Medicinal plants acting against gastric and duodenal ulcer: A review

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Abstract

Nowadays acidity and ulcer are very common, causing huge suffering to humans with ulcers being a matter of concern due to high chances of recurrence and mortality. Nature gives numbers of drugs and possibly has all solutions for human diseases. The aim of this review is to know more about the medicinal plants acting against gastric and duodenal ulcer. An ulcer is erosion in the lining of the stomach and duodenum. There are two types of ulcers -gastric and duodenal ulcer. Together, they are called peptic ulcer. The main cause of peptic ulcer is the increase acids secretion and disturbance of the normal equilibrium either caused by enhanced diminish or aggression in mucosal resistance. Other causes of peptic ulcer are a bacterial infection (*H. pylori*), long-term uses of painkiller such as ibuprofen, naproxen sodium, etc., stress and spicy food habit. Hydrochloric corrosive and pepsin harm the mucous film of the gastrointestinal tract as the outcome both gastric and duodenal ulcers happen. Conventional treatments of peptic ulcers, such as proton pump inhibitors (PPIs) and histamine-2 (H2) receptor antagonists, have demonstrated adverse effects, relapses, and various drug interactions. Herbal plants are considered as safe for peptic ulcer treatment with fewer side effects. There are many herbs and plant products that have been found to play a role in protecting or helping to heal stomach and peptic ulcers. This article reviews drugs derived from plants which are used for the treatment of peptic ulcer and it is evident that plant extracts have significant antiulcer activity in animal models.

Keywords: Medicinal plants, Peptic ulcer, Gastric ulcer, Duodenal ulcer, *H. pylori*.

Introduction

The word ulcer is derived from Latin word “ulcus” (genitive: ulceris) which stands for sore, wound or an ulcer [1]. Ulcer is a common gastrointestinal disorder and can be characterized by inflamed lesions of the mucosa and tissue that protect the gastrointestinal tract. Damage of mucus membrane which normally protects the oesophagus, stomach and duodenum from gastric acid and pepsin causes ulcer. The pathogenesis of gastric ulcers remains widespread, it is multifactorial disease where diverse factors such as a stressful lifestyle, alcohol consumption, irregular food habits, severe illness, shock, burns, severe emotional disturbance, use of steroidal and nonsteroidal anti-inflammatory drugs (NSAIDs) and drugs which stimulate gastric acid and pepsin secretion, smoking, lower socio-economic status [2,3].

There are many types of ulcer such as mouth ulcer, esophagus ulcer, peptic ulcer, and genital ulcer. Of these peptic ulcer is seen among many people. The peptic ulcers are erosion of lining of stomach or the duodenum [4]. Peptic ulcer, also known as PUD or peptic ulcer disease, is an ulcer (defined as mucosal erosions equal to or greater than 0.5 cm) of an area of the gastrointestinal tract that is usually acidic and thus extremely painful [5]. Symptoms includes abdominal pain, classically epigastric with severity relating to mealtimes, after around 3 hours of taking a meal (duodenal ulcers are classically relieved by food, while gastric ulcers are exacerbated by it); bloating and abdominal fullness; waterbrash (rush of saliva after an episode of regurgitation to dilute the acid in esophagus); 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 (foul-smelling feces due to oxidized iron from hemoglobin).

The two most common types of peptic ulcer are called “gastric ulcer” and “duodenal ulcer.” The name refers to the site of ulceration. The main distinction is that they affect different parts of the digestive tract (Figure 1). Gastric ulcer is the lesser common variant of PUD, and usually occurs in the older age groups. The ulcer is localized to the lesser curvature of the stomach. If the ulcer had been chronic it can erode the splenic artery on the posterior surface, and cause excessive bleeding. Gastric ulcers, which are chronic, can lead to carcinoma, and thus, these ulcers are considered malignant till otherwise proven. Duodenal ulcers are more common and occur most commonly over the posterior surface of the 1st part of the duodenum. A chronic ulcer can perforate through the mucosa and all the layer, leading to either fibrosis, perforation (anterior), or if related to a vessel profuse bleeding (posterior). The term “kissing ulcers” was brought up to describe anterior and posterior ulcers, which have healed and given rise to fibrosis. Malignancy from chronic duodenal ulcers is very rare. A person may have both gastric and duodenal ulcers at the same time [6, 7].

