INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Gastric Ulcers: Understanding Pathophysiology and Advances in Treatment

Gaurav Sawant*, Prashant Kumbhar, Dr. Sanganna Burli, Vikas Dhole

Department of Pharmacology, Ashokrao Mane College of Pharmacy, Peth Vadgaon, Kolhapur, Maharashtra, 416112, India.

ARTICLE INFO

Published: 07 Mar. 2025
Keywords:
Gastric ulcer; gastric cancer; Helicobacter pylori; herbal remedies; bioactive Phytochemicals; traditional healing systems.
DOI:
10.5281/zenodo.14986279

ABSTRACT

Despite many advancements in our understanding of the pathophysiology and management of peptic ulcers, they continue to pose a serious public health concern. The availability of conventional therapies has not been sufficient to protect the gastrointestinal mucosa, leading to the exploration of alternative remedies, such as medicinal plants. The goal of this review is to present a thorough analysis of the most popular herbal remedies for peptic ulcer prevention and therapy, together with their available data and possible modes of action. According to the research, using herbal remedies to treat peptic ulcers may be a safe and efficient solution.

INTRODUCTION

A prevalent kind of peptic ulcer disease, gastric ulcers impact millions of people annually and pose a serious threat to world health. Characterized by the erosion of the gastric mucosa, these ulcers can lead to severe complications, including gastrointestinal bleeding, perforation, and even malignancy if left untreated. The prevalence of gastric ulcers has prompted extensive research into their underlying causes, pathophysiology, and effective treatment modalities. [1,2] The incidence of gastric ulcers has fluctuated over the years due to many factors, along with the widespread use of non-steroidal anti-inflammatory drugs (NSAIDs), the prevalence of Helicobacter pyloriinfection, and changes in dietary habits. While the overall occurrence of gastric ulcers has reduced in some regions, certain populations continue to experience high rates, particularly among the elderly and those with chronic health conditions [1] The economic burden of gastric ulcers, due to healthcare costs and loss of productivity, underscores the necessity for effective management strategies [2]. The aggressive and defensive forces interact intricately in the multifaceted pathophysiology of stomach ulcers.

***Corresponding Author:** Gaurav Sawant
Address: Department of Pharmacology, Ashokrao Mane College of Pharmacy, Peth Vadgaon, Kolhapur, Maharashtra, 416112, India.
Email ✉: gauravsawant31072002@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

NSAID use, alcohol intake, smoking, H. pylori infection, and the release of stomach acid and pepsin are all considered aggressive factors. These elements have the potential to upset the delicate equilibrium of the gastric mucosal defense mechanisms, which include the secretion of mucus and bicarbonate, sufficient blood flow, and the turnover of epithelial cells. [3]. H. pylori has been known as a major contributor to gastric ulcer formation, with its tendency to induce chronic inflammation and alter the gastric microenvironment. Recent research has unveiled the role of genetic and epigenetic factors in modulating individual responses to H. pyloriinfection, leading to variations in susceptibility to gastric ulcers [4]. Additionally, emerging studies highlight the influence of the gut microbiome in maintaining gastric mucosal health and how its dysregulation can contribute to ulcer development [5]. Treatment strategies for gastric ulcers have evolved significantly over the years. Traditionally, management has concentrated on the eradication of H. pylori and the lowering of stomach acid secretion through the use of proton pump inhibitors (PPIs). However, recent advances in pharmacotherapy have introduced novel agents and combination therapies aimed at enhancing mucosal protection and healing. Research into the use of probiotics, mucosal protectants, and alternative anti-inflammatory agents has gained traction, offering new avenues for ulcer management [6,7].Moreover, understanding the molecular mechanisms underlying ulcer pathogenesis has paved the way for innovative therapeutic approaches. Targeting specific inflammatory pathways and utilizing personalized medicine based on genetic profiling may lead to more effective and tailored treatment options for patients suffering from gastric ulcers [8,9]

Epidemiology of gastric ulcer: According to epidemiological research, the frequency of PU is correlated with the frequency of H. pylori infections, as well as the use of NSAIDs and ASAs and the elderly population. Prior to a notable decrease in its frequency in the last decades of the 20th century, PUD had a substantial impact on morbidity as well as mortality(10). This significant change in the complaint frequency pattern was attributed to environmental variables, such as modernization. It was also hypothesized that industrialized nations' improved cleanliness and general health could have led to lower rates of H. pylori transmission and nonage infections(11). Two other significant results were also mentioned as having an impact on the decline in PUD rates: the development of strong and efficient acid suppressants as well as the prevention and treatment of H. pylori infections. But by the turn of the century, the increased use of NSAIDs had led to a decrease in duodenal ulcers (caused by an infection associated to H. pylori) and an increase in stomach ulcers (caused by NSAIDs). However, PU is still widespread around the world, particularly in impoverished nations where the prevalence of H pylori infection is high. According to reports, there is a significant likelihood that children may contract H. pylori prior to the age of 10, and in poor nations, Before the age of 50, the frequency peaks at over 80(12). In any event, only a less percentage of H. pylori infection incidents result in ulcers; instead, a greater percentage of patients have non-specific uneasiness, gastritis otherwise stomach pain.

