Journal of Clinical and Nursing Research, 2025, Volume 9, Issue 4
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Alleviative Treatments for Alzheimer's Disease and Early Ecological Intervention Strategies in the Community

Peihua Zhuang, Dongxing Wang, Shuyu Zhao, Peifang Lu*

Zhangjiang Community Health Service Center, Pudong New District, Shanghai 201210, China

**Author to whom correspondence should be addressed.*

Abstract: According to the data from the 7th national population census, the population aged 65 and above in China has reached 13.50%, indicating that the country has entered a deeply aging society. The health issues of the elderly have become a significant concern for society. Common brain diseases among the elderly, including cerebrovascular diseases, genetic factors, or long-term solitary living, can all lead to dementia, with Alzheimer's disease (AD) being the most common. Early symptoms of AD mainly include memory loss and difficulty concentrating, which are often mistaken for normal aging or stress-related issues and thus overlooked. AD lacks specific biomarkers and effective auxiliary diagnostic methods, making it difficult to accurately diagnose with existing imaging and neuroprotein indicators. Therefore, early detection of AD is very challenging. This article explores community-based early detection and intervention strategies from the perspectives of existing mechanism research, clinical manifestations, modern drug treatments, innovative explorations in traditional medicine, and community-appropriate technologies, aiming to construct an ecological management strategy.

Keywords: Alzheimer's disease(AD); Treatment; Community; Intervention

Online publication: April 29, 2025

1. Introduction

Under the trend of deep aging, AD, as a chronic progressive neurodegenerative disease, stealthily steals people's memory, cognition, and ability to live independently like a merciless thief, becoming a major public health issue faced by most countries and regions worldwide. The World Health Organization (WHO) has designated AD as a global public health priority. According to its estimates, the global prevalence of dementia has exceeded 55 million and is expected to rise to 152.8 million by 2050 [1]. In China, the number of existing AD and other dementia cases exceeds 16.99 million, and it has become the fifth leading cause of death among the Chinese population. According to the "Innovative White Paper on the Construction of an Ecological System for Precise Prevention, Diagnosis and Treatment of AD" led by the China Brain Health Action Expert Committee and

others: In 2019, the total cost of AD and related dementias reached approximately RMB 1.35 trillion, and it is estimated that by 2030, the total socioeconomic cost of AD patients will reach about RMB 3.2 trillion RMB. However, early intervention could delay the onset of AD by five years, potentially reducing related expenditures by 45%. Therefore, precise early prevention and intervention for AD are crucial. Integrating existing treatment technologies serves as the foundation, while exploring more accurate community-based intervention ecosystems represents the way forward. The goal is to effectively delay the onset of AD, practice preventive healthcare to stop minor issues from escalating, improve the prognosis and quality of life for the elderly, and significantly alleviate the financial and caregiving burdens on families.

2. Pathophysiological mechanism

The pathophysiology of AD is complex. Genetic susceptibility, glial proliferation, neuroinflammation, imbalance in the production and clearance of reactive oxygen species (ROS), mitochondrial dysfunction, sleep disturbances, reduced brain metabolism, and excessive accumulation of metal ions are all related to the pathogenesis of AD [2 ,3]. Due to AD progressing in a latent neuropathological form, it is considered one of the greatest challenges in modern neuroscience and medical diagnostics [4].

In recent years, theoretical discussions around the pathophysiology of AD have mainly been based on genetic and neuropathological research. The most prominent histopathological feature of AD is the accumulation of abnormally folded proteins in the brain. High concentrations of abnormal proteins lead to intracellular neurofibrillary tangles and extracellular amyloid plaques (β-amyloid peptides are proteolytic fragments of the transmembrane receptor amyloid precursor protein [APP]. Increased enzymatic abnormal cleavage of APP by β-secretase leads to β-amyloid misfolding, making it more likely to aggregate extracellularly and resulting in the formation and accumulation of extracellular β-amyloid plaques and intracellular tau neurofibrillary tangles) [5, 6]. Existing neuropathological, genetic, and molecular biological evidence indicates that aggregates of β-amyloid (Aβ) protofibrils and neurofibrillary tangles in the brain compromise the integrity of neurons and synaptic function in relevant brain regions, leading to cognitive impairment [7].

The following risk factors are commonly recognized, including but not limited to: Low education level, midlife hypertension, midlife obesity, hearing loss, late-life depression, diabetes, lack of physical activity, smoking, and social isolation [8]. In addition, apolipoprotein E (APOE) is considered the strongest genetic risk factor for sporadic AD [9]. Other hypotheses regarding AD, such as the amyloid cascade, Tau hyperphosphorylation, neuroinflammation, oxidative stress, mitochondrial dysfunction, cholinergic, and vascular hypotheses, are not mutually exclusive and all play roles in the development of AD. The amyloid cascade hypothesis remains the most widely studied hypothesis to date, but there are still no sufficiently advanced diagnostic tools for early identification and screening of dementia, and diagnosis and treatment still rely on clinical manifestations.

3. Clinical manifestations

AD is a progressive neurodegenerative disease that primarily affects individuals aged ≥ 65 years. Its typical form usually centers on memory, particularly manifesting as declining cognitive function and accelerated memory

loss, which impairs daily activities [10]. Alzheimer's disease progresses gradually, starting with the preclinical stage, followed by mild cognitive and/or behavioral impairment, and ultimately leading to Alzheimer's dementia. Atypical forms of AD manifest with symptoms unrelated to memory, referred to as heterogeneous clinical features, including, anxiety, agitation, apathy, anhedonia, irritability, delusions, hallucinations, euphoria, abnormal motor changes, and changes in sleep or appetite, which differ from the more common memory-centric typical AD symptoms and are more subtle and less obvious [11, 12]. For example, executive dysfunction AD and behavioral variant AD have replaced the term frontal AD. High-order visual function impairments such as posterior cortical atrophy may mimic other conditions (e.g., depression, anxiety), and are often mistaken for signs of normal aging or stress, thus being overlooked. Moreover, current examinations, including imaging and neuroprotein markers, are insufficient for accurate diagnosis. Unlike common tumors and other diseases, AD lacks specific biomarkers and reliable auxiliary diagnostic tools. Therefore, early detection of AD is extremely challenging. In the face of various atypical manifestations, using tailored therapeutic interventions combining pharmacologic and non-pharmacologic strategies is essential for effective disease control.

