

The Effect of Polysaccharides of Polygonatum Polysaccharides on Memory Impairment in Elderly People

Yiran Zhang

*College of Food Science and Technology, Huazhong Agricultural University, Wuhan, China
2022309210520@webmail.hzau.edu.cn*

Abstract. With the aging of the population, the incidence of memory disorders diseases in the elderly has climbed significantly, and the prevalence rate of people over 60 years old reaches 13%-42%. As the core active ingredient of Polygonatum polysaccharides (PPs), the polysaccharides of PPs have become a research hotspot because of their multi-target neuroprotective effects. Studies have shown that it improves memory function by enhancing hippocampal synaptic plasticity, inhibiting β -amyloid deposition, repairing neuronal damage, and regulating cerebral blood flow and antioxidant and anti-inflammatory responses. However, there are still gaps in current studies such as the lack of clinical data and the unknown conformational relationship of polysaccharides. This paper systematically reviewed the mechanism of action of polysaccharides from PPs on memory disorders, including Alzheimer's disease, chronic cerebral ischemia, and vascular dementia (VD), and found that they can significantly enhance the efficiency of neurotransmitter delivery, reduce neuronal damage in chronic cerebral ischemia, and correct the abnormalities of blood rheology in VD, which can synergistically improve the cognitive function. The results provide an experimental basis for the development of functional foods and drugs to improve memory disorders. In the future, it is necessary to strengthen human clinical trials, deeply analyse the structure-activity relationship of polysaccharides, and expand their application in medicinal food products, so as to provide a new strategy for the health management of the aging society.

Keywords: Polygonatum polysaccharides, elderly people, Alzheimer's disease, chronic cerebral ischemia, vascular dementia.

1. Introduction

Memory disorders are common among the elderly as the brain shrinks and physiological functions deteriorate with age. Currently, the number of people suffering from memory disorders in China has reached 7 million, and the prevalence rate increases significantly with age, with data showing that the prevalence rate of memory disorders is 13% in 60-64 year olds, 17% in 70-74 year olds, 33% in 80-84 year olds, and 42% in ≥ 85 year olds [1]. In the social context of China's aging population, the impact of the problem of memory impairment in the elderly has become more and more prominent, and has become an important topic that needs to be researched and solved nowadays.

A variety of drugs have been found to be able to improve memory impairment, including intellectual stimulants, ergot alkaloids, calcium antagonists, ginkgo biloba extracts, and cholinesterase inhibitors [2]. Among them, polysaccharides of Polygonati Polysaccharides (PPs), as important active extracts from Rhizoma Polygonati, have become a hotspot for research and analysis in recent years due to their diverse compositional patterns and potentially great medicinal value.

Huangjing is a genus of plants in the family of Liliaceae, which has a long history of medicinal use. 2020 edition of the Chinese Pharmacopoeia includes three kinds of medicinal value: Huangjing, Dianhuangjing, and Multiflora Huangjing, which are widely distributed in the three eastern provinces of China, East China, and the Southwest region of China. Huangjing polysaccharide is the most abundant active ingredient in Polygonatum polysaccharides (PPs), which has a series of physiological active functions, such as anti-aging, anti-fatigue, neuroprotection, immune regulation, etc., and it is an important indicator of the quality of PPs.

At present, some research progress has been made on the pharmacological mechanism of polysaccharides of PPs to improve memory problems. Some studies have shown that polysaccharides of PPs improve memory function by enhancing synaptic plasticity in the CA1 region of the hippocampus, improving the efficiency of neurotransmitter transmission, and inhibiting oxidative damage and inflammatory response; in the study of chronic cerebral ischemia, it can reduce the expression of A β 1-42 protein in the brain, reduce the loss of nociceptors, and repair the damage of neuronal ultrastructure. In VD, it can reduce cerebral oxidative damage and inflammation by correcting haemorheological abnormalities, restoring cerebral blood flow and oxygen-carrying capacity. Together, these effects suggest that polysaccharides from PPs ameliorate memory impairment through multi-targeted mechanisms, including neuroprotection, anti-inflammatory and antioxidant effects, and cerebrovascular regulation. In view of its great potential value, there are still many issues that need to be explored, such as the lack of research on the structure and classification of polysaccharides of PPs and their practical applications; the pharmacological mechanism of PPs is mostly deduced from animal experiments and in vitro experiments, and there is a lack of data from clinical trials in human beings. In this paper, we review the effects and mechanisms of polysaccharides of PPs on different memory disorders in the elderly, in order to provide more references for in-depth research on the improvement of memory and the development of functional foods.

