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Indian Medicinal Plants with Antiulcer and Related Beneficial Effects: A Review.

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ABSTRACT

Peptic ulcer disease (PUD) is considered as one of the common diseases in the world. Treatment of peptic ulcer with synthetic drugs such as proton pump inhibitors, H₂ receptor antagonists and other non-steroidal anti-inflammatory drugs has shown adverse effects, relapses, drug interactions. Medicinal plants containing active chemical constituents are useful in prevention and treatment of various diseases. Literatures suggest that polyherbal formulations of medicinal plants are considered to be potential source for the treatment of ulcers. Combination of ayurvedic knowledge with modern medicine can produce better antiulcer drugs of natural origin from medicinal plants with fewer side effects. This study has presented the review of commonly used anti-ulcer plants which are used for the treatment or prevention of peptic ulcers and the other reported activities of these plants.

Keywords: medicinal plants, peptic ulcer, duodenal ulcer, gastric ulcer.

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INTRODUCTION

Peptic ulcer is a gastro intestinal disorder due to an imbalance between the aggressive factors like acid, pepsin, *Helicobacter pylori* and defensive factors like bicarbonate secretion, Prostaglandins, gastric mucus, innate resistance of the mucosal cell factors [1]. Normally peptic ulcer develops when aggressive factors overcome the defensive factors [2]. The major factors that disrupt the equilibrium between aggressive factors and defensive factors are *Helicobacter pylori*, acid-pepsin hyper secretion, non-steroidal anti-inflammatory drugs, sometimes idiopathic due to use of tobacco, psychological stress, rapid gastric emptying and Zollinger-Ellison syndrome where there is a high and uncontrollable production of acid also leads to ulcer formation [3-5]. Synthetic drugs such as proton pump inhibitors, H₂ receptors, cytoprotectants, demulcents, anti cholinergics, antacids and prostaglandin analogues are used for the treatment of ulceration but these drugs produce several side effects. So herbal medicines are considered as better alternatives for the treatment of peptic ulcer [6]. For example, proton pump inhibitors (omeprazole, lansoprazole) may cause nausea, abdominal pain, constipation, diarrhoea and H₂ receptor antagonists (cimetidine) may cause gynaecomastia, loss of libido. Due to the occurrence of many side effects by use of synthetic drugs for many diseases, medicinal plants are considered as the main source of new drugs as they have less or no side effects. As herbal medicines are considered as safe for the treatment of ulcers with lesser adverse effects, economical, effective, relatively less toxic, extensive research is carried out in search for potent antiulcer agents of plant origin [7-8]. This article reviews the features of some of the plants reported to possess antiulcer and ulcer healing properties.

Ulcer

Gastric ulcer, also known as peptic ulcer, is a localized area of erosion in the stomach lining, resulting in abdominal pain, possible bleeding, and other gastrointestinal symptoms. The most common causes of gastric ulcer in a stomach infection associated with the *Helicobacter pylori* (*H. pylori*) bacteria. The spread of *H. pylori* among humans is not understood; it may spread through contaminated food and water. Many people become infected with *H. pylori* at young age, but symptoms most commonly occur in adulthood.[9]

A peptic ulcer, also known as peptic ulcer disease (PUD).[10] is the most common ulcer of an area of the gastrointestinal tract that is usually acidic and thus extremely painful. It is defined as mucosal erosions equal to or greater than 0.5 cm. As many as 70–90% of such ulcers are associated with *Helicobacter pylori*, a helical-shaped bacterium that lives in the acidic environment of the stomach; however, only 40% of those cases go to a doctor [citation needed]. Ulcers can also be caused or worsened by drugs such as aspirin, ibuprofen, and other NSAID.[11]

Four times as many peptic ulcers arise in the duodenum—the first part of the small intestine, just after the stomach—as in the stomach itself. About 4% of gastric ulcers are caused by a malignant tumor, so multiple biopsies are needed to exclude cancer. Duodenal ulcers are generally benign.

By Region/Location

- Duodenum (called duodenal ulcer)
- Esophagus (called esophageal ulcer)
- Stomach (called gastric ulcer)
- Meckel's diverticulum (called Meckel's diverticulum ulcer; is very tender with palpation)

Modified Johnson Classification of peptic ulcers:

- Type I: Ulcer along the body of the stomach, most often along the lesser curve at incisura angularis along the locus minoris resistentiae.
- Type II: Ulcer in the body in combination with duodenal ulcers. Associated with acid over secretion.
- Type III: In the pyloric channel within 3 cm of pylorus. Associated with acid over secretion.
- Type IV: Proximal gastroesophageal ulcer
- Type V: Can occur throughout the stomach. Associated with chronic NSAID use (such as aspirin).

