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Anti-ulcer Potential of *Centella asiatica* in Peptic/ Gastric Ulcer: Molecular Mechanisms and Pharmacological Evidence

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Abstract

A gastric ulcer is defined as an imbalance between defensive factors and aggressive factors. Defensive factors such as the mucus-bicarbonate barrier, prostaglandins, and sufficient blood flow through the mucosa, as well as aggressive factors such as gastric acid secretion, *Helicobacter pylori* infection, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), oxidative stress, and inflammation, all lead to the development of a common gastrointestinal disorder called a gastric ulcer. The drugs used for controlling the level of acid secretion and decreasing the symptoms of gastric ulceration include PPI, H 2 receptor antagonists, antacids, and PCABs, which also have adverse effects, drug interactions, recurrence of ulcers, and antimicrobial resistance when used over the long-term. These issues need to be solved for safer use. This review provides us with a comprehensive overview with a detailed account of gastric ulcer, as well as furnishing us with the information concerning the anti-ulcer properties of herbal remedies, with the focus on *C. asiatica*. The plant's gastro-protective properties are attributed to phytochemical constituents, including the bioactive pentacyclic triterpenoids asiaticoside, madecassoside, asiatic acid, and madecassic acid. Several experimental studies suggest that *C. asiatica* inhibits the secretion of gastric acid, enhances the integrity of the gastric mucosal barrier, promotes angiogenesis and epithelial regeneration, and has anti-inflammatory and antioxidative effects. Such results, together with other experimental evidence, suggest that *C. asiatica* can be used as a potential therapeutic agent for gastric ulcers; however, further studies are necessary to validate its potential use in therapeutic applications such as standardisation, pharmacokinetics, safety and clinical efficacy.

Major Findings: There is evidence from experiments showing that *C. asiatica* exhibits significant gastro-protective and anti-ulcer activity through inhibition of gastric acid secretion, enhancement of the gastric mucosal barrier, promotion of tissue regeneration, and antioxidant and anti-inflammatory effects.

Keywords: *Centella asiatica,* Gastric Ulcers, Gastroprotection, *Helicobacter pylori*, Non-steroidal Anti-inflammatory Drugs, Oxidative Stress

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1. Introduction

The principal symptoms of gastric ulcers are gastrointestinal bleeding, dyspepsia, and gastric discomfort. It is a significant form of gastrointestinal complication characterised by erosion of the mucosal and submucosal layers of the stomach[1]. *H. pylori* infection and long-term use of NSAIDs are responsible for this condition. These factors weaken the mucosal defence by decreasing prostaglandin synthesis and impairing epithelial healing. Patients usually present with dyspeptic symptoms, epigastric discomfort, and bleeding. Treatment depends on reducing acidity[2]. In addition to acid- and NSAID-related damage, several previous studies also show that changes in the level of stomach microorganisms contribute to the development

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of gastric ulcers. Because probiotics can suppress *H. pylori*, improve the gastric mucosal barrier, regulate inflammatory responses, and reduce oxidative stress, they have attracted interest as adjuvant treatments[3]. Recent studies indicate that gastric ulcer healing involves angiogenesis and epithelial restitution[4]. The development of herbal substitutes with multi-targeted gastroprotective and mucosal-healing properties is necessary due to the side effects of conventional antiulcer drugs and the complex pathophysiology of peptic ulcer disease[5]. As a non-vitamin, non-mineral nutraceutical rich in bioactive triterpenoids, *C. asiatica* is known to reduce swelling and Reactive Oxygen Species (ROS) and to promote the formation of a new mucous layer or the recovery of the mucous layer, suggesting its potential role in the prevention and treatment of stomach ulcers[6]. *C. asiatica* is also known as Gotu Kola. Its leaves are rich in vitamins A, C, and certain B-complex vitamins; minerals (calcium, magnesium, iron, potassium); proteins; and amino acids (these nutrients promote ulcer prevention by supporting tissue healing and general gastrointestinal health)[7].

The lifetime risk of developing ulcer disease ranges from 5% to 10%; it's a global health concern that is very important to focus on. Generally, improved hygienic and sanitary conditions, together with the efficient use and treatment of NSAIDs, have reduced the incidence of ulcers worldwide. Compared to stomach ulcers, duodenal ulcers are very common. Men are more likely than women to develop duodenal ulcers[8]. The number of people with gastric ulcers increased from approximately 6.43 million in 1990 to approximately 8.09 million in 2019, according to the 2020 evidence-based guidelines on the condition. However, after adjusting for age, the prevalence rate per 100,000 decreased (from 143.4 to 99.4)[9]. The 2022 study estimates that 8.09 million persons worldwide had Peptic Ulcer Disease (PUD)[10].

2. Risk Factors

Helicobacter pylori infection, long-term NSAID use, smoking, and family history of ulcer disease are the major risk factors for peptic or stomach ulcers, as shown in Figure 1, according to the NCBI "Peptic Ulcer Disease" chapter. These elements substantially increase the risk of ulcer development and impair the stomach mucosal defence mechanism[8]. NSAIDs can damage the protective mucus lining or epithelial layer of the upper, middle, and lower gastrointestinal tract, which results in bleeding that causes melaena or iron deficiency. NSAID use can result in bleeding due to iron deficiency and damage to the small intestine's mucosa, especially when combined with PPI[11]. A study published in Gut and Liver states that *H. pylori* infection and long-term use of NSAIDs also play a vital role in causing ulcers[12]. The 2023 study published in Translational Paediatrics found that following *H. pylori* removal therapy in adolescents, ulcer problems and upper-GI bleeding were more likely if the patient had multiple ulcers, a history of ulcers or bleeding, a preference for spicy or stimulating foods, or an increased level of inflammatory markers (e.g., IL-6, TNF-α)[13].

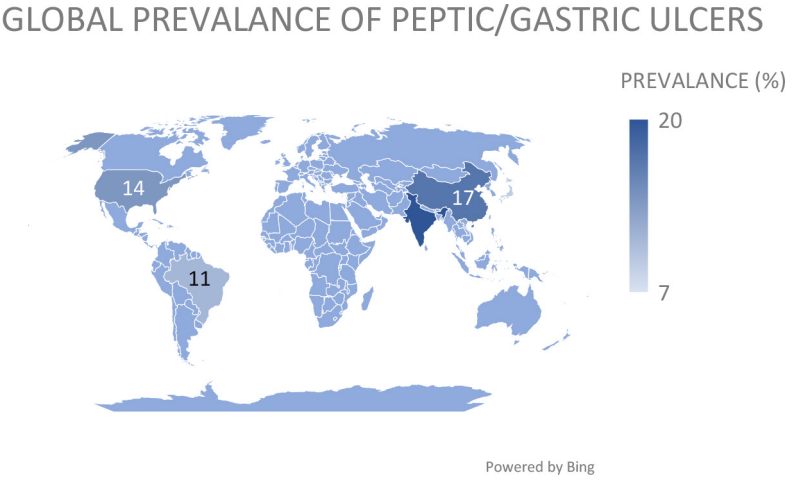


Figure 1. Global prevalence of Peptic/Gastric ulcers.

3. Pathophysiology Overview

3.1 NSAIDs and *H. pylori*

The pathway by which NSAIDs cause the development of peptic ulcers is by preventing cyclooxygenase-1 and 2, which leads to a reduction in the synthesis of prostaglandin, as shown in Figure 2. Prostaglandins normally protect the epithelial lining of the stomach mucosa by balancing mucus and bicarbonate secretion, maintaining adequate epithelial blood flow, promoting epithelial repair, and regulating acid, thereby making the mucosa more vulnerable to mucosal injury, erosion, and ulcer formation[14]. *H. pylori* causes acid imbalance, mucosal layer damage, and chronic inflammation; these factors increase ulcer formation and bleeding[15]. NSAIDs enhance erosion and ulcer development by weakening the gastrointestinal mucosal barrier[16].

3.2 Oxidative Stress and Inflammation

In cases of high ROS production, lipid peroxidation, cytokine-mediated inflammation, and immune reactions are key contributors to the pathophysiology of gastric ulcers. This leads to decreased mucosal integrity, antioxidant defences, mucosal blood flow, and tissue repair, resulting in damage, erosion, and ulcers of the epithelium[17]. Oxidative stress and inflammation are the causes of aspirin-induced gastric ulcer. The excessive release of inflammatory mediators and the initiation of lipid peroxidation, neutrophil inflammation, and cytokine imbalance are triggered by high levels of reactive oxygen species, leading to progressive mucosal damage and the formation of ulcers[18]. Reactive oxygen species generated by oxidative stress and inflammation increase the gastric mucosa's susceptibility to acid-induced ulceration and damage[19].

