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Review

Current Status of Plant-Based Bioactive Compounds as Therapeutics in Alzheimer's Diseases

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Abstract

Alzheimer's disease (AD) is a common central neurodegenerative disease disorder characterized primarily by cognitive impairment and non-cognitive neuropsychiatric symptoms that significantly impact patients' daily lives and behavioral functioning. The pathogenesis of AD remains unclear and current Western medicines treatment are purely symptomatic, with a singular pathway, limited efficacy, and substantial toxicity and side effects. In recent years, as research into AD has deepened, there has been a gradual increase in the exploration and application of medicinal plants for the treatment of AD. Numerous studies have shown that medicinal plants and their active ingredients can potentially mitigate AD by regulating various molecular mechanisms, including the production and aggregation of pathological proteins, oxidative stress, neuroinflammation, apoptosis, mitochondrial dysfunction, neurogenesis, neurotransmission, and the brain-gut microbiota axis. In this review, we analyzed the pathogenesis of AD and comprehensively summarized recent advancements in research on medicinal plants for the treatment of AD, along with their underlying mechanisms and clinical evidence. Ultimately, we aimed to provide a reference for further investigation into the specific mechanisms through which medicinal plants prevent and treat AD, as well as for the identification of efficacious active ingredients derived from medicinal plants.

Keywords: Alzheimer's disease; medicinal plants; neuroprotection; cognitive function; neuroinflammation

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative condition characterized by cognitive deficits, behavioral abnormalities, and impaired social functioning, posing a significant global health threat to older adults and ranking as the fifth leading cause of death worldwide [1,2]. According to a national cross-sectional study in 2020, approximately 9.83 million people aged 60 and above in China were affected by AD [3]. As the global population ages, the incidence, disability, and mortality rates of AD continue to rise annually, promising a growing burden on individuals, families, and societies in the future [4]. Clinical study has identified amyloid-β (Aβ) plaque deposition and hyperphosphorylated Tau protein as primary hallmarks of AD pathology [5]. In addition, numerous studies have demonstrated that oxidative stress, inflammatory responses, programmed cell death (such as apoptosis, autophagy, and ferroptosis), and disturbances in intestinal flora contribute significantly to structural and functional abnormalities in AD progression [6,7].

Currently, the drugs used in the treatment of AD primarily consist of cholinesterase inhibitors and N-methyl-D-aspartate antagonists [8], which can only partially improve the symptoms of patients, but do not reverse disease progression, and prolonged use can lead to various adverse effects. Additionally, surgical interventions used in clinical management are both risky and costly [9]. Hence, there is a critical need to further investigate the pathogenesis of AD and develop effective strategies for its prevention and treatment.

In traditional medical practices, numerous medicinal plants and their active ingredients have been recommended for enhancing cognitive function and alleviating symptoms of AD [10,11], such as cognitive impairment, memory loss, spatial awareness deficits, depression, and dementia. Bioactive compounds derived from medicinal plants are noted for their low incidence of adverse effects and high effectiveness [12]. In recent years, a large number of scholars have carried out studies on active ingredients from medicinal plants for treating AD and elucidating their associated mechanisms [13,14], thereby establishing experimental foundations for AD treatment using medicinal plants. Notably, Huperzine-A derived from *Huperzia serrata* has been clinically employed in the treatment of patients with AD [15,16]. These findings underscored the potential of medicinal plants to offer novel perspectives and strategies for addressing AD in contemporary society.

Currently, there have been a scarcity of reviews focusing on plant-based bioactive compounds for the prevention and treatment of AD. This review provided a comprehensive overview of the current pathogenesis of AD. Furthermore, it summarized recent research on active ingredients derived from medicinal plants targeting AD through global and local databases such as PubMed, Web of Science, and China National Knowledge Infrastructure. The review ex-

amined the mechanisms and clinical efficacy of these compounds, aiming to inform the clinical application of medicinal plants in the treatment of AD and provide a theoretical basis for the development of new drugs to combat this disease.

2. Research Methodology

This review article was conducted using electronic databases such as PubMed, Google Scholar, Springer Link, Science Direct, Cochrane Library, Embase, Web of Science, and Scopus. All published data till the year 2024 have been taken into consideration. The following search keywords were used in the search of materials for this study: "medicinal plants", "active ingredients", "bioactive compounds", "polyphenols", "flavonoids", "alkaloids", "terpenes", "polysaccharides", "quinones", "glycosides", "volatile oils", "biological activity", "pharmacological activities", "Alzheimer's disease", "amyloid β", "tau protein", and other similar keywords in combination with words such as traditional Chinese medicine, Clinical trials, botanical description, toxicity, human health, and nutritional composition. All articles addressing these principal keywords were considered when available in the English language, and in peer-reviewed journals, whether published as review or research articles. Papers were reviewed in their entirety if their abstract mentioned that the article presented any potential relevance to the inclusion criteria. Articles were excluded based on title, abstract, or full text because of their lack of pertinence to the issue concerned. Articles were excluded if they were letters, comments, and not available for access to the full article.

3. Etiology and Pathophysiology of AD

Although AD was first reported by the German physician Alois Alzheimer more than 100 years ago [17], the precise mechanisms underlying its onset and progression remain unclear. Currently, the primary pathological feature of AD has been recognized as the deposition of extracellular amyloid β (Aβ) plaques [18]. Aβ is produced and released through the abnormal cleavage of amyloid precursor protein by β-secretase 1 and γ-secretase enzymes [19,20]. Clinical studies have shown that Aβ plaques can penetrate blood vessels and disrupt the blood supply to the brain [21,22]. Additionally, research has demonstrated that Aβ plaques can damage neurons and trigger activation of microglia and astrocytes [23], leading to increased production of free radicals and influx of Ca^{2+} ions, which exacerbate neuronal apoptosis [24]. It has also been observed that Aβ can enhance the formation of advanced glycation end products on neuron surfaces and stimulate the release of pro-inflammatory cytokines, contributing to impaired neuronal function and eventual cell death [25].

Furthermore, the formation of Aβ plaques typically coincides with additional pathological changes primarily affecting pyramidal neurons and their structural integrity [26]. These changes are induced by increased phosphorylation of tau protein [27], which aggregates into polymers known as tau tangles. Under normal physiological conditions, tau protein plays a crucial role in stabilizing microtubules and facilitating their polymerization to maintain cytoskeletal integrity [28]. Functionally, microtubules are essential for the transport of cellular proteins and enzymes necessary for normal neuronal function [29].

Increasing evidence has observed hyperphosphorylation of tau protein in the brain tissue of patients with AD [30], which in turn leads to the formation of intracellular neurofibrillary tangles, contributing to neuronal degeneration and eventual cell death. At a molecular level, cyclin-dependent kinase 5 (CDK5) can be activated by elevated levels of Ca^{2+} ions within neuronal cells. This activation accelerates microtubule depolymerization, causes cytoskeletal abnormalities, triggers microglial activation, and inflammation, and ultimately impairs neuronal function and leads to apoptotic cell death [31,32].

Recent studies have also confirmed that viral infections [33], mitochondrial dysfunction [34], abnormalities in insulin signaling [35], imbalance in intestinal flora [36], excitotoxicity from amino acids [37], and deficits in cholinergic function [38] are closely associated with the progression of AD. These processes contribute to the aggregation of Aβ plaques, neuroinflammation, oxidative stress, neuronal death, and insulin resistance. Moreover, these factors collectively increase the permeability of the blood-brain barrier, thereby accelerating the pathological advancement of AD.

4. The Therapeutic Effect of Plant-Based Bioactive Compounds on AD and Its Potential Mechanisms

Through extensive research into the pathogenesis of AD, traditional Chinese medicine (TCM) has demonstrated unique therapeutic advantages in AD treatment due to its multi-component, multi-target approach, and emphasis on whole-body integrity [39]. Increasingly, a study has highlighted that medicinal plants and their primary bioactive constituents characterized by diverse structures, exert protective effects against neurodegenerative diseases [40]. The mechanisms by which plant-based bioactive compounds prevent AD are illustrated in Fig. 1 and detailed in Table 1 (Ref. [41–112]). Meanwhile, the majority of Chinese AD patients have incorporated medicinal plants and herbal formulations into their diagnostic and treatment regimens [113,114]. This review aimed to consolidate research progress on natural plant components in the treatment of AD, providing a reference for identifying safe and effective small molecules for AD treatment.

4.1 Polyphenols

Polyphenols are widely found in grapes, *Salvia miltiorrhiza*, tea, *Gastrodia elata*, and other medicinal plants.

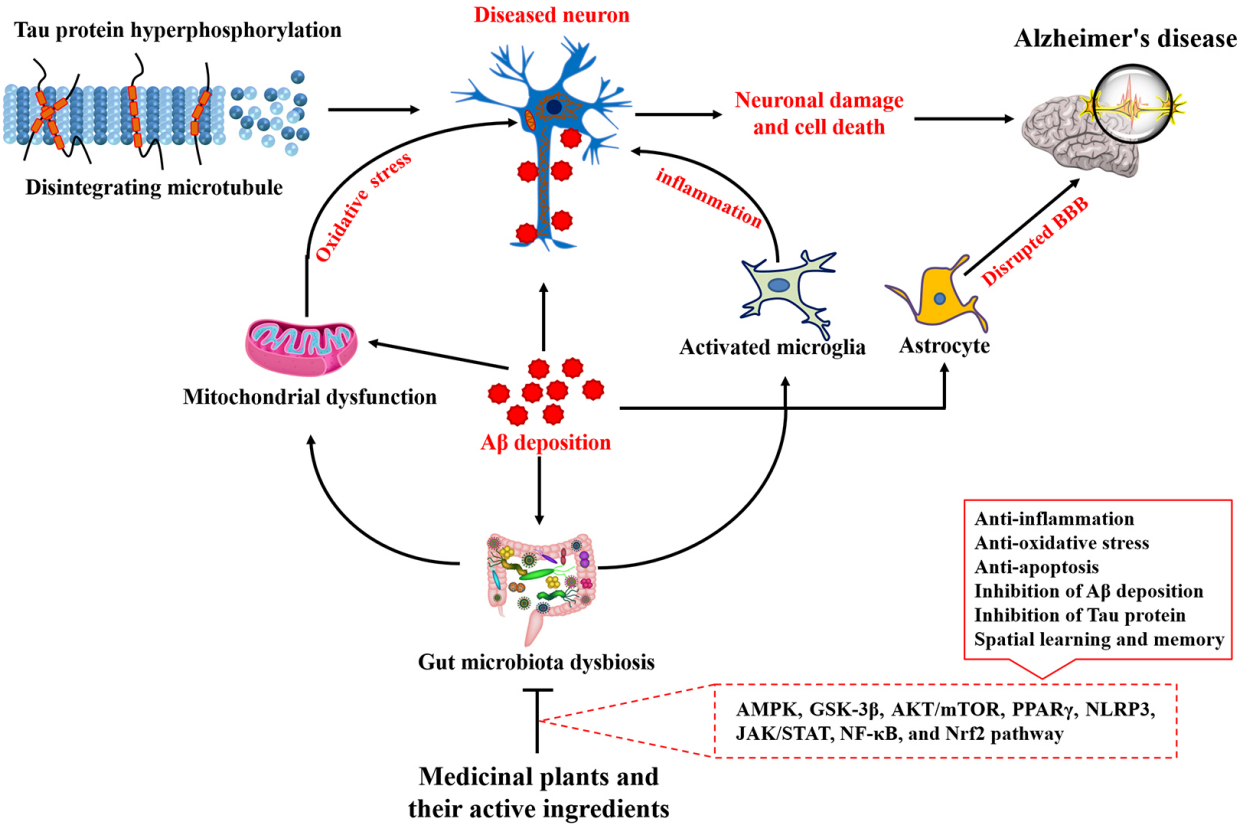

Fig. 1. Therapeutic effects of medicinal plants and their main active ingredients on Alzheimer's disease and the related mechanism. Aβ, amyloid β; BBB, blood-brain barrier; AMPK, AMP-activated protein kinase; GSK-3β, glycogen synthase kinase 3 beta; AKT, protein kinase B; mTOR, rapamycin; PPARγ, Peroxisome proliferator-activated receptor gamma; NLRP3, Nod-like receptor family, pyrin domain containing 3; JAK, Janus kinase; STAT, signal transducer of activation; NF-κB, nuclear factor-κB; Nrf2, nuclear factor erythroid 2-related factor 2. Fig. 1 was created using Microsoft PowerPoint (version 2016, Microsoft, Redmond, WA, USA).