Pathophysiology:

Gastric ulcers, a common form of peptic ulcer disease, occur when there is a breakdown of the gastric mucosa, leading to localized lesions that penetrate through the epithelial lining. A complicated interaction between defensive and aggressive forces influencing the stomach mucosa is part of the pathogenesis of gastric ulcers. Understanding these mechanisms is crucial for effective diagnosis and treatment.

1. Imbalance Between Aggressive and Defensive Factors

An imbalance between aggressive forces that harm the stomach mucosa and defensive factors that shield it leads to the development of gastric ulcers.

1.1 Aggressive Factors

Gastric Acid and Pepsin: Excessive production of gastric acid as well as the digestive enzyme pepsin can erode the gastric lining, contributing to ulcer formation. High levels of gastric acid are linked to various factors, including diet, stress, and certain medications [13,14].

Helicobacter pylori Infection: One of the main causes of gastric ulcers is the gram-negative bacterium H. pylori, which colonizes the stomach epithelium. Its presence leads to chronic inflammation (chronic gastritis) and mucosal damage through the production of toxins and the induction of an inflammatory response [15,16].

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): NSAID's suppresses cyclooxygenase (COX) enzymes, which decreases the production of protective prostaglandins. This reduction leads to diminished mucus and bicarbonate secretion, weakening the gastric mucosal barrier and increasing susceptibility to ulcers [17,13].

Alcohol and Smoking: Both alcohol consumption and smoking have been shown to irritate the gastric mucosa, stimulate gastric acid secretion, and impair mucosal defenses, further predisposing individuals to ulcer development [18,17].

1.2 Defensive Factor:

Mucosal Barrier: The gastric mucosa is protected with a thick mucus layer that traps bicarbonate ions, providing a buffering capacity against gastric acid. The integrity of this barrier is critical in preventing ulceration [13]

Mucosal Blood Flow: Adequate blood supply is essential for the maintenance and repair of the gastric mucosa. Reduced mucosal blood flow can impair healing and contribute to ulcer formation [19].

Epithelial Cell Turnover: The rapid turnover of epithelial cells is vital for repairing any damage to the gastric lining. Disruption of this process can hinder healing and promote ulcer persistence [20].

2. Pathophysiological Mechanisms

Several interrelated mechanisms help explain the pathogenesis of stomach ulcers:

2.1 Mucosal Injury

The stomach epithelium is directly harmed by aggressive substances such pepsin, H. pylori, and too much acid. This mucosal injury compromises the integrity of the protective barrier, allowing gastric acid to penetrate deeper into the tissue [15].

2.2 Inflammatory Response

Immune cells (macrophages and neutrophils) are drawn to the stomach mucosa as part of an inflammatory response brought on by H. pylori and other irritants. Pro-inflammatory cytokines are released as a result of this inflammation. (such as IL-1, TNF-α and IL-6), which exacerbate mucosal injury and contribute to ulcer development [21]

2.3 Inhibition of Prostaglandin Synthesis

NSAIDs block the COX-1 and COX-2 enzymes, which lowers prostaglandin synthesis. The loss of prostaglandins compromises mucosal defenses by reducing mucus as well as bicarbonate secretion and also diminishing blood flow to the mucus membrane, thereby increasing the risk of ulcer formation [18].

2.4 Acid Secretion Dysregulation

Certain conditions, such as Zollinger-Ellison syndrome, can lead to excessive gastric acid production. This hypersecretion overwhelms the protective mechanisms of the gastric mucosa, resulting in ulcer formation [22].

3. Role of Helicobacter pylori

H. pylori play's a crucial role in the pathophysiology of gastric ulcers:

3.1 Urease Production:

Urease, an enzyme produced by H. pylori, neutralizes gastric acid nearby and enables the bacteria to thrive in the acidic environment by

converting urea to ammonia. This action creates a localized alkaline environment that promotes further mucosal damage [15].

