



Review Article

Phytochemical Investigation and Pharmacological Evaluation of *Syzygium cumini* for Anti-Ulcer Activity: A Review

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ABSTRACT

Various studies have shown that many plants possess properties that can help treat ulcers, especially because synthetic drugs can be expensive and not always easily available. One such plant is *Syzygium cumini* L., which is part of the Myrtaceae family and is a large evergreen tree. This tree has several useful chemical components, such as alkaloids, carbohydrates, flavonoids, glycosides, tannins, and phenols. These substances give the plant a wide range of health benefits, including antioxidant, anti-diabetic, antimicrobial, stomach-protecting, anti-inflammatory, antidiarrheal, and liver-protecting effects. The goal of this study was to examine how effective the anti-ulcer properties are in extracts made from the stem of *Syzygium cumini*. Three different extracts were prepared using petroleum ether, acetone, and methanol. A phytochemical analysis was then done to find out what compounds were present. The acetone extract had more phenolic and flavonoid compounds than the methanol and petroleum ether extracts, which may explain why it was more effective. To measure antioxidant activity, the DPPH method was used, and the methanol extract showed the strongest antioxidant ability compared to quercetin, which is a known antioxidant. Ulcers were made in rats using ethanol, and then the animals were treated with the acetone and methanol extracts at doses of 100 and 200 mg/kg, as well as the standard medicine ranitidine. The treatments significantly helped protect the stomach. This was shown by increased gastric pH, lower volume of stomach contents, and fewer ulcers compared to the control group and the standard drug. Also, long-term use of the extracts did not harm the animals, as seen by the stable body weight and normal food intake. These results suggest that these plant extracts could be useful in treating ulcers clinically.

Keywords: *Syzygium cumini* stem, phytoconstituents, phytochemical screening, PUD, antioxidant, antiulcer activity.

INTRODUCTION

Introduction of Peptic Ulcer:

Peptic ulcer disease is a chronic disease characterized by defects in the inner lining of the gastrointestinal (GI) tract. The ulcer penetrates through the layers of the mucosa, extending into the submucosa or muscularis propria.¹ It usually occurs in the stomach and proximal duodenum. It may involve the lower esophagus, distal duodenum, or jejunum. Gastric ulcers and duodenal ulcers are the two most prevalent kinds.

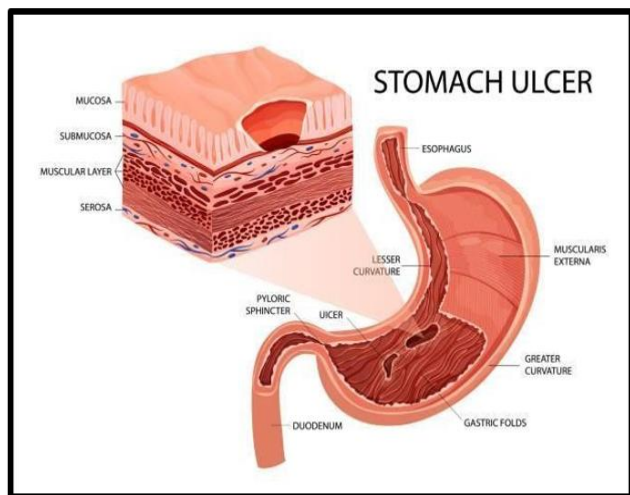


Image 1: Peptic ulcer

Peptic ulcers are caused by an imbalance between aggressive factors like hydrochloric acid (HCL), pepsin, refluxed bile, leukotrienes (LTs), reactive oxygen species (ROS), and defensive factors like the mucus-bicarbonate barrier, prostaglandins (PGs), mucosal blood flow, cell renewal and migration, and nonenzymatic and enzymatic antioxidants. The goal of treating ulcers is to reduce the quantity of acid produced by your stomach, neutralize the acid produced, and protect the wounded area so it can recover.²

TYPES OF PEPTIC ULCER: ³

The peptic ulcers are of two types:

Gastric ulcer: When the ulcers occur in the stomach, they are called gastric ulcers.

Duodenal ulcer: When the ulcer occurs in the duodenum, it is called a duodenal ulcer.

