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Review Article

Herbal Drugs Used in the Management of Alzheimer's Disease: A Comprehensive Review of Phyto-Therapeutic Approaches, Mechanisms and Future Perspectives

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Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the most common cause of dementia, characterized by progressive impairment of memory, cognition, behavior and activities of daily living. Its pathogenesis is multifactorial and involves amyloid-β (Aβ) aggregation, hyperphosphorylation of tau protein, cholinergic dysfunction, oxidative stress, mitochondrial impairment, neuroinflammation, synaptic dysfunction and neuronal loss.[1–4] Although conventional pharmacotherapy includes acetylcholinesterase inhibitors, memantine and, more recently, disease-modifying anti-amyloid antibodies, limitations such as modest symptomatic efficacy, adverse effects, treatment burden, cost and the need for careful patient selection continue to stimulate research into complementary therapeutic approaches.[5–7] Medicinal plants contain diverse bioactive compounds capable of acting simultaneously on several pathological pathways. Important herbal candidates investigated in AD include Ginkgo biloba, Bacopa monnieri, Withania somnifera, Curcuma longa, Crocus sativus, Salvia officinalis, Melissa officinalis, Panax ginseng, Centella asiatica, Huperzia serrata, Nigella sativa and Camellia sinensis.[8–12] Their reported activities include acetylcholinesterase inhibition, antioxidant and anti-inflammatory effects, modulation of amyloid and tau pathology, mitochondrial protection, enhancement of neurotrophic signaling and improvement of synaptic plasticity. Recent systematic reviews of human studies suggest that Ginkgo biloba, Crocus sativus, Salvia officinalis and Melissa officinalis have produced encouraging cognitive or behavioral findings, although study quality, formulations, doses and treatment duration vary substantially.[13,14] Future development should focus on standardized phytopharmaceutical preparations, pharmacokinetic optimization, advanced drug-delivery systems, validated biomarkers, well-designed randomized clinical trials and rational combination therapy. Herbal medicines therefore represent a promising research avenue, but current evidence does not justify considering them universally equivalent or superior to established pharmacological treatment.

Keywords: Alzheimer's disease; herbal drugs; curcumin; Ginkgo biloba; amyloid-β; tau; cognitive impairment.

1. Introduction

Alzheimer's disease (AD) is a chronic, progressive neurodegenerative disease characterized by deterioration of memory, learning, language, executive function and eventually the ability to perform routine activities. It represents the most common form of dementia and constitutes a major public-health challenge because of its increasing prevalence, long disease duration and substantial burden on patients, families and healthcare systems.[1] According to the World Health Organization, dementia affected approximately 57 million people worldwide in 2021, with Alzheimer disease contributing to an estimated 60–70% of dementia cases.[2]

AD is now understood as a complex biological disorder rather than a disease caused by a single pathological pathway. Abnormal accumulation of amyloid-β peptides, tau hyperphosphorylation, neuro-inflammation, oxidative and mitochondrial stress, impaired protein clearance, vascular dysfunction, synaptic failure and neuronal death interact throughout disease development.[1-4] The National Institute on Aging describes the interaction of abnormal amyloid and tau proteins with other biological and environmental factors as an important component of AD pathogenesis.[16] Figure 1. Shows the progressive neurodegenerative disorder of Alzheimer's disease.