3.2 Cytotoxins:

Certain strains of H. pylori produce cytotoxins, such as cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (VacA), which directly harm epithelial cells and aid in the formation of ulcers and chronic inflammation [23].

3.3 Chronic Inflammation:

Chronic gastritis brought on by the ongoing H. pylori infection causes atrophy of the stomach mucosa and raises the risk of stomach ulcers [15].

4. Clinical Manifestations

The clinical manifestations of gastric ulcers can vary, but common symptoms include Epigastric Pain Typically described as burning or gnawing pain, often relieved by food or antacids [21]. Nausea and Vomiting: These symptoms may occur due to gastric irritation or obstruction [23]. Gastrointestinal Bleeding Ulcers can lead to hemorrhage, presenting as melena (black, tarry stools) otherwise hematemesis (vomiting blood) [13]. Weight Losscan result from pain-induced decreased appetite [24].

5. Complications

Gastric ulcers can lead to several complications, including:

Perforation: Ulcers can erode through the gastric wall, leading to peritonitis, which requires immediate surgical intervention [22].

Gastric Outlet Obstruction: Scarring and edema from ulcers can obstruct the pylorus, causing vomiting and weight loss [15]

The etiology of gastric ulcers involves a complicated interaction between protective mechanisms that preserve mucosal integrity and aggressive factors such excess acid and H. pylori infection. Understanding these processes is crucial for effective management and treatment strategies for gastric ulcers.

Current treatments: Lesions in the stomach filling are a hallmark of gastric ulcers, a subtype of peptic ulcer disease (PUD), which is caused by an imbalance between the stomach's defensive mechanisms and aggressive forces including pepsin and stomach acid. Treatment strategies concentrate on relieving symptoms, promoting ulcer mending, precluding rush, and avoiding complications like bleeding or perforation. Current remedial approaches range from pharmacological operation to life revision and, in some cases, surgical intervention.

1. Pharmacological Management

A. Proton Pump Inhibitors (PPIs): PPIs are the foundation of gastric ulcer therapy. They inhibit the H/ K ATPase enzyme found in the stomach's parietal cells, thereby significantly lowering gastric acid stashing. This reduction in acidity promotes ulcer mending and prevents rush. Common PPIs include:

- Omeprazole
- Esomeprazole
- Lansoprazole
- Pantoprazole

These specifics are generally specified for 4- 8 weeks, depending on the inflexibility of the ulcer. [25,26]

B. H2 Receptor Antagonists (H2RAs)

Histamine-2 receptors on stomach parietal cells are blocked by H2 receptor antagonists, reducing acid stashing. While less potent than PPIs, H2RAs remain useful in certain clinical situations, similar as for cases intolerant to PPIs. Common H2RAs include:

- Ranitidine (however now less used due to implicit carcinogenic contaminations)
- Famotidine
- Cimetidine

Efficacy:

H2RAs are effective but generally have a slower and lower mending rate compared to PPIs. They're frequently reserved for mild cases or for cases with

contraindications to PPI remedy. Studies have shown that PPIs are superior to H2 receptor antagonists in promoting mending, with a advanced rate of ulcer resolution and symptom relief. [26]

C. Antacids and Sucralfate

Antacids neutralize gastric acid and give characteristic relief by softening the acid present in the stomach. Sucralfate, a cytoprotective agent, works by forming a defensive hedge over the ulcer point, precluding farther damage from acid and promoting mending. Sucralfate is particularly useful in cases who neednon-acid-suppressing treatments or as peripheral remedy.

Efficacy:

Antacids are less effective in long- term ulcer operation but are useful for short- term symptom relief. Sucralfate has been shown to accelerate mending and ameliorate mucosal protection, although it's frequently used in combination with acid- reducing agents.[27]

D. Prostaglandin Analogues

Prostaglandins cover the stomach mucosa by adding mucus as well as bicarbonate stashing and maintaining mucosal blood inflow. Misoprostol is a synthetic prostaglandin E1 analogue that has been used to help NSAID- convinced ulcers in high- threat cases.

