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Therapeutic potential of indigenous medicinal plants against gastric ulcer

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Article Info	Abstract
Article history	Ulcers are a frequent gastrointestinal condition that affects many different sections of the body. The
Received 8 April 2022	intestinal mucosal layer that lines the gastrointestinal tract can be disrupted or breached by ulcers. Peptic
Revised 24 May 2022	ulceration is now known to be caused by an imbalance of aggressive and defensive elements. There are
Accepted 26 May 2022	already a plethora of synthetic pharmaceuticals available to treat peptic ulcers and their consequences,
Published Online 30 June 2022	but these therapies are either excessively expensive or have a variety of negative effects. Peptic ulcers are
Keywords	currently being treated using a variety of medicinal herbs and polyherbal formulations. In this review
Antioxidant	article, we look at various medicinal plants that can be utilized in both ayurvedic and western medicine to

heal peptic ulcers and reduce their consequences. Apart from their antiulcer activity, the medicinal plants

possesses tremendous therapeutic potentials like Asparagus racemosus L. is known to be quiet effective

in the treatment of problems associated with female reproductive system, Solanum nigrum L. cures

psoriasis and ringworm, inflammatory disorders, menstrual cramps. Carica papaya L. known to possess

antithrombocytopaenic, immunomodulatory and anti-inflammatory potentials.

Antioxidant Bioactive Cyclooxygenase Duodenal ulcers NSAIDs Peptic ulcer Phytochemicals Polyheral formulations

1. Introduction

Herbal drugs have become a matter of worldwide importance in the last decade, affecting both global health and global trade. India has long been renowned as a rich source of therapeutic agents among prehistoric cultures. Herbal medicines continue to play an important part in the healthcare systems of many people across the world. Herbs are harvested from many parts of the plant, including the roots, leaves, barks, seeds, and flowers (Malik et al., 2020). Herbal plants are a source of numerous herbal drugs that are very effective in the treatment of various ailments and are almost widely utilized to cure a wide range of illnesses, and their popularity has been gradually expanded around the world. The indigenous people have a wealth of knowledge about the flora that surrounds them. They nurture and pass on knowledge to ethnobotanists across the world for a variety of purposes, including modern medicine (Alam et al., 2019). The general populace is increasingly turning to herbal medicines to avoid taking modern medicinal pharmaceuticals on their own initiative (Idris et al., 2021). There are an unimaginable number of plants on our green globe that are regarded as wild or weeds due to their lack of clear economic value. Many plant species that were previously thought to be useless, have now been discovered to be extremely valuable in terms of phytochemicals. The major sources of new phytochemicals are found in wild plants, shrubs, and trees (Alam and Khan, 2020).

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Copyright © 2022 Ukaaz Publications. All rights reserved. Email: ukaaz@yahoo.com; Website: www.ukaazpublications.com In this article, we will find out some herbal plants possessing antiulcer potentials. The word "ulcer" originated from the Latin word "ulcus", which means a sore, wound, or ulcer (Ravisankar et al., 2016). Peptic ulcers are most commonly found on the mucosa of the stomach, and duodenal ulcers are found in the duodenum region of the small intestine (Inaparthi et al., 2014; Mohan, 2015), are sores that are open on the skin or mucous membrane of the stomach and duodenum that are characterized by a breach in the inner lining of the gastrointestinal tract because of gastric acid secretion or pepsin (Chan and Graham, 2004). In this situation, the mucosal epithelium is exposed to acid and pepsin. In this condition, gastric ulcers can be exacerbated by stress, smoking, nutritional deficits, and the use of NSAIDs: nonsteroidal anti-inflammatory medicines (Belaiche et al., 2002). The imbalance between aggressive forces such as acid, pepsin, and Helicobacter pylori and defensive factors such as bicarbonate secretion, prostaglandins, gastric mucus, and intrinsic resistance of mucosal cell factors causes peptic ulcers (Dashputre and Naikwade, 2011). Both H. pylori and regular use of nonsteroidal anti-inflammatory drugs (NSAIDs) increase the risk of peptic ulcer development (Teka et al., 2016; Kumar et al., 2011). NSAIDs suppress the production of the enzyme cyclooxygenase (COX), which has been demonstrated to slow the progression of ulcers by blocking the conversion of arachidonic acid to prostaglandins (Vane and Botting, 1998). Complications occurring due to peptic ulcer disease continue to be a major cause of morbidity around the world, putting a significant strain on healthcare resources (Tanih et al., 2010). Peptic ulcer disease is predicted to cause 15,000 fatalities each year. The goal of gastric ulcer treatment is to lower stomach acid production while also encouraging gastric mucosal protection (Valle, 2005). Although, powerful antiulcer drugs are available, the majority of them have a number of side effects, emphasizing the need to seek out new alternatives (Lavnya

