



HERBAL MEDICINES AS ANTIULCER: A REVIEW OF THE SCIENTIFIC EVIDENCE

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ABSTRACT

Ulcer is a common gastrointestinal disease that occurs in many people. An ulcer is an erosion of the lining of the stomach and duodenum. There are two types of gastric ulcer and duodenal ulcer. Together they are called gastric ulcers. Synthetic drugs can be used to treat ulcers. However, these drugs are expensive and may have more side effects than herbal medicines. In recent years, gastric ulcers are also related to *Helicobacter pylori* infection of the lining of the gastrointestinal tract. Many herbs and herbal products have been found to play a role in protecting or treating peptic ulcer and gastric ulcer diseases. Herbs are believed to be safe to treat gastric ulcers with fewer side effects. This

review describes various scientific evidence for the anti-ulcer activity of various plants. Using the following selected medicinal plants, we can prevent and heal ulcers.

KEYWORDS: Antiulcer agents, H.pylori, Peptic ulcer, NSAIDS.

1. INTRODUCTION

Peptic ulcer is defined as the destruction of the integrity of the lining of the stomach or duodenum by taking certain drugs and anti-inflammatory drugs (NSAIDs, and finally non-steroidal anti-inflammatory drugs).^[1] Basically, word “peptic” is derived from Greek term “peptikos” whose meaning is related to digestion. Various reports indicate that old age group patients are more prone to gastric ulcer. Younger individuals have higher risk of duodenal ulcers.^[2,3,4] The pathogenesis of ulcer disease includes gastric acid, pepsin secretion, *Helicobacter pylori* (H. pylori), bile salts, ethanol, some drugs (such as non-steroidal anti-inflammatory drugs), lipid peroxidation, A complex imbalance between aggressive gastric factors such as nitrate. acid. Oxide (NO) and mucosal protective factors, such as prostaglandin

(PG), gastric mucus, cell renewal, blood flow, mucosal cell secretion, glycoprotein, mucin secretion, proliferation, and antioxidant enzymes such as catalase (CAT), superoxide dismutase (SOD) and glutathione levels.^[5] Gastric ulcers can be classified according to the location and severity of the disease. There are many other factors that contribute to the progression of gastric ulcers, such as tumor necrosis factor alpha (TNF alpha), reactive oxygen species (ROS), histamine release, frequency of apoptosis, and bile acid secretion.^[6,7] There is evidence that ulcers caused by non-steroidal anti-inflammatory drugs are very common.^[8] NSAIDs promote ulcer progression by inhibiting the expression of cyclooxygenase (COX), which is reported to inhibit the conversion of arachidonic acid (AA) to PG.^[9] this changes the mucosal barrier and causes the corrosive effect of pepsin, which leads to the progression of gastric ulcers. There is strong evidence that oxygen-derived free radicals play a key role in the pathogenesis of damage to various tissues (including the digestive system).^[10] Stomach ulcers are well known. TNF α is a cytokine that triggers the inflammatory process and stimulates the migration of leukocytes to inflammatory lesions, thus playing an important role in the formation of gastric ulcers.^[11] In addition, TNF α also activates the exogenous cell apoptosis pathway by starting caspase 3, leading to gastric injury.^[12] Increased TNF α levels activate Caspase 3, which is one of the most important effect Caspases involved in apoptotic cell death. Finally, caspase activates neutrophils through various chemical attractants, forming a vicious circle that causes stomach injury.^[13] In addition, *Helicobacter pylori* is also involved in the progression of gastric ulcer. *Helicobacter pylori* is a gram-negative, agile, microaerobic, flagellated, and spiral-shaped bacteria. It secretes a unique urease enzyme that converts urea into ammonia, further reducing gastric acidity, making it a *Helicobacter pylori* nursing home.^[14] *H. Helicobacter pylori* has pathogenic activity and can encode the effector protein of cytotoxin-related gene A (cagA). After translocation into host cells, cagA affects the shape of cells, increases cell movement, and changes the activity of cell attachment, which is the cause of gastric cancer and ulcers.^[15] There are a large number of chemicals that can be used to treat gastric ulcers, but serious side effects such as H₂ antagonists are the triggers for impotence, headache, rash and arrhythmia, and the use of proton pump inhibitors can cause hypergastrinemia and atrophic gastritis. For unpredictable reasons. The use of antacids can cause flatulence, belching, constipation and the risk of ulcer perforation, while other drugs such as anticholinergics can cause constipation, dry mouth, urinary retention, blurred vision, dry mouth and glaucoma precipitation of glaucoma.^[16,17] Ulcer protectives causes constipation, triggers diarrhoea, dizziness, edema and hypophosphatemia whereas abdominal cramps, uterine bleeding and abortion is the probable cause of prostaglandin analogues.^[18]