Efficacy:

Misoprostol is effective in reducing ulcer conformation, especially in cases taking habitual NSAID use. still, side goods similar as diarrhea and abdominal cramps limit its wide use.[28]

Helicobacter pylori Eradication

Antibiotic Therapy

A considerable majority of stomach ulcers are related with Helicobacter pylori (H. pylori) infection. Eliminating H. pylori is essential for ulcer recovery and recurrence prevention. Typical treatment plans consist of:

Triple Therapy: PPI + clarithromycin+ amoxicillin or metronidazole

Quadruple Therapy: PPI + bismuth subsalicylate + tetracycline + metronidazole

Efficacy:

When H. pylori is successfully eradicated, ulcer recurrence is significantly decreased. Meta-analyses have shown high healing rates in H. pylori-positive ulcers treated with combination therapy.[29]

3. Management of NSAID-Induced Ulcers

Gastric ulcers are frequently brought on by long-term usage of nonsteroidal anti-inflammatory drugs (NSAIDs). In these patients, the first step is often discontinuing the offending NSAID, if possible, and initiating PPI therapy.

A. COX-2 Selective Inhibitors

For patients who require ongoing NSAID therapy, the use of COX-2 selective inhibitors (e.g., celecoxib) may reduce the risk of gastric ulcers, as they are less aggressive on the gastric lining compared to traditional NSAIDs.

Efficacy:

COX-2 inhibitors, combined with PPIs or misoprostol, can be effective in reducing ulcer risk, though cardiovascular risks associated with COX-2 inhibitors must be considered. [28,30]

4. Dietary and Lifestyle Modifications

In addition to pharmacological therapy, certain lifestyle changes are recommended to support ulcer healing:

- Smoking cessation: Smoking impairs mucosal healing and increases ulcer recurrence.
- Limiting alcohol intake: Alcohol irritates the gastric mucosa and can worsen symptoms.
- Dietary modifications: Patients are often advised to avoid spicy foods, caffeine, and other irritants.
- Stress management: Psychological stress has been implicated in ulcer formation, and stress-reducing techniques (e.g., yoga, meditation) may aid in the healing process. [31, 32]

Challenges in current treatments and for herbal alternatives:

Herbal alternatives: Gastric ulcers, resulting from the erosion of the stomach's mucosal lining, continue to be a significant global health issue. While conventional treatments like proton pump inhibitors (PPIs) and H2 receptor antagonists are highly effective, they may present long-term side effects such as nutrient malabsorption, osteoporosis, and increased susceptibility to infections. Interest in herbal substitutes has increased in recent years, as they offer a more holistic approach with potentially fewer side effects. Various medicinal plants have been studied for their anti-ulcerogenic properties due to their ability to reduce gastric acid secretion, enhance mucosal protection, or combat Helicobacter pylori infections. This review discusses the most researched herbal alternatives in gastric ulcer management.

Glycyrrhiza glabra (Licorice):

Table no: 1 (characteristics of Glycyrrhiza glabra (Licorice)

Medicinal Plant	Glycyrrhiza glabra (Licorice)
Bioactive Compound	Glycyrrhizin and carbenoxolone
Mechanisms of Action	Enhances mucus and bicarbonate secretion, inhibits acid secretion, and displays anti-inflammatory properties. Licorice also shows antimicrobial action against H. pylori, a common cause of peptic ulcers [33]
Efficacy	Clinical studies have shown that licorice extracts can reduce ulcer size and improve mucosal healing in experimental models and human trials.[34]

Cinnamomum zeylanicum (Cinnamon)

Table no :2 (characteristics of Cinnamomum zeylanicum (Cinnamon)

Medicinal Plant	Cinnamomum zeylanicum (Cinnamon)
Active Compounds	Cinnamaldehyde and eugenol
Mechanisms of Action	Cinnamon has been found to enhance mucus secretion, inhibit acid production, and promote gastric mucosal healing. Its anti-inflammatory and antioxidant properties help reduce gastric damage caused by oxidative stress.[35]
Efficacy	Studies have demonstrated that cinnamon extract significantly reduces gastric ulceration and promotes faster healing in animal models.[36]

Zingiber officinale (Ginger)

Table no :3 (characteristics of Zingiber officinale (Ginger)

Medicinal Plant	Zingiber officinale (Ginger)
Active Compounds	Gingerol and shogaol
Mechanisms of Action	Ginger acts by enhancing mucosal defense, increasing gastric mucus secretion, and reducing inflammatory mediators like prostaglandins. Additionally, it inhibits H. pylori growth, contributing to its ulcer-preventive effects.[37]
Efficacy	Animal studies have shown that ginger extract significantly reduces ulcer formation and speeds up healing in aspirin-induced ulcer models.[38]

Aloe vera

Table no :4 (characteristics of Aloe vera)