Modern pharmacological study has confirmed that polyphenolic compounds have a variety of biological activities [115], including antitumor, antioxidant, anti-inflammation, and anti-oxidative stress properties. Importantly, increasing study has confirmed the anti-AD potential of polyphenolic compounds [116], with their mechanisms summarized in Table 1. For example, proanthocyanidins, a type of polyphenolic compound, possess a spectrum of biological activities that impede the onset and progression of AD [117,118], including anti-inflammatory effects, improvement of insulin resistance, and anti-oxidative stress properties. Resveratrol, capable of crossing the blood-brain barrier, exerts neuroprotective effects by reducing glial activation, amyloid precursor protein levels, and plaque formation [119], and by modulating gut microbiota composition [120] in AD treatment. Research by Fasina *et al.* [45] has demonstrated that gastrodin enhances memory function in AD mouse models by targeting the "gut microbiota-brain" axis, attenuating neuroinflammation, and preserving intestinal barrier integrity. Other studies have indicated that pterostilbene possesses neuroprotective properties against AD through its anti-inflammatory activities and mitigation of mitochondria-dependent apoptosis [43,44]. Additionally, ferulic acid has been shown to ameliorate AD progression by reducing the accumulation of Aβ peptide and tau protein hyperphosphorylation [121]. In conclusion, polyphenolic compounds represent promising therapeutic agents for AD treatment due to their multifaceted mechanisms.

4.2 Flavonoids

Flavonoids, secondary metabolites widely found in medicinal plants, exhibit various pharmacological activities beneficial to human health [122], including their role in treating AD (Table 1). Previous studies have demonstrated that compounds like nobiletin [72] and luteolin [73] exert anti-AD effects by inhibiting oxidative stress, mitochondrial dysfunction, and neuroinflammation. Sun *et al.* [61] have shown that rutin mitigates AD progression by reducing tau aggregation, neuroinflammation, and tau oligomer-induced cytotoxicity. Icariin [123] and genistein [57] have been found to ameliorate memory impairment in AD mouse models by suppressing endoplasmic reticulum stress. Quercetin-3-O-Glucuronide, a type of active flavonol glucuronide, exhibits anti-neuroinflammatory effects in AD by modulating the gut microbiota-brain axis,

Table 1. Experimental research of active components of medicinal plants in the treatment of AD from 2019–2024.

Compound	Evaluation model	Effects and action mechanism	Ref.
Polyphenols			
Paeonol	• D-gal+$AlCl_3$-induced AD rat model	Behavioral dysfunction, Aβ levels, and loss of fibrillar actin ↓ Rho/Rock2/Limk1/cofilin1 pathway ↑	[41]
Carvacrol	• Aβ_{1-42}-induced AD mouse model • Aβ_{1-42}-induced SH-SY5Y cells	Cell viability ↑ Memory impairment and oxidative stress ↓	[42]
Pterostilbene	• Aβ_{25-35}-induced AD mouse model	Neuronal plasticity, expression of SIRT1 and Nrf2, and SOD level ↑ Neuronal loss and mitochondria-dependent apoptosis ↓	[43]
	• Aβ_{1-42}-induced HEK 293T cells • APP/PS1 mice	Learning and memory abilities ↑ Microglial activation, Aβ aggregation, inflammation, and TLR4 pathway ↓	[44]
Gastrodin	• D-gal-induced AD mouse model	Inflammation and gut microbiota dysbiosis ↓ Expression of ZO-1 and occludin ↑	[45]
Ellagic acid	• Scopolamine-induced AD mouse model	Learning and memory abilities and level of SOD and CAT ↑ MDA level ↓	[46]
Salidroside	• Aβ_{1-42}-induced AD mouse model	Cognitive dysfunction, Aβ accumulation, and Tau hyperphosphorylation ↓ TLR4/NF-κB/NLRP3/Caspase-1 pathway ↓	[47]
	• SAMP8 mice	Cognitive impairment, Aβ plaques, neuronal damage, and inflammation ↓ Nrf2/GPX4 pathway ↑	[48]
Resveratrol	• LPS-induced BV2 cells	NLRP3 inflammasome and NF-κB pathway ↓ Expression of CAT and SOD2 ↑	[49]
Curcumin	• Aβ_{1-42}-induced AD mouse model	Cognitive function, spatial memory, SOD content, and AMPK pathway ↑ Damaged neurons and levels of Aβ_{1-42}, TNF-α, IL-6, IL-1β, and MDA ↓	[50]
EGCG	• Aβ_{25-35}-induced AD rat model	Cognitive impairment, Tau phosphorylation, and expression of Aβ_{1-42} ↓ Ach content ↑	[51]
Kaempferol	• Aβ_{25-35}-induced PC-12 cells	Cell death and apoptosis ↓ ERS/ERK/MAPK pathway ↓	[52]
	• STZ-induced AD mouse model	Learning and memory abilities, and expression of GAD67 and p-NMDAR ↑	[53]
Quercetin	• 3xTg mice	Cognitive function and Aβ reduction ↑ Tau phosphorylation ↓	[54]
	• Aβ_{25-35}-induced PC-12 cells	Cell proliferation and levels of SOD, GSH-Px, CAT, and Nrf2 protein ↑ Levels of LDH, AChE, MDA, and HO-1 protein ↓	[55]

Table 1. Continued.

Compound	Evaluation model	Effects and action mechanism	Ref.
Flavonoids			
Genistein	• STZ-induced AD rat model	Aβ level and hyperphosphorylated tau protein ↓ Autophagy and TFEB ↑	[56]
	• D-gal+Aβ_{25-35}-induced AD rat model	Learning and memory ability ↑ Neuronal damage and ERS-mediated apoptosis ↓	[57]
Amentoflavone	• Aβ_{1-42}-induced SH-SY5Y cells • Aβ_{1-42}-induced AD rat model	Neurological dysfunction and pyroptosis ↓ AMPK/GSK-3β pathway ↑	[58]
Q3GA	• Aβ_{1-42}-induced SH-SY5Y cells • Aβ_{1-42}-induced AD mouse model	Neuroinflammation, Aβ accumulation, p-Tau, and gut microbiota dysbiosis ↓ CREB and BDNF levels ↑	[59]
Naringenin	• Aβ_{1-42}-induced neurons	Levels of ULK1, Beclin1, ATG5, and ATG7 ↑ Aβ level, LDH, ROS, and AMPK pathway ↑	[60]
Rutin	• Tau oligomers-induced microglia cells • Tau-P301S mice	Tau aggregation, inflammation, microglial activation, and NF-κB pathway ↓ PP2A level ↑	[61]
DHMDC	• STZ-induced AD mouse model	Learning and memory abilities, and GSH activity ↑ Lipid peroxidation, TBARS level, and AChE activity ↓	[62]
Isoorientin	• APP/PS1 mice	Levels of IL-4 and IL-10 ↑ Aβ_{42} deposition, phospho-Tau, gut microbiota dysbiosis, and NF-κB pathway ↓	[63]
Trilobatin	• 3xTg-AD mouse model	Memory impairment, Aβ burden, neuroinflammation, Tau hyperphosphorylation ↓ TLR4-MYD88-NF-κB pathway ↓	[64]
Eriodictyol	• Aβ_{1-42}-induced HT-22 cells • APP/PS1 mice	Cognitive deficits, Aβ aggregation, and Tau phosphorylation ↓ Nrf2/HO-1 pathway ↑	[65]
Quercitrin	• 5xFAD mice	Microglia activation, inflammation, and Aβ level ↓	[66]
Hesperidin	• 5xFAD mice	Aβ accumulation and memory dysfunction ↓ Neural stem cell proliferation and AMPK/CREB pathway ↑	[67]
Icariin	• 3xTg-AD mouse model	Memory deficits, Aβ level, and hyperphosphorylated tau ↓ Brain glucose uptake, NeuN, and AKT/GSK-3β pathway ↑	[68]
	• Aβ_{1-42}-induced AD mouse model	Content of Aβ_{1-42} and neuronal damage ↓ Learning and memory abilities, synaptic plasticity, and BDNF-TrκB pathway ↑	[69]
Dihydromyricetin	• LPS+ATP-induced BV2 cells • APP/PS1 mice	Inflammation, cell apoptosis, and level of TLR4 and MD2 ↓	[70]
Silibinin	• STZ-induced HT22 cells • STZ-induced AD mouse model	Cognitive impairment and inflammatory cytokines ↓ Level of SLC7A11 and GPX4 ↑	[71]

Table 1. Continued.

Compound	Evaluation model	Effects and action mechanism	Ref.
Nobiletin	• STZ-induced AD mouse model	Memory defects, Aβ level, oxidative stress, and neuroinflammation ↓ SIRT1/FoxO3a pathway ↑	[72]
Luteolin	• Aβ_{1-42}-induced neurons • 3xTg-AD mouse model	Memory impairment, Aβ level, mitochondrial dysfunction, neuronal apoptosis ↓ PPARγ ↑	[73]
Baicalein	• Aβ_{1-42}-induced AD mouse model	Cognitive and memory impairment ↓ Synaptic plasticity and AMP/GMP-CREB-BDNF pathway ↑	[74]
	• 3xTg-AD mouse model	Learning and memory abilities ↑ Neuroinflammation and CX3CR1/NF-κB pathway ↓	[75]
Alkaloids			
Oxymatrine	• Aβ_{1-42}-induced microglia cells • Aβ_{1-42}-induced AD mouse model	Neuronal damage, microglia activation, levels of TNF-α, IL-1β, and COX-2 ↓ NF-κB and MAPK pathways ↓	[76]
Isorhynchophylline	• Aβ_{1-42}-induced neurons • TgCRND8 mice	Cognitive deficits, Aβ level, tau phosphorylated, levels of TNF-α, IL-6, and IL-1β, Iba1$^+$ microglia, and JNK pathway ↓	[77]
Rutaecarpine	• High sucrose-induced AD mouse model	Learning and memory deficits and tau hyperphosphorylation ↓ Synaptic plasticity ↑	[78]
Tetrandrine	• Aβ_{1-42}-induced BV2 cells • 5xFAD mice	Cognitive ability ↑ Aβ plaque deposition, cell apoptosis, inflammation, and TLR4/NF-κB pathway ↓	[79]
Sophocarpine	• APP/PS1 mice	Cognitive impairment, Aβ level, inflammation, and microglial activation ↓	[80]
Rhynchophylline	• APP/PS1 mice	Aβ plaque burden and inflammation ↓	[81]
Homoharringtonine	• APP/PS1 mice	Cognitive deficits, Aβlevel, neuroinflammation, and STAT3 pathway ↓	[82]
DMTHB	• Aβ_{25-35}-induced AD mouse model	Cognitive deficits, microglia activation, and NLRP3 inflammasome ↓	[83]
Magnoflorine	• Aβ-induced PC12 cells • APP/PS1 mice	Cognitive deficits, cell apoptosis, ROS generation ↓ JNK pathway ↓	[84]
Dauricine	• D-gal+$AlCl_3$-induced AD mouse model	Learning and memory deficits, neuronal damage, expression of p-CaMKII, p-Tau, Aβ, and Ca^{2+}/CaM pathway ↓	[85]
Berberine	• 3xTg-AD mouse model	Cognitive disorders, Aβ level, p-tau, neuronal loss ↓ Nrf2 pathway ↑	[86]
Terpenes			
Oleanolic acid	• N2a/APP695swe cells	Cell viability and expression of stanniocalcin-1 ↑ ROS level and Aβ content ↓	[87]
Artemisinin	• Aβ_{1-42}-induced SH-SY5Y cells • 3xTg-AD mouse model	Cognitive impairment, Aβ level, p-tau, inflammation, cell apoptosis, and ROS ↓ ERK/CREB pathway ↑	[88]
	• Aβ_{1-42}-induced BV2 cells • Aβ_{1-42}-induced AD mouse model	NeuN$^+$ cells ↑ Inflammation and NF-κB pathway ↓	[89]

Table 1. Continued.

