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Anti-ulcer potential of *Aegle marmelos* (L.): phytochemistry, pharmacological mechanisms, and therapeutic perspectives

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ABSTRACT

Peptic ulcer disease (PUD) is a prevalent gastrointestinal disorder characterized by mucosal damage in the stomach or duodenum due to on imbalance between aggressive factor and mucosal defence mechanisms. Despite the effectiveness of conventional therapies such as proton pump inhibitors and H_2-receptor antagonists, their long-term use is associated with adverse effects and recurrence. This has led to increasing interest in plant-based therapeutics. *Aegle marmelos* (L.), commonly known as bael, is a medicinal plant widely used in traditional systems of medicine for gastrointestinal disorders. It contains diverse bioactive compounds including flavonoids, alkaloids, coumarins, tannins, and phenolic constituents. Experimental studies have demonstrated its significant anti-ulcer activity through multiple mechanisms such as antioxidant, anti-inflammatory, cytoprotective, and anti-secretory effects. Additionally, it enhances mucosal defence, promotes ulcer healing, and exhibits antibacterial activity against helicobacter pylori. This review summarizes current evidence on the phytochemistry, pharmacological mechanisms, and therapeutic potential of *A. marmelos* in the prevention and management of peptic ulcer disease.

Keywords: Peptic ulcer disease; phytochemicals; gastroprotection; oxidative stress; anti-ulcer activity.

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INTRODUCTION

Peptic ulcer disease (PUD) is a major gastrointestinal disorder affecting millions of individuals worldwide and remains a significant clinical concern [1]. It is characterized by mucosal erosion in the stomach or proximal duodenum due to disruption of the balance between aggressive factors and mucosal defence mechanisms [2].

The major etiological factors involved in ulcer formation include gastric acid hypersecretion, pepsin activity, helicobacter pylori infection, prolonged use of non-steroidal anti-inflammatory drugs (NSAIDS), alcohol consumption, smoking, and oxidative stress [3,4]. These factors impair mucosal integrity by reducing protective mechanisms such as mucus secretion, bicarbonate production, prostaglandin synthesis, and mucosal blood flow [5].

Although conventional anti-ulcer drugs such as proton pump inhibitors and H_2-receptor antagonists are widely used, their prolonged use may result in adverse effects, drug interactions, and relapse of ulcers [6]. Therefore, there is increasing interest in identifying safer and more effective alternatives from natural sources'

Aegle marmelos (L.), belonging to the Rutaceae family, is a well-known medicinal plant traditionally used for treating gastrointestinal disorders including ulcers, diarrhoea and dysentery [7]. Its pharmacological activities are attributed to the presence of bioactive phytochemicals such as flavonoids, alkaloids, coumarins, and tannins [8]. Recent studies have

highlighted its potential gastroprotective effects through multiple mechanisms.

This review aims to critically evaluate the phytochemical composition, pharmacological mechanisms, and therapeutic potential of *A. marmelos* in the management of peptic ulcer disease.

Chronic inflammation and oxidative stress play a critical role in the pathogenesis of various diseases, including peptic ulcer disease, by disrupting cellular homeostasis and promoting tissue injury. Similar inflammatory and immune-mediated mechanisms have been extensively reported in other chronic disorders, highlighting the importance of targeting these pathways for therapeutic intervention [11,12].

Etiology and Risk Factors of Peptic Ulcer

Peptic ulcer disease results from multiple interacting factors that disrupt gastric mucosal homeostasis. Infections with helicobacter pylori is one of the primary causes, leading to chronic inflammation and mucosal damage [9]. Additionally prolonged use of NSAIDs inhibits cyclooxygenase enzymes, resulting in decreased prostaglandin synthesis and compromised mucosal protection [10].

Lifestyle factors such as excessive alcohol consumption, tobacco smoking, and psychological stress further contribute to ulcer formation by increasing gastric acid secretion and impairing mucosal defence mechanisms [13]. Advanced age and severe systemic illness are also associated with increased risk of ulcer development [14].

Clinical Manifestations

The clinical presentation of peptic ulcer disease varies depending on the severity and location of the lesions. The most common symptom is epigastric pain, often described as a burning gnawing sensation [15]. Other symptoms include nausea, vomiting, bloating, and loss of appetite [16].

Complications such as gastrointestinal bleeding, perforation, and obstructions may occur in severe cases, leading to symptoms such as hematemesis, melena, and anaemia [17].

