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### Molecular Insights in to the Gastro protective Potential of Marmin and Imperator in: A Phytochemical and Mechanistic Perspective

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**Abstract:** Peptic ulceration of the stomach continues to represent a common digestive system pathology distinguished by epithelial injury arising from disequilibrium between harmful elements including gastric acidity, reactive oxygen species, and inflammatory processes, and the protective systems of the gastric lining. Although established treatment modalities exist, encompassing proton pump inhibitors and H<sub>2</sub>-receptor antagonists, prolonged administration frequently correlates with undesirable consequences and disease recurrence, creating demand for investigating more secure and efficacious therapeutic options. Within this framework, naturally derived coumarins have attracted substantial interest owing to their varied pharmacological attributes. Marmin and imperatorin, two notable furanocoumarins obtained from therapeutic plants including *Aegle marmelos* and *Angelica* species, demonstrate considerable gastric protective capabilities. This analysis thoroughly examines the phytochemical features, pharmacokinetic characteristics, and fundamental action mechanisms of marmin and imperatorin in gastric ulcer prevention and treatment. Data from laboratory and animal investigations indicate that these substances provide protective benefits via numerous mechanisms, encompassing antioxidant function, suppression of inflammatory factors, strengthening of mucosal protection, and regulation of gastric acid production. Furthermore, their possible anti-*Helicobacter pylori* properties additionally validate their clinical significance. The analysis emphasizes existing constraints, safety aspects, and developing formulation approaches designed to enhance bioavailability. In summary, marmin and imperatorin constitute encouraging prospects for developing innovative gastroprotective compounds. Additional clinical research is required to confirm their effectiveness and safety in human subjects and to enable their progression toward therapeutic implementation.

**Keywords:** Marmin; Imperatorin; Gastro protection; Peptic ulcer; Coumarins; Oxidative stress; Anti-inflammatory; Gastric mucosa.

## Introduction

Digestive system disorders encompass a wide array of pathological conditions that impact various components of the gastrointestinal tract, including gastric, intestinal, hepatic, pancreatic, and related anatomical structures. Within this spectrum, gastric and duodenal ulcerations hold considerable clinical importance owing to their widespread occurrence and potential for serious complications [1]. Peptic ulcer disease manifests as focal erosions within the mucosal surfaces of the stomach or proximal duodenum, arising from disequilibrium between damaging elements including gastric acid secretion, pepsin activity, reactive oxygen species, and bacterial infections and defensive mechanisms such as mucus-bicarbonate production, epithelial cellular integrity, mucosal circulation, and prostaglandin biosynthesis. This homeostatic disruption precipitates mucosal damage, inflammatory responses, and ulcerative lesions, substantially compromising patient well-being [2]. On a worldwide scale, peptic ulcer disease continues to present considerable healthcare challenges, impacting numerous individuals annually throughout both industrialized and developing nations. The occurrence and distribution of peptic ulcerations are modulated by various elements, including economic circumstances, nutritional practices, and medical care availability. *Helicobacter pylori* infection persists as a significant causative factor, promoting chronic gastric inflammation and ulcer development through pathways involving mucosal inflammatory responses, oxidative damage, and epithelial barrier compromise. Additionally, extensive utilization of nonsteroidal anti-inflammatory medications has demonstrated strong correlations with gastric mucosal injury through cyclooxygenase enzyme inhibition and consequent diminishment of protective prostaglandin concentrations [3]. Additional risk factors, including excessive ethanol intake, tobacco use, psychological tension, and poor nutritional choices, further amplify ulcer susceptibility. Critically, complications including gastrointestinal hemorrhage, perforation, and obstruction may lead to considerable morbidity and mortality, underscoring the importance of effective prevention and treatment modalities. Contemporary pharmacological approaches for gastric ulcer management predominantly utilize proton pump inhibitors, H<sub>2</sub>-receptor blockers, antacids, and mucosal protective compounds. These interventions target gastric acid reduction, acid neutralization, and mucosal defense enhancement [4]. Concurrently, antimicrobial protocols are implemented for *H. pylori* elimination. While these treatments have substantially enhanced clinical results, extended administration presents several constraints. Complications including vitamin and mineral malabsorption, heightened vulnerability to gastrointestinal and respiratory infections, and potential renal and cardiovascular complications have been documented with prolonged PPI administration. Moreover, the development of antibiotic-resistant *H. pylori* variants has diminished standard eradication therapy effectiveness, resulting in therapeutic failures and recurring infections. An additional concern involves rebound acid hypersecretion phenomena following acid-suppressive medication cessation, potentially contributing to recurrence. These obstacles emphasize the for more secure, efficacious, and multi-targeted therapeutic strategies [5].

Recently, increasing attention has focused on utilizing phytochemicals as alternative or adjunctive agents for gastrointestinal disorder management. Phytochemicals constitute naturally occurring bioactive substances present in medicinal plants, many historically employed for digestive condition treatment. These molecules, encompassing flavonoids, alkaloids, terpenoids, and coumarins, demonstrate diverse pharmacological activities pertinent to gastric protection. Particularly, phytochemicals exhibit potent antioxidant capabilities, facilitating reactive oxygen species neutralization and reducing oxidative gastric mucosal damage [6]. Furthermore, these compounds exhibit anti-inflammatory properties through the regulation of crucial signaling cascades and the suppression of pro-inflammatory mediator synthesis, including cytokines, prostaglandins, and nitric oxide. Numerous phytochemicals additionally strengthen mucosal protective mechanisms by promoting mucus and bicarbonate production, enhancing mucosal circulation, and facilitating epithelial repair processes. Their multifaceted mechanism of action, combined with comparatively minimal toxicity, positions them as attractive prospects for developing innovative gastro protective treatments. Within the diverse spectrum of phytochemicals, coumarins have garnered significant interest owing to their varied biological functions and therapeutic possibilities [7]. These benzopyrone derivatives occur abundantly throughout nature and are recognized for their antioxidant, anti-inflammatory, antimicrobial, and cytoprotective characteristics. Among this category, furanocoumarins including marmin and imperatorin have emerged as particularly noteworthy compounds.

Marmin is primarily extracted from *Aegle marmelos*, a therapeutic plant widely employed in conventional medical practices for addressing gastrointestinal ailments. Conversely, imperatorin is typically obtained from *Angelica* species and has demonstrated an extensive range of pharmacological actions, encompassing vasorelaxant, anti-inflammatory, and antimicrobial effects. The choice of marmin and imperatorin for this current review stems from their encouraging pharmacological characteristics and accumulating evidence supporting their gastro protective capabilities. Both substances have demonstrated antioxidant efficacy through free radical neutralization and strengthening of endogenous antioxidant systems, consequently reducing oxidative stress-related mucosal injury [8-10]. Moreover, they display anti-inflammatory attributes via suppression of pro-inflammatory mediators and signaling networks, which are fundamental in ulcer

development. Additionally, these compounds have shown enhancement of mucosal protective mechanisms, encompassing elevated mucus synthesis and preservation of epithelial barrier function. Their potential effectiveness against *Helicobacter pylori* further emphasizes their therapeutic significance in peptic ulcer disease treatment. Despite these encouraging observations, the clinical utilization of marmin and imperatorin remains constrained, mainly due to obstacles concerning their bioavailability, pharmacokinetic properties, and absence of extensive clinical investigations [11]. Consequently, a methodical and rigorous assessment of available literature is crucial for advancing understanding of their action mechanisms, therapeutic capacity, and constraints. This current review endeavors to deliver a thorough examination of the chemical properties, pharmacological functions, and gastro protective mechanisms of marmin and imperatorin, alongside perspectives on their safety characteristics and future potential. Through synthesizing contemporary scientific data, this review attempts to emphasize the promise of these naturally sourced compounds as candidates for creating innovative and efficacious gastric ulcer management therapies [12].

### Overview of gastrointestinal disorders

Digestive system pathologies comprise an extensive array of disease states that impact the alimentary canal, encompassing the esophagus, stomach, small and large bowel, hepatic tissue, pancreatic structures, and related anatomical components. These conditions span from functional disturbances, such as irritable bowel syndrome, to structural and inflammatory pathologies, including gastritis, peptic ulceration, inflammatory bowel disease, and digestive tract neoplasms. Within this spectrum, gastric pathologies notably peptic ulcerative conditions continue to represent a significant clinical challenge owing to their widespread occurrence and potential for serious complications [13]. The digestive apparatus serves fundamental functions in food processing, nutrient uptake, immunological control, and preservation of metabolic equilibrium. Gastric mucosal integrity remains vital for safeguarding deeper tissue layers from the aggressive luminal milieu, which contains hydrochloric acid, proteolytic enzymes like pepsin, and diverse external agents. During normal physiological states, the gastric mucosa receives protection through an intricate and adaptive defensive framework involving mucus and bicarbonate production, secure epithelial connections, sufficient mucosal circulation, and protective prostaglandin formation. These protective mechanisms function collaboratively to preserve mucosal structure and prevent tissue damage. When the equilibrium between harmful and protective elements becomes disturbed, mucosal injury occurs, leading to digestive system pathology development. Harmful elements encompass excessive gastric acid production, elevated pepsin function, oxidative damage, inflammatory substances, and bacterial infections including *Helicobacter pylori*. Oxidative damage particularly contributes significantly to GI disorder pathogenesis through reactive oxygen species (ROS) generation that harms cellular structures, including lipids, proteins, and genetic material. Inflammatory cascades further intensify tissue damage via cytokine, chemokine, and additional mediator release [14-16]. Behavioral and environmental elements also substantially influence digestive disorder emergence and advancement. Nutritional patterns, ethanol intake, tobacco use, psychological stress, and specific pharmaceutical agents, particularly NSAIDs, demonstrate strong correlations with gastric mucosal injury. NSAIDs specifically block cyclooxygenase (COX) enzyme function, resulting in diminished prostaglandin production and compromised mucosal protection, thus enhancing ulcer development risk. Additionally, digestive disorders are progressively understood as multifactorial conditions affected by hereditary susceptibility, microbiome modifications, and immune system dysfunction. The intestinal microbiota serves a central function in preserving digestive wellness, and its disruption (dysbiosis) correlates with various GI diseases, including ulcerative and inflammatory disorders. In summary, digestive system disorders demonstrate complex interactions among physiological, environmental, and molecular elements. This complexity further emphasizes the requirement for comprehensive therapeutic strategies capable of targeting the varied pathways involved in disease development [17].