3.3 Impaired mucosal barrier and microcirculation

The pathophysiology of gastric ulcers is also influenced by impaired mucosal barrier function and microcirculation, as shown in Figure 3. This is because mucosal blood flow decreases. As a result, oxygen and nutrient delivery are impaired, which weakens epithelial integrity, disrupts tight junctions, and increases bicarbonate and mucus secretion, thereby increasing the gastric mucosa's susceptibility to acid, ischemia, and ulcerative injury[20]. There is decreased mucus and bicarbonate secretion, impaired epithelial tight junctions, reduced mucosal blood flow, and delayed tissue repair. Additionally, when the gastric mucosal barrier is impaired, microcirculatory changes increase the gastric lining's vulnerability to acid-induced injury[21]. When mucus becomes weak and prostaglandin-mediated repair mechanisms are impaired, gastric and duodenal mucosal barrier defences and microcirculation are compromised, leading to ulcer development and delayed healing[22]. Table 1 contains all the pathophysiological factors of ulcers, along with their mechanisms and activities.

4. Emerging Trends

The increase in primary antibiotic resistance among *H. pylori* worldwide (2013–2023), with significant

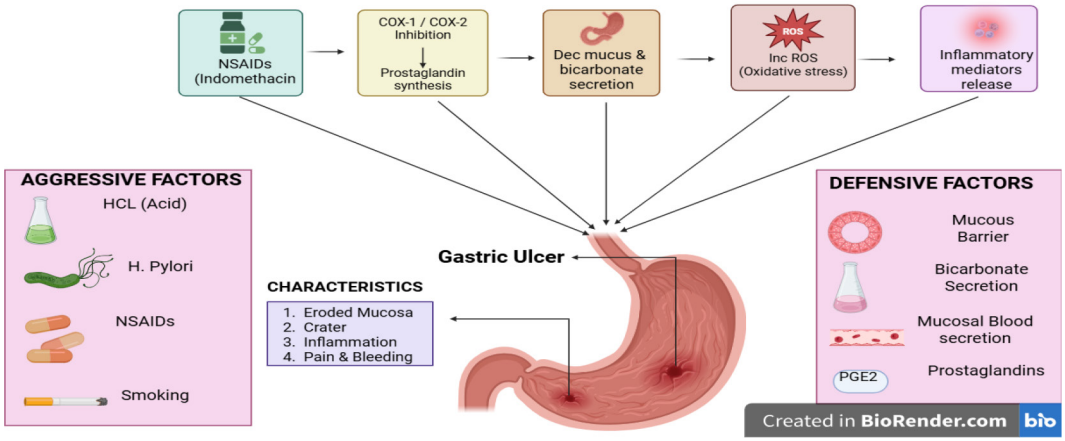


Figure 2. Mechanism of NSAIDs.

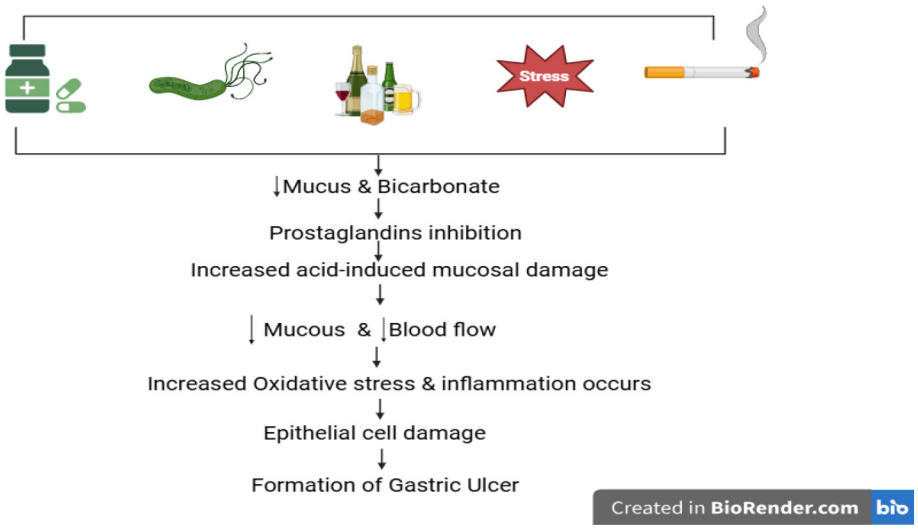


Figure 3. Shows formation of gastric ulcers.

Table 1. Shows the pathophysiological factors of ulcer, their mechanism and activities

Pathophysiological Factors of Ulcer	Mechanism	Activity Shown	References
NSAIDs and Pylori	COX inhibition ⟵ decreases in Prostaglandins Chronic Inflammation occurs	Leads to mucosal damage and ulcer formation	14,15
Oxidative Stress and Inflammation	⟵ Reactive Oxygen Species	Results in Lipid peroxidation	17,19
Impaired Mucosal Barriers and Microcirculation	⟵Microcirculation activity	Ledes to a slow healing process	20,22

regional variations and higher rates in adults, is a concerning emerging trend, according to this 2024 meta-analysis. This development may develop risk regimens and contribute to recurrent peptic/gastric ulcer disease unless there is a perfect treatment strategy available in place[23]. The 2024 systematic study reports a concerning global increase in *H. pylori* resistance to macrolides, particularly clarithromycin; pooled clarithromycin resistance increased from approximately 29% (2015–2019) to approximately 36.5% (2020–2023). If regional surveillance and customised treatment plans are not implemented, this increasing resistance, which varies widely geographically, threatens routine eradication regimens and could lead to more persistent or recurrent peptic/gastric ulcers and associated complications[24]. The efficacy of standard clarithromycin-based triple therapy is being undermined by increasing antibiotic resistance in paediatric *H. pylori*, particularly to clarithromycin and metronidazole, and by rising amoxicillin resistance in recent years, according to a 2024 systematic review and meta-analysis. In addition to highlighting the critical need for regional surveillance and antimicrobial stewardship to guide ulcer drug selection, this trend is driving a shift toward susceptibility-guided treatment and the empirical use of alternative regimens (e.g., bismuth-containing quadruple therapy or rifabutin-based rescue regimens)[25]. The 2023 narrative review states that new drug-related trends in the treatment of peptic and gastric ulcers include a shift from conventional non-selective NSAIDs to gastroprotective approaches, such as selective COX-2 inhibitors, NO-releasing NSAIDs, and dual COX/LOX agents; regular use of acid-suppressive co-therapy (PPIs); and an increased focus on deprescribing and individualised risk assessment to prevent upper and lower GI complications. The review warns that further research is necessary to determine the genuine therapeutic advantages and safety of many new "gastroprotective" NSAID formulations[26].

5. Limitations of Current Anti-ulcer Drugs

5.1 H2 Blockers

H2-receptor antagonists (H2-blockers) decrease gastric acid output by inhibiting histamine-mediated activation of parietal cells and are frequently used as anti-ulcer medications, as stated in Table 2. Works very well to reduce basal and nocturnal acid production, promote ulcer healing, and alleviate symptoms. Have been used safely in clinical settings for a long time and are often well tolerated. Long-term usage, however, may be linked to higher risks, including respiratory infections, some types of cancer, and consequences connected to the bones, according to current research. As a result, doctors are urged to use H2-blockers sparingly and base long-term treatment on a risk-benefit analysis for each patient[27]. H2 blockers, which include famotidine, cimetidine, and nizatidine, inhibit histamine H2 receptors on parietal cells and are acid-suppressive medications used to treat duodenal and stomach ulcers by lowering baseline and nocturnal acid output. Depending on the dosage, they can be purchased over the counter or with a prescription. They are useful for the temporary healing of ulcers and for symptom alleviation. H2 blockers are currently frequently utilised selectively or as adjuncts because proton pump inhibitors are typically favoured for erosive esophagitis and high-risk bleeding ulcers[28]. The FDA requested the removal of all ranitidine products from the U.S. market in April 2020 after it was found that some contained a probable carcinogen (nitrosodimethylamine, or NDMA), which increased over time and at higher storage temperatures. Ranitidine is a commonly used H_2-receptor antagonist that has long been prescribed to suppress stomach acid and treat ulcers and acid-related disorders[29].

5.2 PPIs (Proton Pump Inhibitors)

The most effective acid-suppressants for treating peptic and gastric ulcers are proton pump inhibitors, which significantly lower stomach acid production by inhibiting the H^+/K^+ATPase "proton pump" in gastric parietal cells. PPIs are a crucial part of treatment for *H. pylori*-related ulcers because they efficiently lower acid, speed up the repair of ulcerated mucosa, lessen symptoms, and work in tandem with antibiotics[30]. When used in conjunction with antibiotics, PPIs accelerate mucosal healing, alleviate symptoms, and play a crucial role in *H. pylori* eradication regimens. When recommending prolonged medication, doctors weigh the advantages against the risks because their broad and occasionally prolonged usage has sparked worries about possible side effects[31]. The incidence of type 2 diabetes, increased risk of sensorineural hearing loss, all-cause and cause-specific mortality, and unfavourable outcomes for patients with chronic renal disease are among the side effects of PPIs that have been discussed[32]. To minimise unnecessary PPI exposure and rebound symptoms, a recent agreement highlights deprescribing when there is no long-term justification and recommends step-down procedures (dose reduction or on-demand use with rescue medication) together with patient education and follow-up[33].