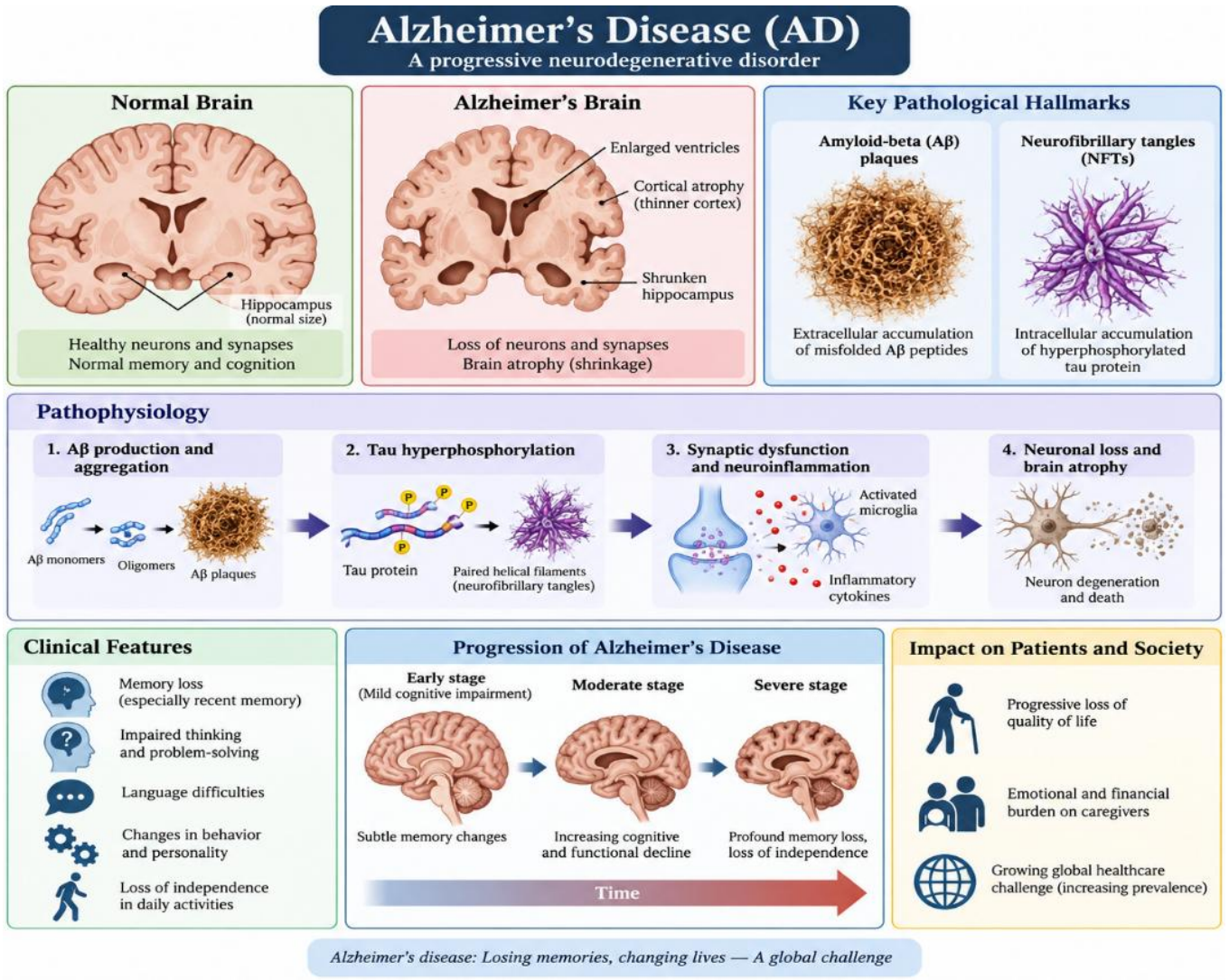


Figure 1. The progressive neurodegenerative disorder of Alzheimer's disease.

Current treatment consists of symptomatic therapies and disease-modifying approaches. Acetylcholinesterase inhibitors such as donepezil, rivastigmine and galantamine improve cholinergic neurotransmission, whereas memantine modulates excessive glutamatergic NMDA-receptor activity.[5,6] In addition, anti-amyloid monoclonal antibodies, particularly lecanemab and donanemab, have introduced a disease-modifying approach for selected patients with early AD.[7,8] Nevertheless, these therapies have limitations, including adverse effects, administration requirements, monitoring requirements, variable treatment response and substantial treatment costs.[5–7]

The limitations of conventional therapy and the multifactorial nature of AD have stimulated interest in medicinal plants and naturally occurring bioactive compounds. Herbal medicines are particularly attractive because many phytochemicals can influence several pathological pathways simultaneously. Recent reviews have identified numerous plants and phytoconstituents with antioxidant, anti-inflammatory, anti-amyloidogenic, anti-tau, cholinergic and neurotrophic activities.[8,9]

Importantly, promising laboratory or animal findings should not be interpreted as proof of clinical efficacy. A recent systematic review of human studies found encouraging signals for several herbal interventions but also emphasized small sample sizes, short intervention periods and methodological heterogeneity.[10] Thus, the development of herbal medicines for AD requires rigorous pharmacological and clinical validation.

