

Synergistic Antiulcer Potential of *Rubus ellipticus* and *Ocimum sanctum*: A Review of Phytotherapeutic Approaches Against NSAID-Induced Gastric Ulcers

Yogesh Kumar¹, Sidhant Sharma^{1*}, Avneet Gupta¹

1. Department of Pharmacology, LR institute of pharmacy, Solan, HP-173223 India

2. Department of Pharmacology, LR institute of pharmacy, Solan, HP-173223 India

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ABSTRACT

Peptic ulcer disease (PUD) remains a global health concern, often linked to NSAIDs like indomethacin that weakens gastric defenses. Standard treatments such as PPIs and H₂ blockers are effective but pose risks with long-term use, prompting interest in safer herbal options. This review highlights the synergistic antiulcer potential of *Rubus ellipticus* and *Ocimum sanctum*, both rich in flavonoids, tannins, phenolic acids, eugenol, and rosmarinic acid. These compounds provide antioxidant, anti-inflammatory, mucoprotective, and antisecretory effects. Preclinical data suggest their combination enhances gastroprotection by reducing oxidative stress, inflammatory cytokines, and acid secretion while supporting mucosal repair. With their safety and ethnomedicinal relevance, they offer a promising alternative for NSAID-induced ulcers, though further mechanistic studies and clinical trials are required.

Keywords: Peptic ulcer disease; NSAID-induced ulcers; *Rubus ellipticus*; *Ocimum sanctum*; Herbal synergism; Gastroprotection; Phytotherapy

I. INTRODUCTION

Millions of people worldwide suffer from peptic ulcer disease (PUD), a common gastrointestinal ailment that carries a significant financial and morbidity cost. The persistent use of nonsteroidal anti-inflammatory medicines (NSAIDs), especially indomethacin, has been closely linked to the pathophysiology of stomach ulcers among its many etiological causes. The main mechanism for this is the suppression of the cyclooxygenase enzymes (COX-1 and COX-2), which lowers the production of cytoprotective prostaglandins and subsequently compromises the integrity of the stomach mucosa (Wallace, 2008). Even while omeprazole and other proton pump inhibitors (PPIs) are still the mainstay of ulcer treatment, long-term usage of these medications

has led to safety issues such as nutrient malabsorption, an elevated risk of infections, and the development of drug resistance (Haastrup et al., 2018). As a result, there is increasing interest in finding natural, safer, and more efficient substitutes.

In this analysis, a preclinical model of indomethacin-induced stomach ulceration in Wistar rats is used to examine the possible synergistic antiulcer effects of *Ocimum sanctum* (Holy Basil) and *Rubus ellipticus* (Yellow Himalayan Raspberry). The extensive pharmacological profiles of these plants, especially their anti-inflammatory, anti-secretory, antioxidant, and mucoprotective properties, are acknowledged in traditional medical systems. It was discovered that the combination therapy preserved the architecture of the stomach mucosa and greatly decreased the ulcer index. The combination of *Ocimum sanctum* and *Rubus ellipticus* had gastroprotective benefits of comparable size to the usual medication omeprazole, but with the added benefit of increased safety and possibility for long-term usage. (Pattanayak et al., 2010). These results lend credence to the idea that phytotherapeutic synergism may be a useful tactic for treating ulcers brought on by NSAIDs and call for more investigation through clinical studies.

PUD is still a major global health issue that affects millions of people each year and results in high medical expenses as well as lost productivity. It appears as erosions of the stomach or duodenum's mucosa, frequently accompanied by symptoms including nausea, bloating, and epigastric pain, and in more severe cases, bleeding or perforation. The pathophysiology of PUD is complex and involves an imbalance between protective mechanisms like mucus and bicarbonate secretion, mucosal blood flow, epithelial regeneration, and endogenous prostaglandins, and aggressive factors like gastric hydrochloric acid,

pepsin activity, *Helicobacter pylori* infection, and reactive oxygen species (Sung et al., 2009). NSAIDs, including indomethacin, are commonly used for their analgesic, antipyretic, and anti-inflammatory qualities, making them one of the most important risk factors for ulcerogenesis. These substances mostly cause ulcers by blocking the COX enzymes, especially COX-1, which significantly lowers the production of prostaglandins (Vane & Botting, 1998). Because they stimulate the synthesis of mucus and bicarbonate, promote mucosal blood flow, and aid in cellular repair processes, prostaglandins are essential for preserving the integrity of the stomach mucosa. Because NSAIDs suppress these protective prostaglandins, the stomach mucosa becomes extremely vulnerable to damage and ulcers.