### Global Burden of Peptic Ulcer Disease

Peptic ulcer disease (PUD) continues to represent a major worldwide health challenge, making considerable contributions to illness burden, medical expenditures, and diminished life quality. Notwithstanding therapeutic progress and enhanced comprehension of disease mechanisms, PUD persists in affecting countless people across the globe [18]. The condition is distinguished by ulcerative lesions developing within gastric or duodenal mucosa resulting from disrupted equilibrium between damaging elements and protective mucosal barriers. Population-based studies demonstrate that lifetime probability for peptic ulcer development spans 5% to 10% among general populations. While PUD occurrence has decreased in certain industrialized nations through enhanced sanitation practices and successful *Helicobacter pylori* elimination protocols, the condition maintains high prevalence in developing areas where healthcare accessibility and disease awareness may be restricted. Disease impact is additionally intensified by socioeconomic determinants, encompassing economic disadvantage, nutritional deficiencies, and insufficient medical infrastructure [19]. *Helicobacter pylori* infection stands as an established causative agent in peptic ulcer pathogenesis, particularly within low- and middle-income nations. This microorganism establishes gastric mucosal colonization and triggers persistent

inflammatory responses, resulting in mucosal deterioration and subsequent ulcer development. Beyond *H. pylori*, extensive NSAID utilization has become another primary PUD contributor, notably within geriatric populations. The synergistic impact of these risk elements substantially elevates ulcer formation probability and related complications. PUD complications, including gastrointestinal hemorrhage, perforation, and gastric outlet obstruction, present severe clinical difficulties and may prove fatal without immediate intervention [20]. Upper gastrointestinal bleeding represents among the most frequent complications and correlates with considerable illness and death rates. Hospital admission frequencies and medical costs associated with PUD and its complications remain extensive, imposing substantial strain on global healthcare frameworks. Furthermore, ulcer recurrence constitutes an ongoing concern following successful therapeutic intervention [21]. Elements including inadequate *H. pylori* elimination, persistent NSAID consumption, and lifestyle-associated hazards contribute to disease relapse. The development of antibiotic-resistant *H. pylori* variants has additionally complicated treatment methodologies, diminishing standard eradication protocol effectiveness. Beyond physical health consequences, PUD carries substantial psychosocial and financial ramifications. Persistent discomfort, nutritional limitations, and repeated medical consultations may negatively influence patient life quality and work performance. Consequently, urgent requirements exist for more efficacious, accessible, and sustainable treatment modalities capable of reducing global PUD burden while enhancing patient outcomes [22].

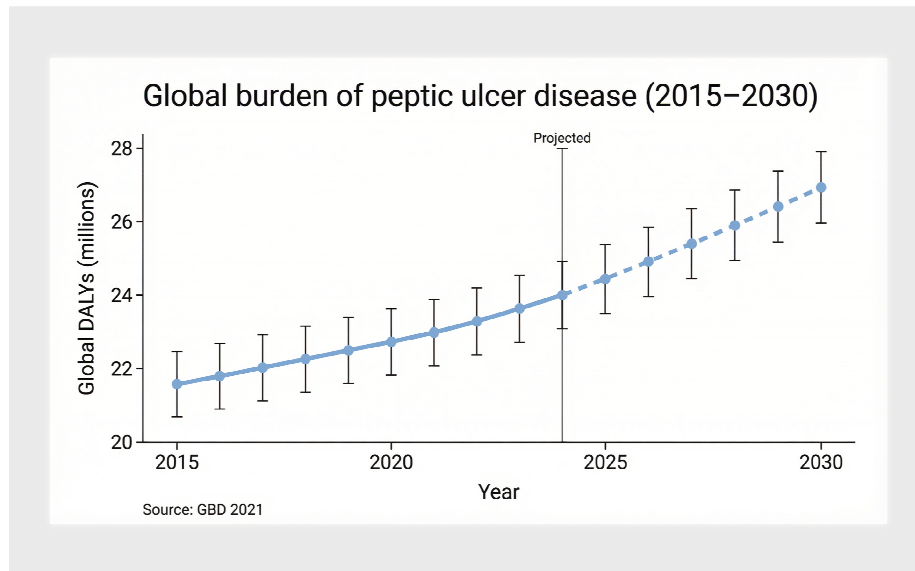


Fig.1: Projected Global Burden of Peptic Ulcer Disease (2015–2030)

### Limitations of Conventional Therapies

Traditional treatment modalities for peptic ulcer disease concentrate on diminishing gastric acid production, neutralizing present acid, safeguarding gastric mucosa, and eliminating *Helicobacter pylori*. Frequently employed pharmaceutical interventions encompass proton pump inhibitors (PPIs), H<sub>2</sub>-receptor antagonists, antacids, and mucosal protective medications including sucralfate and misoprostol [23]. Although these therapeutic interventions have markedly enhanced ulcer recovery rates and symptomatic improvement, they possess inherent constraints. Proton pump inhibitors, regarded as the fundamental component of ulcer management, efficiently reduce gastric acid production through H<sup>+</sup>/K<sup>+</sup>-ATPase enzyme inhibition. Nevertheless, extended PPI administration has been linked to various detrimental outcomes, encompassing vitamin B<sub>12</sub> deficiency, hypomagnesemia, elevated bone fracture risk, and increased vulnerability to gastrointestinal infections including *Clostridioides difficile*. Furthermore, sustained acid suppression may modify gut microbiota structure, potentially resulting in dysbiosis [24–26]. H<sub>2</sub>-receptor antagonists, despite their effectiveness in decreasing acid production, demonstrate lower potency compared to PPIs and may show diminished effectiveness over time through tolerance development. Antacids offer immediate yet temporary relief without addressing fundamental ulcer formation mechanisms. Mucosal protective medications, while advantageous in strengthening mucosal defense mechanisms, may present adverse effects including diarrhea and abdominal discomfort. A primary obstacle in conventional treatment involves *H. pylori* elimination. Standard triple or quadruple antibiotic protocols have demonstrated decreasing efficacy rates attributed to antibiotic-resistant strain emergence. This resistance compromises therapeutic effectiveness while requiring alternative, frequently costlier and more complicated treatment protocols [27]. Another considerable limitation involves ulcer recurrence after therapy cessation. Rebound acid hypersecretion represents a well-established occurrence linked

to PPIs, potentially contributing to disease relapse. Moreover, conventional treatments predominantly focus on specific ulcer pathogenesis components and may inadequately address the disease's multifactorial characteristics, including oxidative stress and inflammation. Economic considerations are also relevant, especially in resource-limited environments where sustained pharmacotherapy access may be restricted. These constraints emphasize the necessity for alternative therapeutic approaches that are safer, economically viable, and capable of targeting multiple pathways in ulcer pathogenesis [28-30].

### **Role of Phytochemicals in Gastro protection**

Plant-derived bioactive compounds, known as phytochemicals, have emerged as promising therapeutic candidates for treating gastrointestinal ailments, particularly peptic ulcer disease. These naturally occurring substances encompass flavonoids, alkaloids, terpenoids, tannins, and coumarins, demonstrating diverse pharmacological properties pertinent to gastric protection. A primary mechanism through which these compounds confer gastro protective benefits involves their antioxidant capabilities. Given that oxidative stress contributes substantially to gastric mucosal damage through the generation of reactive oxygen species that compromise cellular integrity, phytochemicals serve to scavenge these harmful radicals while strengthening intrinsic antioxidant systems, thus safeguarding the gastric mucosa against oxidative injury [31]. Beyond their antioxidant attributes, these plant compounds demonstrate anti-inflammatory properties by regulating crucial inflammatory signaling cascades. They suppress pro-inflammatory cytokine synthesis, diminish the activity of enzymes including cyclooxygenase and lipoxygenase, and prevent the activation of transcription factors such as NF- $\kappa$ B. These mechanisms collectively reduce inflammatory responses and facilitate mucosal repair processes. Furthermore, phytochemicals strengthen mucosal protective systems by promoting mucus and bicarbonate production, enhancing mucosal circulation, and facilitating epithelial cell renewal. Certain compounds demonstrate the capacity to reduce gastric acid production and exhibit antimicrobial properties against *Helicobacter pylori*, thereby augmenting their gastro protective capabilities. Notably, these compounds frequently display multi-faceted therapeutic actions while maintaining relatively minimal toxicity profiles compared to synthetic pharmaceuticals [32]. Their natural origins and extensive utilization in traditional healing practices, including Ayurveda and Traditional Chinese Medicine, provide evidence for their safety and effectiveness. Additionally, developments in formulation science, particularly Nano encapsulation and targeted delivery mechanisms, are improving the bioavailability and therapeutic efficacy of these substances. In summary, phytochemicals offer a comprehensive therapeutic strategy for gastric ulcer management, targeting various pathogenic mechanisms while potentially providing superior benefits relative to conventional treatment modalities [33].