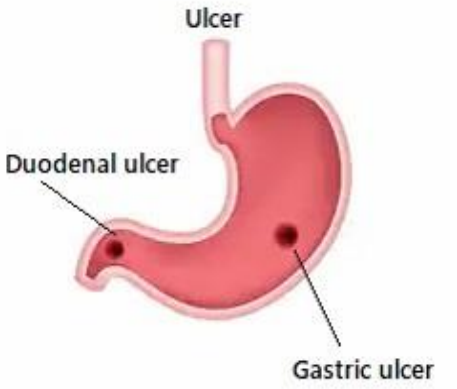

Figure1: Comparing gastric and duodenal ulcers

Plants are a rich resource used for centuries to cure various ailments. In the last few decades there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed

countries owing to its natural origin and lesser side effects. The literature revealed that many medicinal plants and polyherbal formulations are used for the treatment of ulcer. This is an important reason to review medicinal plants with traditional use acting against gastric and duodenal ulcer. The review is drafted via an exhaustive literature review from popular scientific search engines mainly, pubmed, science-direct, google scholar as well as articles present in google search.

Medicinal plants used in the ulcer treatment

There are many herbs, nutrients, and plant products that have been found to play a role in protecting or helping to heal stomach and peptic ulcers. Few human trials are available, but many have show good potential in animal or in vitro studies. A variety of botanical products have been reported to possess antiulcer activity but the documented literature has centered primarily on pharmacological action in experimental animals. A large number of spices and herbs have been evaluated by various researchers for their antiulcer effects to achieve a favorable outcome (Table 1). Large numbers of medicinal plants and dietary nutrients have been shown to possess gastro-protective activities such as Aloe, *Terminalia Chebula*, *Vetiveria Ziziinoides*, Ginseng, Capsicum etc. Except for a few phytogenic compounds (i.e. Aloe, Liquorice and Chilly), limited clinical data are available to support the use of herbs as gastro-protective 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 [8]. 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 [9-11].

Table 1: Some potential medicinal plants with antiulcer activity

S.No.	Botanical name and family	Parts used	Active constituents	Ref.
1.	*Achyrocline satureoides* Asteraceae	Inflorescences	Terpenoids, flavonoids, phenolic compounds, steroids	[12]
2.	*Alhagi maurorum* Leguminosae	Arial plant	Flavonoids, fatty acids, sterols	[13]
3.	*Alstonia scholaris* Apocyanacea	Bark	Alkaloids, coumarins, flavonoids, phlobatannin, phenols, steroids, saponins and tannins	[14]
4.	*Anacardium occidentale* Anacardiaceae	Leaves	Catechins	[15, 16]
5.	*Andrographis paniculata* Acanthaceae	Leaves	Andrographolide	[17]
6.	*Anogeissus latifolia* Combretaceae	Bark	Gallic acid and egallic acid	[18, 19]
7.	*Argemone mexicana* Papavaraceae	Leaves	Carbohydrates, flavonoids, tannins, terpenoids, phenols, saponins	[20]
8.	*Artocarpus integrifolia*	Leaves	Tannins, flavonoids, sterols,	[21, 22]

	Moraceae		phenols, carbohydrates	
9.	*Asparagus racemosus* Liliaceae	Roots	Saponins, polysaccharides	[23]
10.	*Azadirachta indica* Meliaceae	Leaves	Flavonoids, tannins, carbohydrates, and proteins	[24]
11.	*Azadirachta indica* Meliaceae	Bark	Terpenoids, flavones, phenols, glycosides	[25]
12.	*Bacopa monniera* Scrophulariaceae	Plant	Glycosides-bacoside A, Bacoside B	[26]
13.	*Bauhinia purpurea* Fabaceae	Leaves	Flavonoids, sterols, tannins	[27]
14.	*Bambusa arundinacea* Graminae	Leaves	Glycosides, alkaloids, phytosterols	[28]
15.	*Bauhinia variegata* Fabaceae	Leaves	Flavonoids	[29]
16.	*Boswellia serrata* Burseraceae	Bark	Squalene, polyprenol, βsitosterol, lutein, and β-carotene	[30]
17.	*Brassica oleracea* Brassicaceae	Leaves	Flavonoids, sterols	[31]
18.	*Butea frondosa* Fabaceae	Leaves	Butrin, flavonoids	[32]
19.	*Caesalpinia pulcherrima* Caesalpiniaceae	Bark	Flavonoids, alkaloids, steroids, tannins, carbohydrates	[33]
20.	*Calligonum comosum* Polygonaceae	Plant	Phenols, flavonoids	[34]
21.	*Carlina acanthifolia* Asteraceae	Roots	Inulin, flavonoids, essential oils	[35]
22.	*Carum carvi* Apiaceae	Seeds	Proteins, tannins, phenolic compounds, flavonoids	[36]
23.	*Casearia sylvestris* Flacourtiaceae	Leaves	Tannins, triterpenes	[37]
24.	*Cassia sieberiana* Fabaceae	Roots	Glycosides, steroids, flavonoids, tannins	[38]
25.	*Ceiba pentandra* Bombacaceae	Roots	Tannins, flavonoids, reducing sugars, triterpenes	[39, 40]
26.	*Citrullus colocynthis* Cucurbitaceae	Fruit	Saponins, alkaloids, tannins, flavonoids	[41]
27.	*Citrullus lanatus* Cucurbitaceae	Seeds	Phenols, flavonoids, tannins, alkaloids, terpenoids, steroids, saponins, antraquinones	[42]
28.	*Commiphora wightii* Burseraceae	Gum obtained from plant	Sterols, tannins, flavonoids	[43]
29.	*Convolvulus pluricaulis* Convolvulaceae	Plant	Carbohydrates, proteins, amino acids, alkaloids, triterpenoids, steroids	[44, 45]
30.	*Cressa cretica* Convolvulaceae	Plant	Alkaloids, glycosides, tannins, proteins	[46]
31.	*Cucurbita pepo* Cucurbitaceae	Seed	Glycoside terpenoids cucurbitacin	[47]
32.	*Cydonia oblonga* Rosaceae	Fruits	Tannins, phenols, polyphenols, flavonoids	[48]

