



Original Article

Gastroprotective Role of Mogrosides from *Siraitia Grosvenorii* Against Ethanol-Induced Gastric Ulcer

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ABSTRACT

Introduction: An imbalance between aggressive forces and mucosal defence mechanisms causes the destruction of gastric mucosal integrity, which is the hallmark of gastric ulceration, a frequent gastrointestinal illness. A common research model that results in acute oxidative stress, inflammation, and vascular damage is ethanol-induced stomach injury. Potential therapeutic relevance of organic compounds with multiple-target actions, which include mogrosides-cucurbitane-type triterpenoid glycosides produced from *Siraitia grosvenorii* (Monk fruit), in the treatment of stomach ulcers has drawn growing attention. Significantly, recent research indicates that mogrosides have a safe profile for possible therapeutic usage and are well-tolerated with minor side effects.

Methods: Electronic databases such as PubMed, Scopus, Web of Science, and Google Scholar were used to conduct a thorough literature assessment.

Results & Discussion: Preclinical investigations show that mogrosides defend stomach tissue by regulating oxidative stress, inflammation, and apoptotic pathways, which can increase confidence in their therapeutic potential. By blocking the NF- κ B pathway and lowering pro-inflammatory cytokines, including TNF- α , IL-1 β , and IL-6, they also reduce inflammation. Furthermore, mogrosides protect gastric epithelial cells by preventing caspase activation and enhancing the Bcl-2/Bax ratio, which controls apoptosis. However, the majority of research is preclinical, and clinical trials are required to verify safety and efficacy in humans, indicating a research gap.

Keywords: *Siraitia grosvenorii*; Mogrosides; Gastric ulcer; Ethanol-induced gastric injury; Oxidative stress; Reactive oxygen species (ROS).

INTRODUCTION

Gastric ulcers are a global health concern, contributing significantly to morbidity and health care expenditure worldwide [1]. Recent estimates suggest that peptic ulcers affect approximately 4 million people globally each year, with evidence rates from 0.1-0.3% in the general population [2]. Gastric ulcers arise when the balance between aggressive factors such as gastric acid, pepsin, alcohol, nonsteroidal anti-inflammatory drugs, *Helicobacter pylori* infection, reactive oxygen species, and protective mechanisms that maintain mucosal integrity is disrupted [3,4]. The gastric mucosal barrier is a highly organised defence system composed of a mucus-bicarbonate layer, tightly regulated epithelial cells, adequate mucosal blood flow, prostaglandin synthesis, nitric oxide production, and endogenous antioxidant enzymes [5]. When this equilibrium is disturbed, mucosal cell injury occurs, characterized by epithelial erosion, inflammation, hemorrhage, and, in severe cases, ulceration [6].

Among the experimental models used to study gastric ulcerogenesis, ethanol-induced gastric mucosal injury is widely accepted for its reproducibility and mechanistic relevance [7]. Ethanol causes acute and severe damage to the gastric mucosa through multiple interrelated pathways. It disrupts the lipid bilayer of epithelial cell membranes, increasing permeability and leading to cell necrosis [8, 9].

Ethanol also reduces gastric mucus secretion and impairs prostaglandin synthesis, weakening mucosal defence. More importantly, ethanol exposure markedly increases oxidative stress within the gastric mucosa, as evidenced by the excessive production of reactive oxygen species (ROS), including superoxide anion and hydroxyl radicals [10, 11]. These reactive species initiate lipid peroxidation, leading to the formation of malondialdehyde (MDA) and destabilizing cell membranes. Concurrently, ethanol depletes endogenous antioxidants such as reduced glutathione (GSH) and diminishes the activity of key antioxidant enzymes, including superoxide dismutase (SOD) and catalase (CAT) [12, 13, and 14].

Inflammation further amplifies ethanol-induced injury. Ethanol activates redox-sensitive transcription factors such as nuclear factor-kappa B (NF- κ B), which promotes the expression of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF- α), interleukin-1 beta (IL-1 β), and interleukin-6 (IL-6) [15, 16]. These mediators enhance neutrophil infiltration, increase vascular permeability, and exacerbate tissue damage. Additionally, mitochondrial dysfunction triggered by oxidative stress activates apoptotic pathways via Bax upregulation, Bcl-2 downregulation, and caspase activation [17]. Thus, ethanol-induced gastric injury is a multifactorial process involving oxidative stress, inflammation, vascular impairment, and apoptosis [18].

Conventional pharmacological treatments for gastric ulcers, including proton pump inhibitors (PPIs), H₂-receptor antagonists, and mucosal-protective agents, have significantly improved patient outcomes [19, 20]. However, long-term use of acid-suppressive drugs is associated with adverse effects such as nutrient malabsorption, altered gut microbiota, increased susceptibility to infections, and potential renal and metabolic complications [21]. Moreover, these therapies primarily target acid secretion and may not adequately address oxidative and inflammatory components of mucosal injury. This has prompted increasing interest in natural products with multi-target mechanisms of action, particularly those possessing antioxidant and anti-inflammatory properties [22, 23].

Medicinal plants have long served as sources of therapeutic agents for gastrointestinal disorders. Phytochemicals such as flavonoids, phenolic acids, terpenoids, and glycosides have demonstrated significant gastroprotective effects in experimental models [24, 25]. These compounds can scavenge free radicals, enhance endogenous antioxidant defences, suppress inflammatory signalling pathways, increase mucus production, and promote prostaglandin-mediated cytoprotection [26]. The integration of traditional knowledge with modern pharmacological research has led to the identification of promising plant-derived compounds for the prevention and treatment of ulcers. Notably, monk fruit (*Siraitia grosvenorii*) has been valued in traditional medicine for its gastrointestinal benefits and such historical applications [27, 28].

Siraitia grosvenorii, commonly known as monk fruit or Luo Han Guo, is a perennial vine native to southern China and traditionally used in Chinese medicine for respiratory and gastrointestinal ailments [29]. The fruit is widely known as a natural, non-caloric sweetener due to its high content of mogrosides, cucurbitane-type triterpenoid glycosides that impart intense sweetness. Among these, mogroside V is the most abundant and pharmacologically active component [30, 31]. Beyond their sweetening properties, mogrosides possess significant biological activities, including antioxidant, anti-inflammatory, anti-apoptotic, and immunomodulatory effects [32].

Emerging studies indicate that mogrosides exhibit potent free-radical-scavenging activity and enhance endogenous antioxidant enzyme systems. They have been shown to reduce lipid peroxidation, increase glutathione levels, and activate the Nrf2/ARE signalling pathway, which regulates the expression of cytoprotective enzymes, including heme oxygenase-1 (HO-1). In addition, mogrosides modulate inflammatory pathways by inhibiting NF- κ B activation and suppressing pro-inflammatory cytokine production [33].

Based on these properties, the current review explained, mogrosides may effectively counteract the oxidative and inflammatory mechanisms underlying ethanol-induced gastric mucosal injury. Furthermore, the triterpenoid structure of mogrosides is noteworthy, as triterpenoids from other medicinal plants have demonstrated significant gastroprotective activity by enhancing mucosal defence mechanisms.

