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Evaluation of Chinese herbal medicine's neuroprotective effects: Regulation for neurological disorders

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Abstract. Chinese herbal medicine is a type of medicine composed of plants unique to China, which has been found to have significant neuroprotective effects in recent years. The research on its neuroprotective mechanism has become a hot topic. At present, neuroprotective mechanisms have been found to be closely related to balancing ion channels, inhibiting apoptosis of nerve cells and promoting nerve growth. In this work, we summarize the recent progress of research on neuroprotective mechanisms of Chinese herbal medicine and the existing clinical trials.The significance of this study is not only to summarize its therapeutic mechanism, but also to improve the status of Chinese herbal medicine at the international level. It is hoped that more international scholars will join in the research of Chinese herbal medicine.

Keywords: Herbal medicine,Neuroprotective mechanism, Nervous system disease.

1. Introduction

Chinese herbal medicine is a kind of medicine that cures diseases by regulating the flow of "Qi and blood" in the human body. Since ancient times, it has not been paid much attention by the public because of its slow effect and few doctors who really know herbal medicine. In recent years, the medical community has paid more attention to the research of Chinese herbal medicine. The neuroprotective mechanism of Chinese herbal medicine has reached the molecular level, and there are clinical cases for common neurological diseases, but how to completely eradicate such as Parkinson's disease and Alzheimer's disease has not been discovered. In this work, we summarized the research results of Chinese herbal medicine on neuroprotective mechanism in recent years, found the gaps, and pointed out the future research direction for current scholars.

2. Types and mechanisms of neuroprotective effects of traditional Chinese medicine

2.1. Chinese traditional herbal medicine's and historical research

Herbal medicine is a generic term of all kinds of botanicals and mineral drugs. Most are different parts of the plant, such as roots, stems, leaves, flowers, and fruits. Generally speaking, it is mainly herbaceous. In ancient China, traditional Chinese medicine was widely used in the treatment and rehabilitation of diseases [1]. Through the unique formula and treatment method of herbal medicine, the balance of Yin and Yang of the human body and the function of the zang-fu organs are regulated to achieve the cure of diseases and the rehabilitation of the body. In the folk traditional culture, the application of Chinese medicine is also very common. For example, in rural areas, many elderly people and village doctors are

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good at using traditional Chinese medicine to treat some common diseases and minor injuries, which allows them to reduce the need for modern medical facilities.

2.2. Nervous system and diseases

The nervous system is a system in the body that plays a leading role in the regulation of physiological functional activities, mainly composed of nervous tissue, divided into the central nervous system and peripheral nervous system. The central nervous system includes the brain and spinal cord, and the peripheral nervous system includes the cranial and spinal nerves. The nervous system diseases are divided into five different types. Headache, like Low cranial pressure headache, tension headache, migraine, cluster headache, and etc; Brain diseases, like intracranial infection, or inflammatory demyelinating diseases, such as multiple sclerosis, MOG antibody encephalitis, autoimmune encephalitis, NMOSD spectrum disease; Metabolic diseases: such as acute myelitis, spinal cord tumors, spinal vascular diseases, syringomyelia, etc; Peripheral neuropathy:alcoholic peripheral neuropathy, diabetic peripheral neuropathy and so on; Muscle lesions: polymyositis, inclusion body myositis, muscular dystrophy, motor neurone disease, myasthenia gravis, neuromuscular junction disease; Parkinson's disease, epilepsy and so on.

2.3. Interactions between Chinese herbs and Nerve cells

In the acute phase of cerebral infarction, cysteine aspartate protease (cysteinyl aspartate specific proteinase, caspase) -3 is the key protease initiating cell apoptosis and can induce cell apoptosis, leading to neuronal death. The effect of it are promoting blood circulation and removing blood stasis, clearing collaterals and relieving pain. Breviscapine also plays an important role in preventing blood stasis of brain and heart. Breviscapine can significantly inhibit the expression of caspase-3 after cerebral ischemia, reduce brain tissue injury and improve nerves. Function to rescue neurons or glial cells in ischemic penumbra area. The protective mechanism of breviscapines may be related to reducing inflammation, reducing apoptosis, relieving cerebral edema, promoting angiogenesis, and increasing brain-derived neurotrophic factor. As research deepens, breviscapine's neuroprotective mechanism will be clearer, in order to provide a more reliable theoretical basis for the treatment of clinical cerebrovascular disease [1].

