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Research Progress on the Pathogenesis and Traditional Chinese Medicine Treatment of Alzheimer's Disease

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Abstract: ***Alzheimer's disease (AD), the primary causative factor of dementia, is a progressively degenerative neurological disorder that significantly impairs the quality of life in the elderly population and disrupts familial harmony. Concurrent with the intensifying global aging trend, the prevalence of this disease is persistently increasing, thereby imposing an escalating socio-economic burden. This paper systematically reviews the research progress on the pathogenesis of AD. Furthermore, it summarizes the research advancements in the treatment of AD with Traditional Chinese Medicine (TCM), encompassing aspects such as TCM etiology and pathogenesis, compound formulas, single herbs, active constituents, and acupuncture therapy. The limitations of existing studies are analyzed, and future research directions are proposed. This review aims to provide a theoretical foundation for the formulation of clinical prevention and control strategies for AD and for the development of innovative therapeutic agents.***

Keywords: Alzheimer's disease, Pathogenesis, Traditional Chinese Medicine, Syndrome differentiation and treatment, Multi-target therapy, Research progress**.**

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder with an insidious onset. It is characterized by comprehensive dementia manifestations, including memory impairment, aphasia, apraxia, agnosia, visuospatial deficits, executive dysfunction, as well as personality and behavioral changes [1]. In 1906, the German psychiatrist Alois Alzheimer first systematically described the pathological features of this condition, specifically characterized by brain parenchymal atrophy, the formation of neurofibrillary tangles (NFTs), and the deposition of senile plaques (SPs) [2]. With the accelerating aging of the global population structure, AD has emerged as a major public health issue threatening the health of the elderly. According to epidemiological survey data, among the population aged over 60 in China, there are approximately 38.77 million patients with mild cognitive impairment (MCI), about 15.07 million dementia patients, of whom roughly 9.83 million are diagnosed with AD [3]. Longitudinal studies indicate that 16.8% to 35.6% of MCI patients progress to the dementia stage within 3 to 5 years, imposing a heavy burden on families and society.

The treatment of AD in modern medicine primarily involves the use of cholinesterase inhibitors (e.g., donepezil, galantamine) and N-methyl-D-aspartate (NMDA) receptor antagonists (e.g., memantine). However, these drugs only alleviate symptoms without halting disease progression, and are associated with side effects such as gastrointestinal reactions and hepatorenal impairment [4]. In recent years, the approval of monoclonal antibody drugs such as Lecanemab and Donanemab has brought new breakthroughs in AD therapy. Nevertheless, their clinical application is limited by high costs, the necessity for early intervention, and risks including cerebral edema [5].

The treatment of Alzheimer's disease using Traditional Chinese Medicine (TCM) boasts a long history. The medical text *Hua Tuo's Secret Medical Formulas* from the Han Dynasty already documented the disease entity "dementia." It was not until the Ming Dynasty, in Zhang Jingyue's *Jingyue Quanshu* (The Complete Works of Jingyue), that this condition was systematically elucidated as an independent disease category [6]. TCM compound formulas, by virtue of their multicomponent chemical profile, broad range of action sites, and holistic regulatory characteristics, have demonstrated distinctive clinical value in alleviating cognitive impairments and improving the quality of life in AD patients [7]. In recent years, with the advancement of technologies such as molecular biology and network pharmacology, research into the mechanisms of action of TCM against AD has deepened, providing a scientific basis for the modernization and internationalization of TCM. This paper systematically reviews the pathogenesis of AD and the research progress in its treatment with TCM, aiming to provide an academic reference for optimizing prevention and control strategies and for the development of innovative drugs in this field.

2. Research Progress on the Pathogenesis of AD

The pathogenesis of Alzheimer's disease is complex, involving multiple pathophysiological processes. Current academic discourse has proposed several mainstream theories concerning its etiology, primarily including the amyloid-β (Aβ) cascade, Tau protein hyperphosphorylation, cholinergic dysfunction, neuroinflammation, mitochondrial dysfunction, and oxidative stress hypotheses [1]. These theories do not exist in isolation but are intricately intertwined and mutually influential, collectively constituting the complex pathological network system of AD.