### **Rationale for Selecting Marmin and Imperatorin**

Marmin and imperatorin represent naturally occurring furanocoumarins that have garnered considerable scientific attention owing to their varied pharmacological characteristics and prospective therapeutic utility [34]. These substances are primarily extracted from medicinal flora including *Aegle marmelos* and *Angelica* species, traditionally employed in treating digestive ailments. The rationale for focusing on marmin and imperatorin in this review stems from multiple persuasive considerations. Initially, both substances are classified within the coumarin family, recognized for its extensive spectrum of biological functions, encompassing antioxidant, anti-inflammatory, antimicrobial, and cytoprotective activities. Such characteristics hold substantial relevance to the etiology and treatment of peptic ulcer pathology. Furthermore, recent preclinical investigations have revealed that marmin and imperatorin exhibit notable gastro protective properties [35]. These substances have demonstrated efficacy in diminishing gastric mucosal injury in experimental ulceration paradigms, including ethanol-mediated and NSAID-mediated ulcerative conditions. Their operational mechanisms encompass reactive oxygen species neutralization, inflammatory mediator suppression, mucus production enhancement, and mucosal barrier preservation [36]. Moreover, both substances have exhibited prospective antimicrobial efficacy against *Helicobacter pylori*, thereby augmenting their therapeutic significance. Their multifaceted mechanism of action renders them especially appealing as potential candidates for developing innovative gastro protective therapeutics. Notwithstanding these encouraging observations, comprehensive reviews synthesizing existing evidence regarding marmin and imperatorin within gastro protective contexts remain insufficient. Additionally, obstacles concerning their bioavailability and pharmacokinetic profiles require continued exploration [37]. Consequently, this review seeks to deliver an exhaustive and analytical assessment of the chemical, pharmacological, and therapeutic dimensions of marmin and imperatorin, emphasizing their promise as phytochemical alternatives for peptic ulcer disease management while establishing foundations for subsequent research and clinical implementation.

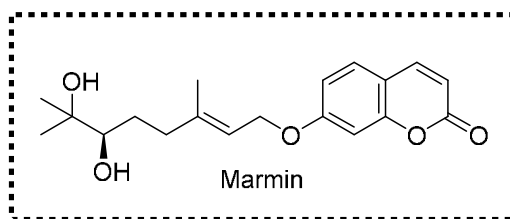
### **Classification of Coumarins**

Coumarins represent a varied group of naturally occurring benzopyrone compounds that are extensively found in higher plants, fungi, and certain bacterial species. From a structural perspective, these compounds feature a

characteristic fused benzene and  $\alpha$ -pyrone ring framework (2H-1-benzopyran-2-one), which functions as the fundamental structural foundation for multiple derivatives possessing unique biological properties [38]. According to their chemical modifications and structural variations, coumarins can be systematically organized into various groups, encompassing simple coumarins, furanocoumarins, pyranocoumarins, dicoumarins, and substituted coumarins. Simple coumarins represent the fundamental derivatives featuring modifications such as hydroxyl, methoxy, or alkyl substituents on the benzene moiety. These molecules demonstrate various biological properties, including antioxidant and anti-inflammatory activities. Furanocoumarins, representing an important subcategory, arise through the incorporation of a furan ring with the coumarin structure. According to the furan ring's location, these compounds are subsequently divided into linear (psoralen-type) and angular (angelicin-type) configurations [39-41]. Marmin and imperatorin are members of this subcategory, particularly demonstrating structural characteristics linked to increased biological potency. Pyranocoumarins are distinguished by the incorporation of a pyran ring into the coumarin framework, whereas dicoumarins comprise two coumarin moieties connected together, frequently demonstrating anticoagulant characteristics. Substituted coumarins include an extensive array of derivatives containing diverse functional groups, enhancing their pharmacological variability [42]. The categorization of coumarins extends beyond structural considerations to encompass pharmacological importance, as various subcategories demonstrate unique action mechanisms. Furanocoumarins, particularly, are recognized for their capacity to engage with biological membranes and enzymes, supporting their antimicrobial, anti-inflammatory, and cytoprotective characteristics [43]. Their planar configuration promotes interaction with nucleic acids and proteins, improving their biological effectiveness. Coumarins are synthesized through the phenylpropanoid pathway, deriving from phenylalanine. Enzymatic hydroxylation, lactonization, and additional modifications result in the production of various coumarin derivatives. Their prevalence in medicinal plants and their varied pharmacological characteristics have established them as significant prospects for drug discovery and development. In summary, the categorization of coumarins offers a systematic approach for comprehending their structural variability and biological capabilities, especially regarding gastro protection, where their antioxidant and anti-inflammatory characteristics serve essential functions [44].

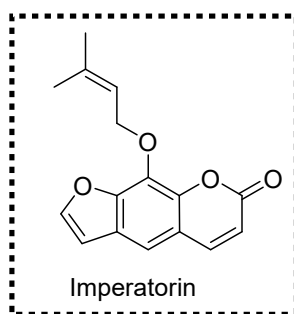
### Chemical Structure of Marmin

Marmin represents a naturally derived furanocoumarin compound primarily extracted from *Aegle marmelos*. From a structural standpoint, marmin is classified within the linear furanocoumarin family and exhibits a distinctive architecture featuring a coumarin core integrated with a furan moiety, accompanied by supplementary substituents that define its characteristic chemical and therapeutic attributes. The fundamental architecture of marmin encompasses a benzopyrone scaffold coupled with a strategically positioned furan ring, generating a planar conjugated framework [45]. This molecular configuration amplifies its capacity for interaction with biological substrates, encompassing enzymatic systems and cellular membrane structures. Marmin's structural identity is further characterized by the incorporation of functional moieties including methoxy groups and alkyl appendages, which modulate its lipophilic nature, dissolution characteristics, and systemic availability. The incorporation of a prenylated substituent within marmin's structure substantially enhances its pharmacological efficacy. Prenylation elevates the molecule's hydrophobic properties, promoting membrane association and improving permeation across biological interfaces. This characteristic proves particularly significant in gastro protective mechanisms, where mucosal membrane interaction is fundamental [46]. The extended conjugation network spanning the coumarin and furan components enables marmin to function as a potent antioxidant agent by neutralizing reactive species through resonance stabilization. This capability is instrumental in counteracting oxidative damage within gastric tissues. Furthermore, marmin's structural characteristics permit modulation of inflammatory cascades, thereby augmenting its therapeutic value. Regarding stereo chemical considerations, marmin may demonstrate particular conformational arrangements that impact its biological efficacy [47]. The three-dimensional orientation of substituent groups can influence target binding specificity and overall pharmacokinetic characteristics. In summary, marmin's molecular architecture is intrinsically connected to its physiological functions. The combination of its planar conjugated framework with hydrophobic modifications underlies its antioxidant, anti-inflammatory, and protective cellular properties, establishing it as a viable candidate for gastro protective therapeutic applications.



## Chemical Structure of Imperatorin

Imperatorin represents a significant furanocoumarin extensively found throughout plants of the Apiaceae family, especially within *Angelica* genera. This compound belongs to the linear furanocoumarin category and possesses the characteristic benzopyrone-furan fused framework common to this chemical class [48]. The molecular architecture of imperatorin features a coumarin backbone integrated with a furan moiety at positions 6 and 7, creating a planar and extensively conjugated framework. A notable structural characteristic of imperatorin involves an isoprenyl (prenyl) substituent connected to the coumarin core. This lipophilic group considerably increases its fat-soluble properties and promotes interaction with cellular membranes. The flat molecular geometry of imperatorin permits effective  $\pi$ - $\pi$  stacking with nucleic acids and proteins, thereby contributing to its varied biological effects. Its delocalized  $\pi$ -electron network enables ultraviolet light absorption and participation in photochemical processes, which represents a typical characteristic of furanocoumarin compounds. Imperatorin demonstrates potent antioxidant capabilities through its electron-donating capacity and free radical scavenging ability [49]. This functionality stems from the resonance stabilization afforded by its conjugated framework. Furthermore, the incorporation of functional moieties such as methoxy groups enhances its chemical reactivity and biological potency. The lipophilic character of imperatorin also affects its pharmacokinetic behavior, including uptake and tissue distribution. Although enhanced lipophilicity may improve membrane penetration, it can create difficulties regarding water solubility and bioavailability [50]. From a structural perspective, imperatorin is optimally configured for targeting essential molecular components involved in inflammatory and oxidative stress pathways. Research has demonstrated its capacity to suppress enzymes and signaling cascades linked to inflammatory reactions, establishing it as a promising therapeutic agent. In conclusion, imperatorin's chemical architecture, distinguished by its fused benzopyrone-furan framework and lipophilic substituents, is fundamental to its pharmacological properties, especially regarding gastric protection [51].



## Natural Sources (*Aegle marmelos*, *Angelica species*)

Marmin and imperatorin are primarily obtained from therapeutic plants that have undergone extensive utilization within conventional medical practices. *Aegle marmelos*, frequently referred to as bael, represents a prominent botanical species in Ayurvedic medicine and receives widespread application for managing digestive system ailments [52]. The fruit, foliage, and root systems of *Aegle marmelos* encompass numerous bioactive constituents, including coumarin derivatives such as marmin, which enhance its medicinal efficacy. *Angelica* genus, classified within the Apiaceae family, serves as an additional reservoir of furanocoumarins, notably imperatorin. These botanical specimens are typically distributed across Asian and European regions and have received implementation in traditional Chinese and European therapeutic systems due to their anti-inflammatory, pain-relieving, and digestive enhancement characteristics [53]. The presence of these compounds within medicinal flora emphasizes their safety profile and therapeutic promise. The recovery and purification of marmin and imperatorin from these natural sources encompasses diverse methodologies, including solvent-based extraction, chromatographic separation, and spectroscopic identification.

