



## A Review of the Phytochemicals Found in Medicinal Plants that may have Antiulcer Properties

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<b>Abstract:</b> The risk of peptic ulcer is also increased by non-steroidal anti-inflammatory medications and Helicobacter pylori infection. Adverse effects and concurrent usage of antibiotics result from the careless use of synthetic medicines. Compounds drug-drug interactions; thus, it is vital to look for medications made from natural sources, particularly plants. Numerous ulcer-inducing models in lab animals have been used to assess the antiulcer effectiveness of numerous herbal remedies. The current study is to examine putative medicinal plants with gastro-protective and ulcer-healing properties and compile relevant data. The antiulcer effectiveness of medicinal plants is the exclusive focus of this essay. This study provides details on the anti-ulcer properties of medicinal plants as well as the many anti-ulcer models that are used to evaluate them.	<b>Review Paper</b>
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### INTRODUCTION

Ulcer pepticum, another name for peptic ulcer, is now a frequent illness affecting a significant portion of the global population in various nations. Peptic ulcers are referred to as Amlapitta in Ayurveda [1]. In humans, peptic ulceration is a frequent, persistent, recurring, and occasionally fatal condition with an unclear etiology. A peptic ulcer occurs when there is a breach in the stomach, duodenum, or digestive tract's continuous mucosal barrier, exposing the underlying tissue to the corrosive effects of hydrochloric acid and pepsin. An ulcer is also defined as a defect in the stomach or duodenum's mucosa that may extend into the sub-mucosa or deeper [2]. The imbalance between aggressive or harmful forces, such as excessive acid-pepsin production, and defensive or protective factors, including gastric integrity, bicarbonate, and prostaglandin secretion, leads to peptic ulcers. The integrity of the mucosa may be compromised by ulceration as a result of repeated injury to the endothelium layer or inability of the mucosal layer to repair or restore itself [3, 4].

Eating spicy food and experiencing stress can cause peptic ulcers. It has been shown that these two elements are only intense ones. The actual reasons, however, were shown to be an H. pylori bacterial infection or a medication response, primarily from NSAIDs [5]. The main etiological causes for peptic

ulcers are often the H. pylori bacteria, NSAIDs, mental stress, alcohol misuse, and smoking [6]. Many medications, including those classified as anti-secretory agents like omeprazole, an inhibitor of the irreversible proton pump, and ranitidine, an antagonist of the histamine H2 receptor, are used to treat stomach ulcers [7]. However, prolonged use of these medications may result in a number of negative side effects, including hepatotoxicity, nephrotoxicity, gynecomastia, thrombocytopenia, and impotence [8]. Medicinal plants are considered a significant source of modern pharmaceuticals because synthetic treatments for many ailments have several adverse effects. Extensive study is conducted to identify the potent anti-ulcer compounds derived from plants, since herbal medicines are recognized as nontoxic for treating ulcers with fewer side effects [9-11]. This communication aimed to evaluate recent research in the field and provide insight into the potential medical uses of some chemicals produced from medicinal plants for the treatment of ulcers.

### Potential Medicinal Plants Used in Ulcer

To get a good outcomes, many researches have assessed the antiulcer properties of a wide variety of spices and herbs. Gastro-protective properties have been demonstrated in a wide range of nutritional supplements and medicinal plants, including aloe, terminalia chebula, vetiveria zizanioides, ginseng, and capsicum [12]. Despite being one of the well-known medicinal plants

used in Indian traditional medicine to cure a variety of illnesses, there are relatively few research on the pharmacological characteristics of certain medicinal plants. We investigated certain medicinal plants' acute toxicity and antiulcer efficacy. Our study demonstrated the dose-dependent ulcer-prevention potential of these examined medicinal herbs in rats. These therapeutic herbs did not exhibit any acute toxicity, according to histological investigations.

Important secondary metabolites including tannins and flavonoids were found in this medicinal plant during preliminary photochemical screening. Many botanical preparations have been claimed to have antiulcer properties, although the majority of the research that has been published has focused on the pharmacological effect of these products in experimental animals. There are few clinical studies supporting the use of herbs as gastro-protective agents, with the exception of a few phytochemicals (such as licorice, chilly, and aloe), and as a result, there are little data on efficacy and safety. In spite of this, a number of botanical compounds have the potential to be used therapeutically due to their high potency and low toxicity. Lastly, it should be mentioned that since the majority of anti-inflammatory medications used in modern medicine are ulcerogenic, compounds with antiulcer action, such as flavonoids, aescin, aloe gel, and many others, are particularly important from a therapeutic standpoint [13-15].

