MAHSA International Journal of Health and
Medicine, V5, Issue 2; July, 2025
e-ISSN: 2805-5705

Original Article Open Access

RESEARCH PROGRESS ON THE PHARMACOLOGICAL EFFECTS OF MOGROSIDE

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Received: 5th July 2025 Accepted: 14th July 2025 Published: 31st July 2025

Abstract

Mogroside, a naturally occurring sweetener derived from *Siraitia grosvenorii*, showcases a remarkable spectrum of pharmacological properties. This comprehensive review encapsulates the salient pharmacological effects of mogroside, encompassing its anti-diabetic, antioxidant, anti-inflammatory, and anti-cancer capabilities, while also delving into its therapeutic potential in domains such as neuroprotection and cardioprotection. Investigations have elucidated mogroside's therapeutic efficacy against a multitude of ailments, achieved through intricate mechanisms involving the activation of the AMPK signaling pathway, inhibition of the NF-κB signaling pathway, and modulation of the cell cycle. Furthermore, this review critically examines the challenges encountered in mogroside research and application, including its limited bioavailability and partially understood mechanisms of action. It proposes future research avenues, emphasizing the validation of its efficacy and safety through clinical trials and the optimization of its therapeutic potency utilizing advanced drug delivery technologies. This review aspires to serve as a valuable resource for the continued exploration and development of mogroside, offering a comprehensive foundation for future scientific endeavors.

Keywords: Mogroside; Pharmacological Activities; Anti-diabetic; Antioxidant; Anti-inflammatory; Anti-cancer; Future Research Directions

1. Introduction

Siraitia grosvenorii, commonly known as monk fruit in English, is a medicinal plant primarily cultivated in southern China and has been utilized in traditional medicine for over three centuries. Its fruit contains a high concentration of mogrosides, a class of natural sweeteners, which are widely used as sugar substitutes and therapeutic ingredients [1]. Mogrosides are characterized by their intense sweetness and low caloric content, making them an ideal alternative for individuals with diabetes or those seeking to reduce caloric intake. Beyond their use as food additives, mogrosides have garnered significant scientific interest due to their diverse pharmacological activities, particularly in the areas of anti-inflammatory, antioxidant, anti-diabetic, and anti-cancer research [2].

Mogrosides are a group of sweet glycosides, with over 20 monomers identified to date. These monomers are classified based on the position, number, and bonding pattern of glucose moieties on the triterpene saponin backbone, including variants such as MGIIE, MGIII, MGIIIE, and mogroside V (MGV), the latter being the most prevalent [3]. Notably, these compounds exhibit sweetness levels several hundred times greater than sucrose, rendering monk fruit not only a valuable natural sweetener but also a subject of intensive pharmacological investigation due to their bioactive properties.

Pharmacological studies have demonstrated that mogrosides possess significant anti-diabetic and antioxidant effects. For instance, in a study using a high-fat diet and streptozotocin (STZ)-induced diabetic model, mogroside (MGE) exhibited notable hypoglycemic and hypolipidemic effects, which were associated with the activation of the AMP-activated protein kinase (AMPK) signaling pathway in the liver [4]. Furthermore, mogrosides have been shown to reduce lipid peroxide levels and enhance antioxidant enzyme activity in vivo, underscoring their crucial role in the antioxidant defense system [5].

The anti-inflammatory properties of mogrosides also represent a key dimension of their pharmacological profile. Research indicates that mogrosides can effectively inhibit the production of inflammatory mediators through suppression of the nuclear factor kappa-B (NF-κB) signaling pathway, thereby reducing the expression of pro-inflammatory cytokines [6]. This anti-inflammatory potential extends beyond in vitro studies, as evidenced by animal models. For example, in a lipopolysaccharide (LPS)-induced inflammation model, mogrosides significantly mitigated inflammatory responses, highlighting their therapeutic relevance.