Compound	Evaluation model	Effects and action mechanism	Ref.
Linalool	• Aβ_{1-42}-induced AD rat model	Neurodegeneration, ROS levels, oxidative stress, and inflammatory response ↓	[90]
Tanshinone IIA	• Aβ_{1-42}-treated BV2 cells • APP/PS1 mice	Spatial learning, memory deficits, Aβ level, and pro-inflammatory cytokines ↓ Synapse-associated proteins (Syn and PSD-95) ↑ RAGE/NF-κB pathway ↓	[91]
Bilobalide	• Aβ_{42}-induced primary astrocytes • APP/PS1 mice	Aβ plaque deposition, expression of TNF-α, IL-1β, and IL-6, neuronal deficiency, and STAT3 pathway ↓	[92]
Geniposidic Acid	• Aβ_{1-42}-induced primary neurons • APP/PS1 mice	Cognitive impairment, Aβ level, neuronal apoptosis, and inflammation ↓ GAP43 expression and PI3K/AKT pathway ↑	[93]
Ginkgolide	• APP/PS1 mice	Levels of TNF-α, IL-1β, and IL-6 ↓ NF-κB pathway ↓	[94]
Cucurbitacin B	• STZ-induced AD rat model	Cognitive impairment, neuron apoptosis, and inflammation ↓	[95]
Ginkgolide B	• ATP+LPS-induced BV2 cells • SAMP8 mice	Cognitive behavior and γ-aminobutyric acid level ↑ Pro-inflammatory cytokines and NLRP3 inflammasome ↓	[96]
OABL	• 5xFAD mice • LPS-induced BV2 cells	Cognitive function ↑ Neuroinflammation, Aβ level, p-Tau, oxidative stress, and NF-κB pathway ↓	[97]
Ginsenoside Rg1	• Aβ_{25-35}+D-gal-induced AD tree shrew model	Cognitive impairment, p-Tau, Aβ_{1-42} level, and Wnt/β-catenin pathway ↓ Activity of SOD, CAT, GSH-Px ↑	[98]
Artesunate	• Aβ_{1-42}-treated BV2 and neurons • APP/PS1 mice	Deficits in memory and learning, Aβ deposition, inflammation, and neuronal cell apoptosis ↓	[99]
Celastrol	• 3xTg-AD mouse model	Memory dysfunction, cognitive deficits, p-Tau ↓ TFEB ↑	[100]
Patchouli alcohol	• Aβ_{25-35}-induced primary neurons • APP/PS1 mice	Cognitive defects, Aβ plaque deposition, oxidative stress, and apoptosis ↓ Microglial phagocytosis and synaptic integrity ↑ BDNF/TrkB/CREB pathway ↑	[101]
Paeoniflorin	• APP/PS1 mice	Cognitive ability and SOD expression ↑ Cell ferroptosis ↓	[102]
Catalpol	• Aβ_{1-42}-induced BV2 cells • APP/PS1 mice	Levels of Aβ, TNF-α, IL-6, and iNOS, IBA-positive microglia, GFAP-positive astrocytes, and NF-κB pathway ↓	[103]
Astragaloside IV	• Aβ_{1-42}-induced BV2 cells	Microglial activation, inflammation, and EGFR pathway ↓	[104]
Polysaccharides			
Coptis chinensis	• Aβ_{25-35}-induced PC-12 cells	Cell viability ↑; Oxidative stress and JNK pathway ↓	[105]
Lycium barbarum	• APP/PS1 mice	Aβ level ↓; Cognitive functions, neurogenesis, and synaptic plasticity ↑	[106]
Angelica sinensis	• Aβ_{25-35}-induced AD mouse model	Learning and memory deficiency, AchE level, MDA, and inflammation ↓ Activity of SOD and CAT and BDNF/TrkB/CREB pathway ↑	[107]

Table 1. Continued.

Compound	Evaluation model	Effects and action mechanism	Ref.
Codonopsis pilosula	• APP/PS1 mice	Cognitive defects and expression of Aβ_{42} and Aβ_{40} ↓ Synaptic plasticity ↑	[108]
Astragalus membranaceus	• APP/PS1 mice	Apoptosis of brain cells and content of Aβ ↓ Spatial learning and memory abilities and Nrf2 pathway ↑	[109]
Taxus Chinensis	• D-gal-induced AD mouse model	Cognitive defects, level of caspase-3, Bax, MDA, ROS, and Aβ_{1-42} ↓ Level of SOD and Nrf2 pathway ↑	[110]
Cistanche deserticola	• D-gal-induced AD mouse model	Memory and learning disorders, inflammation, and gut microbiota dysbiosis ↓	[111]
Polygonatum sibiricum	• D-gal-induced HT-22 cells • D-gal-induced AD mouse model	Cell death, memory impairment, oxidative stress, and inflammation ↓	[112]

Note: AchE, Acetylcholinesterase; AD, Alzheimer's disease; AMPK, adenosine monophosphate-activated protein kinase; Aβ, amyloid-β; CAT, catalase; CREB, cAMP-response element-binding protein; D-gal, D-galactose; DMTHB, Demethylenetetrahydroberberine; EGCG, epigallocatechin-3-gallate; EGFR, epidermal growth factor receptor; ERS, Endoplasmic reticulum stress; FoxO, Forkhead box-containing protein, O subfamily; GSH-Px, glutathione peroxidase; GSK-3β, glycogen synthase kinase 3β; IL, interleukin; MDA, malondialdehyde; NeuN, Neuronal nuclear antigen; NF-κB, nuclear factor-κB; Nrf2, nuclear factor erythroid 2-related factor 2; OABL, 1,6-O,O-diacetylbritannilactone; PPARγ, peroxisome proliferator-activated receptor gama; Q3GA, quercetin-3-O-glucuronide; SAMP8, senescence-accelerated mouse prone 8; SIRT1, sirtuin-1; SOD, superoxide dismutase; STZ, streptozotocin; TNF-α, tumor necrosis factor-α; DHMDC, 2′,6′-dihydroxy-4′-methoxy dihydrochalcone; Rho, Ras homology; Rock2, Rho-associated coiled-coil containing protein kinase 2; HEK, human embryonic kidney; APP/PS1, amyloid precursor protein/presenilin 1; TLR4, Toll-like receptor 4; ZO-1, zonula occludens-1; NLRP3, Nod-like receptor family, pyrin domain containing 3; GPX4, glutathione peroxidase 4; LPS, lipopolysaccharide; ERK, extracellular signal-regulated kinase; MAPK, mitogen-activated protein kinase; GAD67, glutamate decarboxylase 67; p-NMPAR, phosphorylated N-methyl D-aspartate receptor; LDH, lactate dehydrogenase; HO-1, heme oxygenase-1; TFEB, transcription factor EB; ULK1, UNC-52-like kinase 1; ATG, autophagy-related gene; ROS, reactive oxygen species; PP2A, protein phosphatase 2A; GSH, glutathione; TBARS, thiobarbituric acid reactive substance; MYD88, myeloid differentiation primary response 88; AKT, protein kinase; BDNF, brain-derived neurotrophic factor; TrkB, tropomyosin receptor kinase B; MD2, myeloid differentiation factor 2; AMP, adenosine monophosphate; GMP, good manufacturing practice; CX3CR1, CX3C chemokine receptor 1; COX, cyclooxygenase; JNK, c-Jun N-terminal kinase; p-CaMKII: phosphorylated Ca^{2+}/calmodulin-dependent protein kinase II; PSD, postsynaptic density protein; RAGE, receptor for advanced glycation end product; GAP43, growth-associated protein 43; PI3K, phosphatidylinositol 3-kinase; iNOS, inducible nitric oxide synthase; IBA, ionized calcium binding adapter; GFAP, glial fibrillary acidic protein; BCL-2, B-cell leukemia/lymphoma 2; Bax, BCL-2 associated X.

as evidenced by its ability to reduce short-chain fatty acids and address gut microbiota dysbiosis [59]. Overall, flavonoids possess a diverse array of biological activities that can prevent the development and progression of AD.

4.3 Alkaloids

Alkaloids, a class of nitrogen-containing basic organic compounds widely found in medicinal plants, exert protective effects against AD by suppressing inflammation, oxidative stress, and neuronal apoptosis (Table 1). Matrine, a natural quinolizidine alkaloid isolated from *Sophora flavescens*, reduces proinflammatory cytokines and Aβ deposition, alleviating memory deficits in AD transgenic mice by inhibiting the Aβ/receptor for advanced glycation end product (RAGE) pathway [124]. Similarly, oxymatrine demonstrates anti-neuroinflammatory effects in an Aβ_{1-42}-induced AD rat model by inhibiting nuclear factor-κB (NF-κB) and mitogen-activated protein kinase (MAPK) pathways [76], suggesting it as a potential candidate for the treatment of AD. Research by Li *et al*. [77] has shown that isorhynchophylline reduces Aβ deposition, tau hyperphosphorylation, and neuroinflammation, while improving cognitive deficits in AD mice by inactivating the c-Jun N-terminal kinase (JNK) pathway. Berberine, a natural isoquinoline alkaloid derived from *Rhizoma coptidis*, suppresses the formation of Aβ plaques, tau protein hyperphosphorylation, and neuronal loss in the brains of AD mice by activating the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway [86]. Furthermore, a recent study highlights that palmatine, a natural alkaloid found in various plants, enhances cognitive function and restores mitochondrial function in AD mouse models [125].

4.4 Terpenes

Terpenoids, a diverse group of organic compounds found in medicinal plants, are increasingly recognized for their potential in treating various diseases [126,127]. Their preventive and therapeutic effects on AD have garnered significant attention (Table 1), owing to their remarkable biological activities, such as anti-inflammatory, antioxidant, and anti-apoptotic properties. Huperzine-A, a natural sesquiterpene alkaloid derived from *Huperzia serrata*, demonstrates a neuroprotective effect in AD by reducing Aβ accumulation, preserving mitochondrial function, and maintaining Fe^{2+} homeostasis [128]. Paeoniflorin, commonly found in Paeoniaceae plants, improves cognitive function and mitigates neuronal ferroptosis in AD mice through inhibition of the P53 pathway [102]. Administration of geniposidic acid attenuates AD progression by enhancing cognitive function, reducing Aβ accumulation, neuronal apoptosis, and neuroinflammation [93]. Patchouli alcohol, a bioactive tricyclic sesquiterpene from Pogostemonis herba, exerts neuroprotective effects against AD by suppressing Aβ plaque deposition, tau protein hyperphosphorylation, neuroinflammation, and gut dysbiosis via inhibition of the CCAAT/enhancer-binding protein β/asparagine endopeptidase (C/EBPβ/AEP) pathway [129]. Ginkgolide B, a terpene lactone derived from *Ginkgo biloba* leaves, prevents AD progression by inhibiting NLRP3 (Nod-like receptor family, pyrin domain containing 3) inflammasome activation and improving learning and memory impairments [96]. Tanshinone IIA, a fat-soluble component of *Salvia miltiorrhiza*, protects against AD by enhancing Aβ transport [130], reducing tau phosphorylation, oxidative stress, and neuroinflammation [91, 131]. Celastrol, a friedelane-type triterpene from *Tripterygium wilfordii*, activates transcription factor enhancer bindings (EBs) to suppress phosphorylated tau aggregates, thereby improving memory and cognitive deficits in AD mouse models [100]. A recent study has shown that catalpol rescues cognitive deficits in AD by preventing Aβ plaque formation and neuroinflammation [103].

4.5 Polysaccharides

Currently, plant polysaccharides have been gaining significant global attention due to their versatile biological activities, including antioxidation, anti-inflammation, and anti-oxidative stress properties, coupled with minimal side effects [132]. Particularly noteworthy are their potential roles in mitigating risk factors associated with AD [133] (Table 1), such as modulation of neuroplasticity, promotion of neurogenesis, normalization of neurotransmission, and suppression of neuroinflammation. For instance, *Angelica* polysaccharides have been shown to alleviate AD progression by reducing inflammation, oxidative stress, neuronal apoptosis, and improving memory impairment [107]. Polysaccharides from *Coptis chinensis* protect Aβ-induced neurotoxicity, reduce phosphorylated tau protein, and mitigate oxidative stress in AD rat models [105]. Zhou *et al*. [106] reported that polysaccharides from *Lycium barbarum* act as a novel therapeutic agent for AD by reducing Aβ plaque deposition and improving cognitive functions. In D-galactose-induced mouse models, polysaccharides from *Polygonatum sibiricum* exhibit antioxidative stress and anti-inflammatory effects against AD [112]. Additionally, polysaccharides from *Cistanche deserticola* have been shown to improve cognitive function by restoring homeostasis in the gut microbiota-brain axis [111].

4.6 Others

In addition to the previously mentioned compounds isolated from medicinal plants for the prevention of AD, various other plant-based bioactive compounds have shown therapeutic potential against AD. Studies have highlighted that quinones such as sennoside A [134], rhein [135], and shikonin [136], phenylpropanoids, including magnolol [137] and forsythoside A [138], glycosides such as tenuifolin [139] and ginsenoside compound K [140], and volatile oils from plants like *Acorus tatarinowii*

Schott [141], *Rosmarinus officinalis* and *Mentha piperita* oils [142], alleviate AD progression through antioxidant, anti-inflammatory, and anti-apoptotic activities. Furthermore, several medicinal plants have demonstrated potential in preventing or treating AD, including *Moringa oleifera* [143], *Rosmarinus officinalis* [144], *Nardostachys jatamansi* [145], and *Tinospora cordifolia* [146]. For example, plant-derived alkaloids [147,148], polyphenols [149], flavonoids [150,151], saponins [152,153], alkaloids [154], terpenes [155], and essential oils [156,157] showed multi-targeted activity against acetylcholinesterase, butyrylcholinesterase, tyrosinase, monoamine oxidase, and pancreatic lipase, which helped to prevent the occurrence and development of AD. However, the functional roles of these plant-based bioactive compounds in the treatment of AD remain poorly understood, with limited knowledge of their mechanisms. In conclusion, plant-based bioactive compounds exhibit multi-target and versatile biological activities in experimental AD studies, suggesting their potential as therapeutic agents for AD treatment in clinical settings.

