Gastroprotective effects of herbal medicines (roots)

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ABSTRACT
Herbal medicines are now commonly used all over the world and this has increased global demand. Quality, safety, and efficacy of these drugs have become a serious concern. This review presents the medicinal plants cited in folklore that are used to treat gastrointestinal ulcers. Electronic databases, that is, Web of Science, PubMed, Scopus, and Google Scholar were searched to identify the gastroprotective effects of each plant. Ethnopharmacological studies have reported various botanical products with antiulcer activities, but there has been limited scientific research, presenting clinical data to validate the efficacy and safety of medicinal herbs as gastroprotective agents. Most studies centered on pharmacological properties of medicinal herbs as used animals models. This information has prompted us to compile a list of the medicinal herbs cited in folklore with gastroprotective activity.

INTRODUCTION

Peptic ulcer disease (gastric or duodenal) has been a major menace to world populations for more than a century. It has caused significant morbidity and substantial mortality. There is a discrepancy in the pathophysiology of peptic ulcer disease between protective factors (bicarbonate, mucin, prostaglandin, nitric oxide, and other peptides and growth factors) and aggressive agents (acid and pepsin). Treatment and prevention of acid-related disorders are achievable either by reducing levels of gastric acidity or by elevating mucosal protection. Several factors might contribute to peptic ulcer, such as sedentary lifestyle, genes, diet (e.g., alcohol intake and spicy food), drugs (e.g., NSAIDs), smoking, exposure to various bacterial infections and free radicals, sex, emotional stress, and psychosocial factors. Helicobacter pylori (H. pylori) is a major etiologic factor that has a significant influence on susceptibility to peptic ulcer disorder. It is spiral-shaped, highly motile bacteria, induces peptic ulcer by injuring the mucosal cover protecting the lining of the gastrointestinal (GI) track. Then accordingly it is reasonable that the main aim of clinicians in treating peptic ulcer is eradication of H. pylori from the gastric lumen. Basically, treatment of peptic ulcer has been focused on mitigation of symptoms, healing ulcers, and avoiding reappearance of the ulcer. H pylori is present under the mucus layer of the stomach so its eradication is difficult. Before the bacterium had been detected in the stomach, it was accepted as true that stomach ulcers occurred when gastric mucosa was damaged from excess acid secretion; so management had focused on diminution or neutralization of the mentioned acid. Treatment of peptic ulcer disease should mainly include eradication of H. pylori in cases of this infection. Antimicrobial drugs are recommended effective agents for eradicating this type of infection (e.g., metronidazole, clarithromycin, amoxicillin, and tetracycline) as well as antisecretory agents or inhibitors of proton pump that block the H⁺,K⁺ ATPase pump (e.g., omeprazole and lansoprazole) and antagonists of the H₂-receptor (cimetidine, ranitidine, and famotidine) and Bismuth salt is recommended as an agent that acts...
directly on disruption of the bacterial cell wall or membrane.\cite{9-14} Humans have used herbal medicines since early civilization.\cite{15} As an alternative treatment method, they present an effective source of drugs; nowadays, the use of herbal medicine is now considered integral to practicing a healthy lifestyle.\cite{16,17} According to the previous literatures, there are several articles about GI effects of plants, but these studies are limited to a particular geographical regions or mentioned to the different parts of plants.\cite{18-22} The aim of this review was to evaluate the use of roots of herbal plants for the prevention and treatment of GI ulcers from publications over the period of 1980–2016.

**Materials and method**

In this review, most of the medicinal plants’ roots traditionally used to treat gastric ulcer have been collected from searches in electronic databases including Web of Science, PubMed, Scopus, and Google Scholar. All articles were searched for \textit{in vitro}, \textit{in vivo}, and clinical evidence of therapeutic effects and pharmacological mechanisms of herbal plants. Data were gathered from publications over the period of 1980–2016 and only those in English language were reviewed.

**Results and discussion**

The medicinal plants used to treat peptic ulcer are listed in the succeeding text together with their possible mechanisms and active phytochemical constituents. Table 1 summarizes the results obtained from the evaluation of 34 medicinal plants with gastroprotective or antiulcer effects.

**Aegle marmelos**

\textit{Aegle marmelos} (L.) Correa (Family: Rutaceae) or Bael tree is a medium sized, armed deciduous tree that grows in tropical and subtropical climates. It is indigenous to India, found in South East Asia, and has been introduced to Florida and Hawaii, USA.\cite{23,24} Some parts of the plant have been used to treat diarrhea, dyspepsia, dysentery, and diabetes mellitus.\cite{24} Previous studies have reported anti-inflammatory, antipyretic, analgesic, antifungal, antibacterial, antiviral, antioxidant, antiulcer, antimalarial, anticancer, antihyperlipidemic, and radioprotective activities from different parts of \textit{A. marmelos}.\cite{25} Further investigations on fruits and roots of \textit{A. marmelos} suggested gastroprotective and antiulcer properties through its related antioxidant mechanism. The 50\% ethanolic extract of root showed dose-dependent ulcer protective activity in different chronic and acute gastric ulcer models in rats. \textit{A. marmelos} reduced the ulcer index with decreasing significantly in lipid peroxidation, superoxide dismutase, and increasing in the catalase activities. Phytochemical analyses of \textit{A. marmelos} showed the positive results for the alkaloids, flavonoids, saponins, steroids, terpenoids, and tannins.\cite{26,27}