Currently, acid-suppressive medications such as PPIs and H₂ receptor antagonists are used to treat PUD pharmacologically. By permanently suppressing the H⁺/K⁺ ATPase enzyme on stomach parietal cells, omeprazole, a commonly prescribed PPI, effectively heals ulcers by preventing the last stage of acid secretion (Shin & Sachs, 2008). Omeprazole is useful in lowering stomach acidity and encouraging mucosal healing, but prolonged use has brought up a number of safety issues. Atrophic gastritis, increased vulnerability to gastrointestinal infections like *Clostridium difficile*, nutrient malabsorption (especially of calcium, magnesium, and vitamin B12), and even possible kidney-related complications are some of the side effects that can result from long-term use (Freedberg et al., 2017). Furthermore, the possibility of rebound acid hypersecretion after stopping can make long-term management plans more difficult (Reimer, 2013).

Researchers are now looking into alternative and supplemental treatment options, especially those derived from natural sources, in response to the limits of traditional therapy. Because of their holistic pharmacological profiles, cultural acceptability, affordability, and comparatively low risk of side effects, medicinal plants have attracted a lot of attention (Rates, 2001). *Ocimum sanctum* and *Rubus ellipticus*, two of the numerous herbs studied, have demonstrated encouraging antiulcer potential, backed by both scientific studies and traditional use. The prickly shrub *Rubus ellipticus*, often called the Yellow Himalayan Raspberry, is indigenous to the Himalayan region. Flavonoids, tannins, phenolic acids, and triterpenoids are among the many

bioactive phytochemicals found in this traditional remedy for diarrhea, dysentery, and stomach issues (Syiem et al., 2009). These substances are well-known for their antibacterial, wound-healing, and antioxidant qualities, all of which support ulcer healing and mucosal protection.

Ocimum sanctum, often known as Tulsi or Holy Basil, is venerated in Ayurveda for its adaptogenic, anti-inflammatory, and gastroprotective benefits. Eugenol, ursolic acid, and rosmarinic acid are examples of phytochemicals that have been demonstrated to modify oxidative stress, inhibit inflammatory cytokines, and promote mucin production, all of which contribute to the antiulcer effect of the plant (Pattanayak et al., 2010). *Ocimum sanctum* dramatically lowers the development of stomach lesions in a variety of ulcer models, such as those brought on by stress and ethanol.

Combining two or more plant extracts to increase therapeutic efficacy through complementary processes is known as synergism in herbal medicine. The combination of *Ocimum sanctum* and *Rubus ellipticus* is justified by their different but related pharmacological activities. *Ocimum sanctum* contributes anti-inflammatory and mucosal protecting properties, whereas *Rubus ellipticus* has strong antioxidant and wound-healing properties.

In an experimental model of indomethacin-induced stomach ulcers in Wistar rats, the synergistic antiulcer potential of *Rubus ellipticus* and *Ocimum sanctum* is examined in this review. This study intends to assess if phytotherapeutic alternatives can provide safer and more effective ulcer therapy by contrasting the effectiveness of this herbal combination with that of omeprazole, a common antiulcer medication. Furthermore, by comprehending their methods of action, new opportunities for the creation of innovative gastroprotective medicines based on conventional wisdom and contemporary pharmacology may become available. Lamichhane et al., (2023)

