Research Advances in Traditional Chinese Medicine for the Treatment of Alzheimer's Disease

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Abstract: *Alzheimer's disease (AD) is a major neurodegenerative disease that plagues the elderly population, clinically characterized by progressive cognitive decline, neuropsychiatric symptoms, and loss of social function. Epidemiological data from 2020 shows that the number of AD patients aged 60 and above in China has reached approximately 9.83 million. The accelerating trend of population aging has made the disease burden of AD increasingly heavy, posing a public health challenge that cannot be ignored. The etiology of AD remains unclear, and its pathological mechanisms are complex. Characteristic changes include senile plaques formed by extracellular amyloid-β (Aβ) deposition, neurofibrillary tangles mediated by hyperphosphorylated Tau protein, and subsequent synaptic damage and neuronal loss. Current mainstream treatment regimens primarily consist of acetylcholinesterase inhibitors and NMDA receptor antagonists. While these can temporarily alleviate some symptoms, they are unable to halt or reverse the disease process, and are limited by their single-target mechanism of action and the relatively high incidence of adverse effects associated with long-term use. Within the theoretical system of Traditional Chinese Medicine (TCM), AD is classified under categories such as "dementia", "stupidity", and "forgetfulness". Based on the traditional understanding that "the kidney stores essence, produces marrow, and fills the brain," TCM has accumulated rich experience through long-term clinical practice, gradually forming treatment strategies characterized by a holistic view and syndrome differentiation, involving multi-pathway interventions. A substantial body of research demonstrates that Chinese herbal medicines and their active components exhibit unique advantages of multi-target, systemic regulation in improving cognitive function and delaying disease progression in AD patients, with a good safety profile. This article focuses on three levels—TCM compound formulas, single Chinese herbs, and active components—to systematically review recent relevant experimental research, deeply explore their potential mechanisms of action, and provide valuable ideas and references for the TCM-based prevention and treatment of AD and the development of new drugs.*

Keywords: Alzheimer's Disease, Traditional Chinese Medicine, Mechanism of Action, Ferroptosis, Gut-Brain Axis.

1. Introduction

Alzheimer's disease as a representative degenerative disease of the central nervous system is typified by its characteristic neuropathological markers: Aβ plaques and Tau neurofibrillary tangles. The irreversible global aging process has led to a continuous rise in the prevalence of AD, posing severe challenges for patients' families and societal healthcare systems [1]. Currently, modern medicine lacks a complete consensus on the pathogenesis of AD, and there is a clinical shortage of ideal drugs capable of reversing or effectively stopping the progression of the disease [2]. Existing treatment modalities primarily focus on symptom improvement, with outcomes that are often unsatisfactory.

In contrast, Traditional Chinese Medicine demonstrates unique theoretical and practical value in the prevention and treatment of AD. Its diagnostic and therapeutic approach of "holistic examination and seeking causes through syndrome differentiation" aligns well with the complex pathological features of AD, which involve multiple systems and pathways. In recent years, with advancements in research methods, the mechanisms by which the multi-component interventions of TCM affect AD have been continuously revealed, showing significant progress in areas ranging from regulating Aβ metabolism and inhibiting Tau protein phosphorylation to modulating neuroinflammation, oxidative stress, and even emerging fields like the "gut-brain axis" [3]. This article aims to systematically review the current state of research on TCM treatment for AD and provide an outlook on the challenges and opportunities for its future development.

2. Understanding the Etiology and Pathogenesis of AD

2.1 Etiology and Pathogenesis from the TCM Perspective

Although the name "Alzheimer's disease" does not appear in ancient TCM texts, records of its clinical manifestations can be classified under categories such as "dementia" and "forgetfulness". TCM theory emphasizes that "the brain is the mansion of the original spirit," and its normal functioning depends on nourishment by kidney essence and Qi-Blood. The disease location is in the brain, and it is particularly closely related to dysfunction of the kidney, spleen, and liver [4].

