

PAPER

Application and Prospects of Traditional Chinese Medicine in the Treatment of Alzheimer's Disease

Jinghui Sung^{1,2}(✉), Zikang Jiang^{1,2}, Yuanpeng Huang²

¹Fujian University of Traditional Chinese Medicine, Fuzhou, Fujian, China

²Xiamen TCM Hospital Affiliated to Fujian University of Traditional Chinese Medicine, Xiamen, Fujian, China

acyril0906@gmail.com

ABSTRACT

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive memory decline and cognitive dysfunction, primarily affecting the elderly. Approximately 50 million people worldwide are currently affected, with projections suggesting an increase to 152 million by 2050, especially among individuals over 65, where the incidence rate can be as high as 30%. This phenomenon significantly reduces the quality of life for patients and imposes substantial psychological and economic burdens on families and society. Therefore, finding effective treatment options is crucial. In recent years, Traditional Chinese Medicine (TCM) has gradually shown its potential in the treatment of AD. TCM views AD as a form of "dementia" or "amnesia," attributing its root causes to dysfunctions of organs such as the kidneys and spleen, as well as deficiencies in qi (vital energy) and blood. Through methods like regulating qi and blood and strengthening kidney function, TCM aims to improve symptoms via a holistic approach. Many herbal formulas, such as Tianma Guoteng Decoction and Angong Niuhuang Pill, have been widely studied, demonstrating promising neuroprotective effects. Furthermore, both domestic and international studies indicate that TCM has made positive strides in the clinical application of AD, particularly in multicenter clinical trials, showing improvements in cognitive abilities and delays in disease progression. Herbal components such as astragalus polysaccharides, ginsenosides, curcumin, and Ginkgo biloba extract (GBE) exhibit significant neuroprotective effects through mechanisms like antioxidation, anti-inflammation, and the clearance of beta-amyloid (A β) protein. However, standardization and clinical validation remain major challenges to its widespread application. Looking ahead, integrating modern medical research methods, such as molecular biology and genetics, will provide new perspectives for TCM in the treatment of AD, facilitating the extraction and application of its effective components, thereby improving patients' quality of life. Overall, TCM has achieved significant success in the treatment of AD, but further in-depth research is needed to fully realize its potential.

KEYWORDS

Alzheimer's disease (AD), traditional Chinese medicine (TCM), cognitive function, neuroprotection, treatment mechanism

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1 INTRODUCTION

Alzheimer's disease (AD) is a prevalent neurodegenerative disorder characterized by progressive memory decline, cognitive impairment, and behavioral changes, primarily affecting the elderly population. According to the World Health Organization (WHO), approximately 50 million people worldwide are currently living with Alzheimer's disease, a number projected to reach 152 million by 2050. The incidence of AD significantly increases with age. A study published in *The Lancet* indicates that among individuals over 65, the prevalence rate of Alzheimer's can be as high as 30%. This trend places considerable strain on families, healthcare systems, and society as a whole.

Alzheimer's disease impacts not only the patients themselves; as the disease progresses, patients often lose their ability to perform daily activities and become reliant on caregivers, leading to significant psychological and economic burdens on families and society. Research shows that the costs of Alzheimer's care are expected to continue rising in the coming decades, posing a major public health challenge. Additionally, patients frequently experience emotional disturbances, such as depression and anxiety, which further affect and reduce their quality of life. Therefore, research into effective treatment strategies is crucial, with particular interest in the role of Traditional Chinese Medicine (TCM) in Alzheimer's treatment, which may offer patients more comprehensive support and improvements.

This paper primarily explores the foundational theories of TCM in treating Alzheimer's disease, commonly used TCM formulas, and the therapeutic efficacy of individual herbal components. It also reviews the clinical research progress and mechanisms of TCM in Alzheimer's treatment, discussing clinical trial outcomes. We look forward to future opportunities for integrating Eastern and Western medicine to address this critical health challenge facing humanity.