Mogrosides have also demonstrated substantial anti-cancer potential. They not only inhibit tumor cell proliferation but also induce apoptosis and cause cell cycle arrest. In a pancreatic carcinoma cell model, mogrosides significantly suppressed tumor cell growth and promoted apoptosis through modulation of the STAT3 signaling pathway [7]. These findings underscore the potential of mogrosides as candidates for oncological therapeutics and justify further exploration into their anti-cancer mechanisms.

In addition to their pharmacological effects, understanding the pharmacokinetics of mogrosides is essential for optimizing their therapeutic application. Studies indicate that mogrosides exhibit favorable bioavailability and are metabolized primarily in the gastrointestinal tract, where they are hydrolyzed into bioactive metabolites. These metabolites, in turn, exert pharmacological effects systemically. However, comprehensive pharmacokinetic studies remain limited, and further research is needed to elucidate the absorption, distribution, metabolism, and excretion (ADME) profiles of mogrosides. A deeper understanding of these processes will facilitate the development of mogroside-based interventions and improve their clinical efficacy.

Given their extensive pharmacological effects across multiple biomedical domains, mogrosides have emerged as promising candidates for functional food and pharmaceutical applications. This article aims to provide a comprehensive review of the pharmacological research on mogrosides, elucidate their mechanisms of action and pharmacokinetic characteristics, and outline potential clinical applications while offering directions for future investigations.

2. Pharmacokinetics and Metabolism

The pharmacokinetic properties and metabolic pathways of mogrosides are crucial for evaluating their efficacy and safety as therapeutic agents. A comprehensive understanding of the absorption, metabolism, distribution, and excretion of mogrosides in the human body provides deeper insight into the mechanisms underlying their pharmacological actions.

2.1 Absorption and Biotransformation

The in vivo biotransformation of *Siraitia grosvenorii* sweeteners involves complex biochemical reactions, including diverse degradation processes catalyzed by gut microbiota. These microbial activities convert *Siraitia grosvenorii* sweeteners into various small-molecule metabolites with distinct bioactivities [8, 9]. For instance, mogroside V (MGV) can be transformed in vivo into 11-oxo-mogroside V, a metabolite exhibiting enhanced antioxidant and anti-inflammatory properties [10]. Moreover, studies suggest that these metabolites may exert more potent pharmacological effects, including anti-cancer and anti-diabetic activities, than the original mogrosides [11].

2.2 Distribution

The in vivo distribution pattern of mogrosides and their metabolites directly influences their pharmacological activity. Research indicates that mogrosides and their metabolites primarily accumulate in vital organs such as the liver, kidneys, and pancreas [4]. This organ-specific distribution is closely associated with key pharmacological effects, including blood sugar regulation, anti-inflammatory activity, and organ protection. In particular, the hepatic accumulation of mogrosides facilitates their role in regulating lipid and glucose metabolism [5].

A comparative analysis of the metabolic transformation of lohanuoside V in healthy and type 2 diabetic model rats, conducted using ultra-high-performance liquid chromatography/quadrupole time-of-flight mass spectrometry combined with differential metabolite screening, revealed significant differences in metabolite profiles between the two groups. Notably, the metabolites detected in the blood and urine varied substantially, indicating that disease status may influence the metabolic pathways of mogrosides [12].

Further studies comparing the effects of *Siraitia grosvenorii* extract (SGFE) and MGV on hepatic metabolism in murine models of allergic pneumonitis demonstrated that both compounds inhibit inflammatory cytokine expression and alleviate inflammatory responses in lung tissue. However, MGV was more effective in mitigating oxidative stress-induced liver injury. Metabolomic analysis indicated that MGV primarily exerts its effects through the riboflavin and glutathione metabolism pathways, while SGFE influences a broader array of metabolic pathways [13].

2.3 Excretion

The excretion pathways of mogrosides and their metabolites are critical for assessing their safety and pharmacokinetic behavior. Studies indicate that mogrosides are primarily excreted through urine and feces [14]. Metabolites detected in urine reflect their bio-transformed active forms, while fecal excretion suggests that a portion of mogrosides remains unabsorbed in the digestive tract [6]. Furthermore, the variability in excretion patterns among individuals implies that the bioavailability of mogrosides may differ, which has significant implications for their development and clinical application as therapeutic agents [15].