## Physicochemical Properties

The molecular characteristics of marmin and imperatorin significantly influence their pharmacokinetic profiles and clinical effectiveness. These compounds demonstrate moderate to elevated lipophilic nature owing to hydrophobic moieties, including prenyl substituents. While this attribute facilitates membrane permeation, it simultaneously restricts water solubility. Both substances present limited aqueous solubility, creating obstacles for oral absorption. Enhanced dissolution may be achieved through pharmaceutical approaches including nano-formulation techniques and solubility enhancers [54]. Under physiological environments, these compounds maintain stability yet experience hepatic biotransformation, predominantly via oxidative and conjugative enzymatic pathways. The molecular mass, polarity characteristics, and structural attributes of these molecules affect their ADME parameters. Stability and chemical reactivity represent critical determinants in their

biological target interactions. Comprehensive knowledge of the physicochemical attributes of marmin and imperatorin remains fundamental for formulation optimization and maximizing their therapeutic efficacy in gastric protection applications [55].

### Pathophysiology of gastric ulcers

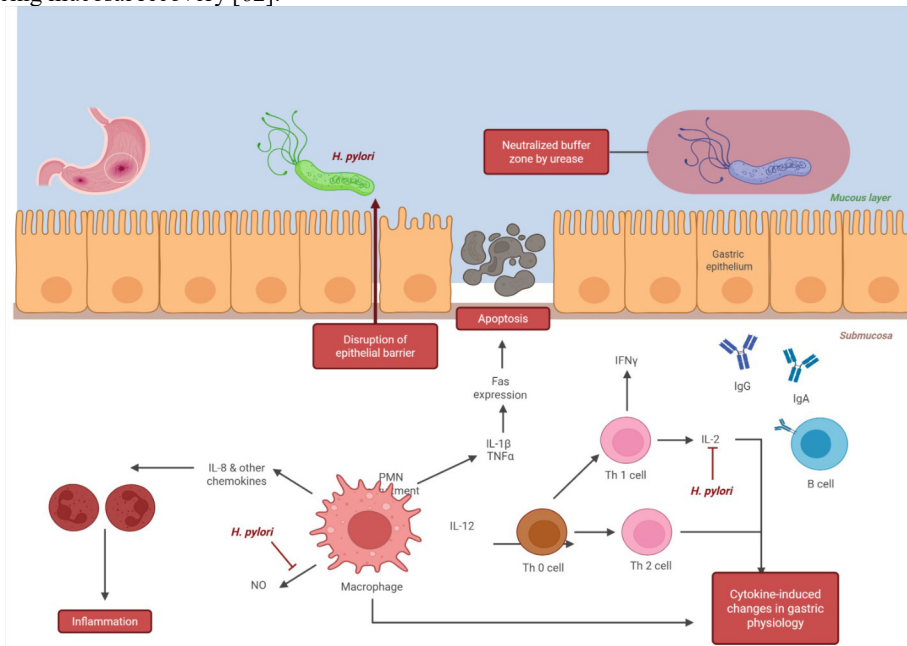
Gastric ulcer formation represents a complex pathological phenomenon resulting from the intricate balance between destructive luminal elements and weakened mucosal protective systems, consequently causing breakdown of gastric epithelial barrier function and subsequent tissue damage. The fundamental aspect of this mechanism involves gastric acid production, which serves vital physiological functions in digestion and antimicrobial protection under normal circumstances, yet becomes harmful when overproduced or when defensive mechanisms fail [56]. Parietal cells secrete gastric acid via  $H^+/K^+$ -ATPase proton pump activity, with regulation occurring through neural, endocrine, and paracrine mechanisms involving acetylcholine, gastrin, and histamine stimulation. Excessive gastric acid production or heightened mucosal acid sensitivity substantially contributes to ulcer development by promoting epithelial erosion and enabling pepsin activation, a proteolytic enzyme that subsequently degrades epithelial structures. Nevertheless, acid secretion alone cannot induce ulceration when mucosal defenses remain functional, suggesting involvement of supplementary pathogenic processes [57]. Oxidative stress constitutes a crucial element in this pathophysiology, marked by overproduction of reactive oxygen species including superoxide anions, hydroxyl radicals, and hydrogen peroxide, which exceed the capacity of endogenous antioxidant mechanisms such as superoxide dismutase, catalase, and glutathione systems. These reactive molecules cause lipid peroxidation, protein modification, and genomic damage, resulting in gastric mucosal cell apoptosis and necrosis. Oxidative stress additionally intensifies inflammatory processes and impairs microvascular function, thereby worsening mucosal damage [58].

Inflammatory processes represent an essential pathophysiological element in gastric ulcer formation, orchestrated by cascading pro-inflammatory cytokines, chemokines, and enzymatic mediators. Critical inflammatory substances including tumor necrosis factor- $\alpha$ , interleukins, and prostaglandins become elevated following mucosal damage, resulting in immune cell recruitment and activation, particularly neutrophils and macrophages. These cellular elements release supplementary reactive oxygen species, proteolytic enzymes, and inflammatory substances, establishing a continuous cycle of tissue destruction. Nuclear factor- $\kappa$ B activation further enhances inflammatory gene expression, promoting persistent inflammation and impaired healing processes. Moreover, cyclooxygenase enzyme inhibition, especially COX-1, through nonsteroidal anti-inflammatory drug administration reduces protective prostaglandin synthesis, compromising mucosal defense and enhancing ulcer susceptibility [59].

*Helicobacter pylori* infection represents a significant etiological component in gastric ulcer pathogenesis, as this gram-negative microorganism establishes gastric mucosal colonization and triggers chronic inflammatory responses. *H. pylori* demonstrates multiple virulence mechanisms, including urease, cytotoxin-associated gene A, and vacuolating cytotoxin A, which enable survival within the acidic gastric milieu and contribute to mucosal destruction. Urease facilitates urea conversion to ammonia, neutralizing gastric acidity and establishing optimal bacterial growth conditions. The organism adheres to epithelial surfaces and compromises intercellular junction integrity, increasing permeability and inflammation. Cytotoxin-associated gene A injection into host cells modifies cellular signaling mechanisms, enhancing inflammation and apoptosis, while vacuolating cytotoxin A causes cellular vacuolation and mitochondrial impairment. Chronic *H. pylori* presence results in persistent gastritis, potentially progressing to ulceration and occasionally gastric neoplasia. Additionally, the relationship between *H. pylori* colonization and host immune mechanisms leads to continuous inflammatory mediator production and oxidative stress generation, further intensifying mucosal damage [60].

Opposing these harmful elements, the gastric mucosa possesses a comprehensive protective mechanism aimed at preserving structural integrity and facilitating repair processes. This mucosal protection encompasses a physical barrier established through mucus and bicarbonate production, generating a protective gel coating that prevents direct exposure of acid and pepsin to epithelial surfaces. The epithelial cellular layer functions as a defensive barrier via tight junctions that control permeability and inhibit hydrogen ion back-diffusion. Sufficient mucosal circulation remains vital for supplying oxygen and nutrients, eliminating harmful metabolites, and sustaining cellular equilibrium [61]. Prostaglandins serve a critical function in strengthening mucosal protection by promoting mucus and bicarbonate production, preserving circulation, and facilitating epithelial restoration and regeneration. Furthermore, intrinsic antioxidant mechanisms safeguard the mucosa against oxidative injury through neutralization of reactive oxygen species. Growth factors and cytokines additionally support mucosal recovery by encouraging cellular proliferation, migration, and blood vessel formation. Nevertheless, when these protective processes become impaired through factors including NSAID usage, alcohol intake, tobacco use, stress, or infectious agents, the equilibrium favors harmful elements, resulting in mucosal damage and ulcer development. The pathophysiology of gastric ulcers therefore represents a dynamic disequilibrium between destructive and defensive forces, encompassing interconnected mechanisms of acid production, oxidative stress, inflammation, microbial infection, and compromised mucosal protection. Comprehending these processes

remains fundamental for developing effective treatment approaches focused on reestablishing this equilibrium and enhancing mucosal recovery [62].



**Fig.2:** Interaction of *H. pylori* with gastric epithelial cells and immune response

## Mechanisms of Gastro protective Action

### Antioxidant Activity

The function of antioxidant mechanisms is fundamental to gastric protection through the reduction of oxidative stress, which contributes significantly to damage of the gastric mucosal lining. During periods of stress, inflammatory responses, and contact with ulcer-inducing substances such as ethanol and NSAIDs, reactive oxygen species (ROS) including superoxide anions, hydroxyl radicals, and hydrogen peroxide are produced. These ROS cause lipid peroxidation, protein deterioration, and DNA breakdown, resulting in cellular damage and programmed cell death. Gastroprotective substances like marmin and imperatorin demonstrate antioxidant properties through direct neutralization of free radicals and strengthening of intrinsic antioxidant protective mechanisms, encompassing superoxide dismutase, catalase, and glutathione. Through the mitigation of oxidative harm, these substances assist in preserving both structural and functional characteristics of gastric mucosal tissue while facilitating tissue repair processes [63].

### Anti-inflammatory effects

Inflammatory processes play a pivotal role in gastric ulcer initiation and advancement. Gastroprotective compounds demonstrate anti-inflammatory properties through the regulation of essential inflammatory cascades and signaling molecules. Substances such as marmin and imperatorin have demonstrated the capacity to suppress pro-inflammatory cytokine synthesis, encompassing TNF- $\alpha$ , IL-1 $\beta$ , IL-6, and prostaglandins. These agents also prevent the stimulation of transcriptional regulators like NF- $\kappa$ B, which controls inflammatory gene expression. Furthermore, such compounds may block enzymatic activity of COX and LOX, consequently diminishing inflammatory mediator production. Via these pathways, they mitigate inflammatory responses, minimize tissue injury, and promote mucosal repair processes [64].