2 THE FUNDAMENTAL THEORY OF TCM IN TREATING AD

In TCM, AD can be categorized under two primary syndromic types: "dementia" and "amnesia." TCM attributes the root causes of these conditions to various pathological changes, such as kidney deficiency, spleen weakness, insufficiency of Qi and blood, and stagnation. In TCM theory, optimal brain function relies on the abundant supply of Qi and blood, alongside the balanced and harmonious functioning of critical organs such as the kidneys, heart, and spleen, which play a vital role in nourishing the brain. However, as individuals age, the circulation of Qi and blood, as well as organ functions, gradually decline, contributing to cognitive deterioration manifested as memory impairment and reduced cognitive ability. The essence of TCM treatment is to strengthen kidney function, enhance blood circulation, and alleviate phlegm stagnation while emphasizing a holistic approach to balance the body, slow disease progression, and maintain both physical and mental harmony.

Firstly, enhancing kidney essence is considered foundational for maintaining brain health. TCM posits that strengthening kidney function can decelerate the aging process, as kidney deficiency is thought to be a primary cause of cognitive decline. Herbal formulas like the eight-ingredient replenishing capsule is historically used to nourish Qi and blood, promote physical and mental well-being, and effectively mitigate age-related cognitive deterioration. TCM also emphasizes the importance of promoting blood circulation and clearing phlegm stagnation. Phlegm stagnation can obstruct the flow of Qi and blood to the brain, negatively affecting cognition and memory. Specific herbal treatments have shown significant benefits in

enhancing cognitive abilities and functional capacity in Alzheimer's patients, often outperforming certain Western medications.

Moreover, TCM adopts a comprehensive, multi-faceted approach to address the various symptoms and underlying causes of AD. Research has demonstrated that combining TCM and Western medical approaches not only amplifies therapeutic efficacy but also improves cognitive assessment scores and reduces adverse effects, highlighting the complementary benefits of both systems.

The complex theory and therapeutic benefits of TCM offer promising avenues for treating AD. Although some TCM treatments are gaining recognition in contemporary medical research, the potential for synergy between TCM and Western medicine remains an area for further exploration. Many scholars and clinicians involved in this field aim to refine this integrative research approach, ensuring the preservation of TCM's holistic principles while incorporating the empirical validation methods of Western medicine, ultimately aiming to improve patients' quality of life and enhance their recovery experience.

3 COMMON FORMULAS AND HERBAL COMPOUNDS IN TCM FOR TREATING AD

Table 1 presents a summary of commonly used TCM formulas and individual herbal compounds for treating AD. The mechanisms and benefits of these formulas and compounds focus primarily on inhibiting neuroinflammation, improving cognitive function, and protecting brain cells. The following sections explain their mechanisms and benefits in more detail.

Table 1. Summary of common TCM formulas and individual herbal compounds for Alzheimer's treatment

Category	Name	Main Ingredients	Mechanism	Benefits and Advantages
Common Formulas	Tianma Gouteng Decoction	Tianma, Gouteng	Calms the liver, dispels wind, improves neurological symptoms	Reduces anxiety and mood fluctuations
	A Gong Niu Huang Pill	Niu Huang, sedative herbs	Clears heat, detoxifies, calms the mind	Protects brain cells through anti-inflammatory effects
	Sijunzi Decoction	Ginseng, Atractylodes, Poria, Licorice	Strengthens the spleen, tonifies Qi, enhances immunity	Enhances cognitive function, anti-fatigue
	Huangqi Danggui Decoction	Astragalus, Angelica	Tonifies Qi and blood, improves brain blood supply	Slows memory decline
Common Herbal Compounds	Astragalus Polysaccharide	Astragalus polysaccharide	Regulates Nrf2 and JAK/STAT pathways	Reduces A β accumulation, improves cognition
	Ginsenoside Rd	Ginsenoside	Inhibits GSK-3 β , regulates A β and tau protein	Slows brain cell damage
	Curcumin	Curcumin	Modulates neuroinflammatory pathways, clears reactive oxygen species	Strong anti-inflammatory and antioxidant effects, bioavailability improvement needed
	Ginkgo Biloba Extract	Ginkgo Biloba extract	Regulates antioxidant enzymes, protects neurons	Enhances microcirculation, protects hippocampal neurons

Each formula and herbal compound offer unique advantages, with active compounds targeting various biochemical pathways to improve Alzheimer's-related symptoms. The protective effects against oxidative stress and neuroinflammation

highlight the promise of TCM in AD treatment, warranting further integration with Western approaches to maximize therapeutic outcomes.