4. Modern pharmacologic treatment

The etiology of AD is complex, as genetic susceptibility, aging, inflammation, oxidative stress, and protein homeostasis imbalance all contribute to its development and progression. The histological hallmarks of AD are the formation and accumulation of amyloid-β plaques and tau tangles in the central nervous system. These histological features trigger neuroinflammation and disrupt the physiological structure and function of neurons, leading to cognitive dysfunction. Currently, most treatment approaches available for AD primarily focus on symptomatic relief. In recent years, research in neuroprotection and the promotion of neuroplasticity has increased, exploring disease-modifying therapies (DMT) targeting the biology of the disease, aiming to improve AD subtypes through target diversity and potentially slow or reverse disease progression.

4.1. Medications to alleviate cognitive symptoms

Cholinesterase inhibitors are currently the most widely used drugs in the treatment of AD. Acetylcholinesterase inhibitors (AChEIs) are believed to increase acetylcholine at neuromuscular junctions to counter the damaged cholinergic pathways observed in AD. However, as AChEIs increase systemic acetylcholine, they can cause adverse effects similar to overstimulation of the parasympathetic nervous system (PNS), such as bradycardia, diarrhea, hypotension, and urinary incontinence. PNS overstimulation increases the risk of syncope in patients with hypotension and cardiac conduction disorders, thereby further raising the risk of fractures and concussions [13]. Donepezil, the first second-generation non-competitive, reversible acetylcholinesterase (AChE) inhibitor, was approved by the FDA in 1996 for the treatment of mild, moderate, and severe AD dementia [14–16]. It is one of the most commonly prescribed medications for AD patients. As an orally administered reversible AChEI, it has high affinity for AChE, binds reversibly to it, thereby reducing synaptic ACh hydrolysis and improving cholinergic neurotransmission. It also activates the PI3K/Akt pathway and enhances oligodendrocyte differentiation to reduce Aβ-induced toxicity, or activates the sigma-1 receptor to regulate calcium signaling, cell defense, and neurotransmitter release to prevent Aβ toxicity. Meta-analyses have shown that among 2,847 patients, Donepezil improved Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) scores, but also caused adverse effects such as nausea, vomiting, diarrhea, fatigue, headache, and dizziness [17].

Rivastigmine, available as both oral and transdermal patch formulations, was approved by the FDA in 2000 for the treatment of AD and Parkinson's disease [18–21]. It is a slow, reversible dual inhibitor of AChE and butyrylcholinesterase, selectively targeting the G1 subtype of AChE. This mechanism enhances cholinergic function and improves psychological functions like memory and thinking, without hepatotoxicity, but its effects may diminish as the disease progresses. Studies have shown that it improves cognitive and overall clinical function in moderate to late-stage AD patients, but adverse reactions such as diarrhea, nausea, vomiting, dizziness, blurred vision, weight loss, tremors, confusion, and abdominal pain have also been reported [22–25]. Galantamine, an alkaloid derived from the plant *Galanthus nivalis* discovered in the early 1950s, was approved by the FDA in 2001 for the treatment of mild to moderate AD [26–28]. As an orally administered AChEI, it is well-tolerated and known to improve function, cognition, and daily activities in mild to moderate AD patients over a short period (approximately 6 months). It acts as a reversible competitive AChE inhibitor that enhances ACh accumulation in the brain and increases its action on nicotinic receptors, thereby facilitating cholinergic neurotransmission in the CNS. Studies have shown its efficacy in improving or slowing cognitive impairment, but mild to moderate nausea, as well as reports of risk factors of syncope, delirium, and QT interval prolongation, have also been noted [29–32].

Glutamate modulators are often used in clinical settings alongside cholinesterase inhibitors to enhance efficacy. Memantine, an N-methyl-D-aspartate (NMDA) receptor antagonist, was approved by the FDA in 2003 for the treatment of moderate to severe AD [33]. It prevents excessive NMDA stimulation and neuronal death by blocking current through NMDA receptor channels and inhibiting calcium influx caused by chronic glutamate-induced NMDA receptor activation. Compared to a placebo, it can delay cognitive and functional decline and is well-tolerated. Most adverse reactions, such as agitation, dizziness, falls, accidental injury, flu-like symptoms, headache, and diarrhea, are mild to moderate, but patients allergic to memantine hydrochloride should avoid it [34, 35].

4.2. Disease-modifying therapies

Monoclonal antibody-mediated plaque-clearing therapies have also been reported in numerous studies. Based on the amyloid cascade hypothesis, these interventions target β-amyloid accumulation in brain parenchyma, aiming to counteract the neurofibrillary tangles, vascular changes, microglial and astrocyte activation, as well as neuronal atrophy and loss associated with AD pathophysiology. Recent studies have found that monoclonal antibodies can clear tau or β-amyloid plaque aggregates and alter disease progression [36]. Aducanumab, approved in 2021, was the first FDA-approved monoclonal antibody targeting Aβ [37, 38]. It works by targeting and removing aggregated Aβ to reduce amyloid plaque burden in the brain and is used to treat mild AD. Studies have shown that high-dose use significantly slows cognitive decline in research subjects, lowers plasma tau levels, and reduces amyloid burden on amyloid PET scans [39].

