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REVIEW ARTICLE

Therapeutic Potential of Traditional Medicinal Plants in the Treatment and Management of Ulcer

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Abstract

Peptic ulcers are lesions in the stomach or duodenal mucosa, caused by an imbalance between protective and aggressive factors, including gastric acid, pepsin, and mucosal defences. Despite the availability of several synthetic medicines for treatment, they frequently involve adverse effects, substantial expenses, and restricted long-term effectiveness. In comparison, natural products are emerging as viable alternatives owing to their therapeutic efficacy, cost-effectiveness, and limited side effects. The rising global inclination towards herbal formulations indicates a heightened interest in traditional and folk medicine as legitimate alternatives to contemporary therapies. This study highlights the significance of advancing research on medicinal plants with antiulcer capabilities and examines the therapeutic benefits of herbal medicines compared to the conventional treatments. It particularly highlights and examines results from the literature addressing around 14 medicinal plants historically utilized for ulcer treatment. These medicinal plants exhibit antiulcer activity by reducing gastric acid secretion, enhancing mucosal protection, and combating oxidative stress and inflammation. Their bioactive phytoconstituents and favorable safety profiles make them strong candidates for development into marketable, plant-based antiulcer formulations.

Major Findings: The traditional medicinal plants exhibit potential antiulcer activity by modulating gastric acid secretion and strengthening mucosal defense, having fewer side effects and better suitability for long-term use. This review highlights 14 traditionally used antiulcer plants and underscores the need for further scientific and clinical validation of their efficacy and safety.

Keywords: Antiulcer Activity, Peptic Ulcer, Pathophysiology, Traditional Medicinal Plants

1. Introduction

These days, people suffer from frequent illnesses such as gastroduodenal ulcers and hyperacidity in the stomach area. Gastric and duodenal ulcers are frequently caused by anatomically peptic ulcers in the stomach and duodenum. When the mucosal epithelium is subjected to harsh or damaging stimuli, peptic ulcersores in the stomach or duodenal mucosa. It is now commonly accepted that the imbalance between harmful elements in the lumen and defensive mechanisms in the gastroduodenal mucosa causes gastric lesions to form. Gastric acid, Nonsteroidal Anti-inflammatory Drugs (NSAIDs), *Helicobacter pylori* (*H. pylori*), pepsin, bile salts, are the main aggravating or damaging agents, whereas mucus, bicarbonate secretion, blood flow, prostaglandins E_2 and I_2 and nitric oxide are the key defending elements of the gastric mucosa[1-6]. Anxiety that persists for a long time, emotional tension, hemorrhagic surgical shock, burns, trauma, cigarette smoking, and drinking alcohol is additionally recognised to produce significant stomach

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irritation, however, the mechanism is still not entirely understood[7-10]. The aggressive and defending factors for peptic ulcer (Figure 1).

2. Pathophysiology of Peptic Ulcer

An ulcer primarily happens as a result of disturbance between the factors that promote aggression and those that support defense within the gastric region. All types of ulcers are characterised by oxidative damage to the mucosa, which is primarily brought on by Reactive Oxygen Species (ROS), particularly the hydroxyl radical[11,12]. To digest food, the human body produces powerful acids. These acids are shielded from the stomach and duodenum's interior by a lining. The stomach wall is vulnerable to acid injury if there is a sore or rupture in its lining, *H. pylori* and NSAIDs weaken the lining[13-15]. The damage to mucosal integrity can cause discomfort, hemorrhage, obstruction, perforation, and even death. The damage can occur in the mucosa, muscularis mucosa, submucosa, and, in some circumstances, the layers that are deep. Mucosal integrity can be retained by providing a homeostatic balance between the damaging and defensive factors. One of the numerous factors that contribute to ulcers is gastric hyperacidity, sometimes referred to as hyperchlorhydria, which is the excessive or hypersecretion of gastric acid (hydrochloric acid) from the parietal cell of the stomach mucosa through proton pumping H+-K+-ATPase[16-18]. Nearly all types of ulcers are caused by Reactive Oxygen Species (ROS), particularly the hydroxyl radical (SOH), which also causes oxidative damage to the mucosa[19,20]. It was found that gastric mucosal damage in ulcers is caused by both accelerated cell death through apoptosis and concurrent suppression of the cell development process. It has been demonstrated that stress-induced stomach erosions are accompanied by an imbalance between the apoptotic-promoting Bax protein and the antiapoptotic Bcl-2 family of proteins, as well as a reduction in gastric blood flow and the proliferating cell nuclear antigen labelling index[21-23]. Due to the stimulation of Tumour Necrosis Factor-α (TNF-α), apoptosis, DNA damage, ethanol and indomethacin (NSAID) harm the stomach mucosa[24]. Pathogenesis of duodenal ulcer (Figure 2).

3. Treatment Approaches for Ulcers

Reduction in the production of stomach acid, blocking apoptosis, encouraging epithelial cell proliferation, and promoting gastro protection are all necessary for successful healing and control of ulcers. An antacid (aluminum hydroxide and magnesium hydroxide), cytoprotective (misoprostol), Histamine (H2) receptor antagonist (ranitidine, famotidine), proton pump inhibitor (pantoprazole, lansoprazole,