33.	*Cynodon dectylon* Poaceae	Aerial parts	Flavonoids	[49]
34.	*Eucalyptus maculate* Myrtaceae	Leaves	Quercetin	[50]
35.	*Eugenia jambolana* Myrtaceae	Seeds	Flavonoids, tannins, triterpenes	[51]
36.	*Excoecaria agallocha* Euphorbiaceae	Leaves	Polyphenols, oxygenated diterpenoids	[52, 53]
37.	*Ficus religiosa* Moraceae	Leaves	Proteins, sterols, tannins, flavonoids, carbohydrates	[54, 55]
38.	*Genista rumelica* Fabaceae	Whole plant	Genistin, luteolin-7- glycoside	[56]
39.	*Glycyrrhiza glabra* Fabaceae	Dried roots and rhizomes	Flavonoids	[57]
40.	*Hibiscus rosa* Malvaceae	Leaves	Flavonoids, anthocyanins	[58]
41.	*Jasminum grandiflorum* Oleaceae	Leaves	Phenolics, flavonoids, carotenoids	[59]
42.	*Kaempferia parviflora* Zingiberaceae	Rhizome	Alkaloids, anthrones, flavonoids	[60]
43.	*Madhuca indica* Sapotaceae	Leaves	Triterpenoids, β-sitosterol, flavonoids	[61, 62]
44.	*Maytenus robusta* Celastraceae	Leaves	Triterpenes, steroids, flavonoids	[63]
45.	*Melia azedarach* Meliaceae	Leaves	Quercetin, rutin	[64]
46.	*Mimosa pudica* Fabaceae	Leaves	Flavonoids, steroids, saponins, tannins, gums and mucilages	[65]
47.	*Momordica charantia* Cucurbitaceae	Fruits	Flavonoids, alkaloids, steroids, sterols	[66]
48.	*Moringa oleifera* Moringaceae	Leaves	Alkaloids, flavonoids, saponin, tannins, zeatin, quercetin, kaempferol, and terpenoid	[67]
49.	*Moringa olifera* Moringaceae	Leaves	β-sitosterol	[68]
50.	*Mucuna pruriens* Fabaceae	Seeds	Alkaloids, glycosides, triterpenoids, tannins, saponins, β-sitosterol, amino acids	[69,70]
51.	*Murrya koenigii* Rutaceae	Root stem and leaves	Monoterpenes, monoterpene hydrocarbons sesquiterpenes	[71]
52.	*Musa sapientum* Musaceae	Leaves	Alkaloids, flavonoids, carbohydrates, glycosides	[72]
53.	*Neolamarckia cadamba* Rubiaceae	Leaves and bark	Terpenoids, glycosides, tannins, saponins, flavonoids	[73]
54.	*Nigella sativa* Ranunculaceae	Seeds	Saponins, tannins, quinines, sterols, triterpenes	[74, 75]
55.	*Ocimum sanctum* Lamiaceae	Leaves	Alkaloids, tannins, saponins, flavonoids (Apigenin)	[76, 77]
56.	*Osyris quadripartita Decne* Santalaceae	Leaves	Saponins, tannins, flavonoids, phenols	[78]
57.	*Paederia foetida*	Plant	Sitosterol, stigmasterol, ursolic	[79]