Medicinal Plant	Aloe vera
Active Compounds	Polysaccharides, vitamins, and enzymes
Mechanisms of Action	Aloe vera increases the production of gastric mucus and inhibits gastric acid secretion. Its anti-inflammatory and antioxidant properties further help reduce gastric mucosal

	injury. Aloe vera also has antimicrobial activity against H. pylori.[39]
Efficacy	Several studies have indicated that aloe vera gel promotes ulcer healing, decreases ulcer area, and enhances mucosal regeneration.[40]

Curcuma longa (Turmeric)

Table no :5 (characteristics of Curcuma longa (Turmeric)

Medicinal Plant	Curcuma longa (Turmeric)
Active Compounds	Curcumin
Mechanisms of Action	Curcumin reduces oxidative stress and inflammation in the gastric mucosa, inhibits gastric acid secretion, and enhances the production of gastric mucus. It also exhibits anti-H. pylori activity, which is crucial in ulcer management.[41]
Efficacy	Animal and human studies have shown that curcumin is effective in reducing ulcer size, accelerating healing, and preventing recurrence in chronic ulcer models.[42]

Matricaria chamomilla (Chamomile)

Table no :6 (characteristics of Matricaria chamomilla (Chamomile)

Medicinal Plant	Matricaria chamomilla (Chamomile)
Active Compounds	Flavonoids, including apigenin and quercetin
Mechanisms of Action	Chamomile inhibits gastric acid secretion, reduces inflammation, and increase the secretion of gastric mucus, neutralize free radicals that cause oxidative damage to the gastric lining.[43]
Efficacy	chamomile extract can significantly reduce the size and number of gastric ulcers in animal models, promoting faster healing.[44]

Allium sativum (Garlic)

Table no :7 (characteristics of Garlic (Allium sativum)

Medicinal Plant	Garlic (Allium sativum)
Active Compounds	Sulfur-containing compounds, particularly allicin, which have anti-inflammatory and antimicrobial effects
Mechanisms of Action	Protection of Gastric Mucosa: Enhances mucus production and reduces gastric acid secretion. - Antimicrobial Action: Combats H. pylori infection, linked to ulcer formation.[45]
Efficacy	-Studies demonstrate gastroprotective effects in various ulcer models, including: - Reduction in ulcer severity. - Promotion of healing.[46]

Phytochemicals responsible for anti-ulcer activity: Peptic ulcers, characterized by lesions in the gastric or duodenal lining, arise due to an imbalance between protective and damaging factors in the gastrointestinal system. In recent years, there has been growing interest in natural compounds and plant-derived chemicals, known as phytochemicals, as therapeutic agents for managing gastric ulcers. Phytochemicals offer a range of protective mechanisms, such as reducing gastric acid secretion, enhancing mucosal defense, exerting anti-inflammatory effects, and combating Helicobacter pylori (H. pylori) infections. This review explores key phytochemicals with anti-ulcer properties, their mechanisms of action, and their potential as therapeutic agents in ulcer treatment.

Table no :7 This table summarizes the key phytochemical classes, their mechanisms of action, and notable compounds with anti-ulcer properties.

Phytochemical Class	Description	Mechanism of action	Key Compounds
Flavonoids	Polyphenolic compounds with antioxidant, anti-inflammatory, and cytoprotective properties.	Increase mucus and bicarbonate secretion -Inhibit gastric acid secretion Display anti-H. pylori activity -Neutralize free radicals	**Quercetin**: Found in fruits, vegetables; enhances mucus production. [47] **Kaempferol**: Present in tea, broccoli; promotes mucosal defense.[48] **Naringenin**: Found in citrus; enhances gastric mucus secretion.[49]
Alkaloids	Nitrogen-containing compounds known for analgesic, anti-inflammatory and antimicrobial properties.	-Inhibit gastric acid secretion -Reduce inflammation -Promote tissue regeneration	-**Berberine**: From Berberis; potent anti-inflammatory, promotes mucus secretion.[50] -**Solanine**: From Solanum; reduces gastric acid secretion. [51] - **Palmatine**: From Coptis chinensis; enhances mucosal protection.[52]
Tannins	Polyphenolic compounds with astringent properties, capable of forming complexes with proteins.	- Form protective layers over ulcerated tissues - Promote tissue healing - Reduce gastric acid secretion	- **Catechin**: In green tea; increases mucus secretion.[53] - **Ellagic acid**: In pomegranates; reduces oxidative stress.[54] - **Proanthocyanidins**: In grape seeds; potent antioxidant.[55]
Saponins	Glycoside compounds with surfactant properties, enhancing mucosal defense.	- Increase mucus and bicarbonate secretion - Inhibit gastric acid secretion - Promote cell regeneration	- **Ginsenosides**: In Panax ginseng; increases mucus production.[56] - **Dioscin**: In Dioscorea; promotes healing of gastric ulcers.[57]
Terpenoids	Diverse organic compounds derived from isoprene units with gastroprotective effects.	- Reduce gastric acid secretion - Increase gastric mucus production - Possess anti-H. pylori properties	- **Carvacrol**: In oregano, thyme; strong antioxidant.[58] - **Limonene**: In citrus peels; reduces gastric acid secretion.[59] - **Menthol**: In peppermint; soothes gastrointestinal tract.[60]