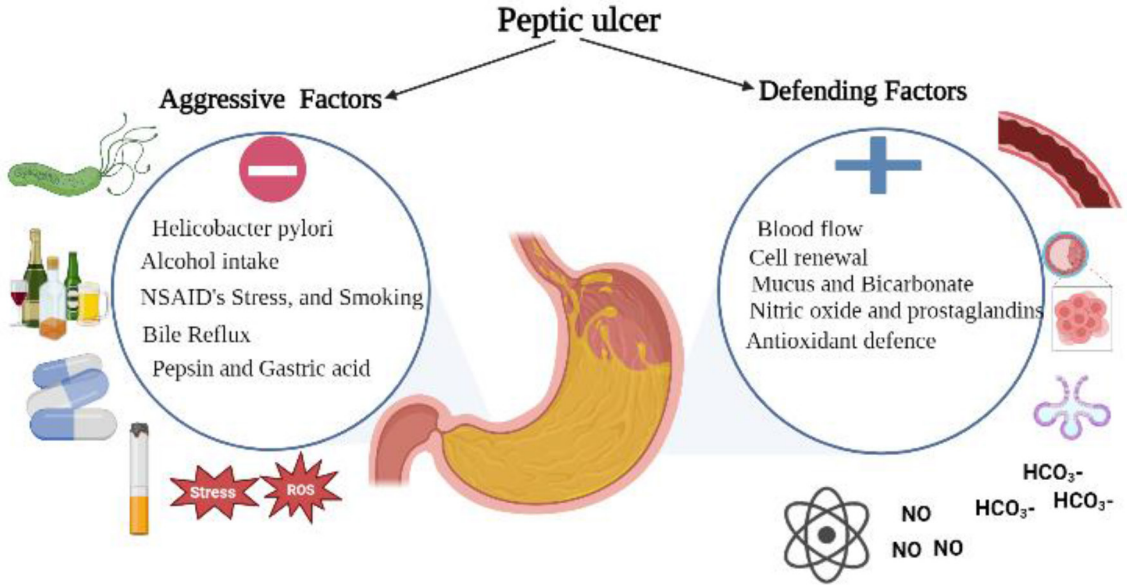


Figure 1. Schematic representation of aggressive and defensive factors involved in the pathogenesis of peptic ulcer.

and omeprazole), anticholinergic (pirenzepine, telenzepine), and other conventional medications for ulcer treatment primarily neutralise gastric acid secretion by acting on the damaging factors[25-28]. The most commonly prescribed proton pump inhibitors and H2 receptor blockers are employed to address a variety of acid-related issues, including as elevated acid secretion caused by stress, NSAIDs, and *H. pylori*[29]. These medications may be useful for treating an acute ulcer, but long-term treatment is not advised due to a variety of unfavorable side effects, drug interactions, and relapse. Most of these medications boost the gastric mucosa's protective mucosal elements, which are crucial. They function by reducing stomach acid output. Ironically, though, people with ulcers frequently have low levels of acid. Calcium carbonate, the most common type of calcium in food, requires an acid gastric environment for bioavailability, which is impaired by stomach acid suppression. Iron, magnesium, and vitamin B-12 absorption could be hampered by this acid suppression as well[30-32]. The market's traditional therapies and the adverse effects they cause (Figure 3).

4. Traditional Gastro Protective Crude Drugs

Ayurveda, an ancient Indian medical system, categorises gastrointestinal disorders into three groups: *Sula*, *parinamasula*, and *amlapitta*. Interestingly, these classifications align with modern clinical conditions such as peptic ulcer and functional dyspepsia, commonly known as non-ulcer dyspepsia[33-35]. The current worldwide situation is moving toward the development of a unique nontoxic antisecretory-antiulcer product, ideally from the medicinal plant of traditional usage, due to the limits of the traditional system of treatment with synthetic medication. This is opening the avenues for "Green Medicine", which is believed to be safer, more accessible, and more reasonably priced[36-39]. India is home to a variety of medicinal plants. To regain the balance, between gastro-protective and aggressive factors different therapeutic drugs including herbal extract are used. Herbal medications derived from plant sources are typically cheaper, safe, clinically effective, globally competitive, and well-tolerated even at larger doses in ulcer therapy[40,41]. Peptic ulcers and other gastrointestinal issues have long been treated with a

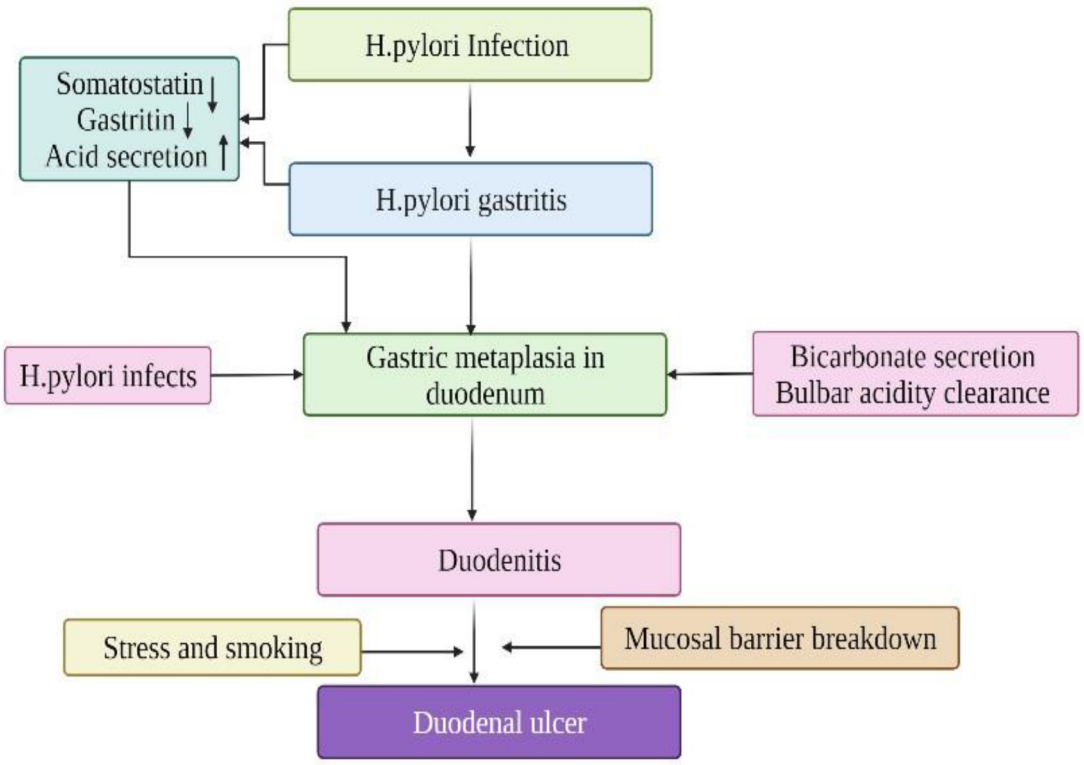


Figure 2. Illustration showing the pathophysiological mechanisms involved in the development of duodenal ulcer.

