***Minireview Article***

**GASTRODIA ELATA AS A NEUROPROTECTIVE AGENT: A MINI REVIEW OF ITS BIOACTIVE COMPOUNDS AND MECHANISMS OF ACTION**

Abstract

Gastrodia elata (Blume) is a traditional medicinal herb widely used in East Asia for its purported neuroprotective effects. This mini-review summarizes the current understanding of the bioactive compounds within G. elata and their potential mechanisms of action related to neuroprotection. Evidence suggests that compounds like gastrodin, gastrodial, and parishin exhibit antioxidant, anti-inflammatory, and anti-apoptotic properties, contributing to the protection of neuronal cells against various stressors. Further research is needed to fully elucidate the specific pathways involved and to translate these findings into clinically relevant applications for neurodegenerative diseases and other neurological disorders.

**Keywords:** Gastrodia elata, neuroprotection, gastrodin, anti-inflammatory, anti-apoptotic, neurodegenerative diseases.

**Introduction**

**Neurodegenerative diseases, including Alzheimer's disease (AD), Parkinson's disease (PD), and stroke, constitute a formidable and escalating global health challenge (**Reddy *et al*., 2024; Mukherjee *et al*., 2020)**.** These debilitating conditions, fundamentally defined by the gradual and irreversible decline in neuronal structure and function, inflict a devastating toll on individuals, placing immense strain on their quality of life and independence. Beyond the personal impact, neurodegenerative diseases exert a significant economic burden on families, caregivers, and healthcare systems worldwide, encompassing the costs of long-term care, medication, and lost productivity (Safiri *et al*., 2024). **Despite decades of intensive research and substantial financial investment, current therapeutic interventions for these disorders predominantly focus on managing symptoms rather than addressing the underlying pathology.** While these symptomatic treatments can provide temporary relief and improve patients' quality of life, they offer limited efficacy in halting or reversing the relentless progression of neuronal degeneration. This inherent limitation highlights a critical and unmet need for the development of innovative neuroprotective strategies. Such strategies would ideally target the mechanisms responsible for neuronal damage, aiming to prevent or significantly mitigate the loss of neurons and preserve cognitive and motor functions.

**In the search for novel neuroprotective agents, natural products have emerged as a promising avenue for exploration (**Rahman *et al*., 2021)**. Gastrodia elata (GE), a distinctive orchid species with a long history of medicinal use in Eastern traditional medicine across China, Korea, and Japan, has gained increasing recognition for its potential in this area.** This herb, traditionally prescribed for treating a diverse array of neurological ailments, including headaches, epilepsy, vertigo, and even stroke-related sequelae, has attracted considerable scientific interest due to accumulating evidence suggesting its neuroprotective capabilities (Liu *et al*., 2024; Hong & Soh, 2019).

**This review is therefore undertaken with the objective of providing an evaluation of the current state of knowledge concerning the neuroprotective potential of Gastrodia elata (GE).** The study will delve into the scientific literature to identify and characterize the bioactive compounds present in GE, elucidating their specific mechanisms of action at the cellular and molecular levels. This includes examining their potential antioxidant, anti-inflammatory, anti-apoptotic, and neurotrophic effects. By synthesising the available evidence, this review aim to highlight the compelling rationale for further, rigorous investigation into *Gastrodia elata* as a rich and accessible source of novel neuroprotective compounds. Ultimately, the goal is to pave the way for the development of more effective and disease-modifying therapeutic strategies for neurodegenerative diseases, offering hope for improved outcomes and a better quality of life for affected individuals and their families.

**Methodology**

This review was conducted to investigate the existing evidence regarding the neuroprotective and cognitive-enhancing properties of Gastrodia elata. To ensure a thorough and unbiased identification of relevant research, the study implemented a comprehensive search strategy across multiple databases. Specifically, the study systematically searched PubMed, Scopus, Web of Science, and CNKI (China National Knowledge Infrastructure) from their respective inception dates. The search terms employed were carefully selected to capture the breadth of research in this area and included a combination of keywords and their synonyms, such as "Gastrodia elata," "Tianma" (the Chinese name for Gastrodia elata), "neuroprotection," "brain," "cognition," "cognitive function," "memory," "bioactive compounds," "secondary metabolites," and "clinical trials." These terms were combined using Boolean operators to optimize search sensitivity and specificity. The inclusion criteria were designed to capture studies directly relevant to this research question. This review included studies that investigated the effects of Gastrodia elata or its constituent bioactive compounds on neuronal function, neuroprotection against various insults (e.g., oxidative stress, inflammation, excitotoxicity), or cognitive performance, including memory, learning, and executive functions. Studies were also deemed eligible if they were published in either English or Chinese, expanding the scope of the search to encompass a wider body of research, particularly from Chinese traditional medicine.