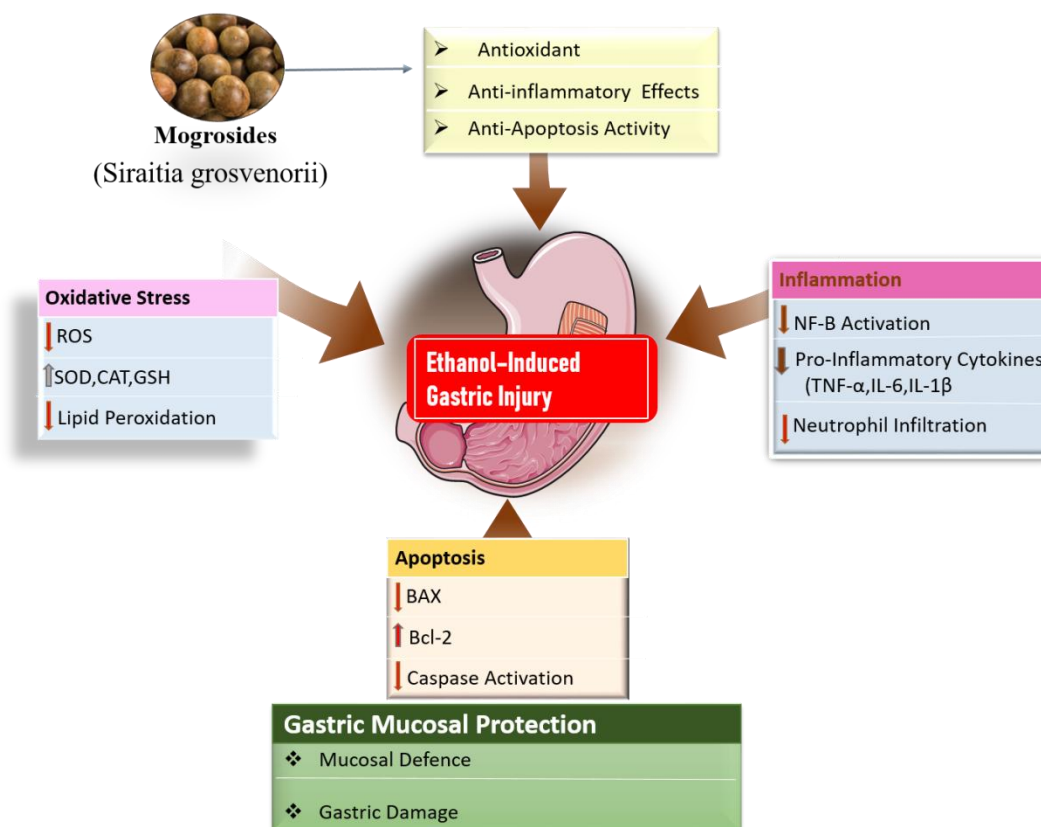


Figure1: Mogrosides from *Siraitia grosvenorii* reduce oxidative stress(ROS, SOD, CAT, and GSH) and inhibit inflammation (NF-κB, TNF-, IL-1β, AND IL-6) to prevent ethanol-induced stomach damage.

MECHANISM OF MOGROSIDE-MEDIATED GASTRIC PROTECTION

Antioxidant Mechanism

Oxidative stress is a pivotal event in ethanol-induced gastric mucosal injury and represents one of the earliest and most destructive pathological processes. Ethanol exposure leads to excessive generation of reactive oxygen species (ROS), including superoxide anions (O_2^-), hydroxyl radicals (OH), and hydrogen peroxide (H_2O_2). These reactive molecules initiate lipid peroxidation, protein oxidation, DNA damage, mitochondrial dysfunction, and ultimately epithelial cell death[34]. Therefore, attenuations are a critical therapeutic strategy for preventing gastric ulcer formation. Mogroside, derived from *Siraitia grosvenorii*, exhibits potent antioxidant actions through multiple complementary mechanisms that collectively restore redox balance and protect gastric tissue [35, 36].

Direct free radical scavenging

Mogrosides possess a highly oxygenated cucurbitane-type triterpenoid backbone with multiple hydroxyl groups that contribute to their electron-donating capacity. Their structural configuration enables direct neutralization of free radicals by donating hydrogen atoms or electrons, thereby stabilizing reactive species. Experimental studies have demonstrated that mogroside effectively scavenges superoxide anions and hydroxyl radicals, which are particularly damaging in ethanol-induced injury. By limiting radical propagation reactions, mogroside reduces oxidative chain reactions that compromise membrane integrity and cellular viability [37, 38, and 39]

Inhibition of Lipid Peroxidation

Lipid peroxidation is a hallmark of ethanol-induced gastric damage and is commonly assessed by measuring malondialdehyde(MDA), a secondary byproduct of polyunsaturated fatty acid oxidation. Elevated MDA levels reflect membrane disruption and cellular injury. Mogroside administration has been associated with a significant reduction in gastric MD level, indicating suppression of lipid peroxidation [40]. This protective effect preserves phospholipid membrane stability, maintains epithelial barrier function, and prevents leakage of intercellular components by stabilizing cellular membranes [41].

Enhancement of endogenous antioxidant defence systems

Beyond direct radical scavenging, mogroside enhances endogenous antioxidant defences. Ethanol exposure typically depletes reduced glutathione (GSH) and decreases the activities of antioxidant enzymes, including superoxide dismutase (SOD) and catalase (CAT). These enzymes are essential for detoxifying reactive oxygen species (ROS) and maintaining intercellular redox homeostasis(42). Mogrosides have been shown to restore GSH levels and increase SOD and CAT activities in experimental models, thereby reinforcing intrinsic cellular defence mechanisms. The replenishment of GSH is

particularly important because glutathione plays a central role in detoxification, maintains thiol status, and protects against oxidative mitochondrial damage(43).

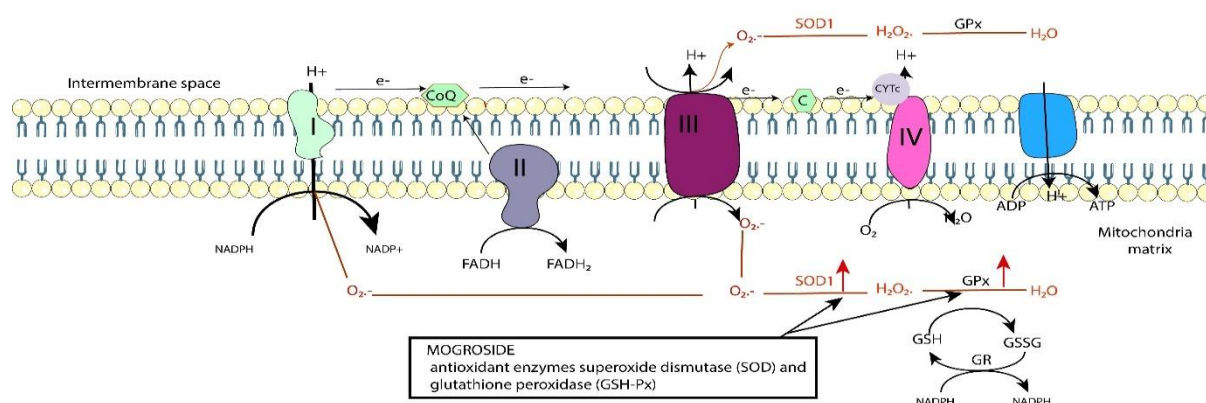


Figure 2:Schematic of antioxidant action of mogrosides in the mitochondrial ETC, where electron leakage generates ROS ($O_2^{\bullet-}$). SOD converts $O_2^{\bullet-}$ to H_2O_2 , which is reduced to water by GPx using GSH.

Activation of the Nrf2/ARE Signalling Pathway

A critical molecular mechanism underlying mogroside-mediated antioxidant effects involves activation of the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway. Under basal conditions, Nrf2 remains bound to its cytoplasmic inhibitor Keap1 and is targeted for proteasome degradation. Oxidative stress or electrophilic compounds disrupt the Nrf2-Keap1 complex, allowing Nrf2 to translocate into the nucleus. Once in the nucleus, Nrf2 binds to antioxidant response elements (AREs) in the promoters of cytoprotective genes, initiating transcription of antioxidant and phase II detoxifying enzymes. Mogrosides appear to facilitate Nrf2 activation by either modulating redox-sensitive cysteine residues of Keap1 or influencing upstream kinases that regulate Nrf2 stability(44). Activation of Nrf2 leads to upregulation of several antioxidant enzymes, including:

- Heme oxygenase-1 (HO-1)
- NAD(P)H: quinone oxidoreductase 1 (NQO1)
- Glutamate-cysteine ligase (GCL) is involved in GSH synthesis
- Superoxide dismutase and catalase

HO-1 induction is particularly relevant in gastric protection. HO-1 catalyses the degradation of heme into biliverdin, free iron, and carbon monoxide, molecules that possess antioxidant, anti-inflammatory, and cytoprotective properties. Through Nrf2-mediated HO-1 activation, mogrosides not only reduce oxidative burden but also enhance mucosal resilience against subsequent injury(45).