However, adverse effects include ARIA-E, ARIA-H, nasopharyngitis, superficial siderosis, dizziness, altered mental status, delirium, gait disturbance, generalized tonic-clonic seizures, and headache. Lecanemab, administered intravenously, was the second drug targeting AD pathophysiology to receive accelerated FDA approval in January 2023 [40, 41]. It is a humanized monoclonal antibody that binds with high affinity to neurotoxic soluble Aβ protofibrils, reducing Aβ protofibril aggregation in astrocytes and thus lowering amyloid plaque burden to yield clinical benefits and disease improvement. Studies have shown that it reduces amyloid burden on amyloid PET, delays cognitive decline and overall functional deterioration, but adverse reactions include infusion-related reactions, ARIA-H, headache, and falls [42]. Other monoclonal antibody therapies

include: Donanemab is mainly used to clear insoluble β-amyloid plaques in the brain; Semorinemab is an anti-tau monoclonal antibody, among others.

4.3. Medications for treating behavioral and psychological symptoms of dementia

Brexpiprazole is a partial agonist of 5-HT1A, D2, and D3, as well as an antagonist of 5-HT2A, 5-HT2B, 5-HT7, α1A, α1B, α1D, and α2C receptors, and was approved by the FDA on May 11, 2023, as an atypical antipsychotic for the treatment of agitation associated with AD dementia [43, 44]. Due to its effects on dopaminergic and serotonergic receptors, it reduces neuronal excitability and also leads to mood improvement in patients with BPSD. Brexpiprazole binds effectively to serotonergic and α1B receptors, thereby reducing extrapyramidal symptoms associated with antipsychotic drugs. Due to its reduced binding to H1 receptors, it also exhibits mild sedative effects. However, some studies have documented mild to moderate adverse reactions such as nasopharyngitis, headache, dizziness, urinary tract infection, insomnia, and somnolence, and have suggested close monitoring of cognitive impairment, dystonia, akathisia, neutropenia, and agranulocytosis during treatment [43, 45]. Suvorexant is a dual orexin receptor antagonist that blocks the action of orexin-1 and -2 receptors, thereby aiding in sleep initiation and maintenance [46, 47]. It was initially developed for the management of insomnia and was approved by the FDA in 2020 for treating sleep disturbances in mild to moderate AD. Some studies have shown its most common adverse reaction is somnolence; other common reactions include diarrhea, dry mouth, upper respiratory tract infection, headache, dizziness, fatigue, dyspepsia, and peripheral edema, but it is contraindicated in patients with narcolepsy with cataplexy [47–50].

4.4. Clinical exploratory new applications based on the brain-gut axis theory and other mechanisms

In recent years, an increasing number of studies have begun to focus on dietary and gut microbiota changes for the prevention and management of neurodegenerative diseases, and have re-evaluated drug selection based on mechanisms such as the brain-gut axis theory, including pharmacological investigations into antagonizing the toxicity of abnormal amyloid-β and tau proteins, reducing oxidative stress and pro-inflammatory responses, and restoring neural plasticity [51–53]. Among them, the representative drug GV-971 (Sodium oligomannate) is an oligosaccharide drug extracted from algae that can alleviate neuroinflammatory responses and improve the pathological progression of AD by regulating the balance of gut microbiota and reducing the overgrowth of pro-inflammatory bacteria [54–57]; it protects neurons from damage by inhibiting Aβ aggregation and abnormal tau phosphorylation [58, 59]; through modulation of gut microbiota and direct neuroprotective effects, it shows certain therapeutic potential. In the future, with more clinical and basic research, these exploratory new applications are expected to offer new treatment options for AD patients.

5. Traditional Chinese medicine treatment

There is no specific term for “AD” in ancient TCM texts, but it is classified under syndromes such as “idiocy”, “dementia”, and “forgetfulness” according to syndrome differentiation and treatment. Traditional Chinese medicine has a long history of understanding this condition, and ancient texts include:

(1) Records of Yijianzhi: “In old age, sudden memory loss may occur, making it difficult to distinguish worldly matters and recognize familiar guests or friends”.

(2) Lingshu·Tiannian Pian: Chapter on Natural Lifespan: "At sixty, the heart Qi begins to decline, leading to anxiety, sadness, and weakened Qi and blood, hence a preference for lying down".
(3) Zhang Jiebin in Ming Dynasty's Jingyue's Complete Works: Miscellaneous Diseases, "In dementia… may result from depression, melancholy, unfulfilled desires, overthinking, doubts, or fright, gradually leading to dementia…".
(4) The Compendium of Materia Medica·Xinyi (Magnolia Bud) by Li Shizhen in Ming Dynasty stated "The brain is the residence of the original spirit".
(5) Shen Jin'ao's The Illuminating Guide to the Origins and Development of Miscellaneous Diseases in Qing Dynasty: "Forgetfulness after stroke".

The term "dementia" first appeared in the Han Dynasty's Biography of Hua Tuo and was also named "idiocy" in A-B Classic of Acupuncture and Moxibustion written in Western Jin Dynasty and The Great Compendium of Acupuncture and Moxibustion written in Ming Dynasty. Records of Syndrome Differentiation first established the "Idiocy Disorder" section for differentiation and treatment. Traditional TCM theory believes that the kidneys store essence and are the root of congenital constitution. Essence generates marrow, and the brain is the sea of marrow and the residence of the original spirit. As people age, the true yin and yang in the kidney decline, leading to insufficient transformation of essence, resulting in deficiency of essence and blood and emptiness of the marrow sea, causing the brain to lack nourishment and wither. Withering leads to loss of mental clarity, dullness, and dementia. In addition, as Qi and blood gradually decline and the meridians become obstructed, the residence of the original spirit loses its acuity, and cognitive abilities fail to manifest externally, resulting in progressive dementia.