### Cytoprotective mechanisms

Cytoprotection encompasses the capacity of compounds to safeguard gastric epithelial cells against damage while not necessarily modifying gastric acid production. Marmin and imperatorin augment cytoprotective mechanisms through membrane stabilization, maintenance of epithelial structural integrity, and inhibition of programmed cell death. These compounds facilitate the preservation of intercellular tight junction complexes, consequently diminishing mucosal permeability and inhibiting the retrograde diffusion of hydrogen ions. Additionally, these substances may enhance endogenous prostaglandin synthesis, which serves a crucial function in sustaining mucosal protective mechanisms. Through the reinforcement of cellular durability and

reparative processes, cytoprotective compounds contribute to ulcer prevention and facilitate accelerated tissue regeneration [65].

### **Modulation of gastric acid secretion**

Heightened gastric acid production represents an aggressive element in ulcer formation. Stomach-protective agents can regulate acid production through diverse mechanisms, such as blocking the H<sup>+</sup>/K<sup>+</sup>-ATPase proton pump, reducing histamine discharge, and disrupting gastrin-mediated signaling cascades. Marmin and imperatorin may indirectly diminish acid production by influencing signaling networks that control parietal cell stimulation. Through decreasing acid generation or minimizing mucosal susceptibility to acid exposure, these compounds assist in reestablishing equilibrium between harmful and protective elements within the gastric milieu, consequently preventing tissue injury [66].

### **Enhancement of mucus production**

The mucus coating represents an essential component of the gastric mucosal protective mechanism, functioning as a physical shield that safeguards epithelial tissue from acidic conditions, pepsin, and other detrimental substances. Gastroprotective compounds augment mucus synthesis and release, thus reinforcing this defensive barrier. Marmin and imperatorin potentially promote the discharge of mucus and bicarbonate, forming a gel-like coating that buffers acidity and avoids direct interaction with the mucosal interface. Enhanced mucus synthesis additionally supports epithelial restoration and renewal, facilitating ulcer recovery and prophylaxis [67].

### **Anti Helicobacter pylori activity**

*Helicobacter pylori* infection represents a primary causative agent in the pathogenesis of gastric ulceration. Gastroprotective agents possessing antimicrobial properties against *H. pylori* may substantially facilitate ulcer prophylaxis and therapeutic management. Marmin and imperatorin have exhibited promising inhibitory potential against *H. pylori* via various mechanisms including bacterial membrane disruption, urease enzyme suppression, and interference with bacterial adherence to gastric epithelial surfaces. Through diminishing bacterial establishment and concurrent inflammatory responses, these compounds facilitate the prevention of mucosal injury and support tissue repair processes. The combined antimicrobial and anti-inflammatory properties of these agents augment their therapeutic efficacy in addressing *H. pylori*-related gastric pathologies [68].

### **Synergistic and comparative effects**

The assessment of combined and comparative impacts of bioactive plant compounds is crucial for comprehending their healing capabilities and enhancing their utilization in multifaceted conditions like gastric ulcer formation. As structurally similar furanocoumarin derivatives, marmin and imperatorin demonstrate both shared and unique pharmacological characteristics that enhance their stomach-protective effectiveness. Comparative investigations and research examining their joint actions, along with their relationships with additional phytochemicals, offer important understanding regarding their multiple-target pathways and possible benefits compared to individual compound treatments [69].

### **Marmin vs Imperatorin**

Marmin and imperatorin possess a shared coumarin-derived structural foundation, yet minor modifications in their molecular architecture lead to distinct pharmacokinetic characteristics and biological effects. Marmin, distinguished by its particular substitution arrangement and prenyl chain attachment, demonstrates robust cellular protective and antioxidant capabilities. This compound has been especially recognized for its capacity to strengthen mucosal protective systems, encompassing enhanced mucus production and maintenance of epithelial barrier function. The relatively equilibrated hydrophilic-lipophilic nature of marmin may promote its engagement with both water-soluble and fat-soluble elements within gastric mucosal tissue, thereby supporting its comprehensive protective actions [70].

Conversely, imperatorin, possessing heightened lipophilic characteristics attributed to its isoprenyl moiety, exhibits enhanced membrane penetration capacity and powerful anti-inflammatory effects. Imperatorin has demonstrated effective suppression of pro-inflammatory factors and cellular signaling cascades, notably NF- $\kappa$ B and COX pathways, thus diminishing inflammation-related mucosal injury. Furthermore, imperatorin displays significant antimicrobial efficacy, especially against *Helicobacter pylori*, which increases its therapeutic significance in peptic ulcer treatment. From a comparative perspective, although both molecules demonstrate antioxidant and anti-inflammatory capabilities, marmin proves more efficient in strengthening mucosal protection and cellular defense, while imperatorin exhibits superior effectiveness in regulating inflammatory mechanisms and microbial suppression. These synergistic characteristics indicate that each molecule addresses

distinct components of ulcer development, rendering them individually beneficial and collectively advantageous for therapeutic implementation [71].

### **Combined Effects**

The concurrent administration of marmin and imperatorin may yield synergistic outcomes, augmenting gastro protective effectiveness beyond the capabilities of individual compounds. Synergism occurs when multiple agents interact to amplify their respective therapeutic effects, typically through complementary action mechanisms. Within gastric ulceration contexts, where diverse pathogenic processes are implicated, such multi-target strategies prove especially beneficial. Combining marmin's cytoprotective and mucus-stimulating characteristics with imperatorin's robust anti-inflammatory and antimicrobial properties could generate more comprehensive gastric mucosal protection. While marmin fortifies the mucosal defense system and mitigates oxidative injury, imperatorin concurrently attenuates inflammatory pathways and prevents *H. pylori* establishment. This coordinated approach targets both causative factors and consequences of mucosal damage. Research investigations examining comparable phytochemical combinations have shown that synergistic interactions can enhance antioxidant capabilities, improve inflammatory mediator regulation, and better maintain mucosal structural integrity. Despite limited direct research on marmin-imperatorin combinations, their complementary pharmacological characteristics strongly indicate synergistic gastro protective potential. Additionally, utilizing combined phytochemicals may permit reduced individual concentrations, minimizing toxicity risks and enhancing safety parameters. This consideration becomes particularly relevant for long-term treatment of chronic disorders like peptic ulcer disease. Creating combination preparations, including botanical extracts incorporating both constituents, constitutes a promising domain for future investigation and therapeutic advancement [72].

### **Interaction with Other Phytochemicals**

Beyond their individual contributions, marmin and imperatorin may engage with additional phytochemicals found in therapeutic plants, resulting in enhanced or synergistic gastro protective benefits. Botanical formulations typically comprise intricate combinations of bioactive constituents, encompassing flavonoids, alkaloids, tannins, and terpenoids, with each component contributing to the comprehensive therapeutic efficacy. Flavonoids, recognized for their antioxidant and anti-inflammatory characteristics, may augment the radical-scavenging capabilities of coumarins. The simultaneous presence of flavonoids alongside marmin and imperatorin in botanical extracts can yield strengthened defense mechanisms against oxidative damage and inflammatory processes. Likewise, tannins support mucosal defense by establishing a protective barrier across the gastric epithelium, potentially complementing marmin's mucus-promoting properties. Alkaloids and terpenoids may similarly interact with coumarins to regulate gastric acid production, enhance mucosal circulation, and provide antimicrobial benefits. These interactions can generate comprehensive therapeutic outcomes, simultaneously targeting various components of ulcer development. This approach corresponds with traditional medicine philosophies, where complete plant extracts are employed instead of individual compounds to achieve superior therapeutic results. Nevertheless, consideration must be given to the possibility that phytochemical interactions may produce antagonistic outcomes or affect pharmacokinetic characteristics, including absorption and metabolic processes. Consequently, systematic investigations are essential to assess the characteristics and magnitude of these interactions and to determine optimal therapeutic combinations. Progress in analytical and pharmacological methodologies, including metabolomics and network pharmacology, is enhancing comprehension of phytochemical interactions and their effects on biological systems. These methodologies can assist in identifying synergistic combinations and developing effective multi-constituent preparations [73].