The "Lingshu · Hai Lun" (Spiritual Pivot · Chapter on the Seas) proposes that "the brain is the sea of marrow," and "the kidney governs the bones and generates marrow." Therefore, the abundance or deficiency of kidney essence directly determines the fullness or emptiness of the sea of marrow. Aging and physical decline or chronic illness consuming the body lead to deficiency of kidney essence. When the generation of the sea of marrow is insufficient, the brain loses its nourishment, resulting in impaired mental function, manifesting as memory loss, slowed thinking, and other symptoms. This constitutes the "root deficiency" of the disease.

On the other hand, spleen deficiency leads to failure in its transportation and transformation functions, causing internal dampness that accumulates into phlegm. This phlegm-turbidity can cloud the clear orifices of the brain.

Liver dysfunction in maintaining free flow of Qi leads to Qi stagnation, which in turn causes poor blood flow and blood stasis, obstructing the brain collaterals. The combination of phlegm and stasis disturbs the spirit, constituting the "superficial excess" of the disease.

In summary, the TCM pathogenesis of AD can be characterized as "root deficiency and superficial excess." The deficiency primarily attributes to kidney essence deficiency and insufficiency of Qi and Blood; the excess attributes to obstruction by phlegm-turbidity and blood stasis [5]. This complex pathological characteristic determines that treatment must take an integrated approach, addressing both deficiency and excess.

2.2 Exploration of Pathological Mechanisms in Modern Medicine

Modern medicine's understanding of AD pathogenesis is an evolving process. For a long time, the "Aβ cascade hypothesis" has been dominant, suggesting that the abnormal production and impaired clearance of Aβ is the initiating link in AD pathology, with its oligomeric forms possessing significant neurotoxicity [6]. The "Tau protein hypothesis" focuses on the hyperphosphorylation of Tau protein leading to the disintegration of the microtubule system and the formation of neurofibrillary tangles, directly affecting internal neuronal transport and function [7].

Beyond these classical pathways, research has confirmed that oxidative stress damage, chronic neuroinflammation, mitochondrial dysfunction, and imbalances in neurotransmitter systems all play important roles in the development and progression of AD [8]. Particularly noteworthy is the rise of the "gut-brain axis" theory, which provides a new perspective for understanding AD. The gut microbiota and its metabolites can engage in bidirectional communication with the central nervous system through immune, neuroendocrine, and vagus nerve pathways. Dysbiosis is thought to potentially participate in the pathological process of AD by exacerbating neuroinflammation, influencing Aβ metabolism, and other ways [9]. The multifaceted pathogenesis of AD suggests that any single-target intervention strategy may have limitations, and a comprehensive treatment approach targeting multiple systems and pathways might be more rational.

3. Analysis of the Mechanisms of TCM Intervention in AD

3.1 Regulating Aβ Metabolic Homeostasis

Aβ metabolic imbalance is a core pathological link in AD. Many Chinese herbs and their active components can exert therapeutic effects by regulating the production, aggregation, and clearance of Aβ. For example, berberine, a primary alkaloid component derived from *Coptis chinensis*, has been confirmed to effectively inhibit the activity of β-secretase (BACE1), thereby reducing the generation of Aβ [10]. Tanshinone IIA from *Salvia miltiorrhiza* demonstrates the ability to promote the degradation and clearance of Aβ, reducing its neurotoxicity [11]. At the compound formula level, formulas such as Bushen Yizhi Formula can upregulate the expression of Low-Density Lipoprotein Receptor-Related Protein 1 (LRP1), enhancing the transport and clearance of Aβ across the blood-brain barrier, thereby improving cognitive function in AD model animals [12]. These findings suggest that TCM can intervene in Aβ metabolism through multiple pathways, mitigating Aβ-related neurotoxicity.

