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# A Systematic Review on Potential Phytoconstituents with Antiulcer Activity

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## Abstract

A frequent gastrointestinal illness that affects many people is ulcer. Basically, it is a swollen tear in the skin or the mucous membrane lining the digestive tract. When the natural equilibrium is upset by increased aggression or decreased mucosal resistance, ulceration results. It might be brought on by consistent drug use, strange eating patterns, stress, and other factors. Peptic ulcers are a general name for digestive system ulcers in the stomach or duodenum. The presence of acid and peptic activity in gastric juice, as well as a breakdown in mucosal defences, all contributes to the development of peptic ulcers. There are several synthetic medications available to treat ulcers. But compared to herbal remedies, these medications are more expensive and likely to have greater negative effects. According to the literature, many Ayurveda doctors and traditional healers utilize a variety of medicinal herbs and polyherbal combinations to cure ulcers. Pain relief, ulcer healing, and postponing ulcer recurrence are the ideal goals of treatment for peptic ulcer disease. An attempt has been made in this review to learn about various medicinal plants that could be used in both Ayurvedic and modern science for the treatment or prevention of peptic ulcer.

**Keywords:** Peptic ulcer; Helicobacter pylori; gastric cancer; bioactive phytochemicals; traditional healing systems

## Introduction

An open sore on the skin or mucous membrane is known as an ulcer, and it is characterized by the shedding of inflammatory dead tissue.[1] Lesions on the skin's or mucous membranes surface known as ulcers are characterized by a superficial loss of tissue. Although they can occur practically everywhere, ulcers are most frequently found on the skin of the lower limbs and in the gastrointestinal tract. There are numerous different forms of ulcers, including vaginal, esophageal, peptic, and oral ulcers. Of these, many people experience peptic ulcers. Peptic ulcers are an erosion of the duodenal or stomach lining.[2] The terms "gastric ulcer" and "duodenal ulcer" refer to the two most prevalent varieties of peptic ulcer. The term alludes to the ulceration's location. A person may simultaneously have duodenal and stomach ulcers. Stomach ulcers, which are located there and cause pain, are more common in older age groups. Eating could make discomfort worse rather than better. Nausea, vomiting, and weight loss are

possible additional symptoms. Although patients with stomach ulcers produce normal or lessened amounts of acid, ulcers can still develop even when acid is completely absent.[3] At the start of the small intestine, duodenal ulcers cause acute discomfort and a burning sensation in the upper abdomen that cause patients to wake up from their sleep. Pain typically starts when the stomach is empty and goes away after eating. Duodenal ulcers are more prevalent in younger people and primarily affect men. Both the front and posterior walls of the duodenum may develop ulcers.[4] Bloody stools, excruciating cramps, and bloody vomiting are all signs of peptic ulcers, which can sometimes be fatal.[5]

**Pathophysiology of Peptic Ulcer**

A conflict between offensive (acid, pepsin, and Helicobacter pylori) and defensive (mucin, prostaglandin, bicarbonate, nitric oxide, and growth hormones) components underlies the Pathophysiology of peptic ulcer disease.[6] Research has shown that Helicobacter pylori infection or adverse drug reactions, notably to NSAIDS (nonsteroidal anti-inflammatory drugs), are the underlying causes of peptic ulcers rather than the previously thought aggravating factors of spicy food and stress.[7] The main etiological causes of peptic ulcers are Helicobacter pylori, NSAIDS, mental stress, alcoholism, and smoking. In order to survive in the hostile environment of the stomach, the Gram-negative bacterium Helicobacter pylori persists between the mucous layer and the gastric epithelium. Initially found in the antrum, Helicobacter pylori gradually moves toward the stomach's more proximal regions.[8] 10% of the world's population suffers from peptic ulcers, one of the most common gastrointestinal conditions.[9] Duodenal ulcers make up for 19 out of 20 peptic ulcers. The estimated annual death toll from peptic ulcers is 15,000. Peptic ulcer bleeding and perforation incidence estimates for each year were 19.4-57 and 3.8-14 per 100,000 people, respectively. The average long-term recurrence of perforation was 12.2%, and the average bleeding recurrence within 7 days was 13.9%.[10] Antacids and antiulcer medications account for 6.2 billion rupees and 4.3% of the market in the Indian pharmaceutical sector. Due to its higher cultural acceptance, better compatibility with the human body, and less side effects, 75–80% of the world's inhabitants still use herbal medicine for primary healthcare in this modern period.[11] These medicinal plants did not exhibit any acute toxicity, according to histological investigations. This medicinal plant's existence of significant secondary metabolites such flavonoids and tannins, which are the key components of antiulcer action, was discovered during preliminary pho to chemical screening.[12] In the current study, medicinal plants that are thought to be gastro-protective and therapeutic agents for ulcers in ayurvedic resources were reviewed. Additionally, evidence for their efficacy and biological mechanisms in contemporary research was gathered. This goal was accomplished by researching each of the medicinal plants for peptic ulcers in the Indian ayurvedic book Meteria Medica and electronic databases such as science direct, pubmed, scopus, and google scholar. All retrieved articles were then assessed for any in vitro, in vivo, or clinical evidence for their efficacy and potential mechanisms. The

research found either directly or indirectly shows that these herbs are beneficial at treating peptic ulcers by influencing the mechanisms involved.[13] Numerous researchers have investigated and demonstrated the antiulcer activity of ethnomedicinal herbs used in experimentation, which are valuable as antiulcer agents, in Meteria Medica. According to accumulated data, there are medicinal plants that are clearly known for their antiulcer activity.