5.1. Chinese medicine treatment

Syndrome differentiation and treatment is the essence of TCM theory. Under its guidance, herbal medicines differ from chemically synthesized drugs. Chinese medicine expands blood vessels, effectively improves cerebral blood supply, scavenges free radicals, and counters excitatory amino acid toxicity, mainly by regulating the balance of Yin and Yang and the circulation of Qi and blood to improve AD symptoms. Many single-compound extracts from traditional Chinese medicine have been confirmed to exert neuroprotective effects [60–66]. For instance, the Ginkgo biloba extract EGb761 can reverse ischemia-induced reductions of cyclooxygenase III mRNA in hippocampal CA1 neurons, inhibit nitric oxide synthesis, scavenge free radicals, and reduce lipid peroxidation, thereby providing neuroprotection.

Salidroside, a component of *Rhodiola rosea*, protects neural stem cells by eliminating intracellular free radicals and enhances hippocampal neurogenesis. Ganoderma polysaccharides from *Ganoderma lucidum* can inhibit apoptosis and possess antitumor, immunomodulatory, hypoglycemic, antioxidant, lipid-lowering, and anti-aging properties. *Polygala tenuifolia*, known for its sedative and cognition-enhancing effects, is commonly used to treat memory disorders, insomnia, and neurasthenia. Its extract, tenuigenin (TEN), can alleviate oxidative damage in cells, reduce the expression of inflammatory factors, and provide cellular protection. *Ophiopogon japonicus*, used to moisten the lungs, nourish Yin, clear the heart, and relieve restlessness, contains ophiopogonin D, which has anti-inflammatory, antioxidant, and antithrombotic pharmacological effects.

Chinese herbal compound preparations intervene in the complex pathogenesis of AD through multi-target and multi-pathway actions, especially in neuroprotection, neurotrophic/regenerative effects, and mitochondrial and synaptic protection [67–71]. Recent studies based on gut microbiota have further explored how herbal formulas

may promote AD progression by increasing gut and blood-brain barrier permeability, activating central nervous system inflammation, enhancing oxidative stress, and modulating neurotransmitter levels.

5.2. Acupuncture treatment

Acupuncture is a vital traditional medical therapy in China and has long played a key role in the treatment of AD. Modern studies show that[72–74] traditional acupuncture improves AD symptoms by regulating the abnormal neuronal cell cycle, such as electroacupuncture promoting synaptic plasticity and damage repair in hippocampal neurons in AD model mice, thereby improving learning and memory in AD rats [75,76]. Acupuncture stimulation improves learning and memory in AD rats by degrading β-amyloid (Aβ) [77]. Signaling pathways triggered by acupuncture can ameliorate AD-related pathological changes such as abnormal Aβ deposition, tau hyperphosphorylation, synaptic dysfunction, and neuronal apoptosis [78,79]. Electroacupuncture can reduce Aβ neurotoxicity to improve AD symptoms [80]. Acupuncture alleviates AD symptoms by targeting mitochondrial dynamic damage and dysfunction [81, 82]. Moxibustion on the Governing Vessel accelerates autophagic clearance of abnormal Aβ1-42 deposition in the brains of APP/PS1 double-transgenic AD mice [83]. Acupoint catgut embedding can improve cognition and compliance in AD patients [84]. Auricular acupoint therapy improves symptoms like forgetfulness and insomnia commonly seen in early AD and MCI patients by stimulating specific areas, unblocking meridians, and adjusting cerebral qi-blood circulation [85].

5.3. Other therapies

TCM emphasizes physical exercise and mental cultivation. Besides taking herbal medicine, this disease can also be managed through external TCM therapies, emotional care, and five-tone music therapy. Music is an art that transcends language and resonates with the soul, and music therapy offers unique advantages unmatched by other psychological therapies. The use of vocalization for health preservation has a rich history in ancient China; the Book of Music from the Spring and Autumn Period stated, “Music can regulate people’s hearts” and “Use music to govern the mind”. Studies show that after musical intervention, negative emotions, loneliness, and feelings of neglect and pain in elderly populations significantly improve. It also supports residual memory, emotional wellbeing, and thinking speed in early-stage dementia patients, and is considered a low-cost but important method for enhancing neuropsychological, cognitive, and social functioning [86–89].

Traditional Chinese Daoyin therapy, guided by theories of visceral Yin-Yang balance and meridian Qi-blood circulation, is a practice involving traditional physical exercises that integrate voluntary control of bodily movements, breathing, and mental focus. This therapy aims to enhance the body’s immunity and regulate sub-health conditions. It is believed to strengthen the body, prevent and treat diseases, facilitate meridian flow, promote Qi and blood circulation, harmonize internal organs, regulate emotions, and promote longevity [90–92]. This method originated in the Spring and Autumn Period and matured during the Han Dynasty; the Yellow Emperor’s Internal Classic: On the Appropriate Methods for Different Conditions was the first to document it as a treatment: “The central region is flat and moist, where heaven and earth produce all things. The people eat mixed food and do not work hard, so diseases like atrophy and cold-heat are common and should be treated with qigong and massage”. The Inscription on the Jade Pendant for Guiding Qi unearthed at Mawangdui details Qigong health methods, stating: “Breath movement, when deep, stores energy; when stored, it extends... in harmony, life is nurtured; in opposition, death ensues”. Traditional routines such as Wuqinxi, Eight-Section Brocade, Muscle-Tendon Change Classic, and Tai Chi are considered moderate-intensity aerobic exercises.

Practicing Tai Chi has been shown to have positive effects on cardiovascular health, balance, and emotional regulation in the elderly, and can effectively improve both cognitive and physical functions, thereby enhancing their quality of life.

