

Development of Pharmacological Mechanism of Chinese Medicine *Gastrodia Elata* in the Treatment of Parkinson's Disease

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Abstract

Parkinson's disease is a neurodegenerative disease with a high prevalence in the elderly population and is characterized by resting tremor, muscle tension, limited movement and postural balance disorders. The cause of Parkinson's disease remains unknown and there are no viable treatment options. Although Western medications can sometimes replace dopamine, there may be serious consequences due to their persistent nature, including diminished therapeutic efficacy and side effects such as the "on-off phenomenon". Chinese medicine has achieved remarkable results in the treatment of Parkinson's disease, in which the efficacy of *Gastrodia elata* is particularly prominent, it has a variety of pharmacological functions such as quenching the wind and opening the collaterals, calming the liver and suppressing the yang, balancing the yin and yang, and it has a long history of medicinal use, and it can be an effective treatment for Parkinson's disease. *Gastrodia elata* is one of the herbs used to treat Parkinson's disease. In this article, we outline the mechanism of action of *Gastrodia elata* in Parkinson's disease through in-depth exploration of relevant information. We focused on alleviating neuroinflammatory responses, anti-oxidative stress and inhibiting apoptosis, and analyzed these signaling pathways in detail, hoping to provide valuable references for the research and treatment of Parkinson's disease.

Keywords

Gastrodia elata, Parkinson's disease, pharmacological mechanism, research progress

Parkinson's disease (PD) is a very dangerous degenerative neurological disease, and its typical manifestations include resting tremor, muscle tension, slowed movement, and postural instability [1]. Parkinson's disease is a serious neurological disorder that can affect the daily life and work of patients. PD occurs due to impaired function of nigrostriatal dopamine (DA) neurons, apoptosis, and Lewy vesicle formation, and the DA content of striatal regions is significantly reduced, a phenomenon that may be due to oxidative stress, impaired mitochondrial function, apoptosis, and immune system disorders [2]. Currently, the etiology of Parkinson's disease is unknown and there are no viable therapeutic strategies. Dopamine replacement therapy in Western medicine has become the preferred regimen for patients with PD, in which compound levodopa is widely used in clinical practice and is regarded as the preferred anti-PD drug in the world, and has gained a high degree of international acceptance [3]. The purpose of PD treatment is to improve the patient's symptoms; however, if it is used consistently, it may lead to side effects such as decreased therapeutic efficacy and the "on-off phenomenon" [4]. Through the use of herbal medicines, PD

can overcome the shortcomings of western medicines and have lower toxicity and long-term efficacy [5].

PD is categorized as a "trembling disease", and it is widely believed in contemporary medicine that the root cause of this disease is the failure of the liver and kidneys, which leads to a loss of qi and blood, resulting in internal heat, phlegm stagnation and other pathological changes. *Gastrodia elata* is a plant of the orchid family, and its dried tubers are sweet in flavor and flat in nature, belonging to the liver meridian. It is capable of quenching wind and opening channels, calming the liver and suppressing yang, and balancing yin and yang. The drug has shown various effects in pharmacology, such as lowering blood pressure, calming mood, suppressing convulsions, reducing blood lipids, enhancing immunity, and protecting the nervous system. In this paper, by summarizing the pathological mechanisms of PD and the related pharmacological studies of *Gastrodia elata*, we comprehensively analyze the advantages of *Gastrodia elata* in the treatment of PD in order to provide reference for the clinical Chinese medicine treatment of PD.

1. Overview of the study of *Gastrodia elata*

Gastrodia elata can quench wind and open channels, calm the liver and suppress yang, and balance yin and yang. Through the pharmacological study of *Gastrodia elata*, we found that its main chemical constituents are tianmuin, tianmuoside, tianmu ether glycoside, tianmu polysaccharide, and B-sterol [6]. It has a variety of pharmacological effects, including but not limited to anticonvulsant, antioxidant, antidepressant, analgesic, sedative, antiepileptic, anti-inflammatory, and neuroprotective [7]. It is also used in the treatment of Parkinson's disease and the sequelae of traumatic brain injury. Despite the fact that *Gastrodia elata* and its active ingredients are widely used in clinical practice, relatively few studies have been conducted on their use in the treatment of neurodegenerative diseases, especially in the treatment of PD. Therefore, the present study aimed to reveal the pharmacological mechanism of *Gastrodia elata* in the treatment of PD by analyzing the pathogenesis of PD and the pharmacological effects of *Gastrodia elata* in depth.