Conversely, the study established specific exclusion criteria to ensure the focus remained on the neurological and cognitive aspects of Gastrodia elata. Studies primarily focusing on non-neurological applications (e.g., cardiovascular effects, anti-inflammatory effects outside the nervous system) were excluded. Similarly, in vitro studies lacking clear relevance or translatability to in vivo effects were excluded to prioritize research with direct implications for living organisms. Review articles, meta-analyses, and commentaries were excluded, as they do not contribute original data. Finally, studies lacking sufficient methodological rigor, such as those with inadequate controls, unclear reporting of methods, or significant sources of bias, were excluded to maintain the quality of the evidence base. Data extraction from the selected studies was performed by two independent reviewers to minimize bias and ensure accuracy. A standardized data extraction form was used to record detailed information on key study characteristics, including the study design (e.g., randomized controlled trial, cohort study, animal study), sample size, participant characteristics (e.g., age, health status), intervention details, encompassing the specific dosage of Gastrodia elata or its extracts, the duration of the intervention, the type of extract used (e.g., crude extract, specific fraction), the route of administration, outcome measures assessed (e.g., cognitive tests, neuroimaging findings, biochemical markers), and the key findings reported by the study authors.

To evaluate the robustness and reliability of the evidence base, the study rigorously assessed the quality of the included studies. For clinical trials, Cochrane Risk of Bias tool was employed, which evaluates various sources of bias, including selection bias, performance bias, detection bias, attrition bias, and reporting bias. For preclinical studies involving animal models, the study utilized the ARRIVE (Animal Research: Reporting of In Vivo Experiments) guidelines checklist, a standardized tool for assessing the completeness and transparency of reporting in animal research, thereby ensuring that studies adhered to ethical and methodologically sound practices. This comprehensive quality assessment allowed this study to critically evaluate the strengths and limitations of the existing evidence and to draw informed conclusions about the neuroprotective and cognitive-enhancing effects of Gastrodia elata.

**Bioactive Compounds of *Gastrodia elata***

Gastrodia elata, a herb that has been traditionally utilized in medicine, possesses a wide range of bioactive compounds, which contribute to its therapeutic capabilities. These compounds can be classified into two main categories, namely phenols and glycosides. Gastrodin (C13H18O7), a phenolic glycoside, is one of the most critical components that can be found in varying concentrations throughout the plant, with a higher concentration typically found in the rhizome. This compound is known for its neuroprotective and antioxidant properties. Another important constituent of Gastrodia elata is Gastrodial (C11H12O4), a compound that exists in smaller quantities and contributes to the plant's sedative effects. p-Hydroxybenzyl alcohol (HBA) (C7H8O2), a simple phenolic compound, is also isolated from G. elata and exhibits both antioxidant and anti-inflammatory activities. In addition to these compounds, other phenolic compounds like parishin A, parishin B, and various glycosides are also present in varying quantities. The process of isolating these compounds typically involves the use of solvents with different polarities, such as methanol, ethanol, and ethyl acetate, followed by purification techniques such as column chromatography and HPLC (High-Performance Liquid Chromatography). (Yang *et al*., 2025; El Menyiy *et al*., 2024). The bioavailability and metabolism of these compounds are crucial for their efficacy. For example, Gastrodin is known to be metabolized into HBA in the body, which may contribute to some of its effects. The specific metabolic pathways and the extent of absorption, distribution, and excretion of G. elata's bioactive compounds are still ongoing areas of research (Wu et al., 2023).

Understanding the chemical structures of these key compounds is essential for comprehending their chemical properties and potential mechanisms of action. By studying the structure-activity relationships of these compounds, researchers can gain insight into how these compounds interact with biological systems and develop more targeted therapies for various medical conditions. Furthermore, understanding the biosynthetic pathways of these compounds in Gastrodia elata can provide valuable information for optimizing cultivation conditions and developing new methods for large-scale production of these valuable bioactive compounds.

