RESEARCH ARTICLE

Ophiopogon japonicus: Traditional Uses, Pharmacological, and Cosmetic Applications

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ABSTRACT

Ophiopogon japonicus (Thunb.) Ker-Gawl., commonly known as Maidong, is a perennial herb of the Liliaceae family, revered in traditional East Asian medicine for its therapeutic benefits. The plant's roots, *Ophiopogonis Radix*, have long been used in Traditional Chinese Medicine (TCM) for their nourishing properties, particularly for promoting yin, moistening the lungs, easing the mind, and dispelling heart fire. It is commonly prescribed for respiratory, gastrointestinal, and cardiovascular issues, as well as conditions like insomnia, dry cough, and psychological disturbances. Modern research has identified a rich array of bioactive compounds in *O. japonicus*, including homoisoflavonoids, steroidal saponins, polysaccharides, and monoterpene glycosides, which contribute to its diverse pharmacological activities. These include antioxidant, anti-inflammatory, cardioprotective, anti-tumor, anti-aging, immunomodulatory, and anti-hyperglycemic effects. Additionally, the plant's polysaccharides exhibit strong antioxidant properties and radical scavenging abilities, supporting its role in protecting against oxidative stress. *O. japonicus* has also been recognized for its skin-soothing and moisturizing effects, promoting hydration and enhancing the skin's barrier function. A patented cosmetic application of the plant has been developed, focusing on its ability to improve skin hydration and barrier integrity. The review of its medicinal and cosmetic applications was conducted using databases such as Scispace, Google Scholar, and PubMed. Despite its extensive use and therapeutic potential, further systematic research on its chemical constituents, pharmacokinetics, toxicology, and quality control is needed to ensure the sustainable development of this valuable herb.

Keywords: *Ophiopogon japonicas*, Cardiovascular issues, Homoisoflavonoids, Pharmacological activities.

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INTRODUCTION

Ophiopogon japonicus (Thunb.) Ker-Gawl., commonly known as Maidong in Chinese, is a perennial herbaceous plant of the Liliaceae family. Its roots, referred to as *Ophiopogonis Radix*, are highly esteemed in traditional medicine systems across East Asia, including China, Japan, and other Southeast Asian countries. As a crucial component of Traditional Chinese Medicine (TCM), Ophiopogonis Radix has been utilized for thousands of years, valued for its nourishing and therapeutic properties. TCM principles attribute yin-nourishing qualities to this herb, which is believed to promote the production of body fluids, moisten the lungs, ease the mind, and dispel heart fire. These properties make *O. japonicus* a cornerstone for treating various conditions associated with yin deficiency and dehydration.The plant's ethnomedicinal importance lies in its extensive application for addressing respiratory diseases, gastrointestinal disorders, cardiovascular ailments, and inflammatory conditions. Traditionally, it has been prescribed for managing fever, dry cough, sore throat, epistaxis, constipation, palpitations, insomnia, and psychological disturbances such as anxiety and restlessness. The plant's cooling and moistening attributes make it particularly effective in combating symptoms of dryness, inflammation, and fluid loss. [1-3]

Modern research has reinforced the plant's traditional uses by uncovering its rich phytochemical profile. *O. japonicus* is abundant in bioactive compounds, including homoisoflavonoids, steroidal saponins, amides, monoterpene glycosides, and polysaccharides. These compounds exhibit significant pharmacological activities such as anti-inflammatory, antioxidant, cardioprotective, anti-tumor, anti-aging, immunomodulatory, and anti-hyperglycemic effects. Notably, homoisoflavonoids, a specialized class of flavonoids unique to this plant, are associated with potent biological activities, including phosphodiesterase inhibition and blood glucose regulation. The roots of *O. japonicus* are also recognized for their high medicinal and nutritional value. Polysaccharides extracted from the roots exhibit robust antioxidant properties, immune-enhancing effects, and radical scavenging abilities. These properties contribute to the herb's role in protecting against oxidative stress and promoting overall health. Moreover, the plant's traditional classification into regional varieties, such as Zhe Maidong (from Zhejiang province) and Chuan Maidong (from Sichuan province), highlights its diverse therapeutic potential and the

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importance of cultivation practices in determining quality and efficacy. Despite its rich therapeutic potential, systematic research on *O. japonicus* remains limited. Studies addressing the complexity of its chemical constituents, pharmacokinetics, toxicology, and quality control are necessary to standardize its use and optimize its efficacy in clinical settings. This highlights the importance of continued research to bridge the gap between traditional knowledge and modern pharmacological applications, ensuring the sustainable development and broader utilization of this valuable medicinal herb.