### Herbal Potential Drug to Reduce Synthetic Drug Effect

An adverse response is any unpleasant, unanticipated, or unwanted consequence that a medication has on the body in addition to its intended effect. The use of synthetic medications for the treatment of peptic ulcers has been restricted for an extended length of time due to several reported side effects [16]. There have been reports of mild adverse effects with proton pump inhibitors (PPIs), including nausea, constipation, gas, and diarrhea. Major adverse effects from PPIs include intestinal nephritis, arthralgia, arrhythmias, and sub-acute myopathy. Prolonged PPI usage has been linked to an increased risk of dementia and chronic kidney disease, according to recent research [17]. H<sub>2</sub> receptor antagonists have been linked to headaches, slurred speech, sleepiness, headaches, muscle soreness, and disorientation. Cimetidine impairs libido, induces impotence, and may cause gynecomastia. Misoprostol is not recommended for use during pregnancy since it increases uterine contractility and can lead to clinical exacerbations of inflammatory bowel disease [18]. Antacids can cause an imbalance in the electrolyte levels, which can exacerbate the condition of a patient with renal insufficiency. Antacids containing Al<sup>+3</sup> may increase the risk of bone fracture in older people by causing osteoporosis, proximal myopathy, and

encephalopathy. Nowadays, cytoprotectant medications such as pirenzepine, an M1 muscarinic receptor antagonist, are rarely utilized due to their tendency to induce hemopoietic alterations and blood problems, as well as their potential for anticholinergic side effects [19]. Humanity can benefit from the search for herbal remedies since natural remedies have been shown to have less adverse effects than manufactured ones. The current research thus attempts to gather information about documented antiulcer activity from medicinal herbs. Few possible anti-ulcer herbs in (Table-1).

### Several Herbs That Are Used to Cure Ulcers Include *Ficus Arnottiana*:

This significant traditional medicinal plant is found all across India, primarily on stony hillsides up to an altitude of 1350 meters. It goes by a number of colloquial names, such as kodiarasu and Para's pipal. Friedelin, glucose, and  $\beta$ -sitosterol acetate are found in the plant's fruits. The bark extracts contain tannins, phenols, carbohydrates, alkaloids, and steroids, among other substances. Traditional medicine makes use of this plant's bark and leaf extract. The plant's bark has depurative, emollient, demulcent, astringent, and aphrodisiac properties. Additionally, it helps with wounds, ulcers, diabetes, burning sensations, leprosy, scabies, and inflammation in addition to skin conditions. Uses: Beneficial for wounds, ulcers, diabetes, burning sensation, leprosy, scabies, and inflammation as well as skin conditions [20]. Alkaloids, reducing sugars, simple phenolic compounds, coumarins, flavonoids, tannins, phthalobatanin, and steroids. Lipoprotein and saponin were detected in greater quantities than other phytochemicals, whereas the alkaloid content was 0.86%. *A. scholaris* may be helpful in treating a variety of illnesses and may one day provide valuable drugs for human usage thanks to the aforementioned many chemical components found in the plant [21].

### *Asparagus Racemosus*:

Shatavarin, a steroidal saponin, is the main chemical component displaying therapeutic effects. Shatavarin I-IV, which are four different kinds, are found in roots. In addition, fruits and seeds contain unidentified saponins, stigmasterol, quercetin-3-glucosinide, rutin in shoots, and sitosterol [22]. Satamuli, the Sanskrit name, refers to the many fusiform tubers that this plant produces. These are used both internally and in the creation of various therapeutic oils. They are said to have cooling, demulcent, diuretic, tonic, and aphrodisiac properties. Sincere, the tubers are regarded as sweet flesh. Nonetheless, the only flavor or taste in this concoction is that of the sugar. Fresh root juice is administered with honey as a demulcent for diarrhea or bilious dyspepsia [12].