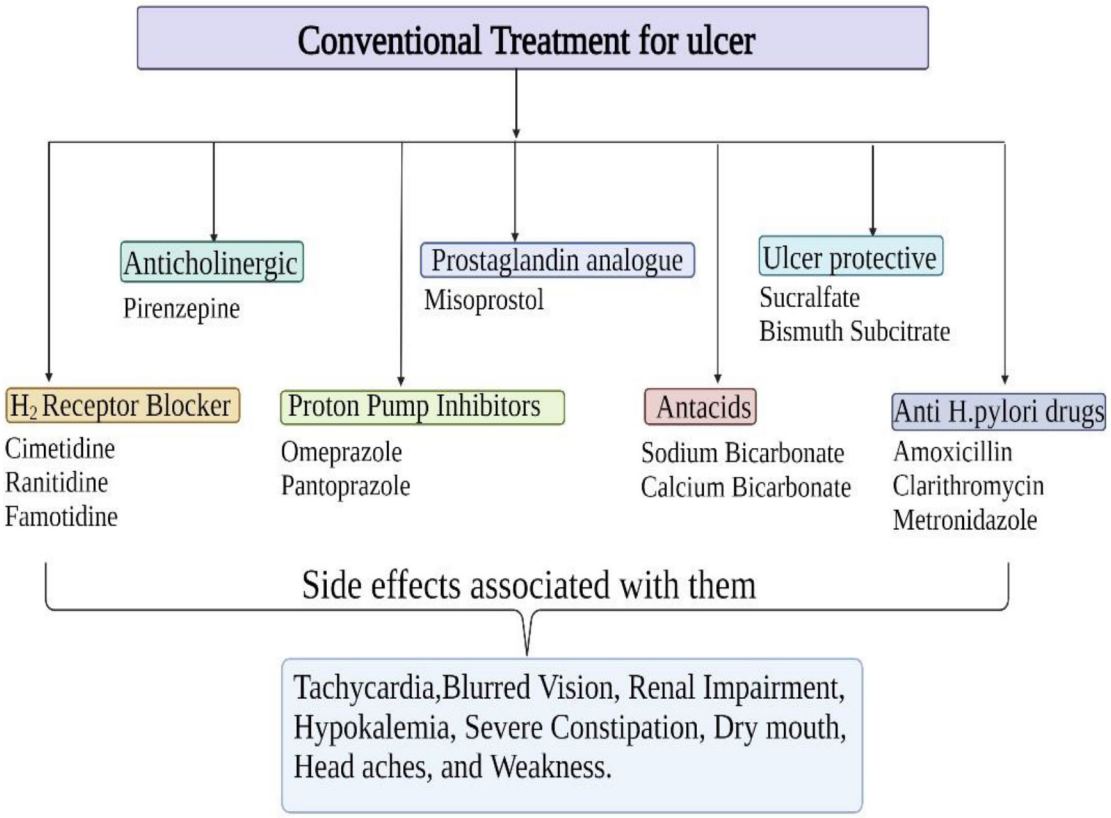


Figure 3. Overview of conventional therapies available in the market and their associated adverse effects.

variety of plants and herbs in traditional medicine. Even throughout the *Vedic* era, natural components were a common source of new drugs. However, plant extracts have been discovered to have promising results in ulcer healing and recurrence prevention, making them one of the most tempting sources of innovative treatments. An agent with a combination of anti-secretory, anti-*H-pylori*, and gastro-protective action that has longer residence duration at the site of action and fewer side effects is required for the effective treatment of ulcers. As no single synthetic compound have all these properties, without any side effect, the natural drugs having the anti-ulcer action are found to be the best alternative with fewer side effect[42,43]. The symptoms of an ulcer include poor absorption, hypo- or hyperacidity, bleeding, loose stools, infection and sepsis, disturbed flora and candidiasis, spasms and pain, and anxiety. Since no one, straightforward herbal remedy can treat all these conditions, anti-ulcer herbs are typically administered in combinations that are optimally catered to the patient's particular issues. The formula may be changed or reformulated frequently using combinations with related features. It is essentially necessary to step up research on conventional and folk medicines to assess the potential and encourage the use of herbal remedies[44].

5. Natural Ingredients Exhibiting Antiulcer Activity

5.1 *Emblica officinalis*

For a very long time, *E. officinalis* (EO) Gaertn (*Euphorbiaceae*), often known as *amla*, has been referenced as a *rasayna* in several *ayurvedic* books, such as the Charaka Samhita and Sushruta, for a variety of diseases[45]. According to *Ayurveda*, *rasayana* is a specific kind of medication that enhances mental health, extends life, and avoids disease by boosting strength and immunity[46]. EO is used to treat dyspepsia and has been shown to have strong adaptogenic effects[47,48]. Fresh EO juice has been shown to have anti-ulcerogenic properties. To examine the potential mechanism of action, Sairam and Rao conducted a study in 2002[49]. They examined the effects of an EO

methanolic extract on defence variables such as cell shedding, cell proliferation, cellular mucus, and mucin secretion, as well as aggressive aspects like the synthesis of acid-pepsin. Their study also looked into the effects of stomach mucosal variables. The results showed that the extract improved mucin secretion, cellular mucus synthesis, and mucosal cell longevity while dramatically lowering acid and pepsin levels.

Because EOE affects both offensive and defensive mucosal variables, it has been found to have important ulcer-protecting and healing capabilities[50]. Research was also done on EO's antioxidant properties as a possible defence against lipid peroxidation, which is a major contributing factor to ulcer development. It is discovered that embicanin A and B, two low-molecular-weight hydrolysable tannoids from EO, are active components with strong *in vitro* antioxidant activity[51].