6. Conclusion

Alzheimer's disease is a complex neurodegenerative disorder, and early intervention can significantly slow progression and improve quality of life. However, patients usually seek medical help only after developing obvious memory impairments, by which time the disease has often advanced to irreversible mid-to-late stages with limited treatment efficacy. Due to its progressive nature and the lack of definitive treatments to halt or reverse its course, AD remains a major public health challenge. Although no cure currently exists, with ongoing scientific progress, the key to conquering AD will be found, preserving memory, and restoring vitality to life. While seeking a path through the fog, it is essential to provide proactive and effective symptomatic relief, improving or delaying disease onset through functional reconstruction and compensatory mechanisms. Specific drugs and pathological mechanisms are still under continuous investigation, and their safety and optimal dosing require further research and observation. Addressing the challenges of globalization requires concerted efforts from the entire society. It is essential to leverage all known and effective diagnostic and therapeutic approaches, eliminate regional biases, and shift appropriate treatment strategies toward early-stage preventive interventions. Enhancing public science education, building a community-based ecosystem for intervention and prevention, and narrowing the gap between the current realities of aging and rising disease prevalence and the arrival of transformative therapies are of critical importance. Such efforts not only benefit individuals and families affected by AD, but also provide support for all those approaching old age. This may become a key point of action at the community level to delay or halt the progression of AD. Exploring and innovatively applying the long-standing practices of traditional medicine can help establish an AD treatment and intervention model with distinctive Chinese characteristics. Implementing more preventive and interventional measures at earlier stages may help reduce the disease burden, diversify treatment options, enhance health awareness within ecological communities, and generate collective health benefits, potentially opening up new possibilities.

Funding

Pudong New District "National Comprehensive Reform Experimental Zone for Traditional Chinese Medicine Development" Construction Project (Project No.: PDZY-2024-1003)

Disclosure statement

The authors declare no conflict of interest.

References

[1] GBD 2019 Dementia Forecasting Collaborators, 2022, Estimation of the Global Prevalence of Dementia in 2019 and Forecasted Prevalence in 2050: An Analysis for the Global Burden of Disease Study 2019. Lancet Public Health, 7: e105–25.

[2] Al-Ghraiybah NF, Wang J, Alkhalifa AE, et al., 2022, Glial Cell-Mediated Neuroinflammation in Alzheimer's Disease. Int J Mol Sci, 23: 10572.

[3] Monteiro AR, Barbosa DJ, Remiao F, et al., 2023, Alzheimer's Disease: Insights and New Prospects in Disease Pathophysiology, Biomarkers and Disease-Modifying Drugs. Biochem Pharmacol, 211: 115522.

[4] Nasreddine Z, Garibotto V, Kyaga S, et al., 2023, The Early Diagnosis of Alzheimer's Disease: A Patient-Centred Conversation with the Care Team. Neurol Ther, 12: 11–23.

[5] Da Mesquita S, Ferreira AC, Sousa JC, et al., 2016, Insights on the Pathophysiology of Alzheimer's Disease: The Crosstalk Between Amyloid Pathology, Neuroinflammation and the Peripheral Immune System. Neurosci Biobehav Rev, 68: 547–562.

[6] Serrano-Pozo A, Das S, Hyman BT, 2021, APOE and Alzheimer's Disease: Advances in Genetics, Pathophysiology, and Therapeutic Approaches. Lancet Neurol, 20: 68–80.

[7] Chouliaras L, Rutten BP, Kenis G, et al., 2010, Epigenetic Regulation in the Pathophysiology of Alzheimer's Disease. Prog Neurobiol, 90: 498–510.

[8] Livingston G, Huntley J, Sommerlad A, et al., 2020, Dementia Prevention, Intervention, and Care: 2020 Report of the Lancet Commission. Lancet, 396: 413–446.

[9] Serrano-Pozo A, Das S, Hyman BT, 2021, APOE and Alzheimer's Disease: Advances in Genetics, Pathophysiology, and Therapeutic Approaches. Lancet Neurol, 20: 68–80.

[10] 2021 Alzheimer's Disease Facts and Figures, 2021, Alzheimers Dement, 17(3): 327–406.

[11] Cerejeira J, Lagarto L, Mukaetova-Ladinska EB, 2012, Behavioral and Psychological Symptoms of Dementia. Front Neurol, 3: 73.

[12] Jones D, Pelak V, Rogalski E, 2024, Atypical Presentations of Alzheimer Disease. Continuum (Minneap Minn), 30(6): 1614–1641.

[13] Singh R, Sadiq NM, 2024, Cholinesterase Inhibitors. StatPearls, Treasure Island, FL: StatPearls Publishing, Florida.

[14] Adlimoghaddam A, Neuendorff M, Roy B, et al., 2018, A Review of Clinical Treatment Considerations of Donepezil in Severe Alzheimer's Disease. CNS Neurosci Ther, 24: 876–888.

[15] Cui X, Guo YE, Fang JH, et al., 2019, Donepezil, a Drug for Alzheimer's Disease, Promotes Oligodendrocyte Generation and Remyelination. Acta Pharmacol Sin, 40: 1386–1393.

[16] Solntseva EI, Kapai NA, Popova OV, et al., 2014, The Involvement of Sigma1 Receptors in Donepezil-Induced Rescue of Hippocampal LTP Impaired by Beta-Amyloid Peptide. Brain Res Bull, 106: 56–61.

[17] Zhang X, Lian S, Zhang Y, et al., 2022, Efficacy and Safety of Donepezil for Mild Cognitive Impairment: A Systematic Review and Meta-Analysis. Clin Neurol Neurosurg, 213: 107134.

[18] Jann MW, 2000, Rivastigmine, a New-Generation Cholinesterase Inhibitor for the Treatment of Alzheimer's Disease. Pharmacotherapy, 20: 1–12.