Etiology: Peptic ulcer disease (PUD) has various causes; however, *Helicobacter pylori*-associated PUD and NSAID-associated PUD account for the majority of the disease etiology.⁴

CAUSES OF PEPTIC ULCER DISEASE:

Common

- H. pylori infection
- NSAIDs



- Medications

Rare:

- Zollinger-Ellison syndrome
- Malignancy (gastric/lung cancer, lymphomas)
- Stress (Acute illness, burns, head injury)
- Viral infection
- Vascular insufficiency
- Radiation therapy
- Crohn's disease
- Chemotherapy

Helicobacter Pylori-Associated PUD: *H. pylori* is a gram-negative bacillus that is found within the gastric epithelial cells. This bacterium is responsible for 90% of duodenal ulcers and 70% to 90% of gastric ulcers. *H. pylori* infection is more prevalent among those with lower socioeconomic status and is commonly acquired during childhood.

NSAID-associated PUD: Nonsteroidal anti-inflammatory drug use is the second most common cause of PUD after *H. pylori* infection.^{5,6} The secretion of Prostaglandin normally protects the gastric mucosa. NSAIDs block prostaglandin synthesis by inhibiting the COX-1 enzyme, resulting in decreased gastric mucus and bicarbonate production and a decrease in mucosal blood flow.

Medications: Apart from NSAIDs, corticosteroids, bisphosphonates, potassium chloride, and fluorouracil have been implicated in the etiology of PUD. Smoking also appears to play a role in duodenal ulcers, but the correlation is not linear. Alcohol can irritate the gastric mucosa and induce acidity.

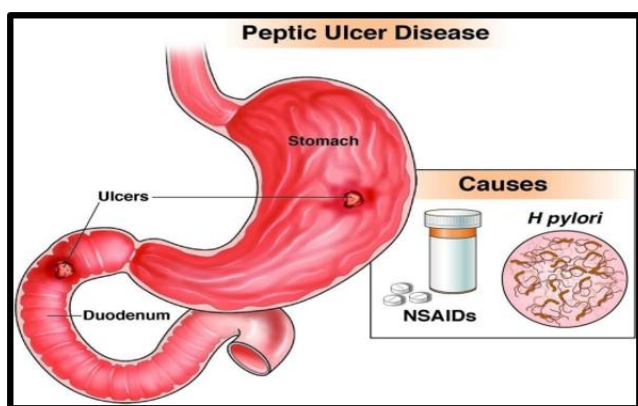


Image 2: Causes of Peptic Ulcer

SYMPTOMS OF PUD:

Common signs and symptoms include:

- Epigastric abdominal pain
- Bloating
- Abdominal fullness
- Nausea and vomiting

- Weight loss/weight gain
- Hematemesis
- Melena

Warning symptoms or alarm symptoms that should prompt urgent referral include:⁷

- Unintentional weight loss
- Progressive dysphagia
- Overt gastrointestinal bleeding
- Iron deficiency anaemia
- Recurrent emesis
- Family history of upper gastrointestinal malignancy

TREATMENT/ MANAGEMENT OF PUD:

Medical Treatment: It includes histamine receptor antagonists, Prostaglandin Analogues, Proton Pump Inhibitors, Cytoprotective agents, antacids, and anticholinergics.

Refractory Disease and Surgical Treatment: Surgical treatment is indicated if the patient is unresponsive to medical treatment, noncompliant, or at high risk of complications. A refractory peptic ulcer is one over 5 mm in diameter that does not heal despite 8-12 weeks of PPI therapy. The common causes are persistent *H. pylori* infection, continued use of NSAIDs, or significant comorbidities that impair ulcer healing, or other conditions like gastrinoma or gastric cancer. If the ulcer persists despite addressing the above risk factors, patients can be candidates for surgical treatment. Surgical options include vagotomy or partial gastrectomy.⁸

Complications: Peptic ulcer disease (PUD), if not diagnosed and treated promptly, can lead to serious complications.

The following complications can occur in PUD:

- Upper gastrointestinal bleeding
- Gastric outlet obstruction
- Perforation
- Penetration
- Gastric cancer

PLANT PROFILE:

Syzygium cumini L. belongs to the family Myrtaceae and is a large evergreen tree indigenous to the Indian subcontinent. However, today these trees are found growing throughout the Asian subcontinent, Eastern Africa, South America, Madagascar and have also naturalized to the warmer regions of the United States of America (in Florida and Hawaii).⁹ The synonyms of *S. cumini* are *Eugenia jambolana*, *Myrtus cumini*, *Syzygium jambolana*, *Eugenia cumini*, etc. It is commonly known as jambolan, black plum, jamun, java plum, Indian blackberry, Portuguese plum, Malabar plum, purple plum, Jamaica plum, and damson plum. For a long

time in the period of recorded history, the tree is known to have grown in the Indian subcontinent, and many other regions of South Asia, such as India, Bangladesh, Burma, Nepal, Pakistan, Sri Lanka, and Indonesia. It was long ago introduced into and became naturalized in Malaysia. In southern Asia, the tree is venerated by Buddhists, and it is commonly planted near Hindu temples because it is considered sacred to Lord Krishna.¹⁰ The plant has also been introduced to many different places where it has been utilized as a fruit producer, as an ornamental and also for its timber. In India, the plant is available throughout the plains from the Himalayas to southern India.