5.3 Antacids

Antacids are anti-ulcer agents, which are fast-acting and neutralise gastric acid to relieve dyspepsia, heartburn, and discomfort. The review highlights that contemporary antacid preparations (aluminium, magnesium, calcium, or mixed salts) are important in self-management due to their rapid onset, good safety profile, and availability as over-the-counter preparations. Antacids provide short-term relief of symptoms and may be administered alongside other ulcer therapies, although they may not be as effective as PPIs and H2 blockers in treating ulcers[34]. Thus, the sole intervention in the treatment of ulcers, they should be applied as a supplement or symptom management. Antacids are weak bases that quickly neutralise pH in the stomach and consequently reduce acidity, prevent the action of pepsin, and instantly alleviate symptoms of acid-related discomfort[35].

5.4 PCABs (Potassium-competitive Acid Blockers)

The 2024 review of PCABs affirms that the newer acid-suppressing drugs, such as vonoprazan, have a faster, stronger and longer-lasting effect on gastric acid compared to the older drugs, which causes a higher and more stable intragastric pH with the initial dose and controls acidity during the day and at night[36]. These findings imply that PCABs are highly promising as a first-line or other intervention

treatment of peptic/gastric ulcers, especially in cases where acid suppression is urgent. However, longer-term safety data and more extensive clinical experience are still being evaluated[35]. It offers advantages, such as more consistent acid control regardless of CYP2C19 genotype, making it a promising alternative for treating peptic and gastric ulcers[37].

5.5 Clinical Limitations

Renal disorders (acute interstitial nephritis, AKI, CKD), increased risk of infections (Clostridium difficile, community-acquired pneumonia), fractures, micronutrient deficiencies (hypomagnesemia, vitamin B12 deficiency), and potential associations with cardiovascular disease and cancer have been linked to long-term PPI use[38].

6. Need and Relevance of Herbal/ Alternative Therapies

This review elaborates on medicinal plants and their phytochemicals that are promising alternatives to pharmacological agents for treating ulcers (e.g., NSAIDs, PPIs, and H_2-blockers). These drugs, most of the time, have various side effects, drug interactions, and mucosal damage. Many plant extracts exhibit anti-ulcer activity by protecting the gastric mucosa, reducing inflammation, inhibiting acid secretion, and combating *H. pylori,* thereby offering effective treatment for ulcers with fewer side effects[39]. Bioactive compounds found in many herbs, such as flavonoids, tannins, and terpenoids, have gastroprotective properties that reduce oxidative stress and inflammation and inhibit *H. pylori*[40]. Such flora-based products are worth attention because they may be viewed as safer, more accessible, and less costly options that may prevent or treat ulcers, given that stress-related ulcers are common and currently used acid suppressants can lead to undesirable outcomes[41]. The 2023 systematic review indicates that a range of Ethiopian medicinal herbs with high phytochemical contents of flavonoids, phenols, tannins, and saponins exhibit significant anti-ulcer properties in animal models, and, in most cases, these effects are comparable to those of conventional ulcer medications[42]. The majority of therapeutic plants and their phytochemicals have a generally good safety profile. The quality of variations in extract extracts, variable dosage, and standardisation, the lack of large-scale clinical trials, and possible herb-drug interactions (through CYP enzymes and transporters) still pose a challenge to safety. Thus, before extensive therapeutic application, a rigorous toxicological screening, standardisation, and well-thought-out clinical research are essential[43].

7. *Centella asiatica*: A Botanical Review

7.1 Taxonomy and Morphology

Common names for *C. asiatica* include Indian pennywort, Mandukaparni, and Gotu kola. The medicinal creeping perennial herb *C. asiatica* Urban is an *asiatica* member of the *Apiaceae* (*Umbelliferae*) family. Small pinkish-white blooms, slender stolon,

Table 2. Shows drug names, their mechanism, effectiveness, limitations and examples

Drugs Name	Mechanism of Action	Effectiveness of Drug	Limitations	Example	References
H2 Blockers	Decreases gastric acid Output by inhibiting Histaminic mediated Parietal cells	Lowers and reduces nocturnal acid	Drug tolerance	Cimetidine	27,29
PPIs	Lowers stomach acid Production by the H^+/k^+ ATPase Proton Pump	Most effective acid suppressants	Long term problems	Omeprazole	30,31
Antacids	Acts by neutralising Gastric acid	Rapid Acting	Short time/ Duration risks	Aluminium Hydroxide	35
PCABs	Works by acting k+ Competitive blockers	Faster Action	Limited risks	Vonoprazan	36



Figure 4. *C. asiatica* showing leaves.



Figure 5. *C. asiatica* showing flowers.

Table 3. Shows plant parts and their main phytochemicals present

Plant Part	Main Phytochemicals Released	Relative Abundance	References
Leaves	Asiaticoside, Madecassoside, Asiatic acid, Madecassic acid, Flavonoids, Phenolics	High	[49]
Stem	Phenolic compounds, Moderate triterpenoids	Moderate	[50]
Roots	Asiatic acid, Madecassic acid (aglycones)	Low	[51]
Whole Plant	Triterpenoid saponins, Flavonoids, Tannins, Phenolics	Variable / Synergistic	[51]

and round to kidney-shaped leaves are characteristics of *C. asiatica,* as shown in Figures 4 and 5. In terms of taxonomy, it was formerly assigned to the genus Hydrocotyle; however, it is now appropriately categorised as *Centella*[44].

7.2 Distribution

Originally from tropical and subtropical Asia, *C. asiatica* is currently cultivated commercially in wet, marshy, or irrigated habitats (e.g., rice fields and streambanks) in India, Sri Lanka, Nepal, China, and other parts of Southeast Asia. Additionally, it is widely distributed across the tropics in damp, swampy, and irrigated areas (rice paddies, streambanks)[45,46].

7.3 Ethnomedical Background

Centella asiatica has long been used in traditional Chinese medicine, Ayurveda, and folk medicine throughout Asia and Africa. It has historically been used as a brain tonic (*Medhya Ras Ayana*) to improve mental clarity, memory, and cognition. The plant is commonly used to treat wounds, ulcers, and skin conditions like leprosy, eczema, and burns. It has been used to treat gastrointestinal disorders such as dysentery, diarrhoea and stomach ulcers. *C. asiatica* is an ancient herb that finds use as an antibacterial, antioxidant and anti-inflammatory agent[47].

7.4 Traditional Ayurvedic Uses

"*Medhya Ras Ayana*" is the term used to refer to *C. asiatica* in Ayurveda, and this plant is used to enhance cognitive, memory, and intelligence. It is also used to treat mental stress, anxiety, and epilepsy in addition to supporting the health of the nervous system. It is a plant that facilitates the repair and regeneration of tissues and is very common in the treatment of ulcers and wounds. In Ayurveda, it has been applied in the management of skin diseases such as chronic ulcers, leprosy and eczema. The *C. asiatica* was used as a treatment for digestive disorders such as diarrhoea, dysentery, and stomach ulcers[48].

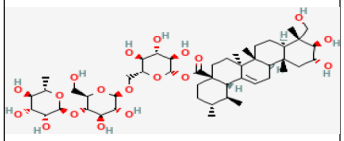
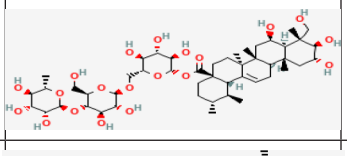
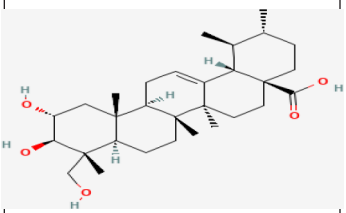
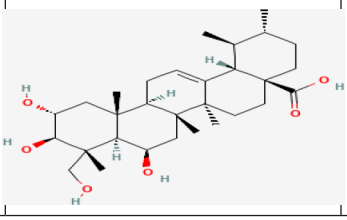
8. Phytochemistry

Asiaticoside and madecassoside, pentacyclic triterpenoid glycosides and their aglycones asiatic acid and madecassic acid are the predominant bioactive constituents of *C. asiatica*, as stated in Tables 3 and 4. Asiaticoside aids in the treatment of ulcers because it enhances the defence of the stomach lining. It enhances the renewal of the epithelium, stimulates the synthesis of collagen and angiogenesis, as well as decreases inflammation and generates free radicals, etc. This helps in the quick healing of ulcers and prevents acid damage to the stomach wall[52]. Asiaticoside is a good anti-ulcer drug that serves as a protective factor against the stomach, keeps the mucosal condition healthy and helps in the quicker healing process[53]. Asiaticoside activates the Wnt/ -catenin signalling pathway, a requirement of tissue growth and wound healing. It enhances repaired tissue development by supporting the formation of collagen and extracellular remodelling. It should be used as an anti-inflammatory and antioxidant agent to help heal wounds and decrease tissue damage[54]. Asiaticoside can be transported by nanotechnology-based methods through hydrogels and nanoparticles to ensure stability, bioavailability and specific delivery to the site of the ulcer[55].