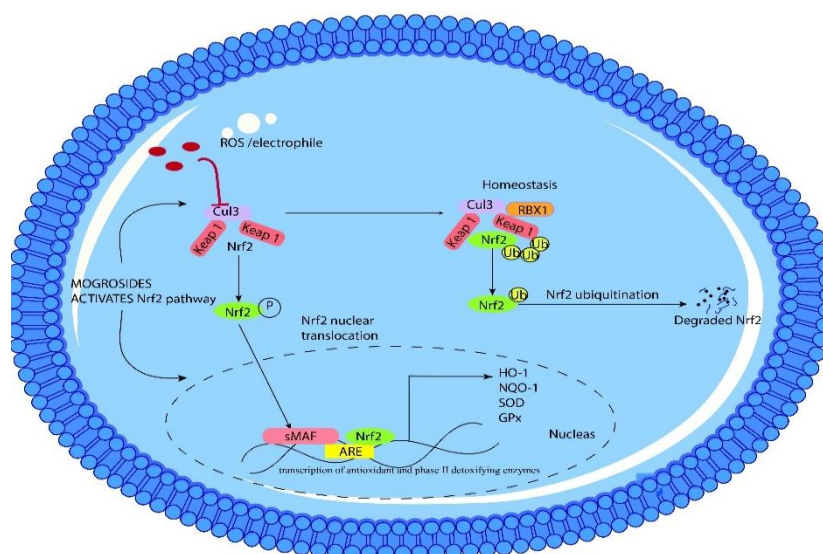


Figure 3: Illustration of mogrosides-induced activation of the Nrf2-Keap1 pathway. Disruption of the Keap1-Nrf2 complex prevents Nrf2 degradation, enabling nucleartranslocation and induction of antioxidant genes (HO-1,NQO1, SOD, and GPx)

Preservation of Mitochondrial Function

Mitochondria are both major sources and primary targets of ROS during ethanol-induced injury. Excessive oxidative stress disrupts mitochondrial membrane potential, leading to cytochrome c release and activation of apoptosis (46). By limiting ROS generation and enhancing antioxidant defences, mogrosides preserve mitochondrial integrity and prevent redox-driven apoptosis. Maintenance of mitochondrial function is essential for sustaining cellular ATP production and epithelial regeneration(47).

Integrated Redox Modulation

Importantly, mogrosides do not merely act as passive antioxidants but also modulate cellular redox signalling. By restoring oxidative balance, they interrupt the feed-forward cycle in which ROS activate inflammatory pathways such as NF- κ B, further amplifying tissue damage. Thus, the antioxidant activity of mogrosides indirectly contributes to their anti-inflammatory and anti-apoptotic effects, demonstrating a coordinated protective mechanism(48).

In summary, mogrosides exert robust antioxidant effects through direct radical scavenging, inhibition of lipid peroxidation, restoration of endogenous antioxidant systems, activation of the Nrf2/ARE signalling pathway, and preservation of mitochondrial function. These integrated mechanisms position mogrosides as promising natural agents for attenuating oxidative stress-mediated gastric mucosal injury in ethanol-induced ulcer models(49).

Anti-Inflammatory Effects

Inflammation is a central amplifier of ethanol-induced gastric mucosal injury and closely interacts with oxidative stress to exacerbate tissue damage. Ethanol exposure activates redox-sensitive transcription factors, particularly nuclear factor-kappa B (NF- κ B), which plays a pivotal role in orchestrating inflammatory gene expression (50). Under basal conditions, NF- κ B remains sequestered in the cytoplasm by its inhibitor NF- κ B. Ethanol-induced oxidative stress promotes phosphorylation and degradation of NF- κ B, allowing NF- κ B to translocate into the nucleus and initiate transcription of pro-inflammatory cytokines, chemokines, and enzymes (51).

Mogrosides have demonstrated the capacity to modulate this inflammatory cascade at multiple levels. One primary mechanism involves inhibition of NF- κ B nuclear translocation(51). By suppressing upstream signalling pathways-possibly through redox modulation or inhibition of IKK activation-mogrosides prevent NF- κ B-mediated transcription of inflammatory genes. This regulatory effect limits the amplification of inflammatory responses within the gastric mucosa(52).

Consequently, mogroside treatment has been associated with reduced production of key pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1 β). These cytokines are critical mediators of mucosal damage, as they enhance vascular permeability, recruit immune cells, and perpetuate oxidative injury. By attenuating cytokine release, mogrosides help to limit inflammatory cell infiltration and secondary tissue destruction (53).

In addition, mogrosides suppress the expression of inducible enzymes such as cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS)(55). COX-2 overexpression contributes to excessive prostanoid production and inflammation, while iNOS produces high levels of nitric oxide, which can react with superoxide to form peroxynitrite, a highly cytotoxic reactive nitrogen species. Inhibition of COX-2 and iNOS reduces nitrosative stress and inflammatory burden (56).

Another significant aspect of mogroside-mediated protection is the reduction of neutrophil infiltration. Activated neutrophils release myeloperoxidase (MPO), proteolytic enzymes, and additional ROS, which intensify mucosal injury(57). By decreasing cytokine-mediated chemotaxis and adhesion molecule expression, mogrosides limit neutrophil accumulation and associated oxidative damage (58).

Overall, through coordinated suppression of NF- κ B signalling, cytokine production, inflammatory enzyme expression, and immune cell infiltration, mogrosides attenuate the inflammatory cascade and prevent progression of ethanol-induced gastric lesions (57).

Enhancement of Mucosal Defence

The gastric mucosal barrier is maintained by a sophisticated defence system that includes mucus secretion, bicarbonate production, prostaglandin-mediated cytoprotection, and adequate microcirculation (59). Ethanol compromises these defences by reducing mucus content, impairing prostaglandin synthesis, and disrupting mucosal blood flow. Restoration of these protective mechanisms is therefore essential for effective gastroprotection (60).

Mogrosides may enhance mucosal defence by stimulating mucus secretion and increasing the content of gastric mucosal glycoproteins (61). The mucus layer serves as a physical barrier that prevents back-diffusion of hydrogen ions and shields epithelial cells from direct contact with luminal irritants. Enhancing glycoprotein synthesis strengthens this barrier and improves mucosal resilience to ethanol-induced disruption (62).

Prostaglandins, particularly prostaglandin E₂ (PGE₂), are crucial mediators of gastric cytoprotection. They regulate mucus and bicarbonate secretion, maintain mucosal blood flow, and promote epithelial regeneration (63). Ethanol decreases prostaglandin synthesis by inhibiting cyclooxygenase activity and damaging epithelial cells. Mogrosides may indirectly support prostaglandin production either by reducing oxidative damage to prostaglandin-synthesizing enzymes or by modulating COX activity toward a protective balance. Improved prostaglandin signalling enhances mucosal repair and barrier stability (64).

Furthermore, adequate mucosal blood flow is critical for oxygen delivery, nutrient supply, and removal of toxic metabolites. Ethanol-induced vascular damage leads to ischemia and haemorrhagic lesions. Through antioxidant and anti-inflammatory actions, mogrosides may preserve endothelial function and microcirculatory integrity, thereby sustaining mucosal perfusion (65). Enhanced blood flow facilitates rapid epithelial restitution and prevents the progression of superficial lesions into deeper ulcers (66).

By reinforcing the structural and biochemical components of mucosal defence, mogrosides strengthen the gastric barrier and provide a first line of protection against ethanol-mediated injury (67).

2.9. Anti-Apoptotic and Cytoprotective Actions

Apoptosis is a significant contributor to ethanol-induced loss of gastric epithelial cells. Excessive oxidative stress and inflammatory signalling disrupt mitochondrial function, thereby activating the intrinsic apoptotic pathway (68). Ethanol increases the expression of pro-apoptotic proteins, such as Bax, while decreasing the expression of anti-apoptotic proteins, such as Bcl-2. This imbalance promotes mitochondrial outer membrane permeabilization, cytochrome c release, and activation of downstream caspases, particularly caspase-3, culminating in programmed cell death (69).

Mogrosides exert cytoprotective effects by modulating these apoptotic pathways. They downregulate pro-apoptotic Bax and upregulate anti-apoptotic Bcl-2, thereby restoring the Bax/Bcl-2 ratio toward cell survival. This shift stabilizes mitochondrial membranes and prevents the release of cytochrome c (70).

Additionally, mogrosides inhibit caspase-3 activation, the key executioner enzyme responsible for DNA fragmentation and cellular dismantling. Suppression of caspase activation interrupts the apoptotic cascade and preserves epithelial integrity (71). Preservation of mitochondrial membrane potential is another crucial mechanism. By limiting oxidative stress and maintaining mitochondrial stability, mogrosides sustain ATP production and prevent energy depletion (72). This is particularly important in gastric epithelial cells, where rapid turnover and repair processes require an adequate energy supply.