2.1 The Amyloid-β (Aβ) Cascade Hypothesis

The Aβ cascade hypothesis is the most classic theory in the study of Alzheimer's disease pathogenesis. This hypothesis

posits that the abnormal cleavage of amyloid precursor protein (APP) by β-secretase (BACE1) and γ-secretase generates an excess of Aβ42 peptides. These peptides aggregate to form oligomers and fibrils, which deposit in brain tissue as senile plaques, triggering a cascade of neurotoxic events and ultimately leading to neuronal apoptosis and cognitive dysfunction [8]. The formation of Aβ plaques can activate resident microglia and astrocytes in the brain, initiating a cascade of inflammatory responses, impairing the integrity of the blood-brain barrier, and causing synaptic transmission dysfunction and neuronal loss [9]. However, immunotherapeutic strategies targeting Aβ have failed to meet their primary endpoints in several clinical trials, suggesting that simply clearing Aβ may be insufficient to reverse the pathological process of AD; Aβ may act as a triggering factor rather than the sole determinant of AD pathogenesis.

2.2 The Tau Protein Hyperphosphorylation Hypothesis

Tau protein is a microtubule-associated protein primarily located in neuronal axons, where it functions to maintain microtubule stability and facilitate axonal transport. In the central nervous system of AD patients, tau protein exhibits an abnormally hyperphosphorylated state, losing its ability to bind to microtubules and aggregating to form paired helical filaments (PHFs), which subsequently constitute neurofibrillary tangles [8]. Tau pathology exhibits prion-like propagation properties, capable of spreading from one brain region to another along neural networks, closely correlating with the progression of AD [10]. Notably, tau protein hyperphosphorylation may represent a downstream event of Aβ neurotoxicity, with both processes forming a vicious cycle that synergistically drives AD progression.

2.3 The Cholinergic Hypothesis

The central tenet of the cholinergic hypothesis is that degenerative changes and necrosis of cholinergic neurons in the basal forebrain of AD patients lead to reduced synthesis of acetylcholine (ACh) and impaired cholinergic neurotransmission, thereby causing deficits in memory and cognitive function [11]. This hypothesis provided the theoretical foundation for the application of cholinesterase inhibitors. However, damage to the cholinergic system is not the initiating factor of AD but rather a consequence of the neurodegenerative process; therefore, simply enhancing cholinergic function cannot halt disease progression.

2.4 The Neuroinflammation Hypothesis

The neuroinflammation hypothesis emphasizes the critical role of the innate immune system in the pathogenesis of AD. Activated microglia and astrocytes release a plethora of pro-inflammatory cytokines, such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α), creating a neuroinflammatory microenvironment that exacerbates neuronal injury [12]. Chronic neuroinflammation can induce Aβ production and tau protein hyperphosphorylation, thereby perpetuating a vicious pathological cycle. In recent years, modulating neuroinflammation has emerged as a novel therapeutic target for AD. However, the results from clinical trials of anti-inflammatory interventions remain inconsistent, suggesting that inflammatory responses may play a dual role in AD [13].

2.5 The Mitochondrial Dysfunction and Oxidative Stress Hypothesis

Mitochondria, as the core organelles for cellular energy metabolism, are also the primary sites for the generation of reactive oxygen species (ROS). In the brain tissue of AD patients, mitochondrial structure and function exhibit significant abnormalities, leading to impaired energy production and excessive accumulation of ROS, which in turn induces oxidative stress damage [14]. This state of oxidative stress can cause multifaceted damage to DNA molecules, protein structures, and lipid components, while simultaneously accelerating the formation of Aβ plaques and promoting abnormal tau protein phosphorylation. These pathological processes mutually reinforce each other, constituting a self-amplifying positive feedback loop [15]. Furthermore, mitochondrial dysfunction is closely linked to the activation of apoptotic pathways, representing a crucial mechanism underlying neuronal loss in AD.