5. Clinical Trials of Medicinal Plants for AD Management and Challenges

Accumulating evidence indicates that medicinal plants offer a wide range of pharmacological effects in AD, with beneficial efficacy demonstrated *in vitro* cell models and animal experiments. Gul *et al.* [158] have reported that Huperzine-A acts as an acetylcholinesterase inhibitor, improving cognition and task-switching abilities in patients with AD. Moreover, ongoing clinical studies are exploring the safety and efficacy of medicinal plant decoctions and injections for the treatment of AD (Table 2). A randomized controlled clinical trial found that Di-Tan decoction is a safe method for treating AD and improving cognitive symptoms [159]. Another study demonstrated that a medicinal plant formula was beneficial for cognitive improvement in AD patients by reducing Aβ plaque deposition [160]. Recently, Huanglian Jiedu decoction has been found to reduce inflammation and oxidative stress in AD patients by regulating lipid and glutamic acid metabolism [161]. Furthermore, clinical trials have indicated that the Jiannao Yizhi formula's efficacy and safety in treating AD are comparable to Western medicine (donepezil) [162]. Meanwhile, Western medicines are expensive and have side effects. A study in Australia showed that EGb 761® (a standardized extract from *Gingkgo biloba*) treatment improved the activities of daily living deterioration by 22.3 months in patients with AD, and EUR 531 for one additional therapy success (defined as improvement in clinician's global judgment) with EGb 761® while cholinesterase inhibitors require between EUR 3849 and EUR 14,224 [163]. A randomized controlled trial (NCT00391833) showed that AD patients treated with *Panax ginseng* powder (4.5 g/day) for 12 weeks, the cognitive subscale of the Alzheimer's Disease Assessment Scale and the Mini-Mental State Examination score began to show improvements. Moreover, Chinese medicinal plants' adjunctive therapy could improve cognitive impairment and enhance immediate response and quality of life in AD patients [12,164]. Based on these findings, plant-based bioactive compounds present a promising alternative for AD, offering diverse therapeutic benefits.

However, it is also necessary to explore the several challenges of translating preclinical findings into clinical applications. The biggest challenge to plant-based drug delivery into the brain is circumventing the blood-brain barrier, which prevents the entry of numerous potential therapeutic agents. Another challenge is related to approval of the drug for commercialization because enough resources are unavailable. Since some compounds cannot be synthesized in a semi-synthetic manner or by growing or engineering the plant artificially, this will increase the product's dependency on natural resources. As per the reports, nearly 25,000 plants will go extinct, which imposes an ethical issue for extracting bioactive compounds from plants. In addition, there is still a lack of sufficient clinical data and their mechanisms of action. Finally, plant-based bioactive compounds have solubility & absorption, intellectual property, absence of drug-likeness, and purity issues.

6. Current Status of Plant-Based AD Treatments in Different Countries

Medicinal plants have been used for thousands of years and have been broadly used in clinical practice in China and several other Asian countries (such as Japan and Korea) [165], and Chinese people have a wealth of clinical experience in medicinal plants. Currently, medicinal plants account for more than 40% of China's pharmaceutical market [166]. Meanwhile, the world health organization (WHO) stated that about 80% of the world population depends on medicinal plants to satisfy healthcare requirements [167,168]. For example, *Evalvulus alsinoides*, *Centella asiatica*, *Myristica fragrans*, *Andrographis paniculata*, *Nardostachys jatamansi*, and *Nelumbo nucifera* widely used in Indian traditional medicine systems for cognitive enhancement were known for their acetylcholinesterase inhibitory activity [169]. Lobbens *et al.* [170] reported that a total of 29 ethanolic extracts from European traditional medicine plants served as new drug candidates for the treatment of AD by inhibition of acetylcholinesterase and amyloidogenic activities. Kumar *et al.* [171] found that medicinal plants from the Australian rainforest possessed anti-AD activity by suppressing neuroinflammation. In the West Africa region, over 10,000 medicinal plants have been utilized in curing neurodegenerative diseases [172], such as *Pyllanthus amarus*, *Crysophyllum albidum*, *Rauwolfia vomitora*, *Abrus precatorius*. A clinical study confirmed that administration with ninjin'yoeito (NYT), a traditional Japanese medicine (Kampo medicine),

Table 2. Registered clinical trials of plant species and compounds in Alzheimer's disease.

Sources	Year of registration	Enrollment	Sponsor	Clinical trial ID
Yizhi Baduanjin	2023	30	The University of Hong Kong, China	NCT06453941
Rhizoma acori Tatarinowii, *Poria cum* Radix Pini, and *Radix polygalae*	2022	180	Peking Union Medical College Hospital, China	NCT05538507
Centella asiatica	2022	48	Oregon Health and Science University, USA	NCT05591027
Yangxue Qingnao Pills	2021	216	Dongzhimen Hospital, China	NCT04780399
Yi-gan-san, Huan-shao-dan, *Salvia miltiorrhiza*, *Rhizoma gastrodiae*, *Ramulus uncariae* cum Uncis, and *Morindae officinalis*	2020	28	Taipei Veterans General Hospital, China	NCT04249869
Bupleurum+Ginkgo	2019	60	Xuanwu Hospital, China	NCT04279418
GRAPE granules	2017	120	Dongzhimen Hospital, China	NCT03221894
Jian Pi Yi Shen Hua Tan Granules	2016	300	Dongfang Hospital Beijing University of Chinese Medicine, China	NCT02641886
Ginkgo biloba Extract	2016	240	The First Affiliated Hospital with Nanjing Medical University, China	NCT03090516
EGb761®	2008	49	Ipsen, France	NCT00814346
Nootropics (*Ginkgo biloba*, nicergoline, piracetam, or others)	2006	1134	Janssen-Cilag G.m.b.H, USA	NCT01009476
Curcumin and Ginkgo	2004	36	Chinese University of Hong Kong, China	NCT00164749
Curcumin	2003	33	John Douglas French Foundation, USA	NCT00099710
Ginkgo biloba	2000	3069	National Center for Complementary and Integrative Health, USA	NCT00010803

improved impairments and depressive states in twelve AD patients [173]. Meanwhile, *Ginkgo biloba* extract (EGb 761®) was registered as an ethical drug in Western countries and has been widely used in clinical therapy to treat AD [174]. Galantamine (Razadyne®) serves as a selective competitive and reversible inhibitor of acetylcholinesterase and has received regulatory approval in 29 countries [175], such as Sweden, Austria, United States, Europe, and other countries. Rivastigmine (Exelon®) was approved to treat mild to moderate AD in over 40 countries in North and South America, Asia, and Europe [176]. Currently, the U.S. Food and Drug Administration has approved tacrine (Cognex®), donepezil (Aricept®), galantamine, memantine, and rivastigmine for the treatment of AD patients in clinical [177,178]. Taken together, medicinal plant-based bioactive compounds exhibited their powerful roles in the management of AD progression and helped to relieve the symptoms related to AD.

7. Conclusions and Future Directions

With increasing research into the pathogenesis of AD, the role of medicinal plants in its treatment has advanced significantly in recent years. TCM has been particularly prominent in treating various diseases, including AD, and offers a new perspective in the modern era for both the prevention and treatment of coronavirus disease 2019 (COVID-19). This review underscored that plant-based bioactive ingredients can prevent and manage AD through multiple mechanisms, including reducing the production and aggregation of pathological proteins, enhancing their degradation, antioxidative and anti-inflammatory activities, improving mitochondrial function and energy metabolism, regulating intestinal flora, inhibiting neuronal apoptosis, and promoting neurogenesis. Clinical trials have demonstrated the efficacy and safety of medicinal plants in alleviating the symptoms of AD. However, the treatment of AD with medicinal plant-based bioactive ingredients still faces some challenges that must be addressed. (1) With the rapid development of science, there is a need to elucidate the physiological functions and mechanistic explanations of medicinal plants against AD using network pharmacological approaches and multi-omics techniques, such as nutrigenomics, metabolomics, proteomics, gut microbial macrogenomics, and immunomics. (2) Further validation of the metabolic, toxicity, and pharmacokinetic profiles of medicinal plants in clinical trials for AD is essential. (3) Research on active ingredients from medicinal plants is limited by unstable chemical structures, low bioavailability, and susceptibility to oxidation. Consideration of strategies like liposome embedding or nanoparticle formulation may mitigate these challenges. (4) Many active compounds from medicinal plants cannot effectively cross the blood-brain barrier to reach the brain. Exploring how plant-based bioactive compounds that regulate intestinal flora based on the "brain-gut microbiota" axis can mitigate AD is warranted.

Due to the synergistic effects, systematic analytical tools must be developed to study the multi-component, multi-rule, and multi-target characteristics of TCM. Network-based approaches in medicinal plants use computational algorithms to elucidate the underlying mechanisms of bioactive compounds and identify the underlying synergistic effects. Moreover, the development of network pharmacology diminishes the cost, reduces the risk, and saves time in researching new bioactive compounds for the treatment of various diseases, including AD [179]. Researchers can use these tools and experimental knowledge to determine effective substances in medicinal plants for AD. For example, Wu *et al.* [180] presented a novel algorithm based on entropy and random walk with the restart of the heterogeneous network was proposed for predicting active ingredients for AD and screening out the effective TCMs for AD, and results showed that the top 15 active ingredients may act as multi-target agents in the prevention and treatment of AD, Danshen, Gouteng and Chaihu were recommended as effective TCMs for AD, Yiqitongyutang was recommended as effective compound for AD. Recent studies have proved that integrating network pharmacology and experimental verification to reveal the potential pharmacological ingredients and mechanisms of different medicinal plants (*Paeonia lactiflora* [181], *Acoritatani-nowii rhizome* [182], *Ginkgo biloba* [183], *Panax ginseng* [184], *Corydalis rhizome* [185]) in curing AD, and TCM decoction (Erjingwan [186], Jin-Si-Wei [187], Guhan Yangshengjing [188], and Tian-Si-Yin [189]). Therefore, using network pharmacology to discover the relationship between medicinal plants, AD, and cellular responses was easily achievable.

In conclusion, medicinal plants exhibit promising anti-AD effects and serve as essential active agents for treating neurodegenerative diseases. In addition to experimental studies, bioinformatics approaches provide valuable insights into the mechanisms by which plant-based bioactive compounds exert their therapeutic effects on AD. Incorporating molecular docking studies, molecular dynamics simulations, quantitative structure-activity relationship models, network pharmacology, and genomics/transcriptomics analyses can significantly enhance our understanding of the multi-target effects and potential efficacy of these compounds. Integration of these bioinformatics methods could validate experimental findings and guide the development of novel therapeutic strategies for AD. This review synthesized the current understanding of AD's pathogenesis, systematically analyzed and explored the mechanisms of medicinal plants in preventing AD, and reviewed their clinical trial outcomes. The aim was to offer a scientific and comprehensive reference for the treatment of AD with medicinal plants, enhancing the utilization and development of TCM resources.

Abbreviations

AchE, acetylcholinesterase; AD, Alzheimer's disease; AMPK, adenosine monophosphate-activated protein kinase; Aβ, amyloid-β; BACE1, β-site amyloid precursor protein-cleaving enzyme 1; CAT, catalase; CDK5, cyclin-dependent kinase 5; CREB, cAMP-response element-binding protein; D-gal, D-galactose; DMTHB, demethylenetetrahydroberberine; EGFR, epidermal growth factor receptor; ERS, endoplasmic reticulum stress; FoxO, forkhead box-containing protein, O subfamily; GSH-Px, glutathione peroxidase; GSK-3β, glycogen synthase kinase 3β; IL-1β, interleukin-1β; MDA, malondialdehyde; NeuN, neuronal nuclear antigen; NF-κB, nuclear factor-κB; Nrf2, nuclear factor erythroid 2-related factor 2; PPARγ, peroxisome proliferator-activated receptor gama; SAMP8, senescence-accelerated mouse prone 8; SIRT1, sirtuin-1; SOD, superoxide dismutase; STZ, streptozotocin; TCM, traditional Chinese medicine; TNF-α, tumor necrosis factor-α; WHO, world health organization.

Author Contributions

DC and YS conceptualized and designed the study. DC designed the figures and conducted a literature review. Both authors contributed to editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Hodson R. Alzheimer's disease. Nature. 2018; 559: S1.

[2] Knopman DS, Amieva H, Petersen RC, Chételat G, Holtzman DM, Hyman BT, *et al*. Alzheimer disease. Nature Reviews. Disease Primers. 2021; 7: 33.

[3] Jia L, Du Y, Chu L, Zhang Z, Li F, Lyu D, *et al*. Prevalence, risk factors, and management of dementia and mild cognitive impairment in adults aged 60 years or older in China: a cross-sectional study. The Lancet. Public Health. 2020; 5: e661–e671.