**Aerva persica**

\textit{Aerva persica} Burm. (Family: Amaranthaceae) is a hoary-tomentose, annual herb located in the warmer parts of Asia and Africa. It is frequently found in western Himalaya, Punjab, and Kashmir.\cite{28} It is universally used in traditional medicine for its diuretic and demulcent properties. Roots of the plant are chewed on to clean teeth and they can be made into a paste for removing acne from the face. It has been said that the wooly seeds are useful for relieving headaches. Several biological activities have been reported from \textit{A. persica} such as antioxidant, antibacterial, antifungal, hypoglycemic, and antiulcer effects. In addition, its roots and flowers have demonstrated medicinal properties against rheumatism and kidney troubles.\cite{28,29} According to an investigation about antiulcer properties of \textit{A. persica} roots, the histopathological evaluation of tested rat gastric mucosa revealed that management with ethanol extract of \textit{A. persica} roots reduced ethanol-induced hemorrhagic necrosis in rat stomach.\cite{29}
| Botanical name | Family            | Part used in peptic ulcer | Remark                                                                                                                                 |
|---------------|-------------------|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| Aegle marmelos | Rutaceae          | 50% Ethanolic extract of root | Gastroprotective and antiulcer properties related to antioxidant mechanism.                                                                                     |
| Aerva persica | Amaranthaceae     | Ethanolic extract          | Pretreatment with the ethanolic extract reduces ethanol- and pylorus ligation-induced hemorrhagic necrosis in rats.                                                               |
| Alhagi camelorum | Fabaceae          | Aqueous extract            | Protection of the rats gastric ulcer against water immersion restraint-stress and ethanol-induced ulcers in a dose-dependent manner.                                |
| Althaea officinalis | Malvaceae       | Aqueous extract            | Stimulation and soothing of the mucosal membrane.                                                                                              |
| Anchusa strigosa | Boraginaceae     | Aqueous extracts           | Protection and treatment of ethanol induced ulcers in rats and guinea pigs.                                                                            |
| Angelica archangelica | Apiaceae    | Hydroalcoholic or lyophilized extracts | Reduction of acid output, increasing the mucus secretion.                                                                                     |
| Aralia elata | Araliaceae        | Araloside A (70% methanolic extract) | Prevention of the ulcerogenesis induced by HCl/ethanol.                                                                                     |
| Arctium lappa | Asteraceae        | Chloroform and ethanol extract | Noticeable protective effect in the ethanol-induced stress gastric ulcer test in rats.                                                                 |
| Asparagus racemosus | Liliaceae      | Fresh juice                | Noticeable protective effect in the ethanol-induced stress gastric ulcer test in rats.                                                                 |
| Asparagus pubescens | Liliaceae      | Methanolic extract          | Possession of significant gastric cytoprotective prostaglandin properties.                                                                 |
| Bupleurum falcatum | Apiaceae        | Water-soluble crude polysaccharides | Antisecretory activity and stimulation of a protective barrier of the mucosa of the gastric tract.                                      |
| Carthamus acanthifolia | Asteraceae | Essential oil              | Antiulcer activity via antihistamine and anticholinergic actions.                                                                 |
| Cassia Sieberiana | Caesalpiniaeae  | Water-soluble crude         | Embarrassment of H\textsuperscript{+}, K\textsuperscript{+}-ATPase, inhibition of H. pylori growth, exhibiting antioxidant potential. |
| Cichorium intybus | Compositae       | Water-soluble crude         | Inhibition of gastric acid secretion by means of blocking H\textsubscript{2} histamine receptors.                                                                 |
| Combretum dolichopetalum | Combretaceae   | Ethanolic extract           | Anti-secretory and cytoprotective properties.                                                                                                  |
| Curcuma amada | Zingiberaceae     | Phenolic compound           | Enhancement of the mucosal defensive factors via the prostaglandin pathway in the cell membrane.                                                                 |
| Curcuma longa | Zingiberaceae     | Ethylacetate extract and curcumin | Anti-H. pylori action.                                                                                                                                 |
| Ficus religiosa | Moraceae          | Ethanolic extract           | Stimulation of PG synthesis, increasing the gastric mucus or leukotriene antagonism.                                                                 |
| Gentiana lutea | Gentianaceae      | Methanolic extract (secoiridoid glycosides) | Reduction of the Ulcer Index of the lesions induced by several ulcerogenic substances.                                                               |
| Glycyrrhiza glabra | Leguminosae    | Glycyrrhetic acid, flavonoids and polysaccharides | Anti-H. pylori action.                                                                                                                                 |
| Guiera Senegalensis | Combretaceae | Aqueous extract            | An absence of halitosis, H. pylori, and gastritis.                                                                                           |
| Hippocratea excelsa | Hipocrateaceae | Aqueous and ethanol extracts | Reduction of the Ulcer Index of the lesions induced by several ulcerogenic substances.                                                               |