2.6 Emerging Mechanisms: Ferroptosis and the Gut-Brain Axis

Ferroptosis, a recently identified form of regulated cell necrosis, has progressively been incorporated into research on the pathological mechanisms of Alzheimer's disease. This mode of cell death is fundamentally characterized by iron-dependent peroxidation of membrane lipids, and its occurrence is closely pathologically associated with iron homeostasis imbalance and elevated oxidative stress levels in the brain tissue of AD patients [16]. Studies have shown abnormal iron accumulation in specific anatomical regions of the brains of AD patients, and this metal ion overload can accelerate Aβ plaque deposition and exacerbate neurodegenerative damage [9]. Furthermore, the gut-brain axis theory offers a novel perspective for AD research. Dysbiosis of the gut microbiota can influence brain function through inflammatory, metabolic, and neuroendocrine pathways, and AD patients often exhibit alterations in their gut microbiota composition [17]. These emerging mechanisms provide new intervention targets for the formulation of prevention strategies and therapeutic development for AD.

3. Understanding of AD Etiology and Pathogenesis in Traditional Chinese Medicine

3.1 Origin and Historical Evolution of the Disease Name

Although the specific term "Alzheimer's disease" does not exist in Traditional Chinese Medicine, based on its clinical manifestations, it falls within the categories of "dementia" (痴呆) and "amnesia" (健忘). The term "dementia" was first documented in the Han Dynasty text *Hua Tuo's Secret Medical Formulas*, which recorded "prescriptions for treating dementia" [4]. In the Ming Dynasty, Zhang Jingyue, in his work *Jingyue Quanshu* (The Complete Works of

Jingyue), explicitly established “dementia” as an independent disease entity for the first time, describing its clinical manifestations such as “incoherent speech and unusual behavior” and offering a prognostic assessment stating that “some cases are curable, while others are not.”

3.2 Analysis of Etiology and Pathogenesis

The onset of AD is closely associated with factors such as aging and constitutional deficiency, emotional dysregulation, and prolonged illness leading to consumption. The disease is located in the brain and involves dysfunction of multiple viscera, including the heart, kidney, liver, and spleen. It is characterized by a syndrome of root deficiency and branch excess [18].

3.2.1 Kidney Essence Deficiency as the Root of Pathogenesis

The kidney governs the bones and produces marrow, and the brain is the sea of marrow. When kidney essence is sufficient, the sea of marrow is replenished, resulting in acute thinking. As stated in the *Lingshu* (Spiritual Pivot): “When the sea of marrow is deficient, it leads to dizziness, tinnitus, soreness of the legs, blurred vision, and a desire to lie down.” With aging, kidney essence gradually declines, or prolonged illness damages the kidney, leading to emptiness of the sea of marrow, malnutrition of the brain, and failure of the spirit mechanism, ultimately manifesting as dementia [19].

3.2.2 Phlegm Turbidity and Blood Stasis as the Manifestations of the Branch

Spleen dysfunction in transportation and transformation leads to the accumulation of fluids, which coalesce into phlegm. Alternatively, emotional distress can cause stagnation of liver qi, and qi stagnation can engender phlegm. When phlegm turbidity clouds the clear orifices, it impairs the function of the spirit, resulting in a dull expression and sluggish response. Furthermore, qi deficiency impairs the power to propel blood, or qi stagnation leads to blood stasis, causing obstruction of the brain collaterals. This obstruction prevents nourishment from reaching the brain, which can also contribute to dementia [20].

3.3 Syndrome Differentiation and Treatment Principles/Methods

Based on the clinical manifestations and pathogenetic characteristics of AD, contemporary TCM practitioners primarily classify the disease into the following syndrome types:

(1) Kidney Essence Deficiency Type: Characterized by memory loss, disorientation, soreness and weakness of the waist and knees, dizziness, tinnitus, a pale tongue with white coating, and a deep, thready pulse. The therapeutic principle is to tonify the kidney and replenish essence, and to benefit marrow and strengthen the brain. Representative formulas include Liuwei Dihuang Pill, Zuogui Pill, and Dihuang Yinzi.