[4] Ren R, Qi J, Lin S, Liu X, Yin P, Wang Z, *et al*. The China Alzheimer Report 2022. General Psychiatry. 2022; 35: e100751.

[5] Arnsten AFT, Datta D, Del Tredici K, Braak H. Hypothesis: Tau pathology is an initiating factor in sporadic Alzheimer's disease. Alzheimer's & Dementia: the Journal of the Alzheimer's Association. 2021; 17: 115–124.

[6] Jiang C, Li G, Huang P, Liu Z, Zhao B. The Gut Microbiota and Alzheimer's Disease. Journal of Alzheimer's Disease: JAD. 2017; 58: 1–15.

[7] Behl T, Makkar R, Sehgal A, Singh S, Sharma N, Zengin G, *et al*. Current Trends in Neurodegeneration: Cross Talks between Oxidative Stress, Cell Death, and Inflammation. International Journal of Molecular Sciences. 2021; 22: 7432.

[8] Fink HA, Linskens EJ, MacDonald R, Silverman PC, McCarten JR, Talley KMC, *et al*. Benefits and Harms of Prescription Drugs and Supplements for Treatment of Clinical Alzheimer-Type Dementia. Annals of Internal Medicine. 2020; 172: 656–668.

[9] Berger M, Burke J, Eckenhoff R, Mathew J. Alzheimer's disease, anesthesia, and surgery: a clinically focused review. Journal of Cardiothoracic and Vascular Anesthesia. 2014; 28: 1609–1623.

[10] Fang Z, Tang Y, Ying J, Tang C, Wang Q. Traditional Chinese medicine for anti-Alzheimer's disease: berberine and evodiamine from *Evodia rutaecarpa*. Chinese Medicine. 2020; 15: 82.

[11] Gregory J, Vengalasetti YV, Bredesen DE, Rao RV. Neuroprotective Herbs for the Management of Alzheimer's Disease. Biomolecules. 2021; 11: 543.

[12] Moreira J, Machado M, Dias-Teixeira M, Ferraz R, Delerue-Matos C, Grosso C. The neuroprotective effect of traditional Chinese medicinal plants-A critical review. Acta Pharmaceutica Sinica. B. 2023; 13: 3208–3237.

[13] Manoharan S, Essa MM, Vinoth A, Kowsalya R, Manimaran A, Selvasundaram R. Alzheimer's Disease and Medicinal Plants: An Overview. Advances in Neurobiology. 2016; 12: 95–105.

[14] Hassan NA, Alshamari AK, Hassan AA, Elharrif MG, Alhajri AM, Sattam M, *et al*. Advances on Therapeutic Strategies for Alzheimer's Disease: From Medicinal Plant to Nanotechnology. Molecules (Basel, Switzerland). 2022; 27: 4839.

[15] Ha GT, Wong RK, Zhang Y. Huperzine a as potential treatment of Alzheimer's disease: an assessment on chemistry, pharmacology, and clinical studies. Chemistry & Biodiversity. 2011; 8: 1189–1204.

[16] Yang G, Wang Y, Tian J, Liu JP. Huperzine A for Alzheimer's disease: a systematic review and meta-analysis of randomized clinical trials. PloS One. 2013; 8: e74916.

[17] Ferrari C, Sorbi S. The complexity of Alzheimer's disease: an evolving puzzle. Physiological Reviews. 2021; 101: 1047–1081.

[18] Zhang Y, Chen H, Li R, Sterling K, Song W. Amyloid β-based therapy for Alzheimer's disease: challenges, successes and future. Signal Transduction and Targeted Therapy. 2023; 8: 248.

[19] Hampel H, Vassar R, De Strooper B, Hardy J, Willem M, Singh N, *et al*. The β-Secretase BACE1 in Alzheimer's Disease. Biological Psychiatry. 2021; 89: 745–756.

[20] Hur JY. γ-Secretase in Alzheimer's disease. Experimental & Molecular Medicine. 2022; 54: 433–446.

[21] Armstrong RA, Cairns NJ, Patel R, Lantos PL, Rossor MN. Relationships between beta-amyloid (A beta) deposits and blood vessels in patients with sporadic and familial Alzheimer's disease. Neuroscience Letters. 1996; 207: 171–174.

[22] Armstrong RA. Spatial correlations between beta-amyloid (Abeta) deposits and blood vessels in familial Alzheimer's disease. Folia Neuropathologica. 2008; 46: 241–248.

[23] Moonen S, Koper MJ, Van Schoor E, Schaeverbeke JM, Vandenberghe R, von Arnim CAF, *et al*. Pyroptosis in Alzheimer's disease: cell type-specific activation in microglia, astrocytes and neurons. Acta Neuropathologica. 2023; 145: 175–195.

[24] Quintana DD, Garcia JA, Anantula Y, Rellick SL, Engler-Chiurazzi EB, Sarkar SN, *et al*. Amyloid-β Causes Mitochondrial Dysfunction via a Ca2+-Driven Upregulation of Oxidative Phosphorylation and Superoxide Production in Cerebrovascular

Endothelial Cells. Journal of Alzheimer's Disease: JAD. 2020; 75: 119–138.
[25] Mangalmurti A, Lukens JR. How neurons die in Alzheimer's disease: Implications for neuroinflammation. Current Opinion in Neurobiology. 2022; 75: 102575.
[26] Ashrafian H, Zadeh EH, Khan RH. Review on Alzheimer's disease: Inhibition of amyloid beta and tau tangle formation. International Journal of Biological Macromolecules. 2021; 167: 382–394.
[27] Busche MA, Hyman BT. Synergy between amyloid-β and tau in Alzheimer's disease. Nature Neuroscience. 2020; 23: 1183–1193.
[28] Rawat P, Sehar U, Bisht J, Selman A, Culberson J, Reddy PH. Phosphorylated Tau in Alzheimer's Disease and Other Tauopathies. International Journal of Molecular Sciences. 2022; 23: 12841.
[29] Ju Y, Tam KY. Pathological mechanisms and therapeutic strategies for Alzheimer's disease. Neural Regeneration Research. 2022; 17: 543–549.
[30] Stefanoska K, Gajwani M, Tan ARP, Ahel HI, Asih PR, Volkerling A, *et al*. Alzheimer's disease: Ablating single master site abolishes tau hyperphosphorylation. Science Advances. 2022; 8: eabl8809.
[31] Turab Naqvi AA, Hasan GM, Hassan MI. Targeting Tau Hyperphosphorylation *via* Kinase Inhibition: Strategy to Address Alzheimer's Disease. Current Topics in Medicinal Chemistry. 2020; 20: 1059–1073.
[32] Lee HJ, Jeon SG, Kim J, Kang RJ, Kim SM, Han KM, *et al*. Ibrutinib modulates Aβ/tau pathology, neuroinflammation, and cognitive function in mouse models of Alzheimer's disease. Aging Cell. 2021; 20: e13332.
[33] Huang SY, Yang YX, Kuo K, Li HQ, Shen XN, Chen SD, *et al*. Herpesvirus infections and Alzheimer's disease: a Mendelian randomization study. Alzheimer's Research & Therapy. 2021; 13: 158.
[34] Ashleigh T, Swerdlow RH, Beal MF. The role of mitochondrial dysfunction in Alzheimer's disease pathogenesis. Alzheimer's & Dementia: the Journal of the Alzheimer's Association. 2023; 19: 333–342.
[35] Akhtar A, Sah SP. Insulin signaling pathway and related molecules: Role in neurodegeneration and Alzheimer's disease. Neurochemistry International. 2020; 135: 104707.
[36] Angelucci F, Cechova K, Amlerova J, Hort J. Antibiotics, gut microbiota, and Alzheimer's disease. Journal of Neuroinflammation. 2019; 16: 108.
[37] Greenamyre JT, Young AB. Excitatory amino acids and Alzheimer's disease. Neurobiology of Aging. 1989; 10: 593–602.
[38] Giacobini E, Cuello AC, Fisher A. Reimagining cholinergic therapy for Alzheimer's disease. Brain: a Journal of Neurology. 2022; 145: 2250–2275.
[39] Li L, Zhang L, Yang CC. Multi-Target Strategy and Experimental Studies of Traditional Chinese Medicine for Alzheimer's Disease Therapy. Current Topics in Medicinal Chemistry. 2016; 16: 537–548.
[40] Liao Y, Wang X, Huang L, Qian H, Liu W. Mechanism of pyroptosis in neurodegenerative diseases and its therapeutic potential by traditional Chinese medicine. Frontiers in Pharmacology. 2023; 14: 1122104.
[41] Han F, Xu H, Shen JX, Pan C, Yu ZH, Chen JJ, *et al*. RhoA/Rock2/Limk1/cofilin1 pathway is involved in attenuation of neuronal dendritic spine loss by paeonol in the frontal cortex of D-galactose and aluminum induced Alzheimer's disease like rat model. Acta Neurobiologiae Experimentalis. 2020; 80: 225–244.
[42] Celik Topkara K, Kilinc E, Cetinkaya A, Saylan A, Demir S. Therapeutic effects of carvacrol on beta-amyloid-induced impairments in in vitro and in vivo models of Alzheimer's disease. The European Journal of Neuroscience. 2022; 56: 5714–5726.
[43] Zhu L, Lu F, Zhang X, Liu S, Mu P. SIRT1 Is Involved in the Neuroprotection of Pterostilbene Against Amyloid β 25-35-Induced Cognitive Deficits in Mice. Frontiers in Pharmacology. 2022; 13: 877098.
[44] Xu J, Liu J, Li Q, Li G, Zhang G, Mi Y, *et al*. Pterostilbene participates in TLR4- mediated inflammatory response and autophagy-dependent Aβ_{1-42} endocytosis in Alzheimer's disease. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology. 2023; 119: 155011.
[45] Fasina OB, Wang J, Mo J, Osada H, Ohno H, Pan W, *et al*. Gastrodin From *Gastrodia elata* Enhances Cognitive Function and Neuroprotection of AD Mice *via* the Regulation of Gut Microbiota Composition and Inhibition of Neuron Inflammation. Frontiers in Pharmacology. 2022; 13: 814271.
[46] Assaran AH, Akbarian M, Amirahmadi S, Salmani H, Shirzad S, Hosseini M, *et al*. Ellagic Acid Prevents Oxidative Stress and Memory Deficits in a Rat Model of Scopolamine-induced Alzheimer's Disease. Central Nervous System Agents in Medicinal Chemistry. 2022; 22: 214–227.
[47] Cai Y, Chai Y, Fu Y, Wang Y, Zhang Y, Zhang X, *et al*. Salidroside Ameliorates Alzheimer's Disease by Targeting NLRP3 Inflammasome-Mediated Pyroptosis. Frontiers in Aging Neuroscience. 2022; 13: 809433.
[48] Yang S, Wang L, Zeng Y, Wang Y, Pei T, Xie Z, *et al*. Salidroside alleviates cognitive impairment by inhibiting ferroptosis via activation of the Nrf2/GPX4 axis in SAMP8 mice. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology. 2023; 114: 154762.
[49] Bartra C, Yuan Y, Vuraić K, Valdés-Quiroz H, Garcia-Baucells P, Slevin M, *et al*. Resveratrol Activates Antioxidant Protective Mechanisms in Cellular Models of Alzheimer's Disease Inflammation. Antioxidants (Basel, Switzerland). 2024; 13: 177.
[50] Shao S, Ye X, Su W, Wang Y. Curcumin alleviates Alzheimer's disease by inhibiting inflammatory response, oxidative stress and activating the AMPK pathway. Journal of Chemical Neuroanatomy. 2023; 134: 102363.
[51] Nan S, Wang P, Zhang Y, Fan J. Epigallocatechin-3-Gallate Provides Protection Against Alzheimer's Disease-Induced Learning and Memory Impairments in Rats. Drug Design, Development and Therapy. 2021; 15: 2013–2024.
[52] Zhang N, Xu H, Wang Y, Yao Y, Liu G, Lei X, *et al*. Protective mechanism of kaempferol against Aβ_{25-35}-mediated apoptosis of pheochromocytoma (PC-12) cells through the ER/ERK/MAPK signalling pathway. Archives of Medical Science: AMS. 2020; 17: 406–416.
[53] Uysal M, Celikten M, Beker M, Polat N, Huseyinbas O, Terzioglu-Usak S, *et al*. Kaempferol treatment ameliorates memory impairments in STZ induced neurodegeneration by acting on reelin signaling. Acta Neurobiologiae Experimentalis. 2023; 83: 236–245.
[54] Paula PC, Angelica Maria SG, Luis CH, Gloria Patricia CG. Preventive Effect of Quercetin in a Triple Transgenic Alzheimer's Disease Mice Model. Molecules (Basel, Switzerland). 2019; 24: 2287.
[55] Yu X, Li Y, Mu X. Effect of Quercetin on PC12 Alzheimer's Disease Cell Model Induced by Aβ_{25-35} and Its Mechanism Based on Sirtuin1/Nrf2/HO-1 Pathway. BioMed Research International. 2020; 2020: 8210578.
[56] Pierzynowska K, Podlacha M, Gaffke L, Majkutewicz I, Mantej J, Węgrzyn A, *et al*. Autophagy-dependent mechanism of genistein-mediated elimination of behavioral and biochemical defects in the rat model of sporadic Alzheimer's disease. Neuropharmacology. 2019; 148: 332–346.

