

Phytoconstituent based interventions for gastric ulcer management: A review of efficacy and mechanisms



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Abstract

Peptic ulcer is a very common disease of the gastrointestinal system that can cause serious health problems like internal bleeding, perforations and obstruction. In India, it affects about 5 to 10% of the population, particularly men in their fifties. Main cause of peptic ulcers is *H. Pylori* infection and inappropriate use of non-steroidal anti-inflammatory medications. Traditional treatment is becoming ineffective due to the development of resistance in *H.Pylori*. Newer strategies can focus on natural products that are derived from plants. Phytochemicals like alkaloids, flavonoids and saponins present in extracts can promote healing of ulcers by their anti-microbial activity, free radical scavenging effects and anti-inflammatory property.

Keywords: Gastric Ulcer, *H. Pylori*, Phytochemicals

1. Introduction

Gastric ulcer or peptic ulcer disease (PUD) is a very common condition that causes damage to the lining of gastrointestinal tract, resulting in sores larger than 3–5 mm, deep enough to reach the sub mucosa. PUD is estimated to occur in about 5–10% of the population at any time during their lifetime. The disease can cause serious problems, namely, internal bleeding, perforation into the wall of stomach or duodenum, penetration into nearby organs, and obstruction of gastrointestinal tract (1). Approximately 1 in 9 individuals in India, particularly men aged in their fifties, may develop peptic ulcer. About 5,00,00 new patients are diagnosed with peptic ulcer annually (2). Major reasons of PUD are *Helicobacter pylori* (*H. pylori*) infection and inappropriate usage of non-steroidal anti-inflammatory drugs (NSAIDs) (2). Research also indicates that prevalence of PUD is more common in South India compared to North India (2-4).

Time taken off from work, the cost of hospitalization and drugs and requirement of surgeries used to treat PUD is a significant burden on the society leading to significant out-of-pocket expenditures and loss in productivity (5).

2. Pathophysiology and treatment of peptic ulcer disease

Peptic ulcers develop on the walls of the stomach or the duodenum because of an imbalance between aggressive and defensive factors that are present in the gastrointestinal tract. This condition is influenced by the presence of gastric acid, pepsin, and bile which are considered aggressive factors.

In addition *H. pylori* infection also contributes to disruption of the mucosal barrier. The protective mechanisms in the stomach and duodenum include the presence of mucous, prostaglandins and rich supply of blood. Under normal conditions, a healthy gastro-duodenal mucosa maintains an equilibrium between both aggressive and defensive factors. However, when aggressive factors overpower the defensive mechanisms—due to increased acid secretion, *H. pylori* infection, or use of NSAID's—ulcers can develop. The condition may also be exacerbated by other factors such as stress or smoking (6-7).

3. Management of peptic ulcer

Before the discovery of *H. pylori*, it was known that peptic ulcers recurred. The patients were maintained on drugs that suppress acid production like proton pump inhibitors, prostaglandin analogues, and histamine-2 receptor antagonists. These drugs were designed to defend the mucosal lining from damage resulting from gastric acid and promote the healing of existing damage. They formed the first line of treatment and are still prescribed for the treatment of PUD (8). These medications have several side effects and studies indicate the development of antibiotic resistance in *H. pylori*. New strategies for managing the challenging *H. Pylori* infection are the need of the hour. Natural products, from medicinal plants, are being explored as potential sources because of their diverse chemical structures (9,10). They can serve as complementary treatments alongside conventional therapies for PUD. Extensive research conducted on various plant-derived compounds has shown protective effects against gastric ulcers through multiple mechanisms.

4. Phytoconstituents with anti-ulcer activity

Several medicinal plants containing phytochemicals that belong to flavonoids, alkaloids, saponins, terpenes, and polyphenols can help in mitigating the symptoms of peptic ulcers. Many of these phytochemicals have antibacterial activity against *H. pylori*. Table 1 gives a list of a few phytochemicals that have a protective role in the management of PUD.

