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ANTIULCER HERBAL DRUGS- A REVIEW

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ABSTRACT

Peptic ulcer disease is a serious gastrointestinal disorder that requires a well targeted therapeutic strategy. This article reviews the gastro-protective and/or anti-ulcer properties of the most commonly employed herbal medicines and their identified active constituents. Botanical compounds with anti-ulcer activity include flavonoids (i.e. quercetin, naringin, silymarin, anthocyanosides and sophoradin derivatives), saponins, tannins, gums and mucilages. We have highlighted some of the important plants reported for their anti-ulcer and ulcer healing properties. Ayurvedic knowledge supported by modern science is necessary to isolate, characterize and standardise the active constituents from herbal sources for antiulcer activity. This study has presented the recent advancements of herbal medicine as an antiulcer agent with the view to aid the further research to prepare antiulcer agents scientifically.

INTRODUCTION:

There is a balance in the stomach between the aggressive digestive capabilities of acid plus pepsin and the mucosal barrier. Ulceration occurs when there is a disturbance of the normal equilibrium caused by either enhanced aggression or diminished mucosal resistance. Several factors are implicated in the pathogenesis of gastric ulcer. These include increased acid-pepsin secretion, impaired bicarbonate neutralization, impaired mucus secretion and precipitate lesions on the mucosal layer. Acid and pepsin secretion must be considered together because in practice it is difficult to distinguish the effects of each alone. Drug treatment of peptic ulcers is targeted at either counteracting aggressive factors (acid plus pepsin, active oxidants, PAF, leukotrienes, endothelins, bile or exogenous factors including NSAIDs) or stimulating the mucosal defences (mucus, bicarbonate,

normal blood flow, prostaglandins, nitric oxide). The ideal aims of treatment of peptic ulcer disease are to relieve pain, heal the ulcer and delay ulcer recurrence. To date, no drug meets all the goals of therapy. In recent years, gastric ulcer has also been associated with infection of gastrointestinal mucosal tissue by *Helicobacter pylori*.¹

This article reviews drugs derived from botanical sources more commonly used (or extensively studied) in the world for peptic ulcer. Also, ethnomedical systems employ several plant extracts for the treatment of peptic ulcer. An indigenous drug possessing fewer side effects is the major thrust area of the present day research, for a better and safer approach for the management of peptic ulcer.^{2,3} This review summarises the features of some of these plants reported to possess antiulcer and ulcer healing properties. Recent studies with significant findings involving *Aspilia Africana*, *Camellia sinensis*

L., *Centella asiatica*, *Ficus hispida*, *Ficus arnottiana*, *Jasminum grandiflorum* *L.*, *Leucas lavandifolia*, *Morinda citrifolia* *linn.*, *Mentha arvensis*, *Phyllanthus niruri* *L.*, *Polyscias balfouriana*, *Polyalthia longifolia*, *Terminalia chebula* are reported here.

HERBAL DRUGS WITH ANTIULCER ACTIVITY:

Aspilia africana

Aspilia Africana *C.D. Adams* (AA) (family: Compositae) is a semi woody herb occurring throughout the region of the savannah and tropical Africa on wastelands. The plant has been reported in literature to possess antimicrobial, haemostatic, antifertility, and antiinflammatory activity. Also earlier studies in West-Africa have reported the wound healing and antiulcer activity of its n-hexane and methanolic extracts.⁵

Aqueous extract of AA leaf was shows significant inhibition of ulcer formation at a dose 50mg/kg and 100mg/kg p.o. in dose dependent

manner. Phytochemical screening showed that the extract contains alkaloids, glycosides, saponins, tannins, flavonoids, and resins.^{5,6,7}

***Camellia sinensis* Linn.**

Tea is made from freshly harvested tender shoots, comprising two or three top most immature leaves and buds of *camellia sinensis* *linn.* (CS) (family: Theaceae) plant. Depending on the manufacturing technique there are three main type of tea: black (fully aerated or fermented), green (unaerated or unfermented) and oolong (partially aerated or semifermented).Of these black tea accounts for about 78% of world tea production.