2. Therapeutic mechanism of *Gastrodia elata* in PD

2.1 Reduce neuroinflammatory response

Microglia plays an important role in the brain in that they provide autoimmunity. Microglia appears in various morphologies when subjected to various stimuli, of which M1 and M2 are the most common. Activation of M1-type microglia is a common phenomenon [8], and their production of pro-inflammatory factors, such as TNF- α , IL-6, IL-12, and IL-1 β , has the potential to cause damage to neuronal cells or even to trigger death, but at the same time, it also leads to an increase in the activity of the microglia that thereby triggering the development of PD, creating a continuous vicious cycle. One study found that the expression levels of TLR4, NF-Kb, p65, and p38MAPK were significantly increased in the brain of Parkinsonian rats [9]. The expression of these substances can be significantly reduced by using tensin, and furthermore, the expression and decline of these substances become greater with the increase of tensin dose. This suggests that the brain tissue of Parkinson's rats shows inflammatory response, and the application of tianphenin can regulate the expression of TLR4/F-Kb pathway proteins, thus reducing the level of downstream inflammatory factors and effectively alleviating the inflammatory response of the brain tissue of Parkinson's rats. In this way, the neuroprotective mechanism was exerted. Studies have shown that C20, a natural plant active substance, can inhibit lipopolysaccharide-induced BV2 cytotoxicity [10] and has a good neuroprotective effect. After 20C treatment, we found that it significantly ameliorated the toxic effects of 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine in a mouse model, and also effectively reduced the aggregation of α -synaptic nuclear proteins, which effectively inhibited the inflammatory response [11]. Wu Xiaoying et al. [12] also found that aspalathin was able to reduce TNF- α and IL-1 β mRNA expression to a certain extent, and down-regulate the expression of lipopolysaccharide-induced BV2 inflammation-related proteins, iNOS, TLR4, p-IKB α , NLRP3, cleavedcaspase-1, and cleavedIL-1 β , and the mechanism may be that aspalathin was able to inhibit the secretion and expression of lipopolysaccharide-induced inflammation-related factors in BV2 cells.

2.2 Anti-oxidative stress

Studies have shown that excessive accumulation of dopamine (DA) leads to oxidative stress in neurons, which triggers severe damage, and this is the main reason why dopaminergic neurons in PD patients are damaged by oxidative stress [13]. Aspalathin can effectively inhibit oxidative reactions and exert antioxidant protective effects [14]. It has been found that 20C aspalathin active substance can effectively alleviate the oxidative stress and inhibit

apoptosis in PC12 cells caused by fisetinone [15, 16], and it can effectively inhibit the endoplasmic reticulum stress caused by clostridium difficile [17]. The presence of 6-OHDA in the toxic products of DA oxidation was explored in depth by some researchers [18], and the 6-OHDA-induced PC12 cell model showed that 20C could significantly improve the survival of the cells and also effectively reduce the oxidative stress damage of the cells, this result provides an important basis for the protection of PC12 cells. It has been experimentally confirmed [19] that the ethyl acetate extract of asparagus can effectively inhibit the growth of H₂O₂ oxidative damage PC12 model cells and greatly increase their survival rate, and it also has the efficacy of antioxidant damage. By activating intracellular antioxidant enzymes (T-SOD), it can effectively reduce the production of oxygen free radicals, thus exerting its unique antioxidant action mechanism; by enhancing the antioxidant capacity of the cells, it can effectively prevent the destruction and damage of free radicals to the cells in many ways; and it protects the cell membranes and other structures from the damage caused by the free radicals, so as to improve the health of the organism. The study of Duan Xiaohua et al. showed that *Gastrodia elata* extract can effectively block lipid peroxidation [20], reduce oxidative damage, and has a significant anti-oxidative stress effect. There are other studies [21] found that the antioxidant effect of asparagus alcohol is obvious, and has a certain protective effect on neurons, the mechanism may be asparagus alcohol can then reduce the serum content of LPO to a certain extent, elevate the serum SOD, GSH-Px value, thus scavenging the role of peroxides in brain tissue.

2.3 Inhibit apoptosis

The occurrence of neurodegenerative diseases is closely related to apoptosis [22]. Relevant studies have found [23] that there are a large number of damaged neurons in the brains of patients with neurodegenerative diseases, and their death process is characterized by distinctive features, which include abnormal replication of chromosomes, degradation of DNA, and elevated levels of activation of cysteine proteases and cysteoaspartic enzymes. It has been shown [24] that tensin injection is able to block the effect of Bcl-2 family members on apoptosis by modulating their activity, as well as preventing Bax phosphorylation, which leads to the inhibition of apoptosis.

3. Summary

As a common treatment for PD, *Gastrodia elata* has a variety of pharmacological effects, including modulation of multiple receptors and signaling pathways. It has a variety of therapeutic approaches that can effectively improve the symptoms of PD patients and has great potential for application. Studies have shown that the traditional Chinese medicine *Gastrodia elata* can effectively alleviate the suffering of PD patients, as evidenced by the reduction of neurological inflammatory response, anti-oxidative stress, and inhibition of apoptosis. However, although its mechanism of action is very diverse, due to the complexity and variability of the regulatory molecules and signaling pathways involved and the close connection between them, there is no complete and systematic mechanism combining analysis to explain its action; with the increasing number of patients with PD, the traditional animal and cellular experiments can no longer meet the clinical needs, so the future must vigorously implement randomized clinical trials to better validate the effectiveness of *Gastrodia elata*, and to provide new ideas and ways to better develop and apply *Gastrodia elata* to treat PD.

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