2. Historical Perspective of Alzheimer's Disease

Alzheimer's disease was named after the German psychiatrist and neuropathologist Alois Alzheimer, who presented the clinical and neuropathological findings of a patient with progressive memory impairment and behavioral abnormalities in the early twentieth century[11]. The patient, Auguste Deter, died in 1906, and examination of her brain revealed extracellular plaques and intracellular neurofibrillary changes. Alzheimer subsequently described these pathological abnormalities, and the condition became associated with his name.[12]

For many decades, AD was regarded primarily as a disorder associated with severe dementia in relatively

young patients. During the latter part of the twentieth century, advances in neuropathology, molecular biology and neurochemistry established that amyloid plaques and neurofibrillary tangles are major pathological characteristics of the disease. The cholinergic hypothesis subsequently provided the rationale for developing acetylcholinesterase inhibitors.

The modern understanding of AD has progressively expanded from the cholinergic hypothesis to amyloid and tau pathology and subsequently to neuroinflammation, oxidative stress, mitochondrial dysfunction, vascular factors, impaired proteostasis and genetic susceptibility. This evolution has encouraged the development of multitarget therapeutic strategies, including investigations of medicinal plants. [13-14]

3. Pathophysiology of Alzheimer's Disease

3.1 Amyloid-β accumulation

Amyloid precursor protein (APP) can undergo different proteolytic processing pathways. Abnormal processing involving β- and γ-secretase contributes to the generation of amyloid-β peptides, particularly Aβ42, which has a high propensity for aggregation. Accumulation of soluble oligomers and extracellular amyloid plaques can disrupt synaptic signaling and activate glial inflammatory pathways.[15]

Although the amyloid hypothesis has strongly influenced AD drug development, recent evidence indicates that amyloid accumulation alone does not completely explain the clinical heterogeneity of AD[16]. This has been encouraged investigation of multiple interacting disease mechanisms.

3.2 Tau hyperphosphorylation

Tau is a microtubule-associated protein that contributes to neuronal cytoskeletal stability. In AD, abnormal phosphorylation causes tau to detach from microtubules and form paired helical filaments and neurofibrillary tangles. Tau pathology is associated with impaired intracellular transport, synaptic dysfunction and neuronal degeneration.[16-17]

3.3 Cholinergic dysfunction

The cholinergic hypothesis proposes that degeneration of cholinergic neurons and reduced acetylcholine availability contribute significantly to cognitive dysfunction. Reduced acetylcholine signaling provides the pharmacological basis for acetylcholinesterase inhibition using donepezil, rivastigmine and galantamine.[18]

3.4 Oxidative stress and mitochondrial dysfunction

The brain has high metabolic activity and consumes considerable oxygen, making it particularly vulnerable to oxidative injury. Excessive reactive oxygen species can damage lipids, proteins, DNA and mitochondrial components. Oxidative stress can interact with amyloid accumulation, tau phosphorylation and neuroinflammation, thereby accelerating neuronal dysfunction.[19]

3.5 Neuroinflammation

Microglia and astrocytes respond to abnormal proteins and tissue injury. Persistent activation can result in the release of inflammatory cytokines, chemokines, reactive oxygen species and other mediators. Chronic neuroinflammation may therefore contribute to synaptic loss and neuronal degeneration.[20-22]

3.6 Synaptic dysfunction and neuronal death

Cognitive decline is closely associated with loss of synaptic integrity and neuronal networks. Amyloid-β, tau pathology, inflammation, oxidative stress, metabolic abnormalities and excitotoxicity can converge on synaptic dysfunction and regulated cell-death pathways.[23]