(Continued)
| Botanical name     | Family       | Part used in peptic ulcer                        | Remark                                                                                                                                 |
|-------------------|--------------|-------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| Mikania cordata   | Asteraceae   | Methanolic extract (Alkaloids)                  | Activation of cyclooxygenase Enzyme, subsequent stimulation of prostaglandin synthesis and increasing bicarbonate level.            |
| Moringa oleifera  | Moringaceae  | Ethanalic extract                              | Antisecretory, anti-H. pylori, activation of mucous membrane protective factor and cytoprotective effects.                      |
| Mukia maderaspatana | Cucurbitaceae | Ethanalic extract                              | Exhibition potent antiulcer effect by increasing hexeamine and carbohydrate protein ratio and decreasing pepsin content.      |
| Panax ginseng     | Araliaceae   | Aqueous extract                                | Gastroprotective effect via antioxidant and anti-inflammatory activities.                                                             |
| Plumbago auriculata | Plumbaginaceae | Ethanol extract                              | Gastroprotective effect via antioxidant activity, anti-H. pylori.                                                                   |
| Polygonum bistorta | Polygonaceae | Hydroalcoholic extract                          | Inhibition of IL-8 secretion.                                                                                                        |
| Pongamia pinnata  | Fabaceae     | Methanol extract                               | Protection via mucosal offensive and defensive factor.                                                                                   |
| Rumex patientia   | Polygonaceae | Aqueous extract                                | Gastroprotective effects via antioxidant properties.                                                                                   |
| Sophora flavescens | Fabaceae     | Methanol extract (vexibinol, Trifolirhizin)     | Protection of gastric mucosal layer, Inhibition of gastric acid secretion, anti H. pylori.                                              |
| Withania somnifera | Solanaceae   | Withanolides                                    | Inhibition of H. pylori-induced production of IL-1β in dendritic cells.                                                               |
| Zingiber officinale | Zingiberaceae | Beta-sesquiphellandrene, beta-bisabolene, ar-curcumene, 6-shogaol, gingerol, 6-gingesulphonic acid | Thromboxane synthetase property, embarrassment of gastric H+ , K+-ATPase, and H. pylori growth via phenolic antioxidants.         |
| Zizyphus lotus    | Rhamnaceae   | Aqueous extract (saponins, alkaloids, tannins, and flavonoids) | Reduction of gastric juice secretion, antiacid, demulcent effects, and inhibition of H. pylori growth.                             |
**Alhagi camelorum**

*Alhagi camelorum* Fisch. (Family: Fabaceae) or camel thorn is a medicinal plant in folklore. Traditionally, the whole plant is used to treat metabolic, GI and liver disorders, diuretic, wound healing, rheumatic conditions, migraines, fever, warts, and rash.\[^{30}\] Other biological activities such as antioxidant, antidiarrheal, antinociceptive, ureteral stone expulsion, antiulcerogenic, and gastroprotective effects were reported from this plant. Previous knowledge has revealed that aqueous extract of *A. camelorum* showed significantly protective and antisecretory effects in gastric mucosa of rat.\[^{31}\] Another species of Alhagi genus is *Alhagi maurorum* that was applied in management of gastric disturbance in folk medicine. Experimental studies on *A. maurorum* extract demonstrated significant mucosal defense and antisecretory action on gastric mucosa of rat.\[^{32}\]

**Althaeae officinalis**

*Althaea officinalis* L. or marshmallow (Family: Malvaceae) is a downy, annual, or perennial plant native of Asia, Europe, and the United States.\[^{33,34}\] Roots, flowers, and leaves of the plant have been used to treat catarrh in the respiratory system, irritating cough, asthma, bronchitis, sore throat, skin wounds, peptic ulceration, cystitis, gastritis, ventricular ulcer, quinsy, diabetes, urethritis, urinary gravel, and a variety of inflammations in nasal or oral cavities. *A. officinalis* is also used as a demulcent, diuretic, emollient, laxative, anti-infective, and immunomodulation remedy.\[^{35}\] According to previous reports in the literature, aqueous extracts and polysaccharides in this plant present medicinal attributes.\[^{33,34}\] *A. officinalis* contains mucilage, and is very soothing for the mucosal membranes and it coats lining of the esophagus and stomach wall, also Deters et al. have proved effective stimulation of epithelial cells using aqueous extracts and polysaccharides of *A. officinalis* roots, which can demonstrate the traditional use of this plant for treatment of irritated mucous membranes with tissue regeneration.\[^{35,36}\]

**Anchusa strigosa**

*Anchusa strigosa* Bank et Sol, bugloss or alkanet (Family: Boraginaceae) is widely dispensed in the Mediterranean zone. The plant is used in folk medicine for its antimicrobial, antidiabetic, hypotensive, antioxidant, analgesic, sedative, sudorific, diuretic, anti-inflammatory, and gastroprotective effects.\[^{37}\] According to previous research, aqueous extracts of *A. strigosa* roots have shown gastric protective effect on healing of stomach ulcer induced by ethanol. This action involves inhibition of pepsin activity, according tests on animals.\[^{38,39}\]

**Angelica archangelica**

*Angelica archangelica* Linn. (Family: Apiaceae) or garden angelica is a biennial plant distributed throughout tropical and subtropical areas of the world.\[^{40,41}\] It has been widely used in folk medicine. Traditionally, it has been applied to treat respiratory catarrh, bronchitis, asthma, leukoderma, nervous headaches, migraine, chronic fatigue, menstrual and obstetric complaints fever, skin rashes, wounds, rheumatism, toothache, flatulent dyspepsia, anorexia nervosa, and gastric ulcer.\[^{40}\] It has demonstrated stimulation of gastric and pancreatic secretions. *A. archangelica* has also been used as an antiseptic, expectorant, emmenagogue, and as a diuretic agent. *A. archangelica* showed antiulcerogenic effects against gastric ulcers induced by indomethacin in rat. It also shows antisecretory and cytoprotective properties. Its antiulcerogenic activity is related to reduced acid output and increased mucus secretion. Also prostaglandin E2 release and decreased leukotrienes activities were observed in tests on this plant.\[^{42,43}\]
Aralia elata

*Aralia elata* Seem (Family: Araliaceae) is a woody shrub or small tree, widely distributed in China, some parts of Japan, Korea, and Russia.\cite{44} It is used in folk medicine to treat cough, rheumatism, diabetes, cancer, neurasthenia, hepatitis, gastric ulcer, and stomach spasms.\cite{44,45} Several biological activities have been reported from the root bark of *A. elata*, from properties such as cytotoxic, anti-inflammatory, liver-protective, antioxidant, antiviral, and hypolipidemic. Based on findings of investigations of antiulcer effects of *A. elata* root, Araloside A, as a triterpenoid saponin, was determined as the main substance with antiulcer activity. Its action may be due to its inhibitory property on gastric acid secretion.\cite{46}

