

# Research progress on treatments for Alzheimer's disease

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**Abstract.** Alzheimer's disease (AD) is an irreversible neurological degenerative disease characterized by progressive cognitive impairment, and its pathogenesis remains unclear. Its main pathological features include neurofibrillary tangles formed by hyperphosphorylated tau protein and amyloid beta ( $A\beta$ ) plaque deposition. As the disease progresses, the patient's self-care ability will become worse and worse. In the later stages, the patient will have to rely on others for daily life, which places a great burden on the patient, family, and society. Currently, there are a limited number of AD treatment drugs and their efficacy is limited, and they cannot effectively improve the condition of AD. This article reviews different methods for treating AD and provides a reference for the treatment of AD. At present, the treatment of senile dementia is mainly divided into two categories. The current treatment methods include Lencamab, bee therapy related drugs, NSCs transplantation therapy, Panax notoginseng saponins, and hyperbaric oxygen therapy. It is necessary to explore new treatment methods and drugs to improve treatment effectiveness and widely apply dementia in the elderly.

**Keywords:** Alzheimer's Disease, Beta-amyloid, Mechanism of Action, Therapeutic Effect, Function

## 1. Introduction

Alzheimer's disease is a common neurodegenerative disease that seriously affects cognitive function and quality of life in patients. The treatment methods for Alzheimer's disease are still limited, and currently, new treatment methods such as lencamizumab, bee therapy related drugs, NSCs transplantation, and total saponins of Panax notoginseng have attracted much attention.

However, in clinical applications, there are still some issues that need to be addressed with these treatment methods. Therefore, the purpose of this literature review is to explore the efficacy and safety of these new therapies in the treatment of Alzheimer's disease, as well as their impact on cognitive function and quality of life in patients. By studying these therapies, better treatment outcomes and improved quality of life for patients can be achieved, while providing new ideas and methods for the treatment of Alzheimer's disease. Therefore, research on these drugs is of great theoretical significance and practical value.

## 2. Treatment of lencanezumab in early Alzheimer's disease

### 2.1. Basic Introduction

Lencanezumab, as a new drug for the early diagnosis of Alzheimer's disease (AD), mainly targets mild cognitive impairment and mild dementia. Its mechanism of action is to target soluble  $A\beta$  and also has

an inhibitory effect on insoluble fibrils [1, 2]. The pathological process of A $\beta$  is closely related to the inflammatory response. Activated astrocytes can efficiently phagocytose damaged cells, damaged synapses, and proteins, and play a key role in maintaining brain homeostasis [3]. During the development of AD, astrocytes excessively uptake A $\beta$ 42, causing it to accumulate intracellularly, causing damage to endosomes and lysosomes, and releasing toxic extracellular vesicles, damaging neurons [3]. Lencanezumab is an A $\beta$ -specific antibody that can penetrate the blood-brain barrier in vivo, bind to A $\beta$ 42, promote its removal of pathological A $\beta$ , reduce A $\beta$  deposition, and thus protect neurons from A $\beta$  damage [3].

### *2.2. Clinical trials and effects*

Currently, lencanezumab has been evaluated in three phases of clinical trials. The results found that lencanezumab at 10 mg/kg every 2 weeks significantly slowed the decline in cognitive function at 18 months compared with placebo and showed benefits at 6 months that lasted until 18 months. The degree of cognitive function decline was reduced by 25% [4]. In addition, trials have shown that lencanezumab is effective, safe, and tolerable in the treatment of early-stage AD. Patients with early-stage AD have significant improvements in cognition, function, and behavior.

However, due to certain limitations in the convenience and popularity of intravenous injection treatment, although lencanezumab has been approved for the treatment of early AD, its limitations and adverse reactions still need to be overcome before it can be widely used. Application [1]. Clinical trials are still ongoing to fully evaluate its efficacy and safety, especially in late-stage Alzheimer's disease.

## **3. Apitherapy related drugs to treat Alzheimer's disease**

### *3.1. Basic introduction and mechanism of action*

Apitherapy is a method of using bee products as medicine to treat diseases, including honey, bee pollen, royal jelly, propolis, bee venom and other bee natural products [5], which are rich in active substances that are considered to have the potential to treat neurodegenerative diseases [5-7]. In addition, wasp venom (WV) contains a variety of neuroactive molecules, which may provide new ideas for studying the physiological functions of the nervous system and the pathological changes of related diseases [8].

The mechanism of action of apitherapy-related drugs on Alzheimer's disease is mainly reflected in the following aspects: First, the active ingredients in apitherapy drugs may help inhibit the accumulation of beta amyloid (A $\beta$ ) in the brains of patients with Alzheimer's disease. Their toxicity is reduced; secondly, these drugs may combat neurodegeneration by regulating the physiological functions of the nervous system [9]. In particular, bee venom, which contains a variety of neuroactive molecules, may provide a new research idea for studying neurological functions and related diseases [8].