3.7 Gut-brain axis

Increasing evidence suggests an interaction between intestinal microbiota, systemic inflammation and brain function. Dysbiosis may influence neuroinflammation, intestinal permeability, microbial metabolites and immune signaling. Herbal medicines are being investigated for their ability to modify the gut microbiota as one component of their possible anti-AD effects.[24]

4. Current Conventional Pharmacological Treatment of Alzheimer's disease

4.1 Acetylcholinesterase inhibitors

Donepezil, rivastigmine and galantamine inhibit acetylcholinesterase and/or related cholinesterase activity, thereby increasing acetylcholine availability in synaptic spaces. These drugs are commonly used for symptomatic management of AD.[5,25]

Their benefits are generally symptomatic rather than curative. Gastrointestinal disturbances, nausea, vomiting, diarrhea, appetite changes, dizziness and other adverse effects may occur, and individual tolerability varies.

4.2 Memantine

Memantine is an NMDA receptor antagonist used particularly in moderate-to-severe AD. It reduces pathological glutamatergic excitotoxicity while preserving physiological neurotransmission to a clinically useful extent.[26]

4.3 Anti-amyloid monoclonal antibodies

Lecanemab and donanemab represent an important change in AD treatment because they target amyloid pathology rather than providing only symptomatic neurotransmitter modulation. Lecanemab received FDA approval in 2023, while donanemab received FDA approval in July 2024 for appropriately selected patients with early AD.[27]

These therapies require careful diagnostic confirmation, treatment monitoring and consideration of risks including amyloid-related imaging abnormalities. Their use is therefore different from conventional oral symptomatic treatment.[28]

5. Disadvantages and Limitations of Conventional Pharmacotherapy

Conventional treatment has substantially improved symptomatic management and introduced disease-modifying therapy; however, several limitations remain.

Limited symptomatic magnitude: Cholinesterase inhibitors and memantine generally provide symptomatic or functional benefits rather than reversing established neurodegeneration.[29]

Adverse effects: Cholinesterase inhibitors may cause gastrointestinal, cardiovascular and neurological adverse effects in susceptible patients.

Long-term treatment burden: Treatment frequently requires prolonged administration and monitoring.

Variable response: Patients differ considerably in their response and tolerability.

Disease heterogeneity: AD involves multiple interacting pathological mechanisms, making single-target treatment insufficient for many patients.[2–4]

Anti-amyloid treatment limitations: Lecanemab and donanemab are intended for selected patients with early disease and require appropriate diagnostic evaluation and monitoring.[30]

Cost and accessibility: Advanced disease-modifying therapies can involve substantial healthcare-resource requirements.

Need for combination strategies: The multifactorial nature of AD suggests that future therapies may need to address several pathological pathways simultaneously.

These limitations provide a scientific rationale for investigating multi-target natural products, while not implying that herbal therapies have already demonstrated equivalent clinical efficacy.[31]

6. Herbal Drugs and Medicinal Plants Investigated in Alzheimer's disease

Medicinal plants contain alkaloids, flavonoids, polyphenols, terpenoids, glycosides and other secondary metabolites that may affect several AD-associated pathways. Recent reviews have identified Ginkgo biloba, Bacopa monnieri, Curcuma longa, *Withania somnifera*, *Crocus sativus*, Salvia officinalis, *Melissa officinalis*, *Panax ginseng*, *Centella asiatica* and *Huperzia serrata* among the most frequently investigated plants.[32-36] all plants which have been investigated for the treatment of AD is given in Table 1.