Arctium lappa

*Arctium lappa* L. (Family: Asteraceae) or burdock has carrot-like roots and is commonly used in Asian cooking as a vegetable. It is used therapeutically as a depurative, diuretic, digestive stimulant agent, and to treat dermatological conditions. Additionally, it shows hepatoprotective, antioxidant, antibacterial, and antiulcer properties.\cite{47} Previous investigations have reported that chloroform extract of *A. lappa* roots showed a protective effect in gastric lesions by lowering gastric acid secretion via gastric H⁺, K⁺-ATPase inhibition in animals.\cite{48} In addition, ethanol extract of roots endorsed renewal of damaged gastric mucosa by its antisecretory and antioxidative mechanisms.\cite{47}

Asparagus racemosus

*Asparagus racemosus* Willd. (Family: Liliaceae) is a spinous undershrub, with tuberous, short root-stock bearing numerous succulent tuberous roots. It is available throughout tropical and subtropical Australia as well as India, Africa, and Asia and is well liked as a vegetable and eaten in many countries.\cite{49} Medicinal application has been reported in the British and Indian Pharmacopoeias and in indigenous systems of medicine. *A. racemosus* is used in traditional medicine as an anodyne, galactagogue, diuretic, aphrodisiac, antispasmodic, and nerve tonic agent. It is also applied in the management of diarrhea, dysentery, peptic ulcer, neurodegenerative disorders, alcohol abstinence-induced withdrawal symptoms, rheumatism, and for nervous breakdowns.\cite{49,50} *A. racemosus* has potent antioxidant, immunostimulant, styptic, adaptogenic, geriatric tonic, immunoadjuvant, antibacterial, cardioprotective, and antitussive effects. The plant is mainly known for its phytoestrogenic properties effective as a lactagogue and for treatment of menopausal and premenstrual symptoms.\cite{51} According to previous findings about antiulcer activity, *A. racemosus* extract of root significantly increased mucosal protective factors such as mucus secretion, cell life span, cellular mucus, and has demonstrated a noticeable antioxidant effect as well as only slight or no outcome on offensive factors such as acid and pepsin.\cite{50,52}

*Asparagus pubescens* bak is another species of *Asparagus* genus; it is an evergreen plant and grows abundantly in the region Valleys of Jos Metropolis and the rocky hills.\cite{53} The root of the plant is widely used in the management of GI disorders and pain caused by inflammation. Studies about antidiarrheal and antiulcer effects of *A. pubescens* root indicated that they might be caused by its α₂-adrenoceptor stimulation and active constituents, respectively.\cite{53,54}

Bupleurum falcatum L

*Bupleurum falcatum* L. (Family: Apiaceae) is one of the best-known crude drugs and broadly applied in Asia for managing many diseases during the past 2000 years.\cite{55} The roots of this plant have been used in chronic hepatitis, inflammatory diseases, and ulcers in GI organs. Peptic polysaccharides (e.g., Bupleuran 2IIb and 2IIc) obtained from *B. falcatum* showed anticomplementary macrophage Fc receptor upregulating and antiulcer effects. Previous studies in
mice demonstrated that a water-soluble crude polysaccharide portion of \textit{B. falcatum} root prevented significant ulcerogenesis induced by HCl/ethanol.\cite{56,57}

\textbf{Carlina acanthifolia}

\textit{Carlina acanthifolia} All. (Family: Asteraceae) is a perennial species widespread in the hills and mountains of Eastern Serbia. \textit{C. acanthifolia} root is used for its diuretic, anti-inflammatory therapy for the urinary tract, antioxidant, antimicrobial, and antiulcer agent.\cite{58,59} It has also strongly hypotensive effects and in cases of faintness, overtiredness, brain-fag, and skin rash.\cite{59} Previous investigations of the effect of essential oil of the root showed significant dose-dependent gastro-protective effect in rat that had undergone an ethanol induced stress gastric ulcer test.\cite{60}

\textbf{Cassia siberiana}

\textit{Cassia Sieberiana} DC (Family: Caesalpiniaceae) was described as an open savannah tree found in drier areas of forests and thickets. It has widespread distribution in Senegal, Nigeria, and East Africa. Some parts of the plant are used to treat fever, jaundice, aches, gonorrhea, pile, ulcer, debility, arthritis, and rheumatism.\cite{61} Previous studies demonstrated that \textit{C. sieberiana} root extract had antiparasitic, myorelaxant, antispasmodic, antimicrobial, antiviral, antioxidant, anti-inflammatory, and analgesic properties.\cite{62} The roots of this plant are commonly applied as a phytotherapeutic to treat stomach disorders including indigestion, stomach pain, and gastric ulcer. \textit{C. sieberiana} root extract possessed significant gastric cytoprotective prostaglandin properties. Additionally, because of embarrassment from lessening gastric antioxidant enzymes activity and myeloperoxidase and inhibition of gastric lipid hydroperoxide levels it is suggested that antioxidant property may also be an antiulcer mechanism of \textit{C. sieberiana} activity.\cite{62,63}

\textbf{Cichorium intybus}

\textit{Cichorium intybus} L. or chicory (Family: Compositae) is a customary Uighur medicine frequently using in China and some of other Asian countries.\cite{64} It has potent antihepatotoxic property and is employed for managing diabetes mellitus, rheumatism, jaundice, gout, liver enlargement, diarrhea, enlarged spleen, pyorrhea, or gingival inflammation. Root extract showed anti-inflammatory activity against formalin-induced edema.\cite{64,65} It was also reported to have a quinidine-like property on isolated heart. Its root and leaves are used widely as wound-healing agent, appetizer, chologogue, depurative, digestive, gastric secretion stimulant, diuretic, laxative, and tonic. Previous pharmacological experiments have demonstrated that root extract possessed significant stomach protection in animal models attributed to antisecretory activity and stimulation of a protective barrier of the mucosa of the gastric tract.\cite{65,66}

