



A REVIEW ON ANTIULCER MEDICINAL PLANTS

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ABSTRACT

Peptic ulcer is the most common gastrointestinal disorder in clinical practice. Peptic ulcer is a conglomerate of heterogeneous disorders, which manifests itself as a break in the lining of the gastrointestinal mucosa bathed by acid and/or pepsin. A number of drugs including proton pump inhibitors and H₂ receptor antagonists are available for the treatment of peptic ulcer, but these drugs has shown incidence of relapses, side effects, and drug interactions. Thus the development of new antiulcer drugs and the search for novel molecules has been extended to herbal drugs that offer better protection and decreased relapse. Medicinal plants provide an effective and safer way in disease management. Many medicinal plants exhibit antiulcer activity and found useful in the treatment of peptic ulcer. In this review attempts have been made to know about some plants which may be used in treatment or prevention of peptic ulcer. Various plants like *Nerium indicum*, *Ocimum sanctum*, *Argyrea speciosa*, *Bauhinia purpurea*, *Benincasa hispida* and *Croton zambesicus* proved active in antiulcer therapy.

Keywords: Peptic ulcers, Proton pump inhibitors, Medicinal plants, Antiulcer therapy.

INTRODUCTION

Peptic ulcer disease is an imbalance of aggressive gastric luminal factors like acid and pepsin and defensive mucosal barrier function may be environmental and host factors contribute to ulcer formation by increasing gastric acid secretion or weakening the mucosal barrier¹. Elaborately, peptic ulcer disease is characterized by the imbalance between gastric offensive factors like acid, pepsin secretion, lipid peroxidation, nitric oxide and defensive mucosal factors like mucin secretion, mucosal cell shedding, glycoproteins, proliferation & antioxidant enzymes like catalase, superoxide dismutase & glutathione levels². Annual incidence estimates of peptic ulcer hemorrhage and perforation were 19.4-57.0 and 3.8-14 per 100,000 individuals, respectively. The average 7-day recurrence of hemorrhage was 13.9% and the average long-term recurrence of perforation was 12.2%³.

Pathophysiology

Peptic ulcer is an excoriated area of the gastric or duodenal mucosa caused by action of the gastric juice. It is generally recognized that peptic ulcer is caused by a lack of equilibrium between the gastric aggressive factors and the mucosal defensive factors¹. A peptic ulcer is a break in the lining of the stomach or duodenum. The break can involve the mucosa, muscularis mucosa, submucosa, and in some cases, the deeper layers of the muscle wall. This compromise of mucosal integrity can cause pain, bleeding, obstruction, perforation, and even death. Peptic ulcers are caused by an imbalance between protective factors and damaging factors in the gastrointestinal mucosa². Pepsin is the one of the proteolytic enzymes that is secreted along with hydrochloric acid in the stomach. These substances are essential for food digestion but at the same time have the ability to erode the cell linings of the digestive system if secreted in excess amount. The stomach defends itself from hydrochloric acid and pepsin by creating a mucus coating and producing bicarbonates. *H. pylori* infection and NSAIDs can impair these protective functions. This makes the cell linings of the gastrointestinal tract susceptible to hydrochloric acid and pepsin and leads to the formation of ulcer².

It is well known that the gastric mucosa can resist autodigestion although it is exposed to numerous noxious stimuli like aggressive secretions of hydrochloric acid, pepsin, reflex of bile, spicy food, microorganisms, formation of free radicals, stress, alcohol, 5-hydroxy tryptamine, substance-P(SP), slow releasing substance, irritant receptors and platelet activating factor⁴.

Peptic ulcer therapy has undergone many strides over the past few years and a number of drugs are now available for treatment. These drugs are broadly classified into two, those that decrease or counter acid pepsin secretion and those that afford cytoprotection by virtue of their effects on mucosal defensive factors. These drugs act by different mechanisms. It is now assumed that these drugs ultimately balance the aggressive factors (acid, pepsin, *H. pylori*, bile salts) and defensive factors (mucin secretion, cellular mucus, bicarbonate secretion, mucosal blood flow and cell turnover). Although these drugs have brought about remarkable changes in ulcer therapy, the efficacy of these drugs is still debatable. Reports on clinical evaluation of these drugs show that there are incidences of relapses and adverse effects and danger of drug interactions during ulcer therapy. Hence, the search for an ideal anti-ulcer drug continues and has also been extended to herbal drugs in search for new and novel molecules, which afford better protection and decrease the incidence of relapse⁵.