Phytoconstituents like flavonoids, catechin, quercetin, rutin, etc. are present in CS. Experimentally it was investigate gastric healing potential of back tea brew (BTB). This was tested in rats and significant gastroprotective effect found at a dose 501 mg/ml. BTB, in dose dependent manner. Also shows

antihistaminic and antioxidant activity.⁸

Centella asiatica

Centella asiatica linn. (CA) is an ethno medical plant used in different countries by diverse ancient culture and tribal groups. It is one of the local herbs that is claimed to possess various physiological effects and it occupies an important place in the indigenous system of medicine as a tonic in skin diseases and leprosy. Different uses are claimed for plant, the more common being its use for wound healing, memory improvement, treatment of mental fatigue, bronchitis, asthma, dysentery, kidney trouble, urethritis, allergy, leucorrhea and toxic fever.

In addition, it has been shown to promote fibroblast proliferation, collagen synthesis and to have antiulcer activity, antioxidant activity and anti-inflammatory activity. Anti-ulcerogenic properties of methanol extract of CA leaf in rats investigated significantly at a dose 400 mg/kg.^{9,}

¹⁰

Ficus hispida

Ficus hispida linn. (FH) (family: Moraceae) moderate sized tree, upto the level of 3.0m, with spreading branches and many aerial roots. It is widely distributed throughout India, Srilanka, Myanmar, southern region of the republic of china and Australia as well as grows in secondary forests, open lands and banks up to 1200m in altitude. All parts of the plant have been reported to be bitter, cooling, astringent, antidysentric, psoriasis, anemia, piles, jaundice and hemorrhage. The root and leaves are of particular interest from a medicinal point of view as an antidiarrhoeal, antidiabetic, hepatoprotective, antibacterial and cardioprotective among others.

Phytochemical screening showed the presence of alkaloids, carbohydrates, proteins, amino acids, phenols, flavonoids, gums and muscilage, glycosides, saponins and terpenes. Methanolic root extract of FH at doses 200 and 400 mg/kg was found to be effective by 63.8 and 68.44%

respectively in aspirin (ASP) induced ulcer model and significantly reduced free and total acidity.¹¹

Ficus arnottiana

Ficus arnottiana miq. (FA) (family: Moraceae) is an important traditional medicinal plant distributed throughout India, mostly in rocky hills of 1350m elevations. It has several vernacular names including paras pipal and kodiarasu. The fruits of the plant contain β -sitosterol, gluanol acetate and glucose, friedelin; sterol, alkaloids, carbohydrates, tannins, phenols, etc. are present in bark extract. Bark of the plant in traditional medicine is used as astringent, aphrodisiac, demulcent, depurative and emollient. It is also useful against inflammation, diarrhea, diabetes, burning sensation, leprosy, scabies, wounds and skin diseases.

Methanolic leaf extract of FA significantly prevent ulcer in rats at a doses 250mg/kg and 500mg/kg in a dose dependent manner.¹²

Jasminum grandiflorum

Jasminum grandiflorum linn(JG) (family : Oleaceae) is used in folk medicine for treating ulcerative stomatitis, skin diseases, ulcers, wounds etc. literature suggest the use of this plant as a diuretic and spasmolytic agent, which is given during child birth.

Antiulcer activity of hydroalcoholic extract of leaves of JG was evaluated employing aspirin plus pylorus ligation induced acute gastric ulcer model in albino rats. There was a significant ($P<0.01$) dose dependent decrease in the ulcerative lesion index at a dose 100 and 200mg/kg, b.w., orally.¹³

Leucas lavandulifolia

The genus leucas contains about 100 Asiatic and African species, but the most common species found in india is *Leucas lavandulifolia* sm. (family: Labiatae).it is an erect herb, 01-02m tall, much branched from base having gray pubescent stem slender. It is commonly known as gumma or dronpuspi in India. In rural area of west champaran, Bihar (India). It is

used to counteract abdominal and liver diseases.

Antiulcer activity of methanolic extract of the herb was studied in rats, in which gastric ulcers were induced by oral administration of indomethacin (20mg/kg) followed by pylorus ligation method. The extract in the dose of 100 and 200 mg/kg intraperitoneally exhibited ulcer protection activity in dose dependent manner.¹⁴

Morinda citrifolia

Morinda citrifolia linn. (MC) (family: Rubiaceae) known commercially as Noni grows widely throughout the Pacific and is one of the most significant sources of traditional medicines among Pacific island societies. The fruit juice is in high demand in medicine for different kinds of illnesses such as arthritis, diabetes, high blood pressure, muscle aches and pains, gastric ulcers, menstrual difficulties, headaches, heart disease, cancers, sprains etc. a number of major components has been identified in

the Noni plant such as octanoic acid, potassium, vitamin C, scopoletin, terpenoids, alkaloids, anthraquinones (such as morindone, rubiadin, rubiadin-1-methyl ether, anthraquinone glycosides) β -sitosterol, carotene, vitamin A, flavone glycosides, linoleic acid, amino acids, caproic acid, caprylic acid, ursolic acid, rutin etc.