Pharmacokinetic studies of mogrosides provide a theoretical framework for their clinical use. Continued research into their specific biotransformation pathways and distribution patterns will facilitate the optimization of their therapeutic potential and improve their applicability in medical treatments.

3. Pharmacological Activity

3.1. Anti-diabetic and metabolic effects

Mogroside exhibits remarkable potential in combating diabetes and ameliorating metabolic dysfunctions. Extensive research has demonstrated that mogroside exerts anti-diabetic effects and combats diabetic complications by modulating glucose and lipid metabolism through the activation of specific signaling pathways[16-19].

Mogroside can significantly reduce fasting blood glucose levels in diabetic mice induced by a high-fat diet combined with streptozotocin (STZ). In a study, by supplementing with mogroside-containing extracts, the fasting blood glucose levels of diabetic mice were significantly reduced, and insulin sensitivity was improved[4]. In addition, another study revealed that lo han guo can lower blood glucose and lipid levels in diabetic mice via activation of the AMP-activated protein kinase (AMPK) pathway. [20]Employing an in vitro cellular paradigm, the researchers evaluated the impact of *Siraitia grosvenorii* and its primary constituent, mogroside V (MGV), on insulin secretion. The findings demonstrated that both the crude extract of *Siraitia grosvenorii* and purified MGV significantly stimulated pancreatic β-cell production of insulin, potentially elucidating the mechanism underlying the insulinotropic activity of *Siraitia grosvenorii* and its extracts. This study corroborates the potential of *Siraitia grosvenorii*/extracts as natural sweeteners with a low glycemic index, while also revealing the potential health benefits of compounds like MGV via stimulation of insulin secretion[21]. MogrosideIIIE, through the activation of the AMPK/SIRT1 signaling pathway, mitigates hyperglycemia-induced inflammation, oxidative stress, and apoptosis, thereby reducing glomerular cell damage and enhancing cell viability[18].

A study investigated the effects of mogroside (MG) and low-polarity mogroside glycoside (L-SGgly) from *Siraitia grosvenorii* extract on gut microbiota and fecal metabolites in type 2 diabetic rats. After 14 days of treatment, the gut microbiota of T2DM rats was restored, while the concentration of short-chain fatty acids in feces increased significantly, and the contents of deoxycholic acid and Iβ-hydroxycholic acid decreased. Correlation analysis showed that the gut microbiota and its metabolites might be the targets of SG and L-SGgly in exerting anti-hyperglycemic effects[22]. These studies suggest that mogroside can serve as a potential natural anti-diabetic agent.

Mogroside also plays a regulatory role in fat metabolism. Studies have shown that mogroside can reduce fat accumulation, lower total cholesterol and low-density lipoprotein levels in serum, which is of great significance for the prevention and treatment of cardiovascular diseases related to diabetes[7]. Mogroside antidiabetic activity is also related to its antioxidant properties, which can reduce oxidative stress, thereby protecting islet cells and maintaining their normal function[6, 19].In a high-fat diet mouse model and free fatty acid-treated LO2 cells, Mogroside V significantly inhibited de novo lipogenesis and promoted lipolysis and fatty acid oxidation via activation of the AMPK-dependent pathway, thereby alleviating fatty liver[23].

Researchers utilized a high-fat diet (HFD)-induced mouse model of obesity to evaluate the intervention effects of Momordica grosvenori-enriched sweet glycoside extract (MGE) and its impact on gut microbiota. Results demonstrated that MGE not only significantly reduced weight gain and adipose tissue accretion in mice but also ameliorated glycometabolism-related parameters. 16S rDNA analysis revealed that HFD feeding induced dysbiosis in the gut microbiota of mice, as evidenced by an elevated Firmicutes/Bacteroidetes (F/B) ratio, while MGE administration effectively rectified this imbalance, decreasing the abundance of obesity-associated taxa. This study meticulously designed an in vivo animal model, preliminarily

elucidating a novel mechanism by which MGE alleviates obesity symptoms, involving the modulation of gut microbiota homeostasis, thus providing novel insights for the development of probiotics or microbiome-based therapeutics[24].