Beyond inhibiting apoptosis, mogrosides may also provide cytoprotection by stimulating cellular repair pathways and maintaining tight junction integrity, although these mechanisms require further investigation.

Collectively, the anti-apoptotic and cytoprotective actions of mogrosides ensure survival of gastric epithelial cells, prevent structural breakdown, and facilitate mucosal recovery following ethanol exposure (74).

Preclinical Evidence

Although studies specifically investigating purified mogrosides in ethanol-induced gastric ulcer models remain relatively limited, accumulating preclinical evidence from monk fruit extracts enriched in mogroside V strongly supports their gastroprotective potential (74). Experimental investigations using ethanol-induced ulcer models in rodents have consistently demonstrated significant attenuation of gastric mucosal injury following treatment with monk fruit extracts, suggesting that mogrosides are likely the principal bioactive constituents responsible for these protective effects (75).

One of the most consistently reported findings is a significant reduction in ulcer index. Animals pre-treated with monk fruit extract exhibit markedly smaller lesion areas and fewer erosive bands compared to untreated ethanol-exposed controls. Macroscopic examination typically reveals decreased severity and extent of haemorrhagic streaks, indicating effective protection against acute mucosal damage (76).

In addition to lowering the ulcer index, monk fruit extract treatment has been associated with reduced haemorrhagic lesions and oedema formation. Ethanol-induced injury is characterized by vascular congestion, increased permeability, and submucosal bleeding. The attenuation of these vascular disturbances suggests preservation of microcirculatory integrity, likely secondary to antioxidant and anti-inflammatory actions (77).

Biochemically, significant reductions in malondialdehyde (MDA) levels have been observed in gastric tissue following the administration of the extract. Since MDA is a reliable marker of lipid peroxidation, its decrease indicates suppression of oxidative membrane damage. This finding aligns with the proposed free radical-scavenging activity of mogrosides and supports their role in mitigating oxidative stress (78).

Furthermore, monk fruit extract has been shown to enhance endogenous antioxidant defence systems. Studies report increased activity of superoxide dismutase (SOD) and catalase (CAT), along with restoration of reduced glutathione (GSH) levels in gastric tissue. These improvements reflect reinforcement of intrinsic cellular antioxidant capacity, which is typically compromised by ethanol exposure. Restoration of redox homeostasis plays a central role in preventing progression from superficial mucosal injury to deeper ulceration (79).

Histopathological analyses provide additional confirmation of gastroprotection. Compared to ethanol-treated controls, animals receiving monk fruit extract demonstrate improved mucosal architecture, reduced epithelial exfoliation, decreased inflammatory cell infiltration, minimal submucosal oedema, and preservation of glandular structures. The maintenance of structural integrity at the microscopic level further supports the cytoprotective properties of mogroside-rich preparations (80).

Comparative Advantages of Mogrosides

Mogrosides derived from *Siraitia grosvenorii* offer several distinct advantages over conventional anti-ulcer therapies, primarily due to their multi-target pharmacological profile and favourable safety characteristics. Unlike standard treatments that predominantly focus on gastric acid suppression, mogrosides exert protective effects across multiple pathogenic pathways involved in ethanol-induced ulcerogenesis (81). To clarify this comparative advantage, Table 1 provides a numerical overview contrasting the multi-target actions of mogrosides with the predominantly single-target mechanism of proton pump inhibitors (PPIs), highlighting the broader spectrum of protective effects afforded by mogrosides (82).

Table 1: Comparison of gastroprotective effects of mogrosides from *Siraitia grosvenorii* and proton pump inhibitors (PPIs) in ethanol-induced gastric ulcers.

Parameter	Mogrosides (from <i>Siraitia grosvenorii</i>)	Proton Pump Inhibitors (PPIs)
Primary Mechanism	Multi-target pharmacological action	Inhibition of H ⁺ /K ⁺ -ATPase
Target Pathways	ROS scavenging, Nrf2 activation, NF-κB inhibition, mucus protection	Gastric acid secretion only
Oxidative Stress	↓ Lipid peroxidation, ↓ ROS	Indirect/minimal effect
Inflammation	↓ TNF-α, IL-6, NF-κB signalling	Limited anti-inflammatory action
Mucosal Defence	↑ Mucus secretion, ↑ prostaglandins	No direct enhancement
Apoptosis Regulation	Anti-apoptotic (↓ Bax, ↑ Bcl-2)	Not significant
Healing Effect	Promotes mucosal repair and regeneration	Supports healing via acid reduction
Onset of Action	Moderate	Rapid
Side Effects	Minimal, natural compound	Long-term risks
Therapeutic Scope	Broad (multi-pathway protection)	Narrow (acid suppression)

Multifactorial Mechanism of Action

One of the most significant advantages of mogrosides is their multifactorial mechanism of action. Ethanol-induced gastric injury is not solely an acid-mediated condition but rather a complex interplay of oxidative stress, inflammation, vascular impairment, and apoptosis (83). They directly scavenge reactive oxygen species, activate endogenous antioxidant pathways such as Nrf2/ARE, inhibit NF-κB-mediated inflammatory signalling, enhance mucosal defence factors, and suppress mitochondrial apoptotic cascades. This broad-spectrum activity enables mogrosides to intervene at multiple stages of ulcer development, providing comprehensive mucosal protection rather than targeting a single pathogenic factor (84).

Natural Origin with Low Reported Toxicity

Mogrosides are naturally occurring phytochemicals widely found in monk fruit, a commonly used non-caloric sweetener. Toxicological evaluations have generally reported a favourable safety profile, with low acute and chronic toxicity in experimental studies (85). The long-standing traditional use of monk fruit in herbal medicine further supports its tolerability. In contrast, prolonged use of proton pump inhibitors (PPIs) and H₂ receptor antagonists has been associated with adverse effects such as altered nutrient absorption, increased infection risk, and potential renal complications. The natural origin and relatively low toxicity of mogrosides enhance their appeal as adjunctive or preventive therapeutic agents (86).

Water Solubility and Formulation Advantages

Structurally, mogrosides contain multiple glycosidic moieties that confer high water solubility. This physicochemical property facilitates formulation into aqueous preparations, including oral solutions, syrups, and functional beverages (87). Water solubility may also enhance bioavailability within the gastric lumen, allowing direct interaction with the mucosal

surface during ethanol exposure. From a pharmaceutical perspective, improved solubility simplifies dosage standardisation and the development of controlled-release systems (88).

Synergistic Antioxidant and Anti-Inflammatory Effects

A notable strength of mogrosides lies in their synergistic modulation of oxidative and inflammatory pathways. Oxidative stress and inflammation are tightly interconnected processes in gastric ulcerogenesis. Reactive oxygen species activate NF- κ B signalling, which in turn amplifies inflammatory cytokine production and further ROS generation (89). By simultaneously reducing oxidative stress and suppressing inflammatory mediators, mogrosides interrupt this feed-forward cycle. This dual regulatory action enhances therapeutic efficacy and may reduce the likelihood of recurrent mucosal injury (38).

Comparison with Conventional Anti-Ulcer Therapies

Conventional anti-ulcer medications, particularly PPIs and H₂ receptor antagonists, primarily act by reducing gastric acid secretion. While effective in acid-related ulcers, these drugs do not directly address oxidative damage, inflammatory cascades, or apoptotic pathways triggered by chemical irritants such as ethanol. Cytoprotective agents, such as sucralfate, provide surface protection but lack systemic antioxidant or anti-inflammatory activity (90).

In contrast, mogrosides target the oxidative and inflammatory mechanisms central to ethanol-induced mucosal injury. Rather than merely reducing luminal acidity, they reinforce intrinsic cellular defences, preserve epithelial integrity, and promote mucosal repair. This broader mechanism of action suggests potential utility not only in ulcer treatment but also in preventing gastric mucosal injury under oxidative stress conditions (91).

Advantages of Monk Fruit (*Siraitia grosvenorii*) as a Therapeutic Candidate

Monk fruit (*Siraitia grosvenorii*) possesses several pharmacological and practical attributes that make it a promising therapeutic candidate for gastric mucosal protection and broader gastrointestinal applications (92). Its advantages extend beyond the activity of isolated mogrosides, as the whole fruit contains a spectrum of bioactive compounds that may exert synergistic effects.