Madecassoside is a potent phytoconstituent with anti-ulcer and gastroprotective effects; it enhances the mucosal defence mechanisms of the stomach. It exhibits strong anti-inflammatory activity and reduces mucosal inflammation by suppressing pro-inflammatory cytokines, including TNF-α and IL-1β[52]. The potent antioxidant activity of madecassoside reduces lipid peroxidation and oxidative stress, which are harmful to the gastric mucosa. Madecassoside promotes tissue remodelling and supports collagen formation, which are beneficial for faster ulcer healing[56]. Madecassoside speeds up ulcer healing by increasing mucus secretion and epithelial cell renewal[57].

By protecting the gastric mucosal barrier, asiatic acid exhibits significant gastroprotective and antiulcer efficacy. It blocks pro-inflammatory mediators, including TNF-α, IL-1β, and COX-2, and exerts anti-inflammatory effects[58]. It also promotes mucosal healing by modulating key molecular signalling pathways implicated in inflammation and tissue damage. Asiatic Acid repairs the epithelial lining and reduces ulcer-related damage. It stimulates

Table 4. Shows the compound name, its chemical structure, and mechanism

Compound Name	Chemical Structure	Mechanism of Action	References
Asiaticoside		Reduces collagen as well as ROS	45
Madecassoside		Reduces and lowers TNF-α and IL-1β	49
Asiatic acid		Regulates NF-κB modulation	7
Madecassic acid		Helps in regulating immunomodulation	62

histopathological architecture. The substance promotes tissue regeneration and barrier function, underscoring its therapeutic potential in ulcer-related conditions[59].

Madecassic acid has a potent immunomodulatory activity. It helps prevent ulcers by protecting the mucosa. This acid helps shift the immunological balance from pro-inflammatory Th17 cells to regulatory T (Treg) cells, thereby reducing inflammation. The PPARγ/AMPK/ACC1 signalling pathway inhibits inflammatory responses. This pathway is activated to facilitate the immunoregulation[60]. It strengthens the antioxidant defence system by reducing ROS levels linked to ulcer aetiology. It lowers and reduces oxidative stress. Madecassic acid also reduces the risk of ulceration by maintaining epithelial integrity and barrier function[61].

9. Pharmacological Activities Relevant to Anti-Ulcer Effects

9.1. Antioxidant

Antioxidant activity is demonstrated by a reduction in ROS and oxidative stress. As a result, there is an increase in ulcer-healing and antioxidant activities that protect the stomach mucosa. The integrity of the stomach epithelial cell membrane is maintained by inhibiting lipid peroxidation[63]. Gastric mucosal defence is strengthened by increasing endogenous antioxidant enzymes (SOD, CAT, and GPx). Antioxidant activity reduces subsequent tissue damage by limiting oxidative burst and neutrophil infiltration. Together, these benefits protect the integrity of the gastric mucosa and accelerate ulcer healing[64]. By limiting oxidative stress-induced inflammation, antioxidants lessen the severity of ulcers[65]. For example, Cheng *et al.* conducted a study that demonstrated that *C. asiatica* extract has the ability to reduce ulcer index and enhance mucosal regeneration in acetic acid-induced gastric ulcer rats.

9.2 Anti-inflammatory

When mucosal damage worsens due to pro-inflammatory mediators such as TNF-α and IL-1β, These Mediators are suppressed by anti-inflammatory actions. Secondary tissue injury at ulcer sites is reduced when neutrophil infiltration is reduced. For the improvement and healing of mucosal and ulcer lesions, both antioxidant and anti-inflammatory properties are required[63]. This anti-inflammatory activity plays an important role in reducing and preventing ulceration by protecting the stomach mucosa. It maintains mucosal integrity and barrier function and helps prevent ulcer progression. Inflammation suppression promotes quicker ulcer healing and less severe stomach tissue lesions[67]. In addition to reducing oedema and leukocyte infiltration, which lessens tissue damage at ulcer sites, anti-inflammatory action is essential[68].

9.3 Cytoprotective Action

Cytoprotective effect is an activity that is essential in the prevention of ulceration by preventing chemical and stress-induced mucosal injury of the stomach[69]. When mucus production is high, it provides a protective layer over the stomach epithelium, protecting it from pepsin and acid. Proper blood flow in the stomach mucosa promotes tissue oxygenation and healing. Ulcer occurrence is less when acid-induced and stress-related mucosal damage is reduced. It promotes faster ulcer healing and protects the stomach epithelium[70]. For example, Selenium has strong cytoprotective activity and helps reduce ulcer formation. It strengthens the antioxidant defence mechanisms and reduces oxidative damage to stomach epithelial cells, as Selenium strengthens the protective mucosal barrier by sustaining the formation of stomach mucus. It reduces stomach tissue erosion and necrosis by promoting cellular defence and repair processes[71].

9.4 Anti-*H. pylori* Potential

Epithelial damage and gastric mucosal inflammation are reduced when *H. pylori* growth is inhibited. Neutrophil infiltration and the secretion of pro-inflammatory cytokines are reduced when *H. pylori* is suppressed—the anti-H. The effect of *H. pylori* promotes ulcer healing and helps restore the integrity of the stomach mucosa[72]. Through antibacterial and anti-adhesive mechanisms, medicinal plant extracts inhibit the growth and survival of *H. pylori*. Antibiotic resistance problems and ulcer recurrence may be avoided using plant-based anti-*H. pylori* medications[73].

9.5 Wound Healing and Angiogenesis

Angiogenesis is crucial for ulcer healing because it replenishes the blood supply to the gastric mucosa.

At ulcer sites, improved microcirculation speeds up tissue remodelling and repair. While angiogenesis activation facilitates ulcer resolution more quickly and consistently, impaired angiogenesis delays healing[74]. Re-epithelialization, granulation tissue formation, and tissue remodelling are wound-healing mechanisms that directly contribute to the repair of stomach ulcers. Stable ulcer healing and mucosal regeneration are accelerated by improved angiogenesis and wound-healing pathways. Growth factors (such as VEGF, TGF-β, and FGF), which promote endothelial cell proliferation and the development of new vessels, are stimulated by natural chemicals[75].

9.6 Mucous Barrier Protection

One important anti-ulcer strategy is to strengthen the gastric mucus barrier, which shields epithelial cells from pepsin and acid. Mucus output and glycoprotein content provide protection and strength to the mucus barrier within the stomach. This barrier helps reduce mucosal exposure to aggressive factors, such as reduced acid secretion, thereby enhancing mucosal protection. This process supports ulcer healing and maintains the integrity of the stomach mucosa[76]. The stomach epithelium is protected from acid and digestive enzymes by increased mucus and bicarbonate production. Mucus Barrier function is maintained by reducing oxidative stress and inflammatory damage[77].

10. Detailed Mechanism of Anti-Ulcer Activity of *Centella asiatica*

Centella asiatica possesses several anti-ulcer properties or mechanisms, such as anti-oxidant, downregulation of inflammatory cytokines, enhancement of mucosal regenerations, gastric acid modulation, angiogenesis promotion, strengthening of the gastric mucosal barrier[79,80,86] as shown in Figure 6.

10.1 Oxidative Stress

Centella asiatica exhibits potent antioxidant activity due to its phytochemical compounds[70]. Due to these phytochemical compounds, the gastric epithelial cells of the stomach prevent attacks by ROS and lipid peroxidation[78]. It also preserves the integrity of the gastric mucosa by enhancing endogenous antioxidant defence systems, such as SOD, CAT, and GSH. Less oxidative stress tends to facilitate gastroprotection and faster recovery of ulcers[79] as shown in Figure 7.