These findings not only underscore the promising therapeutic applications of mogrosides for diabetes and its complications but also provide scientific substantiation for their further development as health food additives.

3.2.Antioxidant and anti-inflammatory properties

Mogrosides exhibit remarkable pharmacological activities, particularly in their antioxidant and anti-inflammatory effects. Their antioxidant properties are primarily achieved by scavenging free radicals and enhancing the endogenous antioxidant defense system, while their anti-inflammatory effects are exerted through modulating inflammatory mediators and suppressing inflammatory pathways.

Mogroside V mitigates oxidative stress through multiple mechanisms. Studies demonstrate that Mogroside V significantly reduces the production of lipid peroxidation products while enhancing the activities of intracellular superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), thus protecting cells from oxidative damage [4, 5, 10]. Additionally, mogrosides enhance the activity of antioxidant enzymes in the liver, further underscoring their antioxidant efficacy in vivo [25, 26]. These effects collectively protect against cellular oxidative stress and prevent oxidative damage [27].

Regarding anti-inflammatory properties, mogrosides effectively reduce the production of inflammatory mediators, such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), by inhibiting the nuclear factor kappa B (NF-κB) signaling pathway [6, 28]. This modulation alleviates inflammatory conditions and related disorders. Mogrosides also demonstrate the ability to mitigate acute inflammatory responses induced by lipopolysaccharide (LPS) in animal models [7]. Mogroside V specifically attenuates inflammation induced by particulate matter (PM2.5), alleviating pulmonary tissue infiltration, restoring the balance between Th17 and Treg cytokines, and suppressing the expression of pro-inflammatory factors. Furthermore, Mogroside V regulates the lung microbiota by increasing beneficial bacteria and reducing inflammation-associated strains, which contributes to its protective effects against LPS-induced lung injury [29, 30]. It also inhibits inflammatory responses in RAW264.7 cells by suppressing LPS-induced COX-2 expression and reactive oxygen species (ROS) production through the blockade of AKT1 phosphorylation, thereby reducing NF-κB and C/EBPδ activation [31]. In LPS-induced acute lung injury (ALI) mouse models, Mogroside V significantly suppresses airway inflammation, reduces cytokine production, and inhibits COX-2 and iNOS activity, thereby alleviating lung tissue damage [32].

Mogroside III E (MGIII) exhibits a potent antifibrotic effect by suppressing pulmonary inflammation and extracellular matrix deposition through modulation of the TLR4/MyD88-MAPK signaling pathway. In a murine model of pulmonary fibrosis, MGIII effectively reduced fibrosis markers and alleviated inflammation, highlighting its potential as a therapeutic agent [33]. Integrated miRNA-seq and mRNA-seq analyses in OVA-induced asthmatic mice identified miR-21-5p as a key mediator of Mogroside V's anti-inflammatory effects. Mogroside V downregulates miR-21-5p while upregulating SPRY1, which reduces the expression of inflammatory factors and ROS in LPS-treated RAW 264.7 cells and OVA-induced asthmatic mice. Experimental manipulation of miR-21-5p and SPRY1 expression confirmed their pivotal role in mediating the anti-inflammatory effects of Mogroside V, highlighting their potential as therapeutic targets [34].

Further studies using a mouse model of LPS-induced ALI showed that MGIII alleviates inflammation in a dose-dependent manner by inhibiting pro-inflammatory cytokines and

increasing myeloperoxidase (MPO) activity. Molecular studies revealed that MGIII activates AMPK phosphorylation while suppressing TLR4/MyD88 expression and the MAPK/NF-κB pathway. The protective effects of MGIII were significantly reversed by the AMPK inhibitor compound C, confirming the involvement of the AMPK signaling pathway in its anti-inflammatory mechanisms [35].