So herbal drugs have preserved their importance due to relatively less toxic, better cultural acceptability, better compatibility with human body, lesser adverse effects. This paper outlines the scientific evidence of some medicinal plants that exhibit antiulcer activity.

1.1 Screening models for anti ulcer^[20-24]

- Hydrochloric acid-induced ulcers.
- Ulcers caused by histamine-induced.
- Ulcers caused by Acetic acid-induced.
- Ethanol-induced ulcers.
- Aspirin-induced ulcers.
- Ulcer caused by giving water immersion stress.
- Pylorus ligation-induced ulcers.
- Ulcer caused by reserpine-induced.
- Indomethacin-induced ulcers.
- Serotonin-induced ulcer.

Table 1: Some plants with Bioactive compounds containing Anti-ulcer activity.

Plant name	Active constituents	Reference
Acacia Arabica (Leguminosae)	Polyphenolic, Flavonoids, Glucoside, Tannin, Rhamnose, Iso-Quercitrin, Leucocyanidin, Galactose, Arabinose, Aldobiouronic Acids, Peroxidase.	[25]
Acorus Calamus (Acoraceae)	Flavonoids, Saponins, Tannins, Glycosides, Volatile Oils, Mucilage, Polyphenolic Compounds, A-Pinene, Camphene, B-Pinene, Borynl Acetate Etc.,	[26]
Adansonia digitata (Malvaceae)	Phobaphenes, Mucilage, Gum, Glucose, Tartrate, Acetate of Potash, Wax, Glucose, Salts, Gum, And Albuminoids. Tannin, AcidGum, Albuminous Carbonate and Chloride of Sodium And Potassium, And A Glucoside Adansonin.	[27]
Aegle marmelos (Rutaceae)	Alkaloids, Terpenoids, Coumarins, Gum or Resins, Essential Oil, Poison, Phenylpropanoids, Polysaccharides, Flavonoids.	[28, 29]
Allium sativum (Liliaceae)	Carbohydrates, Proteins, Steroids Saponins, And Fats. Mucilage And, Ally, Properly Disulphide And Dially, And Disulfyl, Volatile Oil, Alliin, And Allicin, Ajoene, Peroxidase, Arginine, Selenium, Germanium and Tellurium.	[30]
Aloevera (Euphorbiaceae)	Amino Acids, Anthraquinones, Enzymes, Minerals, Vitamins, Lectins, Monosaccharide, Polysaccharides, Salicylic Acid, Saponins, And	[31]

