, which plays a vital role in neutralizing gastric hydrochloric acid and protecting the gastric epithelium. Notably, root extracts collected during the flowering stage exhibit greater anti-ulcer potential than those obtained during the vegetative stage. This difference is likely attributed to variations in the phytochemical profile, particularly the presence and concentration of saponins, terpenoids, and amino acids known for their gastroprotective effects. These constituents may contribute to the extract's ability to reduce mucosal injury and promote ulcer healing.[38-40]

Terminalia chebula **(Chebulic Myrobalan)** has demonstrated significant anti-ulcer activity, particularly through its hydroalcoholic extract, which markedly reduces ethanol-induced gastric ulceration. The extract demonstrates potent gastroprotective activity by reinforcing the gastric mucosal barrier. Chebulinic acid, a principal bioactive compound, has been identified to exert both antisecretory effects by reducing gastric acid secretion and mucosal protective actions that aid in preserving gastric tissue integrity. It reduces free and total gastric acidity while simultaneously enhancing mucin secretion, thereby reinforcing the gastric barrier. Furthermore, chebulinic acid inhibits H^+/K^+-ATPase activity, contributing to reduced gastric acid output. The compound has also shown therapeutic potential in managing *Helicobacter pylori*-associated gastrointestinal disorders, highlighting its dual role in both ulcer prevention and microbial control.[41-43]

Bacopa monnieri (Brahmi) exhibits both preventive and therapeutic effects on gastric mucosa, primarily attributed to its potent antioxidant activity rather than effects on cellular proliferation. The antioxidant properties of Bacopa monnieri extract (BME) contribute to mucosal protection by neutralizing reactive oxygen species that contribute to gastric injury. In vitro studies have demonstrated its spasmolytic activity on intestinal smooth muscle, likely mediated through the inhibition of calcium influx across cell membrane channels. These smooth muscle relaxant and anti-inflammatory properties support its role in gastrointestinal protection. Additionally, experimental research confirms the anti-ulcerogenic potential of BME, indicating its efficacy in both preventing and managing gastric ulcers.[44-46]

CONCLUSION

Peptic ulcer disease continues to pose a significant global health burden, primarily associated with *Helicobacter pylori* infection, NSAID use, and lifestyle-related factors. Although conventional therapies such as proton pump inhibitors and antibiotics offer symptomatic relief and bacterial eradication, issues like drug resistance, recurrence, and adverse effects necessitate the exploration of safer alternatives. In this context, herbal medicines offer a promising and multi-targeted therapeutic strategy. Medicinal plants including *Asparagus racemosus*, *Glycyrrhiza glabra*, *Emblica officinalis*, *Ocimum sanctum*, *Plumbago zeylanica*, and *Solanum nigrum* have demonstrated significant anti-ulcerogenic potential through diverse mechanisms—such as enhancing mucosal protection, scavenging free radicals, inhibiting *H. pylori*, and modulating acid secretion. The therapeutic efficacy of these botanicals is largely attributed to their rich phytochemical composition, particularly flavonoids, tannins, saponins, and phenolic compounds. These bioactive constituents

contribute synergistically to ulcer healing by restoring antioxidant enzyme levels, reinforcing the gastric mucus barrier, and reducing inflammation. Extensive in vitro and in vivo research supports the gastro-protective effects of these herbs, highlighting their potential as complementary or adjunct therapies. Future efforts should focus on rigorously designed clinical trials to establish their safety profiles, therapeutic efficacy, and optimal dosing regimens. Standardization of plant extracts, elucidation of molecular mechanisms, and development of novel delivery systems will further enhance their clinical applicability. With increasing global interest in evidence-based phytotherapy, antiulcer herbs hold significant potential in shaping future strategies for holistic and sustainable ulcer management.

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Abbreviations: H^+/K^+-ATPase: Hydrogen-Potassium Adenosine Triphosphatase enzyme, BME: Bacopa monnieri Extract, SOD: Superoxide Dismutase, CAT: Catalase, and RNS: Reactive Nitrogen Species.

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