In a murine model, mogroside IV E (MGIVE) (25 mg/kg) significantly ameliorated CCl4-induced hepatic inflammation and fibrosis. It improved liver function while suppressing the expression of fibrosis markers such as type I collagen and hypoxia-inducible factor-1α (HIF-1α). MGIVE also reduced the overexpression of transforming growth factor-β1 (TGF-β1) and MAPK phosphorylation by modulating TLR4-mediated signaling pathways. In vitro, MGIVE demonstrated antifibrotic effects on TGF-β1- or LPS-stimulated hepatic stellate cells (HSCs) and RAW 264.7 cells, further supporting its therapeutic potential in hepatic fibrosis [36].

To explore its anti-pneumonia mechanisms, researchers evaluated the effects of Mogroside V in asthmatic mice using LC-MS metabolomics. Mice treated with Mogroside V exhibited significant reductions in lung inflammation induced by ovalbumin (OVA), with organ indices comparable to control levels. Metabolomic analysis identified six key metabolic pathways affected by Mogroside V, including vitamin B6 metabolism, taurine and hypotaurine metabolism, ascorbic acid and aldose metabolism, histidine metabolism, pentose and glucuronic acid interconversion, and the tricarboxylic acid (TCA) cycle. This study provided the first comprehensive elucidation of Mogroside V's metabolic regulatory mechanisms in pneumonia using metabolomics analysis [37].

Using chemiluminescence (CL) techniques, researchers assessed the antioxidant activity of Mogroside V and its derivative, 11-oxo-mogroside V, in vitro. Both compounds, characterized by a tetracyclic triterpenoid skeleton, effectively scavenged singlet oxygen (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl radicals (•OH) while protecting against oxidative DNA damage. Notably, 11-oxo-mogroside V exhibited superior scavenging of O_2^- and H_2O_2, while Mogroside V was more effective in neutralizing •OH. Importantly, 11-oxo-mogroside V showed exceptional efficacy in preventing •OH-induced DNA damage [38].

These findings provide robust evidence supporting the potential of mogrosides as natural antioxidants and anti-inflammatory agents. The diversity of their mechanisms and the significance of their effects establish a solid foundation for further pharmacological research and future clinical applications.

3.3. Anticarcinogenic properties

Mogenin exhibits significant antitumor properties, primarily through its ability to inhibit cancer cell proliferation, induce apoptosis, and regulate the cell cycle. These mechanisms collectively demonstrate its therapeutic potential across various cancer models.

Mogrosides effectively suppress the growth of different cancer types. In pancreatic cancer models, mogrosides not only inhibit cancer cell proliferation but also induce apoptosis by modulating the STAT3 signaling pathway [7]. Similarly, in colorectal cancer cells, mogrosides exert anticancer effects through cell cycle arrest and the enhancement of apoptotic mechanisms [14].

Studies utilizing network pharmacology and molecular docking have further elucidated the therapeutic mechanisms of *Siraitia grosvenorii* mogroside V (MGV) against ovarian cancer in COVID-19 patients. Researchers identified 24 potential targets of MGV relevant to ovarian cancer and COVID-19, with 10 core targets, including Jun, IL2, HSP90AA1, AR, PRKCB, VEGFA, TLR9, TLR7, STAT3, and PRKCA. Enrichment analysis highlighted key biological processes and signaling pathways associated with these targets, while molecular docking demonstrated a favorable binding affinity between MGV and proteins such as vascular endothelial growth factor A (VEGFA) [39].

MGV also reverses epithelial-mesenchymal transition (EMT) in lung cancer cells under hyperglycemic conditions, thereby inhibiting cancer cell migration and invasion. In A549 and H1299 lung cancer cells, MGV suppresses the expression of EMT markers such as N-cadherin, vimentin, and Snail while increasing E-cadherin expression. This modulation reduces the activity of Rho-GTPase family proteins (Rho A, Rac1, Cdc42, and p-PAK1), which are critical in regulating cell migration and invasion [16].