The ethyl acetate extract of fruits of MC was found to be significantly antiulcer properties at a dose 400mg/kg orally.¹⁵

Mentha arvensis

Mentha arvensis linn. (MA) (family: Lamiaceae) is distributed throughout the western Himalayas and is cultivated throughout the world for use as a vegetable. It is an erect aromatic herb that grows up to 60cm. in height with suckers; the stem is cylindrical and the leaves are simple and opposing type. MA is used as a carminative, anti-spasmodic, antiulcer agent and has been given to treat indigestion, skin diseases, coughs and colds in folk medicine.

It contains monoterpenes such as (menthone, menthofuran, methyl acetate and limonine), sesquiterpenes (viridiflorol), flavonoids (caffeic, chlorogenic and rosmarinic), triterpenes (squalene, ursolic acid and sitosterol), phytol, tocopherols, tannin and minerals. The whole herb extracts of MA prepared by using solvent pet ether, chloroform and water. The ulcer index was significantly reduced at a dose 375 mg/kg b.wt. Orally in all extracts.¹⁶

Phyllanthus niruri

Phyllanthus niruri linn. (family: Euphorbiaceae) is an annual and field weed widespread in temperate and tropical climates. It is popularly used in Asia, Africa and south America as a stomachic, aperitive, antispasmodic, anti-hepatotoxic, antiviral, antibacterial, laxative, diuretic, carminative, in the management of diabetes, constipation, fever including malaria jaundice, hepatitis B, dysentery, gonorrhoea, syphilis, diarrhoea, vaginitis, tumors, kidney stones.

Studies on extracts from various parts of the plant have revealed the antioxidant and nitric oxide scavenging, antimalarial, analgesic, diuretic, hepatoprotective, urolithiatic activities. Several Phytochemical constituents of this plant have been isolated and these include alkaloids-4-methoxy-securinine, ellagic acid, β -sitosterol, gallic acid, hypophyllanthin etc. Phytochemical analysis of the extract revealed the presence of alkaloids, saponins, tannins, flavonoids, carbohydrates and glycosides. The methanolic aerial parts extract at a dose 400mg/kg significantly ($P < 0.05$) inhibited the development of ulcer induced by indomethacin and moderately inhibited ethanol-acid induced ulcer.^{17, 18}

Polyscias balfouriana

Polyscias balfouriana is an ornamental plant which belongs to the family Araliaceae. The plant is a bushy shrub with glossy green coloured leaves with white margins. The chemical nature of the active

principles is high content of triterpenoids saponins. The family and the chemical nature of this plant are same as that of panax ginseng. Since ginseng is well established for its antistress property, it was used as the standard drug for evaluating the antiulcer activity. Ulcer was induced by physical and chemical method. The leaf and root extract was given in two different concentrations of 250mg/kg and 500mg/kg body weight. It was observed that the leaf extract of 500mg/kg body weight showed better antiulcer activity.²¹

Terminalia chebula

Terminalia chebula (TC) (family: Combretaceae) was one of the traditional medicine used in many folk claims and it is called as “king of medicine”. It is an middle-sized tree, leaves are ovate or elliptic, flowers are yellowish white, fruits are yellowish brown in colour distributed throughout in India. The plant was extensively used in the Ayurveda and siddha for constipation, diarrhea, ulcers,

gastroenteritis, asthma, cough, hepatomegaly, skin diseases, urinary discharges, rheumatism, arthritis, gout etc.

Phytochemical screening of TC revealed that presence of alkaloids, flavonoids, carbohydrates, glycosides, tannins, terpenoids, phenols and absence of fixed oils and steroids. The methanolic extract of TC fruits produced significant inhibition of the gastric lesions induced by pylorus ligation and ethanol induced gastric ulcer at a dose 250mg/kg and 500mg/kg p.o.^{22, 23, 24}

Miscellaneous plants

Several other plant species that have utility in ulcer therapy have also been reported in the literature. Some of these plants like *Albizia lebbek* and *Benincasa hispida* along with other plants reportedly possessing antiulcerogenic property are summarized in table 1. Some of these herbal drugs characterized chemically along with used model.