2. Memory problems in the elderly

As age increases, the brain of the elderly will gradually deteriorate and memory loss occurs. Elderly people suffering from memory disorders will have problems with cognitive functions, such as memory, computation, judgement, orientation, etc., which affects the quality of their daily life, and in severe cases, may develop into amnesia. Ten to fifteen percent of the elderly population suffering from memory disorders will be further converted to Alzheimer's disease, which in turn develops cognitive dysfunction, and may be accompanied by chronic cerebral ischaemia, VD, cerebral atherosclerosis, and other diseases [3].

2.1. Epidemiological features

Memory disorders are clinically characterised by full-blown dementia manifestations such as memory impairment, aphasia, dysarthria, and behavioural changes, and are affected by a variety of factors such as age and changes in stress, but the exact etiology is hitherto unknown, and for the time being, only pharmacological interventions are available without a complete cure.

The core symptoms usually begin with the gradual onset of memory impairment, particularly near memory loss. Patients present with difficulties in remembering recent events, recounting the same content or questions over and over again, confusing familiar names, and reduced vocabulary. As the disease progresses, near memory impairment worsens and eventually involves distant memory. Cognitive deficits are the hallmark of the disorder and are multifaceted: in language function, early vocabulary loss, decreased fluency, empty expressions and word-finding difficulties, and gradual loss of conversational ability, which may eventually progress to complete aphasia, or even to the production of meaningless sounds. Surveys have shown [4] that one-third of Alzheimer's disease worldwide can be attributed to seven major controllable factors, and that modification of these risk factors contributes to risk factor control for memory impairment disorders.

2.2. Alzheimer's disease

The main feature of AD is progressive cognitive and behavioural impairment, including neuronal loss, senile plaques, neurofibrillary tangles and neuroinflammation. Evidence suggests that inflammatory stress may be causative in the early stages of the disease [5], during which glial cell activation releases pro-inflammatory factors such as TNF- α , IL-1 β , and L-6, leading to neuroinflammation in AD. The pathological features of AD also include oxidative stress damage, and the Nrf-2/HO-1 signalling pathway is an important pathway to reduce oxidative damage in the body. Nrf-2 can regulate the endogenous anti-oxidative stress system, and its specific receptor is Kelch-like ECH-associated protein-1. In normal physiological state, Keap-1 forms a complex with Nrf-2, which inhibits the activity of Nrf-2; however, in pathological state, Keap-1 dissociates from N.2, and Nrf-2 enters into the nucleus, binds to antioxidant response elements, and activates its regulated antioxidant enzyme gene expression, which in turn enhances cellular oxidative stress resistance [6].

2.3. Pathological mechanisms of chronic cerebral ischemia

Chronic cerebral ischemia is a chronic, fluctuating cerebral dysfunction syndrome in which the brain is in a state of malfunction caused by structural lesions of the cerebral vasculature and/or anomalous hypoperfusion of the blood concentration and haemodynamics [7]. In chronic cerebral ischaemia, cerebral blood flow is in a state of prolonged hypoperfusion, which can directly lead to cerebral cortical or subcortical infarcts, cerebral white matter damage, and disruption of the vascular endothelium and the blood-brain barrier, resulting in impairment of memory function. Unlike acute stroke caused by steep reduction of local cerebral blood flow, chronic cerebral hypoperfusion is a persistent neurodegenerative change caused by slow and continuous reduction of cerebral blood flow, leading to gradual progression and aggravation of cognitive dysfunction, and even causing dementia.