### **Safety and Toxicological Profile**

The toxicological assessment and safety evaluation of bioactive substances represents a fundamental component in establishing their appropriateness for clinical therapeutic use. Marmin and imperatorin, being naturally derived furanocoumarins, have exhibited encouraging pharmacological properties; nevertheless, comprehensive safety characterization remains essential to guarantee their secure and efficacious application in gastric protective treatments. Preliminary toxicological investigations indicate that both marmin and imperatorin demonstrate comparatively minimal acute toxicity when delivered at clinically relevant concentrations. Within experimental animal studies, these substances have exhibited substantial safety margins, with no notable mortality or serious adverse reactions documented at concentrations providing gastro protective advantages. Behavioral modifications, weight fluctuations, and tissue pathological changes in experimental subjects typically remained within acceptable parameters, suggesting favorable tolerance profiles. Nevertheless, similar to numerous plant-derived chemicals, toxic manifestations may emerge at elevated concentrations or extended administration periods, requiring meticulous dosage refinement. A significant factor in the safety assessment of furanocoumarins, particularly imperatorin, involves their capacity for inducing phototoxic reactions [74]. Through their UV radiation absorption properties, furanocoumarins can generate reactive metabolites that

interact with cellular macromolecules, potentially resulting in cutaneous photosensitization and genetic material damage following UV exposure. While this phenomenon primarily concerns dermatological applications, it emphasizes the necessity of comprehending the comprehensive toxicological ramifications of these substances. Hepatic biotransformation constitutes another essential element affecting the safety characteristics of marmin and imperatorin. These substances undergo primary hepatic metabolism via cytochrome P450 enzymatic pathways, presenting possibilities for drug-botanical interactions through enzymatic inhibition or activation. Imperatorin specifically has been documented to influence CYP450 enzymatic activity, potentially modifying the biotransformation of simultaneously administered pharmaceuticals, resulting in either enhanced toxicity or diminished therapeutic effectiveness [75]. Consequently, prudence is advised when combining these substances with other therapeutic agents. Long-term toxicity information for marmin and imperatorin remains insufficient, necessitating extended safety investigations to completely characterize their toxicological behaviors. Factors including mutagenic potential, reproductive safety, and oncogenic risk have received inadequate research attention, constituting a knowledge deficiency. Furthermore, variations in botanical sources, isolation procedures, and preparation methodologies may impact the safety and reliability of these compounds. Notwithstanding these constraints, the natural derivation of marmin and imperatorin and their traditional medicinal applications suggest acceptable safety characteristics when utilized properly. Developments in delivery technologies, including nanoencapsulation and selective targeting mechanisms, may additionally improve their safety through enhanced bioavailability and decreased systemic distribution. In summary, marmin and imperatorin demonstrate promising safety characteristics in preliminary studies, exhibiting minimal acute toxicity and acceptable tolerance at therapeutic concentrations. However, potential issues concerning phototoxic reactions, pharmaceutical interactions, and insufficient chronic toxicity information underscore the requirement for thorough toxicological assessments. Subsequent investigations, including properly structured clinical trials, are crucial for confirming their safety and enabling their clinical implementation [76].

### **Clinical perspectives and future directions**

The standardization and quality assurance of phytochemical compounds present substantial obstacles in their clinical implementation. Variations in botanical sources, growing environments, isolation techniques, and preparation methodologies may result in fluctuations in bioactive component concentrations and efficacy. Consequently, establishing uniform extraction protocols and comprehensive quality control measures is imperative for ensuring consistency and dependability in therapeutic applications. Regulatory frameworks are equally important, as the categorization of these substances as nutraceuticals or medicinal products will determine their authorization processes, documentation requirements, and clinical utilization. Regarding mechanistic understanding, additional investigation is required to clarify the precise molecular networks through which marmin and imperatorin demonstrate their gastric protective properties. Sophisticated methodologies including genomic analysis, protein profiling, and metabolic mapping can offer enhanced comprehension of their biological system interactions and reveal potential indicators of therapeutic efficacy. This knowledge would prove instrumental in developing precision therapies and individualized treatment approaches. Furthermore, safety assessment remains paramount, especially concerning prolonged administration, possible botanical-pharmaceutical interactions, and demographic-specific reactions. Particular focus should be directed toward susceptible groups, encompassing geriatric patients, expectant mothers, and persons with concurrent medical conditions. Extensive toxicity investigations and post-approval monitoring will be required to guarantee their secure incorporation into medical practice. In summary, marmin and imperatorin demonstrate considerable potential as innovative gastric protective compounds with diverse action mechanisms. Nevertheless, their effective clinical translation will require addressing obstacles concerning bioavailability enhancement, product standardization, regulatory compliance, and clinical verification. Subsequent research should emphasize connecting preclinical discoveries with clinical implementation through systematic trials, novel delivery approaches, and enhanced mechanistic comprehension. Through sustained scientific exploration and technological progress, these plant-derived compounds possess the capacity to make substantial contributions to developing improved and safer therapeutic options for gastric ulcer treatment.

### **Conclusion**

To summarize, gastric ulceration continues to represent a major worldwide health challenge, distinguished by an intricate balance between damaging elements such as gastric acid production, oxidative damage, inflammatory responses, and bacterial infections, versus the defensive capabilities of the gastric lining. Although established pharmaceutical treatments including proton pump inhibitors, H<sub>2</sub>-receptor antagonists, and antibiotic protocols for *Helicobacter pylori* elimination are accessible, their prolonged administration frequently correlates with side effects, therapeutic resistance, and ulcer recurrence. These constraints emphasize for more secure, efficacious, and multi-faceted treatment strategies capable of addressing the diverse nature of ulcer development. Within this framework, plant-derived bioactive compounds have surfaced as encouraging alternatives or supplementary treatments to standard therapies. Among these, the furanocoumarins marmin and imperatorin have attracted

substantial interest owing to their varied pharmacological characteristics and potential gastric protective benefits. This review has systematically examined the chemical features, botanical origins, physicochemical attributes, and therapeutic mechanisms of these substances. Both marmin and imperator in exhibit notable antioxidant capabilities, efficiently neutralizing reactive oxygen molecules and strengthening inherent antioxidant systems, thus reducing oxidative stress-related mucosal injury. Moreover, their anti-inflammatory characteristics, facilitated through suppression of inflammatory mediators and crucial signaling cascades including NF- $\kappa$ B, support inflammation reduction and mucosal recovery promotion. These compounds also display protective cellular effects by promoting mucus synthesis, preserving epithelial structure, and regulating gastric acid release, thereby reestablishing equilibrium between harmful and protective elements within the gastric milieu. Their possible antimicrobial effectiveness against *Helicobacter pylori* further enhances their therapeutic significance in peptic ulcer management. Research from laboratory and animal studies confirms their effectiveness in decreasing gastric injuries and improving mucosal protection across diverse experimental paradigms, encompassing ethanol-induced, NSAID-induced, and stress-induced ulcerations. The comparative and combined assessment of marmin and imperator in indicates that their complementary action mechanisms may provide superior gastro protective advantages when utilized together or within multi-ingredient botanical preparations. Additionally, their comparatively acceptable safety characteristics and natural derivation render them appealing options for extended use, though additional toxicological and clinical assessments to confirm their safety and effectiveness in human subjects. Notwithstanding these encouraging results, various obstacles persist, including insufficient clinical evidence, bioavailability concerns, and requirements for standardized preparations. Overcoming these obstacles through sophisticated delivery mechanisms, thorough clinical investigations, and detailed mechanistic research will be crucial for converting preclinical findings into clinical applications. In summary, marmin and imperator in constitute encouraging phytochemical prospects for developing innovative gastro protective treatments. Their multi-targeted effects, coupled with their potential for incorporation into current therapeutic approaches, establish them as significant contributors to future progress in gastric ulcer disease management.

## References

1. Gopakumar G, Ramesh B, Michaelson DI, Kunjiappan S, Kabilan SJ, Pavadai P. In silico analysis of phytocompounds from aegle marmelos against potential targets of irritable bowel syndrome. *Journal of Computational Biophysics and Chemistry*. 2023 Nov 17; 22(07):863-79.
2. Asnaashari S, Dastmalchi S, Javadzadeh Y. Gastroprotective effects of herbal medicines (roots). *International Journal of Food Properties*. 2018 Jan 1; 21(1):902-20.
3. Shetty A, Fernandes L, Shambhavi D, Mahadev M, Dubey A. Phytochemical and pharmacological profile of *Aegle marmelos* (L.) Correa: A comprehensive review of therapeutic potential, mechanisms of action, and translational relevance. *Journal of Applied Pharmaceutical Science*. 2026 Jan 5; 16(2):006-18.
4. Tiwari N, Kaushik AC, Rajdev B, Naidu VG, Shanker K. Chemo-preventive and anti-inflammatory potential of *Bilvamooola* [*Aegle marmelos* (L.) Correa] root extract and its bioactive: Chemical standardization, in-vitro and in-silico validation. *Journal of Ethnopharmacology*. 2026 Mar 6:121448.
5. Shajil UK, Jaleel UC, Sathish S, Sandesh EP, Sujith A, Nair BG. Knowledge graph integration of clustered medicinal plants, molecules, diseases, and targets. *Computational Biology and Chemistry*. 2026 Jan 8:108895.
6. Chandran NN, Thomas RP. Virtual Screening for Lead Molecules in *Aegle Marmelos* (L.) Correa. on Mutated Ras Proteins. *Biosciences Biotechnology Research Asia*. 2026 Feb 12; 23(1).
7. Shah B, Solanki N. Exploring the bioactive properties and mechanism of *Aegle marmelos* in the treatment of inflammatory bowel disease through network pharmacology and a molecular docking approach. *American Journal of Translational Research*. 2025 Feb 15; 17(2):748.
8. Dhamne S, Shinde P, Agrawal SA. IN-SILICO PHARMACOKINETICS PREDICTION OF MAJOR COUMARINS PRESENT IN AEGLE MARMELOS L. *Journal of Research in Pharmacy*. 2023 Jul 2;27:1-3.
9. Abd-Alla HI, Ibrahim Fouad G, Ahmed KA, Shaker K. Alloimperatorin from Ammi majus fruits mitigates Piroxicam-provoked gastric ulcer and hepatorenal toxicity in rats via suppressing oxidative stress and apoptosis. *Biomarkers*. 2022 Nov 17; 27(8):727-42.
10. Gajbhiye N, Makasana J, Thorat T. Simultaneous determination of marmin, skimmianine, umbelliferone, psoralene, and imperator in in the root bark of *Aegle marmelos* by high-performance thin-layer chromatography. *JPC-Journal of Planar Chromatography-Modern TLC*. 2012 Aug 1;25(4):306-13.
11. Shah B, Solanki N. Exploring the bioactives and the mechanism of *Aegle marmelos* in the treatment of inflammatory bowel disease through network pharmacology and molecular docking approach.