In summary, *Ophiopogon japonicus* serves as a vital medicinal resource with significant ethnomedicinal, pharmacological, and nutritional importance. Its integration into modern medicine promises to expand its therapeutic applications, benefiting a wide range of health conditions.[4,5]

Pharmacological and cosmetic Applications of *Ophiopogon japonicus*

Antioxidant Activity

O. japonicus exhibits significant antioxidant activity, largely due to its rich content of bioactive compounds such as homoisoflavonoids and polysaccharides. Studies have identified 17 homoisoflavonoid compounds in its root extracts, with methylophiopogonanone A and methylophiopogonanone B being the primary contributors. Among various extracts, the chloroform/methanol (1:1, v/v) fraction demonstrated the highest antioxidant potential, correlating with its substantial homoisoflavonoid content. Notably, methylophiopogonanone A exhibited the strongest radical-scavenging activity across multiple antioxidant assays, emphasizing its therapeutic potential as a natural antioxidant.[6,7]

Polysaccharides derived from *O. japonicus* also contribute significantly to its antioxidant properties. Ultrasonically extracted polysaccharides, such as POJ-U1a, exhibit potent free radical scavenging activity, including DPPH, hydrogen radical, and superoxide anion scavenging. Structural analysis revealed that POJ-U1a is a highly branched α-configuration polysaccharide, which enhances its antioxidant efficacy. Advanced isolation of sulfated polysaccharides (OJP-1, OJP-2, OJP-3, and OJP-4) further confirmed their antioxidant activity, with the degree of sulfation and hexuronic acid content positively correlating with their radical-scavenging capabilities. Among these, OJP-4 showed stronger DPPH radical and hydroxyl radical scavenging activities compared to less sulfated counterparts. These findings underline the robust antioxidant potential of *O. japonicus*, derived from its diverse bioactive compounds. The synergistic effects of homoisoflavonoids and polysaccharides make this plant a promising candidate for natural antioxidant applications, offering potential benefits in therapeutic and nutraceutical fields.[8,9]

Anti-Inflammatory activity

Ophiopogon japonicus exhibits notable anti-inflammatory properties, supported by various studies. Extracts of *O. japonicus* have been found to alleviate inflammation, such as reducing ear swelling and paw edema in animal models. *O. japonicus* extract effectively inhibited leukocyte migration in response to inflammatory stimuli without altering prostaglandin levels. Two bioactive compounds, ruscogenin and ophiopogonin D, were identified as key contributors, showing significant effects in reducing inflammatory cell adhesion and migration. Several homoisoflavonoids, including newly identified ones such as ophiopogonone E and ophiopogonanone H, along with other known compounds from the roots of *O. japonicus*, demonstrated strong anti-inflammatory effects. These compounds were effective in suppressing the production of nitric oxide and other inflammatory mediators in activated immune cells. Another investigation revealed that specific chromones and a newly identified compound from the rhizome of *O. japonicus* reduced inflammatory markers such as nitric oxide, IL-1β, and IL-6. The anti-inflammatory effects were attributed to the inhibition of signaling pathways that regulate inflammatory responses, specifically through reducing the activation of key proteins involved in these processes. These findings highlight the potential of *O.*

Figure 1. *Ophiopogon japonicus*

japonicus as a natural source of anti-inflammatory agents, supporting its traditional use in treating various inflammation-related conditions (10-12).