The majority of the disease's classifications are based on the anatomical origins of the ulcers, such as gastric (found along the stomach's minor curvature) and duodenal (occurring in the duodenal bulb—the area most exposed to stomach acid) ulcers.[14] According to studies, an imbalance between aggressive injurious agents like pepsin and HCl and defensive mucosa-protective factors is what causes peptic ulcer disease (PUD) (e.g., prostaglandins, mucus and bicarbonate barrier and adequate blood flow).[9] The aggressive action of pepsin and stomach acid on mucosa was first believed to be the cause of all upper gastrointestinal tract ulcers. However, the term "peptic ulcer" has recently been associated with Helicobacter pylori infection, where chronic NSAID and acetylsalicylic acid (ASA) use are some of the disease-causing variables.[15] The current report seeks to provide a general overview of peptic ulcers, taking into account their epidemiology, primary symptoms and clinical features, pathogenesis—with a focus on H. pylori infection—pharmacological agents used in an effective management—as well as the most recent challenges and opportunities in this field, all in light of the fact that PUD is an important cause of morbidity and health care costs. Last but not least, a specific emphasis was placed on the safety and security of plant products in order to pique interest in developing deeper knowledge in this area and to guarantee effective managerial competence for health-related systems.

## Epidemiology of Peptic Ulcer

According to epidemiological research, the incidence of PU rises with the use of NSAIDs and ASA, as well as with population ageing, and is a mirror of the incidence of H. pylori infection. Up until the later decades of the 20th century, when a considerable reduction in its prevalence was noticed, PUD had a significant impact on morbidity and mortality.[16] Changes in environmental factors, like modernization, were linked to this abrupt change in the disease's pattern of prevalence. In addition, it was speculated that improved hygiene and general health standards in developed nations may have led to a decline in childhood infections and the transmission of H. pylori.[17] Additionally, the identification of potent and effective acid suppressants as well as the management and prevention of H. pylori infection were noted as having a significant impact on the decline in PUD rates. By the turn of the century, however, the increased use of NSAIDs had led to an increase in stomach ulcers (NSAID-caused ulcers) and a decrease in duodenal ulcers (H. pylori-associated infection).[18] However, PU is still widespread, particularly in developing nations where H pylori infection is very common. In poor nations, according to studies the frequency of H. pylori infection peaks at more than 80% before the age of 50 and is

highest in children under the age of 10.[19] In affluent nations like the US, serologic evidence of H. pylori infection is rare before the age of 10, but it climbs to 10% between the ages of 18 and 30 and to 50% in people over the age of 60. Throughout fact, it is predicted that 10% of people will develop a PU in their lifetime.[20]

**Pathogenesis**

It has been discovered that PU etiology is intricate and complicated. The imbalance between aggressive luminal factors (gastric acid and pepsin) and protective mucosal barrier function, however, is a common aspect of its pathophysiology.[21] Several host and environmental variables that increase stomach acid secretion and/or impair mucosal barriers are crucial in initiating gastric ulceration. Smoking, poor diet, excessive alcohol use, emotional stress, and long-term NSAID use are key etiological environmental variables that affect PU development.[22] Additionally, H. pylori infection has been linked to the emergence of chronic gastritis, duodenal ulcers, gastric cancer, and ulcers of the stomach. By invading the stomach epithelium and the lamina propria beneath it with immune cells such neutrophils, macrophages, lymphocytes, and mast cells, H. pylori causes' chronic gastritis.[23] Additionally, H. pylori produces several biomolecules that are harmful to epithelial cells, including vacuolating cytotoxin A, proteases, and ammonia, which is produced to control stomach pH and damages epithelial cells and may result in apoptosis and specific phospholipases.[24] Although it has been demonstrated that biomolecules originating from H. pylori, such as lipopolysaccharide (LPS) and cysteine-rich proteins (Hcp), in particular HcpA, can induce an inflammatory response and an immunological response.[25] Therefore, it is possible to think of chronic gastritis as being caused by the colonisation of stomach bacteria at infection sites. Studies have shown a link between long-term NSAID use and the prevalence of PU in the industrialized world. In fact, chronic NSAID use has been linked to a number of mechanisms that can harm the gastric and duodenal mucosa, including topical epithelial irritation from the drugs, impairment of the barrier functions of the mucosal membrane, suppression of prostaglandin synthesis in the gastric area, decreased blood flow to the gastric mucosa, and interference with the healing of superficial wounds.[26] However, by compromising hemostasis and suppressing growth factors necessary for mucosal defence and repair, acid in the stomach lumen also plays a role in the pathophysiology of NSAID-induced ulcers and bleeding.[27]