Taxonomical Classification:

Table 1: Taxonomical classification of *Syzygium cumini* L.

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Myrtales
Family	Myrtaceae
Genus	<i>Syzygium</i>
Species	<i>Cumini</i>
Binomial Name	<i>Syzygium cumini</i> L

Morphology/Botany of *Syzygium cumini* L.

The trees reach heights of up to 50 feet and exhibit a large canopy. Young leaves are pale brown, transitioning to darkish brown and scaly as they mature. They are characterized by their elliptic to broadly oblong shape, being smooth, glossy, leathery, and fibrous. The flowering occurs annually, primarily in June and July within the Indian subcontinent. Flowers are small (7–12 mm), white, sessile, with thin, membranous petals, typically grouped in threes and emerging from leaf scars. The fruits grow in clusters of four to twenty, ripening asynchronously. Each fruit varies in shape from round to oblong or ellipsoid, measuring between 1/2 to 2 inches long, containing a centrally placed large seed. Initially green, the fruits mature to light-magenta, eventually dark purple or black when fully ripe, offering a sweet, mildly sour, and astringent flavor along with a purple stain on the tongue.¹¹



Image 3: Jamun Tree



Image 4: Plant Parts

A) Fruit, B) Stem, C) Flowers, D) Seeds, E) Leaves

MEDICINAL PROPERTIES

The leaves are acrid, sweet, digestive, astringent to the bowels, anthelmintic and used for the treatment of sore throat, bronchitis, asthma, thirst, biliousness, dysentery and ulcers. It is also a good blood purifier. The fruit is acrid, sweet, cooling and astringent to the bowels and removes bad smell from the mouth, biliousness, stomachic, astringent, diuretic and antidiabetic.¹² The fruit has a very long history of use for various medicinal purposes and currently has a large market for the treatment of chronic diarrhea and other enteric Disorders.¹³ Vinegar prepared from the juice of the ripe fruit is an agreeable stomachic and carminative and used as a diuretic.¹⁴ Jambolan fruit can be eaten raw and can be made into tarts, sauces and jams. Good quality jambolan juice is excellent for sherbet, syrup and “squash”, an Indian drink. The seed is sweet, astringent to the bowels and good for diabetes. The seed extract is used to treat cold, cough, fever and skin problems such as rashes and the mouth, throat, intestines and genitourinary tract ulcers (infected by *Candida albicans*) by the villagers of Tamil Nadu.¹⁵ The ash of the leaves is used for strengthening the teeth and gums. Juice of tender leaves of this plant, leaves of mango and myrobalan are mixed and administered along with goat's milk and honey to treat dysentery with bloody discharge, whereas juice of tender leaves alone or in combination with carminatives such as cardamom or cinnamon is given in goat's milk to treat diarrhoea in children.¹⁶

USES IN TRADITIONAL MEDICINE:

All parts of the jambolan plant, recognized for its medicinal properties, have a rich history in alternative medicine. Globally, its fruits have been utilized to address issues such as cough, diabetes, dysentery, inflammation, and ringworm.¹⁷ With over a century of classical reviews, the jambolan is particularly noted in India, where ayurvedic medicine acknowledges its effectiveness in treating diabetes mellitus. Traditional practitioners leverage various plant parts to remedy conditions like blisters, cancer, colic, diarrhea, dysentery, piles, pimples, and stomachache.¹⁸ Over the past four decades, numerous folk reports have

highlighted the plant's antidiabetic benefits. Additionally, in Unani medicine, jambolan is employed as a liver tonic, to enrich blood, strengthen teeth and gums, and provide a lotion for ringworm infections on the scalp.¹⁹

VALIDATED PHARMACOLOGICAL PROPERTIES OF JAMUN:

A] Antibacterial and antifungal activity: Essential oils extracted from the Jamun leaves have been reported to exert antibacterial properties against *Bacillus sphaericus*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Salmonella typhimurium*. The 70% ethanol extract of Jamun leaf, bark, pulp and seed showed a potent antimicrobial activity against various Gram-positive bacteria (including *B. subtilis*, *B. cereus* and *S. aureus*) and Gram-negative bacteria (including *S. flexneri*, *P. aeruginosa* and *V. cholera*). The ethanol extract of Jamun seeds was found to inhibit the growth of *E. coli*, *B. subtilis*, and *P. aeruginosa* and *S. aureus*. The aqueous extract of Jamun stem and leaf showed antibacterial activity against all strains of bacteria, including *S. aureus*, *Staphylococcus saprophyticus*, *E. coli*, *P. aeruginosa* and *Proteus vulgaris*. The fruit extract was active against *P. aeruginosa* only and the maximum antifungal activity was recorded for *Penicillium chrysogenum* and *Candida albicans*. The root extract of Jamun was found to be more effective against Gram-positive bacteria than Gram-negative bacteria.^{20,21}

B] Anti-inflammatory effects: Ethanol extract of the bark possesses anti-inflammatory effects in both acute (carrageenan, kaolin– carrageenin, and formaldehyde-induced) and chronic (cotton pellet granuloma) models in rats.²²

C] Gastroprotective effects: Tannins isolated from Jamun were effective against the HCl/ethanol-induced gastric ulceration in rats.²³ Fruits are effective in preventing ulcerations in both normal and streptozotocin- induced diabetic rats.²⁴

D] Hepatoprotective effects: Pulp extract was effective in preventing paracetamol-induced hepatotoxicity in rats.²⁵ Aqueous extract of the leaf and methanolic extract of the seed were effective against CCl₄- induced hepatotoxicity in rats.²⁶

E] Antidiabetic activities: Jamun has been thoroughly investigated for its antidiabetic effects and the seed, pulp and bark have been found to have effective antidiabetic action.^{27,28}

F] Cardioprotective effects: The methanolic extract of the seeds is shown to possess cardioprotective effects in the isoproterenol-induced myocardial infarction model in rats. Oral feeding of the extract (250 mg/kg and 500 mg/kg) for thirty consecutive days resulted in a concentration-dependent protection against the induced myocardial infarction. Administration of isoproterenol caused a significant elevation in the levels of AST, ALT, LDH, and CPK profiles and feeding the seed extract caused a reversal and retained the activity of these enzymes to near normal levels. Of the two doses studied, 250 mg/kg showed a marginal

effect, while the next higher dose of 500 mg/kg was effective. Collectively, all these observations emphasize the usefulness of Jamun as a cardioprotective agent.²⁹

E] Radioprotective effects: Administration of the hydroalcoholic extract of the seed and the dichloromethane extract of the leaf possesses radioprotective effects.³⁰

F] Antineoplastic effects: Jamun fruit extract induced cytotoxic effects against the human cervical cancer cells.³¹

G] Hypolipidemic effect: Feeding ethanolic extract of the seeds to allaxon-induced seed kernel (100 mg/kg body weight) to streptozotocin-induced and flavonoid-enriched extract from seeds to diabetic rats caused a hypolipidemic effect.³²

PHYTOCHEMISTRY OF JAMUN:³³⁻³⁷

Table 2: Chemical constituents present in *Syzygium cumini*

Sr. no:	Parts	Chemical constituents
1.	Leaves	β-sitosterol, betulinic acid, mycaminose, quercetin, myricetin, acylated flavonol glycosides. ^{[5],[6]} The essential oil from the leaves is shown to contain the phytochemicals pinocarveol, α-terpeneol, myrtenol, eucarvone, muurolol, α-myrtanal, cineole, geranyl acetone, α-cadinol, and pinocarvone ⁷
2.	Stem Bark	myricetine, friedelin, friedelan-3-α-ol, betulinic acid, βsitosterol, kaempferol, β-sitosterol-D-glucoside, gallic acid, ellagic acid, gallotannin and ellagitannin ^{6,8}
3.	Flowers	oleanolic acid, ellagic acids, isoquercetin, quercetin, kampferol, and myricetin ⁶
4.	Fruit pulp	anthocyanins, delphinidin, petunidin, malvidin-diglucosides, and these compounds are responsible for their bright purple colour. ^{6,9}
5.	Seeds	Jambosine, gallic acid, ellagic acid, corilagin, 3,6-3,6-hexahydroxydiphenoylglucose, 4,6-hexahydroxydiphenoylglucose, 1-galloylglucose, 3-galloylglucose, quercetin, β-sitoterol

EXTRACTION OF PLANT MATERIAL:

Selection of Solvent: A study of literature survey revealed that the stem of *Syzygium cumini* contain proteins, carbohydrates, fibres, flavonoids like myricetin, Tannins on the basis of literature and the solubility of chemical constituents, solvents selected for extraction were.