et al., 2012). Due to the numerous adverse effects associated with the use of modern medications for a variety of ailments, medicinal plants are increasingly being regarded as the primary source of novel drugs, as they have fewer or no deleterious effects. Because, herbal medications are thought to be safe for treating ulcers with fewer side effects, are cost-effective, and substantially less hazardous, significant research is being done to find potent antiulcer drugs of plant origin (Srinivas *et al.*, 2013). This article examines the characteristics of a few of the plants that have been claimed to have antiulcer potential and ulcer-healing abilities.

2. Symptoms and clinical features of peptic ulcer

Peptic ulcers (PU) extend throughout the muscularis mucosae and are typically characterized by various stages of necrosis, neutrophil infiltration, decreased blood flow, and inflammation enhanced oxidative stress (Silva *et al.*, 2013). Most of the patients having peptic ulcer often have abdominal pain, feeling of nausea and discomfort, one of the most striking symptom of gastric and duodenal ulcer is epigastric pain, this pain often worsen and feels like a burning sensation after having food. Antacids can usually ease the pain of a duodenal ulcer (Najm, 2011), meals on the other hand, frequently worsen gastric ulcer pain. Other symptoms includes bloating and a feeling of abdominal fullness in the abdomen melena, hematemesis and acute peritonitis is a rare complication (Ramasubramaniaraja and Babu, 2011), stools that are dark or black (Roy, 2016).

3. Approaches for treatment of peptic ulcers

Peptic ulcers are treated with a variety of medications; however, the most of them have substantial side effects such as arrhythmias, gynecomastia, impotence, arthralgia, hypergastrinemia, and haemopoeitic alterations (Akthar *et al.*, 1992).

In recent years, an alternative strategy has been to investigate medicines from the ayurvedic or traditional medicinal system. The use of phytoconstituents as a pharmacological therapy to treat major disorders has been shown to be clinically successful and less toxic than currently available medications, as well as reducing offensive factors and functioning as a tool to prevent the peptic ulcers (Jainu *et al.*, 2006). The main advantages of medicinal plants are, they are economical, readily available and has no side effects. (Bhatt *et al.*, 2019).

A number of medicinal plants have been claimed to have antiulcer properties. In this review, we have organized the medicinal plants and their parts that have been utilized in various animal models to effectively lessen the repercussions of peptic ulcer disease in a variety of animal models.

4. Various experimental animal models for peptic ulcer induction

Physiological, pharmacological, and surgical interventions can cause peptic ulcers in a variety of animal species. However, rats are used in the majority of peptic ulcer research. Several models are employed in experiments to test or evaluate antiulcer action of medications or treatments, some of them are listed below in Table1.

There are several compounds called bioactive chemicals that are found in a variety of plants. Bioactive natural compounds always have played an important role as innovative potential therapeutic agents. They have a significant direct and indirect impact on human health, as well as extensive therapeutic characteristics. They possess antioxidant, anti-inflammatory properties which justify their role as an antiulcer compounds (Karasawa and Mohan, 2018). Some important bioactive compound that are being obtained from these medicinal plants and are listed below in Table 2.