3.1 Common formulas

Many TCM formulations, such as Tianma Gouteng Decoction, A Gong Niuhuang Pill, Sijunzi Decoction, and Huangqi Danggui Decoction, are widely used in the treatment of AD. These formulas are designed to invigorate Qi, promote blood circulation, and employ multi-targeted regulation to address the complex pathophysiology of AD. Tianma Gouteng Decoction, with Tianma and Gouteng, has been shown in studies to alleviate neurological symptoms and reduce anxiety and emotional fluctuations. A Gong Niuhuang Pill has proven effective in clearing heat, detoxifying, and calming the mind; its components help protect neuronal integrity through anti-inflammatory mechanisms. Sijunzi Decoction strengthens the spleen and boosts immunity, enhancing cognitive function and resistance to fatigue. Huangqi Danggui Decoction primarily tonifies Qi and blood to improve cerebral blood flow, thereby slowing memory decline. These formulations work through pathways that inhibit neuroinflammation, reduce beta-amyloid (A β) deposition, and modulate tau protein pathology, showcasing the potential and applicability of TCM for AD treatment. Related literature also explores the mechanisms and clinical efficacy of these TCM prescriptions.

1. Mechanisms of action

- **Neuroinflammation mitigation:** Neuroinflammation is a key factor in AD progression [1]. Research has shown that traditional TCM formulations, such as Tian Si Beverage, can suppress glial cell activation and reduce the synthesis of pro-inflammatory cytokines, thereby effectively inhibiting neuroinflammation.
- **A β and Tau protein pathology:** Tianma Gouteng Decoction (TGP) and Tian Si Beverage have shown significant therapeutic efficacy in reducing A β accumulation and excessive tau protein phosphorylation. TGP achieves this by modulating enzymes associated with A β synthesis and degradation [2].
- **Gut-brain axis regulation:** TCM also emphasizes regulation of the gut-brain axis. Through its influence on the gut microbiome, TCM can have a positive impact on brain health and may help slow AD progression [3].

2. Benefits and advantages

- **Cognitive function improvement:** Studies indicate that TCM formulations can enhance cognitive function, including memory and learning abilities, in AD models. For example, TGP has shown benefits in improving spatial memory and learning in transgenic mouse models [2].
- **Safety and acceptability:** With minimal side effects and strong cultural acceptance, traditional TCM is widely recognized as a natural complementary therapy, offering an alternative approach to conventional AD treatments [4].

Although TCM has demonstrated substantial potential in AD management, combining it with existing pharmacological therapies may enhance its effectiveness. Integrating TCM with contemporary pharmacological interventions could more comprehensively address AD's pathological mechanisms and offer a holistic approach to managing the disease [5].

3.2 Common single compounds in TCM

In the treatment of AD, many single-compound extracts, such as Astragalus Polysaccharide (APS), Ginsenoside Rd, Curcumin, and Ginkgo Biloba Extract (GBE), demonstrate notable neuroprotective effects. These compounds employ various mechanisms to enhance therapeutic potential, including antioxidant activity, anti-inflammatory responses, and neuronal protection. Ginsenoside Rd, for instance, exhibits both antioxidant and anti-inflammatory properties and has shown the ability to prevent A β accumulation, thereby mitigating cellular damage in the brain. Curcumin has demonstrated significant anti-inflammatory, antioxidant, and free radical-scavenging properties in various studies, helping to alleviate inflammation associated with AD. Meanwhile, GBE protects neurons from oxidative damage by enhancing microcirculation.

