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# Effect of Ginsenosides on Prevention of Alzheimer's Disease

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**Abstract.** Alzheimer's disease (AD), as a neurodegenerative disease that conceals the progressive development of early disease, has a long onset time and complicated etiology. As the number of Alzheimer's patients increases year by year, it is a hot issue that looking for effective drug prevention and treatment. As the king of Chinese herbal medicine, ginseng contains a variety of pharmacologically active substances, especially ginsenosides can affect multiple metabolic pathways in the body, and its efficacy is relatively complicated. This article reviews the pathogenesis of AD and the preventive effects of five ginsenosides such as Rg1, Rb1, Rg2, Rg5 and Rh1 on AD, in order to provide a basis for the development of functional foods for preventing AD.

## 1. Introduction

Alzheimer's disease (AD), a dementia caused by chronic progressive central nervous system degeneration, which characterized by persistent advanced neurological function disorder, that is, the disorder of memory, thinking, analysis and judgment, emotional and others under the circumstance of no consciousness disorder. The cognitive decline, behavioral disorders, and gradually decline in living ability have a serious impact on the quality of life of patients [1].

Ginseng has an important position in Chinese herbal medicine. It is known as the "King of Herbs". Ginseng has a wide range of good medicinal and health care function in cardiovascular diseases, nervous system diseases, digestive diseases, blood hematopoietic immune system diseases, endocrine system diseases, anti-tumor, anti-aging, etc [2]. In recent years, Ginsenosides of the main active ingredient in ginseng has become a research hotspot for prevention and treatment of AD. This article reviews the pathogenesis of AD and the preventive effects of five ginsenosides such as Rg1, Rb1, Rg2, Rg5 and Rh1 on AD, in order to provide a basis for the development of functional foods for preventing AD.



## 2. Understanding on Pathogenesis of Alzheimer's disease.

### 2.1. Western medicine's understanding on pathogenesis of Alzheimer's disease

There are more than 30 possible factors and hypotheses about the onset of Alzheimer's disease, including the factors of head trauma, progressive failure of the immune system, weakening of the body's detoxification function, and viral infections, and the hypotheses of free radical damage theory, cholinergic neuron theory,  $\beta$  amyloid deposition theory, Tau protein and genetic theory [3]. Studies have shown that under pathological Alzheimer's disease conditions, excessive free radicals, such as reactive oxygen species (ROS) and reactive nitrogen species (RNS), lead to an imbalance between the oxidation mechanism and the antioxidant mechanism in the body. The internal environment tending to oxidize conditions, is called oxidative stress conditions [4]. Oxidative stress conditions are a negative effect caused by free radicals in the body and are associated with certain neurological diseases and aging. Like the above factors, oxidative stress conditions are studied by researchers as one of the influencing factors of Alzheimer's disease.

### 2.2. Chinese medicine's understanding on pathogenesis of Alzheimer's disease

In the field of traditional Chinese medicine, many scholars believe that the cause of Alzheimer's disease is that when people reach to a certain number of years of age, their body is weak qi, blood loss, sparse medulla in bone, nutrient supply insufficient in the brain, so that the brain is blocked by metabolic poisons [5], unconscious, confused thinking and finally inducing the dementia. Some scholars refer to this as the virtual standard, that is, physical weakness is its fundamental point. From the perspective of the elderly body itself, it is caused by disordered organs in the weak body.

## 3. Effects of ginsenosides on anti-Alzheimer's disease.

At present, there are more than 150 kinds of ginsenoside monomers isolated, of which more than 50 kinds of ginsenosides have been identified their structures. Due to the different structure of ginsenoside monomer, its target and biological effects in the body also differ. It has been found that various ginsenosides such as Rg1, Rg2, Rb1, Rg5, and Rh1 have pharmacological effects against AD and defensive neuroprotective.

### 3.1. Anti-AD effect of ginsenoside Rg1.

Ginsenoside Rg1 is a common ginsenoside monomer. Its main target organ is the central nervous system, which has the functions of rapidly relieving fatigue, improving learning and memory, delaying aging, and exciting the central nervous system. Xu [6] found Rg1 could improve  $\beta$ -amyloid-induced hippocampal neuronal damage through activating the NF- $\kappa$ B in neurons and might slow down the progression of AD in their study of the inhibitory effect of Rg1 on  $H_2O_2$ -induced apoptosis in hippocampal neurons of SD rats. The hippocampus is an important part of the learning and memory of mammals, and it is also the most frequently involved part of many neurological diseases.  $H_2O_2$  can easily enter cells, form hydroxyl radicals or oxygen free radicals and induce the increase of reactive oxygen species (ROS) production, which increase the pressure of oxidative scavenging system in the body, lead to oxidative stress damage, and directly participate in a variety of pathological processes of neurodegenerative diseases, such as AD. The ginsenoside monomer Rg1 can effectively increase the activity of antioxidant enzymes such as SOD in the mitochondria of the body, thereby inhibiting the oxidative stress damage caused by  $H_2O_2$  entering the cells and protecting the central nervous system.