\textbf{Combretum dolichopetalum}

\textit{Combretum dolichopetalum} Engl. and Diels (Family: Combretaceae) is applied in traditional medicine to treat diarrhea, stomachache, cramp, blood in the stool, and associated GI disorders. It was shown that this plant possesses hepatoprotective, anti-inflammatory, antiulcer, and anti-diabetic activity.\cite{67}

Research has shown that root extract had a significant protective effect against duodenal and gastric ulcer in rat induced by indomethacin administration and cold stress. Tannin and Saponin structures were known as effective agents in this function.\cite{68} In the other study, ethanol extract of the plant had a protective effect in a dose-dependent manner against gastric ulcer induced by pyloric ligation with histamine administration in rats. Antiulcer activity was associated with the content of
extract, Tannins, alkaloids, glycosides, flavonoids, and saponins that showed antihistamine and anticholinergic activities.\footnote{69}

**Curcuma amada**

The genus *Curcuma* (Family of Zingiberaceae) consists of over 80 species of rhizomatous herb. These are native plants of the Indo-Malayan region and widely dispersed in the tropics from Africa to Asia and Australia.\footnote{70} *Curcuma amada* Roxb. or mango ginger is a permanent herb and widely employed in preparation of particular foods, pickles, drinks, and in pharmaceutical and cosmetic production.\footnote{71} Rhizomes of *C. amada* have traditionally been applied to treat bronchitis, biliousness, skin diseases, fever, asthma, gleet, hiccups, inflammation, flatulence, colic, anorexia, scabies, dyspepsia, ulcers of the male sex organs, bruises, wounds, pruritus, sprains, gout, halitosis, otalgia, cooling, lumbago, stomatitis, rheumatic, GI, and respiratory disorders. Research has shown that bioactive compounds in the rhizomes expressed significant analgesic, antibacterial, anticancer, and antioxidant effects.\footnote{71–73} Moreover, phenolic compound of *C. amada* introduced as inexpensive and potential multistep blockers of ulcers. Its antiulcer property is due to embarrassment of $H^+$, $K^+$-ATPase, inhibition of *H. pylori* growth, exhibiting antioxidant potential.\footnote{72,73}

*C. amada* or mango ginger is another species of the *Curcuma* genus. In old tests, it has been attributed with aromatic, carminative, and stimulant properties. Additionally, it is used against coryza, biliary disorders, cough, anorexia, diabetic wounds, rheumatism, hepatic disorders, sinusitis, ulcer, and inflammatory conditions. Previous studies have shown that *C. longa* reduced secretion of gastric acid and demonstrated protective property against the creation of gastric mucosal lesions. Findings have suggested that the plant extract had the property of inhibition of gastric acid secretion by means of blocking $H_2$ histamine receptors in a competitive way.\footnote{74}

**Ficus religiosa**

*Ficus religiosa* L. (Family: Moraceae), popularly known as peepal, a sacred (bodhi) is a large perennial tree, found in the sub-Himalayan region, across central India and in Bengal. It has been applied for ailments of the GI tract, central nervous system, respiratory and endocrine systems, reproductive organisms, and infectious diseases in traditional medicine.\footnote{75} In folklore, it has been introduced as an excellent source of medicine in the management of diarrhea, asthma, inflammation, diabetes, epilepsy, infectious disorders, gastric problems, and sexual disorders. Outcomes of pharmacological investigations and bioactive metabolites previously reported in *F. religiosa* showed its potential for properties against neuroinflammation, cancer, neuropsychiatric, cardiovascular and oxidative stress-related diseases, bacterial, parasitic, and viral infections.\footnote{75} Investigations on gastroprotective activities of different parts of *F. religiosa* in tests on rat models suggest significant antiulcer activity. The probable mechanism for antiulcer activity may be due to its anti-secretary and cytoprotective properties.\footnote{76,77}

**Gentiana lutea**

Root of *Gentian* (*Gentianae radix*) composed of dried rhizomes and roots of *Gentiana lutea* L. (Family: Gentianaceae), which take place as single or branched subcylindrical parts of different lengths and typically with thickness of 10–40 mm.\footnote{78} These roots have traditionally been used as an appetite stimulant during recovery from acute atonic dyspepsia. It has also been introduced as an antihypotoxic, adaptogenic, anti-inflammatory, and wound-healing agent in many experiments.\footnote{78,79} Research has tested its effect as a medicine for eye troubles, stomach, and liver inflammation. The gastrodefensive effect of *Gentian* root methanolic extract was evaluated and results indicated that healing properties of *Gentian* roots on gastric lesions related to boosted mucosal protective factors by prostaglandin pathway, and that secoiridoid glycosides are responsible for this action.\footnote{80}
**Glycyrrhiza glabra**

*Glycyrrhiza glabra* L. or Liquorice (Family: Leguminosae) is a ligneous perennial shrub native of the Middle East, Mediterranean region, and Asia Minor. It is also farmed extensively in southern Russia. It is one of the most commonly used plant medicines and has biological activities such as antinephritis, anticoagulative antimutagenic, antimicrobial, antiulcer, protective action against hepatotoxicity, antitumor promoting activity, and antidepressant-like effects.\(^{[81,82]}\) Stolon and roots of this plant were widely regarded as the main remedy for peptic ulcer. Glycyrrhetinic acid, as the major metabolite of glycyrrhizin and flavonoids of *G. glabra*, was identified as an active agent against *H. pylori*.\(^{[83,84]}\)