Alternative approach in recent days is the research of medicaments from ayurvedic or traditional medicinal system. The use of phytoconstituents as drug therapy to treat major ailments has proved to be clinically effective and less relatively toxic than the existing drugs and also reduces the offensive factors serving as a tool in the prevention of peptic ulcer. In this modern era also 75-80% of the world populations still use herbal medicine mainly in developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side effects. The chemical constituents present in the herbal medicine or plant are a part of the physiological functions of living flora and hence they are believed to have better compatibility with human body¹. Histological studies

revealed that these medicinal plants did not show any acute toxicity. Preliminary photochemical screening of this medicinal plant identified the presence of important secondary metabolites like flavonoids and tannins. There are several botanical products with potential therapeutic applications because of their high efficacy and low toxicity. Finally, it should be noted that substances such as flavonoids, aescin, aloe gel and many others, that possess antiulcer activity are of particular therapeutic importance as most of the anti-inflammatory drugs used in modern medicine are ulcerogenic. Active principles of antiulcer activity are Flavonoids, terpenoids and tannins⁶.

This paper outlines the properties of some medicinal plants that exhibit antiulcer activity. Although extensive research has been conducted in this area, recent studies with significant findings involving *Nerium indicum*, *Dioscorea oppositifolia*, *Argyrea speciosa*, *Zanthoxylum rhoifolium*, *Bauhinia purpurea*, *Ocimum sanctum*, *Allium sativum*, *Andrographis paniculata* are emphasized here.

Nerium indicum

Antiulcer activity of flowers extract of *Nerium indicum* in the dose of 500 and 1000 mg/kg orally was reported in rats in which gastric ulcers were induced by oral administration of indomethacin and pylorus ligation. Report of earlier study suggests that methanolic flowers extract of *Nerium indicum* possesses significant antiulcer activity. It has been found to also possess major therapeutic activities such as analgesic, anti-inflammatory and antinociceptive, anti-tumor, immune-stimulating, antibacterial, antiviral, antidiabetic, neuroprotective, molluscicidal, immunomodulatory and depressant activity⁶.

Ocimum sanctum

Ocimum sanctum, popularly known as Tulsi in Hindi, is a sacred plant that belongs to the family Labiatae. *Ocimum sanctum* contains a number of chemical constituents that interact in a complex way to elicit their pharmacodynamic responses. The fixed oil obtained from *Ocimum sanctum* L. showed significant antiulcer activity against aspirin, indomethacin, alcohol, histamine, reserpine, serotonin and stress induced ulceration in rats. Significant inhibition of gastric secretion was observed in aspirin induced gastric ulceration in pylorus ligated rats. *Ocimum sanctum* is highly effective in a wide spectrum of diseases and reported to possess anticarcinogenic, anthelmintic, antiseptic, antirheumatic, antistress, and antibacterial properties. Clinical trials have reported the usefulness of *Ocimum sanctum* in heart diseases and diabetes. *Ocimum sanctum* also possess anti-inflammatory and immunomodulatory properties, attributed to its potential to inhibit cyclooxygenase and lymphokines¹.

Argyrea speciosa

Argyrea speciosa (L.f), Sweet (Convolvulaceae) is used traditionally in Indian System of Medicine as aphrodisiac, rejuvenating agent, intellect promoting agent, brain tonic and in the therapy of hepatomegaly, diabetes and chronic ulcer. The butanol fraction of *Argyrea speciosa* leaf (ASE; 50, 100 and 200 mg/kg body weight) was useful for prevention from Aspirin (ASP)-, ethanol (EtOH), cold-restraint stress (CRS) and pylorus ligation (PL) induced ulcers. Result: ASE showed dose-dependent ulcer protective and is regarded as the first line of defence against EtOH-induced gastric ulcers

showing cytoprotective property. ASE showed a marginal decrease in volume, acid pepsin concentration and acid pepsin output. The results of reported study revealed that *Argyrea speciosa* possess significant dose dependent gastroprotective activity, probably due to its free radical scavenging activity. The leaves are used by natives as a local stimulant and rubefacient in skin diseases. The plant also has been reported to possess anti-inflammatory, wound healing, antimicrobial, immunomodulatory, nootropic activity and flower possesses antidiarrheal activity⁷.

Bauhinia purpurea

Bauhinia purpurea (Fabaceae) is a medicinal plant traditionally used to treat various ailments, including ulcers. The *Bauhinia purpurea* aqueous extract (BPAE) in the doses of 100, 500 and 1000 mg/kg reported as antiulcer activity against absolute ethanol- and indomethacin induced gastric ulcer, and pyloric ligation models. The dose dependent activity was observed only in the absolute ethanol-induced gastric ulcer model. Histological studies supported the observed antiulcer activity of BPAE. In pyloric ligation assay, BPAE increased the gastric wall mucus secretion. The BPAE exhibits antiulcer activity, which could be due to the presence of saponins or sugar-free polyphenols. Several pharmacological studies have been carried out on different parts of *Bauhinia purpurea* as antidiarrheal, antispasmodic, antimicrobial, antinociceptive, anti-inflammatory, antipyretic, in vitro antiproliferative, antioxidant, antimycobacterial, antimalarial, antifungal, cytotoxic, anti-inflammatory, thyroid stimulating, anti-hypothyroidism activity⁸.