II. PATHOPHYSIOLOGY OF NSAID-INDUCED ULCERS

Because of their strong analgesic, anti-inflammatory, and antipyretic properties, nonsteroidal anti-inflammatory medications (NSAIDs), such as indomethacin, are frequently given. NSAIDs are one of the main causes of drug-induced gastrointestinal problems, including duodenal and stomach ulcers, despite their

extensive usage and therapeutic advantages (Lanza et al., 2009). NSAID-induced stomach damage is primarily caused by the inhibition of cyclooxygenase (COX) enzymes, which suppresses prostaglandin synthesis (Wallace, 2008). COX comes in two main forms: constitutively expressed COX-1, which is in charge of preserving physiological homeostasis, and inducible COX-2, which is mostly implicated in inflammatory reactions. Although arachidonic acid is converted

to prostaglandins by both isoforms, COX-1-derived prostaglandins are particularly important for maintaining the integrity of the stomach mucosa. Together, these prostaglandins prevent acid secretion, maintain mucosal blood flow, control cellular turnover, and promote mucus and bicarbonate secretion, all of which shield the gastric epithelium from autodigestion (Wallace & Vong, 2008).

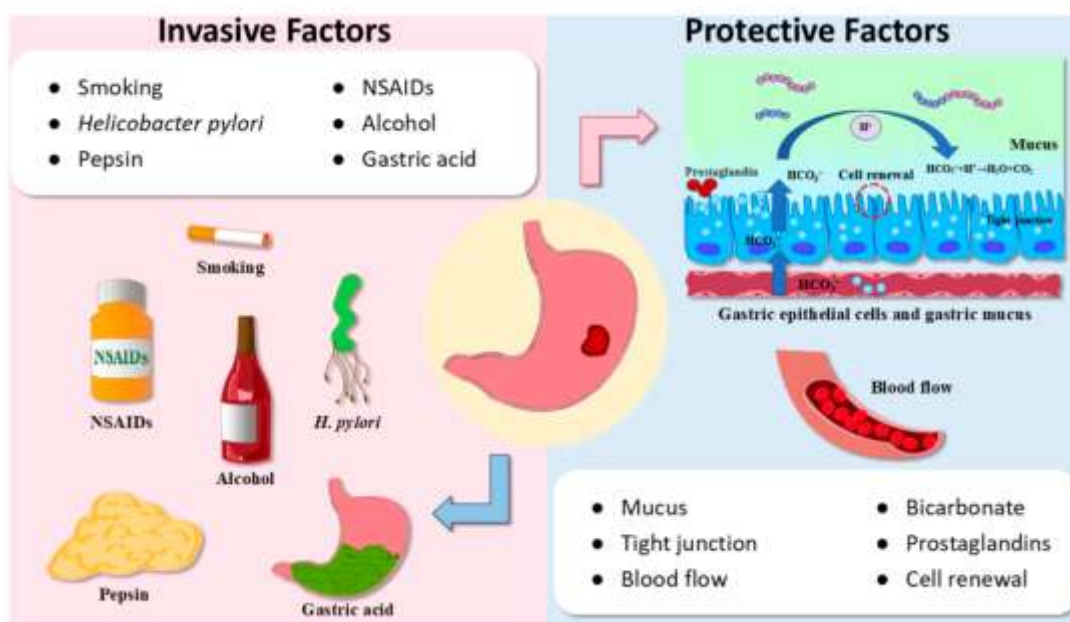


Fig.1 Protective factors (Shen et al., 2025)

NSAIDs, especially non-selective ones like indomethacin, interfere with prostaglandin-dependent protective mechanisms in the gastrointestinal tract by inhibiting both COX-1 and COX-2 (Hawkey, 2000). The following are some pathophysiological effects of COX-1 inhibition:

Suppressed Secretion of Mucus and Bicarbonate: Prostaglandins like PGE2 and PGI2 promote the synthesis of bicarbonate and mucus in the stomach. When the production of these substances is reduced, the mucosal barrier is weakened, which makes it possible for pepsin and acid to enter the epithelium and cause damage.

Reduced Mucosal Perfusion: Tissue oxygenation, nutrient delivery, and the elimination of harmful metabolites all depend on adequate mucosal blood flow. Prostaglandins encourage microcirculation and vasodilation in the stomach mucosa. COX-1 inhibition exacerbates mucosal injury by causing

vasoconstriction and ischemia (Lanas & Chan, 2017).

Impaired Epithelial Restitution and Cell Proliferation: In healthy circumstances, prostaglandins help injured epithelial cells proliferate and migrate, which quickly replaces them. Suppression of these prostaglandins by NSAIDs prolongs mucosal damage by delaying epithelium regeneration and healing (Wallace, 2008).