Rich Source of Bioactive Phytochemicals

Monk fruit contains high concentrations of mogrosides, particularly mogroside V, along with flavonoids, phenolic compounds, and polysaccharides. This phytochemical diversity supports multiple biological activities, including antioxidant, anti-inflammatory, anti-apoptotic, and immunomodulatory effects. The presence of multiple active constituents may provide synergistic protection against oxidative and inflammatory gastric injury (93).

Multifunctional Pharmacological Profile

Unlike single-target synthetic drugs, monk fruit exhibits broad pharmacological activity. Its constituents can modulate oxidative stress (via Nrf2 activation), suppress inflammatory signalling (via NF- κ B inhibition), enhance mucosal defences, and protect against mitochondrial dysfunction. This multi-target approach is particularly advantageous in complex conditions such as ethanol-induced gastric injury, where several pathogenic mechanisms operate simultaneously (94).

Natural Origin and Traditional Use

Monk fruit has been used for centuries in traditional Chinese medicine for respiratory and gastrointestinal ailments. Its long history of human consumption supports its safety and tolerability. As a natural product widely consumed as a non-caloric sweetener, monk fruit enjoys strong public acceptance, which may facilitate translational application as a nutraceutical or functional therapeutic (87).

Favourable Safety Profile

Toxicological studies have generally reported low acute and chronic toxicity of monk fruit extracts. Unlike long-term use of proton pump inhibitors or NSAIDs, monk fruit has not been associated with major systemic adverse effects in preclinical evaluations (95). This favourable safety margin supports its potential use in both preventive and therapeutic settings (96).

Antioxidant Potency

Monk fruit exhibits strong free radical-scavenging activity, often comparable to established natural antioxidants. By reducing lipid peroxidation and restoring endogenous antioxidant enzyme activity, monk fruit directly addresses oxidative stress, a central mechanism in ethanol-induced gastric injury (97).

Anti-Inflammatory Properties

By modulating inflammatory mediators such as TNF- α , IL-1 β , and IL-6, monk fruit reduces amplification of inflammation in gastric tissue. Its ability to suppress COX-2 and iNOS expression further contributes to the reduction of inflammatory and nitrosative stress (98).

Water Solubility and Formulation Flexibility

The glycosidic nature of mogrosides confers high water solubility, facilitating formulation into oral solutions, syrups, capsules, and functional beverages. This enhances bioavailability within the gastric lumen and simplifies pharmaceutical development. The fruit can be administered as juice, an extract, or a purified compound, depending on therapeutic goals (99).

Potential for Synergistic Therapy

Monk fruit may complement conventional anti-ulcer drugs by addressing oxidative and inflammatory components that acid-suppressive therapies do not directly target. It may therefore serve as an adjunct therapy, potentially reducing required doses of synthetic drugs and minimising side effects(100).

Nutraceutical and Functional Food Potential

Given its established use as a natural sweetener, monk fruit has strong potential as a functional food ingredient. Its incorporation into dietary formulations could provide preventive gastroprotective benefits, particularly in individuals exposed to alcohol, stress, or NSAIDs. Mogroside exhibits anti-inflammatory and antioxidant activities that help protect the gastrointestinal mucosal membrane.

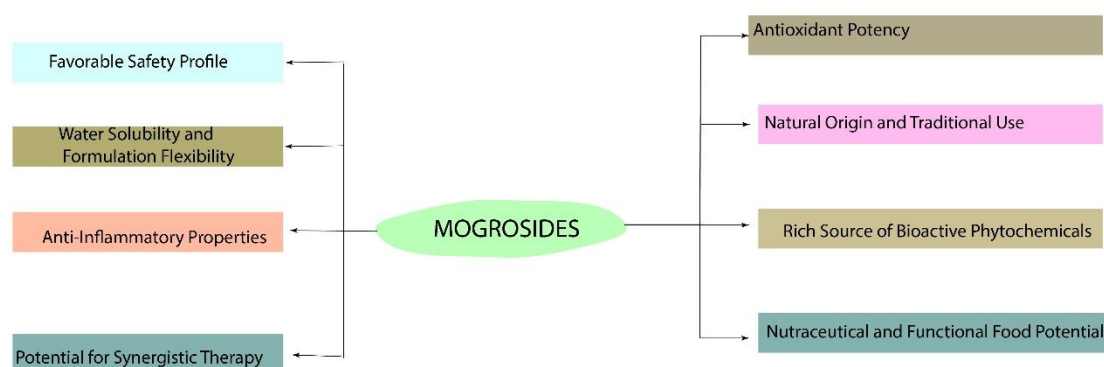


Figure 4: Schematic representation of the multifunctional advantages of mogrosides, highlighting their pharmacological, formulation, antioxidant, and nutraceutical potential derived from *Siraitia grosvenorii*.

CONCLUSION:

As a result of their strong and versatile gastro-protective qualities, mogrosides are an intriguing category of naturally occurring bioactive chemicals for the treatment and prevention of stomach ulcers. The coordinated management of important pathological processes, such as oxidative stress, inflammation, and apoptosis, involved in ethanol-induced stomach injury, is the main reason for their protective effects. By increasing enzymes, including glutathione peroxidase, catalase, and superoxide dismutase, mogrosides mechanistically improve endogenous antioxidant defence systems and reduce mucosal damage caused by epithelial cells; they simultaneously decrease pro-inflammatory signalling pathways, such as NF- κ B and associated cytokines (such as TNF- α and IL-1 β) and control apoptotic markers. Mogrosides support the preservation of the structural integrity and homeostasis of the stomach mucosa using these coordinated effects.

Due to their natural origin, low toxicity, and favourable safety profile, mogrosides provide essential translational benefits in addition to their pharmacological efficacy, making them viable substitutes or supplements to traditional anti-ulcer treatments like proton pump inhibitors and H₂ receptor antagonists. However, despite robust preclinical evidence, the current understanding of their therapeutic potential remains largely confined to in vitro studies and animal models.

Future research should focus on well-designed clinical trials to validate their efficacy and safety in human populations. Comprehensive pharmacokinetic and pharmacodynamic studies are essential to elucidate their absorption, bioavailability, metabolism and tissue distribution. Furthermore, optimization of formulation strategies such as nanocapsulations, lipid based delivery systems or synergistic combinations with existing therapeutics may enhance their stability and therapeutic efficacy. Investigations into structure activity relationships of different mogrosides derivatives could also provide insights for developing more potent analog. Additionally, exploring their role in other gastrointestinal disorders such as *Helicobacter pylori* associated ulcers, inflammatory bowel disease, and gastric carcinogenesis, may broaden their therapeutic applicability. Integration of omics-based approaches (genomics, proteomics, and metabolomics) could further clarify molecular targets and pathway involved in their action.

REFERENCES

1. Abbasi-Kangevari M, Ahmadi N, Fattahi N, Rezaei N, Malekpour MR, Ghamari SH, Moghaddam SS, Azadnajafabad S, Esfahani Z, Kolahi AA, Roshani S. Quality of care of peptic ulcer disease worldwide: A systematic analysis for the global burden of disease study 1990–2019. *PloS one*. 2022 Aug 1;17(8):e0271284.