[19] Jann MW, Shirley KL, Small GW, 2002, Clinical Pharmacokinetics and Pharmacodynamics of Cholinesterase Inhibitors. Clin Pharmacokinet, 41: 719–739.

[20] Rosler M, Anand R, Cicin-Sain A, et al., 1999, Efficacy and Safety of Rivastigmine in Patients with Alzheimer's Disease: International Randomised Controlled Trial. BMJ, 318: 633–638.

[21] Khoury R, Rajamanickam J, Grossberg GT, 2018, An Update on the Safety of Current Therapies for Alzheimer's Disease: Focus on Rivastigmine. Ther Adv Drug Saf, 9: 171–178.

[22] Farlow M, Anand R, Messina J Jr, et al., 2000, 52-Week Study of the Efficacy of Rivastigmine in Patients with Mild to Moderately Severe Alzheimer's Disease. Eur Neurol, 44: 236–241.

[23] Inglis F, 2002, The Tolerability and Safety of Cholinesterase Inhibitors in the Treatment of Dementia. Int J Clin Pract Suppl, 127: 45–63.

[24] Karaman Y, Erdoğan F, Köseoğlu E, et al., 2005, 12-Month Study of the Efficacy of Rivastigmine in Patients with Advanced Moderate Alzheimer's Disease. Dement Geriatr Cogn Disord, 19: 51–56.

[25] Hansen RA, Gartlehner G, Webb AP, et al., 2008, Efficacy and Safety of Donepezil, Galantamine, and Rivastigmine for the Treatment of Alzheimer's Disease: A Systematic Review and Meta-Analysis. Clin Interv Aging, 3: 211–225.

[26] Scott LJ, Goa KL, 2000, Galantamine: A Review of its Use in Alzheimer's Disease. Drugs, 60: 1095–1122.

[27] Lilienfeld S, 2002, Galantamine – A Novel Cholinergic Drug with a Unique Dual Mode of Action for the Treatment of Patients with Alzheimer's Disease. CNS Drug Rev, 8: 159–176.

[28] Raskind MA, 2003, Update on Alzheimer Drugs (Galantamine). Neurologist, 9: 235–240.

[29] Razay G, Wilcock GK, 2008, Galantamine in Alzheimer's Disease. Expert Rev Neurother, 8: 9–17. doi:10.1586/14737175.8.1.9.

[30] Richarz U, Gaudig M, Rettig K, et al., 2014, Galantamine Treatment in Outpatients with Mild Alzheimer's Disease. Acta Neurol Scand, 129: 382–392.

[31] Olin J, Schneider L, 2002, Galantamine for Alzheimer's Disease. Cochrane Database Syst Rev, 3: CD001747.

[32] Fisher AA, Davis MW, 2008, Prolonged QT Interval, Syncope, and Delirium with Galantamine. Ann Pharmacother, 42: 278–283.

[33] Johnson JW, Kotermanski SE, 2006, Mechanism of Action of Memantine. Curr Opin Pharmacol, 6: 61–67.

[34] Reisberg B, Doody R, Stöffler A, et al., 2003, Memantine in Moderate-to-Severe Alzheimer's Disease. N Engl J Med, 348:1333–1341.

[35] Farlow MR, Graham SM, Alva G, 2008, Memantine for the Treatment of Alzheimer's Disease: Tolerability and Safety Data from Clinical Trials. Drug Saf, 31: 577–585.

[36] Vitek GE, Decourt B, Sabbagh MN, 2023, Lecanemab (BAN2401): An Anti-Beta-Amyloid Monoclonal Antibody for the Treatment of Alzheimer Disease. Expert Opin Investig Drugs, 32(2):89–94.

[37] Tampi RR, Forester BP, Agronin M, 2021, Aducanumab: Evidence from Clinical Trial Data and Controversies. Drugs Context, 10: 1–9.

[38] Cummings J, Aisen P, Apostolova L, et al., 2021, Aducanumab: Appropriate Use Recommendations. J Prev Alzheimers Dis, 8: 398–410.

[39] Budd Haeberlein S, Aisen P, et al., 2022, Two Randomized Phase 3 Studies of Aducanumab in Early Alzheimer's Disease. J Prev Alzheimers Dis, 9: 197–210.

[40] Esai Inc, Biogen, 2023, Lequembi: Prescribing Information. Nutley, NJ: Esai Inc, United Kingdom.

[41]van Dyck CH, Swanson CJ, Aisen P, et al., 2023, Lecanemab in Early Alzheimer's Disease. New England Journal of Medicine, 388: 9–21.

[42]Lecanemab in Early Alzheimer's Disease. N Engl J Med. van Dyck CH, Swanson CJ, Aisen P, et al 2023. 388(1):9-21.

[43] Grossberg GT, Kohegyi E, Mergel V, Josiassen MK, Meulien D, Hobart M, et al., 2020, Efficacy and Safety of Brexpiprazole for the Treatment of Agitation in Alzheimer's Dementia: Two 12-Week, Randomized, Double-Blind, Placebo-Controlled Trials. American Journal of Geriatric Psychiatry, 28: 383–400.

[44] Stahl SM, 2016, Mechanism of Action of Brexpiprazole: Comparison With Aripiprazole. CNS Spectrums, 21: 1–6.

[45] Yunusa I, Rashid N, Demos GN, et al., 2022, Comparative Outcomes of Commonly Used Off-Label Atypical Antipsychotics in the Treatment of Dementia-Related Psychosis: A Network Meta-Analysis. Advances in Therapy, 39: 1993–2008.

[46] Merck, 2023, Merck Receives Approval for BELSOMRA (Suvorexant) C-IV Label Update to Include Findings From Study of Insomnia in Patients With Mild-to-Moderate Alzheimer's Disease. Internal Report.