(2) Phlegm Turbidity Obstructing the Orifices Type: Characterized by a dull expression, sluggish response, halting speech, chest tightness, copious phlegm, a greasy white tongue coating, and a slippery pulse. The therapeutic principle is to resolve phlegm and open the orifices, and to awaken the spirit and boost intelligence. Representative formulas include Banxia Baizhu Tianma Decoction, Ditan Decoction, and Wendan Decoction.

(3) Blood Stasis Obstructing the Collaterals Type: Characterized by memory loss, fixed headaches, a darkish complexion, a purplish dark tongue or tongue with ecchymosis, and a choppy pulse. The therapeutic principle is to invigorate blood and resolve stasis, and to unblock the orifices and awaken the brain. Representative formulas include Tongqiao Huoxue Decoction and Xuefu Zhuyu Decoction.

(4) Heart and Spleen Deficiency Type: Characterized by palpitations, insomnia, forgetfulness, fatigue, poor appetite, lassitude, a sallow complexion, a pale tongue with thin white coating, and a thready, weak pulse. The therapeutic principle is to boost qi and nourish blood, and to fortify the spleen and calm the spirit. Representative formulas include Guipi Decoction and Bazhen Decoction.

4. Research Progress on the Treatment of AD with Chinese Materia Medica

The treatment of Alzheimer’s disease with Chinese materia medica offers advantages through its multicomponent nature, multi-target action, and holistic regulatory effects. Modern research has delved into its mechanisms of action at three levels: compound formulas, single herbs, and active constituents.

4.1 Research on TCM Compound Formulas in the Treatment of AD

TCM compound formulas represent the primary form of clinical medication in Traditional Chinese Medicine. Adhering to the compatibility principles of “sovereign, minister, assistant, and courier,” they demonstrate unique advantages in addressing the multi-target pathological characteristics of AD [7].

4.1.1 Formulas for Tonifying the Kidney and Replenishing Essence

Liuwei Dihuang Pill is a representative formula for tonifying the kidney and replenishing essence. Modern studies have shown that Liuwei Dihuang Pill can ameliorate cognitive dysfunction in AD animal models by regulating energy metabolism, enhancing autophagic function, and reducing apoptosis [21]. Dihuang Yinzi, formulated by adding yang-tonifying herbs such as Fuzi (Aconiti Lateralis Radix Praeparata) and Rougui (Cinnamomi Cortex) to the Liuwei Dihuang Pill base, simultaneously tonifies both yin and yang, resolves phlegm, and opens the orifices. Research indicates that Dihuang Yinzi can alleviate hippocampal neuronal damage and improve cognitive function [22].

4.1.2 Formulas for Expelling Phlegm and Opening the Orifices

Yuanzhi San (Polygala Powder) features Yuanzhi (Polygalae

Radix) as the sovereign herb, combined with Shichangpu (Acori Tatarinowii Rhizoma), Fuling (Poria), and others. It possesses functions of expelling phlegm, opening the orifices, calming the spirit, and boosting intelligence. Modern pharmacological studies have confirmed that Yuanzhi San can reduce p-Tau levels in the brain, alleviate oxidative stress damage, and protect neuronal structure [23].

4.1.3 Formulas for Invigorating Blood and Resolving Stasis

Buyang Huanwu Decoction, formulated by Wang Qingren in the Qing Dynasty, was originally used to treat sequelae of stroke but has been extended in modern practice for AD treatment. Research indicates that Buyang Huanwu Decoction can regulate Aβ metabolism, protect the blood-brain barrier, improve cerebral microcirculation, and attenuate AD pathological damage [24].

4.1.4 Formulas for Draining Fire and Resolving Toxin

Huanglian Jiedu Decoction, composed of Huanglian (Coptidis Rhizoma), Huangqin (Scutellariae Radix), Huangbo (Phellodendri Chinensis Cortex), and Zhizi (Gardeniae Fructus), exhibits effects of draining fire and resolving toxin. Studies have demonstrated that this formula can enhance cholinergic system function, inhibit neuroinflammatory responses, and improve learning and memory abilities in AD animal models [25]. Jiedu Yizhi Formula, with Huanglian as the sovereign herb combined with Yizhiren (Alpiniae Oxyphyllae Fructus) and Huangqi (Astragali Radix), has shown in clinical studies that it can significantly inhibit Aβ peptide aggregation and improve cognitive function in AD patients [26].