2.4. Pathogenesis of vascular dementia symptoms

Vascular dementia (VD) refers to impaired brain function due to ischaemic or haemorrhagic stroke, which in turn affects neurocognitive function. Haemorrhage, ischaemic brain injury and insufficient cerebral perfusion caused by a variety of risk factors can lead to VD. Clinical syndromes manifesting as dysfunction of cognitive ability, daily living and work ability. Studies have shown that neuronal loss or damage in the cortex and hippocampus caused by neuronal cell death and neuroinflammatory abnormalities due to inadequate cerebral perfusion is a key factor in the pathological mechanism of

VD. Regulatory cell death is a genetically regulated form of cell death encompassing a large cascade of proteins and associated signalling pathways [8].

3. Assessment of the application value of flavonoid polysaccharides

3.1. Compositional analysis

It has been found that the monosaccharide molecules in polysaccharides of PPs include glucose, mannose, galacturonic acid rhamnose, etc [9]. However, the diverse species of PPs result in significant differences in the composition of monosaccharides and the content of polysaccharides, among which PPs has the highest content of polysaccharides. In recent years, 14 polysaccharides of flavonoids have been successfully isolated and characterised, and their structures have been determined to include fructans, glucomannans and galactans.

3.2. Improvement

The hippocampus is an important brain area for learning and memory, and in the hippocampus the synapses are the structural basis for the connection between neurons and the transmission of information, and changes in the plasticity of the synapses are closely related to learning and memory behaviours. Cheng Wei et al. showed that flavonoid polysaccharides can improve the plasticity of the synaptic interface structure in the CA1 region of the hippocampus, increase the effectiveness of neurotransmitter information transfer, and better realise the information transfer and functional connection between neurons and between neurons and effectors, so as to improve the memory function of AD patients. The mechanism may be related to the fact that flavonoid polysaccharides can reduce oxidative damage and inflammatory responses [10].

It has been pointed out that flavonoid polysaccharides can reduce the protein expression of A β 1-42 in prefrontal cortex and hippocampus. In an animal study, the results showed that polysaccharides from *Rhizoma Polygoni Multiflori* were administered to rats with chronic cerebral ischemia by gavage and compared with the control group, and the results showed that polysaccharides from *Rhizoma Polygoni Multiflori* were able to reduce the neuronal damage in rats with chronic cerebral ischemia and improve the memory of learning.

Tang Wei et al. showed that PPs could reduce the loss of nociceptors, alleviate the damage and destruction of hippocampal neurons, significantly raise the number of neuronal cells in the hippocampus of rats, and repair neuronal cells in the cerebral cortex and hippocampal CA1 area, thus improving the ability of learning and memory. And through the electron microscopic observation of the ultrastructure of the cerebral cortex (layers 3 and 4) and hippocampal CA1 area, it can be seen that the lesions in the cerebral cortex and hippocampal CA1 area of the flavonoid polysaccharide group are lighter, the swollen neurons are rare, the cell boundaries are clear, and the cytoplasm of neuronal cells is rich and the nuclei are clear [11]. The protective effect of flavonoid polysaccharides on chronic cerebral ischaemia symptoms can also be confirmed morphologically.

Studies have confirmed that blood rheological abnormalities occur before vascular dementia presents typical clinical symptoms. Lu Liandi's study found that after administration of flavonoid polysaccharides, model rats showed a reduction in abnormal haemorheological conditions, a decrease in blood lipids, a gradual recovery of cerebral blood flow, blood oxygen-carrying capacity, and a significant reduction in symptoms of cerebral oxidative damage and inflammation [12]. It suggests that flavonoid polysaccharides have a good therapeutic effect on vascular dementia model

rats, which can delay aging, improve blood composition and flow, and ensure the normal brain activity.