2. Wang FW, Tu MS, Mar GY, Chuang HY, Yu HC, Cheng LC, Hsu PI. Prevalence and risk factors of asymptomatic peptic ulcer disease in Taiwan. *World journal of gastroenterology: WJG*. 2011 Mar 7;17(9):1199.
3. Ji W. Prostaglandins, NSAIDs, and gastric mucosal protection: why doesn't the stomach digest itself?. *Physiol Rev*. 2008;88:1547-65.
4. Malfertheiner P, Camargo MC, El-Omar E, Liou JM, Peek R, Schulz C, Smith SI, Suerbaum S. *Helicobacter pylori* infection. *Nature reviews Disease primers*. 2023 Apr 20;9(1):19.
5. Wallace JL. Cooperative modulation of gastrointestinal mucosal defence by prostaglandins and nitric oxide. *Clinical and investigative medicine*. 1996 Oct 1;19(5):346-51.
6. Wallace JL. Mechanisms, prevention, and clinical implications of nonsteroidal anti-inflammatory drug-enteropathy. *World Journal of Gastroenterology: WJG*. 2013 Mar 28;19(12):1861.
7. SHAY H, Komarov SA, Fels SS, MERANZE D, Gruenstein M, Siplet HA. A simple method for the uniform production of gastric ulceration in the rat.
8. Elamin EE, Masclee AA, Dekker J, Jonkers DM. Ethanol metabolism and its effects on the intestinal epithelial barrier. *Nutrition reviews*. 2013 Jul 1;71(7):483-99.
9. Guth PH. Gastric blood flow in ethanol injury and prostaglandin cytoprotection. *Scandinavian Journal of Gastroenterology*. 1986 Jan 1;21(sup125):86-91.
10. Pan JS, He SZ, Xu HZ, Zhan XJ, Yang XN, Xiao HM, Shi HX, Ren JL. Oxidative stress disturbs energy metabolism of mitochondria in ethanol-induced gastric mucosa injury. *World journal of gastroenterology: WJG*. 2008 Oct 14;14(38):5857.
11. Hernández-Muñoz R, Montiel-Ruiz C, Vázquez-Martínez O. Gastric mucosal cell proliferation in ethanol-induced chronic mucosal injury is related to oxidative stress and lipid peroxidation in rats. *Laboratory investigation*. 2000 Aug 1;80(8):1161-9.
12. Fahmi AA, Abdur-Rahman M, Aboul Naser AF, Hamed MA, Abd-Alla HI, Nasr MI. *Pulicaria crispa* mitigates gastric ulcer induced by ethanol in rats: role of treatment and auto healing. *Biomarkers*. 2019 Apr 3;24(3):286-94.
13. Bhardwaj P. Oxidative stress and antioxidants in gastrointestinal diseases. *Tropical Gastroenterology*. 2008 Jul 1;29(3):129-35.
14. Kwiecień S, Jasnos K, Magierowski M, Sliwowski Z, Pajdo R, Brzozowski B, Mach T, Wojcik D, Brzozowski T. Lipid peroxidation, reactive oxygen species and antioxidative factors in the pathogenesis of gastric mucosal lesions and mechanism of protection against oxidative stress-induced gastric injury. *J Physiol Pharmacol*. 2014 Oct 1;65(5):613-22.
15. Paulraj RS, Anbazhagan S, Perumal P, Ramachandran A, Paulraj SG. A Comprehensive Analysis of Therapeutic Potential of Medicinal Plant Extracts to Treat Ethanol-Induced Gastric Ulcer. *Biomedicines*. 2026 Feb 28;14(3):562.
16. Fukumura D, Kurose I, Miura S, Tsuchiya M, Ishii H. Oxidative stress in gastric mucosal injury: role of platelet-activating factor-activated granulocytes. *Journal of gastroenterology*. 1995 Oct;30(5):565-71.
17. Wang Z, Han X, Xiao W, Wang P, Wang J, Zou D, Luo X, Shi L, Wu J, Guo L, Mu Y. Mussel-inspired adhesive drug-loaded hydrogels for oral ulcers treatment. *Acta Biomaterialia*. 2024 Oct 1;187:98-109.
18. Bhattacharyya A, Chattopadhyay R, Mitra S, Crowe SE. Oxidative stress: an essential factor in the pathogenesis of gastrointestinal mucosal diseases. *Physiological reviews*. 2014 Apr;94(2):329-54.
19. Howden CW, Hunt RH. Relationship between gastric secretion and infection. *Gut*. 1987 Jan;28(1):96.
20. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Official journal of the American College of Gastroenterology| ACG*. 2013 Mar 1;108(3):308-28.
21. Willems RP, van Dijk K, Ket JC, Vandenbroucke-Grauls CM. Evaluation of the association between gastric acid suppression and risk of intestinal colonization with multidrug-resistant microorganisms: a systematic review and meta-analysis. *JAMA internal medicine*. 2020 Apr;180(4):561-71.
22. Repetto MG, Llesuy SF. Antioxidant properties of natural compounds used in popular medicine for gastric ulcers. *Brazilian journal of medical and biological research*. 2002 May 6;35(5):523-34.
23. Bhattacharyya A, Chattopadhyay R, Mitra S, Crowe SE. Oxidative stress: an essential factor in the pathogenesis of gastrointestinal mucosal diseases. *Physiological reviews*. 2014 Apr;94(2):329-54.
24. Chen D, Wang W, Chen X, Liang N, Li J, Ding W, Zhang H, Yang Z, Zhao H, Liu Z. Plant-derived extracts or compounds for *Helicobacter*-associated gastritis: a systematic review of their anti-*Helicobacter* activity and anti-inflammatory effect in animal experiments. *Chinese Medicine*. 2025 Apr 22;20(1):53.
25. Shahzad N, Ibrahim IA, Alzahrani AR, Al-Ghamdi SS, Alanazi IM, Ahmad MP, Singh AK, Alruqi MA, Shahid I, Eqbal A, Azlina MF. A comprehensive review of 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.
26. Zayachkivska OS, Gzhegotsky MR, Terletska OI, Lutsyk DA, Yaschenko AM, Dzhura OR. Influence of *Viburnum opulus* proanthocyanidins on stress-induced gastrointestinal mucosal damage. *Journal of physiology and pharmacology*. 2006 Sep 14;57:155.
27. Wu J, Jian Y, Wang H, Huang H, Gong L, Liu G, Yang Y, Wang W. A review of the phytochemistry and pharmacology of the fruit of *Siraitia grosvenorii* (Swingle): A traditional Chinese medicinal food. *Molecules*. 2022 Oct 5;27(19):6618.