10.2 Downregulation of Inflammatory Cytokines

It is shown that *C. asiatica* ethanolic extract possesses a strong anti-inflammatory impact on the models of gastric ulcers induced by indomethacin[80]. It inhibits JAK/STAT3 signalling, which coordinates the synthesis of several pro-inflammatory cytokines. The production of inflammatory mediators known as TNF-α, IL-6, and IL-17, among others, is suppressed, thus decreasing

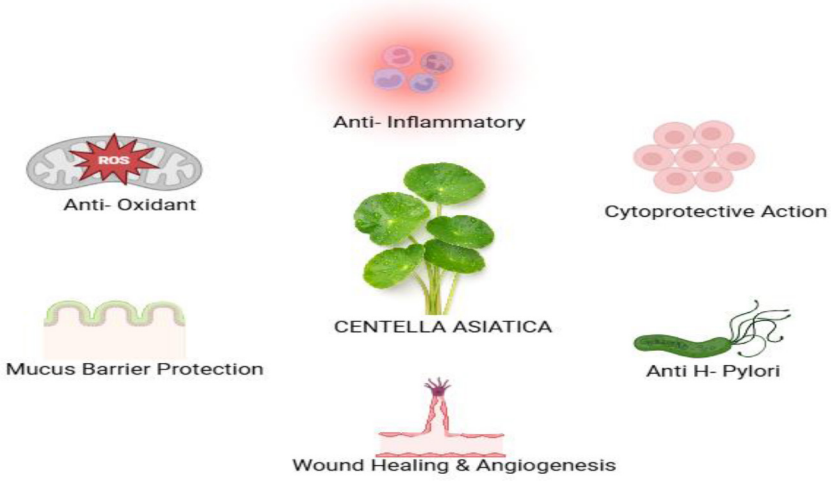


Figure 6. Use of *Centella asiatica* in various protective.

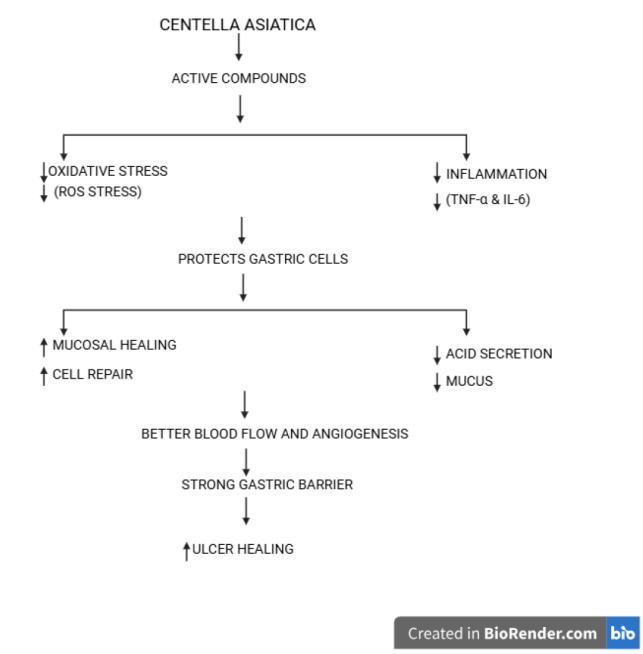


Figure 7. Flowchart of how *Centella asiatica* helps in ulcer healing.

tissue inflammation and cellular destruction[81]. It silences the production of cytokine genes by blocking signalling pathways which are implicated in inflammation, such as NF-KB. The consequences of this anti-inflammatory cytokine regulation are increased healing of ulcers and gastroprotection[82]. Sriepindonnta *et al.* reported that the ethanolic extract of *C. asiatica* reduced TNF-α expression in indomethacin-induced ulcer rats.

10.3 Enhancement of Mucosal Regeneration

The significant bioactive components of *C. asiatica* that have a healing effect on ulcers are constituents such as Pentacyclic triterpenes (asiaticoside, madecassoside, asiatic acid and madecassic acid). These triterpenes have been reported to induce re-epithelialization of ulcerated mucosa, which is a necessary step in the healing of ulcers, through migration and proliferation of epithelial cells. The positive effect of *C. asiatica* on the activation of fibroblasts and the production of collagen, in particular, type I collagen, leads to faster tissue remodelling and structural healing of injured mucosa[83].

10.4 Gastric Acid Modulation

According to one article, *C. asiatica's* anti-ulcer effect under stressful conditions may be mediated by modulating stress-related neurochemical pathways (e.g., by increasing brain GABA), thereby indirectly protecting the stomach mucosa from stress-induced ulceration[84]. Rather than acting primarily as an antisecretory agent to reduce gastric acid, *C. asiatica* increases protective mucosal factors, particularly mucus and glycoproteins, which buffer and resist acid-induced damage and contribute to its anti-ulcer benefits[78]. By increasing angiogenic factors like bFGF, *C. asiatica* promotes neo-vascularisation and enhanced microcirculation, which speeds up mucosal regeneration and restores tissue integrity, improving the healing of gastric ulcers[85].

10.5 Angiogenesis Promotion

Rather than directly suppressing or modifying gastric acid, *C. asiatica's* anti-ulcer actions are primarily mediated by promoting mucosal repair (angiogenesis and epithelial regeneration)[86].

10.6 Strengthening of the Gastric Mucosal Barrier

It has been observed that *C. asiatica* has improved epithelial regeneration, strengthened the mucus layer, reduced epithelial permeability, enhanced cytoprotective and antioxidant defences, and, when combined with a pentacyclic triterpene-rich *C. asiatica* extract, fortified the stomach mucosal barrier, ultimately accelerating ulcer healing[87].

11. Future Perspective

Centella asiatica's pentacyclic triterpenes affect acid regulation in the stomach, mucosal defence regeneration, angiogenesis, and inflammatory signalling pathways; these are the primary focus of anti-ulcer studies[88]. Future studies should focus on enhancing gastrointestinal stability and providing a comprehensive assessment of the availability of chemical constituents, employing advanced drug-delivery methods, such as solid dispersions, phytosomes, and nanoparticles, and also on developing effective herbal anti-ulcer therapies that are needed[89]. Pharmacokinetic and dose-response studies should be conducted to evaluate the gastroprotective benefits of *C. asiatica*[90]. It should also focus on precisely elucidating how specific triterpenoids modulate signalling pathways implicated in gastric ulcer healing

(e.g., NF-κB, MAPK), enabling mechanism-based validation rather than merely symptom reduction, as our understanding of molecular pathways increases[91]. To validate safety and optimal dosing and translate promising preclinical anti-ulcer results into evidence-based human therapeutic use, large-scale, randomised clinical trials are required. The use of *C. asiatica* as an anti-ulcer drug will be more accepted by law and clinicians if the international regulation of botanical drugs is enhanced. Future efforts to promote the production of scalable anti-ulcer products should include sustainable agriculture, biodiversity protection, and fair supply chains[92,93].

12. Conclusion

Gastric ulcer is a complex and multi-factorial pathogenesis with gastric acid imbalance, *H. pylori* infection, mucosal damage caused by NSAIDs, oxidative stress, inflammation, and impaired mucosal defence mechanisms, which makes this condition a major gastrointestinal condition. The conventional anti-ulcer pharmacotherapies include pharmacological agents, including proton pump inhibitors, H 2 -receptor antagonists, antacids and potassium-competitive acid blockers, which are all effective in the management of symptoms and the inhibition of acid secretion. However, they have been mostly linked to side effects, recurrence, and rise in drug resistance against antimicrobials, and therefore, it is obvious that more economical and holistic treatment approaches are required.

As its review indicates, *C. asiatica* has a high anti-ulcer potential due to its ability to protect the gastrointestinal tract in multifactorial ways, including the reduction of ROS and inflammation, the improvement of gastric epithelial barrier integrity, facilitation of angiogenesis and epithelial regeneration, and inhibition of *H. pylori.* In contrast to the traditional medications that mainly focus on acid secretion, *C. asiatica* has demonstrated its ability to stimulate epithelial and tissue healing and is a viable treatment option for long-term ulcer management.