12. Yogesh M, Kumar AK. Phytochemicals and phytotherapeutic studies on different parts of *Aegle marmelos*: A critical overview. *Research Journal of Biotechnology*. 2024 Jan; 19:1.
13. Upadhyay RK. Bel plant: A source of pharmaceuticals and ethno medicines. *International Journal of Green Pharmacy (IJGP)*. 2015 Dec 14; 9(4).
14. Thakur M, Kaur T, Sobti RC. Exploring pharmacological potential of *Aegle marmelos*: integrating traditional knowledge with modern physiology and molecular biology. *Physiology and Molecular Biology of Plants*. 2025 Apr; 31(4):521-43.
15. Rahman S, Parvin R. Therapeutic potential of *Aegle marmelos* (L.)-An overview. *Asian Pacific journal of tropical disease*. 2014 Feb 1; 4(1):71-7.
16. Gupta E, Shakyawar S, Sundaram S. Therapeutic and nutraceutical potential of bioactive compounds in *Aegle marmelos* (L.): An overview. *Current Nutrition & Food Science*. 2019 Jun 1; 15(4):306-17.
17. Choudhary Y, Saxena A, Kumar Y, Kumar S, Pratap V. Phytochemistry, pharmacological and traditional uses of *Aegle marmelos*. *Pharmaceutical and Biosciences Journal*. 2017 Oct 20:27-33.
18. Kumawat N, Pantwalawalkar J, Vispute Y, Tade R, Nangare S. An overview on phytochemistry, pharmacology, pharmaceutical, traditional and economical aspects of *aegle marmelos*. *Asian Journal of Pharmacy and Technology*. 2021; 11(2):166-74.
19. Dutta A, Lal N, Naaz M, Ghosh A, Verma R. Ethnological and Ethno-medicinal importance of *Aegle marmelos* (L.) *Corr (Bael)* among indigenous people of India. *American journal of ethnomedicine*. 2014; 1(5):290-312.
20. Singh P, Garg A, Srivastava RK. The phytochemistry and therapeutical values of *Aegle marmelos* L: A review. *MEDICINAL PLANTS-INTERNATIONAL JOURNAL OF PHYTOMEDICINES AND RELATED INDUSTRIES*. 2024; 16(3):401-9.
21. Ahmed SR, Rabbee MF, Roy A, Chowdhury R, Banik A, Kubra K, Hassan Chowdhury MM, Baek KH. Therapeutic promises of medicinal plants in Bangladesh and their bioactive compounds against ulcers and inflammatory diseases. *Plants*. 2021 Jul 1; 10(7):1348.
22. Zaib S, Javed H, Ogaly HA, Khan I. Evaluating the anti-gastric ulcer activity of *Aegle marmelos*: A brief review. *ChemistrySelect*. 2023 Mar 13; 8(10):e202204193.
23. Nugroho AE, Wijayanti A, Mutmainah M, Susilowati R, Rahmawati N. Gastroprotective effect of combination of hot water extracts of Licorice (*Glycyrrhiza glabra*), Pulasari Stem Bark (*Alyxia reinwardtii*), and Sembung Leaf (*Blumea balsamifera*) against aspirin-induced gastric ulcer model rats. *Journal of evidence-based complementary & alternative medicine*. 2016 Oct; 21(4):NP77-84.
24. Li W, Wang X, Zhi W, Zhang H, He Z, Wang Y, Liu F, Niu X, Zhang X. The gastro protective effect of nobiletin against ethanol-induced acute gastric lesions in mice: impact on oxidative stress and inflammation. *Immunopharmacology and immunotoxicology*. 2017 Nov 2; 39(6):354-63.
25. Cherrada N, Chemsal AE, Gheraissa N, Laib I, Gueboudji Z, EL-Shazly M, Zaater A, Abid A, Sweilam SH, Emran TB, Nani S. Gastroprotective efficacy of North African medicinal plants: A review on their therapeutic potential for peptic ulcers. *Food Science & Nutrition*. 2024 Nov; 12(11):8793-824.
26. Duan WQ, Cai MC, Ma QQ, Huang P, Zhang JH, Wei TF, Shang D, Leng AJ, Qu JL. Exploring the chemical components of Kuanchang-Shu granule and its protective effects of postoperative ileus in rats by regulating AKT/HSP90AA1/eNOS pathway. *Chinese Medicine*. 2024 Feb 21; 19(1):29.
27. Hendawy MS, Hashem MM, Zaki AA, Salah El Dine R, El-Halawany AM. Geographical Distribution, Ethnomedicinal Uses, Phytochemistry, and Potential Health Benefits of Genus *Aster*: A Comprehensive Review. *Egyptian Journal of Chemistry*. 2026 May 1; 69(5):203-31.
28. Majeed W, Khaliq T, Aslam B, Khan JA, Iftikhar A. Medicinal plants with gastro protective potential. *Bangladesh Journal of Pharmacology*. 2015 Jul 9; 10(3):588-603.
29. Zayachkivska OS, Konturek SJ, Drozdowicz D, Konturek PC, Brzozowski T, Ghegotsky MR. Gastroprotective effects of flavonoids in plant extracts. *Journal of Physiology and Pharmacology. Supplement*. 2005; 56(1):219-31.
30. Goswami S, Karmakar S, Brahmachari K, Sarkar P, Sharma N, Ghosh M, Maji S, Koley S, Shaw S, Goswami D. Gastroprotective Potential of Indian Medicinal Plants-A Comprehensive Review. *Mathews Journal of Gastroenterology & Hepatology*. 2024 Jun 3; 9(1):1-37.
31. Cherrada N, Chemsal AE, Gheraissa N, Laib I, Gueboudji Z, EL-Shazly M, Zaater A, Abid A, Sweilam SH, Emran TB, Nani S. Gastroprotective efficacy of North African medicinal plants: A review on their therapeutic potential for peptic ulcers. *Food Science & Nutrition*. 2024 Nov; 12(11):8793-824.

32. Ben Mansour R, Wasli H, Serairi-Beji R, Bourgou S, Dakhlaoui S, Selmi S, Khamessi S, Hammami M, Ksouri R, Megdiche-Ksouri W. In vivo gastro protective effect and biological potentialities of six Tunisian medicinal plants using multivariate data treatment. *Plant Biosystems-An International Journal Dealing With all Aspects of Plant Biology*. 2022 Jan 2; 156(1):152-63.
33. Abdelhafez OH, Shady NH, Hisham M, Essa awad K, Hashem RA, Fouad RA, Ahmed H, Hassan RK, Gomaa RS, Abdelmohsen UR. A comprehensive overview on the role of phytochemicals as gastro protective agents. *Natural Product Communications*. 2025 Apr; 20(4):1934578X251329870.
34. Asnaashari S, Dastmalchi S, Javadzadeh Y. Gastroprotective effects of herbal medicines (roots). *International Journal of Food Properties*. 2018 Jan 1; 21(1):902-20.
35. de Lira Mota KS, Dias GE, Pinto ME, Luiz-Ferreira Â, Monteiro Souza-Brito AR, Hiruma-Lima CA, Barbosa-Filho JM, Batista LM. Flavonoids with gastro protective activity. *Molecules*. 2009 Mar 3; 14(3):979-1012.
36. de Oliveira Leite G, Penha AR, da Silva GQ, Colares AV, Rodrigues FF, Costa JG, Cardoso AL, Campos AR. Gastroprotective effect of medicinal plants from Chapada do Araripe, Brazil. *J Young Pharm*. 2009; 1(1):54.
37. El-Din MI, Youssef FS, Said RS, Ashour ML, Eldahshan OA, Singab AN. Chemical constituents and gastro-protective potential of *Pachira glabra* leaves against ethanol-induced gastric ulcer in experimental rat model. *Inflammopharmacology*. 2021 Feb; 29(1):317-32.
38. de Almeida AL, Beleza ML, Campos A, da Rosa RL, de Andrade SF, Filho VC, Nesello LA. Phytochemical profile and gastro protective potential of *Myrcianthes pungens* fruits and leaves. *Nutrire*. 2017 Jul 20; 42(1):24.
39. Majeed W, Khaliq T, Aslam B, Khan JA, Iftikhar A. Medicinal plants with gastro protective potential. *Bangladesh Journal of Pharmacology*. 2015 Jul 9; 10(3):588-603.
40. Kumar B, Pandey HK, Kaur R, Mishra S, Kalam MA. Phytochemical profiling, antioxidant capacity, acute toxicity, and gastro protective potential of *Angelica glauca* root: A promising high-altitude medicinal herb. *Fitoterapia*. 2025 Jun 1; 183:106565.
41. Abdelhafez OH, Shady NH, Hisham M, Essa awad K, Hashem RA, Fouad RA, Ahmed H, Hassan RK, Gomaa RS, Abdelmohsen UR. A comprehensive overview on the role of phytochemicals as gastro protective agents. *Natural Product Communications*. 2025 Apr; 20(4):1934578X251329870.
42. SANTOS LD, Campos A, Cechinel Filho V, Nesello LA. Phytochemical profile and gastro protective activity of *Eugenia mattosii* fruits. *Arquivos de Gastroenterologia*. 2018; 55(02):138-41.
43. Raafat K, El-Darra N, Saleh FA. Gastroprotective and anti-inflammatory effects of *Prunus cerasus* phytochemicals and their possible mechanisms of action. *Journal of Traditional and Complementary Medicine*. 2020 Jul 1; 10(4):345-53.
44. Ben Mansour R, Wasli H, Serairi-Beji R, Bourgou S, Dakhlaoui S, Selmi S, Khamessi S, Hammami M, Ksouri R, Megdiche-Ksouri W. In vivo gastro protective effect and biological potentialities of six Tunisian medicinal plants using multivariate data treatment. *Plant Biosystems-An International Journal Dealing With all Aspects of Plant Biology*. 2022 Jan 2; 156(1):152-63.
45. Enciso-Roca EC, Arroyo-Acevedo JL, Común-Ventura PW, Tinco-Jayo JA, Aguilar-Felices EJ, Ramos-Meneses MB, Carrera-Palao RE, Herrera-Calderon O. The Phytochemical Profile and Antioxidant and Gastroprotective Effects of Three Varieties of *Chenopodium quinoa* Willd. Sprouts Cultivated in Peru. *Scientia Pharmaceutica*. 2025 Feb 13; 93(1):10.
46. Elshamy AI, Farrag AR, Ayoub IM, Mahdy KA, Taher RF, Gendy AE, Mohamed TA, Al-Rejaie SS, Ei-Amier YA, Abd-ElGawad AM, Farag MA. UPLC-qTOF-MS phytochemical profile and antiulcer potential of *Cyperus conglomeratus* Rottb. alcoholic extract. *Molecules*. 2020 Sep 15; 25(18):4234.
47. Said A, El-Fishawy AM, El-Shenawy S, Hawas UW, Aboelmagd M. Hepatoprotective and gastro protective studies of *Terminalia arjuna* leaves extract and phytochemical profile. *Banat's Journal of Biotechnology*. 2014 Jul 1; 5(10).
48. Sharifi-Rad M, Fokou PV, Sharopov F, Martorell M, Ademiluyi AO, Rajkovic J, Salehi B, Martins N, Iriti M, Sharifi-Rad J. Antiulcer agents: From plant extracts to phytochemicals in healing promotion. *Molecules*. 2018 Jul 17; 23(7):1751.
49. Sen S, Chakraborty R, De B, Mazumder J. Plants and phytochemicals for peptic ulcer: An overview. *Pharmacognosy reviews*. 2009 Jul 1; 3(6):270.
50. Alsabri SG, Rmeli NB, Zetrini AA, Mohamed SB, Meshri MI, Aburas KM, Bensaber SM, Mrema IA, Mosbah AA, Allahresh KA, Hermann A. Phytochemical, anti-oxidant, anti-microbial, anti-inflammatory