	Sterols, Bradykinase, Cellulase, Carboxypeptidase, Catalase, Amylase And Oxidase, Antioxidant Vitamins A, C And E. Vitamin B1 (Thiamine), Niacin, Vitamin B2 (Riboflavin), Choline And Folic Acid, Polysaccharides, Comprising Glucose And Mannose, Known as the Glucomannans, Xylose, Rhamnose, Galactose And Arabinose, Lupeol (A Triterpenoid), Cholesterol, Campesterol And B- Sitosterol.	
<i>Annona muricata</i> (Annonaceae)	Tannic Acid, Alkaloids, Flavonoids, Saponins, And Tannins, Vitamins, Carotenoids, Amides, Cyclopeptides and Megastigmanes,	[32]
<i>Betavulgaris</i> (Chenopodiaceae)	Flavonoids, Saponins, Sterols, And Alkaloids.	[33, 34]
<i>Carica Papaya</i> (Caricaceae)	Alkaloids, Saponins, Phenols, Tannins, Flavonoids, Choline and Carposide, Anthraquinone, Vitamin C And Vitamin E, Oxygen Calcium, Magnesium, Potassium, Aluminum, Phosphorus, Chloride, Sulphur, Stannous, Strontium, Zinc, Vanadium, Titanium, Cobalt, And Tantalum	[35, 36]
<i>Euphorbia neriifolia</i> Linn. (Euphorbiaceae)	E Glut-5-En-3 β -Ol, Glut- 5(10)-En-1-One, Taraxerol and B-Amyrin. Antiquorin, Neriifolione, A Triterpene, Tetracyclic Triterpene, Phlobotannins, Flavonoids, Saponins, Tannins, Terpenoids, Phenols And Cardenoloids, Alkaloid, Caoutchouc, Chlorophyll, Sugar, Mucilage, Tannin, Carbohydrates, Calcium Oxalate, Quercetin, Gallic Acid And Traces Of Essential Oil.	[37, 38]
<i>Ficus religiosa</i> (Moraceae)	Flavonoids, Amino Acids, Steroids, Saponins, Carbohydrates, Tannins, Flavonoids, Polyphenolic, Phenols, Sugars, Alkaloids, Methionine, Terpenoids, Glycosides, Proteins, Separated Amino Acids, Essential And Volatile Oils and Steroids.	[39, 40]
<i>Ficus religiosa</i> (Moraceae)	Flavonoids, Amino Acids, Steroids, Saponins, Carbohydrates, Tannins, Flavonoids, Polyphenolic, Phenols, Sugars, Alkaloids, Methionine, Terpenoids, Glycosides, Proteins, Separated Amino Acids, Essential And Volatile Oils And Steroids.	[41, 42]
<i>Hibiscus rosasinesis</i> (Malvaceae)	Anthocyanins, Quercetin, Cyanidin, Kaempferol, Hydrocitric Acid, Phlobatannins, Glycosides, Saponins, Flavonoids, Terpenoids, Thiamine, Riboflavin, Niacin, Glucosides, Phytosterols, Terpenoids, Tannins, Phenolic Compounds, Calcium.	[43]
<i>Mangifera indica</i> (Anacardiaceae)	Provitamin, Beta-Carotene, Lutein And Alpha-Carotene, Polyphenols Such As Quercetin, Kaempferol, Gallic Acid, Caffeic Acid, Catechins, Tannins, and The Unique Mangoxanthone, Mangiferin, Polyphenolics, Flavonoids, Triterpenoids. Mangiferin A Xanthone Glycoside	[44]

	Major Bio-Active Constituent, Isomangiferin, Tannins &	
Mangifera indica (Anacardiaceae)	Provitamin, Beta-Carotene, Lutein And Alpha-Carotene, Polyphenols Such As Quercetin, Kaempferol, Gallic Acid, Caffeic Acid, Catechins, Tannins, And The Unique Mangoxanthone, Mangiferin, Polyphenolics, Flavonoids, Triterpenoids. Mangiferin A Xanthone Glycoside Major Bio-Active Constituent, Isomangiferin, Tannins & Gallic Acid, Protocatechic Acid, Catechin, Mangiferin, Alanine, Glycine, Γ -Aminobutyric Acid Kinic Acid, Shikimic Acid.	[45]
Nymphaea alba (Nymphaeaceae)	Annecic Acid, Gallic Acid, Alkaloids, Sterols, Flavonoids, Glycosides, Hydrolyzable Tannins, B-Sitosterol,	[46]
Ocimum sanctum (Lamiaceae)	Phenolics, Flavonoids, Neolignans, Terpenoids And Fatty Acid, Mucilage, Polysaccharides and B-Sitosterol, Oleanolic Acid, Ursolic Acid, Rosmarinic Acid, Eugenol, Carvacrol, Linalool And B-Caryophyllene.	[47, 48]
Phyllanthus niruri (Euphorbiaceae)	Lignans, Phyllanthin, Hypophyllanthin, Flavonoids, Glycosides, Tannins, Alkaloids, Ellagitannins, Triterpenes, Phenyl Propanoids, Steroids, Ricinolic Acid, Niruric Acid, Phylltetralin, Ricinoleic Acid, and Linolenic Acid,	[49, 50]
Nymphaea alba (Nymphaeaceae)	Annecic Acid, Gallic Acid, Alkaloids, Sterols, Flavonoids, Glycosides, Hydrolyzable Tannins, B-Sitosterol,	[50]
Ocimum sanctum (Lamiaceae)	Phenolics, Flavonoids, Neolignans, Terpenoids and Fatty Acid, Mucilage, Polysaccharides and B-Sitosterol, Oleanolic Acid, Ursolic Acid, Rosmarinic Acid, Eugenol, Carvacrol, Linalool And B-Caryophyllene.	[51, 52]
Phyllanthus niruri (Euphorbiaceae)	Lignans, Phyllanthin, Hypophyllanthin, Flavonoids, Glycosides, Tannins, Alkaloids, Ellagitannins, Triterpenes, Phenyl Propanoids, Steroids, Ricinolic Acid, Niruric Acid, Phylltetralin, Ricinoleic Acid, and Linolenic Acid,	[53, 54]
Rhus coriaria	Phenolic Acids, Tannins, Anthocyanins, Organic Acids, Proteins, Essential Oils, Fatty Acids, Fiber, Minerals, Gallic Acid, Methyl Gallate, M-Digallic Acid, Ellagic Acid, Amenthoflavone, Agathisflavone, Hinokiflavone, Sumaflavone, B-Caryophyllene Alcohol, A-Terpineol, Carvacrol. Terpene Hydrocarbons, Cembrene, A-Pinene,	[55]
Sesbania grandiflora (Fabaceae)	Carbohydrates, Steroids, Terpenoids, Alkaloids, Flavonoids, Alkaloids, Cardiac Glycosides, Flavonoids, Glycosides, Saponins, Steroids, Tannins,	[56, 57]