Beyond direct tumor suppression, mogrosides impede angiogenesis, a key process in tumor growth and metastasis. Animal studies have shown that mogrosides suppress tumor vasculature formation by downregulating the expression of vascular endothelial growth factor (VEGF), thereby restricting tumor growth and metastasis [40]. Furthermore, mogrosides demonstrate potential in cancer prevention by reducing DNA damage and cellular mutations through their antioxidant properties, which may help prevent the development of liver cancer [41].

These findings highlight the potential of mogrosides as natural anticancer agents, providing a scientific basis for their further development in pharmaceutical research and cancer therapy.

3.4. Other Therapeutic Potentials

Mogroside shows significant therapeutic potential across several areas, including neuroprotection, cardioprotection, psychiatric disorders, anti-aging, immunomodulation, and reproductive health.

Mogroside demonstrates remarkable neuroprotective effects in both in vivo and in vitro studies. In a rotenone-induced Parkinson's disease model, MGV (10 mg/kg) reverses motor deficits and protects dopaminergic neurons by reducing ROS overproduction, restoring mitochondrial membrane potential, and enhancing ATP generation. These protective effects are mediated by the activation of deacetylase Sirtuin3 and its downstream target, SOD2, and are abolished when Sirtuin3 is inhibited. In vitro studies indicate that MGV and its metabolite, 11-oxo-mogrol, protect against MK-801-induced neuronal damage by promoting neurite outgrowth, inhibiting apoptosis, and preventing calcium ion release. Furthermore, MGV mitigates neuroinflammation by inhibiting the TLR4-MyD88 pathway and activating AKT/AMPK-Nrf2 signaling, reducing LPS-induced proinflammatory cytokines while enhancing antioxidant enzymes.

Mogroside also exhibits antidepressant properties in chronic unpredictable mild stress (CUMS) models. MGV protects PC12 cells from corticosterone-induced injury and alleviates depression-like behaviors in stressed rats by reducing inflammation, oxidative stress, and hippocampal apoptosis through modulation of the BDNF/TrkB/AKT pathway. Additionally, *Siraitia grosvenorii* saponins delay β-amyloid-induced paralysis in Alzheimer's models by reducing oxidative stress and modulating antioxidant gene expression.

Mogrosides improve cardiac function and reduce myocardial injury via the AMPK pathway, which enhances the heart's antioxidant capacity and protects against damage from high-fat diets. In an isoproterenol-induced myocardial fibrosis mouse model, Momordica grosvenori glycoside III E (MG III E) suppresses inflammation and fibrosis by downregulating the TLR4/MyD88/NF-κB signaling pathway, decreasing collagen deposition and inflammatory factor release.

Mogroside IIE (MGEIIE) shows promise in diabetic cardiomyopathy (DCM) by improving blood glucose, lipid profiles, and cardiac function while inhibiting apoptosis-related proteins (caspase, Bax, and Cyt-C) in vivo and in vitro. These findings suggest that MGEIIE mitigates DCM by suppressing apoptosis pathways.

Siraitia grosvenorii glycosides inhibit cellular senescence and promote cell viability, contributing to their anti-aging effects. These compounds also regulate the immune system by modulating cytokine release. In immunosuppressed mice, mogroside enhances macrophage phagocytosis and T

lymphocyte proliferation without affecting normal mice.

Mogrosides protect pancreatic islets in streptozotocin-induced diabetic mice by restoring the CD4+/CD8+ ratio and enhancing IL-4 expression, suggesting a role in restoring immune balance in insulin-dependent diabetes mellitus (IDDM). Mogroside also strengthens antiviral immunity. In restraint stress-induced influenza models, it inhibits Mfn2-mediated MAVS ubiquitination, enhancing MAVS-mediated IFN-β responses and reducing susceptibility to H1N1 infection.

Mogrol suppresses osteoclastogenesis by inhibiting TRAF6-dependent NF-κB signaling and key transcription factors (NFATc1 and c-Fos), thereby reducing bone loss in ovariectomized mice. This suggests a potential role for mogrol in osteoporosis prevention and treatment.