[57] Gao H, Lei X, Ye S, Ye T, Hua R, Wang G, *et al*. Genistein attenuates memory impairment in Alzheimer's disease via ERS-mediated apoptotic pathway in vivo and in vitro. The Journal of Nutritional Biochemistry. 2022; 109: 109118.
[58] Zhao N, Sun C, Zheng M, Liu S, Shi R. Amentoflavone suppresses amyloid β1-42 neurotoxicity in Alzheimer's disease through the inhibition of pyroptosis. Life Sciences. 2019; 239: 117043.
[59] Xu M, Huang H, Mo X, Zhu Y, Chen X, Li X, *et al*. Quercetin-3-O-Glucuronide Alleviates Cognitive Deficit and Toxicity in Aβ_{1-42} -Induced AD-Like Mice and SH-SY5Y Cells. Molecular Nutrition & Food Research. 2021; 65: e2000660.
[60] Ahsan AU, Sharma VL, Wani A, Chopra M. Naringenin Upregulates AMPK-Mediated Autophagy to Rescue Neuronal Cells From β-Amyloid $_{(1-42)}$ Evoked Neurotoxicity. Molecular Neurobiology. 2020; 57: 3589–3602.
[61] Sun XY, Li LJ, Dong QX, Zhu J, Huang YR, Hou SJ, *et al*. Rutin prevents tau pathology and neuroinflammation in a mouse model of Alzheimer's disease. Journal of Neuroinflammation. 2021; 18: 131.
[62] Gonçalves AE, Malheiros Â, Casarin CA, de França L, Palomino-Salcedo DL, Ferreira LLG, *et al*. 2',6'-dihydroxy-4'-methoxy Dihydrochalcone Improves the Cognitive Impairment of Alzheimer's Disease: A Structure-activity Relationship Study. Current Topics in Medicinal Chemistry. 2021; 21: 1167–1185.
[63] Zhang Z, Tan X, Sun X, Wei J, Li QX, Wu Z. Isoorientin Affects Markers of Alzheimer's Disease via Effects on the Oral and Gut Microbiota in APP/PS1 Mice. The Journal of Nutrition. 2022; 152: 140–152.
[64] Ding J, Huang J, Yin D, Liu T, Ren Z, Hu S, *et al*. Trilobatin Alleviates Cognitive Deficits and Pathologies in an Alzheimer's Disease Mouse Model. Oxidative Medicine and Cellular Longevity. 2021; 2021: 3298400.
[65] Li L, Li WJ, Zheng XR, Liu QL, Du Q, Lai YJ, *et al*. Eriodictyol ameliorates cognitive dysfunction in APP/PS1 mice by inhibiting ferroptosis via vitamin D receptor-mediated Nrf2 activation. Molecular Medicine (Cambridge, Mass.). 2022; 28: 11.
[66] Wang L, Sun J, Miao Z, Jiang X, Zheng Y, Yang G. Quercitrin improved cognitive impairment through inhibiting inflammation induced by microglia in Alzheimer's disease mice. Neuroreport. 2022; 33: 327–335.
[67] Lee D, Kim N, Jeon SH, Gee MS, Ju YJ, Jung MJ, *et al*. Hesperidin Improves Memory Function by Enhancing Neurogenesis in a Mouse Model of Alzheimer's Disease. Nutrients. 2022; 14: 3125.
[68] Yan F, Liu J, Chen MX, Zhang Y, Wei SJ, Jin H, *et al*. Icariin ameliorates memory deficits through regulating brain insulin signaling and glucose transporters in 3×Tg-AD mice. Neural Regeneration Research. 2023; 18: 183–188.
[69] Wan M, Sun S, Di X, Zhao M, Lu F, Zhang Z, *et al*. Icariin improves learning and memory function in Aβ_{1-42}-induced AD mice through regulation of the BDNF-TrκB signaling pathway. Journal of Ethnopharmacology. 2024; 318: 117029.
[70] Pei H, Han C, Bi J, He Z, Guo L. Dihydromyricetin suppresses inflammatory injury in microglial cells to improve neurological behaviors of Alzheimer's disease mice via the TLR4/MD2 signal. International Immunopharmacology. 2023; 118: 110037.
[71] Liu P, Chen W, Kang Y, Wang C, Wang X, Liu W, *et al*. Silibinin ameliorates STING-mediated neuroinflammation via downregulation of ferroptotic damage in a sporadic Alzheimer's disease model. Archives of Biochemistry and Biophysics. 2023; 744: 109691.
[72] El-Maraghy SA, Reda A, Essam RM, Kortam MA. The citrus flavonoid "Nobiletin" impedes STZ-induced Alzheimer's disease in a mouse model through regulating autophagy mastered by SIRT1/FoxO3a mechanism. Inflammopharmacology. 2023; 31: 2701–2717.
[73] He Z, Li X, Wang Z, Cao Y, Han S, Li N, *et al*. Protective effects of luteolin against amyloid beta-induced oxidative stress and mitochondrial impairments through peroxisome proliferator-activated receptor γ-dependent mechanism in Alzheimer's disease. Redox Biology. 2023; 66: 102848.
[74] Shi J, Li Y, Zhang Y, Chen J, Gao J, Zhang T, *et al*. Baicalein Ameliorates Aβ-Induced Memory Deficits and Neuronal Atrophy *via* Inhibition of PDE2 and PDE4. Frontiers in Pharmacology. 2021; 12: 794458.
[75] Xie XM, Hao JJ, Shi JZ, Zhou YF, Liu PF, Wang F, *et al*. Baicalein ameliorates Alzheimer's disease via orchestration of CX3CR1/NF-κB pathway in a triple transgenic mouse model. International Immunopharmacology. 2023; 118: 109994.
[76] Dong P, Ji X, Han W, Han H. Oxymatrine exhibits anti-neuroinflammatory effects on Aβ_{1-42}-induced primary microglia cells by inhibiting NF-κB and MAPK signaling pathways. International Immunopharmacology. 2019; 74: 105686.
[77] Li HQ, Ip SP, Yuan QJ, Zheng GQ, Tsim KKW, Dong TTX, *et al*. Isorhynchophylline ameliorates cognitive impairment via modulating amyloid pathology, tau hyperphosphorylation and neuroinflammation: Studies in a transgenic mouse model of Alzheimer's disease. Brain, Behavior, and Immunity. 2019; 82: 264–278.
[78] Zhao B, Wang Y, Liu R, Jia XL, Hu N, An XW, *et al*. Rutaecarpine Ameliorated High Sucrose-Induced Alzheimer's Disease Like Pathological and Cognitive Impairments in Mice. Rejuvenation Research. 2021; 24: 181–190.
[79] Ren D, Fu Y, Wang L, Liu J, Zhong X, Yuan J, *et al*. Tetrandrine ameliorated Alzheimer's disease through suppressing microglial inflammatory activation and neurotoxicity in the 5XFAD mouse. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology. 2021; 90: 153627.
[80] Ye JY, Hao Q, Zong Y, Shen Y, Zhang Z, Ma C. Sophocarpine Attenuates Cognitive Impairment and Promotes Neurogenesis in a Mouse Model of Alzheimer's Disease. Neuroimmunomodulation. 2021; 28: 166–177.
[81] Fu WY, Hung KW, Lau SF, Butt B, Yuen VWH, Fu G, *et al*. Rhynchophylline Administration Ameliorates Amyloid-β Pathology and Inflammation in an Alzheimer's Disease Transgenic Mouse Model. ACS Chemical Neuroscience. 2021; 12: 4249–4256.
[82] Jiang X, Wu Q, Zhang C, Wang M. Homoharringtonine Inhibits Alzheimer's Disease Progression by Reducing Neuroinflammation via STAT3 Signaling in APP/PS1 Mice. Neuro-degenerative Diseases. 2021; 21: 93–102.
[83] Zhang Y, Liu D, Yao X, Wen J, Wang Y, Zhang Y. DMTHB ameliorates memory impairment in Alzheimer's disease mice through regulation of neuroinflammation. Neuroscience Letters. 2022; 785: 136770.
[84] Zhong L, Qin Y, Liu M, Sun J, Tang H, Zeng Y, *et al*. Magnoflorine improves cognitive deficits and pathology of Alzheimer's disease via inhibiting of JNK signaling pathway. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology. 2023; 112: 154714.
[85] Xue JS, Li JQ, Wang CC, Ma XH, Dai H, Xu CB, *et al*. Dauricine alleviates cognitive impairment in Alzheimer's disease mice induced by D-galactose and $AlCl_3$ via the Ca^{2+}/CaM pathway. Toxicology and Applied Pharmacology. 2023; 474: 116613.
[86] Li X, Chen J, Feng W, Wang C, Chen M, Li Y, *et al*. Berberine ameliorates iron levels and ferroptosis in the brain of 3 × Tg-AD mice. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology. 2023; 118: 154962.
[87] Guo Q, He J, Zhang H, Yao L, Li H. Oleanolic acid alleviates oxidative stress in Alzheimer's disease by regulating stanniocalcin-