Cardiac protective activity

Polysaccharides and steroidal saponins extracted from *O. japonicus* have shown significant benefits in mitigating cardiac injuries caused by various pathological conditions. Studies on *O. japonicus* polysaccharide (OJP1) indicate its potential to protect against cardiovascular complications in diabetes and myocardial ischemia. In diabetic rats, OJP1 enhanced antioxidant enzyme activities (SOD, CAT, and GPx), reduced oxidative stress markers like MDA, and regulated cardiovascular biomarkers, including AGE, hs-CRP, sICAM-1, NO, and ET-1. It also normalized mRNA expression levels of ET-1 and eNOS, improving cardiac tissue integrity and reducing histological damage. In models of isoproterenol -induced myocardial ischemia, OJP1 attenuated cardiac dysfunction, reduced ST-segment elevation, and improved enzymatic markers of cardiac injury (AST, LDH, CK, CK-MB). The cardioprotection was linked to enhanced endogenous antioxidant defenses and decreased lipid peroxidation. Steroidal saponins from *O. japonicus*, such as ophiopogonin B, D, and D', have shown robust cardioprotective effects, particularly in models of doxorubicin (DOX)-induced chronic heart failure (CHF). These compounds ameliorated oxidative stress by increasing antioxidant enzyme activities (SOD, CAT, GSH-Px) and reducing MDA levels. Inflammatory markers, including TNF-α, IL-6, and IL-1β, were significantly decreased, alongside inhibition of p38 MAPK activation—a key pathway in DOX-induced cardiac damage. Improvements in cardiac function parameters, such as enhanced LVESP, EF, FS, and reduced LVEDP, were also observed. Together, the polysaccharides and saponins of *O. japonicus* offer multifaceted cardioprotection through their antioxidant, anti-inflammatory, and tissue-preserving activities, making it a promising therapeutic agent for cardiovascular disorders.[13-15]

Antidiabetic activity

Ophiopogon japonicus, a traditional Chinese medicinal herb, has shown significant antidiabetic properties in various studies. A water-soluble polysaccharide (OJP1) extracted from its roots was found to reduce blood glucose levels, enhance insulin levels, and protect pancreatic islets in streptozotocin (STZ)-induced diabetic rats. OJP1, demonstrated hypoglycemic effects comparable to untreated diabetic controls.Further research on oligosaccharides of *O. japonicus* (OOJ) indicated that oral administration to high-fat diet and STZ-induced type 2 diabetic rats improved glucose tolerance, decreased fasting blood glucose levels, enhanced glycogen storage, and alleviated pancreatic histopathological damage. OOJ also positively influenced glucagon-like peptide-1 (GLP-1) levels and reduced glucagon levels, supporting its antidiabetic potential. Another polysaccharide fraction (OJP-W1) ameliorated insulin resistance and glucose intolerance in high-fat diet-induced diabetic mice. *O. japonicus* also regulated gut microbiota dysbiosis, increasing beneficial bacteria like *Bifidobacterium* while reducing diabetes-associated taxa. The compound MDG-1, derived from *O. japonicus*, demonstrated antidiabetic activity via the InsR/IRS-1/PI3K/Akt/GSK-3/Glut-4 signaling pathway. It improved glucose metabolism, reduced hyperglycemia, and normalized lipid profiles in diabetic models. Overall, these findings highlight the potential of *Ophiopogon japonicus*-derived polysaccharides and oligosaccharides as promising natural antidiabetic agents.[16-20]