In addition, polysaccharides isolated from root extract of *G. glabra* significantly inhibited *H. pylori* from attaching to human stomach tissue, it can therefore be applied as a potent means for advanced development of cytoprotective products with anti-infectious potential.\(^{[85]}\)

**Guiera senegalensis**

*Guiera Senegalensis*, J.F. Gmel (Family: Combretaceae) is widespread in western and central Africa (Fiot et al. 2006). The plant is utilized for GI disorders, respiratory infections (pneumonia, bronchitis, and coughs) and rheumatism, and as antioxidant and antimalarial agents.\(^{[86]}\) According to pharmacological investigations, leaves, and roots of *G. senegalensis* supported folkloric application for healing GI disorders such as diarrhea and ulcer in an animal models.\(^{[87]}\) The mechanism of mucosal protective effect of this plant may be because due to stimulation of prostaglandin synthesis. As we know, endogenous prostaglandins have a fundamental role in gastro cytoprotection. Another proposal is that increased gastric mucus or leukotriene antagonism may be the reason for gastro-defensive properties of *G. senegalensis*.\(^{[87]}\)

**Hippocratea excelsa**

*Hippocratea excelsa* HBK. (Family: Hipocrateaceae) is a climbing plant that grows in Central America and Mexico. “Cancerina” is denoted to the root bark of this plant and is usually applied for inflammatory, peptic ulcers, kidney disease, skin ailments, cancer, and menstruation disorders.\(^{[88]}\) Several biological activities have been reported from *H. excelsa* such as strong insecticidal, antibacterial, antisecretory effects.\(^{[89]}\) Important gastrodefensive properties were reported from root and bark extracts of the mentioned plant in some experimental ulcer models in rat. In the extract of *H. excelsa*, β-amyrin, (−) epicatechin, α-amyrin, β-sitosterol, and its glycoside were recognized as active gastroprotective ingredients. These findings support popular application of this plant in traditional medicine as an antiulcer remedy.\(^{[88,90]}\)

**Mikania cordata**

*Mikania cordata* Burm. f. B.L. Robinson (Family: Asteraceae) or heartleaf hemp vine, a perennial herb found all over the tropical regions of Asia, South America, and Africa.\(^{[91]}\) It is widely used in traditional medicine to treat eye problems, respiratory problems, asthma, scorpion sting and snake bite, dyspepsia, gastric ulcer, dysentery, and other disorders.\(^{[92]}\) Studies about *M. cordata* showed hepatoprotective, anticarcinogenic, antispasmodic, analgesic, antiinflammatory, anti-diarrhea, antiemetic, antibacterial, and anthelmintic effects of this plant.\(^{[91,92]}\) Research has demonstrated that methanolic extract of *M. cordata* roots is effective for healing gastric ulcers in animals. The mentioned property is supposed to be due to modulation of defensive issues via expansion of gastric cytoprotection. Different possible physiological mechanisms have been suggested for *M. cordata* activity on GI lumen. Activation of cyclooxygenase enzyme and subsequent motivation of
synthesis of prostaglandin, increasing bicarbonate level and then GI pH, H2-receptor antagonist and anticholinergic activity are some of the proposed mechanisms.^[93]

**Moringa oleifera**

*Moringa oleifera* Lam. (Family: Moringaceae) is a soft wooded deciduous tree, distributed in numerous tropical and subtropical regions. It is an effective medicinal plant with high nutritional value.^[94] Most of its parts are used in traditional medicine for analgesic, anti-inflammatory and antifertility effects. The plant is reported to have a wide array of pharmacological properties such as antitumor, antioxidant, antipyretic, local anesthetic, antinociceptive, antispasmodic, diuretic, anti-uroliithiatic, antiulcer, hypotensive, cardioprotective, anthelmentic, hypolipidemic, antiatherosclerotic, hepatoprotective, wound healing, antifungal, antibacterial, antitypanosomal, hypoglycemic, and anti-AIDS outcomes.^[94,95] Previous studies have shown antiulcer activity of the ethanolic extract of root bark using ethanol-induced and pylorus ligation-induced gastric ulceration in albino wistar rats, which may be due to its antisecretory, anti *H. pylori*, activation of mucous membrane protective factor and cytoprotective effects of active ingredients such as alkaloids (Moringine and moringinine), antibiotics (Pterygospermin), triterpenoids, saponins and tannins.^[96]

**Mukia maderaspatana**

*Mukia maderaspatana* Linn. (Family: Cucurbitaceae) is an annual monoecious, tendril climber, mostly prevalent in southern India. It is also found in tropical areas of Africa, Australia and Asia. It is a potent herbal medicine with various pharmacological effects and wide therapeutic potential. Different parts of *M. maderaspatana* are used in fever, dyspnea, abdominal disorders, vomiting, ulcer, cough, asthma, neuralgia, odontalgia, as well as in treatment for mental troubles, dysuria, piles, polyuria, and tuberculosis.^[97] It has been shown that the plant poses antimicrobial, antifungal, antirheumatic, antiflatulent, anti-inflammatory, antihypertensive and antilipidemic, anti diabetic, diuretic, stomachic, hepatoprotective, immunomodulatory expectorant, carminative effects, and as a cure for lung diseases and toothache.^[97] Pharmacological investigation on the antiulcer property of the *M. maderaspatana* root extract suggested that it was a nice natural herbal resource for peptic ulcer disorder treatment. Its root extract displayed a strong antiulcer effect by decreasing pepsin content and the elevating hexoamine and carbohydrate protein ratio.^[98]