28. Chen D, Wang W, Chen X, Liang N, Li J, Ding W, Zhang H, Yang Z, Zhao H, Liu Z. Plant-derived extracts or compounds for *Helicobacter*-associated gastritis: a systematic review of their anti-*Helicobacter* activity and anti-inflammatory effect in animal experiments. *Chinese Medicine*. 2025 Apr 22;20(1):53.
29. Chun LI, Li-Mei LI, Feng SU, Zhi-Min WA, Hai-Ru HU, Li DA. Chemistry and pharmacology of *Siraitia grosvenorii*: A review. *Chinese Journal of Natural Medicines*. 2014 Feb 1;12(2):89-102.
30. Duan J, Zhu D, Zheng X, Ju Y, Wang F, Sun Y, Fan B. *Siraitia grosvenorii* (swingle) C. Jeffrey: research progress of its active components, pharmacological effects, and extraction methods. *Foods*. 2023 Mar 23;12(7):1373.
31. Liu C, Dai L, Liu Y, Dou D, Sun Y, Ma L. Pharmacological activities of mogrosides. *Future Medicinal Chemistry*. 2018 Apr 1;10(8):845-50.
32. Wu J, Jian Y, Wang H, Huang H, Gong L, Liu G, Yang Y, Wang W. A review of the phytochemistry and pharmacology of the fruit of *Siraitia grosvenorii* (Swingle): A traditional Chinese medicinal food. *Molecules*. 2022 Oct 5;27(19):6618.
33. Mundkar M, Bijalwan A, Soni D, Kumar P. Neuroprotective potential of *Moringa oleifera* mediated by NF- κ B/Nrf2/HO-1 signalling pathway: A review. *Journal of food biochemistry*. 2022 Dec;46(12):e14451.
34. Takeuchi K. Pathogenesis of NSAID-induced gastric damage: importance of cyclooxygenase inhibition and gastric hypermotility. *World journal of gastroenterology: WJG*. 2012 May 14;18(18):2147.
35. Jin JS, Lee JH. Phytochemical and pharmacological aspects of *Siraitia grosvenorii*, *luo han kuo*. *Oriental Pharmacy and Experimental Medicine*. 2012 Dec;12(4):233-9.
36. Kwiecien S, Jasnos K, Magierowski M, Sliwowski Z, Pajdo R, Brzozowski B, Mach T, Wojcik D, Brzozowski T. Lipid peroxidation, reactive oxygen species and antioxidative factors in the pathogenesis of gastric mucosal lesions and mechanism of protection against oxidative stress-induced gastric injury. *J Physiol Pharmacol*. 2014 Oct 1;65(5):613-22.
37. Guo Q, Shi M, Sarengaowa, Xiao Z, Xiao Y, Feng K. Recent advances in the distribution, chemical composition, health benefits, and application of the fruit of *Siraitia grosvenorii*. *Foods*. 2024 Jul 19;13(14):2278.
38. Mo Q, Fu H, Zhao D, Zhang J, Wang C, Wang D, Li M. Protective effects of mogroside v on oxidative stress induced by H₂O₂ in skin fibroblasts. *Drug Design, Development and Therapy*. 2021 Dec 1:4901-9.
39. Guo Y, Chen X, Gong P, Long H, Wang J, Yang W, Yao W. *Siraitia grosvenorii* as a homologue of food and medicine: a review of biological activity, mechanisms of action, synthetic biology, and applications in future food. *Journal of Agricultural and Food Chemistry*. 2024 Mar 21;72(13):6850-70.
40. Halliwell B, Gutteridge JM. Free radicals in biology and medicine. Oxford university press; 2015.
41. Qi XY, Chen WJ, Zhang LQ, Xie BJ. Mogrosides extract from *Siraitia grosvenorii* scavenges free radicals in vitro and lowers oxidative stress, serum glucose, and lipid levels in alloxan-induced diabetic mice. *Nutrition Research*. 2008 Apr 1;28(4):278-84.
42. Lu R, Hu J, Liu X, Yu L, Hu J, Jiang H, Liu S, Li M, He J, Yang X, Liang X. Mogroside-rich extract from *Siraitia grosvenorii* fruits protects against heat stress-induced intestinal damage by ameliorating oxidative stress and inflammation in mice. *Food & Function*. 2023;14(2):1238-47.
43. Huenchuguala S, Segura-Aguilar J. Natural compounds that activate the KEAP1/Nrf2 signalling pathway as potential new drugs in the treatment of idiopathic Parkinson's disease. *Antioxidants*. 2024 Sep 18;13(9):1125.
44. Tundis R, Loizzo MR, Bonesi M, Menichini F, FilomenaConforti, Statti G, Menichini F. Natural products as gastroprotective and antiulcer agents: Recent developments. *Natural Product Communications*. 2008 Dec;3(12):1934578X0800301234.
45. Wu X, Wei J, Yi Y, Gong Q, Gao J. Activation of Nrf2 signalling : A key molecular mechanism of protection against cardiovascular diseases by natural products. *Front Pharmacol*. 2022; 13 [Internet]. 2022
46. Ott M, Gogvadze V, Orrenius S, Zhivotovsky B. Mitochondria, oxidative stress and cell death. *Apoptosis*. 2007 May;12(5):913-22.
47. Sun AY, Simonyi A, Sun GY. Serial review: alcohol, oxidative stress and cell injury. *Free radical biology and medicine*. 2002 Nov;32:9-4.
48. Reuter S, Gupta SC, Chaturvedi MM, Aggarwal BB. Oxidative stress, inflammation, and cancer: how are they linked?. *Free radical biology and medicine*. 2010 Dec 1;49(11):1603-16.
49. Morgan MJ, Liu ZG. Crosstalk of reactive oxygen species and NF- κ B signalling . *Cell research*. 2011 Jan;21(1):103-15.
50. Chung BS, Yang K, Park C, Ryu T. Prolonged intestinal ethanol absorption and oxidative stress: Revisiting the gut–liver axis in alcohol-associated disease. *International Journal of Molecular Sciences*. 2025 Jun 6;26(12):5442.
51. Nkpaa KW, Adedara IA, Amadi BA, Wegwu MO, Farombi EO. Ethanol via regulation of NF- κ B/p53 signalling pathway increases manganese-induced inflammation and apoptosis in hypothalamus of rats. *Biological Trace Element Research*. 2019 Jul 15;190(1):101-8.
52. Zhang T, Gao Z, Zeng D, Wang Y. Mogroside V: A Review of Its Structure, Synthesis, Pharmacokinetics, and Toxicity. *Archiv der Pharmazie*. 2025 Oct;358(10):e70112.
53. Lawrence T. The nuclear factor NF- κ B pathway in inflammation. *Cold Spring Harbor perspectives in biology*. 2009 Dec 1;1(6):a001651.

54. Wu Y, Jin F, Wang Y, Li F, Wang L, Wang Q, Ren Z, Wang Y. In vitro and in vivo anti-inflammatory effects of theaflavin-3, 3'-digallate on lipopolysaccharide-induced inflammation. *European Journal of Pharmacology*. 2017 Jan 5;794:52-60.
55. Li Y, Zou L, Li T, Lai D, Wu Y, Qin S. Mogroside V inhibits LPS-induced COX-2 expression/ROS production and overexpression of HO-1 by blocking phosphorylation of AKT1 in RAW264. 7 cells. *Acta biochimica et biophysica Sinica*. 2019 Apr;51(4):365-74.
56. Moncada S, Higgs EA. Nitric oxide and the vascular endothelium. *The vascular endothelium I*. 2006 Jan 1:213-54.
57. Grisham MB, Granger DN. Neutrophil-mediated mucosal injury: role of reactive oxygen metabolites. *Digestive diseases and sciences*. 1988 Mar;33(Suppl 3):6S-15S.
58. Huang X, Liu Y, Lu Y, Ma C. Anti-inflammatory effects of eugenol on lipopolysaccharide-induced inflammatory reaction in acute lung injury via regulating inflammation and redox status. *International immunopharmacology*. 2015 May 1;26(1):265-71.
59. Paulraj RS, Sathiyaseelan A, Perumal P, Ramachandran A. Mechanistic Insights into the Therapeutic Potential of Phytochemicals Against Stress-Induced Gastric Ulcer. *Journal of Inflammation Research*. 2025 Dec 31:17961-81.
60. Liu J, Wang F, Luo H, Liu A, Li K, Li C, Jiang Y. Protective effect of butyrate against ethanol-induced gastric ulcers in mice by promoting the anti-inflammatory, anti-oxidant and mucosal defence mechanisms. *International immunopharmacology*. 2016 Jan 1;30:179-87.
61. Zhang T, Gao Z, Zeng D, Wang Y. Mogroside V: A Review of Its Structure, Synthesis, Pharmacokinetics, and Toxicity. *Archiv der Pharmazie*. 2025 Oct;358(10):e70112.
62. Lenders V, Koutsoumpou X, Phan P, Soenen SJ, Allegaert K, de Vleeschouwer S, Toelen J, Zhao Z, Manshian BB. Modulation of engineered nanomaterial interactions with organ barriers for enhanced drug transport. *Chemical Society Reviews*. 2023;52(14):4672-724.
63. Takeuchi K, Amagase K. Roles of cyclooxygenase, prostaglandin E2 and EP receptors in mucosal protection and ulcer healing in the gastrointestinal tract. *Current pharmaceutical design*. 2018 May 1;24(18):2002-11.
64. Guo Y, Chen X, Gong P, Long H, Wang J, Yang W, Yao W. *Siraitia grosvenorii* as a homologue of food and medicine: a review of biological activity, mechanisms of action, synthetic biology, and applications in future food. *Journal of Agricultural and Food Chemistry*. 2024 Mar 21;72(13):6850-70.
65. Sørbye H, Svanes K. The role of blood flow in gastric mucosal defence, damage and healing. *Digestive Diseases*. 1994 Nov 4;12(5):305-17.
66. S Tarnawski A, Ahluwalia A, K Jones M. The mechanisms of gastric mucosal injury: focus on microvascular endothelium as a key target. *Current medicinal chemistry*. 2012 Jan 1;19(1):4-15.
67. Cao S, Liu M, Han Y, Li S, Zhu X, Li D, Shi Y, Liu B. Effects of saponins on lipid metabolism: the gut–liver axis plays a key role. *Nutrients*. 2024 May 17;16(10):1514.
68. Pan JS, He SZ, Xu HZ, Zhan XJ, Yang XN, Xiao HM, Shi HX, Ren JL. Oxidative stress disturbs energy metabolism of mitochondria in ethanol-induced gastric mucosa injury. *World journal of gastroenterology: WJG*. 2008 Oct 14;14(38):5857.
69. Nkpaa KW, Awogbindin IO, Amadi BA, Abolaji AO, Adedara IA, Wegwu MO, Farombi EO. Ethanol exacerbates manganese-induced neurobehavioral deficits, striatal oxidative stress, and apoptosis via regulation of p53, caspase-3, and Bax/Bcl-2 ratio-dependent pathway. *Biological Trace Element Research*. 2019 Sep 15;191(1):135-48.
70. Tan YR, Shen SY, Li XY, Yi PF, Fu BD, Peng LY. Mogroside V reduced the excessive endoplasmic reticulum stress and mitigated the Ulcerative colitis induced by dextran sulfate sodium in mice. *Journal of Translational Medicine*. 2024 May 21;22(1):488.
71. Mosadegh M, Noori Goodarzi N, Erfani Y. A comprehensive insight into apoptosis: molecular mechanisms, signalling pathways, and modulating therapeutics. *Cancer Investigation*. 2025 Jan 2;43(1):33-58.
72. Pan JS, He SZ, Xu HZ, Zhan XJ, Yang XN, Xiao HM, Shi HX, Ren JL. Oxidative stress disturbs energy metabolism of mitochondria in ethanol-induced gastric mucosa injury. *World journal of gastroenterology: WJG*. 2008 Oct 14;14(38):5857.
73. Sheng Y, Li S, Yue-Rong T, Qin S, Tan Z, Song C, Yi P, Peng L, Fu B. Mogroside V inhibits the tunicamycin-induced endoplasmic reticulum stress in Caco-2 cells. *Animals and Zoonoses*. 2026 Jan 12.
74. 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.
75. Wu J, Jian Y, Wang H, Huang H, Gong L, Liu G, Yang Y, Wang W. A review of the phytochemistry and pharmacology of the fruit of *Siraitia grosvenorii* (Swingle): A traditional Chinese medicinal food. *Molecules*. 2022 Oct 5;27(19):6618.
76. Wallace JL. Pathogenesis of NSAID-induced gastroduodenal mucosal injury. *Best practice & research Clinical gastroenterology*. 2001 Oct 1;15(5):691-703.
77. Brzozowski T, Konturek PC, Konturek SJ, Brzozowska I, Pawlik T. Role of prostaglandins in gastroprotection and gastric adaptation. *Journal of physiology and pharmacology*. 2005 Sep 1;56(Suppl 5):33-55.