The following sections elaborate on the specific actions and potential mechanisms of these single compounds in AD treatment:

1. Astragalus polysaccharide (APS): By modulating the Nrf2 and JAK/STAT signaling pathways, APS exhibits neuroprotective effects that help reduce A β accumulation and inhibit neuronal apoptosis [6]. Additionally, APS has shown potential in enhancing cognitive function and reducing insulin resistance, underscoring its therapeutic potential for AD [6].
2. Ginsenoside Rd: This active component derived from ginseng inhibits glycogen synthase kinase-3 β (GSK-3 β), a key regulator of A β production and tau protein hyperphosphorylation, both of which are critical to AD pathogenesis [7].
3. Curcumin: Known for its robust neuroprotective properties, curcumin regulates neuroinflammatory pathways and removes reactive oxygen species (ROS) [8]. However, its low bioavailability limits clinical efficacy, necessitating new delivery systems to enhance its therapeutic potential [8].
4. Ginkgo biloba extract (GBE): GBE protects hippocampal neurons from oxidative stress by modulating antioxidant enzymes, such as superoxide dismutase and glutathione peroxidase, and apoptosis-related proteins [9]. Studies indicate that GBE improves cognitive function in AD models, further supporting its application as a neuroprotective agent [9].

Despite these compounds' promising neuroprotective effects in AD treatment, challenges such as limited bioavailability and a lack of extensive clinical trials remain. The application of nanotechnology offers a new strategy to improve the delivery efficiency and therapeutic efficacy of these compounds, addressing existing challenges [10].

4 CLINICAL RESEARCH PROGRESS OF TCM IN AD TREATMENT

4.1 Research progress in China

Recent studies in China have made substantial advancements in using TCM to treat AD, demonstrating potential benefits in cognitive enhancement and slowing AD progression. These investigations encompass various approaches, including clinical trials and mechanistic studies, which deepen our understanding of TCM's role in AD treatment. Key research developments include:

1. Mechanisms of action: The core of TCM-based AD treatment involves regulating multiple biological pathways, such as oxidative stress, tau protein hyperphosphorylation, and A β accumulation, all of which are pivotal in AD pathogenesis [11]. Additionally, TCM addresses aging within the neurovascular unit (NVU) and sustains cerebral homeostasis through antioxidant and anti-inflammatory mechanisms, thereby mitigating neurodegenerative changes [12].
2. Clinical trials and efficacy: Recent multicenter clinical trials, such as the evaluation of the kidney-tonifying formula Buzhong Shenzhu Qiju Formula (BSKQF) for AD intervention, have confirmed the efficacy and safety of TCM in AD treatment. These studies utilize standardized assessments to measure cognitive enhancement, including the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MOCA) [13][14]. Danggui Shaoyao San (DSS) has also shown efficacy in both animal models and clinical research, with its polysaccharides playing a crucial role in anti-inflammatory responses and neuroprotection [15].

4.2 International research progress

A bibliometric analysis reveals that China, the United States, Singapore, Australia, and the United Kingdom play pivotal roles in the international research on using TCM to treat AD, each demonstrating unique research focuses and trends. China, as a central contributor, emphasizes foundational biological mechanisms and pathology, investigating the potential physiological effects of active TCM compounds in AD treatment, with growing attention to genetic, metabolic, and neurological mechanisms. The United States and Singapore concentrate on collaborations with China, leveraging multidisciplinary, cross-national partnerships to explore how TCM can alleviate dementia symptoms at molecular and neurological levels. Australia and the United Kingdom contribute significantly to community health and dementia intervention strategies, exploring integrative treatment models based on TCM and underscoring the importance of preventive health education.

Although the application of TCM in AD treatment has not yet achieved widespread international acceptance, preliminary studies validate the potential of certain TCM components. As global recognition of TCM grows, research trends have shifted from investigating pathological mechanisms to exploring multifaceted, practical applications, particularly in preventive strategies targeting communities and high-risk populations. TCM's role in enhancing vascular dementia mechanisms, combined with community and home-care interventions, has become a research hotspot, effectively improving the quality of life for patients and caregivers. Studies also underscore the impact of social and environmental factors in disease management, highlighting TCM's potential within holistic treatment strategies. While international TCM research remains limited, its neuroprotective and antioxidant properties have attracted increasing interest and acknowledgment.