 Table 1: In vivo models used for preclinical evaluation of antiulcer activity

S. No.	Animal model	Reference
1.	Water-immersion stress or cold-water-restraint or cold-restraint stress	Kitagawa et al., 1979; Brodie and Hanson, 1960
2.	NSAIDs-(indomethacin, aspirin, and ibuprofen) induced gastric ulcers	Rainsford.,1987
3.	Ethanol-induced gastric ulcers	Sener et al., 2004; Takagi et al., 1970
4.	Histamine-induced gastric ulcers	Adinortey et al., 2013
5.	Reserpine-induced gastric ulcers	Kagoshima et al., 1982
6.	Serotonin-induced gastric ulcers	Hashizume et al., 1978; LePard and Stephens, 1994
7.	Pylorus-ligated-induced peptic ulcers	Shay et al., 1945
8.	Diethyldithiocarbamate-(DDC)-induced peptic ulcers	Oka <i>et al.</i> , 1990
9.	Methylene blue-induced ulcers	Shah et al., 2006
10.	Ischemia-reperfusion-(IR)induced gastric ulcers	Wada <i>et al.</i> , 1996
11.	Cysteamine-induced duodenal ulcers	Szabo, 1978
12.	Indomethacin-histamine-induced duodenal ulcers	Takeuchi et al., 1986
13.	Ferrous iron-ascorbic acid-induced gastric ulcers	Naito et al., 1995
14.	Acetic acid-H. pylori-induced ulcers	Takagi et al., 1970; Okabe and Amagase, 2005
15.	Acetic acid-induced gastric ulcers	Konturek et al., 2003

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S. No.	Plant name	Important chemical constituent	Chemical structure	References
1.	Asparagus racemosus L.	Tannic acid	$HO \rightarrow OH HO \rightarrow OH $	Ahmad, 2014
2.	Hibiscus rosa-sinensis L.	Quercetin		Zhang <i>et al.</i> , 2020
3.	Solanum nigrum L.	Solasodine	$H_{1}C$ $H_{2}C$ $H_{3}C$ $H_{1}C$ H	Al Sinani <i>et al.</i> , 2013
4.	Psidium guajava L.	Gallic acid	О ОН НО ОН	Reckziegel <i>et al.</i> , 2016
5.	Terminalia chebula R.	Chebulinic acid		Lu <i>et al.</i> , 2012
6.	Carica papaya L.	Kaempferol		Lee et al., 2014

 Table 2: Some important major bioactive chemical constituents of selected medicinal plants

5. Pharmacological activities exhibited by selected medicinal plants

5.1 Asparagus racemosus L.

Asparagus racemosus L. commonly known as satavar, is a member of the Asparagaceae family of plants that is known to be quiet effective in the treatment of problems associated with female reproductive system (Sharma and Sharma, 2017). It shows a wide range of pharmacological activities among which, some of the reported activities are antihepatotoxic activity (Muruganadan et al., 2000), aphrodisiac activity (Thakur et al., 2009), antioxidant activity (Kamat et al., 2000), antiurolithiac activity (Narumalla et al., 2012), antistress activity (Sharma et al., 2017), uterine relaxant activity (Suwannachat et al., 2012), antineoplastic activity (Liu et al., 2009), antidepressant activity (Singh et al., 2009), antihyper glycaemic activity (Hannan et al., 2007), versatile female tonic (Sharma et al., 2011), diuretic activity (Kumar et al., 2010), hypolipidemic activity (Visavadiya et al., 2009), antidiarrhoeal effect (Karmakar et al., 2012), antipyretic activity (Vasundra et al., 2013), immunomodulatory action (Gautam et al., 2012) and wound healing activity, etc. (Kodancha et al., 2011). Apart from these pharmacological activities, A. racemosus crude extract also possess significant antisecretory and antiulcer activity, when compared to the control group, crude extract in daily oral dose of 100 mg/kg/day up to 15 days considerably lowered ulcer index. The decrease in stomach lesions was similar to that seen with the conventional antiulcer medicine ranitidine (30 mg/kg/day orally). Crude extract also decreased gastric secretion volume, free and total acidity (Bhatnagar et al., 2006). Some important chemical constituents reported in A. racemosus are asparagine, arginine (Mishra et al., 2017), sarsasapogenin and shatavarin I-IV, isoflavone, 8-methoxy-5,6,42 -trihydroxyisoflavone-7-Oα-d-glucopyranoside (Negi et al., 2010), etc.