Table 1. Few Phytochemicals with protective effect in peptic ulcer disease

S. No.	Phytochemical	Class	Source	Effect	Ref
1	Eucalyptol or 1,8-Cineole	Monoterpene	Eucalyptus oil	Gastroprotective and healing effect	7
2	Limonene	Monoterpene	<i>Artemisia dracunculus L</i> (tarragon)	Cytoprotective action	7
3	Curcumin	Alkaloid	<i>Curcuma longa</i> (turmeric)	Reduction the pro inflammatory cytokines TNF- α , IL-1 β , IL-6, IL-8	9
4	Berberine	Alkaloid	<i>Berberis L.</i> (Barberry)	Increased expression of eNOS mRNA and inhibited expression of iNOS mRNA.	14
5	Quercetin	Polyphenols	<i>Momordica cymbalaria Hook f</i> (Little Wild Gourd)	Decreased gastric acidity through anti-apoptotic mechanisms	11,12
6	Kaempferol-3-O-rutinoside	Polyphenols	<i>Foeniculum vulgare</i> (Fennel)	Reduction in the activity of lipid peroxidation and amplification of the antioxidant activity	15,17
7	Glycyrrhizin	Sapponins	<i>Glycyrrhiza glabra</i> (Licorice)	Protective role against acid and pepsin secretions by covering the site of lesion and promoting the mucous secretion	18

4.1. Flavonoids (Quercetin, Rutin)

Flavonoids are natural anti-inflammatory and antioxidant agents. This property helps in reducing inflammation in the gastric mucosa and provides protection against oxidative stress. The antioxidant effect is helpful in scavenging free radicals, contributing to the healing of damaged tissues and inhibiting the progression of ulcers. Studies have proposed the role of flavonoids from *Momordica cymbalaria* in promoting wound healing in the gastric mucosa. Aqueous extract of *M. cymbalaria* fruits significantly decreases total acidity and ulcer index in experimental models. The presence of flavonoids, particularly quercetin in *M. cymbalaria*, is believed to contribute to ulcer healing. This effect can be ascribed to reduction in oxidative stress which in turn enhances mucosal protection. Histopathological analyses show a marked reduction in gastric lesions and improvements in mucosal integrity in groups treated with aqueous extract of *M. cymbalaria*. The results endorse the traditional use of this plant in the management of PUD (11,12).

4.2. Alkaloids (Berberine)

It has been known for many years that many alkaloids possess antimicrobial and anti-inflammatory effects. Berberine mitigates the inflammatory processes associated with PUD. It enhances the formation of nitric oxide and improves the endothelial function. Nitric oxide is responsible for causing vasodilation and reducing the ulcerogenic risk factors (13). Berberine can decrease the expression of inducible nitric oxide synthase (iNOS), which is responsible for increased production of free radicals that cause cytotoxicity. By decreasing iNOS expression, berberine helps maintain a more stable NO level, which is beneficial for the protection of gastric mucosa and healing of gastric ulcers (14).

4.3. Polyphenols (Tannins, Catechins)

Polyphenols, including tannins and catechins, are responsible for scavenging free radicals and reducing oxidative stress in the gastrointestinal tract. Polyphenols can inhibit inflammatory cytokines, contributing to the prevention and treatment of ulcers. *Zingiber officinale*, *Foeniculum vulgare* and *Curcuma longa* are some plants that are rich in polyphenols and can be potentially used in the mitigation of PUD due to their anti-inflammatory, antioxidant, antimicrobial, and cytoprotective properties (15,16). The ulcer preventive effects of ginger, fennel and turmeric have been investigated in various studies, particularly focusing on their efficacy in experimental models in rats. This activity in part has been attributed to the reduction in the activity of lipid peroxidation and amplification of the antioxidant activity (17).

4.4. Saponins (Glycyrrhizin)

Several studies have been carried out highlighting the role of licorice in the treatment of PUD. A double-blind study involving 40 patients with confirmed peptic ulcers evaluated the efficacy of a quadruple therapy regimen consisting of amoxicillin, metronidazole, omeprazole, and bismuth sub nitrate compared to a similar regimen where licorice replaced bismuth. After one month of treatment, endoscopic evaluations showed that the treatment with licorice extract was similar to that seen with bismuth. Thus, it was concluded that licorice offers a low-cost and well tolerated treatment with minimal side-effects (18). The healing effect of licorice was because of the rise in concentration of prostaglandins in the digestive tract that led to promotion of secretion of mucus in the stomach.

5. Conclusion

The causes of peptic ulcer disease (PUD) are diverse and complex, requiring targeted therapies to effectively manage and reduce complications. PUD being one of the most prevalent gastrointestinal disorder, poses a significant global health concern due to its high morbidity and mortality rates. Preclinical studies have substantiated the anti-ulcer potential of phytochemicals present in plants and their extracts, however, to confirm the efficacy and safety of their use in patients' further clinical trials are necessary. Standardization of plant based medications and the regulations governing them is a big lacuna for ensuring the quality, safety, and effectiveness of these products. Development of guidelines for stringent quality control and ensuring good manufacturing processes will enhance confidence of the consumer in using herbal remedies. Additionally, incorporating plant-based products into dietary practices or as supplements may complement traditional treatment approaches for PUD.

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