4. Application status

4.1. Clinical application

Huangjing has been used as a medicinal and food material since ancient times, and with the in-depth study of its efficacy mechanism, the research and development of proprietary Chinese medicines containing Huangjing has flourished. In clinical practice, Huangjing has been used to treat a variety of neurological diseases. By treating 175 patients with phytoneurological dysfunction with Ning Shen tincture (180 g of Huang Jing, 90 g each of *Lycium barbarum*, *Radix et rhizoma*, *Radix Paeoniae alba*, *Radix et Rhizoma Polygoni Multiflori*, 60 g each of *Astragalus membranaceus*, *Radix et Rhizoma Ginseng*, *Radix Angelicae Sinensis*, *Radix jujube seed* and 30 g each of *Radix et Rhizoma Zizoma Ziziphi*) [13] medication, the results found that 94.9% of the cases had a reduction or disappearance of self-awareness of their symptoms, improvement of their sleep, and a reduction or elimination of their excessive dreaming. Among them, in the whole formula of Ning Shen tincture, Huang Jing, as an important medicine for replenishing the deficiency, not only strengthens the qi replenishing efficacy of *Astragalus* and *Radix et Rhizoma Ginseng*, but also synergises with Yin nourishing medicines to balance yin and yang, and at the same time, provides the material basis for tranquillising drugs, which is the key ingredient for the multi-targeted improvement of insomnia and the related accompanying symptoms.

Based on this, Huangjing has great clinical prospects for improving memory diseases in the elderly.

4.2. Edible applications

The edible products of Huangjing are developed mainly as pastries, meat products and convenience products, all of which have the effect of strengthening the body. Because of the ancient method of the essence of 'nine steam and nine sun' process requires water steaming, modern technology will be wine steaming wine essence in the Pharmacopoeia, water, wine excipients used more frequently, and black beans, honey and other excipients in the concoction of the essence of yellow are applied. Among them, 'vinegar + honey' combination of auxiliary materials used in the process of drying and slicing the Huangjing has been put into the steriliser in the vinegar system to remove astringent taste, put into the aroma machine in the honey system to improve the aroma, and finally fried and dried to get the ready-to-eat Huangjing. 'Water + honey + ginger + corn' combination of excipients used in the process of corn grinding, ginger grinding powder mixed with honey to prepare the soaking solution, adding flavonoids slices soaked until the juice suction, water steaming of flavonoids drink tablets.

In recent years, Huangjing in the field of health food application of research has made greater progress. Such as Huangjing beef soup is to Huangjing, beef, walnut meat, ginger, etc. as the main ingredient of slow simmering made, it has the prevention and treatment of qi and blood deficiencies, enhance immunity, physical fitness and strengthening of the efficacy of the body; Huangjing potpourri is the use of rice, Huangjing of maitake as the main ingredient of a special baking process, with the complementary qi, moistening the dryness, stomach digestion and other effects.

5. Conclusion

The aging of the population is becoming increasingly severe in today's society, and anti-aging has become a global challenge, particularly brain aging that affects neural function. Research indicates that *Polygonatum polysperum* polysaccharides have a certain therapeutic effect on memory disorders such as Alzheimer's disease. This review summarises the role and mechanisms of *Polygonatum polysperum* polysaccharides in improving common memory disorders in the elderly, including Alzheimer's disease, chronic cerebral ischaemia, and vascular dementia. Key studies indicate that *Polygonatum polysperum* polysaccharides significantly improve memory function through mechanisms such as enhancing hippocampal synaptic plasticity, reducing neuronal damage, inhibiting oxidative stress and inflammatory responses, and regulating abnormal blood rheology and lipid levels. These multi-target effects provide a solid experimental basis for *Polygonatum polysaccharides* as an intervention for memory disorders in the elderly. However, current research limitations primarily lie in reliance on animal experiment data, lack of clinical validation, and unclear structure-activity relationships between polysaccharide structure and activity.

In recent years, with the continuous development of *Polygonatum* food-medicine dual-use products, their vast application potential has been demonstrated, and it is anticipated that more products to improve memory disorder symptoms will be developed in the future.

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