5.2 Hibiscus rosa-sinensis L.

This plant is belonging to Malvaceae family, the common name is "changing rose" locally also called gudhal, originally it is a native of China and is widely grown in India. Various chemical constituents present in *H. rosa-sinensis* are flavonoids, anthocyanins, quercetin, cyanidin, kaempferol and hydrocitric acid (Vimala and Shoba, 2014). At different doses, the aqueous and ethanolic extracts of *H. rosa-sinensis* roots possess antiulcer activity in pylorus-ligated rats (Srivastava *et al.*, 2013). Some other activities exerted by *H. rosa-sinensis* are antibacterial activity (Ruban *et al.*, 2012), anticonvulsant activity (Kasture *et al.*, 2000), analgesic activity (Sawarkar *et al.*, 2009), antioxidant activity (Mandade *et al.*, 2011), anti-inflammatory activity (Tomar *et al.*, 2010), antipyretic activity (Sawarkar *et al.*, 2011), wound healing activity (Nayak *et al.*, 2007), antianxiety activity (Khan *et al.*, 2011).

5.3 Solanum nigrum L.

Solanum nigrum L., a member of the Solanaceae family, is popularly referred to as "black nightshade berries." The major chemical constituents are gentisic acid, luteolin, apigenin, kaempferol, and m-coumaric acid, alkaloids, saponins, flavonoids, and phytosterols (Mayilsamy *et al.*, 2013). In rats with pylorus ligation produced stomach ulcers, aqueous extract of leaves of *S. nigrum* showed strong antiulcer potential at 200 and 400 mg/kg doses (Kavitha *et al.*, 2012). It cures psoriasis and ringworm, inflammatory disorders,

menstrual cramps, fevers, diarrhea, eye infections, hydrophobia (Kirtikar *et al.*, 1935; Nadkarni *et al.*, 1976). Other pharmacological activities reported on *S. nigrum* are hepatoprotective activity, antioxidant activity, anticonvulsant activity, immunostimulant activity, antitumor activity, anti-inflammatory activity, cytotoxic activity, anti HCV activity, *etc.* (Goutam *et al.*, 2018).

5.4 Psidium gsajava L.

Psidium guajava L. of the Myrtaceae family, is best known as "guvava. The major chemical constituents are quercetin, avicularin, apigenin (Wang *et al.*, 2010), gallic acid, catechin, epicatechin (Liu *et al.*, 2014), kaempferol (Wang *et al.*, 2017). The methanolic extract of leaf of *P. guajava* was given orally to rats at various doses for 10 days to treat ethanol-induced stomach ulcers. In comparison to the control, the extract reduces ulcer indices significantly when compared to control (Umana *et al.*, 2012). At doses of 500 and 1000 mg/kg body weight, *P. guajava* reported to cause reduction in ulcer index of ethanol induce ulceration in the stomach of wistar rats. *P. guajava* has been shown to have pharmacological actions such as antidiabetic, antidiarrhoeal, hepatoprotective, anticancer, antioxidant, anti-inflammatory, antiestrogenic and antibacterial *in vitro* and *in vivo* studies (Eziuche *et al.*, 2022).