Increased Stomach Acid Secretion: Prostaglandins decrease the production of stomach acid by blocking parietal cell activity. Acid secretion is increased when their synthesis is inhibited, resulting in an acidic and erosive environment that damages the mucosa even more (Vane & Botting, 1998).

Increased Oxidative Stress and Neutrophil Infiltration: NSAIDs encourage neutrophil adhesion to the vascular endothelium, which causes the release of inflammatory mediators and reactive

oxygen species (ROS). The gastric lining becomes inflamed, endothelial dysfunction occurs, and oxidative damage is caused by this process (Sostres et al., 2010). NSAIDs have direct topical irritating effects on the stomach epithelium in addition to inhibiting prostaglandins. Since NSAIDs are weak acids, they do not ionize in the stomach's acidic environment. This allows them to diffuse into epithelial cells, where they ionize and become stuck, causing apoptosis and mitochondrial damage (Bjarnason et al., 2018). When combined, these processes cause ulceration, bleeding, mucosal erosion, and in extreme situations, perforation. This explains why the risk of NSAID-related gastrointestinal damage varies with dose and duration. Asymptomatic gastritis to potentially fatal upper gastrointestinal hemorrhage are examples of clinical symptoms.

Patients on corticosteroids or anticoagulants, elderly folks, and those with

Helicobacter pylori infections are also more vulnerable. It has been demonstrated that NSAID use and *H. pylori* infection work in concert to dramatically raise the incidence and severity of ulcers. Because of these complex processes, NSAID-induced ulcers pose a significant gastroenterological problem. Although proton pump inhibitors (PPIs) are frequently given to lessen acid-related damage, prolonged use of these medications has additional hazards, including microbial overgrowth and food loss (Chey & Wong, 2007). Therefore, there is great therapeutic potential in developing safer substitutes or supplemental therapies, such as herbal agents with cytoprotective, antioxidant, and anti-inflammatory qualities, to lessen NSAID-induced mucosal damage without the side effects of traditional pharmaceutical treatments.