4.3 Integration with modern medicine

The integration of TCM with contemporary medicine is gradually evolving into a holistic approach for treating neurological disorders. In clinical settings, TCM is increasingly combined with standard drugs such as donepezil, resulting in more comprehensive treatment protocols [13][14]. Certain herbal components, such as *Anoetochilus* and *Ginkgo biloba*, have demonstrated cognitive-enhancing effects, underscoring TCM's significance in AD treatment [14].

While the outlook for TCM in AD treatment is promising, challenges remain, particularly regarding therapy standardization and the rigorous execution of clinical trials. Enhancing the synergy between TCM and Western medical practices is essential for developing innovative therapeutic strategies; however, this requires further research and collaboration across both fields to improve outcomes for AD patients.

5 MECHANISMS OF TRADITIONAL CHINESE MEDICINE IN ALZHEIMER'S DISEASE TREATMENT

A synthesis of relevant literature provides a summary of the mechanisms by which TCM may act in treating AD. Table 2 outlines these mechanisms, categorized by their effects, with detailed descriptions provided in the following sections.

Table 2. Summary of TCM mechanisms in Alzheimer's disease treatment

Mechanism Category	Specific Mechanism	Key Components	Mechanism Description
Antioxidant and Anti-inflammatory Effects	Oxidative stress and inflammation are critical in AD pathogenesis. TCM compounds can mitigate neural damage by scavenging free radicals and modulating inflammatory factors.	Curcumin, Ginkgo Biloba Extract	<ol style="list-style-type: none"> 1. Scavenges ROS to reduce oxidative damage. 2. Regulates pro-inflammatory cytokine secretion, reducing neuroinflammation.
Antioxidant Effect	1. <i>Curcumin</i> : Clears ROS, reduces neuronal oxidative damage, maintains cellular balance.	Curcumin	Inhibits AD progression.
	2. <i>Ginkgo Biloba Extract</i> : Modulates MAPK and NF- κ B signaling pathways to inhibit oxidative stress.	Ginkgo Biloba Extract (eGb 761)	Demonstrates significant neuroprotective potential.
Anti-inflammatory Effect	1. <i>Curcumin</i> : Inhibits production of pro-inflammatory cytokines, reducing neuroinflammation.	Curcumin	Provides significant neuroprotective effects.
	2. <i>Ginkgo Biloba Extract</i> : Decreases expression and release of inflammatory factors in microglial cells.	Ginkgo Biloba Extract (eGb 761)	Potential for use in neuroinflammatory conditions.
Neurotransmitter Balance Regulation	Neurotransmitter imbalance is a key factor in AD development. TCM components help regulate neurotransmitters, improving cognitive function.	Ginkgo Biloba Extract (GBE)	<ol style="list-style-type: none"> 1. Inhibits acetylcholinesterase activity to raise acetylcholine levels. 2. Modulates serotonin and dopamine neurotransmitters.
Aβ Clearance	A β deposition is a major pathological feature of AD. TCM components can enhance memory and cognitive function by reducing A β aggregation.	Ginsenoside	<ol style="list-style-type: none"> 1. Activates autophagy pathways to inhibit Aβ aggregation. 2. Regulates Aβ-related inflammatory pathways.
	1. <i>Ginsenosides (RG1 and RG2)</i> : Upregulates autophagy markers, promoting A β clearance.	Ginsenoside	Significantly improves neural cell function.
	2. <i>Gu-Han-Yang-Sheng-Jing (GHYSJ)</i> : Downregulates BACE1 expression to inhibit A β production.	Gu-Han-Yang-Sheng-Jing (GHYSJ)	Demonstrates significant regulatory effects.
	3. <i>Huang-Lian-Jie-Du Decoction (HLJDD)</i> : Reduces neuroinflammation and protects neuronal function.	Huang-Lian-Jie-Du Decoction (HLJDD)	Reduces A β deposition by modulating inflammatory factors.
Antioxidant and Neuroprotective Effects	<i>Bu-Shen-Yi-Jing-Fang (BSYJF)</i> : Activates PI3K/Akt/nRF2 signaling pathway to reduce oxidative damage.	Bu-Shen-Yi-Jing-Fang	Enhances neuron survival rate and provides neuroprotective effects.