Signs and symptoms

Symptoms of a peptic ulcer can be

Abdominal pain, classically epigastric strongly correlated to mealtimes. In case of duodenal ulcers the pain appears about three hours after taking a meal;

Bloating and abdominal fullness;

Water brash (rush of saliva after an episode of regurgitation to dilute the acid in esophagus - although this is more associated with gastroesophageal reflux disease);

Nausea, and copious vomiting;

Loss of appetite and weight loss;

Hematemesis (vomiting of blood); this can occur due to bleeding directly from a gastric ulcer, or from damage to the esophagus from severe/continuing vomiting.

Melena (tarry, foul-smelling feces due to oxidized iron from haemoglobin);

Rarely, an ulcer can lead to a gastric or duodenal perforation, which leads to acute peritonitis. This is extremely painful and requires immediate surgery.

A history of heartburn, gastroesophageal reflux disease (GERD) and use of certain forms of medication can raise the suspicion for peptic ulcer. Medicines associated with peptic ulcer include NSAID (non-steroid anti-inflammatory drugs) that inhibit cyclooxygenase, and most glucocorticoids (e.g. dexamethasone and prednisolone).

In patients over 45 with more than two weeks of the above symptoms, the odds for peptic ulceration are high enough to warrant rapid investigation by esophagogastroduodenoscopy.

The timing of the symptoms in relation to the meal may differentiate between gastric and duodenal ulcers: A gastric ulcer would give epigastric pain during the meal, as gastric acid production is increased as food enters the stomach. Symptoms of duodenal ulcers would initially be relieved by a meal, as the pyloric sphincter closes to concentrate the stomach contents, therefore acid is not reaching the duodenum. Duodenal ulcer pain would manifest mostly 2–3 hours after the meal, when the stomach begins to release digested food and acid into the duodenum.

Also, the symptoms of peptic ulcers may vary with the location of the ulcer and the patient's age. Furthermore, typical ulcers tend to heal and recur and as a result the pain may occur for few days and weeks and then wane or disappear. Usually, children and the elderly do not develop any symptoms unless complications have arisen.

Burning or gnawing feeling in the stomach area lasting between 30 minutes and 3 hours commonly accompanies ulcers. This pain can be misinterpreted as hunger, indigestion or heartburn. Pain is usually caused by the ulcer but it may be aggravated by the stomach acid when it comes into contact with the ulcerated area. The pain caused by peptic ulcers can be felt anywhere from the navel up to the sternum, it may last from few minutes to several hours and it may be worse when the stomach is empty. Also, sometimes the pain may flare at night and it can commonly be temporarily relieved by eating foods that buffer stomach acid or by taking anti-acid medication.[12] However, peptic ulcer disease symptoms may be different for every sufferer.[13]

Complications

Gastrointestinal bleeding is the most common complication. Sudden large bleeding can be life-threatening.[14] It occurs when the ulcer erodes one of the blood vessels, such as the gastro duodenal artery.

Perforation (a hole in the wall) often leads to catastrophic consequences. Erosion of the gastro-intestinal wall by the ulcer leads to spillage of stomach or intestinal content into the abdominal cavity. Perforation at the anterior surface of the stomach leads to acute peritonitis, initially chemical and later bacterial peritonitis. The first sign is often sudden intense abdominal pain. Posterior wall perforation leads to bleeding due to involvement of gastro duodenal artery that lies posterior to the 1st part of duodenum.

Perforation and penetration are when the ulcer continues into adjacent organs such as the liver and pancreas.

Gastric outlet obstruction is the narrowing of pyloric canal by scarring and swelling of gastric antrum and duodenum due to peptic ulcers. Patient often presents with severe vomiting without bile.

Cancer is included in the differential diagnosis (elucidated by biopsy), *Helicobacter pylori* as the etiological factor making it 3 to 6 times more likely to develop stomach cancer from the ulcer.

Cause

A major causative factor (60% of gastric and up to 90% of duodenal ulcers) is chronic inflammation due to *Helicobacter pylori* that colonizes the antral mucosa. The immune system is unable to clear the infection, despite the appearance of antibodies. Thus, the bacterium can cause a chronic active gastritis (type B gastritis), resulting in a defect in the regulation of gastrin production by that part of the stomach, and gastrin secretion can either be increased, or as in most cases, decreased, resulting in hypo- or achlorhydria. Gastrin stimulates the production of gastric acid by parietal cells. In *H. pylori* colonization responses to increased gastrin, the increase in acid can contribute to the erosion of the mucosa and therefore ulcer formation. Studies in the varying occurrence of ulcers in third world countries despite high *H. pylori* colonization rates suggest dietary factors play a role in the pathogenesis of the disease.