	Rubiaceae		acid	
58.	*Passiflora foetida* Passifloraceae	Plant	Proteins, phenols, alkaloids, phenolic compounds, flavonoids	[80]
59.	*Polyalthia longifolia* Annonaceae	Leaves	Alkaloids, terpenoids	[81]
60.	*Pseuderanthemum palatiferum* Acanthaceae	Leaves	Saponin, triterpenoid, flavonoids	[82]
61.	*Rhamnus procumbens* Rhamnaceae	Whole plants	Kaempherol	[83]
62.	*Rosa damascene* Rosaceae	Rose oil	Terpenes, alkaloids, anthocyanins	[84]
63.	*Scutia buxifolia* Rhamnaceae	Bark	Flavonoids, alkaloids, polyphenols, tannins	[85]
64.	*Solanum nigrum* Solanaceae	Fruits	Tannins, alkaloids, saponins, volatile oils	[86]
65.	*Sophora alopecuroides* Fabaceae	Whole plants	Sophoradin	[87]
66.	*Sylibin marium* Asteraceae	Whole plants	Silymarin	[88]
67.	*Syzygium alternifolium* Myrtaceae	Leaves	Flavonoids, tannins	[89, 90]
68.	*Tephrosia purpurea* Fabaceae	Roots	Flavonoiods	[91]
69.	*Terminalia chebula* Combretaceae	Fruits	Alkaloids, flavonoids, glycosides, tannins, terpenoids	[92]
70.	*Terminalia pallida* Combretaceae	Leaves	Tannins, terpenoids, phenols, alkaloids, flavonoids, carbohydrates	[93]
71.	*Toona ciliate* Meliaceae	Heart wood	Terpenoids, sterols, quercetin	[94]
72.	*Trigonella foenum graceum* Fabaceae	Seeds	Flavonoids, polysaccharides	[95]
73.	*Utleria salicifolia* Periplocaceae	Rhizomes	Steroids, saponins, tannins	[96]
74.	*Zingiber officinale* Zingiberaceae	Ginger powder	Gingerol, shogaol	[97]
75.	*Ziziphus jujuba* Rhamnaceae	Bark	Flavonoids, alkaloids, sterols, polyphenols, tannins	[98]

Medicinal plants have achieved their therapeutic properties from their capability to produce renewable and various secondary metabolites, which are known as phytochemical constituents. Hence, numerous plants have used these phytochemicals as a protection mechanism against pathogens [99]. It is important to emphasize that herbal products may contain numerous bioactive constituents with dangerous, but also beneficial effects. Therefore, the higher education of doctors and patients about herbal therapy is necessary, as well as legislation to control the quality of herbal products, especially for further randomized investigations to determine the effectiveness and safety of many products in digestive and other disorders [100]. Finally, the Ayurvedic

knowledge and modern medicine could generate preferable antiulcer drugs derived from medicinal plants with less side effects [101].

Future research perspective

Currently, increasing health concern urged the researchers to revitalize the natural products and to alleviate the diseases without harming the body. Along with the global decline of peptic ulcer disease and in the prevalence of *H. pylori*, there is a rising problem of growing antimicrobial resistance, which reduces the efficiency of eradication therapy, and the overuse of proton pump inhibtors, resulting in unexpected new side effects [102]. Also, the occurrence of idiopathic ulcers associated with high mortality is increasing [103], and there is a need for defining the optimum management of the idiopathic disease. According to the old hypothesis, acid secretion was thought to be the sole cause of ulcer formation and reduction in acid secretion was thought to be the major approach towards therapy. However, in the light of recent evidences this concept has changed. Now treatment of ulcer mainly targets the potentiation of the defensive system along with lowering of acid secretion.

Some plant products, including isolated compounds and plant formulas, significantly decreased such gastric inflammation and injury, and even inhibited gastric cancer progression. Medicinal plant compounds provide effective way to reduce *H. pylori*-induced gastric inflammation and even gastric cancer. However, potential cytotoxicity and adverse side effects might present from those medicinal plant products. Further relevant cytotoxicity studies both in vitro and in vivo will be required. Further evaluation of pharmacokinetics for those products in animals will be also required. Ethno medicinal knowledge supported by modern science is necessary to isolate, characterize, and standardize the active constituents from herbal source. This combination of traditional and modern knowledge can produce better antiulcer drugs with fewer side effects.

Conclusion

The review was designed to highlight the gastrointestinal effects of the medicinal plants to open the door for their clinical uses as a result of efficacy and safety. Various herbal plants and plants extracts have significant antiulcer activity in animal models. It has mucoprotective activity and gastric anti-secretary when compared with that of reference drugs. The extract is non-toxic even at relatively high concentrations. The antiulcer activity is probably due to the presence of flavonoids in all this plants. It is high time efforts should be made to use the vast ethno-pharmacological knowledge our traditional practitioners have to develop safer herbal preparations, for the people which will be less toxic and cheaper than the modern day medicaments.

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