Table 1. Important herbal drugs investigated for Alzheimer's disease

Herbal drug	Important constituents	Proposed major actions
Ginkgo biloba	Ginkgolides, bilobalide, flavonoids	Antioxidant, anti-inflammatory, mitochondrial and vascular effects
Bacopa monnieri	Bacosides	Cholinergic modulation, antioxidant and neuroprotective effects
Withania somnifera	Withanolides	Anti-inflammatory, antioxidant, neurotrophic and anti-amyloid effects
Curcuma longa	Curcumin, demethoxycurcumin	Anti-inflammatory, antioxidant, anti-amyloid effects
Crocus sativus	Crocin, crocetin, safranal	Antioxidant, anti-inflammatory, anti-amyloid and cognitive effects
Salvia officinalis	Rosmarinic acid, terpenoids	Cholinesterase inhibition and antioxidant activity
Melissa officinalis	Rosmarinic acid, essential oils	Cholinergic, antioxidant and anxiolytic effects
Panax ginseng	Ginsenosides	Neuroprotection, antioxidant and anti-inflammatory activity
Centella asiatica	Asiaticoside, asiatic acid	Antioxidant, neurotrophic and synaptic effects
Huperzia serrata	Huperzine A	Acetylcholinesterase inhibition
Nigella sativa	Thymoquinone	Antioxidant and anti-inflammatory activity
Camellia sinensis	EGCG, catechins	Antioxidant, anti-inflammatory and anti-aggregation activity

6.1. Ginkgo biloba

Ginkgo biloba is among the most extensively studied medicinal plants for cognitive impairment and dementia. Standardized preparations such as EGb 761 contain characteristic flavonoid glycosides and terpene lactones, particularly ginkgolides and bilobalide.[37]

The proposed mechanisms include antioxidant activity, modulation of inflammatory pathways, protection against mitochondrial dysfunction, effects on cerebral microcirculation and modulation of neurotransmitter systems.[37,38]

Clinical studies of standardized Ginkgo biloba preparations have produced variable results, partly because extracts, doses, populations and outcome measures differ. A recent review concluded that EGb 761 is the most extensively studied standardized herbal preparation in this area, although heterogeneity remains in clinical findings.[38]

6.2. *Bacopa monnieri*

Bacopa monnieri, commonly known as Brahmi, has a long history of use in Ayurvedic medicine. Bacosides are considered important bioactive constituents.

Experimental studies suggest antioxidant, anti-inflammatory, cholinergic and neuroprotective actions.[38] Proposed mechanisms include modulation of cholinergic transmission, reduction of oxidative damage and enhancement of neuronal signaling.

However, clinical evidence requires cautious interpretation. A systematic review of randomized trials identified only five eligible studies and judged the overall certainty of evidence to be very low because of small sample sizes, heterogeneity and high risk of bias.[38]. Thus, although Bacopa is pharmacologically interesting, more rigorous clinical trials are needed before definitive therapeutic conclusions can be made.

6.3. *Withania somnifera*

Withania somnifera (Ashwagandha) contains steroidal lactones known as withanolides. Preclinical research has suggested antioxidant, anti-inflammatory, neuroprotective and neurotrophic properties.[39]

Proposed anti-AD mechanisms include modulation of amyloid-related pathways, reduction of oxidative stress, and suppression of neuroinflammatory signaling and support of neuronal plasticity. Withanolides may also influence signaling pathways associated with neuronal survival.

However, the translation of these findings into clinically established AD treatment remains incomplete. Standardization of extracts, identification of active constituents, pharmacokinetics and adequately powered randomized clinical trials remain necessary.[40]

6.4. *Curcuma longa* and Curcumin

Curcuma longa (turmeric) contains curcuminoids, with curcumin being the best investigated component. Curcumin has attracted considerable interest because it exhibits antioxidant and anti-inflammatory activities and has been investigated for effects on amyloid aggregation and tau-related mechanisms.[41]

Potential mechanisms include:

- Inhibition of oxidative stress;
- Modulation of NF-κB and inflammatory signaling;
- Reduction of inflammatory cytokines;
- Interaction with amyloid-β aggregation;
- Possible modulation of tau phosphorylation;
- Mitochondrial protection; and
- Activation of endogenous antioxidant pathways.

Despite strong preclinical evidence, clinical translation has been inconsistent. A recent review emphasized poor aqueous solubility, rapid metabolism, limited systemic exposure and uncertain brain availability as important barriers.[41] A recent systematic review of curcumin studies also reported heterogeneous cognitive findings.