Table 1. Herbal plants with antiulcerogenic property⁵⁻⁴⁴

Botanical name	Family	Part used	Extract/Active principle	Ulcer Model
<i>Aspilia africana</i>	Compositae	Leaves	Aqueous; Saponins, tannins, glucoside, alkaloid, flavonoids, resin.	Ethanol, Aspirin, Indomethacin.
<i>Albizia lebeck</i>	Mimosaceae	Leaves	70%Ethanol; Flavon, echinocystic acid, β -sitosterol, vicenin-II.	Ethanol, Pylorus-ligated, Indomethacin.
<i>Anisochilus carnosus</i>	Lamiaceae	Leaves	Methanol; 0.13% v/w oil- carvacol (27.9%), camphor (14.1%), α -cis bergamotene (10.2%).	Pylorus-ligated.
<i>Amomum sabulatum</i> Roxb.	-	Seeds	Pet ether soluble fraction of methonolic extract and essential oil.	Ethanol, Aspirin.
<i>Benincasa hispida</i>	Cucurbitaceae	Fruits	Pet ether, methanol, ethyl acetate, aqueous; triterpenes, alnusenol, multiflorenol, iso-multiflorenol, flavones, iso-vitexin, sterols-lupeol, lupeol acetate, β -sitosterol.	Ethanol, Pylorus-ligated, Cold-restraint-stress.
<i>Centella asiatica</i>	-	Leaves	Ethanol; Antioxidant material.	Ethanol.
<i>Camellia sinensis L.</i>	Theaceae	Leaves	Black tea brews.	Acetic acid, Serotonin.
<i>Calotropis gigantea</i>	Asclepiadaceae	Roots	Pet ether, chloroform, ethanol, aqueous; flavonoids, tannins.	Pylorus-ligated.
<i>Datura alba nees.</i>	Solanaceae	Leaves	Ethanol; alkaloids.	Pylorus-ligated.
<i>Elettaria cardamomum</i>	-	Seeds	Pet ether soluble fraction of methonolic extract and essential oil.	Ethanol, aspirin.

<i>Eclipta alba</i>	-	Whole plant	Methanol.	Ethanol, aspirin, Pylorus-ligated.
<i>Ficus hispida</i>	Moraceae	Roots	Methanolic; alkaloids, flavonoids, tannins, proteins, amino acid, saponins.	Aspirin.
<i>Ficus arnottiana</i>	Moraceae	Leaves	Methanolic; alkaloids, flavonoids, tannins, proteins, amino acid, steroids, carbohydrates.	Ethanol, Pylorus-ligated.
<i>Gossipium arboreum L</i>	-	Leaves	Pet ether, alcohol, chloroform, aqueous; triacontanol, hexatriacontane, dotriacontanol, proteins, condensed tannins, total phenolics.	Aspirin, Pylorus-ligated.
<i>Garcinia cambogia</i>	Culsiaceae	Fruits	Organic acid (-)-erythro-hydroxycitric acid, carbohydrates, protein.	Indomethacin.
<i>Jasminum grandiflorum L.</i>	Oleaceae	Leaves	Hydroalcoholic solvent (30%water +70%alcohol)	Aspirin plus pyloric ligation.
<i>Leucas lavandifolia</i>	Labiatae	Whole plant	Methanol.	Pylorus-ligation plus Indomethacin.
<i>Morinda citrifolia linn.</i>	Rubiaceae	Fruits	Ethyl acetate; Alkaloids, Flavonoid, Glycosides, Proteins, Phenol, Carbohydrates, Gums, Mucilages.	Aspirin, Pylorus-ligated, alcohol, cysteamine HCL.
<i>Mentha arvensis</i>	Lamiaceae	Whole plants	Pet ether, chloroform, aqueous; flavonoids, tannins, proteins, saponin, carbohydrates, alkaloid.	HCL, ethanol, ibuprofen plus pyloric ligation.
<i>Ocimum sanctum</i>	Labiatae	Leaves	Ethanol, aqueous; eugenol, ursolic	Ethanol, cold- restraint,