Polyphenols	Compounds with strong antioxidant properties found in various plant sources.	- Neutralize free radicals - Inhibit gastric acid secretion - Display anti-H. pylori activity	- **Resveratrol**: In grapes, red wine; potent antioxidant.[61] - **EGCG**: In green tea; enhances gastric mucosal defense.[62]

Phytochemicals such as flavonoids, alkaloids, tannins, saponins, terpenoids, and polyphenols offer a natural and promising approach to managing gastric ulcers. These compounds exert gastroprotective effects through a variety of mechanisms, including enhancing mucosal defense, reducing gastric acid secretion, combating oxidative

CONCLUSION: In recent years, significant progress has been made in understanding the pathophysiology and treatment of gastric ulcers. Advances in molecular biology have clarified the crucial role of Helicobacter pylori infection, gastric acid hypersecretion, and impaired mucosal defense mechanisms in ulcer development. In response, treatment approaches have evolved beyond acid suppression alone to include targeted therapies against H. pylori, cytoprotective agents, and novel anti-inflammatory drugs. The standard treatment involving proton pump inhibitors (PPIs) and antibiotics has proven effective in the eradication of H. pylori and healing of ulcers. However, concerns over antibiotic resistance, long-term side effects of PPIs, and relapse have fueled research into alternative therapies. New treatment strategies, such as potassium-competitive acid blockers (P-CABs), improved antibiotics, and therapies targeting the inflammatory pathways, offer promising results. Additionally, there has been renewed interest in natural and herbal remedies, with a focus on phytochemicals that possess anti-ulcer properties. Despite these advances, challenges remain in achieving long-term ulcer remission, managing drug resistance, and preventing recurrence, particularly in patients with underlying conditions like NSAID use. Future directions in gastric ulcer research include the development of more personalized medicine approaches, leveraging biomarkers to predict treatment outcomes, and further exploration of the gut microbiome's role in gastric mucosal protection.

REFRENCES

1. Machicado, Jorge D., Julia B. Greer, and Dhiraj Yadav. "Epidemiology of gastrointestinal diseases." Geriatric Gastroenterology (2020): 1-21.
2. Pohl, Calvin S., Julia E. Medland, and Adam J. Moeser. "Early-life stress origins of gastrointestinal disease: animal models, intestinal pathophysiology, and translational implications." American Journal of Physiology-Gastrointestinal and Liver Physiology 309.12 (2015): G927-G941.
3. Malfertheiner, Peter, et al. "Management of Helicobacter pylori infection—the Maastricht V/Florence consensus report." Gut 66.1 (2017): 6-30.
4. Kamada, T., Satoh, K., Itoh, T., Ito, M., Iwamoto, J., Okimoto, T., ... & Koike, K. (2021). Evidence-based clinical practice guidelines for peptic ulcer disease 2020. Journal of gastroenterology, 56, 303-322.
5. Bäckhed, F., Roswall, J., Peng, Y., Feng, Q., Jia, H., Kovatcheva-Datchary, P., ... & Wang, J. (2015). Dynamics and stabilization of the human gut microbiome during the first year of life. Cell host & microbe, 17(5), 690-703.
6. Uchiyama, I., Mihara, M., Nishide, H., Chiba, H., & Kato, M. (2019). MBGD update 2018:

microbial genome database based on hierarchical orthology relations covering closely related and distantly related comparisons. Nucleic acids research, 47(D1), D382-D389.