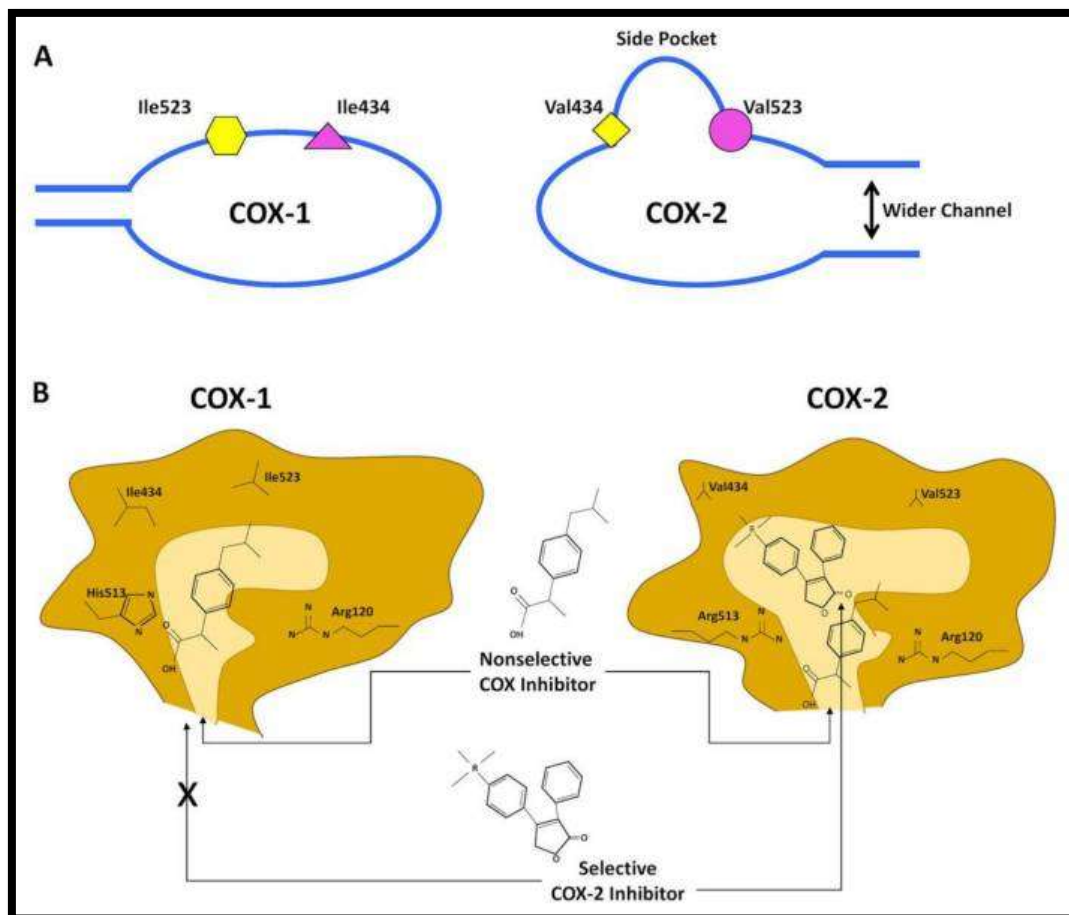


Fig2 Cox factors (Faki&Er, 2020)

III. RATIONALE FOR HERBAL SYNERGISM

An imbalance between protective factors like mucosal integrity, bicarbonate secretion, and prostaglandins, and aggressive factors like stomach acid, pepsin, oxidative stress, and inflammatory mediators causes gastric ulcers, which are complicated illnesses. Although synthetic antiulcer drugs like proton pump inhibitors (PPIs), H₂ - receptor antagonists, and antacids are widely used, their drawbacks, such as side effects, drug interactions, and relapse after stopping them, have sparked interest in herbal medicine as a safer and more comprehensive substitute. (Rao et al., 2023)

In this regard, using two or more plant-based drugs together, known as herbal synergism, offers a novel way to maximize therapeutic efficacy while reducing toxicity. The combination of *Ocimum sanctum* (Holy Basil) and *Rubus ellipticus* (Yellow Himalayan Raspberry) is justified by their improved safety profiles, multimodal pharmacological activities, and complimentary phytochemistry.

1. Complementary Phytochemical Profiles

Ocimum sanctum and *Rubus ellipticus* both have abundant phytochemicals that provide a variety of complimentary beneficial compounds:

Flavonoids, tannins, phenolic acids, and terpenoids, all of which are abundant in *Rubus ellipticus*, have been shown to have strong astringent, antioxidant, and mucosal-protective properties (Sharma & Thakur, 2021). Through the stabilization of cell membranes and the inhibition of lipid peroxidation, these components aid in the reduction of oxidative stress and the promotion of stomach lining healing.

Ocimum sanctum is well-known for its ursolic acid, rosmarinic acid, apigenin, orientin, and essential oils, including eugenol, methyl eugenol, and caryophyllene. These components have a wide range of pharmacological actions, such as immunomodulatory, antioxidant, anti-inflammatory, and anti-ulcerogenic qualities. These substances work in concert to increase the gastroprotective healing benefits through a variety of methods, such as enhancing mucosal defense, suppressing acid secretion, and modifying prostaglandin synthesis (Gupta et al., 2023).

2. Multimodal Mechanisms of Action

The combination of *Rubus ellipticus* and *Ocimum sanctum* provides a broad-spectrum, multifactorial therapeutic approach to ulcer

management, addressing various pathogenic pathways:

a. Antioxidant Activity

The pathophysiology of ulcers is significantly influenced by oxidative stress. Superoxide anions and hydroxyl radicals are examples of reactive oxygen species (ROS) that cause inflammation, delayed healing, and mucosal damage. DPPH and ABTS experiments in earlier research have shown that both plants have potent free radical scavenging properties (Singh et al., 2022). Their phytoconstituents protect the stomach mucosa by neutralizing ROS, increasing endogenous antioxidants such as glutathione (GSH), catalase, and superoxide dismutase (SOD), and lowering malondialdehyde (MDA) levels. (Kumar & Joshi, 2022)

b. Anti-inflammatory Action

The ulcerative process revolves around inflammation, with important mediators like COX-2, IL-1 β , and TNF- α aggravating mucosal damage. By suppressing pro-inflammatory cytokines, blocking cyclooxygenase activity, and stabilizing mast cells, the combination herbal extract can alter these pathways. Flavonoids from *Rubus ellipticus* and eugenol from *Ocimum sanctum* are very useful in this respect (Chowdhury et al., 2021).