4.2 Research on Single Herbs in the Treatment of AD

Single herbs form the foundation of compound formulas, and elucidating their active constituents and mechanisms of action is crucial for optimizing formulations and enhancing therapeutic efficacy. *Renshen* (Ginseng Radix et Rhizoma) is an essential herb for tonifying qi, with ginsenosides as its main active components. Studies have shown that ginsenoside Re can reduce the generation of Aβ1-40 and Aβ1-42 by regulating PPARγ protein and its mRNA levels, thereby ameliorating cognitive dysfunction in AD animal models [27]. *Shichangpu* (Acori Tatarinowii Rhizoma) possesses functions of opening the orifices, resolving phlegm, awakening the spirit, and boosting intelligence, making it a commonly used herb for dementia. The volatile oil of *Shichangpu* exerts anti-AD effects by modulating neurotransmitter levels, protecting neuronal cells, and improving cerebral circulation [28]. *Yuanzhi* (Polygalae Radix) has effects of calming the spirit, boosting intelligence, expelling phlegm, and opening the orifices. Polygala saponins can ameliorate synaptic damage and memory impairment by maintaining the stability of the calpain system and regulating the expression of APP and its sheddases [29]. *Sanqi* (Notoginseng Radix et Rhizoma) is known for dissipating stasis, stopping bleeding, reducing swelling, and alleviating pain. Notoginsenosides can reduce Aβ production by regulating PPARγ levels and improve spatial learning ability in AD animal models [30]. *Hongjingtian* (Rhodiolae Crenulatae Radix et Rhizoma) has functions of supplementing qi, invigorating blood, unblocking meridians, and calming panting. Salidroside, its main active component, has been shown to inhibit neuronal ferroptosis by activating the Nrf2/GPX4 axis and regulating iron transport proteins, thereby improving cognitive impairment in AD [31].

4.3 Research on Active Constituents of Chinese Herbs in the Treatment of AD

The active constituents of Chinese herbs constitute the material basis for their pharmacological effects. Based on chemical structure, they can be classified into flavonoids, phenolics, quinones, phenylpropanoids, terpenoids, alkaloids, and glycosides, among others [6]. Flavonoids, widely present in herbs such as *Yinxingye* (Ginkgo Folium), *Gegen* (Puerariae Lobatae Radix), and *Yinyanghuo* (Epimedii Folium), exhibit diverse pharmacological activities including antioxidant, anti-inflammatory, and cerebral circulation-improving effects. Nobiletin and luteolin can mitigate AD pathological damage by reducing oxidative stress and mitochondrial dysfunction, modulating signaling pathways to inhibit neuroinflammation, and promoting autophagy [32]. Icariin and baicalein can regulate multiple signaling pathways in the brain, inhibit Aβ accumulation and tau protein hyperphosphorylation, and improve cognitive impairment. Quercetin-3-O-glucuronide exerts anti-AD effects by modulating the gut microbiota structure, thereby ameliorating brain inflammation and insulin resistance. Salidroside, a representative phenolic compound, inhibits neuronal ferroptosis by activating the Nrf2/GPX4 axis and regulating iron transport proteins, improving cognitive dysfunction in AD animal models, thereby opening a new direction for research into the anti-AD mechanisms of Chinese herbs [33]. Tanshinone IIA, celastrol, astragaloside IV, and the volatile oil of *Shichangpu* can promote Aβ transport, activate autophagy, and inhibit neuroinflammation, exerting multi-target anti-AD effects [34].

5. Research Progress on Acupuncture Treatment for AD

Acupuncture, as a vital component of Traditional Chinese Medicine, demonstrates unique advantages in the treatment of Alzheimer’s disease. Numerous clinical studies have indicated that acupuncture can improve cognitive function, activities of daily living, and neuropsychiatric symptoms in AD patients [35].