Another major cause is the use of NSAIDs. The gastric mucosa protects itself from gastric acid with a layer of mucus, the secretion of which is stimulated by certain prostaglandins. NSAIDs block the function of cyclooxygenase 1 (cox-1), which is essential for the production of these prostaglandins. COX-2 selective anti-inflammatories (such as celecoxib or the since withdrawn rofecoxib) preferentially inhibit cox-2, which is less essential in the gastric mucosa, and roughly halve the risk of NSAID-related gastric ulceration.

The incidence of duodenal ulcers has dropped significantly during the last 30 years, while the incidence of gastric ulcers has shown a small increase, mainly caused by the widespread use of NSAIDs. The drop in incidence is considered to be a cohort-phenomenon independent of the progress in treatment of the disease. The cohort-phenomenon is probably explained by improved standards of living which has lowered the incidence of *H. pylori* infections.

Although some studies have found correlations between smoking and ulcer formation, others have been more specific in exploring the risks involved and have found that smoking by itself may not be much of a risk factor unless associated with *H. pylori* infection.[13] Some suggested risk factors such as diet, and spice consumption, were hypothesized as ulcerogens (helping cause ulcers) until late in the 20th century, but have been shown to be of relatively minor importance in the development of peptic ulcers.[14] Caffeine and coffee, also commonly thought to cause or exacerbate ulcers, have not been found to affect ulcers to any significant extent. Similarly, while studies have found that alcohol consumption increases risk when associated with *H. pylori* infection, it does not seem to independently increase risk, and even when coupled with *H. pylori* infection, the increase is modest in comparison to the primary risk factor.[15]

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. 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 which are the active principles of antiulcer activity.

Present study was conducted to review medicinal plants considered as gastroprotective and healing agents on ulcers in ayurvedic resources and beside that to gather evidence for their effectiveness and biological mechanisms in modern investigation.

In order to achieve this aim, Indian ayurvedic book Meteria Medica and electronic databases including science direct, pubmed, scopus, and google scholar were explored for each of the medicinal plants for peptic ulcers and all retrieved articles were evaluated to achieve any in vitro, in vivo, or clinical evidence for their efficacy and possible mechanisms. The retrieved studies either demonstrate obviously effectiveness of these herbs or indirectly their efficacy on the involved mechanisms in the treatment of peptic ulcers.

Meteria Medica provides lots of information about ethno medicinal herbs, which are valuable as antiulcer agents and their use experimentally was evaluated and proved by many researchers for its antiulcer activity. Following compiled data suggested that medicinal plant those are evidently reported for its antiulcer activity.

List of Medicinal Plants Reported Anti-ulcer activity [16-79]