5.2 *Azadirachta indica* A Juss

Neem is used extensively in traditional *Ayurvedic* and folk medicine[52,53]. The plant extract from the bark, leaves, fruits, and root has a number of medicinal chemicals that have purportedly been used to cure leprosy, intestinal helminthiasis, and respiratory conditions in children. Because its bitter components are believed to increase the flow of gastric juice and saliva, *A. indica* is used as a stomachic[54-57]. The effectiveness of *A. indica* extract against gastric ulcerogenesis, high blood sugar levels, bacterial and viral infections, antifertility and malaria has been found in various types of research. *A. indica* has been claimed to have insecticidal, immunomodulatory, hypotensive, and minimally chronotropic properties[58-65]. In 2002, the antisecretory and antiulcer properties of *neem* (*A. indica*) aqueous bark extract were studied under conditions including pylorus ligation, restraint-cold stress, Indomethacin, and mercaptomethylimidazole-induced acid secretion. Similar to omeprazole, the bark extract also inhibits H^+-K^+-ATPase activity *in vitro* in a concentration-dependent manner. It provides gastroprotection against stress ulcers by significantly reducing adherent mucus and endogenous glutathione depletion[66]. By drastically lowering lipid peroxidation and scavenging the endogenous hydroxyl radical (OH), the primary cause of ulcers, it protects the stomach mucosa from oxidative damage. Raji *et al.*, conducted another study in 2004 examined the impact of the extract on gastrointestinal ulcers in albino rats[67]. *A. indica* extracts considerably reduced the stomach ulceration brought on by indomethacin (100-800 mg/kg p.o., 100-250 mg/kg i.p.)[67]. The extract's effectiveness on *in-situ* stomach acid secretion was examined both by itself and in conjunction with cimetidine (0.12 mg/kg) and histamine (1 mg/kg). Both baseline and histamine-induced stomach acid production were markedly decreased by *A. indica* when administered at dosages of 250 mg/kg. The suppression of stomach acid secretion by *A. indica* appeared to be enhanced by cimetidine. The findings imply that antiulcer properties exist in *A. indica* stem bark extract, which most likely act via histamine H2 receptor[67].

5.3 *Asparagus racemosus*

In *Ayurveda, A. Racemosus* (AR) wild, belonging to *Liliaceae,* is a famous *rasayna*[68]. This plant's root juice or root paste is reported to cure various diseases, example, gastric ulcers[69]. AR has been described as a powerful adaptogen that boosts nonspecific resistance[70,71]. The polysaccharide portion of AR has been shown to have considerable *in vitro* anti-oxidant activity in the treatment of ulcers making it a potential anti-ulcer medication[72,73]. Additionally, it has been suggested that AR speeds up stomach emptying[74]. A change in stomach emptying has reportedly been linked to the development of ulcers[75]. Fresh AR juice mixed with honey has been found to work well for dyspepsia. The active saponins *shatavarin* I-IV were found to be present in AR[76]. On several gastroduodenal ulcer models, in 2003, Sairam *et al.*, investigated the ulcer-protective qualities of a methanolic extract of fresh AR roots. The extract significantly reduced the risk of developing acute stomach ulcers brought on by Cold Restraint Stress (CRS), pyloric ligation, aspirin paired with pyloric ligation, and duodenal ulcers brought on by cysteamine, but it had no effect on ulcers brought on by ethanol or aspirin. Additionally, studies on gastric juice and mucosa revealed that AR greatly enhanced mucosal defensive factors like mucus output, cellular mucus, and cell life span, while having little to no effect on offensive factors like acid and pepsin. It had a strong antioxidant impact as well. AR also effectively cured persistent stomach ulcers brought on by acetic acid[76].

5.4 *Solanum nigrum*

Known as "Black nightshade", *S. nigrum* Linn. (*Solanaceae*) is widely used in traditional medicine in India and other countries to cure a variety of ailments[77]. Long-term skin conditions, including ringworm and psoriasis, as well as liver and inflammatory diseases, painful periods, fevers, diarrhoea, eye infections, and hydrophobia, are all reportedly treated by the plant[78]. In folk medicine, *S. nigrum* is used as a potential medicine against peptic ulcers[79]. Among the many components of the plant are polyphenolic compounds and tannin (7-10%). Additionally, included are glycoalkaloids such as solanine, solamargine, solanigrine, and solasodine (0.09-0.65%). There are steroidal glycosides such solamargine, solasonine, and solansodamine in addition to steroidal saponins like diosgenin (0.4-1.2%) and steroidal genin (gitogenin)[80-82]. Previous rat investigations have demonstrated the antiulcer, antioxidant, anti-tumour-promoting, and hepatoprotective properties of *S.nigrum* fruits[82-84]. They also protect against free radical-mediated damage[85]. Rats with aspirin-induced ulcerogenesis have shown that the aerial portions had antiulcer activity through acid and peptic suppression[86]. Jainu *et al.*, induced gastric ulcers in rat models using Indomethacin (IND), pyloric Ligation (PL), Cold Restraint Stress (CRU), and Ethanol (EtOH). We looked at the ulcer-healing activity on the acetic acid-induced ulcer model in rats as well as the antiulcer efficacy of *Solanum nigrum* fruit Extract (SNE) on these models. SNE showed antiulcer benefits via reducing gastrin release and inhibiting H+K+ATPase.

5.5 *Momordica charantia* L.