13. References

1. Khan AH, Dar MA, Mir MA. Gastric ulcer: An overview. Int J Curr Res Physiol Pharmacol. 2023; 1-7. Available from: https://ijcrpp.com/index.php/ijcrpp/article/view/63
2. Woolf A, Rose R. Gastric ulcer. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023 Nov 3. Available from: https://pubmed.ncbi.nlm.nih.gov/30725813/
3. Khoder G, Al-Menhali AA, Al-Yassir F, Karam SM. Potential role of probiotics in the management of gastric ulcer. Exp Ther Med. 2016; 12(1):3-17. https://doi.org/10.3892/etm.2016.3293
4. Tarnawski AS, Ahluwalia A. The critical role of growth factors in gastric ulcer healing: the cellular and molecular mechanisms and potential clinical implications. Cells. 2021; 10(8):1964. https://doi.org/10.3390/cells10081964
5. Tripathy S, Afrin R. Herbal treatment alternatives for peptic ulcer disease. J Drug Deliv Ther. 2016; 6(3):27-33. https://doi.org/10.22270/jddt.v6i3.1210
6. Nabavi SM, Sanches Silva A, editors. Nonvitamin and nonmineral nutritional supplements. Academic Press; 2019. https://doi.org/10.1016/C2016-0-03546-5
7. Chandrika UG, Prasad Kumara PAAS. Gotu Kola (*Centella asiatica*): Nutritional properties and plausible health benefits. In: Preedy VR, editor. Advances in Food and Nutrition Research. Vol 76. Academic Press. 2015; 1-28. https://doi.org/10.1016/bs.afnr.2015.08.001
8. Malik TF, Gnanapandithan K, Singh K. Peptic ulcer disease. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jun 5. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534808/
9. Kamada T, Satoh K, Itoh T, Ito M, Iwamoto J, Okimoto T, *et al.* Evidence-based clinical practice guidelines for peptic ulcer disease 2020. J Gastroenterol. 2021; 56(4):303-322. https://doi.org/10.1007/s00535-021-01769-0
10. Xie X, Ren K, Zhou Z, Dang C, Zhang H. The global, regional, and national burden of peptic ulcer disease from 1990 to 2019: a population-based study. BMC Gastroenterol. 2022; 22:58. https://doi.org/10.1186/s12876-022-02130-2
11. Tai FWD, McAlindon ME. Non-steroidal anti-inflammatory drugs and the gastrointestinal tract. Clin Med (Lond). 2021; 21(2):e71-e75. https://doi.org/10.7861/clinmed.2021-0039
12. Joo MK, Park CH, Kim JS, Park JM, Ahn JY, Lee BE, *et al.* Clinical guidelines for drug-related peptic ulcer, 2020 revised edition. Gut Liver. 2021; 15(3):295-307. https://doi.org/10.5009/gnl20246
13. Li R, Wang W, Ma Y, Chen H. Analysis of risk factors for ulcer recurrence and upper gastrointestinal bleeding in children with peptic ulcer treated with *Helicobacter pylori* eradication therapy. Transl Pediatr. 2023; 12(4):618-630. https://doi.org/10.21037/tp-23-155
14. Melcarne L, Garcia-Iglesias P, Calvet X. Management of NSAID-associated peptic ulcer disease. Expert Rev Gastroenterol Hepatol. 2016; 10(6):723-733. https://doi.org/10.1586/17474124.2016.1142872
15. Sostres C, Carrera-Lasfuentes P, Benito R, Roncales P, Arruebo M, Arroyo MT, *et al.* Peptic ulcer bleeding risk: the role of *Helicobacter pylori* infection in NSAID/low-dose

aspirin users. Am J Gastroenterol. 2015; 110(5):684-689. https://doi.org/10.1038/ajg.2015.98
16. Sohail R, Mathew M, Patel KK, Reddy SA, Haider Z, Naria M, *et al.* Effects of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and gastroprotective NSAIDs on the gastrointestinal tract: a narrative review. Cureus. 2023; 15(3):e37080. https://doi.org/10.7759/cureus.37080
17. Ermis A, Aritici Colak G, Acikel-Elmas M, Arbak S, Kolgazi M. Ferulic acid treats gastric ulcer via suppressing oxidative stress and inflammation. Life (Basel). 2023; 13(2):388. https://doi.org/10.3390/life13020388
18. Mahmoud YI, Abd El-Ghaffar EA. *Spirulina ameliorates* aspirin-induced gastric ulcer in albino mice by alleviating oxidative stress and inflammation. Biomed Pharmacother. 2019; 109:314-321. https://doi.org/10.1016/j.biopha.2018.10.118
19. Almasaudi SB, El-Shitany NA, Abbas AT, Abdel-Dayem UA, Ali SS, Al Jaouni SK, *et al.* Antioxidant, anti-inflammatory, and antiulcer potential of Manuka honey against gastric ulcer in rats. Oxid Med Cell Longev. 2016; 2016:3643824. https://doi.org/10.1155/2016/3643824
20. Truse R, Hinterberg J, Schulz J, Herminghaus A, Weber A, Mettler-Altmann T, *et al.* Effect of topical iloprost and nitroglycerin on gastric microcirculation and barrier function during hemorrhagic shock in dogs. J Vasc Res. 2017; 54(2):109-121. https://doi.org/10.1159/000464262
21. Jia X, He Y, Li L, Xu D. Pharmacological targeting of gastric mucosal barrier with traditional Chinese medications for repairing gastric mucosal injury. Front Pharmacol. 2023; 14:1091530. https://doi.org/10.3389/fphar.2023.1091530
22. Yandrapu H, Sarosiek J. Protective factors of the gastric and duodenal mucosa: an overview. Curr Gastroenterol Rep. 2015; 17:24. https://doi.org/10.1007/s11894-015-0452-2
23. Yu Y, Xue J, Lin F, Liu D, Zhang W, Ru S, *et al.* Global primary antibiotic resistance rate of *Helicobacter pylori* in the recent 10 years: a systematic review and meta-analysis. Helicobacter. 2021; 26(4):e12887. https://doi.org/10.1111/hel.12887
24. Kasani SM, Mofid M, Navidifar T, Golab N, Parvizi E, Badmasti F, *et al.* Insights into *Helicobacter pylori* macrolide resistance: a comprehensive systematic review and meta-analysis. Front Microbiol. 2024; 15:1351899. https://doi.org/10.3389/fmicb.2024.1351899
25. Salahi-Niri A, Nabavi-Rad A, Monaghan TM, Rokkas T, Doulberis M, Sadeghi A, *et al.* Global prevalence of *Helicobacter pylori* antibiotic resistance among children in the World Health Organisation regions between 2000 and 2023: a systematic review and meta-analysis. BMC Med. 2024; 22:598. https://doi.org/10.1186/s12916-024-03816-y
26. Sohail R, Mathew M, Patel KK, Reddy SA, Haider Z, Naria M, *et al.* Effects of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and gastroprotective NSAIDs on the gastrointestinal tract: a narrative review. Cureus. 2023; 15(3):e37080. https://doi.org/10.7759/cureus.37080
27. Meng R, Chen LR, Zhang ML, Cai WK, Yin SJ, Fan YX, *et al.* Effectiveness and safety of histamine H2 receptor antagonists: an umbrella review of meta-analyses. J Clin Pharmacol. 2023; 63(1):7-20. https://doi.org/10.1002/jcph.2147
28. Nugent CC, Falkson SR, Terrell JM. H2 blockers. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Aug 11. Available from: https://www.ncbi.nlm.nih.gov/books/NBK525994/
29. U.S. Food and Drug Administration. FDA requests removal of all ranitidine products (Zantac) from the market [Internet]. Silver Spring (MD): FDA; 2020 Apr 1. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-requests-removal-all-ranitidine-products-zantac-market
30. Shanika LGT, Reynolds A, Pattison S, Braund R. Proton pump inhibitor use: systematic review of global trends and practices. Eur J Clin Pharmacol. 2023; 79(9):1159-1172. https://doi.org/10.1007/s00228-023-03534-z
31. Kim SY, Lee KJ. Potential risks associated with long-term use of proton pump inhibitors and the maintenance treatment modality for patients with mild gastroesophageal reflux disease. J Neurogastroenterol Motil. 2024; 30(4):e24059. https://doi.org/10.5056/jnm24059
32. Sizgoric L, Likic R. Proton pump inhibitors: weighing the benefits and risks across various health conditions. Br J Clin Pharmacol. 2024. https://doi.org/10.1111/bcp.15960
33. Kahrilas PJ, Anastasiou F, Bredenoord AJ, El-Serag HB, Labenz J, Mendive J, *et al.* Proton pump inhibitors: rational use and use-reduction - the Windsor Workshop. Gut. 2024. https://doi.org/10.1136/gutjnl-2024-331296
34. Garg V, Narang P, Taneja R. Antacids revisited: review on contemporary facts and relevance for self-management. J Int Med Res. 2022; 50(3):03000605221086457. https://doi.org/10.1177/03000605221086457
35. Ouyang M, Zou S, Cheng Q, Shi X, Zhao Y, Sun M. Comparative efficacy and safety of potassium-competitive acid blockers vs proton pump inhibitors for peptic ulcer with or without *Helicobacter pylori* infection: a systematic review and network meta-analysis. Pharmaceuticals (Basel). 2024; 17(6):698. https://doi.org/10.3390/ph17060698
36. Scarpignato C, Hunt RH. Potassium-competitive acid blockers: current clinical use and future developments. Curr Gastroenterol Rep. 2024; 26:273-293. https://doi.org/10.1007/s11894-024-00939-3
37. Tian L, Xiang D, Yue F, Li R, Zhou Y. Efficacy and safety of vonoprazan versus proton pump inhibitors in the treatment of peptic ulcer disease: a systematic review and network meta-analysis for randomised controlled trials. Front Nutr. 2024; 11:1436993. https://doi.org/10.3389/fnut.2024.1436993
38. Maideen NMP. Adverse effects associated with long-term use of proton pump inhibitors. Clin Mol Hepatol. 2023; 29(2):115-121. https://doi.org/10.3350/cmh.2022.0343