S. No	Common name	Botanical Name	Part Used	Family	Uses
1	Tulsi	<i>Ocimum sanctum</i>	All parts	Labiatae	Antiulcer, Antibacterial
2	Tippani	<i>Allophylus serratus</i>	Leaves	Sapindaceae	Antiulcer, Elephantiasis
3	Shaparni	<i>Desmodim gangeticum</i>	Root Extract	Leguminosae	Typhoid, Piles, Inflammation, Asthma, Antiulcer
4	Neem	<i>Azadirach-ta indica</i>	dried bark extract	Meliaceae	Gastrointestinal disease, Leprosy, Respiratory disorders
5	Indian Sarsaparilla	<i>Hemides-mus indicus</i>	Extract	Asclepiadaceae	Antidiarrhoeal, mucoprotective, Antiulcer
6	Satavari	<i>Asparagus racemosus</i>	Extract of fresh root	Liliaceae	Anti-diarrhoeal, Antibacterial, Antiulcer
7	Triphala	<i>Terminalia pallida</i>	Plant Extract	Combretaceae	Antiulcer
8	Aamla	<i>Emblica officinalis</i>	Fruit Extract	Euphorbiaceae	Antiulcer
9	Gotu Kola	<i>Centella asiatica</i>	Fresh Juice	Apiaceae	Antiulcer
10	Brahmi	<i>Bacopa monniera</i>	Fresh Juice	Scrophulariaceae	Antiulcer
11	Apple bananas	<i>Musa sapientum</i>	Fruits	Scitamineae	Antiulcer
12	Papeeta	<i>Carica papaya</i>	Seeds	Caricaceae	Anti-helminthic, Antiamebic, Antiulcer
13	Pausanto	<i>Kielmeye-ra coriacea</i>	Stem	Guttiferae	Anxiolytic, Antiulcer
14	Brindle berry	<i>Garcinia cambogia</i>	Fruit extract	Clusiaceae	Antiulcer
15	Winter melon	<i>Benincasa hispida</i>	Fruits	Cucurbitaceae	Antiulcer, Epilepsy
16	Wild pipal	<i>Ficus arnottiana</i>	Fruits	Moraceae	Antiulcer, Demulcent
17	Indian devil tree	<i>Alstonia Scholaris</i>	Whole plant	Apocynaceae	Antiulcer,
18	Indian mulberry	<i>Morinda citrifolia</i>	Fruit	Rubiaceae	Antiulcer, Antidiabetic
19	Indian borage	<i>Plectrant-hus amboinic-us</i>	Whole plant	Lamiaceae	Diuretic, Antiulcer
20	Babul	<i>Acacia arabica</i>	Leaves, gums	Mimosaceae	Haemorrhagic ulcer, Wound
21	Garlic	<i>Allium sativum</i>	bulb juice	Liliaceae	Antiulcer
22	Boabab	<i>Adansonia digitata</i>	Leaves and Bark	Malvaceae	Syphilitic ulcer, Irritable inflammatory ulcers, Antiulcer
23	Bael tree	<i>Aegle marmelos</i>	Fruits	Rutaceae	Antiulcer
24	Kattalai	<i>Aloe vera</i>	Leaves and powder	Liliaceae	Antiulcer
25	Custard apple	<i>Annona squamosa</i>	Leaves	Annonaceae	Antiulcer
26	Kanchanara/ orchid tree	<i>Bauhinia variegata</i>	Bark and Root	Caesalpiniaceae	Antiulcer
27	Indian or Nepal barberry	<i>Berberis aristata</i>	Root and Wood	Berberidaceae	Antiulcer
28	Beetroot	<i>Beta vulgaris</i>	Roots	Chenopodiaceae	Antiulcer
29	Slow match tree	<i>Careya arborea</i>	Leaves, Btem and Bark	Myrtaceae	Antiulcer
30	Arasha-maram	<i>Ficus religiosa</i>	Bark and Leaves	Urticaceae	Antiulcer
31	Purple tephrosia	<i>Galega purpurea</i>	Roots	Papilionaceae	Antiulcer
32	Changing rose	<i>Hibiscus rosa</i>	Roots	Malvaceae	Antiulcerogenic agent, Antiulcer

		<i>sinensis</i>			
33	Indian penny-wort	<i>Hydrocotyle asiatica</i>	Leaves	Umbelliferae	Antiulcer
34	Mango tree	<i>Mangifera indica</i>	Leaves and Flowers	Anacardiaceae	Antiulcer
35	Touch me not	<i>Mimosa pudica</i>	Leaves	Fabaceae	Antiulcer, Antioxidant.
36	Bitter gourd	<i>Momordica charantia</i>	Whole plant and Fruits extract	Cucurbitaceae	Antiulcer.
37	Drum-stick	<i>Moringa oleifera</i>	Leaves	Moringaceae	Antiulcer.
38	Rice	<i>Oryza sativa</i>	extract of grains	Gramineae	Antiulcer.
39	Stonebreaker	<i>Phyllanthus niruri</i>	aerial part extract	Euphorbiaceae	Antiulcer
40	Sumach	<i>Rhus coriaria</i>	hydro alcoholic extract of R. coriaria	Anacardiaceae	Antiulcer
41	Sal tree	<i>Shorea robusta</i>	Resin extract of S. robusta	Dipterocarpaceae	Antiulcer, Analgesic
42	black nightshade berries	<i>Solanum nigrum</i>	Leaf extract	Solanaceae	Antiulcer
43	Tamarind tree	<i>Tamarindus indica</i>	Seeds	Caesalpiniaceae	Antiulcer
44	Ink-nut	<i>Terminalia chebula</i>	All parts	Combretaceae	Antiulcer
45	Basna	<i>Sesbania grandiflora</i>	Leaves	Fabaceae	Antiulcer

CONCLUSION

From this study, it is clear that the medicinal plants play a vital role against various diseases. Various herbal plants and plants extracts have significant antiulcer, activity in different animal models. Our review result shows that above-mentioned medicinal plants could prevent from Ulcer with the principle on dose-dependent. A variety of botanical products have been reported to possess that activity. Hence the review study is concluded that the herbal drug possesses antiulcer, activity and it has been proved by different animal models and Ayurveda which give many links to develop the future trials.

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