Momordica charantia L. (*Cucurbitaceae*) fruits, consumed as vegetables globally, having wide variety of therapeutic activities, including hypoglycaemic, antidiabetic, antifungal, inhibition of p-glycoproteins, antihyperlipidemic, and antioxidant effects[87-90]. The fruit has historically been used to treat several illnesses, such as anaemia, jaundice, malaria, and cholera, and has anthelmintic, antiemetic, carminative, and purgative effects[91]. Fresh fruit extracts in olive oil, dried fruit in honey, and dried fruit extract in ethanol have all been shown to have stomach cytoprotective effects in rats, making them effective treatments for peptic ulcers[92,93]. Furthermore, fruits have been said to inhibit the growth of *H. pylori*, the bacteria that cause stomach and duodenal ulcers[94]. It is currently unknown how fruits affect the healing of stomach ulcers, aggressive gastric factors like the release of gastric acid and pepsin, or protective factors like the secretion of mucus[95].

5.6 *Bambusa arundinacea*

The emmenagogue properties of *B. arundinacea* leaves to make them beneficial for inflammatory diseases, wound healing, and controlling bovine diarrhea. The crystalline substance *manna* is found in bamboo plants, and *Ayurvedic* medicine uses its leaves to treat ptosis and paralysis[96,97]. The plant and its extracts have been used extensively in traditional medicine, but respectable, well-established scientific journals have not published any reliable scientific data to back up these claims. According to research, the methanol extract of *B. arundinacea* leaves has anti-inflammatory properties against paw oedema caused by carrageenin and immunological factors, and it also has antiulcer activity in albino rats. When compared to the effects of common drugs, these effects were determined to be considerable. Experimental studies have shown that the combination of phenylbutazone (an NSAID) with methanol extract of this plant leaves had the strongest anti-inflammatory efficacy and the least harmful (no ulcerogenic) activity.This herb may be used to treat rheumatoid arthritis and other chronic inflammatory diseases over time, especially in those who also have peptic ulcers[98].

5.7 *Glycyrrhiza glabra*

Liquorice, scientifically referred to as *G. glabra* (*G. glabra* L.; Family: *Papilionaceae/Fabaceae*), is a widely recognized medicinal herb[99-101]. In traditional medicine, liquorice roots and stolons have been utilized for their tonic, expectorant, demulcent (soothing and protective), and therapeutic properties. They have been employed to alleviate respiratory conditions such as allergies, bronchitis, colds, sore throats, and tuberculosis. Additionally, liquorice has been used to address gastrointestinal issues including stomach burns, gastritis, and peptic ulcers. Additionally, it has been acknowledged for its prospective advantages in the treatment of liver, skin, and inflammatory diseases[102-105]. Liquorice has been shown to have anti-allergic, immunostimulant, and antioxidant

properties[106,107]. The primary ingredients, saponins and flavonoids, are responsible for these stated actions. Liquorice is useful in treating gastrointestinal ulcers and the aglycone of glycyrrhizin, glycyrrhetinic acid, has an anti-inflammatory and antiulcer action[108-110]. According to research, liquorice enhances mucus production and secretion, shielding the GI tract from the acids produced by digestion[111,112]. According to Andersson *et al*., in rats, deglycyrrhised liquorice inhibits stomach ulcers caused by pyloric ligation; in dogs, it prevents mucosal damage from bile; and in humans, it accelerates the healing of peptic ulcers[113,114]. The sodium salt of glycyrrhetinic acid's 3/3-O-hemisuccinate, carbenoxolone sodium, has undergone significant research and is known to have antiulcer properties in both animals and humans. To understand the anti-inflammatory mechanism, Chandrasekaran and colleagues investigated how the phytoconstituents glabridin, glycyrrhizin, and isoliquiritigenin found in *G. glabra* (GutGard) root extract inhibited the synthesis of Lipoxygenase (LOX) and Cyclooxygenase (COX) products[115,116]. *G. glabra* (almost completely lacking in glycyrrhizin) has anti-inflammatory qualities in mammalian cell assay systems, most likely by suppressing PGE2, TXB2, and LTB4, which may be influenced by glabridin and isoliquiritigenin[117]. Another study by Dehpour *et al.* found that liquorice or its derivatives had a preventive effect against stomach ulcers brought on by oral ibuprofen[118]. Mukherjee *et al*., have reported the anti-oxidant and anti-ulcer properties of the standardized extract of *G. glabra* (GutGardTM) in rats with stomach mucosal injury brought on by indomethacin, cold-restraint stress, and pyloric ligation[119]. GutGuard's antioxidant properties included antiulcerogenic effects through a cytoprotective mechanism and high hydrophilic and lipophilic Oxygen Radical Absorbance Capacity (ORAC) values.

Rats with aspirin-induced stomach ulcers were treated with a decoction of the liquorice root, *G. glabra,* as opposed to omeprazole and misoprostol[120]. The study's conclusions suggest that *G. glabra* may be used to treat NSAID-induced ulcers at a lower cost than omeprazole and misoprostol[121]. Three distinct polarity extracts of leaves were described and assessed by Siracusa *et al.* for their antioxidant, anti-inflammatory activity, and anti-genotoxic, which are essential properties of effective chemo-preventive medicines[122]. The most valuable extract was the ethyl acetate extract, which was distinguished by the obvious presence of various polyphenols, including flavonoids and dihydro stilbenes. Wittschier *et al.* investigated how *G. glabra* extract affected *H. pylori's* ability to adhere to stomach tissue[123]. The agar diffusion experiment was used to assess *H. pylori's* cytotoxicity *in vitro*; FITC-labelled bacteria on tissue slides from human stomach resections were used to examine the antiadhesive properties of aqueous extract, raw polysaccharides, and purified polysaccharide fractions *in situ. G. glabra* roots contain strong antiadhesive aqueous extracts and polysaccharides that may be helpful in the continuous creation of cytoprotective preparations with anti-infectious potential[124].