5.5 Terminalia chebula R.

Myrobalan is the common name for Terminalia chebula R., a Combretaceae plant often referred to as "harad." According to a recent study, the methanolic extract of T. chebula was given orally at doses of 250 and 500 mg/kg. Both the pylorus ligation and the ethanol-induced gastric ulcer resulted in stomach damage. The methanolic extract reduces gastric volume, free acidity, and ulcer index when compared to the control (Raju et al., 2009). Some other pharmacological activities exhibited by T. chebula are neuroprotective activity (Yuh-Chiang et al., 2017), antibacterial activity (Phadke et al., 1989), antiepileptic activity (Debnath et al., 2010), antioxidant activity, neuroprotective activity (Chang et al., 2011), hepatoprotective activity (Tasduq et al., 2006), cardiotonic activity (Reddy et al., 1990), cytoprotective activity (Na M et al., 2004), antidiabetic (Sharma et al., 2011), antiarthritic and analgesic activity (Seo et al., 2012), antihyperlipidaemic (Shirin et al., 2010), antifungal activity (Venkatachalam et al., 2020), antiviral activity, anticarcinogenic activity, wound healing activity, etc. (Chattopadhyay et al., 2007). Major chemical constituents present in T. chebula are flavonoids, flavins, terpenoids, steroids, various phenols, tannic acid, ethyl gallate, chebulic acid, chebulagic acid, corilagin, ascorbic acid (vitamin C), gallic acid, ellagic acid, eugenol, chebulinic acid, ethylgallate, methyl gallate, chebulaginic acid, etc. (Riaz et al., 2017).

5.6 Carica papaya L.

Carica papaya L. belongs to the Caricaceae family. The methanolic extract of *C. papaya* reduced stomach ulcers by 56%, 76%, and 82% at 125, 250, and 500 mg/kg doses, respectively (Pinto *et al.*, 2015). Some of the pharmacological activities shown by *C. papaya* are antithrombocytopaenic activity (Dharmarathna et al., 2013), analgesic activity (Suwendar, 2014), antimicrobial activity (Baskaran *et al.*, 2012), antitumor activity and immunomodulatory activity (Otsuki *et al.*, 2010), antidiabetic activity (Juarez-Rojop, 2014), anthelmintic activity (Sanghvi, 1989), nephroprotective activity (Suyono *et al.*, 2016), anti-inflammatory activity (Owoyele

et al., 2008), and wound healing activity (Ukoba *et al.*, 2016), *etc.* The chief constituents present are manghaslin, clitorin, rutin, nicotiflorin, papain, chymopapain, cystatin, tocopherol, and caffeic acid carpaine (Ramasawamy *et al.*, 1960), pseudocarpaine

(Govindachari et al., 1954), and dehydrocarpaine I and II (Tang, 1979).

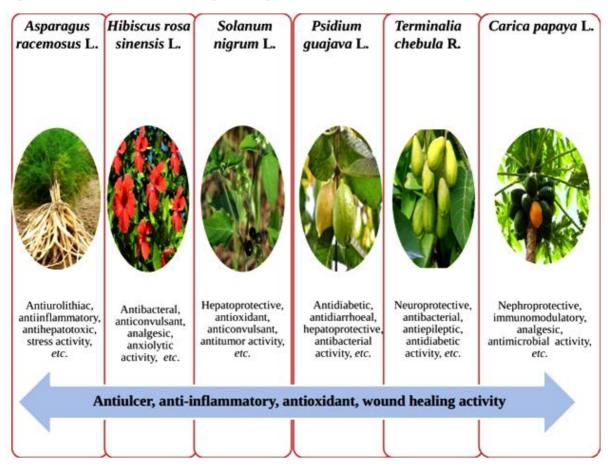


Figure 1: Some important pharmacological activities of indigenous medicinal plants.