### *Maytenus Robusta Reissek*:

Robust *Maytenus* in South America, reissek is traditionally used as a decoction to treat gastrointestinal ailments; it is most popular in nations like Brazil [23]. Using an acetic acid-induced chronic ulcer model, L. Mota da Silva *et al.*, (2015) conducted in vitro and in vivo research to ascertain the ulcer healing efficacy of the hydro alcoholic extract of aerial plants of *Maytenus robusta* Reissek (HEMR). Utilizing an ulcer-induced model generated by Pylorus ligation, the antisecretory property was investigated. Radical scavenging activity, cytoprotective impact, and cell proliferation activity in fibroblast (L929 cells) were assessed along with anti-helicobacter pylori activity to identify in vitro antiulcer activity. The acetic acid-induced chronic ulcer model showed a 53% decrease in stomach ulcer area when HEMR was administered orally at a dosage of 10 mg/kg. HEMR 10 mg/kg applied intradually, however, did not significantly alter volume, pH, total acidity, or pepsin activity in the pylorus ligated ulcer generated model. Research conducted in vitro has demonstrated that HEMR at concentrations of 1-1000µg/ml may effectively scavenge the free radical DPPH. Additionally, fibroblasts have been found to exhibit cytoprotection against hydrogen peroxide at concentrations of 0.1-100µg/m [24].

#### **Rhizophora Mangles:**

Native to the Caribbean, *Rhizophora mangles* L is a plant high in tannins. 14 Studies have found that the medication possesses antioxidant, anti-inflammatory, and wound-healing properties [25]. *Rhizophora mangle* L.'s mode of action for its antiulcer effect was investigated by F. M. de-Faria *et al.*, in 2012. *Rhizophora mangles* L. bark was ground up and macerated in a ratio of acetone to water (7:3) to produce crude extract (CE). This extract was then separated using various solvents to produce three different fractions: aqueous (Aq), ethyl acetate (EtoAc), and butanolic (BuOH). Rats were used as models for gastric ulcers by pylorus ligation and ethanol induction. The findings demonstrated that at every tested dosage, every fraction of *Rhizophora mangle* L. exhibited a gastroprotective effect. Since BuOH extract showed notable antiulcer effect, it was investigated further to look for a potential underlying mechanism of action. Nitric oxide (NO), sulfurydril compounds (SH), mucus sticking to the stomach wall, PGE2 levels, and the expression of COX-1, COX-2, and EGF were all shown to be involved. It was shown that increased PGE2 levels and upregulated COX-2 and EGF may have a role in the gastroprotective, ulcer-healing, and antisecretory effects of BuOH [26].

#### **Vitis Vinifera:**

Known by most as grape seeds, *Vitis vinifera* is a native plant of Europe and the Mediterranean area. It is a member of the Vitaceae family. Because it is a high source of antioxidants, studies have shown that it has antioxidant activity. Its antimicrobial and anti-

inflammatory properties have been discovered [27]. Ingale A. M. *et al.*, (2016) used wistar albino rats to create an ulcer model with hydrochloric acid and ethanol to assess the anti-ulcer efficacy of grape (*Vitis vinifera*) seed extract. After the grapes' seeds were extracted, they were air dried to create grape seed extract (GSE). Afterwards, 95% ethanol was used to remove the seeds. Rats of both sexes were split up into four groups, each with six rats. Group I received 1 milliliter of distilled water as a control, Group II received the normal medication 100 mg/kg of sucralfate, and Groups III and IV received 100 mg/kg and 200 mg/kg of GSE, respectively. Each and every therapy was given orally. Thirty minutes after the therapy, 1 ml of 60% ethanol and 0.3M HCl was given to induce ulcer. GSE was shown to considerably reduce ulcer number 30 + 3.23 and 27 + 2.97 as compared to control 41.66, even though there was no significant change in the stomach volume, pH, total acidity, or bound acidity. The relative rates of ulcer inhibition were 34.67% and 27.98% [28].