5.8 *Aloe barbadensis* Miller

Aloe barbadensis Miller, a very popular household plant commonly known as *Aloe vera* and commercially as *Curacoa aloe* belongs to the family *Liliaceae*[125,126]. Aloe has been used for millennia as a medicinal remedy to heal a variety of illnesses, earning it the moniker "miracle plant"[127,128]. Tropical to subtropical climates are home to the succulent plant aloe. In the African region, *Aloe vera* is also popular as the "desert lily" or the immortality plant[129]. *Aloe vera* plant contained a colourless bitter gel in the inner parts of the fresh leaves. This gel has been reported to have great therapeutic value and is effective against skin ulcer parasites, radiation burn, peptic ulcer wound healing and anti-inflammatory activity as it contains anthraquinones, polysaccharides, saponins and flavonoids, alkaloids, amino acids, enzymes, proteins, fatty acid materials, Vitamins (A, C, and E), glycoproteins, resins, minerals, sterols, gelonins, and biological stimulators[130-135]. The extract of *Aloe vera* produces healing of ulcers by forming a protective coating on the affected areas and through the complex synergistic interaction of the phytochemical constituents of the plant[136]. The gel is popularly utilised nowadays as a moisturizer, as a base in nutritional drinks and foods, and in cosmetics to intensify beauty by treating skin-related problems. Kohli *et al.* examine the entire leaf of Aloe barbadensis using solvent, ether, and aqueous extracts to determine whether it contains carbohydrates, saponins, flavonoids, tannins, alkaloids, anthraquinones, and resins, as well as any anti-inflammatory or antimicrobial properties[137,138].

Aloe vera's antibacterial properties have shown that *S. aureus*, *E. coli*, and *C. albicans* were all successfully suppressed. The results demonstrated that aloe gel had potent anti-inflammatory properties and unrefined sap had antibacterial properties. Patients with stomach ulcers have been treated with *Aloe vera* emulsion, which is a mixture of *Aloe vera* gel and sap and mineral oil[139]. In a 2004 study by Yusuf *et al.* studied in rats with ligated pylori and rats with lumen perfusion, acute gastric mucosal ulcers caused by 0.6M HCl and the effects of different dosages of an ethanol extract of *Aloe vera* (*Liliaceae*) on acid production were examined. Titrating the obtained gastric juice to pH 7.0 allowed for the detection of acid secretion. In a dose-dependent manner, an intraperitoneal injection of *Aloe vera* decreased the generation of stomach acid. The antimicrobial data showed effective inhibitory action against *S. aureus*, *E. coli*, and *C. albicans*. According to the findings, aloe leaf gel had strong anti-inflammatory properties, while crude sap had antibacterial properties. Peptic ulcer patients have been treated with *Aloe vera* emulsion, which is a mixture of *Aloe vera* gel and sap and mineral oil. In an investigation conducted by Yusuf *et al.*, in 2004, the effects of varying dosages of *Aloe vera* (*Liliaceae*) ethanol extract were investigated in connection to acute gastric mucosal lesions brought on by 0.6M HCl and acid production in rats with pylorus ligation and lumen perfusion. Acid secretion was measured by titrating the collected gastric juice to a pH of 7.0. Gastric acid secretion was dose-dependently reduced by an intraperitoneal infusion of *Aloe vera*. *Aloe vera* can inhibit acid secretion in the stomach, which allows it to defend the gastrointestinal mucosa from harmful substances at low concentrations[139].

5.9 *Cinnamomum tamala*

Cinnamomum tamala T. Nees and *Eberm* belongs to the *Lauraceae* family and is also referred to as Bay leaves in Europe and Tejpat in India[140]. Due to its distinctive aromatic odour, these medium-sized tree leaves are used as a spice all over the world. Historically, these leaves have been used to treat colic, dyspepsia, and diarrhoea, and as an anthelmintic, diuretic, and carminative[141]. Pinene, camphene, myrcene, limonene, germacrene A, gurjunene, 1-8-cineole, pcymene, methyl eugenol, eugenol acetate, and methyl ether of eugenol are some of the primary constituents of *C. tamala* leaves[142,143].

According to Shradha *et al.*, and other sources, *C. tamala* leaves have hypoglycemic, stimulant, carminative, and anti-diarrheal effects[144-146]. The antiulcer effects of aqueous extracts of cinnamon (CIAE) and chamomile (CHAE) at dosages of 100, 200, 300, and 400 mg/kg of body weight (b.wt) in rats were examined and compared by Amr *et al.* with Zantac™ (ranitidine)[147]. Oral administration of CIAE or CHAE was associated with a significant reduction in the volume of gastric juice as compared to the positive and control groups. Rats given CIAE or CHAE had a greater success rate at curing stomach ulcers than rats given Zantac. Results showed that CHAE and CIAE exhibited potential antiulcer effects that were superior to those shown with Zantac in area[148]. Eswaran *et al.*, discovered that a hydroalcoholic extract in the gastric mucosa had gastroprotective effects against ulcers brought on by chemicals, stress, and physical trauma; it also reduced the production of gastric acid, most likely by preventing H^+K^+ATPase from working; and it offered antioxidant protection against oxidative stress-induced gastric damage[149].

5.10 *Utleria salicifolia*

The branching shrub *U. salicifolia* Bedd. Ex. Hook. F. (*Periplocaceae*), often known as "*Mahali kizhangu*", is indigenous to the South Western Ghats of peninsular India and is mostly found in the Anamalais (Kerala and Tamil Nadu), Nelliampathy, and Marayaoor forests (Kerala). This herb has historically been found to be useful for digestive issues like colic and bleeding from ulcers. *Utleria salicifolia* (USE) ethanolic extract (50%) was evaluated by Rao *et al.* in 2004 in various rat models of acute and chronic stomach ulcers. In a model of ulceration caused by pylorus ligation, aspirin, cold-restraint stress, ethanol, and acetic acid, the antiulcer impact was investigated. The results of this investigation shown that *U. salicifolia* ethanolic extract has a gastroprotective effect by considerably reducing the development of ulcers brought on by a variety of chemical and physical stimuli[150,151].