**Neuroprotective Mechanisms of Action**

Gastrodia elata, a traditional medicinal herb, possesses remarkable neuroprotective capabilities that stem from the synergistic action of its diverse bioactive compounds (Meng *et al.*, 2025; Andrew *et al*., 2017). These compounds orchestrate a complex interplay of mechanisms to safeguard the delicate neural environment.

**Counteracting Oxidative Stress:** A cornerstone of Gastrodia elata's neuroprotective effect is its robust antioxidant activity (Wang *et al.*, 2025). The bioactive compounds act as scavengers, directly neutralizing harmful free radicals such as reactive oxygen species (ROS) and reactive nitrogen species (RNS). These unstable molecules, when left unchecked, inflict significant oxidative damage to cellular components, contributing to neuronal dysfunction and degeneration. Beyond direct scavenging, Gastrodia elata empowers the body's inherent antioxidant defenses. It achieves this by boosting the activity of critical endogenous antioxidant enzymes, including superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx). These enzymes work in concert to neutralize free radicals and convert them into less harmful substances, ensuring a balanced redox state within the brain (Udi, 2025; Balachandra & Hosamani, 2023).

**Taming Neuroinflammation:** Inflammation plays a significant role in many neurological disorders, exacerbating neuronal damage. Gastrodia elata exerts potent anti-inflammatory effects by modulating the inflammatory cascade. This involves the downregulation of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6). These cytokines are key signaling molecules that amplify the inflammatory response. Furthermore, Gastrodia elata curtails microglial activation. Microglia, the brain's resident immune cells, can become overactive and release inflammatory mediators in response to injury or disease. By suppressing this activation, Gastrodia elata helps to dampen neuroinflammation and protect vulnerable neurons (Oyovwi, & Udi, 2024; Joshee *et al*., 2019).

**Preventing Neuronal Apoptosis:** Apoptosis, or programmed cell death, is a natural process, but its dysregulation contributes to neuronal loss in neurodegenerative diseases. Gastrodia elata exhibits anti-apoptotic properties, safeguarding neurons from premature death. It achieves this by regulating the expression of apoptosis-related proteins, including Bcl-2 (an anti-apoptotic protein), Bax (a pro-apoptotic protein), and caspase-3 (a key executioner caspase). By shifting the balance towards anti-apoptotic pathways, Gastrodia elata promotes neuronal survival under stressful conditions (Gong *et al.*, 2024; Udi *et al.*, 2022).

**Nurturing Neuronal Health:** Beyond protection, Gastrodia elata actively promotes neuronal health and resilience. It exhibits neurotrophic effects, fostering neuronal survival and differentiation. This involves the upregulation of neurotrophic factors, specifically brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF). These growth factors are essential for neuronal development, maintenance, and plasticity, supporting optimal brain function (Ashraf *et al*., 2024).

**Modulating Neurotransmitter Systems:** Neurotransmitter imbalances can disrupt neuronal communication and contribute to neurological disorders. Gastrodia elata modulates key neurotransmitter systems, influencing the levels of acetylcholine, dopamine, and glutamate. By regulating these neurotransmitters, Gastrodia elata optimizes synaptic function, ensuring efficient and accurate communication between neurons (Nimgampalle *et al*., 2024).

**Shielding Against Excitotoxicity:** Excitotoxicity, a process where excessive glutamate stimulation leads to neuronal damage, is implicated in various neurological conditions. Gastrodia elata provides protection against excitotoxicity by attenuating glutamate-induced neuronal damage. This protective effect helps prevent neuronal overstimulation and subsequent cell death (Iovino *et al.*, 2020).

**Combating Alzheimer's Disease Pathology:** Notably, Gastrodia elata exhibits mechanisms relevant to Alzheimer's disease (AD) pathology. It demonstrates inhibitory effects on Amyloid-beta (Aβ) aggregation and tau phosphorylation. Aβ plaques and neurofibrillary tangles formed by hyperphosphorylated tau protein are hallmarks of AD. By targeting these key pathological processes, Gastrodia elata holds promise as a potential therapeutic agent for AD (Shi *et al*., 2023).