Mogroside supports reproductive health and oocyte maturation. It stabilizes microtubules, aligns chromosomes, and reduces oxidative stress-induced oocyte damage, preserving embryo quality. In polycystic ovary syndrome (PCOS) models, MGV promotes follicle development and ovulation by enhancing glycolysis and energy metabolism, offering therapeutic potential for PCOS management.

Mogroside alleviates heat stress-induced intestinal injury in mice by reducing TNF-α levels, restoring superoxide dismutase (SOD) activity, and modulating oxidative stress and inflammatory gene expression. These findings highlight its protective role in maintaining intestinal integrity under extreme conditions.

Mogrosides exhibit a broad range of therapeutic benefits beyond their anticancer, anti-inflammatory, and antidiabetic effects. Their neuroprotective, cardioprotective, immunomodulatory, and anti-aging properties suggest substantial promise for future pharmaceutical development and therapeutic applications across various medical domains.

3.5 Correlation analysis of the pharmacological mechanism of action of mogrosides

There is a certain correlation between the multiple pharmacological mechanisms of mogroside, especially when the same signaling pathway is involved. Mogroside is involved in both antidiabetic and cardioprotective aspects of the AMPK signaling pathway. In the antidiabetic effect, mogroside reduces blood glucose and blood lipid levels and improves insulin sensitivity in diabetic mice by activating the AMPK pathway. [20]In terms of cardioprotection, mogroside also improves the heart's antioxidant capacity by activating the AMPK pathway, protecting the heart from damage caused by a high-fat diet. [48]This suggests that the AMPK signaling pathway plays a key role in the multiple pharmacological effects of mogroside, and its activation not only helps to regulate blood glucose and lipid metabolism, but also enhances the heart's antioxidant defense system, thereby producing synergistic protective effects in different physiological and pathological processes.

The antioxidant and anti-inflammatory effects of mogroside are interrelated and work together to exert a protective effect on the body. On the one hand, mogrosides reduce oxidative stress by scavenging free radicals and strengthening the antioxidant defense system, which helps reduce inflammation. On the other hand, its anti-inflammatory effects also help to reduce oxidative stress levels by modulating inflammatory factors and inhibiting inflammatory pathways. This synergistic mechanism of antioxidant and anti-inflammatory effects has led to mogrosides showing significant therapeutic potential in a variety of inflammatory and oxidative stress-related disease models.

In terms of neuroprotection, the mechanism of mogroside is also closely related to anti-inflammatory and antioxidant effects. Neuroinflammation and oxidative stress are important pathological features of many neurodegenerative diseases. Mogroside protects nerve cells from damage by inhibiting neuroinflammation and reducing oxidative stress.

[44] [45]This neuroprotective mechanism is similar to the anti-inflammatory and antioxidant effects in other systems, reflecting the characteristics of mogroside playing a protective role in different tissues and cells by regulating common pathological processes.

The immunomodulatory effect of mogroside cooperates with other pharmacological mechanisms to maintain the stability of the body's internal environment. Mogroside provides a good internal environment for immune cells through antioxidant and anti-inflammatory effects, and its regulatory effect on cytokine release directly enhances the body's immune response and improves the body's immune defense ability.

4. Challenges and Future Directions

Despite the remarkable pharmacological activities *Siraitia grosvenorii* saponins have demonstrated in multiple fields, their investigation and application still face several challenges, indicating the future research directions.

4.1. Challenges

1. Bioavailability and Stability Concerns: The limited bioavailability and stability of *Momordica grosvenorii* in the gastrointestinal tract pose challenges to its therapeutic efficacy. Studies have shown poor absorption rates of mogrosides in vivo, potentially reducing their clinical effectiveness. To address this, future research should focus on strategies to enhance its bioavailability, such as chemical modifications or novel formulation techniques.

2. Safety and Adverse Effects: Although mogroside is generally considered safe, research on its long-term safety profile and potential adverse effects remains limited. More comprehensive studies are required to evaluate the side effects and toxicological properties of mogroside in clinical settings, ensuring its safety for extended use.