Benincasa hispida

Benincasa hispida (*B.hispida*) is recommended in Ayurveda for the management of peptic ulcer, hemorrhages from internal organs. Anti-ulcerogenic activity of different extracts of *B.hispida* (fresh juice, supernatant and residue fraction of centrifuged juice, alcoholic and petroleum ether extract) were reported in aspirin plus restraint, swimming stress, indomethacin plus histamine and serotonin-induced ulcers in rats and mice. The oral feeding of different doses of the extract significantly reduced the ulcer index produced by various ulcerogens. The anti-ulcerogenic effect was dose dependent in stress induced model of ulcer and not in other models. *B.hispida* probably has a CNS component in prevention of stress induced ulceration. *B.hispida* is also recommended for management of epilepsy and other nervous disorders, inflammations⁹.

Croton zambesicus

The ethanolic root extract of *Croton zambesicus* was reported for its potential to protect gastric mucosa against ulcers induced by indomethacin, ethanol and reserpine. The extract (27-81mg/kg) reported a significant dose-dependent effects against the ulcerogenic effect of different agents used; indomethacin, ethanol and reserpine. *Croton zambesicus* (Euphorbiaceae) is an ornamental tree grown in villages and towns in Nigeria. Ethnobotanically, the leaf decoction is used as anti hypertensive, antimicrobial (urinary infections), antidiabetic, malarial remedy, antiplasmodial, anti-inflammatory, analgesic and antipyretic activities. The root is also used for menstrual pain and as aperients¹⁰. Some other medicinal plants have anti-ulcerogenic activity are listed in Table 1.

Table 1: List of medicinal plants possessing antiulcerogenic activity

Plants	Extracts	Models	Mode of action
<i>Tectona grandis L</i> (Trunk Bark and wood chips) ¹¹	Ethanollic fraction	PL-, RS- and prednisolone induced GU in rats, HIST-induced GU and DU in GP	No effect on acid-pepsin secretion but caused increase in mucin secretion
<i>Withania somnifera</i> (Roots) ¹²	SG-1 [total methanol -H ₂ O (1:1)] SG-2 (sitoindosides VII, VIII and withaferin-A)	RS- induced GU in rats	Anti-stress activity
<i>Emblcia officinalis</i> (Fruits) ^{13,14}	Fresh juice	CRS-, ethanol, ASP- and PL induced GU in rats	Increase in mucin secretion and life span of mucosal cells.
<i>Bacopa monniera</i> (Whole plant) ¹⁵	Fresh juice	CRS-, ethanol-, ASP- and PL induced GU in rats	Increase in mucin secretion and life span of mucosal cells.
<i>Convolvulus pluricaulis</i> (Whole plant) ¹⁶	Fresh juice	CRS-, ethanol-, ASP- and PL induced GU in rats	Increase in mucin secretion and life span of mucosal cells.
<i>Centella asiatica</i> (Whole plant) ¹⁷	Fresh juice	CRS-, ethanol-, ASP- and PL induced GU in rats	Increase in mucin secretion and life span of mucosal cells.
<i>Asparagus acemosus</i> (Roots) ¹⁸	Fresh juice	PL- and CRS- induced GU in rats	Promotes mucosal defensive factors by enhancing mucin secretion and life span of induced mucosal cells
<i>Glycyrrhiza glabra</i> (Roots) ¹⁸	Water decoction	PL- and CRS- induced GU in rats	Promotes mucosal defensive factors by enhancing mucin secretion
<i>Holarrhene antidiysenterica</i> (Barks) ¹⁸	Water decoction	PL- and CRS- induced GU, CYS- DU in rats	Promotes mucosal defensive factors by enhancing mucin secretion
<i>Ficus religiosa</i> (Barks) ¹⁸	Water decoction	PL- and CRS- induced GU, CYS- DU in rats	Promotes mucosal defensive factors by enhancing mucin secretion

ASP-Aspirin; CRS-Cold restraint stress; CYS-Cysteamine; DU-Duodenal ulcer; GP-Guinea pig; GU-Gastric ulcer; HIST-Histamine; PL-Pylorus ligation; RS-Restraint stress

CONCLUSION

From this study we can conclude that studies with plant sources can result in novel and effective pattern of treatment. Various herbal plants and plants extracts have significant antiulcer activity in different animal models. These plants provide leads to find therapeutically useful compounds, thus more efforts should be made towards isolation and characterization of the active principles and their structure activity relationship. The combination of traditional and modern knowledge can produce better drugs for the treatment of peptic ulcer with fewer side effects. From this study, it is clear that the medicinal plants play a vital role against various diseases.

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