**Current Approaches of Treatment of Peptic Ulcer**

Despite the availability of numerous new therapeutic agents, pharmacological therapy of PU continues to advance with the goal of focusing treatment on pain relief, ulcer healing, and in delaying ulcer recurrence. However, a large number of the pharmaceutical treatments for PU are directed either at reducing aggressive factors or at enhancing mucosal defence. Antacids, histamine H2-receptor antagonists, proton pump inhibitors, anticholinergics, and prostaglandins are examples of such medications (Table 1) that are intended to

limit or neutralise gastric acid output.[28]

**Table No.1: Principal Medication Classes Used To Treat Peptic Ulcers [28, 29]**

| Drug Classes | Characteristics | Types |
|---|---|---|
| Antacids | Aid in neutralising stomach acid, lowering duodenal acid absorption, and pepsin activity in addition to binding bile acids | Calcium and magnesium carbonates, aluminum hydroxide and magnesium trisilicate |
| Anti-secretory agents | Reduce gastric acid production, aid in reducing ulcer discomfort and promoting ulcer healing, and prevent the growth and proliferation of H. pylori in the gastric tissues | Histamine H2-receptor antagonist (cimetidine, famotidine, nizatidine and ranitidine), proton pump inhibitors (esomeprazole, lansoprazole, omeprazole, pantoprazole and rabeprazole) |
| Cytoprotective agents | Lessen/eliminate injury to the stomach mucosa (increase mucus and bicarbonate secretion, strengthen gastric mucosal barrier, decrease gastric motility, increase blood flow to gastric mucosa, increase prostaglandins and sulfhydryl biosynthesis, scavenge free radicals, stimulate cell growth and repair and decrease leukotrienes release) | Prostaglandins, fatty acids, sulfhydryl compounds, aluminum-containing antacids, sucralfate, bismuth chelate and liquorice |

## Helicobacter Pylori Eradication

Although the complete eradication of H. pylori is essential for curing related peptic ulcers and preventing relapses, it has become increasingly difficult due to the rising incidence of antibiotic resistance. The first successful treatment was introduced in the 1980s and consisted of a two-week course of bismuth, tetracycline, and metronidazole.[8] A proton pump inhibitor (PPI) and two antibiotics, such as clarithromycin plus amoxicillin or metronidazole, are administered for seven to fourteen days as the conventional first-line treatment.[30] However, during the past 10-15 years, there has been a noticeable drop in the effectiveness of triple therapy due to a rising prevalence of antibiotic resistance, particularly for clarithromycin.[31] Antimicrobial susceptibility tests should be the foundation for the elimination of H. pylori. The selection of first-line treatments should be based on the local prevalence of antibiotic resistance, and clarithromycin-based regimens should be abandoned in areas where the local clarithromycin resistance rate is higher than 15% because susceptibility testing is frequently unavailable in clinical practice.[32] By using high-dose PPI and prolonging the course to 14 days, the rate of elimination can be accelerated. The standard first-line treatment is either a 14-day concomitant therapy for patients who cannot tolerate bismuth (PPI, clarithromycin, amoxicillin,

and metronidazole) or a bismuth-containing quadruple therapy (PPI, a bismuth salt, tetracycline, and metronidazole).[33] Both regimens have eradication rates of more than 90%. If a first-line regimen doesn't work, second-line therapy is recommended, but it shouldn't contain clarithromycin or metronidazole. With eradication rates between 74 to 81%, levofloxacin triple therapy (PPI, amoxicillin, and levofloxacin) for 14 days appears to be an effective treatment.[34] A bismuth quadruple therapy with eradication rates of 77-93% or a high-dose dual-therapy regimen with amoxicillin and a PPI are preferred treatment options if a patient received first-line treatment with a clarithromycin-based regimen.[35] This is because H. pylori rarely develops amoxicillin resistance. Despite comprehensive guidelines for selecting appropriate treatment plans, 5–10% of patients have chronic infection. Subpar compliance or H. pylori resistance to one or more antibiotics are the two most frequent causes of treatment failure after two attempts, in which case susceptibility testing is highly advised. Rifabutin-based triple therapy (PPI, rifabutin, and amoxicillin) for 10 days, with eradication rates of 66-70%, is one of the frequently advised salvage regimens when at least three recommended options have failed.[36]

**NSAID-Associated Ulcer Disease and the Use of PPIs:** There are numerous methods for preventing NSAID- and aspirin-related gastroduodenal ulcers and their side effects. Some of these methods include using NSAIDs in conjunction with PPIs, H2 receptor antagonists, or misoprostol, using COX-2-selective NSAIDs, or combining them with gastroprotective drugs. The most well-liked and efficient preventive medications are PPIs.[37] The greatest defence against peptic ulcer complications is a combination of COX-2-selective NSAIDs and a PPI. H2 receptor antagonists cannot lower the risk of stomach ulcers at standard doses. Misoprostol effectively prevents peptic ulcer complications; however its use for stomach protection is constrained by gastrointestinal discomfort and its abortifacient effects.[38] If the offending drug is stopped, ulcers recover in more than 85% of patients after six to eight weeks of PPI therapy.[39] Repeat endoscopy is necessary for each stomach ulcer in order to determine whether or not it has healed. Checking drug compliance should be done if ulcers don't heal. Although there isn't enough evidence to back it, it's frequently suggested that patients with refractory ulcers double their PPI dosage for another six to eight weeks. After false-negative H. pylori status has been ruled out, uncommon causes of peptic ulcers such as cancer, infections, Crohn's disease, vasculitis, upper abdominal radiation, cocaine usage, and Zollinger-Ellison syndrome should be investigated. PPIs are among the drugs that are prescribed excessively and most frequently worldwide and it has modest and usually treatable side effects include headaches, diarrhoea, constipation, and abdominal discomfort.[40]