Pathophysiology of Peptic Ulcer

The pathogenesis of peptic ulcer involves a complex interplay between aggressive and defensive factors. Excess gastric acid secretion and pepsin activity contribute to mucosal injury, while H. pylori infection induces inflammation and oxidative stress [18].

Reduced synthesis of prostaglandins leads to decreased mucus and bicarbonate secretion, weakening the mucosal barrier [19]. In addition, reactive oxygen species (ROS) and inflammatory mediators further damage the gastric epithelium, impair mucosal blood flow, and inhibit tissue regeneration [20]. These events ultimately result in erosion of the mucosa and ulcer formation. The development of peptic ulcer involves a complex interaction between aggressive factors and impaired mucosal defence mechanisms, leading to mucosal damage and ulcer formation (Figure 1).

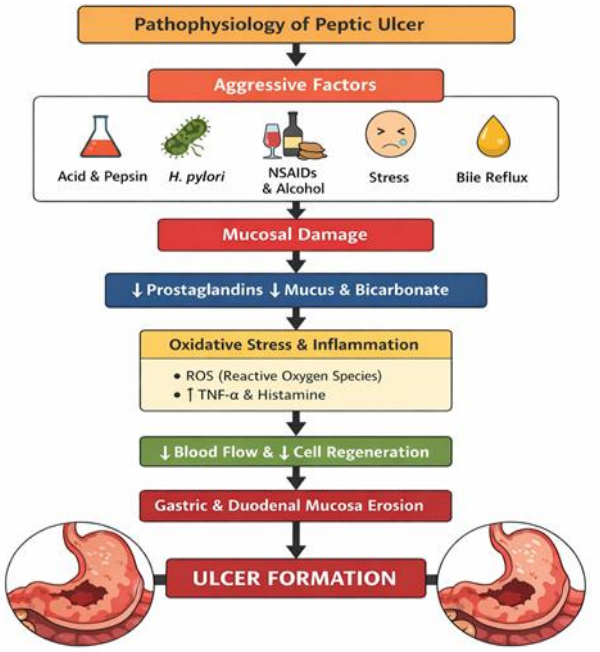

Figure 1: Pathophysiology of Peptic Ulcer Development

Plant Profile of *Aegle marmelos*

Aegle marmelos (L.) correa is a deciduous tree widely distributed in India and Southeast Asia. It is commonly known as bael and has been extensively used in traditional medicine for its therapeutic properties [21].

Various parts of the plant, including leaves, fruits, roots and bark, are used medicinally. The plant exhibits a wide range of pharmacological activities such as antioxidant, anti-inflammatory, anti-microbial, antidiabetic, and gastroprotective effects [22]. The morphological features of *Aegle marmelos,* including its fruit, leaves, and bark, are illustrated in (Figure 2).

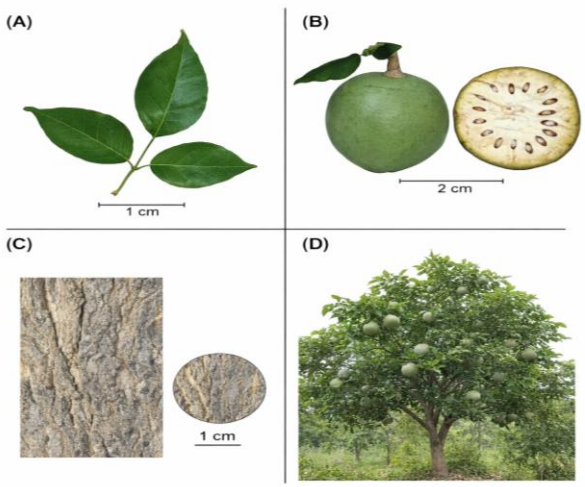

Figure 2: Morphological characteristics of *Aegle marmelos* showing the whole plant, fruit, seeds, leaves, and bark.