39. Prayoga DK, Aulifa DL, Budiman A, Levita J. Plants with anti-ulcer activity and mechanism: a review of preclinical and clinical studies. Drug Des Devel Ther. 2023; 17:3839-3859. https://doi.org/10.2147/DDDT.S446949
40. Cherrada N, Chemsa AE, Gheraissa N, Laib I, Gueboudji Z, EL-Shazly M, *et al.* Gastroprotective efficacy of North African medicinal plants: a review on their therapeutic potential for peptic ulcers. Food Sci Nutr. 2024; 12(11):8793-8824. https://doi.org/10.1002/fsn3.4536
41. Shahzad N, Ibrahim AAI, Alzahrani AR, AlGhamdi SS, Alanazi IMM, Ahmad MP, *et al.* A comprehensive review on phytochemicals as potential therapeutic agents for stressinduced gastric ulcer. J Umm Al-Qura Univ Appl Sci. 2024; 10:793-808. https://doi.org/10.1007/s43994-024-00140-2
42. Mustefa A, Nardos A, Hailu D, Deyno S. Phytochemistry, efficacy, and safety of medicinal plants used traditionally for the management of peptic ulcer diseases in Ethiopia: a systematic review. Clin Phytosci. 2023; 9:95. https://doi.org/10.1186/s40816-023-00362-7
43. Gupta M, Kapoor B, Gupta R, Singh N. Plants and phytochemicals for treatment of peptic ulcer: an overview. S Afr J Bot. 2021; 135:269-279. https://doi.org/10.1016/j.sajb.2020.11.030
44. Gray NE, Magana AA, Lak P, Wright KM, Quinn J, Stevens JF, *et al. Centella asiatica*: phytochemistry and mechanisms of neuroprotection and cognitive enhancement. Phytochem Rev. 2018; 17(1):161-194. https://doi.org/10.1007/s11101-017-9528-y
45. Sun B, Wu L, Wu Y, Zhang C, Qin L, Hayashi M, *et al.* Therapeutic potential of *Centella asiatica* and its triterpenes: a review. Front Pharmacol. 2020; 11:568032. https://doi.org/10.3389/fphar.2020.568032
46. Kandasamy A, Aruchamy K, Rangasamy P, Varadhaiyan D, Gowri C, Oh TH, *et al.* Phytochemical analysis and antioxidant activity of *Centella asiatica* extracts: an experimental and theoretical investigation of flavonoids. Plants (Basel). 2023; 12(20):3547. https://doi.org/10.3390/plants12203547
47. Ethnobotany, phytochemistry, and pharmacological features of *Centella asiatica*: a comprehensive review. In: Ethnobotany, phytochemistry, and pharmacological features of medicinal plants. Cham: Springer. 2021; 451-499. https://doi.org/10.1007/978-3-030-64872-5_25
48. Prakash V, Jaiswal N, Srivastava M. A review on medicinal properties of *Centella asiatica*. Asian J Pharm Clin Res. 2017; 10(10):1-6. https://doi.org/10.22159/ajpcr.2017.v10i10.20760
49. James JT, Dubery IA. Pentacyclic triterpenoids from the medicinal herb, *Centella asiatica* (L.) Urban. Molecules. 2009; 14(10):3922-3941. https://doi.org/10.3390/molecules14103922
50. Diniz LRL, Calado LL, Duarte ABS, de Sousa DP. *Centella asiatica* and its metabolite asiatic acid: wound healing effects and therapeutic potential. Metabolites. 2023; 13(2):276. https://doi.org/10.3390/metabo13020276
51. Ling APK, Marziah M, Tan SE. Triterpenoid distribution in the whole plant and callus cultures of *Centella asiatica* accessions. In: Interdisciplinary approaches in natural products research: proceedings of the 16th National Seminar on Natural Products; 2000 Oct 24-25; Selangor, Malaysia. Selangor: Dept. of Chemistry, University Putra Malaysia; 2001. p. 165-168.
52. Bandopadhyay S, Mandal S, Ghorai M, Jha NK, Kumar M, Radha, *et al.* Therapeutic properties and pharmacological activities of asiaticoside and madecassoside: A review. J Cell Mol Med. 2023; 27(5):593-608. https://doi.org/10.1111/jcmm.17635
53. Patel K, Mishra R, Patel DK. A review on the phytopharmaceutical importance of asiaticoside. J Coast Life Med. 2016; 4(4):204-210. https://doi.org/10.12980/jclm.4.2016J6-161
54. Nie X, Zhang H, Shi X, Zhao J, Chen Y, Wu F, *et al.* Asiaticoside nitric oxide gel accelerates healing of diabetic cutaneous ulcers by activating the Wnt/β-catenin signalling pathway. Int Immunopharmacol. 2019; 74:106109. https://doi.org/10.1016/j.intimp.2019.106109
55. Kumar M, Kumar D, Mahmood S, Singh V, Chopra S, Hilles AR, *et al.* Nanotechnology-driven wound healing potential of asiaticoside: a comprehensive review. Phys Chem Chem Phys. 2024. https://doi.org/10.1039/D3PM00024A
56. Tan SC, Bhattamisra SK, Chellappan DK, Candasamy M. Actions and therapeutic potential of madecassoside and other major constituents of *Centella asiatica*: a review. Appl Sci. 2021; 11(18):8475. https://doi.org/10.3390/app11188475
57. Sivasankaran SM, Pethanasamy M, Surya S, Harish K, Sakthisankaran SM, Kowsalya R. The multifaceted therapeutic profile of madecassoside: a scholarly review. J Drug Deliv Ther. 2024; 14(9):6767. https://doi.org/10.22270/jddt.v14i9.6767
58. Lv J, Sharma A, Zhang T, Wu Y, Ding X. Pharmacological review on asiatic acid and its derivatives: a potential compound. Exp Rev Mol Diagn. 2018; 18(4):391-404. https://doi.org/10.1177/2472630317751840
59. Lokman MS, Kassab RB, Salem FAM, Elshopakey GE, Hussein AA, Aldarmahi AA, *et al.* Asiatic acid protects intestinal tissue by suppressing molecular, biochemical, and histopathological changes associated with ulcerative colitis. Biosci Rep. 2024; 44:BSR20232004. https://doi.org/10.1042/BSR20232004
60. Xu X, Wang Y, Wei Z, Wei W, Zhao P, Tong B, *et al.* Madecassic acid, the contributor to the anti-colitis effect of madecassoside, enhances the shift of Th17 toward Treg cells via the PPARγ/AMPK/ACC1 pathway. Cell Death Dis. 2017; 8:e2723. https://doi.org/10.1038/cddis.2017.150
61. Hsu YM, Hung YC, Hu L, Lee YJ, Yin MC. Anti-diabetic effects of madecassic acid and rotundic acid. Nutrients. 2015; 7(12):10065-10075. https://doi.org/10.3390/nu7125512