Antiosteoporetic activity

Ophiopogon japonicus, a traditional Chinese herbal medicine, contains Ophiopogonin D (OP-D) a steroidal saponin as its chief pharmacologically active component. Recent studies have highlighted the potential of OP-D in addressing osteoporosis by inhibiting osteoclast activity and differentiation. Osteoclasts, derived from the fusion of mononuclear preosteoclasts, are pivotal in bone resorption, and their overactivity leads to conditions such as osteoporosis, tumor-induced bone loss, and peri-prosthetic osteolysis. OP-D administration has been shown to significantly reduce osteoclast numbers and suppress the mRNA expression of osteoclastic genes, including NFATc1 and TRAP, under oxidative stress conditions. This inhibition of osteoclastogenesis is associated with OP-D's antioxidative properties, which decrease reactive oxygen species (ROS) levels—a critical factor in osteoclast formation and activation. Reduced ROS generation, mediated by OP-D, may involve the FoxO3a-β-catenin signaling pathway, which plays an essential role in maintaining bone health under oxidative stress. Additionally, OP-D enhances osteoblastic differentiation and function, potentially counteracting bone loss by promoting bone formation while reducing resorption. These findings underscore OP-D's therapeutic potential as a natural agent for the prevention and treatment of osteoporosis through its dual action on inhibiting osteoclast activity and supporting osteoblast function,[21,22]

Anti-atherosclerotic activity

Atherosclerosis is a chronic disease and a critical pathological process contributing to cardiovascular diseases. It involves endothelial dysfunction, vascular smooth muscle cell (VSMC) proliferation, and neutrophil activation. Radix *O. japonicus*, a traditional Chinese medicine, and its active compounds, such as Ophiopogonin D (OPD), have shown potential therapeutic effects against atherosclerosis. Studies have demonstrated that OPD significantly reduces atherosclerotic plaque formation and serum lipid levels in mice. It improves glucose tolerance, insulin resistance, and hepatocyte steatosis while attenuating oxidative stress. Mechanistically, OPD inhibits mTOR phosphorylation and regulates lipid metabolism through the SREBP1 and SCD1 signaling pathways. Furthermore, OPD alters gut microbiota composition, reducing cholesterol-metabolizing genera like *Erysipelotrichaceae*, thereby contributing to its anti-atherosclerotic effects. Extracts of *O. japonicus* also exhibit protective effects on endothelial cells and VSMCs. EOR decreases oxidative stress markers such as reactive oxygen species (ROS) and nitric oxide (NO) production while improving endothelial function. It inhibits oxidized low-density lipoprotein (ox-LDL)-induced VSMC proliferation

and neutrophil activation, reducing malondialdehyde production and restoring superoxide dismutase activity. Key active constituents of *O. japonicus*, including saponins and homoisoflavonoids, mitigate endothelial injury, suppress VSMC proliferation, and prevent neutrophil activation, thereby providing multi-target protection against atherosclerosis. Additionally, studies indicate that Ophiopogonin D suppresses thrombin-induced proliferation and migration of VSMCs by inhibiting AKT phosphorylation and reducing cyclin D1 expression. It also downregulates MMP-2 expression through the inhibition of NF-κB activity, halting extracellular matrix degradation and limiting the progression of vascular lesions.Collectively, these findings underscore the potential of *O. japonicus* and its active components as promising natural agents for the prevention and treatment of atherosclerosis through multi-faceted mechanisms targeting oxidative stress, lipid metabolism, endothelial function, and VSMC activity.[23-25]

Anti-cancer activity

Ophiopogon japonicus, exhibits significant anticancer properties through various mechanisms. Bioactive compounds such as ophiopogonin B, ophiopogonin D, DT-13, and polysaccharides derived from the plant have been shown to inhibit tumor growth, induce apoptosis, and suppress metastasis and angiogenesis in various cancer cell lines. Notably, these effects are achieved with minimal toxicity, emphasizing its potential for safe therapeutic use. OJP display potent anticancer activities. They inhibit the viability of esophageal cancer cell lines Eca109 and TE-1 and promote their apoptosis. Additionally, acetylated polysaccharides like ROH05A exhibit cytotoxicity against pancreatic cancer cells by triggering apoptotic pathways, including the upregulation of p53 and Bax expression, along with activation of caspase-3 and FasL. These effects highlight the crucial role of OJP in combating oxidative damage and inducing cancer cell death. *O. japonicus* extracts. stronger pro-apoptotic and anti-migratory effects due to its higher content of homoisoflavonoids and unique saponins. The differential composition of steroidal saponins and homoisoflavonoids contributes to selective cytotoxicity across cancer cell lines. The diverse and potent anticancer effects of *O. japonicus*, coupled with its safety, make it a promising candidate for novel cancer therapies, including potential applications in immunotherapy and combination chemotherapy. Further exploration of its bioactive components could enhance its clinical utility.[26-28]