			acid,	aspirin, pylorus-ligated.
<i>Phyllanthus niruri L.</i>	Euphorbiaceae	Aerial Parts	Methanol; flavonoids, tannins, proteins, saponin, carbohydrates, alkaloid.	Ethanol, cold- restraint, Indomethacin.
<i>Polyscias balfouriana</i>	Araliaceae	Root / leaves	70% ethanol; triterpenoids, saponin, steroids.	Immobilization stress.
<i>Polyalthia longifolia</i>	Annonaceae	Leaves	Ethanol.	Aspirin plus pylorus-ligation, HCL-ethanol, water immersion stress.
<i>Terminalia chebula</i>	Combretaceae	Fruits	Methanol; flavonoids, tannins, carbohydrates, alkaloid, glycoside, phenol, terpenoid, steroid.	Ethanol, Pylorus-ligated.

ACTIVE PRINCIPLES WITH ANTIULCER ACTIVITY:

Flavonoids

Flavonoids are a group of compounds with a wide range of biological effects, including anti-ulcer activity. Various mechanisms have been proposed to explain the gastroprotective effect of flavonoids; these include increase of mucosal prostaglandin content, inhibition of *Helicobacter pylori* growth and decrease of histamine secretion from mast cells by inhibition of histidine decarboxylase. Also, flavonoids have been found to be free radical scavengers, free radicals play an important role in ulceration

of the gastrointestinal tract. The most studied Anti-ulcer flavonoids are naringin, quercetin, silymarin, anthocyanosides and sophoradin derivatives. Moreover, several extracts containing flavonoids have been found to exert gastro-protective activity.^{49, 50}

Saponins

Saponins are widely distributed in plants and are a particular form of glycosides. They are so-called because of their soap-like effect, which is due to their surfactant properties. They also have haemolytic properties and, when injected into the blood stream, are highly toxic. When taken by mouth saponins

are comparatively harmless. According to the structure of the aglycone or sapogenin two kinds of saponin are recognized, the steroidal and triterpenoid type. Plant materials often contain triterpenoid saponins in considerable amounts.

The protective activities of some active saponins are not due to inhibition of gastric acid secretion but probably due to activation of mucous membrane protective factors. Several plants containing high amounts of saponins have been shown to possess anti-ulcer activity in several experimental ulcer models.^{11, 12, 51}

Tannins

Tannins are used in medicine primarily because of their astringent properties, which are due to the fact that they react with the proteins of the layers of tissue with which they come into contact. Tannins are known to 'tan' the outermost layer of the mucosa and to render it less permeable and more resistant to chemical and mechanical injury or irritation. However, the correlation between the molecular structures of tannins and the astringent/anti-ulcer activity is not known.

When a low concentration of tannins is applied to the mucosa, only the outermost

layer is tanned, becoming less permeable and affording an increased protection to the subjacent layers against the action of bacteria, chemical irritation, and, to a certain extent, against mechanical irritation. High concentrations of tannins cause coagulation of the proteins of the deeper layer of the mucosa, resulting in inflammation, diarrhea and vomiting.^{11, 12, 51}

Gums and mucilages

Gums and mucilages are usually brittle, amorphous, transparent or translucent substances, which readily absorb water to form gelatinous masses or viscous colloidal solutions. The colloidal character of gums, mucilages and other mucoids accounts largely for their use as therapeutic agents. Mucilaginous drugs have the property of covering and protecting the mucosa of the stomach and are used in the treatment of gastric ulcer. Gum guar increased the healing rate of stress-induced gastric ulcers in the rat; proposed mechanisms are reduced acidity, increased local mucosal supply of energy and mechanical protection. The protective effect of myrrh is attributed to its effect on mucus production or increase in nucleic acid and non-protein sulphydryl

concentration, which appears to be mediated through its free-radical scavenging, thyroid-stimulating and prostaglandin inducing properties.⁵¹

CONCLUSIONS:

A variety of botanical products have been reported to possess anti-ulcer activity (especially from ethnopharmacological studies) but the documented literature has centred primarily on pharmacological action in experimental animals. Except for a few phytochemical compounds, limited clinical data are available to support the use of herbs as gastroprotective agents and thus, the data on efficacy and safety are limited. Despite this, 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, tannins, carbohydrates, alkaloid, glycoside, terpenoid, steroid, saponin and many others, that possess anti-ulcer activity.

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