**Panax ginseng**

*Panax ginseng* C.A. Meyer. (Family: Araliaceae), is recognized worldwide as perennial wild plant that grows in China. It is employed in traditional Chinese medicine as a tonic, prophylactic, and restorative medicine. Most of the pharmacological effects of ginseng are due to ginsenosides, a diverse class of steroidal saponins. It has efficient effects on CNS (central nervous system); promotes immune function, the cardiovascular system, and endocrine secretion; it also aids metabolism. Ginseng has antiaging properties, bio modulation activity, hepatoprotective, anti-stress, antitumor, antinociceptive, antiviral, anti-inflammatory, antioxidant, antidiuretic, antifatigue, antihypothermic, antidiabetic, sedative, and cytoprotective activities. It has also been reported to present considerable gastroprotective effect in ethanol-induced gastric lesions in rats. The rats, that received ginseng showed significant cytoprotective heat shock proteins HSP27 and HSP70 induction, which is suggested as a cytoprotective mechanism in ethanol-induced gastric damages.^[99,100]

**Plumbago auriculata**

*Plumbago auriculata* Lam. (Family: Plumbaginaceae) is one of 500 species perennial herbs, which is indigenous in Africa and grown as an ornamental plant in India. This plant is used traditionally for
treatment of wounds, warts, broken bones, and headaches. The roots are taken as an emetic and its root sap is used for tattoos.\textsuperscript{[101,102]} Phytochemical investigation on the methanol and chloroform extracts of \textit{P. auriculata} root showed the presence of naphthoquinones and steroid structures (e.g. naphthoquinones: plumbagin, diomuscinone, and epi-isoshinanolone steroids: sitosterol, 3-O-glucosylstilostoler, plumbagic, and palmitic acids).\textsuperscript{[102]}

Several studies revealed gastroprotective effects of plumbaginales including \textit{P. auriculata}, \textit{P. indica}, \textit{P. zeylanica} species, and plumbagin as an effective substance. Based on previous results these species root had cytotoxic and anti-\textit{H. pylori} effects.\textsuperscript{[103]} They play a protective role on GI tract. Among these species, \textit{P. auriculata} showed significant antioxidant and acid neutralizing abilities and its gastroprotective capacity was comparable with Ranitidine.\textsuperscript{[104]}

\textbf{Polygonum bistorta}

\textit{Polygonum bistorta} Linn, Bistort or Snakeroot (Family: Polygonaceae) is a small perennial shrub with a woody rootstock. This herb is distributed worldwide, it is found in northern temperate regions such as Europe and North America. It is recognized as an efficient treatment for adenopathy, cancer, amenorrhea, hematuria, carbuncle, cramp, colitis, congestion, diarrhea, dyspepsia, dysentery, dysmenorrhea, irritable bowel syndrome, epilepsy, jaundice, worm infestations, bleeding hemorrhoids, fever, rhinitis sore throat, inflammation, and to applied to heal wounds. Moreover, it is useful in intestinal abrasion, peptic ulcer, ulcerative colitis and stops intestinal bleeding. In a previous study, \textit{P. bistorta} root (100 µg/ml of hydro alcoholic extract) showed evidence of strong inhibitory action on IL-8 secretion as an inflammatory mediator, which could partly confirm the traditional application of this plant for GI diseases mainly related to \textit{H. pylori} infection.\textsuperscript{[105,106]}

\textbf{Pongamia pinnata}

\textit{Pongamia pinnata} (Linn) Pierre (Family: Fabaceae) is a medium in size, glabrous and evergreen tree, distributed throughout tropical and sub-tropical areas, the plant thrives in areas with good drainage and a sunny aspect. Nowadays it is found in Australia, India, Florida, Hawaii, Oceania, Seychelles, Malaysia, and Philippines. Most pieces of \textit{P. pinnata} have been used as therapeutic agents for a variety of illnesses. Its sprouts and fruit have been used for abdominal tumors. Seeds show hypotensive outcome and generate uterine contractions. Seeds are also utilized in bronchitis, fever, whooping cough, painful rheumatic joints, and skin diseases. The oil obtained from seeds is used to treat piles, scabies, chronic fever, leprosy, lumbaro, ulcers, and liver pain as anti-inflammatory and antibacterial agents. Leaves are applied for diarrhea, cold, flatulence, cough, dyspepsia, leprosy, gonorrhea, and are active against \textit{Micrococcus}. The bark is employed for bleeding piles and beriberi internally. Flowers are used for diabetes and its roots for cleaning gums, ulcers and teeth.\textsuperscript{[107]} Other pharmacological effects reported from \textit{P. pinnata} are antiplasmodial, antinociceptive, antilipidperoxidative, antioxidant, antimicrobial, antihyperammonic, CNS depressant, anticonvulsant, and cytotoxic properties.

Different researches have demonstrated significant gastroprotective effects of various parts of this plant. Inhibition of ulcer pathogenicity may be attributed to various mechanisms such as establishment of H\textsuperscript{+}, K\textsuperscript{+}-ATPase action, as a mucosal offensive or defensive factors. But defensive factors (e.g., mucin secretion, life span of mucosal cells, mucosal cell glycoproteins, cell proliferation, and prevention of lipid per oxidase) were more efficient than offensive factors (e.g. acid-pepsin secretion).\textsuperscript{[108,109]}

\textbf{Rumex patientia}

\textit{Rumex patientia} L. (Family: Polygonaceae) is a perennial plant that grows up to 2 m of height and is broadly dispersed in the mid Anatolia region. It has been commonly applied in traditional medicine in Turkey to treat various diseases. \textit{R. patientia} possesses purgative, constipate, depurative, diuretic, laxative, antipyretic, analgesic, injury healing, tonic, antimicrobial, antioxidant, anti-inflammatory,
and gastroprotective characteristics. Previous researches have revealed that aqueous extract of *R. patient* roots decreased number and size of ulcerated areas and these effects may be due to its antioxidant property.\textsuperscript{[110,111]}