- and anti-ulcer properties of *Helianthemum lippii*. Journal of Pharmacognosy and Phytochemistry. 2013 Jul 1; 2(2).
51. Farrag EK, Kassem ME, Bayoumi D, Shaker SE, Afifi MS. Phytochemical study, phenolic profile and antigastric ulcer activity of *Morus macroura* Miq. fruits extract. Journal of Applied Pharmaceutical Science. 2017 May 30; 7(5):152-60.
  52. Parmar NS, Parmar S. Anti-ulcer potential of flavonoids. Indian Journal of physiology and pharmacology. 1998 Jul 1; 42:343-51.
  53. Ukwubile CA, Bingari MS, Mathias SN. Phytochemical Profiles and Toxicological Evaluation of a Nigerian Polyherbal Antiulcer Powder Derived from Aquatic Plants: Implications for Human Health. SPC J. Med. Healthc. 2025; 1(3):153-66.
  54. Shahzad N, Ibrahim IA, Alzahrani AR, Al-Ghamdi SS, Alanazi IM, Ahmad MP, Singh AK, Alruqi MA, Shahid I, Equbal A, Azlina MF. A comprehensive review on phytochemicals as potential therapeutic agents for stress-induced gastric ulcer. Journal of Umm Al-Qura University for Applied Sciences. 2024 Dec; 10(4):793-808.
  55. Abdu H, Ahmad FB, Adamu AU. Phytochemical Screening, Proximate Analysis and Anti-ulcer Activity of Methanolic Seed Extract of *Citrullus lanatus*. African Journal of Agricultural Science and Food Research. 2023 Dec 31; 13(1):42-50.
  56. Singh SE, Balakrishnan M. Phytochemical Profile and Anti-ulcer Activities of Extracts of Unripen Fruits of *Psidium Guajava* Linn by Ethanol In-duced Ulcer Method. International Journal of Pharmaceutics and Drug Analysis. 2016; 4(6):310-7.
  57. Gajbhiye N, Makasana J, Thorat T. Simultaneous determination of marmin, skimmianine, umbelliferone, psoralene, and imperatorin in the root bark of *Aegle marmelos* by high-performance thin-layer chromatography. JPC-Journal of Planar Chromatography-Modern TLC. 2012 Aug 1; 25(4):306-13.
  58. Nugroho AE, Anas Y, Arsito PN, Wibowo JT, Riyanto S, Sukari MA. Effects of marmin, a compound isolated from *Aegle marmelos* Correa, on contraction of the guinea pig-isolated trachea. Pak J Pharm Sci. 2011 Oct 1; 24(4):427-33.
  59. Singh M, Singh AP, Tiwari N, Shanker K. UHPLC-Orbitrap-MS/MS metabolite profiling combined with HPLC-PDA targeted chemical fingerprint reveals the geographic-environment ( $G \times E$ ) effect on chemical constituents of *Bilvamula* (*Aegle marmelos* root). Methods. 2025 Oct 2.
  60. Nugroho AE, Riyanto S, Sukari MA, Maeyama K. Anti-allergic effects of Marmin, a coumarin isolated from *Aegle marmelos* Correa: In vitro study. International Journal of Phytomedicine. 2011 Jan 1; 3(1):84.
  61. Patel DK, Patel K, Rahman M, Chaudhary S. Therapeutic potential of “Aegeline,” an important phytochemical of *Aegle marmelos*: Current health perspectives for the treatment of disease. In *Nanomedicine for Bioactives: Healthcare applications 2020* May 15 (pp. 383-392). Singapore: Springer Singapore.
  62. Lamia SS, Shimo MS, Rashed SS, Prima AA, Mony AT, Dash PR. Phytochemistry and pharmacological properties of *Aegle marmelos* L (Rutaceae): A review. Phytochemistry. 2018 May; 3(3):45-54.
  63. Ghosh MK, Kumar A, Barman RK, Wahed MI. Current status of phytochemical and phytopharmacological study of some medicinal plants used by the tribes in Bangladesh: a review. J Pharmacogn Phytochem. 2018; 7(5):1089-95.
  64. Dugan D, Bell RJ, Brkljača R, Rix C, Taki AC, Gasser RB, Urban S. Phytochemical Profiling Studies of Alkaloids and Coumarins from the Australian Plant *Geijera parviflora* Lindl.(Rutaceae) and Their Anthelmintic and Antimicrobial Assessment. Metabolites. 2024 Apr 30; 14(5):259.
  65. Monika S, Thirumal M, Kumar PR. Phytochemical and biological review of *Aegle marmelos* Linn. Future science OA. 2023 Mar 1; 9(3):FSO849.
  66. Suja KP, Jose L, Lakshmanan D, Vidya AG, Reshmi Nair R, Kumar RA. Isolation and characterization of antimycobacterial compounds from fruits of *Aegle marmelos* (L.) Correa. J Commun Dis. 2017; 49(4):32-8.
  67. Manandhar B, Paudel KR, Sharma B, Karki R. Phytochemical profile and pharmacological activity of *Aegle marmelos* Linn. Journal of integrative medicine. 2018 May 1; 16(3):153-63.
  68. Melappa G. Identification of Bioactive Coumarin (s) from Three Endophytic Fungal Species of *Calophyllum tomentosum*. The Natural Products Journal. 2020 Aug 1; 10(4):502-12.
  69. Shelar PA, Gharge VG, Yadav AV. Pharmacognostic evaluation, phytochemical screening and antimicrobial study of leaves extracts of *Urena lobata* Linn. Current Research in Pharmaceutical Sciences. 2017 Jul 8; 7(02):40-9.

70. Noumi E, Snoussi M, Anouar EH, Alreshidi M, Veettil VN, Elkahoui S, Adnan M, Patel M, Kadri A, Aouadi K, De Feo V. HR-LCMS-based metabolite profiling, antioxidant, and anticancer properties of *Teucrium polium* L. methanolic extract: Computational and in vitro study. *Antioxidants*. 2020 Nov 5; 9(11):1089.
71. Hatami A. Phytochemical profiling and antibacterial activities of *Ziziphora tenuior* root extracts: a molecular docking against VanA of vancomycin-resistant enterococci. *3 Biotech*. 2024 Sep; 14(9):217.
72. Mathappan R, Joe VF, Varirappan K. Pharmacognostical and preliminary phytochemical studies of *Urena lobata* linn. *International Journal of Phytomedicine*. 2010 Oct 1; 2(4).
73. Bruni R, Barreca D, Protti M, Brighenti V, Righetti L, Anceschi L, Mercolini L, Benvenuti S, Gattuso G, Pellati F. Botanical sources, chemistry, analysis, and biological activity of furanocoumarins of pharmaceutical interest. *Molecules*. 2019 Jun 8; 24(11):2163.
74. Mongalo NI, Raletsena MV. Bioactive Molecules, Ethnomedicinal Uses, Toxicology, and Pharmacology of *Peltophorum africanum* Sond (Fabaceae): Systematic Review. *Plants*. 2025 Jan 16; 14(2):239.
75. Hatami A, Paezi M, Sadeghi MM. Phytochemical Profiling and Anti-VanA Activity of Pulegone Extracted from *Ziziphora tenuior* Flower Against Vancomycin-Resistant Enterococci: An In Silico Approach. *Chemistry & Biodiversity*. 2025 Feb; 22(2):e202401536.
76. Monika S, Thirumal M, Kumar PR. Phytochemical and biological review of *Aegle marmelos* Linn. *Future science OA*. 2023 Mar 1; 9(3):FSO849.