[47] Stahl SM, 2016, Mechanism of Action of Suvorexant. CNS Spectrums, 21: 215–218.

[48] Hanazawa T, Kamijo Y, 2019, Effect of Suvorexant on Nocturnal Delirium in Elderly Patients With Alzheimer's Disease: A Case-Series Study. Clinical Psychopharmacology and Neuroscience, 17: 547–550..

[49] Herring WJ, Ceesay P, Snyder E, et al., 2020, Polysomnographic Assessment of Suvorexant in Patients With Probable Alzheimer's Disease Dementia and Insomnia: A Randomized Trial. Alzheimer's & Dementia, 16: 541–551.

[50] Rhyne DN, Anderson SL, 2015, Suvorexant in Insomnia: Efficacy, Safety and Place in Therapy. Therapeutic Advances in Drug Safety, 6: 189–195.

[51] Gates EJ, Bernath AK, Klegeris A, 2022, Modifying the Diet and Gut Microbiota to Prevent and Manage Neurodegenerative Diseases. Reviews in Neuroscience, 33(7): 767–787.

[52] Ettcheto M, Busquets O, Cano A, Sánchez-Lopez E, Manzine PR, Espinosa-Jimenez T, et al., 2021, Pharmacological Strategies to Improve Dendritic Spines in Alzheimer's Disease. Journal of Alzheimer's Disease, 82(S1): S91–S107.

[53] Peng G, Li M, Meng Z, 2023, Polysaccharides: Potential Bioactive Macromolecules for Alzheimer's Disease. Frontiers in Nutrition, 10: 1249018.

[54] Martins M, Silva R, Pinto MM, et al., 2020, Marine Natural Products, Multitarget Therapy and Repurposed Agents in Alzheimer's Disease. Pharmaceuticals, 13(9): 242.

[55] Klose J, Griehl C, Roßner S, et al., 2022, Natural Products From Plants and Algae for Treatment of Alzheimer's Disease: A Review. Biomolecules, 12(5): 694.

[56] Ma Y, Liu S, Zhou Q, et al., 2024, Approved Drugs and Natural Products at Clinical Stages for Treating Alzheimer's Disease. Chinese Journal of Natural Medicine, 22(8): 699–710.

[57] Wang X, Sun G, Feng T, et al., 2019, Sodium Oligomannate Therapeutically Remodels Gut Microbiota and Suppresses Gut Bacterial Amino Acids–Shaped Neuroinflammation to Inhibit Alzheimer's Disease Progression. Cell Research, 29(10): 787–803.

[58] Xiao S, Chan P, Wang T, et al., 2021, A 36-Week Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Phase 3 Clinical Trial of Sodium Oligomannate for Mild-to-Moderate Alzheimer's Dementia. Alzheimer's Research & Therapy, 13(1): 62.

[59] Wang Y, Li H, et al., 2021, Efficacy and Safety of GV-971 in Patients With Mild-to-Moderate Alzheimer's Disease: A Phase 3 Randomized Clinical Trial. Alzheimer's & Dementia, 17(Suppl 10): e058107.

[60] Yang H, 2014, Research Progress on the Treatment of Alzheimer's Disease With Chinese Herbal Extracts. Journal of Hubei University of Chinese Medicine, 16(1): 113–115.

[61] Li Y, Liu Y, Zhang G, et al., 2024, Research Progress on the Treatment of Alzheimer's Disease With Single Chinese Herbal Medicines. Journal of Changzhi Medical College, 38(6): 470–474.

[62] Xue Y, Li Y, Wang Y, et al., 2024, Synergistic Effect and Mechanism of Ginkgo Biloba Extract Combined With Donepezil on Alzheimer's Disease Model Rats. China Pharmaceuticals, 33(10): 59–65.

[63] Zhang N, Nao J, Dong X, 2023, Neuroprotective Mechanisms of Salidroside in Alzheimer's Disease: A Systematic Review and Meta-Analysis of Preclinical Studies. Journal of Agricultural and Food Chemistry, 71(46): 17597–17614.

[64] Li Y, Wang H, Yang L, et al., 2024, Research Progress on the Protective Effect and Mechanism of Ganoderma Lucidum Polysaccharides in Neuroinflammatory Degenerative Diseases. Journal of Shanxi University of Chinese Medicine, 25(9): 1038–1042, 1062.

[65] Lin C, Huang Z, Wen S, et al., 2024, Study on the Effects of Tenuifolin From Polygala Tenuifolia on Liver and Kidney

Based on a Mouse Model of Alzheimer's Disease. Asia-Pacific Traditional Medicine, 20(12): 22–25.

[66] Li Q, Zhang Y, Li R, et al., 2022, Study on the Mechanism of Ophiopogonin D in Improving Cognitive Function of Alzheimer's Disease Model Rats. Journal of Regional Anatomy and Operative Surgery, 31(12): 1046–1051.

[67] Li L, Zhang L, 2012, Characteristics of the Effects of Traditional Chinese Medicine in the Treatment of Alzheimer's Disease. Progress in Biochemistry and Biophysics, 39(8): 816–828.

[68] Zhang L, Wang Y, Zhou J, et al., 2018, Observation on Curative Effect of Dihuang Yinzi in the Treatment of Alzheimer's Disease and Discussion on Its Mechanism. China Journal of Chinese Materia Medica, 33(11): 4948–4952.

[69] Liang C, Wang H, Shen S, et al., 2025, Study on the Pharmacodynamics and Mechanism of Gegen-Zhimu Herb Pair in the Prevention and Treatment of Alzheimer's Disease Based on UHPLC-Q/TOF-MS Metabolomics Strategy. Pharmaceutical Practice and Service, 43(1): 30–40.

[70] Wang Y, Wu M, Song W, et al., 2024, Research Progress on the Pathogenesis of Alzheimer's Disease and the Treatment of Traditional Chinese Medicine Based on Gut Microbiota. Shaanxi Journal of Traditional Chinese Medicine, 45(12): 1718–1721.