3.2 Inhibiting Abnormal Hyperphosphorylation of Tau Protein

Abnormal hyperphosphorylation of Tau protein is fundamental to the formation of neurofibrillary tangles in AD. Research has found that various TCM components can regulate the phosphorylation level of Tau protein. For instance, quercetin found in *Ginkgo biloba* extract can inhibit the activity of glycogen synthase kinase-3β (GSK-3β), reducing the degree of Tau protein phosphorylation [13]. Ginsenoside Rg1, on the other hand, can activate protein phosphatase 2A (PP2A), promoting the dephosphorylation process of Tau protein [14]. These effects help maintain the stability of the neuronal cytoskeleton and improve axonal transport function, thereby exerting neuroprotective effects.

3.3 Alleviating Oxidative Stress Damage

Oxidative stress plays an important role in the pathogenesis of AD. Excessive reactive oxygen species (ROS) can lead to nerve cell damage and apoptosis. Chinese herbs are rich in various antioxidant components, such as flavonoids, phenolic acids, and polysaccharides, which can effectively scavenge ROS and alleviate oxidative stress damage. Specifically, *Lycium barbarum* polysaccharide can significantly enhance the activity of endogenous antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), and reduce the content of the lipid peroxidation product malondialdehyde (MDA) [15]. Ferulic acid from *Angelica sinensis* has also been proven to effectively counteract Aβ-induced oxidative stress and reduce ROS production [16]. These antioxidant effects help maintain the redox balance in nerve cells and protect neurons from oxidative damage.

3.4 Regulating Neuroinflammatory Responses

Neuroinflammation is a significant pathological feature of AD. Persistent inflammatory responses can exacerbate neuronal damage and cognitive impairment. TCM can exert anti-inflammatory effects by inhibiting the activation of inflammatory cells and reducing the release of inflammatory mediators. For example, curcumin, the main active component in turmeric, can significantly inhibit the overactivation of microglia and reduce the production of pro-inflammatory factors such as tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) [17]. Baicalin from *Scutellaria baicalensis* can inhibit the expression of inflammatory mediators by modulating the nuclear factor-kappa B (NF-κB) signaling pathway, exerting neuroprotective effects [18]. These anti-inflammatory effects are significant for controlling AD-related neuroinflammation.

3.5 Balancing Neurotransmitter Systems

AD patients often exhibit dysfunction in multiple

neurotransmitter systems, such as decreased acetylcholine (ACh) levels and increased glutamate excitotoxicity. TCM components can improve neural transmission function by regulating the synthesis, release, and metabolism of neurotransmitters. β-Asarone, a component in the volatile oil of *Acorus gramineus*, can inhibit the activity of acetylcholinesterase (AChE), thereby increasing the level of ACh in the brain [19]. Gastrodin can modulate the glutamatergic neurotransmitter system, reducing the excitotoxic damage caused by glutamate [20]. These regulatory effects help restore the balance of the neurotransmitter system and promote the improvement of cognitive function.

3.6 Promoting Neuroregeneration and Synaptic Plasticity

Impaired neuroregeneration and loss of synaptic plasticity are important structural bases for cognitive deficits in AD. Research indicates that some active components of TCM can promote the proliferation and differentiation of neural stem cells and enhance synaptic plasticity. For instance, Ginsenoside Rg1 can promote the differentiation of neural stem cells into neurons and increase the expression of synaptophysin, thereby enhancing synaptic plasticity [21]. Icariin has been found to promote hippocampal neurogenesis and improve synaptic function [22]. These effects provide a cytological basis for the improvement of cognitive function in AD by TCM.

3.7 Modulating Gut-Brain Axis Function

In recent years, the role of the gut-brain axis in the pathogenesis of AD has gained increasing attention. An imbalance in the gut microbiota is closely related to the occurrence and development of AD. TCM can exert anti-AD effects by modulating the composition and function of the gut microbiota, thereby improving gut-brain axis function. For example, Liuwei Dihuang Wan has been shown to modulate the structure of the gut microbiota in AD model animals, increase the relative abundance of beneficial bacteria, improve gut barrier function, alleviate neuroinflammation, and cognitive impairment [23]. Some single herbs like *Atractylodes macrocephala* and *Poria cocos* also have the effect of regulating the gut microbiota and may participate in AD treatment through the gut-brain axis [24].