Table 1: Major Phytochemical Constituents of *Aegle marmelos* and their Pharmacological activities

S.NO	*Phytochemicals*	*Class*	*Plant part*	*Reported activity*	*Reference*
1	Marmelosin	Coumarin	Fruit	Anti- ulcer, antioxidant	[21]
2	Marmesin	Coumarin	Fruit	Anti-inflammatory, Gastroprotective	[21]
3	Imperatorin	Coumarin	Leaves	Anti-inflammatory, Anti-Microbial	[21]
4	Aegeline	Alkaloid	Leaves	Anti-inflammatory, Anti-diabetic	[22]
5	Skimmianine	Alkaloid	Leaves	Anti-Microbial, Antioxidant	[21]
6	Quercetin	Flavonoid	Leaves, Fruit	Antioxidant, Cytoprotective	[24]
7	Rutin	Flavonoid	Leaves	Anti-Ulcer, Antioxidant	[24]
8	Tannins	Polyphenol	Fruit	Mucosal Protection, Astringent	[22]
9	Phenolic compounds	Phenolics	Whole plant	Antioxidant, Anti-Inflammatory	[24]
10	Carotenoids	Terpenoids	Fruit	Antioxidant	[22]
11	Limonene	Essential oil	Fruit peel	Anti-Microbial	[22]
12	Cineole	Essential oil	Leaves	Anti- inflammatory	[22]
13	Lupeol	Triterpenoid	Bark	Anti-Ulcer, Anti-Inflammatory	[23]
14	Beta-sitosterol	Sterol	Leaves	Anti-Inflammatory	[23]
15	Glycosides	Glycosides	Leaves	Cytoprotective	[22]

Phytochemical Constituents

Phytochemical studies have identified numerous bioactive compounds in *Aegle marmelos.* Major constituents include coumarins (marmelosin, marmesin, imperatorin), alkaloids, (aegeline, skimmianine), flavonoids (quercetin, rutin), tannins, and phenolic compound [23].

These compounds play a significant role in the pharmacological activities of the plant. Flavonoids and phenolic compounds exhibit strong ant-oxidant activity, while alkaloids and coumarins contribute to anti-microbial and anti-inflammatory effects [24]. The major phytochemical constituents of *Aegle marmelos* and their pharmacological activities are summarized in (Table 1).

Mechanisms of Ant-Ulcer Activity

Anti-secretary Activity: *A. marmelos* reduces gastric acid and pepsin secretion while increasing gastric pH, thereby protecting the mucosal lining [25].

Antioxidant Activity: The presence of flavonoids and phenolic compounds enables the plant to scavenge free radicals and inhibit lipid peroxidation, reducing oxidative stress [26]. Oxidative stress plays a crucial role in mucosal damage through the generation of reactive oxygen species, leading to lipid peroxidation and cellular injury. Experimental studies on herbal extracts have demonstrated significant restoration of antioxidant enzymes, supporting their protective role against oxidative tissue damage [34].

Anti- Inflammatory Activity: The plant inhibits inflammatory mediators such as prostaglandins and cytokines, thereby reducing mucosal inflammation [27].

Cytoprotective Effect: It enhances mucus and bicarbonate secretion, strengthening the gastric mucosal barrier [28].

Mucosal Healing: The plant promotes epithelial regeneration and improves mucosal blood flow, facilitating ulcer healing [29].

Anti-Helicobacter pylori Activity

Bioactive compounds present in *A. marmelos* exhibit antibacterial activity against H. pylori, reducing infection-induced ulcer formation [30]. In addition to its gastroprotective effects, *Aegle marmelos* has demonstrated a wide spectrum of pharmacological activities, including anti-inflammatory, antimicrobial, and potential anticancer properties, indicating its broad therapeutic applicability [31]. Furthermore, the plant has shown promising antidiabetic activity, suggesting its potential role in managing metabolic disorders that may indirectly influence gastrointestinal health [32]. Recent advances in novel drug delivery systems for plant-derived anti-inflammatory agents have demonstrated improved bioavailability and targeted therapeutic efficacy, which may further enhance the clinical applicability of herbal medicines in the management of peptic ulcer disease [33].

CONCLUSION

Peptic ulcer disease remains a significant health concern due to its high prevalence and recurrence. Although conventional therapies are effective, their long-term use is associated with limitations. *Aegle marmelos* demonstrate significant anti-ulcer potential due to its rich phytochemical composition and multiple pharmacological mechanisms, including antioxidant, anti-inflammatory cytoprotective, and anti-secretory effects. Experimental evidence supports its traditional use in gastrointestinal disorder. However, further studies, particularly clinical trials, are required to establish its safety, efficacy, and standardization for therapeutic use. Future research should focus isolation of active compounds and development of novel phytopharmaceutical formulation.

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