**Evidence-Based Support:** Each of these mechanisms is supported by a growing body of scientific evidence derived from in vitro (cell-based), in vivo (animal-based), and, in some cases, human studies. These studies meticulously investigate the detailed molecular pathways and specific targets involved in the observed neuroprotective effects. This comprehensive research provides a thorough understanding of the neuroprotective capabilities of Gastrodia elata and solidifies its potential as a valuable therapeutic tool for a range of neurological disorders. In essence, Gastrodia elata presents a multifaceted approach to neuroprotection, addressing oxidative stress, inflammation, apoptosis, and neurotransmitter imbalances, while also promoting neuronal health and targeting disease-specific pathologies (Fu *et al*., 2024; Chen *et al*., 2024; Lee *et al*., 2023).

**Evidence from Preclinical Studies**

**Preclinical studies utilizing animal models have illuminated the potential neuroprotective capabilities of**Gastrodia elata**(GE) across a spectrum of neurological disorders (**Shi *et al*., 2024)**.** These investigations serve as a crucial foundation for understanding GE's therapeutic potential before human trials. **In the context of Alzheimer's disease (AD), a neurodegenerative disorder characterized by cognitive decline, GE has demonstrated encouraging results in preclinical models (**Wu *et al*., 2023; Park *et al.*, 2015)**.** Studies have shown that GE administration can improve cognitive function, potentially by enhancing learning and memory processes **(**Wu *et al*., 2023; Fasina et al., 2022; Park *et al.*, 2015). Furthermore, GE has been observed to reduce the formation and accumulation of amyloid-beta plaques, a hallmark pathological feature of AD (Alsenani, 2024). Evidence also suggests that GE can mitigate tau pathology, another key component of neurodegeneration in AD, by reducing tau phosphorylation and aggregation (Ganapathy *et al.*, 2023; Baek *et al.*, 2020).

**Beyond neurodegenerative diseases, GE has also been explored in the context of stroke, a leading cause of disability and mortality.** In stroke models, GE administration has been associated with a significant reduction in infarct size, the area of brain tissue damaged by the stroke. This reduction in infarct size correlates with improved neurological deficits, such as motor weakness and sensory loss (Gowtham *et al*., 2024). Furthermore, GE has been shown to enhance recovery after stroke, facilitating functional restoration and improving long-term outcomes. **The scope of GE's potential benefits extends to other neurological disorders, including epilepsy and traumatic brain injury (TBI).** Research has explored the effects of GE in these conditions, with preliminary findings suggesting potential benefits in reducing seizure frequency in epilepsy models and mitigating neuronal damage following TBI. **It's important to note that these preclinical studies typically employ various dosage levels and administration methods, including oral gavage, intraperitoneal injection, and intravenous administration (**Linh *et al*., 2022; Ariyanto *et al.*, 2024)**.** The choice of dosage and administration method can influence the observed effects of GE, and these factors need to be carefully considered when interpreting the results and designing future research. **While the preclinical evidence supporting the neuroprotective effects of GE is encouraging, it's crucial to acknowledge its limitations.** One significant challenge lies in translating findings from animal models to human clinical applications. Animal models can only partially mimic the complexity of human neurological disorders, and the effects observed in animals may not always translate directly to humans. Furthermore, further investigation is needed to elucidate the precise mechanisms of action by which GE exerts its neuroprotective effects. Identifying the specific molecular targets and signaling pathways involved will be crucial for optimizing GE's therapeutic potential and developing targeted interventions.

**Evidence from Clinical Studies**

Clinical studies are the cornerstone of evidence-based medicine, providing a crucial foundation for understanding the potential therapeutic benefits of Gastrodia elata, a traditional herb, particularly in the context of neurological disorders. The reviews of these clinical trials often place significant emphasis on the impact of Gastrodia elata on cognitive function and memory, crucial domains of neurological health. These investigations frequently target specific populations, such as older adults experiencing age-related cognitive decline or individuals diagnosed with mild cognitive impairment (MCI), meticulously investigating whether Gastrodia elata can improve these functions, potentially offering a natural avenue for cognitive support.

Beyond cognitive enhancement, the research landscape extends to explore Gastrodia elata's impact on sleep quality and anxiety, two prevalent neurological complaints that significantly affect the overall well-being of individuals. Studies delve into whether the herb can promote restful sleep patterns and alleviate anxiety symptoms, offering a potential alternative or complementary approach to conventional treatments. Furthermore, research endeavors also evaluate the herb's effects on a broader spectrum of neurological conditions, including headaches and dizziness, investigating its potential to provide relief from these often debilitating symptoms (Dobrek & Głowacka, 2023).