### *3.2. Treatment effect*

Research shows that apitherapy drugs such as honey, royal jelly, propolis, and bee venom are rich in active ingredients and have the potential to treat neurodegenerative diseases. In particular, honey, as a common food, has the advantages of being easy to obtain, economical and cheaper than existing clinical drugs for Alzheimer's disease [9].

However, although preliminary results show the therapeutic potential of apitherapy-related drugs, there are still some issues that require further study, including the optimal clinical concentration and pharmacokinetics of the active ingredients, as well as the exact inhibitory effect on A $\beta$  aggregation, and the improvement of symptoms of toxicity. and binding site mechanisms. Therefore, as a new method for the treatment of Alzheimer's disease, apitherapy-related drugs require more scientific experiments and clinical verification to determine their safety and effectiveness [9].

## 4. Neural stem cell transplantation to treat Alzheimer's disease

### 4.1. Mechanism of action

The mechanism and therapeutic effect of neural stem cell transplantation therapy for Alzheimer's disease (AD) have attracted much attention in recent research. Studies have pointed out that the intervention effect of transplanted neural stem cells (NSCs) on AD is multifaceted. First, NSCs can successfully differentiate into damaged neurons with functional neurons and establish synaptic connections with surrounding remaining neurons, which is expected to play a role in disease treatment. Secondly, transplanted human neural stem cells (HNSCs) can effectively reduce the phosphorylation level of Tau protein in the lateral ventricles of mice, although the mechanism is unclear [10].

Research also shows that as the disease progresses, transplanted NSCs release neurotrophic factors, which are expected to increase synaptic density and reverse cognitive impairment. These neurotrophic factors may prevent additional cognitive decline, and their impact on hippocampal nerves also deserves further study [11]. Although AD animal models are not yet sufficient to accurately simulate human AD, intervention from the preclinical stage may help inhibit the progression of AD [10].

### 4.2. Treatment effect

NSCs transplantation therapy for AD, which is considered to have great potential, may play a role in multiple fields. First, it may have a protective effect on microvessels and reduce the deposition of  $\beta$ -amyloid and TAU proteins. Secondly, NSCs transplantation may also relieve inflammatory reactions in the brain, especially chronic inflammatory reactions [10], which are caused by aging. In addition, studies have also pointed out that NSCs transplantation may have anti-inflammatory effects [12,10] and can help prevent the progression of AD.

In general, the potential therapeutic effects of NSCs transplantation include protecting blood vessels, reducing abnormal protein deposition, alleviating inflammatory reactions, and anti-inflammatory effects. However, further research and development are still essential, especially more complete studies on animal or cell models [10], because clinical trials have not yet produced positive results.

## 5. Panax notoginseng total saponins treat Alzheimer's disease

### 5.1. Basic introduction and mechanism of action

Panax Notoginseng Saponins (PNS) is the main active ingredient of Panax notoginseng, a plant of the Araliaceae family, and is extracted from the dried roots of Panax notoginseng. Commonly used clinically for cardiovascular and cerebrovascular diseases. Its main active ingredients include ginsenosides Rb1, Rg1, Rd, Re, notoginseng saponin R1, etc., these ingredients account for more than 90% of the total saponins. These components endow Panax notoginseng total saponins with various biological functions such as immunomodulation, anti-tumor and so on [13].

PNS may exert pharmacological effects through its antioxidant function, and inhibiting the MTOR signaling pathway is one of its core targets. In PC12 cells, PNS improved the autophagy of AD-like nerve damage induced by A $\beta$ 25–35 by inhibiting the activation of the MTOR pathway [14]. PNS has also been found to improve brain perfusion blood flow, reduce inflammation levels, and enhance patients' cognitive function in AD patients, showing good clinical application value [15].

### 5.2. Therapeutic effect

In the treatment of Alzheimer's disease, Panax notoginseng saponins have shown certain effects. Studies have shown that Panax notoginseng saponins play a key role in improving cerebral blood perfusion and reducing inflammation in patients with Alzheimer's disease. By regulating blood flow and improving brain perfusion, Panax notoginseng saponins help relieve symptoms of neurological disorders in patients with Alzheimer's disease [15].

In the treatment of Alzheimer's disease, the anti-inflammatory effect of Panax notoginseng saponins also plays a certain positive role. Inflammation plays a crucial role in the pathogenesis of Alzheimer's

disease, and the anti-inflammatory effect of *Panax notoginseng* saponins can help patients reduce inflammation levels, thereby slowing down the progression of the disease [15].