#### **Muktashukti Bhasma:**

An Ayurvedic treatment called *Muktashukti Bhasma* is made of vinegar, pearl, and aloe vera. Aloe vera and vinegar are used to triturate the oyster shell's outer layer. It is used to treat dyspepsia, asthma, heart disease, and vomiting [29]. The anti-peptic ulcer efficacy of *Muktashukti Bhasma* was investigated by Chouhan Omi *et al.*, (2010). The Ayurvedic medical system uses ash, or pearl oyster paste, known as *Muktashukti Bhasma* (MSB), to treat a variety of stomach issues. Rats of both sexes were split into seven groups in this investigation, each with eight individuals. Group I received no treatment and was retained as the control group. Groups II, III, and IV received doses of 100 mg/kg, 300 mg/kg, and 1000 mg/kg of MSB. The conventional medication ranitidine was administered subcutaneously to Groups V, VI, and VII at doses ranging from 0.5 to 5 mg/kg of body weight. Using a model of ligated stomach ulceration produced by the stomach, the activity of peptic ulcers was evaluated. All dosages of MSB were shown to exhibit encouraging antiulcer action, as evidenced by a reduction in ulcer score and ulcer index. When MSB was administered at doses of 100, 300, and 1000 mg/kg of body weight, the ulcer score was 1.66 ± 0.20, 0.66 ± 0.20, and 0.50 ± 0.22, while the control group had a score of 2.00 ± 0.47. Ulcer index was 200.0 against 166, 44, and 25 for the control group. In comparison to control 2.0, pH was increased by MSB to 2.66, 3.66, and 6.0 at the same dosage levels. It was determined that MSB had anti-ulcer action and a considerable decrease in acid production [30].

#### **Carica Papaya:**

Papaya is a tropical plant that grows quickly and is semi-woody. The stem is hollow, solitary, and straight, with noticeable leaf scars. Papayas seldom branch until the apical meristem is severed or destroyed,

demonstrating strong apical dominance. The fruit is up to 9 kg in weight, melon-like, oval to almost spherical, slightly pyriform, or elongated club-shaped. Its dimensions are 15–50 cm in length and 10–20 cm in thickness. Fruits on semi-wild (naturalized) plants range in length from 2.5 to 15 cm. The skin is thin, waxy, and quite durable. The fruit's skin is hard and green when it is young, and it contains a lot of white latex [31]. Tropical traditional medicine makes use of papaya. Papaya latex is given topically to burns and scalds and is invaluable in the treatment of dyspepsia. The fruit and seeds have antiamebic and anthelmintic properties. Numerous physiologically active substances are included in it. Two significant substances that are well-known for helping with gastrointestinal tract disruptions and digestive issues are chymopapain and papain. Papain, chymopapain, pectin, carposide, carpaine, pseudocarpaine, dehydrocarpines, carotenoids, cryptoglavine, cis-violaxanthin, and antheraxanthin are the principal chemical constituents [32].

#### ***Terminalia Chebula:***

*Terminalia Chebula* is a key component of the Ayurvedic medical system. It is regarded as the king of medicine and possesses exceptional healing potential [33]. The anti-ulcer potential of *Terminalia chebula* fruit was assessed by Raju D *et al.*, (2009) by methanol (METC) extraction. Rats with pylorus ligation and an ethanol-induced ulcer model were used to create ulcers. In comparison to the control, METC at doses of 250 and 500 mg/kg significantly reduced the number of gastric lesions, stomach volume, free acidity, and ulcer index. The anti-secretory activity of METC may account for its anti-ulcerogenic and ulcer-healing qualities, according to the findings [34].

#### ***Gardenia Gummifera:***

Research has shown that the plant *Gardenia gummifera* L., which is native to the southern Indian subcontinent, possesses anthelmintic, antispasmodic, and antiepileptic properties [35]. The antiulcer activity of *Gardenia gummifera* L. (MEGG) in rats was demonstrated by Pradeep Kumar *et al.*, (2015) through their study and extraction of the whole plant. The aspirin plus pylorus ligation caused ulcer model showed a reduction in ulcer index in groups of rats treated with MEGG at oral doses of 150 mg/kg and 300 mg/kg for six days. The percentage protection was 70.66 and 44.61, respectively [36].