3. Chinese herbal medicine in the treatment of neuro diseases

3.1. Parkinson's disease

Parkinson's disease, also known as paralysis tremor, is the most common degenerative disease of the central nervous system in the elderly. Parkinson's disease starts slowly and develops gradually, which is a slow, progressive process of development. Symptoms include dyskinesia, tremors, and muscle rigidity. Science shows that young and middle-aged people are also at the onset of Parkinson's disease [1]. At present, the cause of Parkinson's disease is not fully understood, and research suggests that Parkinson's disease may be related to genetic factors, environmental factors, and diet. Currently, less than 10% of Parkinson's disease is inherited, and the mutation of the alpha-synuclein gene, which we first discovered, may cause Parkinson's disease. In addition, in recent years, many researchers have found that there are many genetic mutations that may eventually aggravate or cause Parkinson's disease under the influence of the external environment. In addition, our current research shows that there is a substance called MTPT, and this substance, early on, was a drug derivative. Some people who take it can cause Parkinson's disease. In addition, aging and age factors are also very big. In fact, Parkinson's disease tends to occur in people over the age of 60 or 65, and although aging is a major cause, it is not inevitable that older people will get Parkinson's disease. Parkinson's disease is also a sporadic and relatively common degenerative disease. Aging may lead to a loss of dopamine neurons in the brain, or degeneration of the nigra striatum. In addition to aging, we have brain injuries, smoking, drinking coffee, etc., can increase or decrease the risk of Parkinson's disease. The link between smoking and Parkinson's disease is not clear, some people think it may reduce Parkinson's disease.

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3.2. Treatment for Parkinson's disease

During the research of Enli Luo, Chunli Bao and Desheng Wang. A total of 180 Wistars were obtained from PD model rats. The cranial horizontal position was fixed on the brain upright position instrument, the rat brain stereotaxic map, and the striatum two-point injection method was used. They use the mix medicine made from Shu di, Gouqi, Zhenzhumu,Roucongrong,Dannanxing, Quanxie,Tianma then mellow them in water. Shake the mixture water and take it for the mice [2].Then they texted three kinds of result,circling behavior, the striatal monoamine neurotransmitters and TH immunohistochemical. Before doing the official text, the double blind clinical trail.

Double-blind test means that in the process of the test, neither the tester nor the tested person knows which group the tested person belongs to (experimental group or control group), and the analyst usually does not know which group the data being analyzed belongs to when analyzing the data. It is designed to eliminate subjective biases and personal preferences that may appear in the consciousness of the experimenter and the participant. In most cases, double-blind experiments require a very high degree of scientific rigor. Double-blind experiments mean that neither the tester nor the tested person knows which group the tested person belongs to (experimental group or control group) during the experiment, and the analyst usually does not know which group the data being analyzed belongs to when analyzing the data. It is designed to eliminate subjective biases and personal preferences that may appear in the consciousness of the experimenter and the participant. In most cases, double-blind experiments require a very high degree of scientific rigor. The result of this research is Qi Feng Dingzhi decoction can pass the upper tone TH. Expression, increase the release of DA in DA neurons, and have a positive effect on dopamine. The warp can improve the rotation behavior of PD model rats by protecting them.

This indicates that Xifeng Dingzhi Decoction is an effective drug in the treatment of PD model rats.It works best at medium doses.Xifeng Dingzhi Decoction can improve the spin behavior of PD model mice by increasing the release of DA neurons and protecting dopaminergic neurons through the expression of TH. It is concluded that Xifeng Dingzhi Decoction is an effective drug for treating PD model mice. The medium dose is the best and its mechanism of action is discovered, which lays a theoretical and experimental basis for the clinical treatment of PD with Xifeng Dingzhi Decoction. With the trend of aging populations, the incidence of osteoarthritis is increasing year after year. It is urgent to improve the treatment effect and quality of life of patients and doctors should pay enough attention [2].

3.3. The advantages of Chinese herbal medicine in treating neurological diseases

Firstly, the price is cheap, the collection of Chinese medicine is simple, the active extract of Chinese medicine is easy to separate and purify, and the administration of Chinese medicine is easy. Secondly, the unique principle: Chinese medicine from the root phase of regulating the function of the viscera, the principle of balancing Yin and Yang, supplemented by clearing phlegm and waking up the brain, dredging the meridians, nourishing the heart and calming the mind, clearing heat and removing fire, strengthening the spleen and kidney, relaxing the liver and regulating qi and other methods, to enhance the microcirculation of brain cells, improve the brain's blood oxygen metabolism, so as to achieve the purpose of truly curing neurological diseases [3].Thirdly, few side effects: The use of Chinese herbal medicine, little pain, low risk, non-toxic side effects, is a natural ecological therapy. Therefore, regardless of age, physical strength, the whole world people can be used [4].