78. Mo Q, Fu H, Zhao D, Zhang J, Wang C, Wang D, Li M. Protective effects of mogroside v on oxidative stress induced by H₂O₂ in skin fibroblasts. *Drug Design, Development and Therapy*. 2021 Dec 1:4901-9.
79. Gusti AM, Qusti SY, Alshammari EM, Toraih EA, Fawzy MS. Antioxidant-related superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), glutathione-S-transferase (GST), and nitric oxide synthase (NOS) gene variants analysis in an obese population: a preliminary case-control study. *Antioxidants*. 2021 Apr 13;10(4):595. Mogrosides from *Siraitia grosvenorii*
80. Paulraj RS, Anbazhagan S, Perumal P, Ramachandran A, Paulraj SG. A Comprehensive Analysis of Therapeutic Potential of Medicinal Plant Extracts to Treat Ethanol-Induced Gastric Ulcer. *Biomedicines*. 2026 Feb 28;14(3):562.
81. Luo Z, Zang Y, Su J, Tang Q, Pan L, Ma X, Wang C, Mo C. A review of *Siraitia grosvenorii*: Applications, breeding, and biosynthesis of mogrosides. *Chinese Herbal Medicines*. 2025 Nov 15.
82. Zhang Z, Adiham A, Han C, Huang F, Yan Y, Li D, Guo K, Gu J, Gong P. Mogroside V derived from *Siraitia grosvenorii* fruit: From evidence of health-promoting benefits to food applications. *Trends in Food Science & Technology*. 2025 Sep 1;163:105141.
83. Liu C, Dai L, Liu Y, Dou D, Sun Y, Ma L. Pharmacological activities of mogrosides. *Future Medicinal Chemistry*. 2018 Apr 1;10(8):845-50.
84. Intharuksa A, Arunotayanun W, Takuathung MN, Boongla Y, Chaichit S, Khamnuan S, Prasansuklab A. Therapeutic potential of herbal medicines in combating particulate matter (PM)-induced health effects: Insights from recent studies. *Antioxidants*. 2024 Dec 27;14(1):23.
85. Jin M, Muguruma M, Moto M, Okamura M, Kashida Y, Mitsumori K. Thirteen-week repeated dose toxicity of *Siraitia grosvenori* extract in Wistar Hannover (GALAS) rats. *Food and Chemical Toxicology*. 2007 Jul 1;45(7):1231-7.
86. Freedberg DE, Kim LS, Yang YX. The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. *Gastroenterology*. 2017 Mar 1;152(4):706-15.
87. Zhang J, Zhang Y, Wang H, Chen W, Lu A, Li H, Kang L, Wu C. Solubilisation and enhanced oral absorption of curcumin using a natural non-nutritive sweetener mogroside V. *International Journal of Nanomedicine*. 2023 Dec 31:1031-45.
88. Bácskay I, Arany P, Fehér P, Józsa L, Vasvári G, Nemes D, Pető Á, Kósa D, Haimhoffer Á, Ujhelyi Z, Sinka D. Bioavailability enhancement and formulation technologies of oral mucosal dosage forms: a review. *Pharmaceutics*. 2025 Jan 22;17(2):148.
89. Kim YJ, Kim EH, Hahm KB. Oxidative stress in inflammation-based gastrointestinal tract diseases: Challenges and opportunities. *Journal of gastroenterology and hepatology*. 2012 Jun;27(6):1004-10.
90. Robinson M. The pharmacodynamics and pharmacokinetics of proton pump inhibitors—overview and clinical implications. *Alimentary pharmacology & therapeutics*. 2004 Nov;20:1-0.
91. Ai R, Tian M, Sun J, He S, Cui Z, Yang Y, Hou X, Zhao Y, Dou T, Chen X, Wang J. Mogroside V prevents ethanol-induced hangover and liver damage by reducing oxidative stress, steatosis and inflammation. *Biochemical and Biophysical Research Communications*. 2025 Jun 20;766:151912.
92. Ahmed KA, Alqaisi KM, Jabbar AA, Ismail PA, Ibrahim NA, Althagbi HI, Hassan RR, Saber MH, Saleh GN, Saleh MI, Alqaisi TS. Grosvenorine (Monk fruit flavonoid) attenuates Indomethacin-mediated gastropathy in vivo: role of P53/Bcl-2, Antioxidant, and inflammatory mediators. *Journal of Pharmaceutical Innovation*. 2025 Oct;20(5):203.
93. Yeung AW. Bibliometric analysis on the literature of monk fruit extract and mogrosides as sweeteners. *Frontiers in nutrition*. 2023 Aug 29;10:1253255.
94. Wen Z, Liu W, Li X, Chen W, Liu Z, Wen J, Liu Z. A protective role of the NRF2-Keap1 pathway in maintaining intestinal barrier function. *Oxidative medicine and cellular longevity*. 2019;2019(1):1759149.
95. Maideen NM. Adverse effects associated with long-term use of proton pump inhibitors. *Chonnam medical journal*. 2023 May 25;59(2):115.
96. EFSA Panel on Food Additives and Flavourings (FAF), Younes M, Aquilina G, Engel KH, Fowler P, Frutos Fernandez MJ, Fürst P, Gürtler R, Gundert-Remy U, Husøy T, Mennes W. Safety of use of Monk fruit extract as a food additive in different food categories. *Efsa Journal*. 2019 Dec;17(12):e05921.
97. Xu Q, Chen SY, Deng LD, Feng LP, Huang LZ, Yu RR. Antioxidant effect of mogrosides against oxidative stress induced by palmitic acid in mouse insulinoma NIT-1 cells. *Brazilian Journal of Medical and Biological Research*. 2013 Nov 18;46(11):949-55.
98. Lee YM, Kim M, Yuk HJ, Kim SH, Kim DS. *Siraitia grosvenorii* residual extract inhibits inflammation in RAW264. 7 macrophages and attenuates osteoarthritis progression in a rat model. *Nutrients*. 2023 Mar 15;15(6):1417.
99. Luo Y, Gong C, Wei M, Chen Y, Song T, Wu C, Mo L, Zhang J. Evaluation of mogroside V as a promising carrier in drug delivery: improving the bioavailability and liver distribution of silybin. *AAPS PharmSciTech*. 2020 Apr 26;21(4):123.

100. Chen N, Cao W, Yuan Y, Wang Y, Zhang X, Chen Y, Yiasmin MN, Tristante NA, Hua X. Recent advancements in mogrosides: A review on biological activities, synthetic biology, and applications in the food industry. Food Chemistry. 2024 Aug 15;449:139277.