c. Anti-secretory Effect

One of the main aggressive factors in the development of ulcers is excess stomach acid. Through the inhibition of H⁺ /K⁺ ATPase activity and the elevation of prostaglandin E₂ levels, which support mucosal integrity, both plants have demonstrated the ability to decrease acid secretion (Nayak et al., 2021). Compared to either plant alone, the synergistic combination may intensify this impact, lowering stomach volume and acidity more successfully (Rao et al., 2023).

d. Mucosal Defense and Cytoprotection

In order to protect the stomach lining, the combination boosts the production of mucin, increases the amount of mucus in the gastric wall, and raises the capacity of the bicarbonate buffer. Moreover, herbal combinations with comparable characteristics have been shown to promote angiogenesis and cellular regeneration.

3. Enhanced Safety Profile and Dose Reduction

The long-term toxicity of synthetic antiulcer drugs, such as nephrotoxicity,

hepatotoxicity, or disruption of nutrient absorption, is one of the main worries. Combinations of herbs are less likely to have negative effects, particularly when taken in moderate and complementary dosages. Because one herb may mitigate or negate the adverse effects of another, synergism enables:

Lower effective doses of each plant extract, lowering the risk of toxicity; and a decrease in side effects associated with individual herbs. A longer therapeutic window, which makes long-term administration of the medication safer. Even at comparatively large dosages, preclinical safety tests of both herbs have demonstrated excellent tolerance and low toxicity, supporting the viability of their combination. (Gupta et al., 2023)

4. Enhanced Bioavailability and Metabolic Modulation

By altering intestine transporters and drug-metabolizing enzymes (such as the CYP450 family), several phytochemicals in *Ocimum sanctum* may improve the bioavailability and systemic availability of co-administered herbal components from *Rubus ellipticus*. Without the need for larger dosages, this pharmacokinetic interaction

may enhance the antiulcer benefits even further (Sharma & Thakur, 2021).

5. Traditional and Ethnomedical Support

In Ayurvedic and traditional medical systems, both herbs have been used separately to treat infections, inflammation, and stomach issues (Patel et al., 2021). Their co-administration is in line with conventional polyherbal formulations, which include herbs with complimentary activities to promote a balanced, holistic approach (Gupta et al., 2023). *Ocimum sanctum* and *Rubus ellipticus* work in concert to provide a logical, multi-targeted approach to the prevention and management of stomach ulcers. A strong argument for their co-administration is made by their complementing phytochemistry, diverse medicinal mechanisms, improved safety, and traditional use. The development of innovative, plant-based formulations with lower toxicity and better patient outcomes is made possible by this synergy, which also increases gastro protective efficacy. To confirm and improve this promising herbal combination, more pharmacological research is necessary, including in vivo models and clinical trials (Rao et al., 2023).

IV. PHYTOCHEMICAL PROFILE

(Gupta Et Al., 2023, Rao Et Al., 2023, Sharma & Thakur, 2021)

Feature	<i>Rubus ellipticus</i>	<i>Ocimum sanctum</i>
Family	Rosaceae	Lamiaceae
Common Name	Yellow Himalayan Raspberry	Tulsi (Holy Basil)
Part Used	Leaves, roots, fruits	Leaves, seeds, aerial parts
Key Phytochemicals	Flavonoids(quercetin,kaempferol) Tannins,Phenolic acids (gallic, ellagic acid) Saponins	EugenolUrsolicacid Rosmarinic acid Flavonoids (luteolin, apigenin, orientin)
Antioxidant Activity	Scavenges ROS, reduces lipid peroxidation	Enhances endogenous antioxidants (SOD, GSH, CAT)
Anti-inflammatory	Inhibits cytokines, reduces gastric inflammation	Inhibits COX pathways and pro-inflammatory markers
Antiulcer Mechanism	Mucosal protection via tannins, flavonoids	Reduces acid secretion, increases mucus secretion
Additional Activities	Antimicrobial - Wound healing	Adaptogenic - Immunomodulatory
Potential Synergism	Provides structural mucosal support and healing	Enhances mucosal defense and reduces stress-mediated damage