Terminalia chebula (Combretaceae)	Ellagitannin, Gallotannin, Gallic Acid, Chebulagic Acid, Chebulinic Acid, Gallotannins, Ellagitannins, Gallic Acid, Chebulic Acid, Chebulagic Acid, Anthraquinone Glycosides.	[58]
Terminalia chebula (Combretaceae)	Ellagitannin, Gallotannin, Gallic Acid, Chebulagic Acid, Chebulinic Acid, Gallotannins, Ellagitannins, Gallic Acid, Chebulic Acid, Chebulagic Acid, Anthraquinone Glycosides.	[59]
Ziziphus Spina.L. (Rhamnaceae)	Flavonoids, Alkaloids, Triterpenoids, Saponins, Lipids, Proteins, Free Sugar and Mucilage, Isoquinoline Alkaloids, Betulinic, Ceanothic Acids, Saponins, Erols, Tannins, Triterpenes, Butic Acid, Ceanothic Acid, Cyclopeptides,	[60]

Findings and Discussion

1. *Acacia arabica*

- **Active constituents:** Phenolic compounds, tannins, and flavonoids are considered.
- **Antiulcer activity**
 - **In ayurvedic:** As gargle it is useful as wash in haemorrhagic ulcer and wounds. Bruised tender leaves formed into apoultice and applied to ulcers act as stimulant and astringent.^[61]
 - **In recent studies:** *Acacia senegal* gum protected against cold restraint stress-induced gastric ulcer in rats.^[62] Aqueous extract of *A. arabica* gum showed protection against meloxicam-induced intestinal damage and attenuated intestinal enzymes activity.^[63]

2. *Adansonia digitata*

- **Antiulcer activity**
- Fresh juice of the leaves mixed with powdered ginger together with the expressed juice of the fresh root of *Salvadora indica* is applied with considerable benefit to indolent syphilitic ulcer. Leaves are used as fomentations and poultices for irritable inflammatory ulcers.^[64]

3. *Aegle marmelos*

Active constituents: Luvangetin, a pyranocoumarin isolated from the seeds,^[65] is considered.