7. Zullo, A. (2020). The current role of dual therapy for treatment of Helicobacter pylori: back to the future?. European Journal of Gastroenterology & Hepatology, 32(5), 555-556.
8. González-González, C. S., Gómez del Río, N., Toledo-Delgado, P. A., & García-Peñalvo, F. J. (2021). Active game-based solutions for the treatment of childhood obesity. Sensors, 21(4), 1266.
9. Fitzgerald, P. C., Bitarafan, V., Omari, T., Cock, C., Jones, K. L., Horowitz, M., &Feinle-Bisset, C. (2024). The herbal preparation, STW5-II, reduces proximal gastric tone and stimulates antral pressures in healthy humans. Neurogastroenterology& Motility, e14755.
10. Malfertheiner, P.; Chan, F.K.; McColl, K.E. Peptic ulcer disease. Lancet 2009, 374, 1449–1461.
11. Graham, D.Y. Changing patterns of peptic ulcer, gastrooesophageal reflux disease and Helicobacter pylori: A unifying hypothesis. Eur. J. Gastroen. Hepat. 2003, 15, 571–572
12. Pounder, R.; Ng, D. The prevalence of Helicobacter pylori infection in different countries. Aliment.Pharm. Therap. 1995, 9, 33–39.
13. Lanas, Angel, and Francis KL Chan. "Peptic ulcer disease." The Lancet 390, no. 10094 (2017): 613-624.
14. Chen, C. M., Huang, W. T., Chang, L. J., Hsu, C. C., & Hsu, Y. H. (2021). Peptic ulcer disease is associated with increased risk of chronic urticaria independent of Helicobacter pylori infection: a population-based cohort study. American Journal of Clinical Dermatology, 22, 129-137.
15. Malfertheiner, P., Mégraud, F., O'Morain, C. A., Gisbert, J. P., Kuipers, E. J., Axon, A. T., ... & El-Omar, E. M. (2017). Management of Helicobacter pylori infection—the Maastricht V/Florence consensus report. Gut, 66(1), 6-30.
16. Suerbaum, S., & Michetti, P. (2002). Helicobacter pylori infection. New England Journal of Medicine, 347(15), 1175-1186.
17. Dudar, G. K., D'Andrea, L. D., Di Stasi, R., Pedone, C., & Wallace, J. L. (2008). A vascular endothelial growth factor mimetic accelerates gastric ulcer healing in an iNOS-dependent manner. American Journal of Physiology-Gastrointestinal and Liver Physiology, 295(2), G374-G381
18. Cleynen, I., Boucher, G., Jostins, L., Schumm, L. P., Zeissig, S., Ahmad, T., ... & Lees, C. W. (2016). Inherited determinants of Crohn's disease and ulcerative colitis phenotypes: a genetic association study. The Lancet, 387(10014), 156-167.
19. Sakaguchi, T., Sugihara, T., Ohnita, K., Fukuda, D., Honda, T., Ogihara, R., ... &Isomoto, H. (2022). Pyloric incompetence associated with helicobactor pylori infection and correlated to the severity of atrophic gastritis. Diagnostics, 12(3), 57
20. Díaz del Arco, C., Alvarez Sanchez, A., & Fernandez Acenero, M. J. (2016). Non-gastric Gastrointestinal Xanthomas: Case Series and Literature Review. Journal of Gastrointestinal & Liver Diseases, 25(3).
21. Fitzgerald, A. J., et al. (2019). Inflammatory responses in gastric ulceration. World Journal of Gastroenterology, 25(34), 5095-5110. DOI: 10.3748/wjg.v25.i34.5095
22. Klein, M., et al. (2019). Zollinger-Ellison syndrome: A rare cause of gastric ulcers. The American Journal of Medicine, 132(9), 1109-1114. DOI: 10.1016/j.amjmed.2019.04.006.
23. Huang, J. Q., et al. (2017). Role of Helicobacter pylori in the pathogenesis of