5.1 Commonly Used Acupoints and Needling Methods

Acupuncture for AD primarily selects acupoints from the Governor Vessel, Conception Vessel, and Gallbladder Channel of Foot-Shaoyang, adhering to the therapeutic principles of awakening the brain and opening the orifices, tonifying the kidney and replenishing essence, and resolving phlegm and unblocking collaterals [8]. Commonly used acupoints include: **Head acupoints:** Baihui (GV20), Sishencong (EX-HN1), Shenting (GV24), Benshen (GB13), Yintang (EX-HN3), and Taiyang (EX-HN5). Baihui, located at the vertex, is a meeting point of all yang channels, capable of raising yang and alleviating collapse, awakening the brain and opening the orifices; Sishencong, an extra point, calms the spirit, boosts intelligence, brightens the eyes, and sharpens

the ears [36]. **Limb acupoints:** Taixi (KI3), Xuanzhong (GB39), Zusanli (ST36), Sanyinjiao (SP6), Fenglong (ST40), and Neiguan (PC6). Taixi, the Yuan-Source point of the kidney channel, tonifies the kidney and replenishes essence; Xuanzhong, the influential point of marrow, benefits marrow and strengthens the brain; Zusanli, the He-Sea point of the stomach channel, fortifies the spleen and resolves phlegm; Fenglong is a key point for resolving phlegm. **Needling methods:** Even reinforcing-reducing or reinforcing methods are commonly applied, once daily or every other day, with needles retained for 20-30 minutes per session. A course of treatment consists of 10-15 sessions, typically continued for 2-3 courses.

5.2 Evaluation of Clinical Efficacy

Multiple randomized controlled trials (RCTs) have demonstrated that acupuncture can significantly improve scores on the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Activities of Daily Living (ADL) scale in AD patients [37]. Meta-analyses indicate that the total effective rate of acupuncture combined with medication for AD is superior to medication alone, with a favorable safety profile [38].

5.3 Research on Mechanisms of Action

Modern research reveals that the anti-AD mechanisms of acupuncture involve multiple levels [39]: 1) **Regulation of neurotransmitters:** Acupuncture can increase the levels of neurotransmitters such as acetylcholine, dopamine, and serotonin in the brain, thereby improving cholinergic neurotransmission; 2) **Inhibition of neuroinflammation:** Acupuncture can reduce the levels of pro-inflammatory cytokines like IL-1β, IL-6, and TNF-α in the brain, modulate the activation state of microglia, and attenuate neuroinflammatory responses; 3) **Promotion of neuroplasticity:** Acupuncture can increase the expression of brain-derived neurotrophic factor (BDNF), promoting synaptic plasticity and neurogenesis; 4) **Improvement of cerebral blood flow:** Acupuncture can increase cerebral blood flow, enhance cerebral microcirculation, and improve oxygen supply and energy metabolism in brain tissue.

6. Strategies for the Integrated Treatment of AD with Chinese and Western Medicine

The integrated treatment of Alzheimer's disease using Chinese and Western medicine represents a current hotspot in clinical research. By combining the advantages of both medical systems, this approach can enhance clinical efficacy and reduce adverse reactions [40].

Chinese Materia Medica Combined with Cholinesterase Inhibitors: Research indicates that the combination of TCM compound formulas (such as Compound Haishe Capsule and Zhinao Capsule) with donepezil can significantly improve cognitive function and activities of daily living in AD patients. The therapeutic effect is superior to that of donepezil alone, and this combination can also mitigate side effects such as gastrointestinal reactions [40].

Chinese Materia Medica Combined with NMDA Receptor Antagonists: The combination of Chinese materia medica with memantine for the treatment of moderate-to-severe AD can ameliorate patients' neuropsychiatric symptoms and improve their quality of life [23].

Acupuncture Combined with Pharmacotherapy: Combining acupuncture with donepezil or memantine can potentiate the drug efficacy and enhance the overall functional status of patients [8].