- **Antiulcer activity**
 - **In folk medicine:** The fruit of *A. marmelos* is traditionally used for the treatment of ulcer among the kani tribes in Kanyakumari district, Tamil Nadu, India.^[66]
 - **In recent studies:** Ulcers are induced by aspirin plus pylorus ligated gastric ulceration in rats and aqueous extract of leaves is to be administered orally for 21 days, daily dose of 1

gm/kg .The result indicated a significant reduction in the ulcer lesion count compared to control.^[67]

4. *Allium sativum*

- **Active constituents.** Volatile oil, alliin, and allicin are considered.
- **Antiulcer activity**
- **In ayurvedic:** Mustard or coconut oil in which garlic has been fried is an excellent application for maggots infesting ulcers, ulcerated surfaces, and wounds. Garlic juice mixed with 3 or 4 parts of ordinary or distilled water has been used as a lotion for washing wounds and foul ulcers.^[68]
- **In recent studies:** The extract of *A. sativum* bulb juice was administered at the doses of 250 and 500 mg/kg orally in rats, against cysteamine induced gastric ulcer. The extract significantly increases healing of gastric ulcer and prevents the development of experimentally induced gastric and duodenal ulcers in rats.^[69]

5. *Aloe vera*

- **Antiulcer activity**
- **Active constituents:** Barbalin, isobarbolin, and saponins are considered.
- **In ayurvedic:** Leaves are being used successfully in America in the local treatment of chronic ulcers. First the pain diminishes and after a few weeks the ulcers heal.^[70]
- **In recent studies:** Aloe vera powder was mixed with gum acacia; the solution was administered orally in rats at dose of 200 mg/kg against indomethacin induced gastric ulcer. The extract showed significant antiulcer activity comparable to control.^[71]

6. *Annona squamosa*

- **Active constituents:** Tannic acid is considered.
- **Antiulcer activity**
- **In ayurvedic:** Leaves made into a paste without adding water are applied to unhealthy ulcers.^[72]
- **In recent studies:** The aqueous leaf extract protected against pylorus ligation and ethanol induced gastric ulcer in rats.^[73]

7. *Azadirachta indica*

- **Active constituents:** Stearic and palmitic acid isolated from the nimbidin fraction of neem seeds oil is considered.^[74]

➤ **Antiulcer activity**

- **In ayurvedic:** A poultice of leaves mixed with sesamum seeds is very useful in unhealthy ulcerations.^[75]
- **In recent studies:** Azadirachta indica leaf extract protected against pylorus ligation and cold restraint stress induced gastric ulcer in rats.^[76]

8. Balsamodendron mukul

➤ **Antiulcer activity**

- **In ayurvedic:** Guggul gum is mixed with lime juice or coconut oil; it is applied as a plaster or in the form of a lotion in indolent ulcers. Gum obtained from other species, *B. pubescens* found in Sind, Karachi, and Baluchistan, is used as ointment in bad ulcers such as Delhi sores, combined with sulphur, catechu, and borax.^[77]

9. Bauhinia variegata

- **Active constituents:** Flavonoids are considered.
- **In ayurvedic.** Decoction of the bark is a useful wash in ulcers. A preparation known as kanchanara guggula made of the following ingredients is useful in ulcers: take the bark of *Bauhinia variegata* (10 parts), 3 myrobalans, ginger, black-pepper, long-pepper, bark of *Crataeva nurvala*, cardamoms, cinnamon, and Tejpatra leaves, each one part. Powder them all and add guggula (15 parts) to make a pill mass. This is given in doses of half a tola every morning with a decoction of *Sphaeranthus mollis* or of Triphala or of catechu.^[78]
- **In recent studies:** The ethanolic and aqueous extract of root of *B. variegata* was administered at the doses of 200 and 400 mg/kg orally, in rats against pylorus ligation, ethanol, and aspirin induced gastric ulcer. The extract significantly inhibited gastric mucosal damage and reduced the basal gastric acid secretion.^[79]

10. Berberis aristata

➤ **Antiulcer activity**

- **In ayurvedic:** Crude extracts known as rasaut (in Hindi) are prepared from the root; bark mixed with honey is useful application to ulcerations of the skin.^[80]

CONCLUSION

Peptic ulcer and other types of ulcer is commonly seen in around us. Patient with usage of high doses of NSAIDS, junk foods, *H. pylori*, excessive consumption of caffeine beverages are main cause of ulcer. In this review we tried to explain scientific evidence of herbal

antiulcer agent. Most drugs mention in the review are easily available around us. By using consumption of these drugs one will can prevent and treat the peptic ulcer.

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