4. Molecular mechanisms of Chinese herbal medicine in Neurological diseases

4.1. The main role of Chinese medicine in resisting calcium ion inflow

Some studies have reported that the flavonoid glycoside of the yellow zen can inhibit the release of calcium ions in nerve cells and the inflow of calcium ions outside the cell, so that it can protect neurons from the damage of cell excitatory toxins. Some researchers have used calcium fluorescence indicators to determine the concentration of free calcium ions in nerve cells [5]. Some studies have shown that the concentration dependence of flavescens significantly reduces the resting calcium concentration in smooth muscle cells and suprarenal adenin and potassium ionoide-induced overloading of intracellular

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calcium concentration. The glial cells have inseparable relation to the structure and function of nerve distant cells. The inhibitory effect of flavonoside and flavonoside on the increase of intracellular calcium ion concentration is realized by decreasing the activity of phosphatase [5].Effectively reduce the incidence of Alzheimer's disease and Parkinson's disease due to neurotoxin release.

4.2. To alleviate vascular endothelial damage and promote angiogenesis

Plasma endothelin 1 can enhance the vasoconstrictor effect, and its high expression can cause vasospasm in the collateral circulation in the area surrounding the ischemic lesion, further increasing the ischemic lesion. The combination of breviscapine injection and edaravone reduced the expression level of plasma endothelin 1 in patients with acute ischemic cerebrovascular disease, contributing to the establishment of collateral circulation and improving tissue damage in the ischemic area. Studies have shown that the more serious the insulin resistance, the more serious the inflammatory state of the body, the worse the plaque stability, the higher the incidence of cerebrovascular disease, and breviscapinin participates in metabolic regulation, inflammatory response, and organic biological processes, such as nitrogen compound metabolism interfere with important signaling pathways in the human body to exert anti-insulin resistance effects [1]. Vascular endothelial growth factor (VEGF) is directly involved in the blood vessels of ischemic and hypoxic tissues or organs. Endothelial cell proliferation and angiogenesis.

4.3. Main signaling pathways

Phosphatidyl inositol 3-kinase is an intracellular phosphatidyl inositol kinase. Various growth factors and neurotrophic factors can initiate the activation of PI3K, including fibroblast growth factor, insulin, insulin-like growth factor, calcium ion, and calcium-regulated egg white. When these growth factor signals bind to the extracellular domain of transmembrane receptors such as tyrosine kinase receptors, the receptors undergo self-phosphorylation, and PI3K is recruited to the receptor phosphorylation site to catalyze phosphosyl inositol diphosphate ribosomal protein S6 kinase on the plasma membrane surface, initiating various proteins to synthesize phosphatase tensin, a negative regulatory mechanism dominated by PTEN. The protein PTEN encoded by the motif is natural dephosphorylation of the PI3K/AKT/mTOR pathway to PIP and inhibition of PI3K/AKT pathway's PIP 3, 4, 5 -triphosphoric acid sequence on the cell membrane. In the case of decreased PTEN activity, this pathway activates phate, the PIPAKT signaling molecule, and initiates the PI3K/AKT pathway. mTOR initiates the synthesis of various proteins by regulating a variety of proteins that play an important role in translation [6].

5. Chinese herbal medicine and mitochondria

Mitochondria are energy sources and organelles of biosynthesis, and play an important role in regulating biological processes such as ATP production and Ca2 + level and distribution in cells [5]. Mitochondria are also one of the key organelles of intracellular signal transduction. Mitochondria function on the electron transport chain, which not only produces ATP, but is also the main source of living oxygen.Mitochondria perform a variety of functions within cells, including producing energy, regulating apoptosis, and synthesizing cell signaling molecules. These functions are closely related to the development of the central nervous system. First, mitochondria provide the necessary energy support for the development of the central nervous system by producing energy. Second, mitochondria also involved in the process of neuronal apoptosis, which plays an important role in the morphogenesis of the central nervous system and the regulation of the number of neurons. In addition, mitochondria are also involved in the synthesis of some nerve signaling molecules, such as nitric oxide and glutathione, which play an important role in neurotransmission and neuroprotection [3].

5.1. Effect of Chinese medicine on mitochondrial energy production

Most of the energy in the body's cells is supplied by mitochondria. The electron transfer process (mitochondrial oxidative phosphorylation) in the mitochondrial electron transport chain is coupled with

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the production of ATP. The deficiency of mitochondrial bioenergetics results in insufficient ATP production, which seriously affects cell and organ functions.

Astragaloside is an organic substance extracted from Astragalus. The main active ingredients in Astragalus are Astragalus polysaccharide, Astragalus saponins and Astragalus isoflavones, which can enhance the immune function of the body, strengthen the heart and reduce blood pressure, reduce blood sugar, diuresis, anti-aging, anti-fatigue and so on.