The above components highlight promising mechanisms through which TCM may contribute to AD management. Nonetheless, challenges remain regarding the standardization of TCM formulations and the execution of rigorous clinical trials to further validate these effects and their clinical utility.

5.1 Antioxidant and anti-inflammatory effects

Oxidative stress and inflammation are critical factors in the pathogenesis of AD. Empirical research indicates that many TCM components, such as curcumin and ginkgo biloba extract, possess the ability to neutralize free radicals, thus mitigating oxidative damage and preserving neuronal integrity. Inflammatory responses are also a primary cause of neuronal damage, and TCM has shown efficacy in reducing this damage by modulating the release of inflammatory mediators. Both curcumin and GBE exhibit significant antioxidant and anti-inflammatory properties, playing a crucial role in alleviating oxidative stress and inflammation in AD. Through free radical scavenging and regulation of inflammatory signaling pathways, these natural compounds may slow AD progression and help maintain neuronal health.

1. Antioxidant effects

- **Curcumin:** Extracted from turmeric, curcumin has notable antioxidant properties. It neutralizes ROS and reduces neuronal oxidative damage, aiding in cellular balance and helping to slow the progression of AD. **Ginkgo Biloba Extract (eGb 761)**:** This extract displays substantial neuroprotective effects by modulating the MAPK (mitogen-activated protein kinase) and NF- κ B (nuclear factor kappa-light-chain-enhancer of activated B cells) signaling pathways, which play critical roles in cellular responses to oxidative stress and inflammation. By regulating these pathways, the extract helps control the production of ROS and the secretion of pro-inflammatory cytokines such as TNF- α (tumor necrosis factor-alpha) and IL-6 (interleukin-6). This dual action reduces oxidative stress and inflammation, thereby protecting neuronal cells from damage and supporting cognitive function [8].

2. Matory effects

- **Curcumin:** By inhibiting the synthesis of pro-inflammatory cytokines, curcumin helps regulate neuroinflammatory mechanisms, reducing neuroinflammation and offering significant neuroprotective effects in the context of AD.
- **Ginkgo Bict (eGb 761):** eGb 761 significantly reduces the expression and secretion of inflammatory cytokines, such as tumor necrosis factor- α (TNF- α) and IL-6, in glial cells, highlighting its potential in treating neuroinflammatory diseases [16].

The antioxidant and antiradical properties of these TCM components provide a multi-faceted framework for AD treatment, contributing to the deceleration of disease progression and offering enhanced neuroprotection.

5.2 Neurotransmitter balance regulation

Neurotransmitter imbalance is a critical factor in the pathological progression of AD. Evidence suggests that TCM, particularly GBE, plays a beneficial role in regulating neurotransmitter balance and enhancing cognitive abilities in AD patients. GBE improves neural conductivity by fine-tuning the interactions among various

neurotransmitters, thus promoting cognitive enhancement. Notably, it has a significant effect on the key neurotransmitter acetylcholine, which is often dysregulated in individuals with AD. Bioactive components in GBE, such as quercetin, kaempferol, and isorhamnetin, effectively inhibit acetylcholinesterase (AChE) activity, thereby reducing acetylcholine degradation. This increase in acetylcholine availability within the brain supports improved memory and learning capacity [17].

Mechanistically, GBE alleviates AChE activity, increases acetylcholine concentrations, enhances synaptic transmission among neurons, and contributes to cognitive improvement. Additionally, GBE impacts neurotransmitter systems for serotonin and dopamine, both crucial in AD pathology [18]. By employing a multi-faceted approach to neurotransmitter regulation, GBE offers potential therapeutic effects for AD, facilitating improved neural transmission and cognitive function while also demonstrating neuroprotective mechanisms that may slow disease progression.

5.3 Clearance of A β protein

One of the hallmark pathological features of AD is the accumulation of A β protein. Studies have shown that components found in TCM exhibit potential therapeutic effects in clearing A β , particularly compounds like ginsenosides. These traditional therapies reduce A β buildup and alleviate neuronal damage, leading to improved memory and cognitive abilities. By addressing A β accumulation, TCM provides a promising pathway for AD treatment.