4. Critical Review of the Current Research Status of TCM for AD

4.1 Research on TCM Compound Formulas

TCM compound formulas are the primary form of TCM treatment for AD. Their multi-component, multi-target characteristics align well with the complex pathogenesis of AD. Formulas commonly used in clinical practice based on therapeutic principles such as "tonifying the kidney and replenishing essence", "resolving phlegm and opening the orifices" and "activating blood and resolving stasis" have shown certain efficacy in AD treatment.

Kidney-Tonifying and Essence-Replenishing Formulas: The kidney stores essence and generates marrow to fill the brain. Kidney deficiency and essence deficiency lead to an empty sea of marrow and intellectual decline. "Tonifying the kidney and replenishing essence" is a key principle in TCM treatment for AD. Numerous studies have shown that kidney-tonifying and essence-replenishing formulas can improve cognitive dysfunction in AD models through various mechanisms. Liuwei Dihuang Wan, whose functions include nourishing Yin and replenishing essence, and tonifying the liver and kidney, has been found to regulate Aβ transport through the Receptor for Advanced Glycation End Products (RAGE)/Low-Density Lipoprotein Receptor-Related Protein 1 (LRP1) receptor system, improve cerebral microvascular damage, reduce neuronal apoptosis in AD mice by regulating autophagy, repair mitochondrial function, increase neuronal ATP levels, and alleviate neuronal damage [25]. Dihuang Yinzi, which nourishes kidney Yin and warms kidney Yang, is a classic warming and tonifying famous formula for benefiting the kidney and filling the marrow. The research group of Ma Tao focused on early energy metabolism disorders in AD and found that Dihuang Yinzi can protect mitochondrial structure and function, reduce oxidative damage, and inhibit energy metabolism in the brain [26].

Phlegm-Resolving and Orifice-Opening Formulas: Phlegm-turbidity clouding the clear orifices is an important pathogenesis of AD. Phlegm-resolving and orifice-opening formulas can improve AD symptoms by clearing phlegm-turbidity and opening the brain orifices. Daotan Tang has the effects of drying dampness, resolving phlegm, moving Qi, and relieving stagnation. Studies show that Daotan Tang can reduce the content of Aβ in the brain of AD model rats, inhibit inflammatory responses, and improve cognitive function [27]. Changpu Yujin Tang, with *Acorus gramineus* and *Curcuma aromatica* as the main drugs, has the effects of resolving phlegm, opening the orifices, awakening the spirit, and boosting intelligence. It can regulate neurotransmitter levels and improve cognitive and neuropsychiatric symptoms in AD patients [28].

Blood-Activating and Stasis-Resolving Formulas: Blood stasis obstructing the brain collaterals can lead to malnourishment of the brain and marrow, causing AD. Blood-activating and stasis-resolving formulas exert therapeutic effects by improving cerebral blood circulation, increasing cerebral blood supply, and promoting the nutrient supply to nerve cells. Tongqiao Huoxue Tang can activate blood, resolve stasis, and unblock the orifices and collaterals. It can reduce oxidative stress levels in the brain of AD model mice, inhibit Aβ deposition, and improve learning and memory abilities [29]. Xuefu Zhuyu Tang can regulate vascular endothelial function and improve cerebral microcirculation, having a certain preventive and therapeutic effect on AD [30].

4.2 Research on Single Chinese Herbs

Single Chinese herbs also play an important role in AD treatment. Their active components are relatively clear, making their mechanisms easier to study. Many single herbs have been confirmed to have effects such as improving cognitive function and reducing neuropathological damage in AD.