gastric ulcers. Clinical Gastroenterology and Hepatology, 15(1), 32-39. DOI: 10.1016/j.cgh.2016.06.021.
24. Vann, S., et al. (2016). The effects of alcohol and smoking on gastric ulcer formation. Gastroenterology Clinics of North America, 45(4), 715-726. DOI: 10.1016/j.gtc.2016.07.
25. Vakil, N. et al., "Proton pump inhibitors in the treatment of gastric ulcers," Gastroenterology Journal, 2018.
26. Howden, C. W., "Comparative efficacy of PPIs vs H2RAs in gastric ulcer healing," Clinical Gastroenterology and Hepatology, 2019.
27. Thorsen, S., et al., "Efficacy of sucralfate in treating gastric ulcers," Annals of Internal Medicine, 2020.
28. Simon, L. S., "Misoprostol for the prevention of NSAID-induced gastric ulcers," Journal of Rheumatology, 2019.
29. Chey, W. D., "Helicobacter pylori eradication therapy for gastric ulcers," The New England Journal of Medicine, 2017.
30. Lanza, F. L., et al., "COX-2 inhibitors and gastric ulcer prevention," American Journal of Gastroenterology, 2021.
31. Katz, P. O., "Lifestyle changes and gastric ulcer healing," Digestive Diseases and Sciences, 2018.
32. Freedberg, D. E., "Impact of alcohol and smoking on gastric ulcers," Journal of Clinical Gastroenterology, 2020.
33. Rafatullah, S., et al., "Evaluation of the gastric anti-ulcerogenic effect of glycyrrhizin," Journal of Ethnopharmacology, 2017.
34. Ali, T., "The gastroprotective effect of glycyrrhizin in gastric ulcers," Phytomedicine, 2020.
35. Khan, A., et al., "Gastroprotective effects of Cinnamomum zeylanicum in experimental models of gastric ulcers," Journal of Pharmacy and Pharmacology, 2019.
36. Jamal, P., "Antioxidant and anti-ulcer activity of cinnamon extract in gastric ulcer models," International Journal of Molecular Sciences, 2020.
37. Nanjundaiah, S. M., et al., "Gastroprotective properties of Zingiber officinale," Phytotherapy Research, 2018.
38. Prakash, P., "Antiulcer and antioxidant properties of ginger in experimental gastric ulcer models," Journal of Gastroenterology and Hepatology, 2021.
39. Tanaka, M., et al., "Aloe vera and its anti-ulcer properties: A review," Journal of Traditional Medicine, 2019.
40. Mishra, S., et al., "Antiulcer activity of Aloe vera gel in ethanol-induced gastric ulcers," Journal of Ethnopharmacology, 2020.
41. Mahady, G. B., "Curcumin and its potential role in gastric ulcer healing," Phytomedicine, 2018.
42. Azuine, M. A., "The gastroprotective effects of curcumin in animal models of gastric ulcer," Journal of Gastrointestinal Research, 2020.
43. Gupta, R. P., et al., "The gastroprotective effect of Matricaria chamomilla in experimental gastric ulcers," Phytotherapy Research, 2019.
44. Ahmed, M., "Anti-inflammatory and gastroprotective activity of chamomile," Journal of Medicinal Plants Research, 2020.
45. Sadiq, A., et al., "Protective effects of garlic against gastric ulcers," Journal of Medicinal Foods, 2019.
46. Azeem, W., "The role of garlic in gastric ulcer management: An experimental study," International Journal of Food Sciences and Nutrition, 2021.
47. Di Carlo, G., et al., "Flavonoids as gastroprotective agents," Journal of Ethnopharmacology, 2019.
48. Kamboj, A., et al., "Kaempferol as a potential anti-ulcer agent," Phytomedicine, 2020.

49. Borrelli, F., et al., "Naringenin and gastric mucosal protection," Phytotherapy Research, 2018.
50. Cui, H. S., et al., "Berberine: An anti-ulcer phytochemical," World Journal of Gastroenterology, 2020.
51. Yoshikawa, T., et al., "Solanine as a gastroprotective agent," Journal of Gastrointestinal Pharmacology and Therapeutics, 2021.
52. Sun, H. Y., et al., "Palmatine and its gastroprotective effects," Phytomedicine, 2019.
53. Shimada, T., et al., "Catechins as anti-ulcer agents," Phytotherapy Research, 2019.
54. Singh, R., et al., "Ellagic acid in the treatment of gastric ulcers," Journal of Medicinal Food, 2020.
55. Santos, A. M., et al., "Proanthocyanidins and their role in gastric ulcer management," World Journal of Gastroenterology, 2021.
56. Liu, Y., et al., "Ginsenosides in the prevention and treatment of gastric ulcers," Journal of Ethnopharmacology, 2018.
57. Kang, J. X., et al., "Dioscin's role in gastric mucosal protection," Phytotherapy Research, 2020.
58. Ulusoy, H. G., et al., "Carvacrol and its anti-ulcer potential," Journal of Food Biochemistry, 2019.
59. De Oliveira, A. P., et al., "Gastroprotective activity of limonene," Phytomedicine, 2020.
60. Gunawardhana, C., et al., "Menthol's role in gastroprotection," Phytotherapy Research, 2021.
61. Bertelli, A. A., et al., "Resveratrol and its potential gastroprotective effects," Gastroenterology Research and Practice, 2020.
62. Singh, B. N., et al., "Gastroprotective effects of EGCG," Journal of Clinical Gastroenterology, 2019

HOW TO CITE: Gaurav Sawant*, Prashant Kumbhar, Dr. Sanganna Burli, Vikas Dhole, Gastric Ulcers: Understanding Pathophysiology and Advances in Treatment, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 3, 304-315. https://doi.org/10.5281/zenodo.14986279