**Potassium-Competitive Acid Blockers:** The quest for an alternate therapy is ongoing because ulcer recurrence occurs in up to 13% of individuals who take lansoprazole.[41] Inhibiting H+, K+-ATPase in stomach parietal cells in the last stage of the acid secretory route is what vonoprazan, a potassium-competitive acid blocker, does.[42] Vonoprazan's mechanism of action differs

from PPIs' in that it inhibits the enzyme in a K+ -competitive and reversible way without needing an acidic environment for activation.[43] Vonoprazan also exhibits a quick onset of action and long-lasting reduction of intragastric acidity. When given to Japanese patients on NSAID therapy, vonoprazan at doses of 10 mg and 20 mg was not worse than lansoprazole at preventing the recurrence of peptic ulcers, [44] or those with good tolerance, a similar safety profile, and no newly discovered safety problems who needed aspirin medication for cardiovascular or cerebrovascular protection. Additionally, compared to PPIs, vonoprazan administration for five weeks significantly reduced post-endoscopic submucosal dissection bleeding. It was also demonstrated to be superior than rabeprazole and esomeprazole for scarring fake ulcers, which may contribute to the safety of an endoscopic submucosal dissection.[45]

**Alternative Therapy for Peptic Ulcer:** As old as humans, the practise of using medicinal plants to treat various illnesses is known as phytotherapy.[46] Additionally, there has been an increase in interest in herbal products, particularly those made from medicinal plants, during the past few years. Additionally, medicinal plants are regarded as the main source of potentially new medications due to the emergence of diverse adverse effects from the use of traditional drugs for a variety of disorders. The most important sources of novel medications are plant extracts and their compounds, which have also been demonstrated to have promising outcomes in the treatment of stomach ulcers.[12] Proton pump inhibitors, anticholinergics, antacids, antimicrobials, H2-receptor antagonists, sucralfate, and bismuth are just a few examples of medications that aren't completely effective and can have a variety of negative side effects, including impotence, arrhythmia, hematopoietic changes, hypersensitivity, and gynecomastia.[40] As a result, research into novel pharmacologically active compounds through the screening of various plant extracts resulted in the identification of efficient and secure medications with gastroprotective function. For the treatment of ulcer disease, plants with antioxidant capacity as the primary mechanism are used in particular.[47] Due to their ability to create a variety of secondary metabolites that are renewable and useful, or phytochemical ingredients, medicinal plants offer therapeutic characteristics. These phytochemicals have thus been utilised by many plants as a defence strategy against infections. The emergence of resistant bacteria, on the other hand, has greatly influenced pharmaceutical corporations to alter their approach to the creation of traditional antibiotics and create novel antimicrobial medications derived from medicinal plants.[48] To highlight several medicinal plants with notable antibacterial and antioxidant action against H. pylori and peptic ulcer disease was one of the goals of this review. However, due to the rise of resistant strains, several plants lose their effectiveness against H. pylori. As a result, it is encouraged to isolate different ingredients from the most potent plant extracts.[49] It is crucial to stress that herbal products may contain a variety of bioactive components with both harmful and advantageous effects. Therefore, legislation to control the quality of herbal products is required, as well as

increased training for doctors and patients about herbal therapy. This is especially true for future randomised studies to ascertain the efficacy and safety of many products in treating digestive and other disorders. Finally, the combination of contemporary medicine with Ayurvedic expertise could result in more effective antiulcer medications made from therapeutic herbs that have fewer side effects. **Table 2** lists several medicinal plants with considerable anti-H. pylori activity and advantages for treating gastric ulcer disease.

**Active Principles for Antiulcer Activity**

**Mangifera Indica:** The popular name for Mangifera indica (Anacardiaceae) is "mango tree." Locally, it is known as "man gaai." It is raised all over India. This plant has alkaloids, sterols, saponins, tannins, and flavonoids among its chemical components.[50]

**Azadirachta Indica:** Azadirachta indica (family Meli aceae) is native to India and Bengal and is grown there as well. Both locally and generally, it is referred to as "neem" or "vembu." Nimbidin, phenolic compounds, saponin, and flavonoids are the chemical components of this plant that have been identified. It includes Margosine, a bitter alkaloid. 10–31% of a yellow, bitter fixed oil is found in seeds. Free and volatile fatty acids are present in the oil. The blend of stearic, oleic, and lauric acids that make up the volatile fatty acids is most likely the case.[51]