### 3.2. Anti-AD effect of ginsenoside Rg2.

Ginsenoside Rg2 has functions of anti-shock, improving myocardial and brain ischemia and hypoxia, and improving the body's memory ability. The cognitive function of the body is strongly related to the central neurotransmitter. At the same time, the level of cholinergic can also affect the brain center [7]. The neurotransmitter content in the brain of patients with AD is significantly different from that of non-pathological patients. So, it can improve the cognitive function of patients by regulating the

content of central neurotransmitters [8]. Shang [9] found that in mice injected with ginsenoside Rg2, the memory ability was higher than that of mice without ginsenoside Rg2 during their experiment of ginsenoside Rg2 effects on memory ability of scopolamine-induced mouse. Its mechanism might be the inhibition of acetylcholinesterase (AChE) activity in hippocampus and forebrain cortex by Rg2, which enhances the acetylcholine transferase (ChAT) activity and increase the acetylcholine (ACh) content.

Liu's results [10] have shown that compared with the vascular dementia control group, ginsenoside Rg2 experimental group could significantly improve the neurological performance and memory ability of vascular dementia rats through the mechanism associated with anti-apoptosis when brain reperfusion induction of vascular dementia rats using ginsenoside Rg2 and observation of its neurological response, memory and apoptosis of caudate-shell nucleus neurons, Y-maze memory evaluation and detection of expression of apoptosis-related proteins such as heat shock protein 70 and P53 by immunocytochemistry.

### 3.3. *Anti-AD effect of ginsenoside Rg5.*

Ginsenoside Rg5 has a good effect in alleviating neuroinflammatory reactions and antidepressant activity by activating hippocampal brain-derived neurotrophic factor. Neuroinflammatory response plays an important role in the pathogenesis of AD [11]. It has been confirmed that ginsenoside Rg5 can attenuate streptozotocin-induced neuroinflammatory response and resist cognitive dysfunction caused thereby. Rg5 can reduce the activity of acetylcholinesterase, while the activity of acetylcholine transferase in the hippocampus is significantly increased, inducing the increase of the acetylcholine content and improving the excitability of the nervous system. Rg5 could attenuate the neuroinflammatory response by reducing the levels of the inflammatory cytokines' TNF- $\alpha$  and IL- $\beta$ . By detecting the role of Rg5 in forced swimming and tail suspension experiments after using Rg5 to treat hippocampal brain-derived neurotrophic factor signaling pathway, and determining the antidepressant effect of Rg5 using the tryptophan hydroxylase inhibitor, Xu [12] found that Rg5 has obvious experimental effects, which proves that Rg5 could resist depression by activating hippocampal neurotrophic factor.

Through the mouse avoidance test, Y maze and Morris water maze, Kim [13] found that Rg5 not only inhibits the activity of acetylcholinesterase, but also effectively protect memory defects by reversing the expression of hippocampal brain-derived neurotrophic factor and phosphorylation of scopolamine-reduced cAMP response element binding protein. They also tested the effect of ginsenoside Rh3 and found that its effect was better than Rg5.

### 3.4. *Anti-AD effect of ginsenoside Rb1.*

Ginsenoside Rb1 is the most abundant in American ginseng and has been extensively studied for its protective effect on the brain. Rb1 can improve memory by increasing the synthesis and release of acetylcholine, and has the function of enhancing the function of choline system. The pathological feature of Alzheimer's disease is mainly the accumulation of  $\beta$ -amyloid, and excessive  $\beta$ -amyloid accumulation in the brain could induce an increase in the activity of superoxide dismutase, while the content increase of lactic acid dehydrogenase and malondialdehyde products lead to neuronal pericytes shrinking and neurites lossing and damage occurred. Du et al. [14] conducted the researches of ginsenoside Rb1 on A $\beta$ -induced neuronal injury by observing primary culture neuronal morphology and biochemical analysis. They found that Rb1 attenuated the activity of superoxide dismutase, decreased the levels of lactate dehydrogenase and malondialdehyde and resisting the toxicity of  $\beta$ -amyloid-induced neurons. Therefore, ginsenoside Rb1 can protect neurons through antioxidant pathways, increase their survival rate, and effectively resist Alzheimer's disease.

### 3.5. *Anti-AD effect of ginsenoside Rh1.*

The content of ginsenoside Rh1 in ginseng plants is relatively rare, mostly converted from Rg1 and Re by intestinal metabolites. Rh1 has a certain protective effect on the nervous system, but due to its

lower content, the research is relatively rare. Rh1 can protect the neurons mainly by antagonizing the release of excitatory neurotransmitters caused by cortical neurohypoxia injury, reducing the release of excitatory neurotransmitters, and relieving excitatory neurotoxicity. Yang [15] reported the protective effect of ginsenoside Rh1 on mouse cortical neurons. Hou found that the mice's learning and memory ability had been significantly improved through mice passive avoidance test feeding the Rh1 for a long time. The main mechanism is to improve the survival rate of cells in the mouse dentate gyrus, regulate the activity of hippocampal neurotrophic factor. This finding provides an important basis for treatment of memory loss and neurodegenerative diseases.