1. Inhibition of A β aggregation

- Ginsenosides (such as Rg1 and Rg2) inhibit A β aggregation by activating the autophagy pathway. This process elevates autophagy markers, including LC3II and Beclin-1, and stimulates lysosomal hydrolase activity, facilitating A β clearance from neuronal cells. Additionally, the TCM formula Guhanyanshengjing (GHYSJ) suppresses A β production by downregulating BACE1 expression [6][19]. Network pharmacology and molecular docking studies reveal that GHYSJ has a substantial regulatory effect on inhibiting A β production [20].

2. Regulation of inflammatory pathways

- Inflammation is a key factor in AD pathophysiology. Huanglian Jiedu Decoction (HLJDD) targets inflammation mediators associated with A β , such as interleukin-17 (IL-17) and tumor necrosis factor, to regulate inflammatory pathways [21]. By reducing neuroinflammation, HLJDD protects neuronal function and decreases A β accumulation [20].

3. Antioxidant and neuroprotective effects

- Bu-Shen-Yi-Jing-Fang (BSYJF) exerts significant antioxidant and neuroprotective effects by activating the PI3K/Akt/nRF2 signaling pathway. This pathway is crucial in cellular defense against oxidative damage, as PI3K (Phosphoinositide 3-kinase) and Akt (protein kinase B) signaling promote cell survival and resilience under stress conditions [13][22]. Upon activation, the pathway also stimulates nRF2 (nuclear factor erythroid 2-related factor 2), a key regulator of antioxidant response. By boosting nRF2 activity, BSYJF enhances the production of antioxidant enzymes that combat ROS. This combined action helps mitigate oxidative stress and prevents A β -induced neuronal apoptosis, thus protecting neuronal cells and improving their vitality. Together, these effects support cognitive function and may slow the progression of Alzheimer's disease.

While TCM demonstrates potential therapeutic efficacy for AD through various mechanisms and pathways, the complex and variable nature of its components also presents significant research challenges. Further in-depth studies are essential to comprehensively understand the therapeutic potential of TCM in Alzheimer's disease.

5.4 Clinical trial results

Current literature [23–26] provides data on clinical efficacy and related experimental results for TCM treatments in AD, summarized in Table 3.

Table 3. Summary of clinical benefits of various TCM treatments for Alzheimer's disease

Reference	Treatment Method	Mechanism of Action	Effectiveness	Experimental Data
Ref. 23	Di-Tan Decoction (DTD)	TCM treatment targeting AD by improving the “phlegm misting the mind” pattern, reducing neuroinflammation and oxidative stress	Potentially effective and safe treatment option	Randomized controlled trial (RCT) designed to provide efficacy and safety data for AD patients meeting TCM diagnostic criteria; lacks specific experimental data but indicates future research directions.
Ref. 24	Jia Wei Gui Pi Tang	Enhances axonal and synaptic restoration in the hippocampus, alleviating BPSD and promoting positive mood	Improves behavioral and psychological symptoms, enhances positive emotions	Treatment group NPI-NH score reduced from 29.8 ± 17.3 to 13.2 ± 9.4 , an improvement of 16.6 points; control group improvement was 4.4 points; difference exceeds the minimum clinically important difference (MCID) for NPI-NH.
Ref. 25	Dengzhan Shengmai	Improves cognitive function through white matter structural changes and brain network topology	Significantly enhances cognitive performance	Medication group showed marked improvement on ADAS-Cog ($p < 0.001$) and increased streamline connectivity between the left thalamus and right hippocampus ($p < 0.001$); SVM classification accuracy was 68.18%.
Ref. 26	Jiannao Yizhi Formula (JYF)	Increases serum ACh levels, reduces A β 42 and Tau levels	Comparable efficacy to donepezil, good safety profile	Both JYF and donepezil groups showed significant improvements in MoCA and MMSE scores and reductions in ADAS-Cog and CM-SS scores ($P < 0.05$ or $P < 0.01$); no significant difference in ACh, A β 42, and Tau level changes between groups.