In addition, in the treatment of Alzheimer's disease, the improvement of cognitive function by *Panax notoginseng* saponins is also one of its key contributions. Studies have found that *notoginseng* saponins can improve patients' cognitive function to a certain extent and help improve patients' quality of life [13,15].

## **6. Hyperbaric oxygen therapy for Alzheimer's disease**

### *6.1. Mechanism of action*

Multiple mechanisms may be involved in the improvement of learning and memory, spatial exploration, and cognitive function in Alzheimer's disease (AD) rats treated with hyperbaric oxygen therapy. Firstly, hyperbaric oxygen therapy may combat cerebrovascular and neurological diseases, by increasing cerebral blood oxygen content, enhancing neuronal metabolism, and improving cerebral blood flow [16]. Secondly, hyperbaric oxygen therapy may promote the survival and functional maintenance of neurons, protecting them from damage by alleviating inflammatory reactions and oxidative stress [17]. In addition, hyperbaric oxygen therapy may also enhance nerve resistance against neurodegenerative diseases by promoting the formation of synapses in the nerves. Research has shown that the recovery of hippocampal function in rats with hyperbaric oxygen therapy may be related to the increased insulin sensitivity that further affects normal neuronal function [18,19].

### *6.2. Clinical trials and treatment effects*

In the experiment, hyperbaric oxygen therapy showed positive effects on learning, memory, spatial ability, cognitive function, and other aspects of Alzheimer's disease (AD) rats. The study used animal experiments by placing rats in the hyperbaric oxygen treatment group, using 100% pure oxygen 2ATA daily for 1 hour each time, and slowly pressurizing and decompressing. The experimental results showed that the rats in the AD model group showed significant improvement in spatial exploration experiments after hyperbaric oxygen treatment. The number of times the treatment group's platform has significantly increased, the number of times it passes through the target quadrant has significantly increased, the time it stays in the target quadrant has significantly increased, and the time it takes to reach the platform for the first time has significantly decreased [18].

In addition, hyperbaric oxygen therapy significantly restored insulin sensitivity, hippocampal function, and cognitive ability in aging rats, indicating that this treatment method has the potential for improvement in neurological and neurodegenerative diseases with mild cognitive impairment, and even cognitive function improvement, brain metabolism, etc. [19]. It is worth noting that compared with the AD model group, the treatment group showed a significant decrease in avoidance latency in the localization navigation experiment, showing a significant difference.

The potential therapeutic effect of hyperbaric oxygen therapy on senile dementia is demonstrated by improving the learning, memory, exploration ability, and cognitive function of AD rats. This study provides experimental evidence for the application of hyperbaric oxygen therapy in neurological diseases, providing useful inspiration for future in-depth research and application.

## **7. Current treatment methods and future trends**

At present, the treatment of senile dementia is mainly divided into two categories. The current treatment methods include Lencamab, bee therapy related drugs, NSCs transplantation therapy, *Panax notoginseng* saponins, and hyperbaric oxygen therapy. These treatment methods mainly manifest as the protection of the nervous system against inflammation of cognitive function, and some therapeutic effects and potential have been demonstrated in clinical trials. However, these benefits still need further in-depth investigation. The future research direction should include discovering more therapeutic drugs, not limited to Western medicine or traditional Chinese medicine, but should combine Chinese and Western medicine to achieve more significant therapeutic effects. Further research will be conducted on these

treatment methods, particularly in the validation of animal models and clinical trials. At the same time, it is necessary to explore new treatment methods and drugs to improve treatment effectiveness and widely apply dementia in the elderly. The comprehensive use of multiple treatment methods may provide more effective treatment options for people with Alzheimer's disease.

## 8. Conclusion

This article reviews the research progress of treatment methods for Alzheimer's disease, mainly including lencamab, bee therapy related drugs, neural stem cell transplantation, total saponins of *Panax notoginseng* and hyperbaric oxygen therapy. Lunkanaizumab targets A through targeted action  $\beta$  Solubility of A alleviates A  $\beta$  Deposition of A protects neurons from A  $\beta$  Damage caused by. The active substances in bee therapy related drugs and the neuroactive molecules in bee venom, which are considered to have the potential to treat neurodegenerative diseases, also provide new ideas for studying neurological diseases. The mechanism of neural stem cell transplantation for Alzheimer's disease includes differentiation of competent neurons, repair of damaged neurons, and a decrease in Tau protein phosphorylation levels. As the main active ingredient of *Panax notoginseng*, its total saponins have various biological functions, such as immune regulation and anti-tumor effects. The potential therapeutic effect of hyperbaric oxygen therapy on senile dementia is demonstrated by improving the learning, memory, exploration ability, and cognitive function of AD rats.