#### 4. Summary

There are many pathological causes of AD, including decreased neurotransmitter levels, brain cell damage in the hippocampus, gliosis, acute or chronic systemic infections of pro-inflammatory signaling transduction, family inheritance, and neurotoxic oxidative stress. AD may also be caused by a combination of factors. There is still a long way of research on the pathological mechanisms of AD and its drugs and preventive treatments. As the king of Chinese herbal medicine, ginsenosides has become a new star for many scholars to study the mechanism of anti-AD due to its multiple targets, non-drug resistance and non-toxicity. In addition to the above five ginseng saponins, ginsenoside Rg3, Rh2, Rh3, Re, etc. also have certain pharmacological activities against AD. At present, the separation of ginsenoside monomers has not been fully realized. It is expected that ginsenoside monomers may be found more pharmacological activities, and to help successfully the prevention of AD in middle-aged and elderly patients and the treatment of pathological patients.

#### References

- [1] Miao Yang, Wang Li. Discussion on the pathogenesis of Alzheimer's disease and its clinical effect on the treatment of traditional Chinese medicine and western medicine, *J. China continuing medical education*, 2016, 8 (02): 193-194.
- [2] Liu Yueping, Cui Jintao. The effect of ginseng on cardiovascular system, *J. Hubei Journal of Traditional Chinese Medicine*, 2006, 28 (7): 56-56.
- [3] Liu Ju. Research Progress in the Pathogenesis of Alzheimer's Disease, *J. Journal of Minnan Medical College*, 2018, 31 (04): 261-263.
- [4] Wang Yongzhen, Xiao Xingjun. Role of Oxidative Stress in the Pathogenesis of Peripheral Neuropathy, *J. Stroke and Nervous Diseases*, 2016, 23(1).
- [5] Nguyen Huu Tung, Takuhiro Uto, Osamu Morinaga, et al. Pharmacological Effects of Ginseng on Liver Functions and Diseases: A Minireview, *J. Evidence-Based Complementary and Alternative Medicine*, 2012.
- [6] Xu Wei, Fu Lina, Zhai Yongjian. Effects of ginsenoside Rg1 on H<sub>2</sub>O<sub>2</sub> induced rat hippocampal neuronal injury and its mechanism, *J. Strait Pharmaceutical Journal*, 2019, 31 (01): 19-22.
- [7] Peng Wenjie, Wu Dahua. Research progress of traditional Chinese medicine on the central cholinergic system of Alzheimer's disease, *J. Chinese Medicine Herald*, 2015, 21 (07): 89-91.
- [8] Zhuang Ying, Shi Bo, Tian Wei, Cui Li. Effect of ginsenoside Rg2 on learning and memory ability and senile plaque formation in Alzheimer's disease model rats, *J. Chinese Journal of Gerontology*, 2010, 30 (02): 202-204.
- [9] Shang Chongzhi, Zhao Mingliang. Effects of ginsenoside Rg2 on learning and memory in mice induced by scopolamine in Alzheimer's disease, *J. Chinese Journal of Practical Diagnosis and Therapy*, 2017, 31(05): 444-447.
- [10] Liu Aizhen. Study on neuronal apoptosis in rats with vascular dementia after ischemia-reperfusion and the influence of ginsenoside Rg2. *Proceedings of the 2003 Academic Annual Conference. China Society of Surveying and Mapping*, 2003: 2.
- [11] Shenghui Chu, Junfei Gu, Liang Feng, et al. Ginsenoside Rg5 improves cognitive dysfunction and beta-amyloid deposition in STZ-induced memory impaired rats via attenuating neuroinflammatory responses, *J. International Immunopharmacology*, 2014, 19 (2): 317-326.

- [12] Xu D, Wang C, Zhao W, et al. Antidepressant-like Effects of Ginsenoside Rg5 in Mice: Involvement of Hippocampus BDNF Signaling Pathway, *J. Neuroscience Letters*, 2017, 645:97-105.
- [13] Kim E J, Jung I H, Van Le T K, et al. Ginsenosides Rg5 and Rh3 protect scopolamine-induced memory deficits in mice, *J. Journal of Ethnopharmacology*, 2013, 146 (1): 294-299.
- [14] Du Xiaoxiang, Chen Bicheng. Research Progress of Three Kinds of Ginsenoside Monomers Against Alzheimer's Disease, *J. West China Journal of Pharmacy*, 2018, 33 (03): 323-327.
- [15] Yang Kai, Wu Xiaomei. Protective Effects of Ginsenoside Rg2, Re and Rh1 on Hypoxia in Mouse Cortical Neurons, *J. Journal of Nantong Medical College*, 2002 (02): 134-135