**Ocimum Sanctum:** The popular name for Ocimum sanctum (Lamiaceae) is "holy basil." Locally, it is known as "tulsi." It flourishes all over India. Tulsi means "the incomparable one" in Sanskrit. Hindus in the Indian subcontinent regard it as one of their sacred herbs. This plant has alkaloids, tannins, saponins, flavonoids, and sterols among its chemical components.[52, 53]

**Annona Squamosa:** Custard apple, or Annona squamosa (Annonaceae), is a common name for this plant. It is grown in gardens across India and is known there as "sitapalam." Alkaloids, flavonoids, saponins, and tannins are some of the chemical components in this plant. Seeds produce oil and resin, and immature fruit, leaves, and seeds all have an acrid principle.[54]

**Mimosa Pudica:** The Fabaceae plant Mimosa pudica is commonly referred to as "touch me not." Locally, it is known as "thottalsinungee." It flourishes throughout the world's subtropical and tropical climates. Flavonoids, quercitin, naringin, saponins, tannins, gums, and mucilage are some of this plant's chemical components.[55]

**Terminalia Chebula:** Common names for Terminalia chebula (Combretaceae) include "myrobalan," "ink-nut," and "gullnut." Locally, it is known as "kaduk-kai." The forests of Northern India, the Central Provinces, and Bengal are home to this tree, which is also prevalent in Madras, Mysore, and the southern regions of the Bombay Presidency. This plant's chemical composition includes lucilage, a brownish yellow colouring substance, 45% tannic acid (also known as tannin), and chebulinic acid, which when cooked in water separates into gallic and tannic acids.[56]

**Ficus Religiosa:** The urticaceae plant Ficus religiosa is usually referred to as "holy fig." Locally, it is known as "arasha-maram." This sacred peepul is a sizable tree that Hindus

have grown throughout India. This plant's bark contains tannin, caoutchouc (cochtone), and wax as chemical components.[57]

**Carica Papaya**: Papaya, or Carica papaya (Caricaceae), is a common name for this plant. Locally, it is known as "papali-pazham." It flourishes throughout the world's subtropical and tropical climates. Papain, chymopapain, pectin, carposide, carpaine, carotenoids, and antheraxanthin are some of the chemical components of this plant.[58]

**Aegle Marmelos:** The plant that primarily grows in India is Aegle marmelos, also referred to as a "bael tree" and a member of the Rutaceae family. Locally, it is known as "vilvam." This plant contains flavonoids, tannins, and saponins as chemical components.[59]

**Moringa Oleifera**: The scientific name for the Moringa oleifera (Moringaceae) plant is "drum-stick, horse radish tree." Locally, it is known as "murungai." It is indigenous to the Western and Sub-Himalayan regions, as well as to Africa, Arabia, Pakistan, India, and Asia Minor. Alkaloids, flavonoids, saponin, tannins, zeatin, quercetin, kaempferom, and terpenoids are some of this plant's chemical components.[60]

**Psidium Guajava:** The Myrtaceae family plant Psidium guajava is used ethnobotanically to treat a variety of gastrointestinal conditions, including peptic ulcer. The plant contains tannins, phenols, triterpenes, flavonoids, saponins, alkaloids, and glycosides, among other phytochemical components.[61]

**Sesbania Grandiflora:** The Fabaceae plant Sesbania grandiflora is usually referred to as "basna." Locally, it is known as "akathi." It is an ornamental plant that can be found from Sri Lanka to the plains of the Western Himalayas. This plant contains triterpenes, tannins, and saponins as chemical components.[62]

**Shorearobusta:** The term "sal tree" refers to the Dipterocarpaceae species Shorearobusta. Locally, it is known as "taloora; kungiliyam." It is widespread in Western Bengal woods and sub-Himalayan regions. Ursolic acid, tri- and tetrahydroxy ursenoic acid, Asiatic acid alpha and beta amyrin, and mangiferonic acid uvaol are among the chemical components of this plant.[63]

**Allium Sativum:** The plant Allium sativum, a member of the Liliaceae family, is also known as "vellapundu" in several parts of the world. It is grown throughout India. The active ingredient in this plant is an acrid volatile oil, which also contains starch, mucilage, albumen, and sugar as its chemical components. Seeds produce fragrant oil. In addition to critical nutrients and complimentary compounds comprising vitamins, the juices, and more specifically its oil contents, are abundant in combinations of salicylic acid, iodine, and sulphur that are organically bonded.[64]

**Aloe Vera:** The term "aloe gel" refers to the Liliaceae family member aloe vera. It is known as "kattalai" locally, and it is common throughout India. This plant contains the chemicals aloin, isobarbaloin, and emodin.[65]

**Dalbergia Sissoo:** Dalbergia sissoo belongs to the family Fabaceae and has beautiful flowers. Also referred to as Indian Rosewood. India is home to three hundred of the twenty-five identified species of Dalbergia.Dalbergia sissoo contains a number of active chemicals in its leaves, including genstein, biochanin A, pratensein, caviunin, quercetin 3-O-rutinoside, caviunin 7- O—D-glucopyranoside, biochanin 7-O-glucoside, kampferol- 3-O-rutinoside, and others.[66]