1 and uncoupling protein-2 signalling. Clinical and Experimental Pharmacology & Physiology. 2020; 47: 1263–1271.
[88] Zhao X, Li S, Gaur U, Zheng W. Artemisinin Improved Neuronal Functions in Alzheimer's Disease Animal Model 3xtg Mice and Neuronal Cells via Stimulating the ERK/CREB Signaling Pathway. Aging and Disease. 2020; 11: 801–819.
[89] Zhao X, Huang X, Yang C, Jiang Y, Zhou W, Zheng W. Artemisinin Attenuates Amyloid-Induced Brain Inflammation and Memory Impairments by Modulating TLR4/NF-κB Signaling. International Journal of Molecular Sciences. 2022; 23: 6354.
[90] Yuan C, Shin M, Park Y, Choi B, Jang S, Lim C, *et al*. Linalool Alleviates Aβ42-Induced Neurodegeneration via Suppressing ROS Production and Inflammation in Fly and Rat Models of Alzheimer's Disease. Oxidative Medicine and Cellular Longevity. 2021; 2021: 8887716.
[91] Ding B, Lin C, Liu Q, He Y, Ruganzu JB, Jin H, *et al*. Tanshinone IIA attenuates neuroinflammation via inhibiting RAGE/NF-κB signaling pathway in vivo and in vitro. Journal of Neuroinflammation. 2020; 17: 302.
[92] Xiang J, Yang F, Zhu W, Cai M, Li XT, Zhang JS, *et al*. Bilobalide inhibits inflammation and promotes the expression of Aβ degrading enzymes in astrocytes to rescue neuronal deficiency in AD models. Translational Psychiatry. 2021; 11: 542.
[93] Chen QY, Yin Y, Li L, Zhang YJ, He W, Shi Y. Geniposidic Acid Confers Neuroprotective Effects in a Mouse Model of Alzheimer's Disease through Activation of a PI3K/AKT/GAP43 Regulatory Axis. The Journal of Prevention of Alzheimer's Disease. 2022; 9: 158–171.
[94] Niu TT, Yin H, Xu BL, Yang TT, Li HQ, Sun Y, *et al*. Protective Effects of Ginkgolide on a Cellular Model of Alzheimer's Disease via Suppression of the NF-κB Signaling Pathway. Applied Biochemistry and Biotechnology. 2022; 194: 2448–2464.
[95] Liu Z, Kumar M, Kabra A. Cucurbitacin B exerts neuroprotection in a murine Alzheimer's disease model by modulating oxidative stress, inflammation, and neurotransmitter levels. Frontiers in Bioscience (Landmark Edition). 2022; 27: 71.
[96] Shao L, Dong C, Geng D, He Q, Shi Y. Ginkgolide B inactivates the NLRP3 inflammasome by promoting autophagic degradation to improve learning and memory impairment in Alzheimer's disease. Metabolic Brain Disease. 2022; 37: 329–341.
[97] Tang JJ, Huang LF, Deng JL, Wang YM, Guo C, Peng XN, *et al*. Cognitive enhancement and neuroprotective effects of OABL, a sesquiterpene lactone in 5xFAD Alzheimer's disease mice model. Redox Biology. 2022; 50: 102229.
[98] Yang Y, Wang L, Zhang C, Guo Y, Li J, Wu C, *et al*. Ginsenoside Rg1 improves Alzheimer's disease by regulating oxidative stress, apoptosis, and neuroinflammation through Wnt/GSK-3β/β-catenin signaling pathway. Chemical Biology & Drug Design. 2022; 99: 884–896.
[99] Qin YR, Ma CQ, Jiang JH, Wang DP, Zhang QQ, Liu MR, *et al*. Artesunate restores mitochondrial fusion-fission dynamics and alleviates neuronal injury in Alzheimer's disease models. Journal of Neurochemistry. 2022; 162: 290–304.
[100] Yang C, Su C, Iyaswamy A, Krishnamoorthi SK, Zhu Z, Yang S, *et al*. Celastrol enhances transcription factor EB (TFEB)-mediated autophagy and mitigates Tau pathology: Implications for Alzheimer's disease therapy. Acta Pharmaceutica Sinica. B. 2022; 12: 1707–1722.
[101] Yan QY, Lv JL, Shen XY, Ou-Yang XN, Yang JZ, Nie RF, *et al*. Patchouli alcohol as a selective estrogen receptor β agonist ameliorates AD-like pathology of APP/PS1 model mice. Acta Pharmacologica Sinica. 2022; 43: 2226–2241.
[102] Zhai L, Pei H, Shen H, Yang Y, Han C, Guan Q. Paeoniflorin suppresses neuronal ferroptosis to improve the cognitive behaviors in Alzheimer's disease mice. Phytotherapy Research: PTR. 2023; 37: 4791–4800.
[103] Li S, Tian Z, Xian X, Yan C, Li Q, Li N, *et al*. Catalpol rescues cognitive deficits by attenuating amyloid β plaques and neuroinflammation. Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie. 2023; 165: 115026.
[104] Bao M, Bade R, Liu H, Tsambaa B, Shao G, Borjigidai A, *et al*. Astragaloside IV against Alzheimer's disease via microglia-mediated neuroinflammation using network pharmacology and experimental validation. European Journal of Pharmacology. 2023; 957: 175992.
[105] Li Y, Wang B, Liu C, Zhu X, Zhang P, Yu H, *et al*. Inhibiting c-Jun N-terminal kinase (JNK)-mediated apoptotic signaling pathway in PC12 cells by a polysaccharide (CCP) from Coptis chinensis against Amyloid-β (Aβ)-induced neurotoxicity. International Journal of Biological Macromolecules. 2019; 134: 565–574.
[106] Zhou Y, Duan Y, Huang S, Zhou X, Zhou L, Hu T, *et al*. Polysaccharides from Lycium barbarum ameliorate amyloid pathology and cognitive functions in APP/PS1 transgenic mice. International Journal of Biological Macromolecules. 2020; 144: 1004–1012.
[107] Du Q, Zhu X, Si J. Angelica polysaccharide ameliorates memory impairment in Alzheimer's disease rat through activating BDNF/TrkB/CREB pathway. Experimental Biology and Medicine (Maywood, N.J.). 2020; 245: 1–10.
[108] Wan L, Zhang Q, Luo H, Xu Z, Huang S, Yang F, *et al*. *Codonopsis pilosula* polysaccharide attenuates Aβ toxicity and cognitive defects in APP/PS1 mice. Aging. 2020; 12: 13422–13436.
[109] Qin X, Hua J, Lin SJ, Zheng HT, Wang JJ, Li W, *et al*. Astragalus polysaccharide alleviates cognitive impairment and β-amyloid accumulation in APP/PS1 mice via Nrf2 pathway. Biochemical and Biophysical Research Communications. 2020; 531: 431–437.
[110] Zhang S, Li L, Hu J, Ma P, Zhu H. Polysaccharide of *Taxus chinensis* var. *mairei* Cheng et L.K.Fu attenuates neurotoxicity and cognitive dysfunction in mice with Alzheimer's disease. Pharmaceutical Biology. 2020; 58: 959–968.
[111] Gao Y, Li B, Liu H, Tian Y, Gu C, Du X, *et al*. *Cistanche deserticola* polysaccharides alleviate cognitive decline in aging model mice by restoring the gut microbiota-brain axis. Aging. 2021; 13: 15320–15335.
[112] Bian Z, Li C, Peng D, Wang X, Zhu G. Use of Steaming Process to Improve Biochemical Activity of *Polygonatum sibiricum* Polysaccharides against D-Galactose-Induced Memory Impairment in Mice. International Journal of Molecular Sciences. 2022; 23: 11220.
[113] Wang S, Kong X, Chen Z, Wang G, Zhang J, Wang J. Role of Natural Compounds and Target Enzymes in the Treatment of Alzheimer's Disease. Molecules (Basel, Switzerland). 2022; 27: 4175.
[114] Zhang Q, Yan Y. The role of natural flavonoids on neuroinflammation as a therapeutic target for Alzheimer's disease: a narrative review. Neural Regeneration Research. 2023; 18: 2582–2591.
[115] Gorzynik-Debicka M, Przychodzen P, Cappello F, Kuban-Jankowska A, Marino Gammazza A, Knap N, *et al*. Potential Health Benefits of Olive Oil and Plant Polyphenols. International Journal of Molecular Sciences. 2018; 19: 686.
[116] Uddin MS, Hasana S, Ahmad J, Hossain MF, Rahman MM, Behl T, *et al*. Anti-Neuroinflammatory Potential of Polyphenols by Inhibiting NF-κB to Halt Alzheimer's Disease. Current Pharmaceutical Design. 2021; 27: 402–414.
[117] Sun Q, Jia N, Li X, Yang J, Chen G. Grape seed proanthocyanidins ameliorate neuronal oxidative damage by inhibiting GSK-3β-dependent mitochondrial permeability transition pore open-

ing in an experimental model of sporadic Alzheimer's disease. Aging. 2019; 11: 4107–4124.
[118] Gao WL, Li XH, Dun XP, Jing XK, Yang K, Li YK. Grape Seed Proanthocyanidin Extract Ameliorates Streptozotocin-induced Cognitive and Synaptic Plasticity Deficits by Inhibiting Oxidative Stress and Preserving AKT and ERK Activities. Current Medical Science. 2020; 40: 434–443.
[119] Subhan I, Siddique YH. Resveratrol: Protective agent against Alzheimer's disease. Central Nervous System Agents in Medicinal Chemistry. 2024. (online ahead of print)
[120] Yang L, Wang Y, Zheng G, Li Z, Mei J. Resveratrol-loaded selenium/chitosan nano-flowers alleviate glucolipid metabolism disorder-associated cognitive impairment in Alzheimer's disease. International Journal of Biological Macromolecules. 2023; 239: 124316.
[121] Mugundhan V, Arthanari A, Parthasarathy PR. Protective Effect of Ferulic Acid on Acetylcholinesterase and Amyloid Beta Peptide Plaque Formation in Alzheimer's Disease: An In Vitro Study. Cureus. 2024; 16: e54103.
[122] Shen N, Wang T, Gan Q, Liu S, Wang L, Jin B. Plant flavonoids: Classification, distribution, biosynthesis, and antioxidant activity. Food Chemistry. 2022; 383: 132531.
[123] Li F, Zhang Y, Lu X, Shi J, Gong Q. Icariin improves the cognitive function of APP/PS1 mice via suppressing endoplasmic reticulum stress. Life Sciences. 2019; 234: 116739.
[124] Cui L, Cai Y, Cheng W, Liu G, Zhao J, Cao H, *et al*. A Novel, Multi-Target Natural Drug Candidate, Matrine, Improves Cognitive Deficits in Alzheimer's Disease Transgenic Mice by Inhibiting Aβ Aggregation and Blocking the RAGE/Aβ Axis. Molecular Neurobiology. 2017; 54: 1939–1952.
[125] Lee DY, Lee KM, Um JH, Kim YY, Kim DH, Yun J. The Natural Alkaloid Palmatine Selectively Induces Mitophagy and Restores Mitochondrial Function in an Alzheimer's Disease Mouse Model. International Journal of Molecular Sciences. 2023; 24: 16542.
[126] Zhou JC, Li HL, Zhou Y, Li XT, Yang ZY, Tohda C, *et al*. The roles of natural triterpenoid saponins against Alzheimer's disease. Phytotherapy Research: PTR. 2023; 37: 5017–5040.
[127] Rivera Rodríguez R, Johnson JJ. Terpenes: Modulating anti-inflammatory signaling in inflammatory bowel disease. Pharmacology & Therapeutics. 2023; 248: 108456.
[128] Friedli MJ, Inestrosa NC. Huperzine A and Its Neuroprotective Molecular Signaling in Alzheimer's Disease. Molecules (Basel, Switzerland). 2021; 26: 6531.
[129] Xu QQ, Su ZR, Yang W, Zhong M, Xian YF, Lin ZX. Patchouli alcohol attenuates the cognitive deficits in a transgenic mouse model of Alzheimer's disease via modulating neuropathology and gut microbiota through suppressing C/EBPβ/AEP pathway. Journal of Neuroinflammation. 2023; 20: 19.
[130] Wan C, Liu XQ, Chen M, Ma HH, Wu GL, Qiao LJ, *et al*. Tanshinone IIA ameliorates Aβ transendothelial transportation through SIRT1-mediated endoplasmic reticulum stress. Journal of Translational Medicine. 2023; 21: 34.
[131] Peng X, Chen L, Wang Z, He Y, Ruganzu JB, Guo H, *et al*. Tanshinone IIA regulates glycogen synthase kinase-3β-related signaling pathway and ameliorates memory impairment in APP/PS1 transgenic mice. European Journal of Pharmacology. 2022; 918: 174772.
[132] Dhahri M, Alghrably M, Mohammed HA, Badshah SL, Noreen N, Mouffouk F, *et al*. Natural Polysaccharides as Preventive and Therapeutic Horizon for Neurodegenerative Diseases. Pharmaceutics. 2021; 14: 1.
[133] Peng G, Li M, Meng Z. Polysaccharides: potential bioactive macromolecules for Alzheimer's disease. Frontiers in Nutrition. 2023; 10: 1249018.
[134] Li X, Wang X, Huang B, Huang R. Sennoside A restrains TRAF6 level to modulate ferroptosis, inflammation and cognitive impairment in aging mice with Alzheimer's Disease. International Immunopharmacology. 2023; 120: 110290.
[135] Yin Z, Gao D, Du K, Han C, Liu Y, Wang Y, *et al*. Rhein Ameliorates Cognitive Impairment in an APP/PS1 Transgenic Mouse Model of Alzheimer's Disease by Relieving Oxidative Stress through Activating the SIRT1/PGC-1α Pathway. Oxidative Medicine and Cellular Longevity. 2022; 2022: 2524832.
[136] Zhong J, Wang Z, Xie Q, Li T, Chen K, Zhu T, *et al*. Shikonin ameliorates D-galactose-induced oxidative stress and cognitive impairment in mice via the MAPK and nuclear factor-κB signaling pathway. International Immunopharmacology. 2020; 83: 106491.
[137] Xian YF, Qu C, Liu Y, Ip SP, Yuan QJ, Yang W, *et al*. Magnolol Ameliorates Behavioral Impairments and Neuropathology in a Transgenic Mouse Model of Alzheimer's Disease. Oxidative Medicine and Cellular Longevity. 2020; 2020: 5920476.
[138] Wang C, Chen S, Guo H, Jiang H, Liu H, Fu H, *et al*. Forsythoside A Mitigates Alzheimer's-like Pathology by Inhibiting Ferroptosis-mediated Neuroinflammation via Nrf2/GPX4 Axis Activation. International Journal of Biological Sciences. 2022; 18: 2075–2090.
[139] Li C, Gao F, Qu Y, Zhao P, Wang X, Zhu G. Tenuifolin in the prevention of Alzheimer's disease-like phenotypes: Investigation of the mechanisms from the perspectives of calpain system, ferroptosis, and apoptosis. Phytotherapy Research: PTR. 2023; 4621–4638.
[140] Li N, Pang Q, Zhang Y, Lin J, Li H, Li Z, *et al*. Ginsenoside ompound K reduces neuronal damage and improves neuronal synaptic dysfunction by targeting Aβ. Frontiers in Pharmacology. 2023; 14: 1103012.
[141] Xu Z, Zhou X, Hong X, Wang S, Wei J, Huang J, *et al*. Essential oil of Acorus tatarinowii Schott inhibits neuroinflammation by suppressing NLRP3 inflammasome activation in 3 × Tg-AD transgenic mice. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology. 2023; 112: 154695.
[142] Al-Tawarah NM, Al-Dmour RH, Abu Hajleh MN, Khleifat KM, Alqaraleh M, Al-Saraireh YM, *et al*. *Rosmarinus officinalis* and *Mentha piperita* Oils Supplementation Enhances Memory in a Rat Model of Scopolamine-Induced Alzheimer's Disease-like Condition. Nutrients. 2023; 15: 1547.
[143] Ghimire S, Subedi L, Acharya N, Gaire BP. *Moringa oleifera*: A Tree of Life as a Promising Medicinal Plant for Neurodegenerative Diseases. Journal of Agricultural and Food Chemistry. 2021; 69: 14358–14371.
[144] Satoh T, Trudler D, Oh CK, Lipton SA. Potential Therapeutic Use of the Rosemary Diterpene Carnosic Acid for Alzheimer's Disease, Parkinson's Disease, and Long-COVID through NRF2 Activation to Counteract the NLRP3 Inflammasome. Antioxidants (Basel, Switzerland). 2022; 11: 124.
[145] Anupama KP, Shilpa O, Antony A, Gurushankara HP. Jatamansinol from *Nardostachys jatamansi*: a multi-targeted neuroprotective agent for Alzheimer's disease. Journal of Biomolecular Structure & Dynamics. 2023; 41: 200–220.
[146] Vig R, Bhadra F, Gupta SK, Sairam K, Vasundhara M. Neuroprotective effects of quercetin produced by an endophytic fungus Nigrospora oryzae isolated from Tinospora cordifolia. Journal of Applied Microbiology. 2022; 132: 365–380.
[147] Cheenpracha S, Jitonnom J, Komek M, Ritthiwigrom T, Laphookhieo S. Acetylcholinesterase inhibitory activity and molecular docking study of steroidal alkaloids from Holarrhena pubescens barks. Steroids. 2016; 108: 92–98.
[148] Freitas TR, Danuello A, Viegas Júnior C, Bolzani VS, Pivatto M. Mass spectrometry for characterization of homologous piperidine alkaloids and their activity as acetylcholinesterase inhibitors. Rapid Communications in Mass Spectrometry: RCM.

