Research Progress of Polygala Tenuifolia in the Treatment of Alzheimer's Disease

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Abstract: Alzheimer's disease (AD), also known as dementia in traditional Chinese medicine, is a progressive neurodegenerative disease, which is progressive and irreversible. The etiology of AD is still unknown, and the current medication can only delay its process. Alzheimer's disease impairs the patient's thinking, memory and independence, affects the patient's social viability and quality of life, and even death. Polygala tenuifolia is a traditional Chinese medicine, which has the functions of tranquilizing mind and improving intelligence, soothing heart and kidney, dispelling phlegm and opening orifices, and reducing swelling, etc. At present, many studies have shown that Polygala tenuifolia and its chemical components can improve the symptoms of Alzheimer's disease, which is a potential ideal drug.

Alzheimer 's disease (Alzheimer 's disease), referred to as AD, also known as dementia in traditional Chinese medicine, is a kind of disease that often occurs in the elderly or pre-elderly, with slow onset and gradual progress. The symptoms are gradually severe cognitive impairment (memory impairment, learning impairment, attention impairment, spatial cognitive function, problem solving ability disorder), gradually unable to adapt to society.The mechanism is usually considered to be related to gene mutation, deposition of Aβ, tau protein hyperphosphorylation, mitochondrial defects, nerve cell apoptosis, oxidative stress, free radical damage and so on. According to the "Chinese Alzheimer 's Disease Report 2021 ", the number of AD patients aged 60 and above in China is as high as 9.83 million, which has become a major disease and social problem that seriously endangers the health of the Chinese people [1].

Polygala tenuifolia is a traditional Chinese medicine commonly used in China. It has bitter, pungent and warm taste, and belongs to the heart, kidney and lung meridians. It has the effects of

tranquilizing mind and benefiting intelligence, communicating heart and kidney, dispelling phlegm and opening orifices, and detumescence. It is often used in the treatment of insomnia, forgetfulness, palpitation, epilepsy, convulsion, cough, carbuncle, sores and ulcers. It is often combined with gladiolus, ginseng and poria (God) and Chinese medical herbs [2]. Li Shizhen, as early as in the "Compendium of Materia Medica", said that "the ability of this herbal suit to enhance intelligence and ambition, so it is called polygonia". "Shennong 's Herbal Classic" recorded in the polygonia : " the main cough reverse injury, tonic deficiency, in addition to evil, nine orifices, benefit wisdom, ears and eyes smart, do not forget, strong will, power. " polygonia tenuifolia is often matched with calamus, jujube kernel and so on. It is a commonly used pair of intelligence-enhancing drugs in the clinical application of traditional Chinese medicine. The two must be used together. After compatibility, it can play a role in soothing the mind, nourishing the mind, resolving phlegm and opening the orifices. It has been used to treat ' forgetfulness ' and other diseases throughout the ages [3].

1. Chemical Composition of Polygala Tenuifolia

Polygala tenuifolia is rich in chemical components, and the effective chemical components mainly include saponins, ketones, oligosaccharide esters and alkaloids. The components that exert pharmacological effects are mainly saponins, ketones and oligosaccharide esters.The pharmacological effects of Polygala tenuifolia are mainly concentrated in the central nervous system, which have the effects of improving cognitive impairment, improving learning and memory ability, anti-aging, protecting neurons, anti-epilepsy, anti-depression, anti-tumor, inhibiting inflammatory response, repairing cartilage damage and protecting liver cells [4]. Polygala tenuifolia is an ideal drug for the treatment of Alzheimer 's disease. This paper summarizes the mechanism of its therapeutic effect.

2. Mechanism of Action

2.1 Promote Proliferation and Differentiation of Neural Stem Cells

Neural stem cells (NSCs) have the characteristics of long-term self-replication and multi-potential differentiation, which can differentiate into various types of cells in the nervous system under certain conditions, providing a new alternative treatment for neurodegenerative diseases. Shi Fang, Liang Zhigang [5-6] et al. have shown that Polygala tenuifolia has a definite neuroprotective effect, and its antioxidant activity is one of the possible mechanisms. The main active ingredient of polygenin (SEN) can promote the proliferation and differentiation of NSCs in vitro, suggesting that the drug has a new biological characteristics to promote nerve regeneration and repair.

2.2 Protecting Neuronal Mitochondria

Huang Yan, Chen Yiqing [7] et al. observed the ultrastructure of brain mitochondria, the expression of cytochrome C, the changes of apoptosis rate, mitochondrial membrane potential and mitochondrial free radical metabolism of brain mitochondria in AD, indicating that polygonin can inhibit the expression of cytochrome C in nerve cells, and the apoptosis rate was significantly decreased. In addition, It is suggested that tenuigenin can significantly enhance the activity of mitochondrial antioxidant enzymes in hippocampal nerve cells and reduce the production of free radicals, significantly reduce the neurotoxicity induced by Aβ1-40, and have a better protective effect on the ultrastructure and function of mitochondria. Shuai Zhifeng, Han Lijun [8]et al. also showed that tenuigenin could significantly inhibit the activity of superoxide

Dismutase (SOD), catalase (CAT) and Glutathione peroxidase (GSH-PX) and the content of malondialdehyde (MDA) while improving mitochondrial membrane potential, showing a dose-dependent effect.