**Pleurotus Tuber-Regium:**Pleurotus tuber-regium (PT), often known as tiger milk mushrooms or sclerotia generating mushroom, is a tropical edible mushroom that may be found in Nigeria.it has wide biological activities such as antioxidant, antigenotoxic, bio-antimutagenic activities, anti-inflammatory activity.[67]

**Euphorbia Thymifolia:** Euphorbia thymifolia is an Ayurvedic herb widely referred to as the Asthma Plant.it is also calledchoti dudhi in indianregion.phytoconstituents present in extract of euphorbia thymifoliaextract contains alkaloids, tannins, saponins, glycosides, flavonoids, and unsaturated steroids.[68]

**Corydalis Yanhusuo:** One of the plant species that belongs to the genus Corydalis is called the Corydalis yanhusuo. yan hu suo is the Chinese name for the plant known as Corydalis yanhusuo.Common names in English for this plant include yanhusuo, corydalis, and Asian corydalis.A dried tuber of Corydalis yanhusuo W. T. Wang (Papaveraceae), Corydalis yanhusuo has been widely used in China, Japan, and Korea for the treatment of a wide range of symptoms, including gastrointestinal (GI) disorders.[69]

**Echinopserinaceus:** Echinopserinaceus Kit Tan is an endemic wild perennial herb found only in Yemen, Saudi Arabia, and Oman. Due to its wide range of bioactive secondary metabolites, which include sesquiterpenoids, triterpenoids, phytosterols, phenolics, flavonoids, alkaloids, and essential oils, plants in the genus Echinop (Asteraceae) are traditional medicinal plants used to cure a number of GIT diseases.[70]

**Ficus Religiosa:**Ficus religiosa (F. religiosa) Miq. (Moraceae) is a significant traditional medicinal plant that can be found all throughout India, although it is most commonly found close to Indian temples because of their spiritual significance. Carbohydrates, flavonoids, amino acids, steroids, saponins, tannins, and a number of other chemical compounds can be found in the bark of the plant.[71]

**Urtica Simensis:** U. simensis belongs to the Plantae kingdom, Magnoliophyta phylum, Magnoliopsida class, Urticales order,Urticaceae family, and the Urtica genus. The genus Urtica is used to treat a variety of diseases with herbal medicine. Active phytoconstituents involvespolyphenols, cardiac glycosides, saponins, plant sterols.[72]

**Centella Asiatica:** The plant known as Centella asiatica (Linn) has a long history of usage in traditional medicine across a wide range of ancient societies and tribal communities. It is one of the native plants that is believed to exhibit a variety of different physiological properties, and it plays an important role in the traditional medical

practise of the area as a tonic in the treatment of skin illnesses and leprosy.[73]

**Polygonum Minus:** The Polygonum minus plant, also known as kesum in its native Malay language, has an odour that can be described as sweet and pleasant. This plant belongs to the family known as Polygonaceae. P. minus has traditionally been used as a treatment for gastrointestinal issues.[74]

**Parkia Speciosa:** is also known by the common names stink bean and petai. It produces elongated bean pods that are flat and filled with green seeds. The people of Southeast Asia, particularly those in Malaysia and the northernmost parts of India, are fond of these beans. The residents of the area believe that P. speciosa possesses medicinal properties, and it has been reported that it demonstrates hypoglycemic, antibacterial, anticancer, and antioxidant activity.75

**Bryophyllumpinnatum:** A common herb in India and Ceylon is Bryophyllumpinnatum (Lam.) Kurz (family, Crassulacea), also known as Kalanchoe pinnata (Lam.) Pers. The herb's leaves have been recommended for use in treating bruises, wounds, boils, and bug bites in India's traditional medical systems.[76]

**Gynura Procumbens:** G. procumbens (Merr.), which is called "Sambungnyawa" in Malaysia, is found in many countries in South East Asia, such as Indonesia, Malaysia, and Thailand. Traditional medicine uses the plant to treat inflammation, rheumatism, skin diseases caused by viruses, kidney diseases, rashes, fevers, migraines, constipation, and even cancer.[77]

**Toona Ciliate:** Toona ciliata Roemer, a member of the Meliaceae family, is widely spread in the Himalayan tract from the Indus eastwards through Chittagang, Assam, Burma, Chottanagpur, Ganjam, the Western Ghats of Bombay to the Nilgiris and Anamalans, as well as other hills in the Western Peninsula.[78]

**Mentha Arvensis:** The herb Mentha arvensis L. (Lamiaceaea) is native to the western Himalayas and is farmed worldwide as a vegetable. Folk medicine uses Mentha arvensis L. as a carminative, anti-spasmodic, and anti-peptic ulcer agent, as well as to treat indigestion, skin problems, coughs, and colds.[79]