1. Unclear Mechanism of Action: The exact mechanism of action of mogrosides is still not fully understood. While some potential pathways, such as AMPK activation and NF-κB inhibition, have been identified, more detailed molecular-level studies are needed to fully elucidate these mechanisms. A deeper understanding of these pathways is crucial for developing more effective therapeutic strategies involving mogrosides.

4.2 Future Direction

1. Expansion of Clinical Research: To validate the efficacy and safety of mogroside in humans, more clinical studies are needed. Most existing research has been conducted on animal models, and there is limited clinical trial data available. Future studies should focus on assessing human responses to different dosages and treatment durations.

2. Employment of Novel Approaches and Emergent Technologies: Novel strategies, such as nanotechnology and drug delivery systems, can enhance the stability and bioavailability of mogroside. Nanoparticles, for example, can protect the active ingredient, preserving its stability in the body and increasing its concentration in target tissues. Additionally, the production of mogroside V through synthetic biology offers a promising solution to challenges related to limited natural resources and high extraction costs. An enzymatic glycosyltransferase approach has also been developed to convert bitter momordica saponin IIE into a sweet triterpenoid saponin mixture. This approach has shown good antioxidant activity and food safety, offering potential for the development of novel sweeteners.

3. Interdisciplinary Study: The integration of biological, chemical, and materials science is essential in exploring the therapeutic potential of mogrosides and addressing existing challenges. Additionally, the application of systems biology and omics technologies will contribute to a more comprehensive understanding of mogrosides' mechanisms of action and their effects on disease. For instance, research using molecular docking and dynamics simulations has shown that *Momordica grosvenorii* V (MGV) can form stable complexes with toll-like receptor 7 (TLR7), suggesting its potential as a TLR7 antagonist. In vitro experiments

have confirmed that MGV can concentration-dependently inhibit B cell differentiation, supporting its potential as a TLR7-targeted therapeutic.

5. Conclusion

This article reviews the pharmacological research progress of mogroside, with a particular focus on its pharmacological activities in anti-diabetes, anti-oxidation, anti-inflammation, and anti-cancer. Studies have shown that mogroside not only has rich biological activities but also exhibits potential clinical application value.

1. Antidiabetic Activity: Mogroside has shown significant effects in regulating blood glucose and improving diabetic conditions. By activating the AMPK signaling pathway, mogroside can effectively reduce high-fat diet-induced blood glucose levels and improve insulin resistance. These properties make it a potential natural supplement for the treatment of diabetes.

2. Antioxidant and Anti-inflammatory Effects: Mogroside exerts antioxidant and anti-inflammatory effects by reducing oxidative stress and modulating the expression of inflammatory factors. It can significantly reduce the expression of IL-6 and TNF-α and alleviate the inflammatory state by inhibiting the NF-κB signaling pathway. These findings provide scientific evidence for the application of mogroside in the prevention and treatment of inflammatory diseases.

1. Antitumor Properties: Mogroside exhibits antiproliferative activities against various cancer cell lines and induces apoptosis in cancer cells. By affecting the cell cycle and inhibiting angiogenesis, mogroside can suppress tumor growth and metastasis. These findings underscore its therapeutic potential in oncology.

2. Other Therapeutic Potential: Mogroside also demonstrates impressive effects in neuroprotection, cardioprotection, and immunomodulation. In particular, mogroside offers therapeutic strategies for combating neurodegenerative diseases and cardiovascular diseases through antioxidant and anti-inflammatory mechanisms.

Mogroside, a versatile natural compound, exhibits a wide spectrum of pharmacological activities and therapeutic potential. While current research provides a solid foundation for future mogroside applications, further exploration of its mechanisms of action, optimization of its formulations, and validation of its safety and efficacy in clinical trials remain key for future research endeavors. Furthermore, advanced drug development technologies, such as nanotechnology and targeted delivery systems, hold promise for further enhancing the therapeutic efficacy of mogrosides, broadening their applications in pharmaceuticals and functional food.

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