A. Pet ether	D. N-Butanol
B. Chloroform	E. Ethanol
C. Ethyl acetate	F. Methanol
D: Acetone	G. Water



Selection of Extraction Method

Based on the literature survey, most of the chemical constituents of the plant extract are heat-stable, and most of the researchers selected Soxhlet extraction. Therefore, the same. Method, i.e., Soxhlet method for extraction, was selected for the present research

PRELIMINARY PHYTOCHEMICAL ANALYSIS: The extracts obtained by successive extraction were subjected to quantitative tests for the identification of various secondary metabolites such as carbohydrates, proteins, tannins, saponins, steroids, flavonoids and glycosides. Phytochemical examinations were carried out for all the extracts as per standard methods.

MECHANISM OF ACTION:

1. **Anti-Secretory and Acid Neutralization:** The agent is noted for its ability to significantly decrease the volume of gastric juice, lower free acidity, and reduce acid-pepsin secretion. Additionally, it raises the gastric fluid pH, thus providing a more alkaline environment in the stomach beneficial for mucosal protection.
2. **Antioxidant and ROS Scavenging:** It addresses oxidative stress by lessening lipid peroxidation (LPO) and replenishing vital endogenous antioxidants, notably reduced glutathione (GSH). This action helps in protecting gastric tissues from oxidative damage.
3. **Mucosal Defense Enhancement:** The therapeutic agent promotes an increase in the production of gastric mucin and mucosal glycoproteins, enhancing the protective barrier of the stomach against harmful hydrogen ions. This fortification of the mucosal layer is crucial for maintaining gastric integrity.
4. **Anti-Inflammatory Pathways:** It exhibits anti-inflammatory effects by inhibiting the activity of pro-inflammatory cytokines and modulating the cyclooxygenase (COX) enzymes. Specifically, it stimulates gastroprotective COX-1 while inhibiting the inflammatory COX-2, leading to reduced inflammation in the gastric tissues.

Overall, the agent displays a multifaceted approach in promoting gastric health through acid neutralization, antioxidant support, mucosal defense, and significant anti-inflammatory actions.³⁸⁻⁴¹

SAFETY AND TOXICITY:

Acute toxicity is involved in the estimation of LD50. As per the reported reference, the safe dose of *Syzygium cumini* L. stem extracts was 2000 mg/kg, carried out as per OECD Guidelines for Acute Toxicity study: Class Method (423). As per the reported reference, studies conducted revealed that the administration of a graded dose of extracts (up to a dose of 2000 mg/kg) of extract did not produce significant changes in behaviours such as alertness, motor activity,

breathing, restlessness, diarrhoea, convulsions, coma, and appearance of the animals. *Syzygium cumini* L. was found to be safe for biological studies, as no lethality was observed up to 2000 mg/kg in rats. Accordingly, the maximum therapeutic experimental dose was calculated as 200 mg/kg.⁴²

CONCLUSION AND FUTURE PERSPECTIVES

This study highlights the significant role of medicinal plants in combating various diseases, particularly their antiulcer activity as demonstrated in animal models. Various herbal extracts exhibit both mucoprotective and gastric anti-secretory effects, proving non-toxic even at high concentrations. The findings indicate that these plants possess the potential to prevent ulcers, primarily attributed to bioactive compounds such as flavonoids and tannins, which are noted for their therapeutic importance. The review underscores that botanical products are a rich source of bioactive molecules with antiulcer potential. Transitioning from traditional use to rigorous scientific inquiry, both in vitro and in vivo studies have substantially examined the efficacy of certain herbal remedies, linking their effectiveness to specific classes of phytochemicals, including alkaloids, tannins, simple phenols, and polyphenols, especially flavonoids. While the literature supports the natural, safe, and effective utilization of these phytochemicals in ulcer prevention and treatment, the lack of extensive clinical studies represents a significant gap. This scarcity limits the validation of preclinical findings and emphasizes the need for more clinical trials to substantiate the promising results. Thus, future research should focus on bridging this gap to enhance the clinical application of these herbal remedies.

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