Evaluating these clinical studies requires a meticulous and rigorous approach, encompassing careful examination of the dosage levels and administration methods employed across different trials. Understanding the optimal dosage and delivery mechanisms is essential for maximizing therapeutic efficacy. Equally important is a rigorous assessment of the safety and tolerability of Gastrodia elata in human subjects. This includes monitoring for potential adverse effects and evaluating the herb's overall safety profile to ensure its responsible use in clinical practice.

Finally, a critical evaluation of the existing clinical evidence is essential to paint a balanced and accurate picture of Gastrodia elata's therapeutic potential. This entails not only highlighting the strengths of the positive findings, such as statistically significant improvements in cognitive performance or sleep quality, but also acknowledging the limitations of the current research. Identifying limitations, such as small sample sizes, methodological flaws, or inconsistent findings, is crucial to inform future study design and clinical application. This critical appraisal helps guide the development of more robust and well-designed studies that can further elucidate the true therapeutic potential of Gastrodia elata in addressing neurological disorders and improving patient outcomes.

**Future Directions and Research Gaps**

Future research on Gastrodia elata should prioritize addressing key gaps in our current understanding to fully unlock its therapeutic potential. While promising, the precise mechanisms by which G. elata and its bioactive compounds exert their neurological effects require further elucidation at the molecular level. This includes identifying specific molecular targets, signaling pathways, and downstream effects involved in its neuroprotective, anti-inflammatory, and cognitive-enhancing actions. Investigations into the synergistic potential of different bioactive compounds within G. elata are also warranted, as these interactions could significantly enhance therapeutic efficacy. This necessitates exploring combinations of compounds and their impact on various neurological parameters both in vitro and in vivo. To translate research findings into practical applications, the development of standardized extracts and formulations is crucial, ensuring consistent quality and predictable outcomes. This includes establishing reliable quality control methods for assessing the content of key bioactive compounds and developing formulations that optimize stability and delivery. Rigorous clinical trials, employing larger sample sizes, diverse patient populations, and extended follow-up periods, are essential to definitively assess the efficacy of G. elata in specific neurological disorders such as Alzheimer's disease, Parkinson's disease, stroke, and epilepsy. These trials should incorporate validated outcome measures and compare G. elata-based interventions to existing treatments.

Moreover, research should focus on optimizing extraction and purification methods to maximize the yield of key bioactive compounds, such as gastrodin and p-hydroxybenzyl alcohol, from G. elata. Sophisticated techniques, including supercritical fluid extraction and advanced chromatography, should be explored. Further evaluation of the bioavailability and metabolism of these compounds within the body is necessary to optimize therapeutic potential. This involves studying their absorption, distribution, metabolism, and excretion (ADME) profiles and identifying potential drug-drug interactions. Finally, exploring sustainable and scalable cultivation practices for G. elata is important to ensure a reliable supply of high-quality raw material for research and therapeutic applications.

**Conclusion**

In conclusion, this review has highlighted the promising neuroprotective potential of Gastrodia elata, showcasing its remarkable effects in mitigating neuronal damage and dysfunction. The evidence presented demonstrates that its beneficial effects are likely mediated through a multifaceted approach, targeting various pathways implicated in neurodegeneration. Specifically, Gastrodia elata exhibits a capacity to modulate oxidative stress by scavenging free radicals and boosting antioxidant defenses, to dampen neuroinflammation by suppressing the release of pro-inflammatory cytokines, and to prevent neuronal apoptosis through the regulation of cell survival signaling pathways. Given its demonstrated ability to combat these key hallmarks of neurodegenerative diseases, Gastrodia elata stands out as a compelling source of novel therapeutic agents for the treatment and prevention of conditions such as Alzheimer's disease, Parkinson's disease, and stroke (Percário *et al*., 2020). This review consolidates existing knowledge from diverse preclinical studies, underscores the significance of further research to identify and isolate the specific bioactive compounds responsible for these neuroprotective effects, elucidate their precise mechanisms of action at the molecular level, and investigate optimal dosages and delivery methods. Ultimately, this work contributes to the growing body of evidence supporting the therapeutic potential of Gastrodia elata in the fight against neurological disorders, paving the way for future clinical trials and potential development of effective treatments for debilitating neurodegenerative conditions.

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