**Garcinia Cambogia:** Garcinia cambogia (Gaertn.) Desr. (Clusiaceae) fruit extract containing the principal organic acid (-)-erythro-Ls-hydroxycitric acid has been traditionally used to cure ulcers, diarrhoea, dysentery, haemorrhoids, tumours, and as an antibacterial agent.[80]

| Sr. No | Medicinal plants | Active constituents | Recent Studies /Dose | Reference |
|---|---|---|---|---|
| 1 | Mangifera indica | Mangiferin | Rats with stomach lesions were given the flower decoction orally at doses of 250, 500, and 1000 mg/kg in a dose-dependent manner. As a result, the extract dramatically decreased the amount of gastric juice and gastric acidity. | 50 |
| 2 | Azadirachta indica | Nimbidin | Rats were protected from pylorus ligation and cold restraint stress-induced stomach ulcers by azadirachta indica leaf extract. | 51 |
| 3 | Ocimum sanctum | Fixed oil eugenol | In rats with ulcers caused by aspirin, indomethacin, alcohol, and stress-induced ulceration, the fixed oil of O. sanctum was administered at doses of 1, 2, and 3 mL/kg intraperitoneally. In a dose-dependent manner, it lowers the ulcer index. | 52 |
| 4 | Annona squamosa | Tannic acid | Rats exposed to ethanol-induced stomach ulcer and pylorus ligation were prevented by the aqueous leaf extract. | 81 |
| 5 | Mimosa pudica | Alkaloid mimosine | Mimosa pudica leaf extracts in ethanol have been found to have antiulcer action in a dose-dependent manner, suggesting that they could be used as a natural antioxidant in the treatment of ulcers. | 82 |
| 6 | Terminalia chebula | Tannins, gallic acid, chebulinic acid, and sorbitol | T. chebulawa methanolic extract was administered orally in doses of 250 and 500 mg/kg. Pylorus ligation-induced ulcer and ethanol-induced gastric ulcer both caused stomach lesions. In comparison to the control, the extract significantly reduced stomach volume, free acidity, and ulcer index. | 83 |
| 7 | Ficus religiosa | Flavonoids Naringenin | Rats were tested at two dose levels of the hydro alcoholic extract of the leaves of F. religiosa (250 and 500 mg/kg, oral) for their ability to prevent stomach ulcers caused by 100% ethanol, aspirin, and pylorus ligation. When compared to the control, the extract dramatically lowers the ulcer index value. | 84 |
| 8 | Carica papaya | Chymopapain and papain | Rats were treated orally with C. papaya aqueous seed extract at doses of 50 and 100 mg/kg to treat ethanol-induced stomach ulcers. The extract defended the stomach mucosa from the effects of ethanol. The amount of gastric juice and stomach acidity were dramatically lowered by C. papaya extract | 85 |
| 9 | Aegle marmelos | Luvangetin | Aspirin combined with pylorus ligation causes stomach ulcers in rats, and aqueous leaf extract must be taken orally for 21 days at a rate of 200mg/kg and 400 mg/kg every day. | 86 |
| 10 | Moringa oleifera | Quercetin, beta sitosterol, and beta carotene | Rats were given oral doses of 125, 250, and 500 mg/kg of the alcoholic leaves extract of M. oleifera to prevent stomach ulcers caused by aspirin, pylorus ligation, ethanol, and cold restraint stress. Acid pepsin and ulcer | 87 |

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| | | | secretion were reduced by the extract. | |
| 11 | Psidium guajava | Quercetin, guaijaverin, and flavonoids | In a study utilising Wistar rats in an ethanol-induced paradigm, higher dosages of the guava leaf's methanol extract (500 mg/kg and 1000 mg/kg) also showed a substantial ulcer-protective action (64.4%) on the stomach wall as compared to the control, which was less than ranitidine (73%) at the same dose. | 88 |
| 12 | Sesbania grandiflora | Tannins and saponins | Rats were given 400 mg/kg of the ethanol leaf extract of S. grandiflora orally to prevent stomach ulcers caused by aspirin, ethanol, and indomethacin. The extract considerably lowered basal stomach acid output and prevented gastric mucosal damage. | 89 |
| 13 | Shorearobusta | Ursolic acid and amyrin | Rats were given oral dosages of 150 and 300 mg/kg of S. robusta extract to treat ethanol- and pylorus-ligation-induced stomach ulcers. When compared to the control, the extract significantly increases the gastroprotective action. | 90 |
| 14 | Allium sativum | Alliin and allicin | Rats were given oral doses of the A. sativum bulb juice extract against cysteamine-induced stomach ulcers of 250 and 500 mg/kg. The extract significantly speeds up the healing of gastric ulcers in rats and inhibits the occurrence of experimentally produced duodenal and gastric ulcers. | 91 |
| 15 | Aloe vera | Barbaloin, isobarbolin, and Saponins | Aloe vera powder and gum acacia were combined, and the resulting solution was given orally to rats at a rate of 200 mg/kg to treat a stomach ulcer brought on by indomethacin. The extract demonstrated strong antiulcer activity that was comparable to the control. | 92 |
| 16 | Dalbergia sissoo | Genstein, biochanin A, pratensein, caviunin | The Dalbergia sissoo plant's leaves were used to treat experimental ulcers. Gastric ligation and ulcers induced by Indomethacin at 250 mg/kg and 500 mg/kg. | 66 |
| 17 | Pleurotus Tuber-Regium: | Sulphar containing amino acids | Peptic ulcer was induced by administration of 1 ml of 80% ethanol orally,pretreatment dose of 500 mg/kg of P. tuber-regium extract was given for 14 days to each group | 67 |
| 18 | Euphorbia Thymifolia | Alkaloids, tannins, saponins, glycosides. | A pharmacological screening of the leaf hydroalcoholic extract of Euphorbia Neriifolia Linn. (Euphorbiaceous) was carried out in order to investigate the plant's potential anti-ulcer effects. All of the experiments were carried out on rats with doses of 100, 200, and 400 mg/kg. | 68 |
| 19 | Corydalis yanhusuo | Benzylisoquinoline alkaloids | To investigate the inhibitory mode against H. pylori, the various extracts of C. yanhusuo at 6.25, 12.5, and 25 mg/mL were used | 69 |
| 20 | Echinopserinaceus | Erinaceolic acid, speranskoside | The evaluation of the gastric ulcer protective activity of the total extract and successive fractions of E. erinaceus, using the in vivo ethanol-inducedulcer in rats model,dose 500mg/kg | 70 |