#### ***Annona Squamoza:***

A deciduous tree that reaches a height of 5 to 10 meters, smooth or almost smooth. The leaves are grouped in pairs and are 6 to 10 centimeters in length. They have whole or undulating borders, a pointed tip, and a pointed, rounded, or heart-shaped base. The white or yellowish-white, stalkless flowers are 7 mm in length and are borne in loose inflorescences that span 5 to 10 cm. There is an oval calyx. The calyx, which has lobes that expand and reflex, is longer than the corolla tube. The corolla and stamens have hairy throats. The fruit is a drupe that is ovoid, 10 to 13 mm long, yellowish white or pinkish, with a firm stone and a sparse pulp [37]. Tannic acid may be found in considerable quantities in bark. Fruit pulp includes ash, gum, sugar, and extractive materials. A substance found in bark is comparable to "cathartin." Fruit is regarded as soothing, while bark is tonic and astringent. The bark is moistened and applied to boils and tumors to hasten ripening. Also used for headaches and stomach aches. Bark is used as antidyspeptic and as febrifuge. Powdered bark is used for mouth ulcers. Infusion of bark is used as gargle. The bark juice, mixed with coconut milk, is used to relieve colicky pains.

**Table 1: Several possible anti-ulcer herbs**

Botanical name	Parts used	Phytoconstituents	Medicinal use
<i>Curcuma longa</i>	Rhizome	Phenolic, tannins, flavonoids	Antiulcer, wound healings, antiinflammatory
<i>Terminalia Chebula</i>	Seed	Tannins, gallic acid, chebulinic acid, sorbitol.	Triphala, wound ulcer, leprosy, inflammation
<i>Ficus arnottiana</i>	Leaf	$\beta$ -sitosterol, gluanol acetate and glucose, Sterols, alkaloids, carbohydrates, tannins, phenols	Useful against inflammation, diarrhea, diabetes, burning sensation, leprosy, scabies, ulcer
<i>Albizia lebbek</i>	Leaves, bark, flowers	Phenolic compounds, saponin, protein, flavonoids	Boils, eruptions and swellings, leprosy ulcers
<i>Rhizophora mangles</i>	Leaf	Quercetin and proanthocyanidins	Antiseptic, astringent, haemostatic and antifungal properties
<i>Vitis vinifera</i>	Leaves and fruit	Phenolic compounds, aromatic acids, flavonoids, proanthocyanidins, and stilbenoids.	Antioxidative, anti-inflammatory, and antimicrobial activities
<i>Gardenia gummifera</i>	Bark and leaf	Glycosides, phytosterols, fats and oils, phenols, resins, tannins, flavonoids, tannins, and terpenoids	Indigestion, constipation, menstrual cycle problem, muscle pain, dental problems, parasitic worms

Botanical name	Parts used	Phytoconstituents	Medicinal use
<i>Glycyrrhiza glabra</i>	Root and rhizome	Glycyrrhizinic acid, a triterpenoids saponin	Antiulcer activity
<i>Basella rubra</i>	Leaf	Saponin, protein, flavonoids	Antiulcer
<i>Momordica charantia</i>	Fruits	Charantin, vicine, and polypeptide	Antiulcer
<i>Citrus aurantifolia</i>	Fruits and leaves	lavonoids including apigenin, hesperetin, kaempferol, nobiletin, quercetin, and rutin, flavones, flavanones and naringenin, triterpenoid, and limonoids	Arthritis, asthma, headaches, abdominal pain, intestinal parasites and psychological problems
<i>Persea americana</i>	Fruits	Alkaloids, flavonoids, saponin, tannins, phenol and cardinolides	Diarrhea, dysentery caused by helminths and amoebas, toothache, intestinal worms

## CONCLUSION

Significant antiulcer and gastroprotective efficacy has been found in a variety of plant extracts and the isolated substances derived from them. Plant extracts including flavonoids and tannins have been shown to have a significant impact on ulcer healing. With the extracts of these therapeutic plants, polyherbal preparations might be designed and developed. This study makes it abundantly clear that medicinal herbs are essential in the fight against a wide range of illnesses. In animal models, a wide variety of herbal plants and plant extracts have strong antiulcer properties. When compared to reference medications, it has stomach anti-secretory and mucoprotective effects. Not even at comparatively large doses is the extract harmful. The antiulcer action in all these plants is most likely caused by the flavonoid content. Our findings demonstrated that the medicinal herbs listed above might, in a dose-dependent way, prevent ulcers in rats. Numerous plant products have been found to have antiulcer properties; in conclusion, it should be highlighted that compounds with antiulcer properties such flavonoids and tannins are especially significant from a medicinal standpoint.

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