Astragaloside can inhibit the activity of mitochondrial Ca2 + unidirectional transporter, reduce mitochondrial Ca2 + level, stimulate cell metabolic enzymes to synthesize ATP, thus solving the problem of mitochondrial energy shortage [5]. Several common genes involved, such as PARKIN, DJ-1, LRRK2, and Pink 1, are closely related to mitochondrial function. Among them, D-1 gene can inhibit the formation of reactive oxygen species and play a protective role, while PARKIV can enhance mitochondrial regeneration by increasing the expression of TFAM. Mutations of these two genes lead to increased intracellular ROS levels and weakened TPAM binding ability to DNA, thus affecting mitochondrial regeneration. On the one hand, TFAM knockout mice showed parkinsonic-like movement disorders, which could be alleviated by levodopa, suggesting that TPAM dysfunction was related to PD. It has also been confirmed that induced overexpression of TFAM can reverse the damage caused by 1-methyl-4-phenyl-tetrahydropyridine ion (MPP+) to dopaminergic neurons, including respiratory chain complex activity, mtDNA expression,ATP content and ROS level1. Therefore, IPAM can be regarded as one of the targets for the future treatment of PD. On the other hand, mitochondrial single nucleotide polymorphism site analysis was conducted in some PD patients and normal population, and no link was found between several common TFAM SNPS and knock, and no TFAM gene mutation was found in tested PD patients. However, new research suggests it may be a risk factor for Parkinson's disease dementia. Compared with the control group, the frequency of rs23066604 genotype was significantly different in male subjects, and the copy number of prefrontal cortex mitochondria was also significantly reduced [7].

5.2. Effects of traditional Chinese medicine on mitochondrial ROS

Electron leakage during electron transport in the mitochondrial respiratory chain may lead to the production of ROS, which can play an important role in cell biology [5]. Shikonin is an organic substance extracted from Lithospermum erythrorhizon Siebold. Shikonin can inhibit mitochondrial ROS production by activating phosphatidylinositol -3-kinase/protein kinaseB/nuclear factor E2-related factor 2 signaling, reducing oxidative low-density lipoprotein cholesterol induced Monocyte inflammatory response.Mitochondrial ROS can act as signaling molecules to regulate cellular function, such as by inducing hypoxic-inducing factors and factors. Nuclear factor E2 related factor 2 is involved in the process of cellular antioxidant. High levels of ROS cause oxidative damage to mPTP, resulting in the disappearance of mitochondrial membrane potential, irreversible damage to both mitochondria and cells, and cell activation. Endogenous apoptosis. It can be seen that the regulation of ROS production by traditional Chinese medicine interferes with cell damage caused by oxidative stress [5].

5.3. Chinese medicine induces stem cell differentiation

Because traditional Chinese medicine is often used in the form of compound medicine in clinical practice, so traditional Chinese medicine compound medicine. The influence on stem cell differentiation has become one of the research directions. And in the actual study. Many Chinese herbal compounds have indeed shown good differentiation induction effect on stem cells.

Qinggu Xiaotong granules are made from a Chinese herb called Qianxiacheng. It contains phenolic components and sterols, flavonoids, amino acids, choline, potassium salts and other components, and has the effect of removing dampness and eliminating yellow, eliminating swelling and detoxificationSome studies have shown that bone marrow mesenchymal stem cells were induced by the drug-containing serum of Qinggu Xiaotong Granule, and the mRNA expression levels of Sox9, Runx2 and Collagen II in the drug-containing serum group were higher than those of the control group, indicating that the drug-containing serum of Qinggu Xiaotong granule could enable the differentiation

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of myeloid mesenchymal stem cells into chondrocytes [8]. Mouse embryonic fibrob-lasts (MEF) is studied during induction into nerve cells at multiple time points. Quasi-time series analysis revealed that the molecular reprogramming pathway was continuous, and the transcription factor Ascl1 promoted MEF to exit the cell cycle and differentiate into nerve cells [9].

6. Conclusion

At present, the relevant neuroprotective effects and mechanisms mainly come from the experimental studies on Parkinson's disease , which has proved that it can cross the blood-brain barrier and further balance ion channels, antioxidant, inhibit apoptosis of nerve cells and promote neurogenesis, improve choline nerve function, to play a neuroprotective role . Therefore, Chinese herbal medicine has the value of further study in neuroprotection. In traumatic diseases of the nervous system various pathological stimulating factors eventually cause nerve cell injury and apoptosis, thus causing neurological function lesions. Herbal medicine can inhibit nerve cell injury and apoptosis through multi-pathway and multi-target has unique advantages for neuroprotection. However, whether herbal medicine has its unique target in inhibiting nerve cell injury and apoptosis, and the root cause of Parkinson's disease are still not completely clear , so its neuroprotective mechanism needs further study. Traditional Chinese medicine has a long time history, played a notable advantage in treating neurological diseases and has a broad perspective. The potential of herbal medicine still have a lot to discover, so it is important for doctors and scientist to do more future research about the Chinese herbal medicine.

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