62. Meeran MFN, Goyal SN, Suchal K, Sharma C, Patil CR, Ojha SK. Pharmacological properties, molecular mechanisms, and pharmaceutical development of asiatic acid: a pentacyclic triterpenoid of therapeutic promise. Front Pharmacol. 2018; 9:892. https://doi.org/10.3389/fphar.2018.00892
63. Phromnoi K, Sinchaiyakij P, Khanaree C, Nuntaboon P, Chanwikrai Y, Chaiwangsri T, *et al.* Anti-inflammatory and antioxidant activities of medicinal plants used by traditional healers in the treatment of ulcers. Sci Pharm. 2019; 87(3):22. https://doi.org/10.3390/scipharm87030022
64. Almasaudi SB, El-Shitany NA, Abbas AT, Abdel-Dayem UA, Ali SS, Al Jaouni SK, *et al.* Antioxidant, anti-inflammatory, and antiulcer potential of Manuka honey against gastric ulcer in rats. Oxid Med Cell Longev. 2016; 2016:3643824. https://doi.org/10.1155/2016/3643824
65. Albayrak A, Alp HH, Suleyman H. Investigation of antiulcer and antioxidant activity of moclobemide in rats. Eurasian J Med. 2014; 46(3):197-203. https://doi.org/10.5152/eajm.2014.0034
66. Mostofa R, Ahmed S, Begum MM, Rahman MS, Begum T, Ahmed SU, *et al.* Evaluation of anti-inflammatory and gastric anti-ulcer activity of *Phyllanthus niruri* L. (*Euphorbiaceae*) leaves in experimental rats. BMC Complement Altern Med. 2017; 17:267. https://doi.org/10.1186/s12906-017-1771-7
67. Bhatia S, Sharma K, Sharma A, Nagpal K, Bera T. Anti-inflammatory, analgesic and antiulcer properties of *Porphyra vietnamensis*. Avicenna J Phytomed. 2015; 5(1):69-77. https://doi.org/10.22038/ajp.2015.4634
68. De Sales IRP, Formiga RDO, Machado FDF, Nascimento RF, Pessoa MMB, Barros MEFX, *et al.* Cytoprotective, antioxidant, and anti-inflammatory mechanisms related to the antiulcer activity of *Cissampelos sympodialis* Eichl. in animal models. J Ethnopharmacol. 2018; 222:190-200. https://doi.org/10.1016/j.jep.2018.04.019
69. Al-Harbi MM, Qureshi S, Raza M, Ahmed MM, Afzal M, Shah AH. Gastric antiulcer and cytoprotective effect of *Commiphora molmol* in rats. J Ethnopharmacol. 1997; 55(2):141-150. https://doi.org/10.1016/S0378-8741(96)01488-2
70. Parmar NS, Tariq M, Ageel AM. Gastric anti-ulcer and cytoprotective effect of selenium in rats. Toxicol Lett. 1988; 42(1):1-6. https://doi.org/10.1016/0378-4274(88)90234-7
71. Wang Y, Wang SL, Zhang JY, Song XN, Zhang ZY, Li JF, *et al.* Anti-ulcer and anti-*Helicobacter pylori* potentials of the ethyl acetate fraction of *Physalis alkekengi* L. var. franchetii (*Solanaceae*) in rodents. J Ethnopharmacol. 2017; 212:150-159. https://doi.org/10.1016/j.jep.2017.09.004
72. Safavi M, Shams-Ardakani M, Foroumadi A. Medicinal plants in the treatment of *Helicobacter pylori* infections. Pharm Biol. 2015; 53(6):939-960. https://doi.org/10.3109/13880209.2014.952837
73. Honnegowda TM, Kumar P, Rao P. Role of angiogenesis and angiogenic factors in acute and chronic wound healing. Plast Aesthet Res. 2015; 2:243-249. https://doi.org/10.4103/2347-9264.165438
74. Vitale S, Colanero S, Placidi M, Di Emidio G, Tatone C, Amicarelli F, *et al.* Phytochemistry and biological activity of medicinal plants in wound healing: an overview of current research. Molecules. 2022; 27(11):3566. https://doi.org/10.3390/molecules27113566
75. Ribeiro ARS, Valença JDDN, Santos JS, Boeing T, da Silva LM, de Andrade SF, *et al.* The effects of baicalein on gastric mucosal ulcerations in mice: protective pathways and anti-secretory mechanisms. Chem Biol Interact. 2017; 264:58-65. https://doi.org/10.1016/j.cbi.2016.10.016
76. Zong Y, Meng J, Mao T, Han Q, Zhang P, Shi L. Repairing the intestinal mucosal barrier of traditional Chinese medicine for ulcerative colitis: a review. Front Pharmacol. 2023; 14:1273407. https://doi.org/10.3389/fphar.2023.1273407
77. Mishra A, Singh Y, Singh R, Kumar R, Shukla S, Prajapati RK, *et al.* Ethano-pharmacology activity and antioxidant activity of *Centella asiatica* plant parts. Neuroquantology. 2022; 20(11):7562-7572. https://doi.org/10.14704/NQ.2022.20.11.NQ66753
78. Zheng HM, Choi MJ, Lee DH. *Centella asiatica* leaf extract protects against indomethacin-induced gastric mucosal injury in rats. J Med Food. 2016; 19(1):38-46. https://doi.org/10.1089/jmf.2015.3464
79. Kaur B, Saxena A, Roy K, Bhardwaj M, Bisht M. Development and *in-vitro* evaluation of phytosomes containing herbal extract of *Centella asiatica* for antiulcer and antioxidant activity. J Adv Sci Res. 2023; 14(3):305-312. https://doi.org/10.55218/JASR.2023140305
80. Sriepindonnta PM, Fitriani FN, Thirza SQ, Pratiwi MD, Noviardi DEP, Kalsum U, *et al.* The potential effects of *Centella asiatica* ethanolic extracts as an anti-inflammatory agent through decreasing TNF-α expression in the indomethacin-induced gastric ulcer model rats. AIP Conf Proc. 2021; 2353:030054. https://doi.org/10.1063/5.0053018
81. Lin P, Shi HY, Lu YY, Lin J. *Centella asiatica* alleviates psoriasis through JAK/STAT3-mediated inflammation: An *in vitro* and *in vivo* study. J Ethnopharmacol. 2023; 307:116746. https://doi.org/10.1016/j.jep.2023.116746
82. Mairuae N, Cheepsunthorn P, Buranrat B. Anti-inflammatory and anti-oxidative effects of *Centella asiatica* extract in lipopolysaccharide-stimulated BV2 microglial cells. Pharmacogn Mag. 2019; 15(62):140-146. https://doi.org/10.4103/pm.pm_197_18
83. Sanguansajapong V, Sakdiset P, Puttarak P. Development of oral microemulsion spray containing pentacyclic triterpenes-rich *Centella asiatica* (L.) Urb. Extract for healing mouth ulcers. Pharmaceutics. 2022; 14(11):2531. https://doi.org/10.3390/pharmaceutics14112531
84. Sairam K, Rao CV, Goel RK. Effect of *Centella asiatica* L. on physical and chemical factors that induce gastric ulceration and secretion in rats. Indian J Exp Biol. 2001; 39(2):137-142.

85. Chatterjee TK, Chakraborty A, Pathak M, Sengupta GC. Effects of plant extract *Centella asiatica* (Linn.) on cold restraint stress ulcer in rats. Indian J Exp Biol. 1992; 30(10):889-891.
86. Mariska E, Sitorus TD, Rachman JA. Effect of *Centella asiatica* leaves on gastric ulcer in rats. Althea Med J. 2015; 2(1):44-47. https://doi.org/10.15850/amj.v2n1.444
87. Cheng CL, Guo JS, Luk J, Koo MWL. The healing effects of *Centella asiatica* extract and asiaticoside on acetic acid-induced gastric ulcers in rats. Life Sci. 2004; 74(18):2237-2249. https://doi.org/10.1016/j.lfs.2003.09.055
88. Wannasarit S, Puttarak P, Kaewkroek K, Wiwattanapatapee R. Strategies for improving healing of the gastric epithelium using oral solid dispersions loaded with pentacyclic triterpene-rich *Centella* extract. AAPS PharmSciTech. 2019; 20:277. https://doi.org/10.1208/s12249-019-1488-7
89. Hein ZM, Gopalakrishna PK, Kanuri AK, Thomas W, Hussan F, Naik VR, *et al. Centella asiatica*: Advances in extraction technologies, phytochemistry, and therapeutic applications. Life. 2025; 15(7):1081. https://doi.org/10.3390/life15071081
90. Bansal K, Bhati H, Vanshita, Bajpai M. Recent insights into therapeutic potential and nanostructured carrier systems of *Centella asiatica*: An evidence-based review. Pharmacol Res - Mod Chin Med. 2024: p. 100403. https://doi.org/10.1016/j.prmcm.2024.100403
91. Wright KM, McFerrin J, Alcázar Magaña A, Roberts J, Caruso M, Kretzschmar D, *et al.* Developing a rational, optimised product of *Centella asiatica* for examination in clinical trials: Real-world challenges. Front Nutr. 2021; 8:799137. https://doi.org/10.3389/fnut.2021.799137
92. Bhagat J, Bhagwat A, Waghmode P, Temkar P, Gunjal S, Walunj A, *et al. Centella asiatica* in the modern therapeutic landscape. Int J Pharm Sci. 2025; 3(10):1973-1982. https://doi.org/10.5281/zenodo.17384310
93. Guo X, Suzuki H, Sawafuji T, Fukuda S, Yamada T, Kobayashi M, *et al.* A clinical trial to evaluate the safety and efficacy of *Centella asiatica* for ulcerative colitis. JGH Open. 2025; 9:e70258. https://doi.org/10.1002/jgh3.70258

Author Contribution

Sweta Kumari: Conceptualization, data collection, and manuscript preparation. Pooja Negi: Supervision, guidance, and critical review of the manuscript. Madhurani and Digvijay Singh: Literature review and manuscript editing. Sagar Kumar and Akshay Chauhan: Data compilation and reference management. All authors have read and agreed to the published version of the manuscript.