**Sophora flavescens**

*Sophora Flavescens* Aiton (Family: Fabaceae) have long been used in traditional medication in the management of fever, dermal burns, diarrhea, mucosal ulcers, viral hepatitis, sores, inflammation, GI hemorrhage, cancer, and cardiac arrhythmia. Other effects of *S. flavescens* dry roots such as antioxidant, vasodilator, antibacterial, antiarthritic, antiasthmatic, apoptosis modulator properties, and antitumor activities have been reported in previous studies.\textsuperscript{[112]} According to the literature, vexibinol is a flavonol that is an active constituent in the root extract and has useful effects for healing gastric ulcers in rats induced by an HCl/ethanol model. Anti-ulcer effect of vexibinol is related to its gastric mucosal protective activity and inhibitory effect on secretion of gastric acid. Trifolirhizin is another active principle extracted from *S. flavescens* root, which has demonstrated noteworthy effects on *Helicobacter pylori* infection and diminished amounts of gastric secretion and acid yield in an animal model.\textsuperscript{[112–114]}

**Withania somnifera**

*Withania somnifera* Dunal or Ashwagandha (Family: Solanaceae) is distributed in northern areas of India, the Mediterranean region and in Africa. It has been widely used as a home remedy for several ailments. It is a dietary supplement composed of various nutrients that possesses antiulcer, anti-inflammatory, antimicrobial, antitumor, antistress, sedative, antioxidant, antihypotoxic, antidiabetic, immunomodulatory, and rejuvenating properties. *W. somnifera* is also active against snake bite and scorpion sting and is taken to relieve conditions of conjunctivitis, senile dementia, epilepsy, insomnia, leprosy, rheumatism, Parkinson’s disease, bronchitis, nervous disorders, arthritis, intestinal infections, impotence, asthma, and as a suppressing agent in HIV/AIDS diseases. The roots of this plant are regarded as a tonic and used as an aphrodisiac. In addition, they are used in cough, dropsy, consumption, emaciation, debility, dyspepsia, rheumatism, and gynecological disorders.\textsuperscript{[115,116]}

Research has shown that pretreatment with *W. somnifera* had possessed significance protection against stress induced gastric ulcers. Another study suggested that Withaferin A, a withanolide obtained from *W. somnifera*, could inhibit *H. pylori*-induced production of IL-1β in dendritic cells and could be utilized as a novel preventive and remedial agent in cases of gastric cancer.\textsuperscript{[115,117]}

**Zingiber officinale**

*Zingiber officinale* Roscoe or ginger (Family: Zingiberaceae) is a widespread medicinal plant and a common condiment used in food and drink. It is used for a broad collection of unrelated disorders such as arthritis, muscular aches, rheumatism, pain, sprains, sore throat, constipation, cramp, stomach upset, indigestion, nausea, diarrhea, vomiting, dementia, hypertension, infectious diseases, fever, and helminthiasis. Additionally, some constituents in ginger have potent antioxidant, anticancer, anti-inflammatory, antimicrobial, antiviral, antiplatelet, cholagog, antitumor, and immunomodulatory effects.\textsuperscript{[118]}

Ground rhizome of *Z. officinale* has been utilized as a traditional treatment in GI disorders. It has frequently been used to treat peptic ulceration. The healing and antiulcer properties of ginger may be due to its powerful thromboxane synthetase property, Inhibition of gastric H\textsuperscript{+}, K\textsuperscript{+}-ATPase, and *H. pylori* growth via phenolic antioxidants. Plant extract demonstrated prevention of incidence of GI ulcers induced by non-steroidal anti-inflammatory drugs (NSAIDs) and hypothermic restraint stress in animal models.\textsuperscript{[52,72,119]}
**Zizyphus lotus**

*Zizyphus lotus* (Family: Rhamnaceae) is a large shrub distributed throughout tropical and subtropical areas: Asia, North America, Africa, Oceania, South America, and in Europe. Pharmacological investigations have confirmed that it has important activities applicable in management or treatment of various ailments and its analgesic, anti-inflammatory, antioxidant, sedative, antidiabetic, antibacterial, antifungal, antispasmodic, and antulcerogenic properties.\[^{120}\]

Antiulcerogenic activity of *Z. lotus* extract on gastric ulcer in experimental models was evaluated and findings suggested that its antiulcerogenic activity could be mediated partially by reduction of gastric juice secretion, antiacid, demulcent effects, and inhibition of *H. pylori* growth. The existence of tannins and flavonoids in root bark aqueous extract can partially explain antisecretory and the cytoprotective activity.\[^{121,122}\]

**Conclusion**

During recent years, research has focused on medicinal plants and properties of herbal medicinal plants. These plants have been tested to evaluate their efficacy as drugs to prevent and treat various diseases. From the aforementioned review, in most cases, there was correspondence between ethnopharmacological and scientific findings and experiments demonstrated that active components in herbal medicines were usually responsible for the biological effects such as antioxidant, anti-inflammatory, and antiulcer properties.\[^{85,104,123–126}\] Natural compounds such as tannins, flavonoids, alkaloids, triterpenoids, steroids, saponins, and coumarins showed significant antiulcerogenic activity.\[^{96,127–130}\] It can be concluded that investigation of new gastroprotective plants and identification of the natural compounds that they contain are important considerations for the discovery of new drugs with less side effects, less toxicity, less cost, and more efficacy in prevention and management of different gastric disorders.

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