7. Existing Problems and Controversies

Despite progress in the intervention of Alzheimer's disease with Traditional Chinese Medicine, its clinical translation and internationalization still face three major bottlenecks. **First, insufficient quality of clinical research:** Existing trials are mostly limited to small-sample, single-center designs, lacking large-sample randomized double-blind controlled studies that meet international standards. Inconsistent criteria for syndrome differentiation and efficacy evaluation, coupled with a scarcity of long-term safety data, result in a low level of evidence that struggles to gain international recognition [41]. **Second, insufficient depth of mechanistic elucidation:** The complex composition of compound formulas, with intertwined synergistic and antagonistic effects, makes them difficult to analyze using single-target theories. The active constituents often suffer from low oral bioavailability and limited ability to penetrate the blood-brain barrier. Current animal models lack TCM syndrome elements, highlighting an urgent need to establish disease-syndrome combination models [42]. **Third, the dilemma of integrating Chinese and Western medical systems:** The significant paradigmatic differences between holistic syndrome differentiation and molecular targeting, along with disparate dimensions of efficacy evaluation, mean a unified standard has yet to be established [43].

Future research should achieve breakthroughs in the following areas: 1) **Elevating the level of clinical evidence:** Conduct internationally standardized, multi-center randomized controlled trials and develop a comprehensive efficacy evaluation system integrating syndrome assessment, cognitive scales, and biomarkers [44]; 2) **Deepening mechanistic research:** Establish animal models combining disease and syndrome, utilize network pharmacology to elucidate compatibility rules, and explore intervention targets from novel perspectives such as the gut-brain axis and ferroptosis [45]; 3) **Advancing new drug development:** Develop nano-formulations and targeted delivery systems to enhance drug concentration in the brain, investigate classic famous formulas, and clarify their material basis [46]; 4) **Promoting deeper integration of Chinese and Western medicine:** Establish collaborative clinical pathways and guidelines for diagnosis and treatment, facilitate the inclusion of research findings in international consensus, and enhance global influence [47].

8. Conclusion

Alzheimer's disease is a complex neurodegenerative disorder whose pathogenesis involves multiple pathological mechanisms, including Aβ deposition, tau protein hyperphosphorylation, neuroinflammation, oxidative stress,

and mitochondrial dysfunction. The single-target therapeutic strategies of modern medicine have demonstrated limited efficacy. In contrast, Traditional Chinese Medicine, with its advantages of multicomponent formulation, multi-target action, and holistic regulation, exhibits unique potential in improving cognitive function and delaying disease progression in AD patients.

In TCM theory, AD falls within the category of "dementia," and its pathogenesis is characterized by root deficiency and branch excess, with kidney essence deficiency as the root, and phlegm turbidity and blood stasis as the manifestations. Treatment emphasizes syndrome differentiation, employing principles such as tonifying the kidney and replenishing essence, resolving phlegm and opening the orifices, and invigorating blood and resolving stasis. Modern research has elucidated the anti-AD mechanisms of TCM at three levels—compound formulas, single herbs, and active constituents—involving multiple targets such as reducing Aβ production and deposition, inhibiting tau protein hyperphosphorylation, exerting anti-inflammatory and antioxidant effects, regulating neurotransmitters, inhibiting neuronal apoptosis, and promoting neuroregeneration. Acupuncture therapy for AD can improve cognitive function, with mechanisms related to neurotransmitter regulation, neuroinflammation inhibition, and neuroplasticity promotion.

Despite significant progress in the treatment of AD with TCM, challenges remain, including insufficient quality of clinical research, inadequate depth of mechanistic elucidation, and incomplete integration of Chinese and Western medicine. Future efforts should focus on strengthening high-quality clinical research, deepening mechanistic studies—particularly the exploration of disease-syndrome combination models and emerging mechanisms (e.g., ferroptosis, gut-brain axis) — advancing new drug development, and promoting deeper integration of Chinese and Western medicine to provide more effective strategies for the prevention and treatment of AD. With the advancement of modern scientific technologies and the progress of TCM modernization research, TCM is poised to play an increasingly significant role in the field of AD treatment, contributing Chinese wisdom to address the health challenges of the global aging society.

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