Panax ginseng: Ginseng is a traditional tonic herb. Its main

active components, ginsenosides, have various pharmacological effects. Studies show that ginsenoside Rg1 can improve cognitive function in AD model animals through multiple pathways, including regulating the neurotransmitter system, inhibiting oxidative stress and inflammatory responses, and promoting neuroregeneration [31]. Ginsenoside Rb1 can inhibit the hyperphosphorylation of Tau protein, reduce the formation of neurofibrillary tangles, and protect neurons [32].

Ginkgo biloba: Ginkgo leaf extract is widely used in AD treatment. Its main components, flavonoids and terpenoids, have antioxidant, anti-inflammatory, and improving cerebral blood circulation effects. Ginkgo leaf extract can inhibit the aggregation and neurotoxicity of Aβ, regulate neurotransmitter levels, and improve the cognitive ability and quality of life of AD patients [33].

Acorus gramineus: Acorus gramineus has the effects of opening the orifices, eliminating phlegm, awakening the spirit, and boosting intelligence. Components like β-asarone in its volatile oil can inhibit AChE activity, increase ACh content in the brain, and improve learning and memory ability. Additionally, Acorus gramineus can regulate neuroinflammatory responses and reduce the neurotoxicity of Aβ [34].

Polygonum multiflorum: The main active component of Polygonum multiflorum, tetrahydroxystilbene glucoside, has antioxidant, anti-inflammatory, and lipid-regulating effects. Research finds that tetrahydroxystilbene glucoside can inhibit the production and aggregation of Aβ, improve cognitive function in AD model mice, and its mechanism may be related to regulating oxidative stress and neuroinflammation-related signaling pathways [35].

4.3 Research on Active Components of Chinese Herbs

Active components are the material basis for the therapeutic effects of Chinese herbs. In-depth research on them helps to reveal the mechanisms of TCM in treating AD and provides a basis for new drug development.

Flavonoids: Flavonoids are widely found in many Chinese herbs and have various biological activities such as antioxidant, anti-inflammatory, and neuroprotective effects. For example, quercetin can inhibit the activity of GSK-3β, reduce Tau protein phosphorylation, and improve learning and memory ability in AD model animals. Simultaneously, quercetin can also inhibit the aggregation and neurotoxicity of Aβ and regulate the neurotransmitter system [36]. Kaempferol can alleviate Aβ-induced nerve cell damage through antioxidant and anti-inflammatory effects, showing a protective effect against AD [37].

Terpenoids: Terpenoids are an important class of active components in Chinese herbs, such as ginkgolides and triptolide, which have attracted attention in AD treatment research. Ginkgolides have anti-Platelet-Activating Factor (PAF) activity, can improve cerebral blood circulation, reduce neuroinflammatory responses, and protect neurons [38]. Triptolide can inhibit the activation of microglia and the release of inflammatory factors, reduce neuroinflammation, and also inhibit Aβ deposition, improving cognitive function in AD model animals [39].

Alkaloids: Alkaloid components have various pharmacological activities and possess certain potential in AD treatment. For example, berberine can inhibit the activity of BACE1, reducing the generation of Aβ. Meanwhile, berberine can also regulate the gut microbiota, improve gut-brain axis function, and exert anti-AD effects [40]. Lycorine can inhibit AChE activity, increase ACh levels in the brain, and improve learning and memory ability [41].

Polysaccharides: Polysaccharide components have effects such as immunomodulation, antioxidant, and neuroprotection. For example, Lycium barbarum polysaccharide can enhance antioxidant enzyme activity, reduce oxidative stress levels, and protect nerve cells from damage. It can also regulate the gut microbiota, improve gut-brain axis function, and have a certain preventive and therapeutic effect on AD [42]. Lentinan from *Lentinula edodes* can enhance immunity, reduce neuroinflammatory responses, and improve cognitive function in AD model animals [43].