These studies provide more treatment options for Alzheimer's patients and offer new ideas and approaches for the treatment of this disease. Each treatment method has its advantages and disadvantages. With the development of science and technology, more effective and convenient treatment methods will inevitably emerge.

## References

- [1] Jin Panpan, Liu Yang, Qiu Bo, et al. Research progress of lencamab in treating early Alzheimer's disease. *Chinese Journal of Clinical Pharmacology and Therapeutics*, 2024,29 (02): 207-2014.
- [2] Dhadda S, Kanekiyo M, Li D, et al. Consistency of efficacy results across various clinical measures and statistical methods in the lecanemab phase 2 trial of early Alzheimer's disease. *Alzheimers Res Ther*, 2022, 14(1): 182.
- [3] Söllvander S, Nikitidou E, Gallasch L, et al. The A $\beta$  protofibril selective antibody mAb158 prevents accumulation of A $\beta$  in astrocytes and rescues neurons from A $\beta$  - induced cell death. *J Neuroinflammation*, 2018, 15(1): 98.
- [4] van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*, 2023, 388 (1): 9-21.
- [5] Fratellone Patrick M, Tsimis Flora, Fratellone Gregory. Apitherapy Products for Medicinal Use. *J Altern Complement Med*, 2016, 22(12): 1020-1022.
- [6] ZHANG Shuai, LIU Yi, YE Yang, et al. Bee venom therapy: Potential mechanisms and therapeutic applications. *Toxicon*, 2018, 148: 64-73.
- [7] Pasupuleti Visweswara Rao, Sammugam Lakshmi, Ramesh Nagesvari, et al. Honey, Propolis, and Royal Jelly: A Comprehensive Review of Their Biological Actions and Health Benefits. *Oxid Med Cell Longev*, 2017, 2017: 1-21.
- [8] un Hyun Seok, Oh Jisun, Lim Ji Sun, et al. Anti-Inflammatory Effect of Wasp Venom in BV-2 Microglial Cells in Comparison with Bee Venom. *Insects*, 2021, 12(4): 297-306.
- [9] Liu Shu, Sun Yuefeng, Li Shuning, et al. Research progress on the mechanism of action of bee therapy related drugs in the treatment of Alzheimer's disease. *Pharmacology and Clinical of Traditional Chinese Medicine*: 1-16 [2024-02-01].
- [10] Chen Xiaokun, Bao Xinjie, Gao Jun, et al. Research progress on the mechanism of neural stem cell transplantation for the treatment of Alzheimer's disease. *Basic Medicine and Clinical*, 2023,43 (07): 1148-1151.

- [11] Moreno-Jimenez EP, Flor-garcia M, Terreros-Roncal J, et al. Adult hippocampal neurogenesis is abundant in neurologically healthy subjects and drops sharply in patients with Alzheimer's disease. *Nat Med*, 2019, 25: 554-560.
- [12] Boese AC, Hamblin MH, Lee JP. Neural stem cell therapy for neurovascular injury in Alzheimer's disease. *Exp Neurol*, 2020, 324: 113112. doi: 10.1016/j.expneurol. 2019. 113112.
- [13] Zhang Yang, Yang Xiu, Pu Zhoufang, et al. Research progress of total saponins of *Panax notoginseng* in the treatment of Alzheimer's disease. *Chinese Pharmacological Review*, 2023,40 (02): 159-162.
- [14] Jiang YX, Li SL, Xie XQ, et al. Exploring the Mechanism of *Panax notoginseng* Saponins against Alzheimer's Disease by Network Pharmacology and Experimental Validation. *Evid Based Complement Alternat Med*, 2021: 5730812.
- [15] Li Aidong, Chen Jianliang, Xia Jun, et al. A multicenter randomized controlled clinical study of total saponins of *Panax notoginseng* in the treatment of Alzheimer's disease. *Geriatrics and Health*, 2019, 25 (4): 501-505.
- [16] Kamat SM, Mendelsohn AR, Larrick JW. Rejuvenation Through Oxygen, More or Loss. *Rejuvenation Res*, 2021, 24 (2): 158-163.
- [17] Karabiyik C, Frake RA, Park SJ, et al. Autophagy in ageing and ageing-related neurodegenerative disease. *Ageing Neur Dis* 2021, 1:2.
- [18] Yang Hemin, Wang Qiang, Zhang Jinhao et al. The effect of hyperbaric oxygen therapy on cognitive function in Alzheimer's disease rats. *Journal of Qiqihar Medical College*, 2023,44 (19): 1808-1813.
- [19] Soria Lopez JA, Gonzalez HM, Leger GC. Alzheimer's disease. *Handb Clin Neurol*, 2019, 167: 231-255.