5.11 *Elettaria cardamomum* Maton

Cardamom is a spice that is used all over the world and has therapeutic potential for gastrointestinal ailments. It is the fruit of the plant *E. cardamomum* Maton (*Zingiberaceae*), which is more generally known as *Choti*

ilaichi in India[152]. The herb has digestive, antiemetic, resolvent, retentive, carminative, and stomachic effects. Additionally, gastritis and acid peptic diseases have been treated with it[153-155]. The fruit is said to include phenolic acids, sterols, essential oil, and lipids[156,157]. The essential oil shows antibacterial, anti-inflammatory, analgesic, and antispasmodic properties[158].

In 2000, Vasudevan *et al.*, found that the aqueous extract of *E. cardamomum* increased the production of stomach acid in rats anesthetized with pentobarbitone[159]. In order to examine the antiulcerogenic properties of different *E. cardamomum* fractions in models of gastric lesions brought on by pylorus ligation, alcohol, and aspirin, Jamal *et al.* examined the cardamomum methanolic extract's crude Methanolic extract (TM), Essential Oil (EO), Petroleum ether Soluble (PS), and Insoluble (PI) fractions in rats. Their effects on the formation of stomach acid and mucus in the wall were also noted. It was discovered that all of the fractions (TM, EO, PS, and PI) significantly reduced the severity of stomach lesions caused by aspirin and ethanol, but not by pylorus ligation[160].

5.12 *Terminalia arjuna*

Terminalia arjuna (Combretaceae) has antibacterial, antimutagenic or anticarcinogenic, antioxidant, and hypocholesterolemic properties. It also helps heal wounds and prevent ulcers[161-164]. Tannins, triterpenoid saponins (arjunolic acid, arjunic acid, arjungenin, and arjunglycosides), flavonoids (arjunone, arjunolone, and luteolin), gallic acid, Oligomeric Proanthocyanidins (OPCs), polyphenols, calcium, magnesium, zinc, and copper are among the chemical substances found in *Terminalia* that exhibit biological activity[165,166].

Devi *et al.* assessed the impact of *T. arjuna* (TA) methanolic extract on experimental rat stomach ulcers brought on by Diclofenac sodium (DC). Non-protein Sulfhydryls (NP-SH), Lipid Peroxide (LPO), reduced Glutathione (GSH), pH, free and total acidity, pepsin concentration, the amount of gastric juice, and the antioxidant activities of the enzymes Glutathione Peroxidase (GPx), Catalase (CAT), glutathione dismutase (SOD), and glutathione-S-trans in the gastric mucosa were measured. When DIC + TA rats were compared to DIC rats, the pH, NP-SH, GSH, enzyme antioxidants, protein-bound carbohydrate complexes, adherent mucus content, and nucleic acids were significantly higher, while the volume of gastric juice, free and total acidity, pepsin concentration, acid output, LPO levels, or MPO activities were significantly lower. *T. arjuna* was found to have gastroprotective effects, most likely as a result of its cytoprotective qualities and ability to scavenge free radicals[167].

5.13 *Strychnos potatorum*

Known as *katakam* in *Ayurvedic* medicine, *S. potatorum* Linn (Family: *Loganiaceae*) is a medium-sized tree that is primarily found in southern and central India, Sri Lanka, and Burma[168]. Hepatopathy, nephropathy, gastropathy, bronchitis, and chronic coagulant aids can all be treated with the plant's seeds. The seeds colloids and alkaloids combine to extract suspended contaminants from muddy water and coal-washery effluent (Wealth of India, 1976)[161]. It has been reported that the seed contains the principal alkaloid diaboline and its acetate, as well as β sitosterol, stigmasterol, oleanolic acid and its 3 βacetate, saponins including oleanic acid, triterpenes, mannogalactans (polysaccharides), *etc*[160].

In a model of stomach ulcers caused by aspirin with pyloric ligation (Aspirin+PL), Sanmugapriya *et al.* discussed how *S. potatorum* Linn. Seed Powder (SPP) and Seed aqueous Extract (SPE) had antiulcerogenic properties[171]. *S. potatorum* seeds prevented ulcers in mice by increasing mucin activity and decreasing acid secretory activity. The mucoprotective properties of SPP and SPE may be caused by the polysaccharides found in seeds.

5.14 *Bryophyllum pinnatum*

This herb belongs to the *Crassulacea*, is frequently utilised in Indian traditional medicine[161]. The leaves are used to treat wounds, boils, bruises, and insect bites because they have antifungal, antibacterial, anti-inflammatory, and analgesic qualities[162]. It was examined how the leaf extract from *B. pinnatum* affected the different pharmacologic models of acute and chronic gastroduodenal ulcers and lesions[174,175]. This study found that the extract greatly decreased stomach lesions caused by alcohol, stress, serotonin, reserpine, aspirin, and indomethacin. Extract treatment was reported to considerably ameliorate duodenal ulcers caused by aspirin and histamine in guinea pigs and rats with pylorus ligation. Rats with persistent stomach

injuries caused by acetic acid also showed remarkable healing[163]. Herbal plants with antiulcerogenic activity are summarized in Table 1.

6. Recent Advancement in the Management of Ulcer using Traditional Medicinal Plants

6.1 Nanotechnology-based Advancement

In recent years, nanotechnology has been utilised to enhance the therapeutic efficacy of herbal antiulcer medicines. Nanoparticles, lipid nano-emulsions, and liposomal compositions have been engineered to improve bioavailability, stability, and stomach mucosal targeting of phytochemicals. *Aloe vera*-encapsulated chitosan nanoparticles and *G. glabra* nanosuspensions have demonstrated enhanced mucosal adherence and extended antiulcer efficacy in experimental animals. Likewise, curcumin and flavonoid nano-emulsions demonstrate improved solubility and absorption, resulting in greater ulcer-healing effectiveness than traditional extracts[178].