5. Conclusion and Outlook

In summary, Traditional Chinese Medicine holds unique advantages in the treatment of Alzheimer's disease through its multi-target, multi-pathway approach. It can exert therapeutic effects by regulating Aβ metabolism, inhibiting Tau protein hyperphosphorylation, combating oxidative stress, suppressing inflammation, modulating neurotransmitter systems, promoting neuroregeneration and synaptic plasticity, and regulating the gut-brain axis. Certain progress has been made in both experimental research and clinical application of TCM compounds, single herbs, and active components, providing new ideas and methods for the prevention and treatment of AD.

However, several issues and challenges remain in the current research on TCM for AD. On one hand, the complex composition of TCM formulas means their mechanisms of action are not fully elucidated. Further in-depth research into their material basis and targets is needed to clarify their mechanisms and provide a more solid theoretical basis for clinical application. On the other hand, problems regarding quality control and standardization of Chinese herbs urgently need resolution. Variations in the geographical origin, processing methods, and extraction techniques can lead to differences in the quality of herbal materials, affecting their clinical efficacy and safety. Furthermore, clinical studies on TCM for AD often suffer from small sample sizes and less rigorous study designs. More high-quality, large-sample clinical research is required to validate the efficacy and safety of TCM.

Looking ahead, with the continuous development of modern scientific technologies such as multi-omics, systems biology, and network pharmacology applied in TCM research, it is expected that the scientific connotation of TCM in treating AD will be further revealed, leading to the identification of more effective Chinese herbs and active components, and the development of safe and effective new TCM drugs for AD. Simultaneously, strengthening research on integrated Chinese

and Western medicine approaches for AD, fully leveraging the advantages of both TCM and modern medicine, will bring new breakthroughs in the prevention and treatment of AD, offering more hope to the vast number of AD patients.

References

[1] Scheltens, P., De Strooper, B., Kivipelto, M., et al. Alzheimer's disease [J]. The Lancet, 2021, 397(10284): 1577-1590.

[2] 2020 Alzheimer's disease facts and figures [J]. Alzheimer's & Dementia, 2020, 16(3): 391-460.

[3] Wang, Y., Wang, H., Chen, H.Z. et al. Traditional Chinese Medicine in the Treatment of Alzheimer's Disease [J]. Current Neuropharmacology, 2022, 20(6): 1077-1095.

[4] Zhang, Y.L., Chen, Z.G. Exploration of Alzheimer's Disease Pathogenesis from the Perspective of Traditional Chinese Medicine [J]. Chinese Journal of Integrative Medicine, 2019, 25(5): 392-396.

[5] Li, H., Qu, M. Syndrome Differentiation and Treatment of Alzheimer's Disease in Traditional Chinese Medicine: A Review [J]. Journal of Traditional Chinese Medicine, 2020, 40(5): 879-885.

[6] Hardy, J., Selkoe, D.J. The Amyloid Hypothesis of Alzheimer's Disease: Progress and Problems on the Road to Therapeutics [J]. Science, 2002, 297(5580): 353-356.

[7] Wang, Y., Mandelkow, E. Tau in Physiology and Pathology [J]. Nature Reviews Molecular Cell Biology, 2016, 17(1): 22-35.

[8] Butterfield, D.A., Halliwell, B. Oxidative Stress, Dysfunctional Glucose Metabolism, and Alzheimer Disease [J]. Nature Reviews Neuroscience, 2019, 20(3): 148-160.

[9] Cryan, J.F., O'Riordan, K.J., Cowan, C.S.M., et al. The Microbiota-Gut-Brain Axis [J]. Physiological Reviews, 2019, 99(4): 1877-2013.

[10] He, W., Wang, C., Chen, Y., et al. Berberine attenuates cognitive impairment and neuroinflammation in a mouse model of Alzheimer's disease [J]. Journal of Neuroinflammation, 2021, 18(1): 1-15.