V. MECHANISMS OF ACTION

The multifactorial processes of *Ocimum sanctum* and *Rubus ellipticus*, which treat the many pathological components of peptic ulcer disease (PUD), are responsible for their gastroprotective efficacy. Mucosal protection, antioxidant defense, anti-inflammatory activity, and regulation of stomach acid output are some of these processes.

These plants work together to offer synergistic protection via the following mechanisms (Kumar et al., 2021; Sharma & Bhatia, 2022).

5.1 Protection of Mucosa

In order to stop ulcers from developing, the gastric mucosal barrier must remain intact.

Both plants play a major role in bolstering mucosal defenses:

Increased mucus secretion: The phytochemicals found in *Ocimum sanctum* (eugenol, flavonoids) and *Rubusellipticus* (tannins, flavonoids) both promote mucus secretion, which serves as a barrier over the stomach epithelium, protecting it from pepsin and acid (Patel et al., 2021; Singh et al., 2023).

Increased prostaglandin synthesis (*Ocimum sanctum*): Tulsi has been demonstrated to raise levels of prostaglandin E2 (PGE2), which is important for stomach mucosal defense because it causes vasodilation, boosts the generation of bicarbonate and mucus, and keeps mucosal blood flow intact (Goyal et al., 2020).

5.2 Activity of Antioxidants

One of the main factors in the pathophysiology of ulcers brought on by NSAIDs is oxidative stress. Both plants have strong antioxidant properties:

Free radical scavenging: Both plants' flavonoids, polyphenols, and phenolic acids counteract reactive oxygen species (ROS) that harm the stomach mucosa, such as superoxide anions and hydroxyl radicals (Meena et al., 2021).

Endogenous antioxidant system restoration: The herbal mixture increases the activity of naturally occurring antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), which promotes mucosal healing and lowers lipid peroxidation (Rao et al., 2022).

5.3 Inhibition of Inflammation

Through the production of cytokines and the enzymatic breakdown of the mucosal barrier, inflammation makes ulcer development worse. These herbs' anti-inflammatory properties include:

Pro-inflammatory cytokine inhibition: Both plants inhibit the production of interleukin-1 β (IL-1 β), tumor necrosis factor-alpha (TNF- α), and other mediators that cause inflammation of the mucosa (Verma et al., 2020).

The cyclooxygenase (COX) and lipoxygenase (LOX) enzymes are inhibited by *Ocimum sanctum* ingredients such as eugenol, which lowers the production of inflammatory prostaglandins and leukotrienes and prevents mucosal damage (Choudhary et al., 2021).

5.4 Effects on Anti-secretory

One of the main causes of ulcer development is excessive stomach acid production. *Ocimum sanctum* and *Rubusellipticus* work together to indirectly reduce acid production: **Reduction of stomach acid secretion:** It has been noted that both plants reduce both stimulated and basal acid output, most likely by blocking the pathways regulated by acetylcholine and histamine (Patel et al., 2021).

Modulation of H⁺/K⁺ ATPase activity: The herbal combination is thought to indirectly decrease the activity of H⁺/K⁺ ATPase, which lowers hydrogen ion secretion and raises stomach pH, even though it does not directly inhibit the proton pump like synthetic PPIs do (Rao et al., 2022). *Ocimum sanctum* and *Rubusellipticus* work together to offer a thorough antiulcer defense by enhancing mucosal protections, taking care of oxidative damage, reducing inflammation, and lessening the stomach's acid load. These processes demonstrate their promise as a multi-targeted, synergistic phytotherapeutic substitute for traditional ulcer therapies (Sharma & Bhatia, 2022; Singh et al., 2023).