Table 3: Indigenous medicina	l plants, their parts used	and major active constituents
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Sr. No.	Medicinal plant	Family	Part(s) used	Major active constituents	Reference
1.	Asparagus racemosus L.	Asparagaceae	Fruits, roots	Asparagine, arginine, tyrosine, flavonoids (kaempferol, tannin quercetin, and rutin) and resin	Negi <i>et al.</i> , 2010
2.	<i>Hibiscus rosa-sinensis</i> L.	Malvaceae	Flowers, leaves root	Phenols, tannins, alkaloids, flavonoids, anthraquinones	Al Snafi <i>et al.</i> , 2018
3.	Solanum nigrum L.	Solanaceae	Leaves, fruits, stem	Polyphenols, entisic acid, luteolin, apige- nin, kaempferol, and m-coumaric acid	Hsiu et al., 2010
4.	Psidium guajava L.	Myrtaceae	Leaves, fruits	Beta sitosterol, uvaol, oleanolic acid, ursolic acid <i>etc</i> .	Sabira <i>et al.</i> , 2014
5.	Terminalia chebula R.	Combretaceae	Leaves, fruits	Tannins (gallic acid, chebulic acid, puni- calagin, corilagin, ellagic acid, chebulegic acid, chebulinic acid), flavonol glycosides, triterpenoids, chebulin, phenolic compounds, <i>etc</i> .	Said <i>et al.</i> , 2012
6.	Carica papaya L.	Caricaceae	Peel, fruits, leaves, roots, seeds, flower	latex Trans-geranylacetone, palmitic acid, myristic acid, methyl palmitate, oleic acid, steric acid, decylene, <i>etc</i> .	Anjana <i>et al.</i> , 2018

6. Utilization of herbal plants in development of antiulcer medicines

It is evident now that the antiulcer effects are now known to exist in a variety of plants. Herbal medicines have been utilized for the treatment of numerous disorders since ancient times. Peptic ulcer disease is a global problem and sometimes it can lead to some serious life threatening side effects. Nowadays, the medicines that are utilized in the treatment of peptic ulcers may also have various side effects like gastrointestinal disturbances such as nausea, vomiting, diarrhea, constipation, headache, rash, dizziness, fatigue, dry mouth, etc. So, it is essential to develop and utilize a formulation of plant origin to minimize the side effects caused by drugs in the modern medicine system. Some medicinal plants with antiulcer effects are discussed in this review article. These plants are A. racemosus, H. rosa-sinensis, S. nigrum, P. guajava, T. chebula, and C. papaya. Apart from antiulcer properties, some of their important chemical ingredients and few other parameters of these plants utilized for antiulcer activity are discussed. Other pharmacological activities exhibited by these medicinal plants are also demonstrated here in this review article. Antiulcer effects are mostly due to chemical ingredients such as alkaloids, flavonoids, terpenoids, and tannins.

7. Conclusion

The peptic ulcer disease (PUD) mechanism results from an imbalance between gastric mucosal protective and aggressive factors. The mucosal protective factors are mucous, bicarbonate, mucosal blood flow and prostaglandins while aggressive factors are H. pylori, acid, pepsin, smoking, NSAIDs, etc. Out of this, prevalence of any one or more aggressive factors can cause peptic ulcers. However, today's ulcer treatment focuses on potentiating defense factors as well as reducing acid secretion. While the currently available treatment options have significant side effects, nowadays, proton pump inhibitors are the most widely used and over prescribed medications. The proton pump inhibitors are reported to possess some side effects, which include a headache, diarrhea, constipation, and cramping, these are minor and easily managed. Recent studies; however, have suggested a link between proton pump inhibitors and other antiulcer medications used and a number of serious side effects, which has caused considerable concern among patients and physicians. Some of the negative effects of proton pump inhibitors are related to their suppression of gastric acid secretion, which allows ingested microbial pathogens that would have been devastated by gastric acid to colonize the upper gastrointestinal tract and cause infections. This article looks at a few of the herbal medications that have been shown to have antiulcer activity in animal studies. Various experimental data now show that various herbal medications are extremely effective in the treatment of stomach ulcers, but only a few have reached the clinical trial stage, and even fewer have been commercialized. As a result, it can be inferred that the advantages of these studies are not reaching the general public. As a result, researchers must devote more time and effort to the standardization of such potential herbal medications in order for them to be clinically effective and competitive.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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