[11] Guo, X.Y., Zhang, D.S. Tanshinone IIA protects against Aβ-induced Alzheimer's disease model rats: mechanism research [J]. Chinese Journal of Pharmacology and Toxicology, 2019, 35(4): 512-517.

[12] Wang, C.Y., Liu, X.M., Wang, Y.Y. Effects of Bushen Yizhi Formula on the expression of LRP1 and RAGE in APP/PS1 transgenic mice [J]. Chinese Journal of Integrated Traditional and Western Medicine, 2017, 37(6): 696-701.

[13] Chen, H., Li, S.C., Zhang, L., et al. Effects of quercetin on tau protein phosphorylation and cognitive function in triple transgenic AD model mice [J]. Chinese Journal of Pharmacology and Toxicology, 2020, 34(2): 81-88.

[14] Li, Y., Chen, N.H. Study on the effect and mechanism of ginsenoside Rg1 promoting Tau protein dephosphorylation [J]. Chinese Traditional and Herbal Drugs, 2019, 50(14): 3430-3435.

[15] Wang, Y., Hao, H.P., Kong, L.Y. Effects of Lycium barbarum polysaccharide on learning memory and oxidative stress in D-galactose-induced aging mice [J].

Journal of China Pharmaceutical University, 2018, 49(3): 350-355.

[16] Zhao, T.T., Wang, N., Lv, G.Y., et al. Protective effect of ferulic acid on Aβ25-35-induced PC12 cell injury [J]. China Journal of Chinese Materia Medica, 2019, 44(17): 3737-3743.

[17] Zhang, L., Xu, T., Wang, S., et al. Curcumin relieves paraquat-induced lung injury through inhibiting the thioredoxin interacting protein/NLRP3 pathway [J]. American Journal of Translational Research, 2022, 14(3): 1787-1799.

[18] Sun, X.B., Guo, L.P. Effect of baicalin on NF-κB signaling pathway in Aβ-induced Alzheimer's disease cell model [J]. Chinese Journal of Experimental Traditional Medical Formulae, 2020, 26(11): 89-95.

[19] Yang, J., Wang, P., Lu, Y.B., et al. Effects of β-asarone on learning memory and cholinergic system in scopolamine model rats [J]. Chinese Journal of Integrated Traditional and Western Medicine, 2018, 38(4): 456-460.

[20] Wu, Q., Shi, J.S., Liu, J., et al. Protective effect of gastrodin on glutamate-induced neuronal excitotoxicity [J]. Acta Pharmaceutica Sinica, 2017, 52(2): 188-194.

[21] Liu, P., Wang, Y.N., Chen, N.H. Study on ginsenoside Rg1 promoting neural stem cell proliferation and differentiation and improving cognitive dysfunction in AD mice [J]. China Journal of Chinese Materia Medica, 2022, 47(10): 2700-2707.

[22] Zhu, Y.C., Zhang, L., Li, L. Effect of icariin on hippocampal neurogenesis in APP/PS1 transgenic AD model mice [J]. Chinese Journal of Nervous and Mental Diseases, 2019, 45(5): 257-262.

[23] Xie, M., Chen, J.X., Wang, M.Q. Regulatory effect of Liuwei Dihuang Wan on intestinal flora and brain inflammatory factors in SAMP8 mice [J]. Modernization of Traditional Chinese Medicine and Materia Medica-World Science and Technology, 2021, 23(4): 1025-1032.

[24] Du, G.H., Shen, Z.F. Comparative study on the regulatory effects of Atractylodes macrocephala and Poria cocos on intestinal flora in spleen deficiency syndrome mice [J]. China Journal of Chinese Materia Medica, 2018, 43(15): 3189-3195.

[25] Wang, Y.Y., Liu, K., Li, C.Y. Effects of Liuwei Dihuang Wan on autophagy and mitochondrial function in Aβ25-35-induced AD rat model [J]. Chinese Journal of Integrated Traditional and Western Medicine, 2020, 40(8): 976-981.