6.2 *In Silico* and Computational Advancement

Advanced *in silico* methodologies, including molecular docking, Absorption, Distribution, Metabolism, Elimination, and Toxicity (ADMET) prediction, and network pharmacology, have become essential for elucidating the molecular processes of phytoconstituents. Recent investigations have revealed substances such as quercetin, gallic acid,

Table 1. Represents the summary of natural ingredients exhibiting anti-ulcers activity

Medicinal Plants	Phytochemical Constituent	Antiulcer Activity	References
E. officinalis	Ascorbic acid, gallic acid, ellagic acid, tannins	Flavonoids possess antioxidant properties, have cytoprotective effects, augment mucin secretion, and diminish gastric acidity.	164
A. indica A. Juss	Azadirachtin, nimbidin, nimbin, quercetin	Anti-inflammatory, suppresses acid release, enhances mucosal protection.	165
A. racemosus	Asparagamine	Enhances mucin secretion, possesses antioxidant properties, and provides cytoprotection.	166
S. nigrum	Solanine, solasodine, flavonoids, tannins	Antioxidant, cytoprotective, mitigates gastric mucosal damage.	167
M. charantia L.	Charantin, momordicin, and cucurbitane-type triterpenoids	Antioxidant, suppresses acid secretion, facilitates mucosal repair.	168
B. arundinacea	Silica, flavonoids, phenolic acids, lignans	Anti-inflammatory, antioxidant, mucosal safeguarding.	169
G. glabra	Glycyrrhizin, liquiritin, glabridin, and flavonoids	Cytoprotective, anti-inflammatory, and improves mucosal defense mechanisms.	170
A. barbadensis	Aloin, aloesin, polysaccharides, anthraquinones	Mucoprotective, cicatrising, antioxidant	171
C. tamala	Cinnamaldehyde, eugenol, linalool, tannins	Antioxidant properties, decrease acid secretion, and enhance mucin formation.	172
U. salicifolia	Flavonoids, phenolic chemicals, and alkaloids	Antioxidant properties and mucosal protection.	173
E. cardamomum	Cineole, α-terpinyl acetate, flavonoids	Antioxidant, gastroprotective, anti-inflammatory properties.	174
T. arjuna	Arjunolic acid, tannins, saponins, and flavonoids	Antioxidant properties, promote mucosal healing, and possess anti-inflammatory effects.	175
S. potatorum	Strychnine, brucine, alkaloids, polysaccharides	Antioxidant, anti-secretory, fortifies mucosal barrier	176
B. pinnatum	Bufadienolides, flavonoids, tannins, glycosides	Anti-inflammatory, antioxidant, and promotes mucosal protection.	177

and glycyrrhizin as effective inhibitors of critical ulcerogenic targets, including H^+/K^+-ATPase, COX-2, and TNF-α. These computer models facilitate the prediction of multi-target interactions, the optimization of lead drugs, and the validation of the pharmacological significance of traditional herbal treatments[179-180].

6.3 Metabolomics and Transcriptomics Advancement

High-throughput omics technologies, including metabolomics, transcriptomics, and proteomics, are increasingly employed to examine the systemic effects of herbal antiulcer medicines. This research has demonstrated that phytochemicals influence oxidative stress pathways, promote mucosal regeneration, and alter genes associated with stomach acid secretion and inflammation. In one study, extracts of *A. racemosus* and *E. officinalis* were observed to affect the production of antioxidant enzymes and growth factors implicated in mucosal healing[181].

6.4 Polyherbal and Synergistic Medicine System

The development of polyherbal combinations is increasing due to the synergistic effects of several bioactive constituents. Recent preclinical data indicate that the combinations of *G. glabra* with *E. officinalis* or *A. barbadensis* yield superior gastroprotective benefits compared to the solo plant extracts. These formulations boost efficacy while reducing dosage requirements and potential adverse effects, in accordance with the holistic principles of *Ayurveda* and integrative medicine[182-183].

6.5 Gut Microbial Environment Modulation System

An increasing amount of research indicates that the gut microbiota is essential in ulcer etiology and repair. Recent research indicates that specific plant extract namely *A. indica, M. charantia*, and *T. arjuna,* demonstrate prebiotic-like properties, fostering the proliferation of beneficial bacteria while inhibiting *H. pylori* colonisation. This modification of microbiota is an innovative therapeutic approach connecting herbal medicine to gastrointestinal health and mucosal protection[184].

7. Conclusion

The present article reviewed various plants having antiulcer activity with the help of various literature having proper pharmacological activities of these plants. India and various countries are rich in green wealth. Since ancient times, plants have been utilized to heal a variety of illnesses. Humans turn to herbal remedies as an alternative to allopathic ones due to a number of issues with manufactured medications. Plants have been found fully loaded with various active constituents. The main objective is to find these constituents and make their use in suitable diseases via proper scientific research. Today, peptic ulcers are a widespread issue throughout the world, and people are looking for a therapy that is less costly, safe, and effective with fewer side effects. The prognosis for patients with gastric ulcers may be improved by using herbal medicines in conjunction with traditional anti-gastric ulcer drugs, which may work in concert to combat *H. pylori* and gastric ulcer illness. In order to treat peptic ulcers and other illnesses, traditional medicinal plants offer a glimmer of hope in meeting the aforementioned criterion. Because there are so few human studies on the effectiveness and safety of medicinal plants with antiulcer action, more clinical research with larger sample sizes is recommended. Last but not least, herbal items used for medicinal purposes need to be licensed in order to enhance their quality and safety and ensure that randomised controlled trials support claims of their possible utility. There is still a problem with insufficient research in this area, and nothing has been done to address it, even though reports of herb-drug interactions have increased. The risks associated with using herbal remedies, either by alone or in combination with other herbal or conventional standard therapies, should be known to chemists and physicians. It would also be advantageous to plan studies to look into and elucidate the mechanisms of action of medicinal plants used to cure or prevent peptic ulcers.

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9. Author Contribution

Conceptualization, YA; investigation, YA and AS; resources, AS, KJ, PK and MB.; data curation, YA and MB; writing-original draft preparation, YA, AS, AS, KJ and PK; writing-review and editing, YA and MB; visualization, YA; supervision, YA, NK, KS. All authors have read and agreed to the published version of the manuscript.

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