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| 21 | Ficus religiosa | Flavonoids, tannins, alkaloids | In stress-induced ulcer animal models, the anti-ulcer activity of F. religiosa ethanolic extract (250 and 500 mg/kg) was investigated. and found significant results. | 71 |
| 22 | Urtica simensis | Polyphenols, cardiac glycosides, saponins, plant sterols | The pyloric ligation paradigm, the cold restraint stress model, and the acetic acid-induced ulcer model were utilised in order to validate the in vivo antiulcer potential of U. simensis. E extracts at doses of 100, 200, or 400 mg/kg daily. According to these findings, U. simensis possesses potent antiulcer properties. | 72 |
| 23 | Centella asiatica | Isoprenoids (sesquiterpenes, plant sterols, pentacyclic triterpenoids and saponins) and phenylpropanoid derivatives. | In rats, anti-ulcerogenic effects of methanol extract of C. asiatica leaf were investigated.at dose 100, 200 and 400 mg/kg | 73 |
| 24 | Polygonum minus | Decanal and dodecanal | Anti-ulcer activity of P. minus aqueous leaf extract (PMALE) against ethanol-induced stomach ulcer in rats was investigated at doses of 250 and 500 mg/kg. | 74 |
| 25 | Parkia speciosa | Djenkolic acid, sulphur-containing amino acids. | The gastroprotective effects of Parkia speciosa against ethanol-induced gastric mucosa injury in rats at doses of 50, 100, 200, and 400 mg/kg of ethanolic leaf extract were investigated in this study. | 75 |
| 26 | Bryophyllum pinnatum | Flavonoids, steroids, terpenoids, phenolics | In nine distinct experimental animal models at various doses, a methanolic fraction from an extract of Bryophyliumpinnatum leaves was investigated for anti-ulcer activity, and it showed considerable anti-ulcer efficacy. | 76 |
| 27 | Gynura procumbens: | Flavonoids, saponins, tannins, and terpenoids | In this work, G. procumbens ethanolic leaf extract (GPELE) was utilised to explore its gastroprotective impact in adult Sprague dawley rats at dosages of 50, 100, 200, and 400 mg/kg and good gastroprotective activity was observed. | 77 |
| 28 | Toona ciliata | Quercetin, -sitosterol, gallic acid | Toona ciliata Roemer (heart wood) was investigated for its anti-ulcer effectiveness against aspirin plus pylorous ligation caused stomach ulcer (antisecretory), HCl–ethanol induced ulcer (cytoprotective), and water immersion stress induced ulcer in rats at a dose of 300 mg/kg, p.o. | 78 |
| 29 | Mentha arvensis | Menthone, menthofuran, methyl acetate cineole and limonene | This study examines the antiulcerogenic effects of several Mentha arvensis Linn extracts at a dose of 375 mg/kg on acid, ethanol, and pylorus-ligated ulcer models in rats. | 79 |
| 30 | Garcinia cambogia | (-)-erythro-Ls-hydroxycitric | This study examined the antiulcerogenic activity of Garcinia cambogia extract at a dose of 1 g/kg against Indomethacin-induced gastric ulcers in rats. | 80 |

## Conclusion

It is obvious that medicinal plants are essential in the fight against many ailments. In animal models, a variety of herbal plants and plant extracts exhibit strong antiulcer properties. When compared to reference herbal medications, it exhibits stomach anti-secretory and mucoprotective properties. Even when present in quite high amounts, the extract is not hazardous. According to the findings of our review, the medicinal herbs described above could prevent ulcers using the dose-dependent principle. Numerous botanical compounds have been said to have antiulcer properties. Finally, it should be highlighted that compounds with antiulcer activity, such as flavonoids and tannins, are particularly significant from a therapeutic standpoint. The findings of this study suggest that several medicinal plant extracts have good potentials for application in peptic ulcer treatment.

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