2.3 Antioxidant Effect

The hippocampus is an important brain region related to learning and memory. The large oxygen consumption of the brain hippocampus itself has a high concentration of easily oxidized substances such as catecholamine, ascorbic acid, myelin and other lipid components as well as intercellular lipid signaling molecules, so the brain hippocampus is more susceptible to involvement [9]. SOD is an important antioxidant enzyme in the body. Geng Zhihui, Xuan Zhaoyu[10] et al. studied the learning ability of D-galactose aging model mice, indicating that Polygala tenuifolia can increase the activity of peroxidase SOD and reduce the content of lipid peroxide, which has oobvious antioxidant effect, thus improving the body 's learning and memory function and protecting nerves to a certain extent.

2.4 Regulate the Abnormal Expression of AB And Reduce Abnormal Cell Death

Neurotoxicity caused by β-amyloid (Aβ) deposition is one of the pathogenic mechanisms of AD.Studies have shown that senile plaques formed by Aβ deposition in the brain are a key event in the pathological process of AD [11]. Yu Hehan and Lu Xiaohua [12] et al studied the neuroprotective effect of Polygala tenuifolia saponins on Aβ-induced cell cycle disorder and apoptosis by regulating the transport and clearance of Aβ. The results showed that polygenin had a regulatory effect on Aβ-induced abnormal expression of Bcl-2, Bax, Caspase-3 and Caspase-8 induced by Aβ, and reduce the abnormal death of cells, so as to play a protective role in nerve cells. The mechanism may be to accelerate the transport and clearance of Aβ, reduce the deposition of Aβ in cells, and block the reactivation of nerve cell cycle, which leads to the apoptosis of nerve cells.

2.5 Reduce the Aggregation of Phosphorylated Tau Protein

Intracellular neurofibrillary tangles (NFTs) have been shown to be caused by abnormal aggregation of hyperphosphorylated tau protein, which is a more critical pathological change in AD pathogenesis [13]. Xie Peijun [14] applied Polygala Powder (Polygala tenuifolia, Acorus tatarinowii Schott, Ginseng, Poria cocos, Coptis chinensis), taking tau protein as the entry point, to qualitatively and semi-quantitatively detect the expression of phosphorylated tau protein by IHC method and Wb method, respectively. The results showed that Polygala powder may have a better degradation effect on abnormal phosphorylated tau protein in AD model by regulating the ubiquitin-proteasome system.

2.6 Improve Direction Discrimination Ability and Improve Cognitive Function

Ma Liben, Wang Futian [15] et al. studied the effects of Polygala tenuifolia extract on memory impairment induced by scopolamine hydrobromide, direction discrimination disorder induced by pentobarbital sodium and cerebral blood flow. The results showed that Polygala tenuifolia extract had a certain protective effect on direction discrimination disorder induced by pentobarbital sodium in mice, and had a significant improvement effect on memory impairment induced by scopolamine in mice, and could significantly improve cerebral blood flow and oxygen supply. Gao Minghuang [16] used the model experiment of cognitive impairment induced by corticosterone, and the results showed that Polygala tenuifolia and its active component Polygala tenuifolia saponins (2.5mg / kg)

had a significant improvement effect on c corticosterone-induced cognitive impairment. The results of the study further confirmed that Polygala tenuifolia has a more obvious therapeutic effect on cognitive impairment diseases caused by dementia and Polygala tenuifolia saponin is one of its main active substances. It may be related to the regulation of Synl, PSD95, NMDAR, P-CREB / CREB and other synaptic proteins and their related downstream proteins to enhance the plasticity and improve the central nervous inflammation.

3. Conclusion

Traditional Chinese medicine believes that the heart governs the mind, and the liver stores blood, the kidney stores essence, the essence is born in the marrow, and the marrow is filled in the brain. The deficiency of heart qi and blood or the deficiency of liver and kidney essence and blood will affect the physiological function of the brain. Polygala tenuifolia belongs to the heart, kidney and lung meridians. The ancients have long studied that Polygala tenuifolia has the effect of improving intelligence, and it has achieved definite curative effect in clinical practice of traditional Chinese medicine. With the development of modern research of traditional Chinese medicine, the chemical constituents and pharmacological activities of Polygala tenuifolia have been further studied. The results of modern research provide strong evidence for its treatment of Alzheimer 's disease and dementia.Of course, the mechanism of Polygala tenuifolia in the treatment of Alzheimer 's disease can be further studied. This paper summarizes its mechanism of action, which is helpful for the treatment of Alzheimer 's disease and dementia. With more research results, it needs to be further improved. The traditional Chinese medicine is extensive and profound, worthy of in-depth study, and can provide more ways and methods for the treatment of diseases.

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