[71] Iyaswamy A, Krishnamoorthi SK, Liu YW, Song JX, et al., 2020, Yuan-Hu Zhi Tong Prescription Mitigates Tau Pathology and Alleviates Memory Deficiency in the Preclinical Models of Alzheimer's Disease. Frontiers in Pharmacology, 11: 584770.

[72] Wang X, 2021, Network Meta-Analysis of the Effects of Acupuncture-Related Therapies on Cognitive Function in Patients With Mild to Moderate Alzheimer's Disease, thesis, Hubei University of Chinese Medicine.

[73] Luo Y, Shan X, Song J, et al., 2024, Exploring the Mechanism of Acupuncture and Moxibustion in Preventing and Treating Alzheimer's Disease Based on Neuronal Cell Cycle Re-Entry. Acupuncture Research, 49(11): 1205–1212.

[74] Tang Y, Zhang M, 2024, Clinical Research Progress of Acupuncture Treatment for Alzheimer's Disease. Traditional Chinese Medicine, 13(11): 3103–3107.

[75] Lu S, Shao X, Tang Y, et al., 2008, Neural Cell Adhesion Mechanism of Electroacupuncture Promoting Synaptic Plasticity of Hippocampal Neurons in Alzheimer's Disease Model Mice (SAMP8). Chinese Journal of Rehabilitation Medicine, 23(12): 1057–1060.

[76] Wang Y, Kong L, Li W, et al., 2017, Effects of Electroacupuncture at Different Frequencies on Learning-Memory Ability and Partial Mechanism in Rats With Alzheimer's Disease. Chinese Acupuncture and Moxibustion, 37(6): 629–636.

[77] Tang S, Du Y, Xiao J, et al., 2018, Effects of Acupuncture and Moxibustion on Up-Regulating Serum Aβ Internalization Enzymes, Learning and Memory Abilities, and β-Amyloid Protein Deposition in Rats With Alzheimer's Disease. Acupuncture Research, 43(11): 692–697.

[78] Ke C, Shan S, Tan Y, et al., 2024, Signaling Pathways in the Treatment of Alzheimer's Disease With Acupuncture: A Narrative Review. Acupuncture Medicine, 42(4): 216–230.

[79] Du K, Yang S, Wang J, Zhu G, 2022, Acupuncture Interventions for Alzheimer's Disease and Vascular Cognitive Disorders: A Review of Mechanisms. Oxidative Medicine and Cellular Longevity, 2022: 6080282.

[80] Yang W, Dong W, 2020, Mechanisms of Electroacupuncture for Improving Alzheimer's Disease From Reducing β Amyloid Protein Level. Acupuncture Research, 45(5): 426–431.

[81] Huang TI, Hsieh CL, 2021, Effects of Acupuncture on Oxidative Stress Amelioration via Nrf2/ARE-Related Pathways in Alzheimer and Parkinson Diseases. Evidence-Based Complementary and Alternative Medicine, 2021: 6624976.

[82] Jiang YH, He JK, Li R, et al., 2022, Mechanisms of Acupuncture in Improving Alzheimer's Disease Caused by Mitochondrial Damage. Chinese Journal of Integrative Medicine, 28(3): 272–280.

[83] Zhang L, Han W, Zhu C, et al., 2019, Study on the Regulation of PI3K/Akt/mTOR Signaling Pathway by Moxibustion at Du Meridian to Enhance Autophagy Level in APP/PS1 Double Transgenic AD Mice. Chinese Acupuncture and Moxibustion, 39(12): 1313–1319.

[84] Zhou Y, Jia J, 2008, Clinical Observation of Acupoint Catgut Embedding Therapy for Alzheimer's Disease. Chinese Acupuncture and Moxibustion, 28(1): 37–40.

[85] Sun X, Song L, Zhuang P, et al., 2019, Intervention Study of Traditional Auricular Therapy Combined With Modern Finger Exercises on Patients With Mild Cognitive Impairment. Chinese Primary Health Care, 33(2): 72–73,82.

[86] Li Y, Wang X, Shan S, et al., 2021, Clinical Application of Music Therapy in the Treatment of Alzheimer's Disease. China Modern Medicine, 28(16): 252–254.

[87] Wang X, Guo Q, Cai M, et al., 2021, The Influence and Mechanism of Music Therapy on Cognitive Function of Senile Dementia. Chinese Journal of Convalescent Medicine, 30(5): 483–485.

[88] Jiang Y, 2024, A Review of the Current Research Status of Music Therapy Intervention in Recent Memory Impairment of Elderly People With Early Dementia. Contemporary Music, 2024(3): 189–192.

[89] Zhang Y, Wang S, Huang R, et al., 2024, Meta-Analysis of the Intervention Effect of Music Therapy on Patients With Alzheimer's Disease. Chinese General Practice, 27(12): 1511–1518.

[90] Yang X, Chen W, Sun J, et al., 2024, Theoretical Discussion on the Prevention and Treatment of Vascular Dementia With Traditional Chinese Medicine Guidance. Chinese and Foreign Medical Research on Cardiovascular and Cerebrovascular Diseases, 22(22): 4207–4209.

[91] Zhang Y, Huang S, Wu R, et al., 2024, Effects of Eight-Section Brocade Combined With Cognitive Training on Elderly Patients With Multiple Chronic Conditions and Cognitive Frailty. Chinese and Foreign Medical Research, 3(31): 135–137.

[92] Yu X, 2021, The Effect of Guided Prescription Combined With Cognitive Training on Cognitive Function and Activities of Daily Living in Patients With Vascular Dementia. Reflexotherapy and Rehabilitation Medicine, 2(8): 7–9.