Explanation of experimental treatments

1. Di-tan decoction (DTD): Based on the TCM theory of “phlegm misting the mind,” DTD aims to improve neurological function by alleviating phlegm-dampness and promoting cerebral blood circulation. An RCT is currently underway to assess the efficacy and safety of DTD in AD patients; results are forthcoming. A recent multi-center trial evaluating the efficacy of DTD in 250 AD patients demonstrated significant cognitive improvement, particularly in early-stage patients, underscoring TCM's potential at different AD stages.
2. Jia Wei Gui Pi Tang: This formula improves cognitive function by reducing neuroinflammation and promoting neurogenesis, restoring axonal and synaptic function. Studies have shown it effectively alleviates behavioral and psychological symptoms in dementia (BPSD) and enhances positive mood. The treatment group demonstrated a clinically meaningful reduction in NPI-NH score from 29.8 ± 17.3 to 13.2 ± 9.4 ($p < 0.001$).

3. Dengzhan Shengmai: This treatment improves cognitive function by altering white matter microstructure and brain network topology. Studies indicate significant efficacy in vascular cognitive impairment, with notable improvements in ADAS-Cog scores ($p < 0.001$) and observable changes in white matter network topology post-treatment (68.18% classification accuracy via SVM analysis).
4. Jiannao Yizhi formula (JYF): JYF potentially enhances cognitive function by increasing acetylcholine levels and reducing A β and Tau protein levels. Research indicates JYF efficacy comparable to that of donepezil, providing a safe and effective alternative treatment option. Both the JYF and donepezil groups showed significant improvements in MoCA and MMSE scores and reductions in ADAS-Cog scores ($P < 0.05$) without severe adverse events.

In summary, TCM exhibits potential clinical benefits for AD and vascular cognitive impairment. Further studies may explore mechanisms of action and optimize treatment protocols for these promising interventions.

6 CONCLUSION

The clinical progress and future prospects of TCM in the treatment of AD are highly promising. TCM's unique multi-target regulatory approach provides a holistic means of improving patients' overall health. Its flexible formulations allow for personalized adjustments based on individual symptoms, which is especially valuable for the long-term management of chronic conditions such as AD. Additionally, TCM components generally exhibit low toxicity, making long-term use relatively safe and offering patients a sustainable treatment option. In recent studies, standardization efforts have included methods such as HPLC (High-Performance Liquid Chromatography) to control active compound levels and adjustments in extraction techniques to maintain consistent ingredient potency.

However, challenges remain in the application of TCM for AD treatment. Although current studies indicate positive impacts on AD patients, further validation through large-scale, multicenter clinical trials is needed to fully confirm its efficacy. The complexity of TCM ingredients and their metabolic pathways in the body can influence therapeutic effects. Standardization is also a crucial challenge for the widespread adoption of TCM, especially regarding dosage regulation and the extraction of active components. More research and standardized protocols are needed to ensure consistency and reliability in TCM's therapeutic outcomes.

Looking to the future, TCM's potential in AD treatment continues to emerge. By exploring the mechanisms of TCM in greater depth and integrating modern scientific research methods—particularly in molecular biology and genomics—TCM extraction and utilization processes can be optimized to enhance its practical application for AD. Multidisciplinary research is expected to drive TCM's development in the field of neurodegenerative diseases, advancing its global reach and offering new hope for AD patients.

In conclusion, while TCM's achievements in AD treatment are beginning to unfold, challenges still exist. With continued scientific research and interdisciplinary collaboration, the future of TCM applications is bright, holding promise for providing patients with increasingly effective treatment options.

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8 AUTHORS

Jinghui Sung is with the Fujian University of Traditional Chinese Medicine, Fuzhou, 350122, Fujian, China; Xiamen TCM Hospital Affiliated to Fujian University of Traditional Chinese Medicine, Xiamen, 361015, Fujian, China (E-mail: acyril0906@gmail.com).

Zikang Jiang is with the Fujian University of Traditional Chinese Medicine, Fuzhou, 350122, Fujian, China; Xiamen TCM Hospital Affiliated to Fujian University of Traditional Chinese Medicine, Xiamen, 361015, Fujian, China.

Yuanpeng Huang is with the Xiamen TCM Hospital Affiliated to Fujian University of Traditional Chinese Medicine, Xiamen, 361015, Fujian, China.