2018; 32: 1303–1310.
[149] Mosbah H, Chahdoura H, Adouni K, Kamoun J, Boujbiha MA, Gonzalez-Paramas AM, *et al*. Nutritional properties, identification of phenolic compounds, and enzyme inhibitory activities of Feijoa sellowiana leaves. Journal of Food Biochemistry. 2019; 43: e13012.
[150] Baek SC, Park MH, Ryu HW, Lee JP, Kang MG, Park D, *et al*. Rhamnocitrin isolated from Prunus padus var. seoulensis: A potent and selective reversible inhibitor of human monoamine oxidase A. Bioorganic Chemistry. 2019; 83: 317–325.
[151] Varshney H, Siddique YH. Effect of Natural Plant Products on Alzheimer's Disease. CNS & Neurological Disorders Drug Targets. 2024; 23: 246–261.
[152] Yang Y, Liang X, Jin P, Li N, Zhang Q, Yan W, *et al*. Screening and determination for potential acetylcholinesterase inhibitory constituents from ginseng stem-leaf saponins using ultrafiltration (UF)-LC-ESI-MS^2. Phytochemical Analysis: PCA. 2019; 30: 26–33.
[153] Li S, Liu C, Liu C, Zhang Y. Extraction and in vitro screening of potential acetylcholinesterase inhibitors from the leaves of Panax japonicus. Journal of Chromatography. B, Analytical Technologies in the Biomedical and Life Sciences. 2017; 1061-1062: 139–145.
[154] Zhan G, Zhou J, Liu J, Huang J, Zhang H, Liu R, *et al*. Acetylcholinesterase Inhibitory Alkaloids from the Whole Plants of Zephyranthes carinata. Journal of Natural Products. 2017; 80: 2462–2471.
[155] Guo J, Liu S, Guo Y, Bai L, Ho CT, Bai N. Chemical characterization, multivariate analysis and comparison of biological activities of different parts of Fraxinus mandshurica. Biomedical Chromatography: BMC. 2024; 38: e5861.
[156] Hung NH, Quan PM, Satyal P, Dai DN, Hoa VV, Huy NG, *et al*. Acetylcholinesterase Inhibitory Activities of Essential Oils from Vietnamese Traditional Medicinal Plants. Molecules (Basel, Switzerland). 2022; 27: 7092.
[157] Al-Mijalli SH, Mrabti HN, Ouassou H, Flouchi R, Abdallah EM, Sheikh RA, *et al*. Chemical Composition, Antioxidant, Anti-Diabetic, Anti-Acetylcholinesterase, Anti-Inflammatory, and Antimicrobial Properties of *Arbutus unedo* L. and *Laurus nobilis* L. Essential Oils. Life (Basel, Switzerland). 2022; 12: 1876.
[158] Gul A, Bakht J, Mehmood F. Huperzine-A response to cognitive impairment and task switching deficits in patients with Alzheimer's disease. Journal of the Chinese Medical Association: JCMA. 2019; 82: 40–43.
[159] Chua KK, Wong A, Kwan PWL, Song JX, Chen LL, Chan ALT, *et al*. The efficacy and safety of the Chinese herbal medicine Di-Tan decoction for treating Alzheimer's disease: protocol for a randomized controlled trial. Trials. 2015; 16: 199.
[160] Zhang Y, Lin C, Zhang L, Cui Y, Gu Y, Guo J, *et al*. Cognitive Improvement during Treatment for Mild Alzheimer's Disease with a Chinese Herbal Formula: A Randomized Controlled Trial. PloS One. 2015; 10: e0130353.
[161] Xu M, Yue Y, Huang J. Efficacy evaluation and metabolomics analysis of Huanglian Jiedu decoction in combination with donepezil for Alzheimer's disease treatment. Journal of Pharmaceutical and Biomedical Analysis. 2023; 235: 115610.
[162] Wang HC, Liu NY, Zhang S, Yang Y, Wang ZY, Wei Y, *et al*. Clinical Experience in Treatment of Alzheimer's Disease with Jiannao Yizhi Formula () and Routine Western Medicine. Chinese Journal of Integrative Medicine. 2020; 26: 212–218.
[163] Rainer M, Mucke H, Schlaefke S. Ginkgo biloba extract EGb 761 in the treatment of dementia: a pharmacoeconomic analysis of the Austrian setting. Wiener Klinische Wochenschrift. 2013; 125: 8–15.
[164] Zeng L, Zou Y, Kong L, Wang N, Wang Q, Wang L, *et al*. Can Chinese Herbal Medicine Adjunctive Therapy Improve Outcomes of Senile Vascular Dementia? Systematic Review with Meta-analysis of Clinical Trials. Phytotherapy Research: PTR. 2015; 29: 1843–1857.
[165] Yu W, Ma M, Chen X, Min J, Li L, Zheng Y, *et al*. Traditional Chinese Medicine and Constitutional Medicine in China, Japan and Korea: A Comparative Study. The American Journal of Chinese Medicine. 2017; 45: 1–12.
[166] Traditional Chinese Medicine. Traditional Chinese medicine accounted for 40% of China's pharmaceutical market in 2019, as Stated by Insightslice GlobeNewswire News Room. 2021. Available at: https://www.globenewswire.com/en/news-release/2021/02/15/2175561/0/en/Traditional-Chinese-Medicine-Accounted-for-40-of-China-s-Pharmaceutical-Market-in-2019-as-stated-by-insightSLICE.html (Accessed: 18 February 2022).
[167] Calixto JB. Twenty-five years of research on medicinal plants in Latin America: a personal view. Journal of Ethnopharmacology. 2005; 100: 131–134.
[168] World Health Organisation. Global report on traditional and complementary medicine. World Health Organization: Geneva. 2019.
[169] Mukherjee PK, Kumar V, Houghton PJ. Screening of Indian medicinal plants for acetylcholinesterase inhibitory activity. Phytotherapy Research: PTR. 2007; 21: 1142–1145.
[170] Lobbens ESB, Vissing KJ, Jorgensen L, van de Weert M, Jäger AK. Screening of plants used in the European traditional medicine to treat memory disorders for acetylcholinesterase inhibitory activity and anti amyloidogenic activity. Journal of Ethnopharmacology. 2017; 200: 66–73.
[171] Kumar P, Mathew S, Gamage R, Bodkin F, Doyle K, Rossetti I, *et al*. From the Bush to the Brain: Preclinical Stages of Ethnobotanical Anti-Inflammatory and Neuroprotective Drug Discovery-An Australian Example. International Journal of Molecular Sciences. 2023; 24: 11086.
[172] Ayeni EA, Gong Y, Yuan H, Hu Y, Bai X, Liao X. Medicinal Plants for Anti-neurodegenerative diseases in West Africa. Journal of Ethnopharmacology. 2022; 285: 114468.
[173] Kudoh C, Arita R, Honda M, Kishi T, Komatsu Y, Asou H, *et al*. Effect of ninjin'yoeito, a Kampo (traditional Japanese) medicine, on cognitive impairment and depression in patients with Alzheimer's disease: 2 years of observation. Psychogeriatrics: the Official Journal of the Japanese Psychogeriatric Society. 2016; 16: 85–92.
[174] Kandiah N, Ong PA, Yuda T, Ng LL, Mamun K, Merchant RA, *et al*. Treatment of dementia and mild cognitive impairment with or without cerebrovascular disease: Expert consensus on the use of Ginkgo biloba extract, EGb 761®. CNS Neuroscience & Therapeutics. 2019; 25: 288–298.
[175] Olin J, Schneider L. Galantamine for Alzheimer's disease. The Cochrane Database of Systematic Reviews. 2002; CD001747.
[176] Marucci G, Buccioni M, Ben DD, Lambertucci C, Volpini R, Amenta F. Efficacy of acetylcholinesterase inhibitors in Alzheimer's disease. Neuropharmacology. 2021; 190: 108352.
[177] Peng Y, Jin H, Xue YH, Chen Q, Yao SY, Du MQ, *et al*. Current and future therapeutic strategies for Alzheimer's disease: an overview of drug development bottlenecks. Frontiers in Aging Neuroscience. 2023; 15: 1206572.
[178] Varadharajan A, Davis AD, Ghosh A, Jagtap T, Xavier A, Menon AJ, *et al*. Guidelines for pharmacotherapy in Alzheimer's disease - A primer on FDA-approved drugs. Journal of Neurosciences in Rural Practice. 2023; 14: 566–573.
[179] Jarrell JT, Gao L, Cohen DS, Huang X. Network Medicine for Alzheimer's Disease and Traditional Chinese Medicine. Molecules (Basel, Switzerland). 2018; 23: 1143.
[180] Wu X, Cao S, Zou Y, Wu F. Traditional Chinese Medicine studies for Alzheimer's disease via network pharmacology based on

entropy and random walk. PloS One. 2023; 18: e0294772.
[181] Zhang M, Zheng H, He J, Zhang M. Network pharmacology and *in vivo* studies reveal the neuroprotective effects of paeoniflorin on Alzheimer's disease. Heliyon. 2023; 9: e21800.
[182] Qiu ZK, Zhou BX, Pang J, Zeng WQ, Wu HB, Yang F. The network pharmacology study and molecular docking to investigate the potential mechanism of Acoritataninowii Rhizoma against Alzheimer's Disease. Metabolic Brain Disease. 2023; 38: 1937–1962.
[183] Huang XY, Li TT, Zhou L, Liu T, Xiong LL, Yu CY. Analysis of the potential and mechanism of Ginkgo biloba in the treatment of Alzheimer's disease based on network pharmacology. Ibrain. 2021; 7: 21–28.
[184] Kim BJ, Bak SB, Bae SJ, Jin HJ, Park SM, Kim YR, *et al*. Protective Effects of Red Ginseng Against Tacrine-Induced Hepatotoxicity: An Integrated Approach with Network Pharmacology and Experimental Validation. Drug Design, Development and Therapy. 2024; 18: 549–566.
[185] Lyu Y, Wang Y, Guo J, Wang Y, Lu Y, Hao Z, *et al*. Integrating serum pharmacochemistry and network pharmacology to reveal the active constituents and mechanism of Corydalis Rhizoma in treating Alzheimer's disease. Frontiers in Aging Neuroscience. 2023; 15: 1285549.
[186] Xu Y, Zhang J, Li X. Erjingwan and Alzheimer's disease: research based on network pharmacology and experimental confirmation. Frontiers in Pharmacology. 2024; 15: 1328334.
[187] Zhi J, Yin L, Zhang Z, Lv Y, Wu F, Yang Y, *et al*. Network pharmacology-based analysis of Jin-Si-Wei on the treatment of Alzheimer's disease. Journal of Ethnopharmacology. 2024; 319: 117291.
[188] Cheung S, Zhong Y, Wu L, Jia X, He MQ, Ai Y, *et al*. Mechanism interpretation of Guhan Yangshengjing for protection against Alzheimer's disease by network pharmacology and molecular docking. Journal of Ethnopharmacology. 2024; 328: 117976.
[189] Zhou L, Yang C, Liu Z, Chen L, Wang P, Zhou Y, *et al*. Neuroprotective effect of the traditional decoction Tian-Si-Yin against Alzheimer's disease via suppression of neuroinflammation. Journal of Ethnopharmacology. 2024; 321: 117569.