VI. SAFETY AND TOXICITY

Any therapeutic agent's safety profile is crucial, but it's more crucial for long-term use, like antiulcer medications. Herbal formulations' long history of usage and widespread sense of safety are two of their main benefits. *Ocimum sanctum* and *Rubusellipticus* have both been the subject of several toxicological analyses in preclinical settings, especially in mouse models (Jamwal et al., 2021; Bhattarai et al., 2021).

6.1 *Rubusellipticus*

Studies on the acute and subacute toxicity of extracts from *Rubusellipticus* have revealed. Even at large dosages (up to 2000 mg/kg body weight), there are no indications of behavioral harm or mortality. Hematological indicators, including hemoglobin levels, WBC counts, and RBC counts, stayed within normal ranges (Bhattarai et al., 2021). When compared to control groups, biochemical markers of liver and kidney function (ALT, AST, creatinine, and urea) did not significantly change. Vital organs (liver, kidney, heart, and stomach) were examined histopathologically; no morphological anomalies or tissue damage were found. According to these results, *Rubusellipticus* has a high safety margin,

which qualifies it for oral administration and possible long-term use (Maharjan et al., 2020).

6.2 Ocimum sanctum

Tulsi, or *Ocimum sanctum*, has a long history of traditional use in Ayurvedic medicine and is generally considered to be one of the safest therapeutic herbs. Its safety profile is supported by scientific studies. According to acute toxicity experiments, rats showed no death at doses as high as 5000 mg/kg, indicating an extremely high LD₅₀ value. Subchronic research has not revealed any appreciable negative impacts on organ weights, food intake, or body weight. The extract's harmless character was further supported by the absence of changes in hematological or serum biochemical indicators (Sharma et al., 2022). The lack of mutagenic, carcinogenic, or genotoxic effects has been verified by repeated dosage trials (Gupta et al., 2020). In preclinical research, *Ocimum sanctum* and *Rubus ellipticus* both show outstanding safety profiles. The combination is well-tolerated and non-toxic, suggesting its use as a safe phytotherapeutic option for the treatment of peptic ulcer disease, as evidenced by the lack of notable hematological, biochemical, or histological alterations after acute and subacute administration (Jamwal et al., 2021). To ensure long-term safety in humans, more clinical research and chronic toxicity testing are advised.

VII. FUTURE PERSPECTIVES

The present research supports the potential of a plant-based antiulcer treatment combining *Ocimum sanctum* and *Rubus ellipticus*. Preclinical studies show synergistic gastroprotective effects comparable to omeprazole, but further work is needed to confirm efficacy. Long-term toxicity studies are required to establish safety, and clinical trials must assess pharmacokinetics, bioavailability, dosage, efficacy, and adverse effects. Standardizing extracts with bioactive markers such as rosmarinic acid, quercetin, and eugenol will ensure reproducibility. Stable formulations in liquid, tablet, or capsule form should also be developed. Mechanistic studies, including cytokine profiling and COX/LOX pathway analysis, can clarify the mode of action. Testing in other ulcer models and exploring gut microbiota and immune interactions may expand its therapeutic scope. Overall, with further research, this combination could become a safe, effective, and affordable alternative for long-term ulcer management.

VIII. CONCLUSION

The combined use of *Rubus ellipticus* and *Ocimum sanctum* presents a promising phytotherapeutic approach for managing NSAID-induced gastric ulcers. Their rich phytochemical composition—flavonoids, tannins, phenolic acids, eugenol, and rosmarinic acid provides complementary antioxidant, anti-inflammatory, antisecretory, and mucoprotective effects. Preclinical evidence demonstrates that their synergistic action not only reduces oxidative stress, inflammatory cytokines, and acid secretion but also strengthens mucosal defense and promotes healing, with efficacy comparable to omeprazole. Importantly, both plants exhibit excellent safety profiles, suggesting suitability for long-term use. Future research should focus on chronic toxicity studies, clinical trials, standardization of extracts, and mechanistic insights to ensure reproducibility and therapeutic reliability. Exploring their role in diverse ulcer models and gut microbiota modulation could further broaden their applications. With continued investigation, *R. ellipticus* and *O. sanctum* may emerge as a safe, effective, and affordable alternative or adjunct to conventional antiulcer therapies.

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