Antiobesity activity

Ophiopogon japonicus contains MDG-1, a water-soluble polysaccharide, has demonstrated strong anti-obesity effects in diet-induced obese mice. In a 16-week study, MDG-1 was administered at 300 mg per body weight, resulting in significant weight loss and a reduction in adipose tissue mass by approximately 50%. Remarkably, this weight loss occurred without suppressing appetite or increasing physical activity. The primary effect of MDG-1 was a reduction in fat mass, while lean mass remained unaffected. MDG-1 also improved plasma lipid profiles, reduced leptin secretion, and alleviated hepatic lipid accumulation. Additionally, it enhanced the expression of genes related to lipid and energy metabolism in the liver, further supporting its role in weight regulation. The polysaccharide increased oxygen consumption and energy expenditure, indicating its potential to boost metabolic activity and promote fat burning. These results suggest that MDG-1 is a promising candidate for treating obesity and associated metabolic disorders. Its ability to reduce fat mass without the adverse effects often seen with other weight-loss treatments makes it an attractive natural alternative. Overall, MDG-1 shows promise as a safe and effective therapeutic option for managing obesity and improving metabolic health.[30,31]

Neuroprotective activity

Eight novel long-chain anacardic acid derivatives, janohigenins, were isolated from the endosperm of *Ophiopogon japonicus* seeds. The neuroprotective effects of these compounds were evaluated in SH-SY5Y human neuroblastoma cells, demonstrating significant protection against rotenone-induced cellular damage at a concentration of 1 μM. Anacardic acids, the parent compounds of janohigenins, are known for a broad range of biological activities, including antioxidant, anti-inflammatory, and antitumor properties. These acids have also been studied for their potential to treat neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS). The observed neuroprotective activity of janohigenins highlights the therapeutic potential of O. japonicus-derived compounds in promoting brain health and preventing neurodegeneration.[32,33]

Skin-Soothing and Moisturizing Properties

Ophiopogon japonicus, commonly known as Japanese lilyturf, is increasingly utilized in cosmetic formulations for its exceptional skin-soothing and moisturizing properties. The plant's roots are rich in polysaccharides that help alleviate skin irritation by deactivating the TRPA1 itch receptor, providing a calming effect, particularly for sensitive skin. These polysaccharides also play a crucial role in enhancing skin hydration by stimulating the synthesis of claudin-1 and Zonula occludens-1 (ZO-1), which are essential proteins that maintain tight junctions and promote cell-cell cohesion. This action strengthens the skin's barrier function and helps to restructure the epidermis, making it more resilient and less prone to irritation. Furthermore, *O. japonicus* increases the levels of filaggrin, a vital component of natural moisturizing factors (NMF), helping to prevent trans-epidermal water loss and maintain moisture. These properties make *O. japonicus* an ideal ingredient in a wide range of cosmetic products, such as facial serums, balms, repair creams, cleansers, night oils, and soothing tonics, as well as body care products like hand creams and makeup foundations. Rich in antioxidants, this plant enhances skin hydration, alleviates irritation, and fortifies the skin's barrier, offering significant benefits for dry and sensitive skin. [34-36]

Conclusion,

Ophiopogon japonicus (Maidong) demonstrates significant therapeutic potential, particularly in promoting health through its antioxidant, anti-inflammatory, and cardioprotective properties. Its traditional uses in treating

respiratory, gastrointestinal, and psychological conditions are supported by modern research, revealing a rich phytochemical profile. Furthermore, its skin-soothing and moisturizing benefits make it a valuable ingredient in cosmetics, with patented formulations enhancing skin hydration and barrier function. While the plant's diverse pharmacological activities are promising, continued research on its chemical composition, pharmacokinetics, and safety profile is essential for optimizing its use in both medicinal and cosmetic applications. This will ensure the plant's sustainable development and wider clinical and commercial utilization.

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