Consequently, advanced formulations such as nanoparticles, phospholipid complexes, micelles, liposomes, nanoemulsions and other bioavailability-enhancing systems represent an important future direction.

6.5. *Crocus sativus*

Crocus sativus (saffron) contains crocin, crocetin, safranal and related constituents. These compounds have demonstrated antioxidant, anti-inflammatory and neuroprotective activities in experimental models.

Saffron has received particular attention because clinical studies have investigated its effects on cognition and neuropsychiatric symptoms. A systematic review published in 2024 identified numerous randomized clinical trials investigating saffron across neurological and psychiatric conditions and reported beneficial effects on several cognitive and psychological outcomes, although the studies were not all specific to AD.[33]

Recent systematic evidence concerning herbal treatments for dementia has also identified Crocus sativus among the plants associated with encouraging clinical findings.[42]

6.6. *Salvia officinalis*

S. officinalis (sage) contains rosmarinic acid and several volatile and phenolic constituents. Its potential relevance to AD is associated particularly with cholinergic modulation and antioxidant activity.

A randomized, double-blind, placebo-controlled clinical trial involving patients with mild-to-moderate AD reported improvement in cognitive outcomes after 16 weeks of S. officinalis extract compared with placebo. Although this historical clinical finding is noteworthy, replication using standardized preparations and larger multicenter trials is required.[43]

6.7. *Melissa officinalis*

Melissa officinalis (lemon balm) contains rosmarinic acid, phenolic compounds and volatile constituents. Experimental evidence suggests antioxidant, cholinergic and neuroprotective effects.

Its potential mechanisms include inhibition of cholinesterase activity, reduction of oxidative stress and modulation of neurotransmitter systems. Recent human-trial evidence has identified Melissa officinalis among herbal interventions associated with improvements in some dementia-related outcomes, although clinical evidence remains heterogeneous.[44]

6.8. *Panax ginseng*

Panax ginseng contains ginsenosides, which have been investigated for their effects on neuronal signaling,

inflammation, oxidative stress and synaptic function. Ginsenosides may influence multiple pathways associated with neuronal survival and cognitive function.

Experimental evidence indicates potential antioxidant and anti-inflammatory effects, while some studies suggest modulation of amyloid-related pathways. However, standardized clinical evidence specifically demonstrating disease modification in AD remains insufficient. [45]

6.9. *Centella asiatica*

Centella asiatica contains triterpenoid compounds such as asiaticoside and asiatic acid. It has traditionally been associated with cognitive and neurological benefits.

Potential mechanisms include antioxidant activity, neurotrophic signaling, and neuronal protection, reduction of neuroinflammation and enhancement of synaptic plasticity. Recent medicinal-plant reviews have included *Centella asiatica* among promising candidates for AD research.[46]

6.10. *Huperzia serrata* and *Huperzine A*

Huperzia serrata is a natural source of *huperzine A*, a potent acetylcholinesterase inhibitor. Unlike many phytochemicals investigated primarily for antioxidant or anti-inflammatory actions, huperzine A has a direct pharmacological relationship with the cholinergic hypothesis.

It has additionally been investigated for possible antioxidant, neuroprotective and NMDA-related effects. Nevertheless, clinical evidence varies, and issues concerning preparation quality, dosage, interactions and regulatory status must be considered.[47-48]

6.11. *Nigella sativa*

Nigella sativa contains thymoquinone, a bioactive compound with antioxidant and anti-inflammatory properties. Experimental investigations suggest that thymoquinone may reduce oxidative damage, inflammatory signaling and neuronal injury.[49]

Although promising preclinical evidence exists, robust clinical trials specifically establishing efficacy in AD are limited.

6.12. C*amellia sinensis*

Camellia sinensis (green tea) is rich in catechins, particularly epigallocatechin-3-gallate (EGCG). EGCG has been investigated for antioxidant, anti-inflammatory and anti-protein-aggregation properties.

Experimental studies have suggested possible effects on amyloid aggregation, oxidative stress and neuronal signaling. However, clinical results remain insufficient to establish green-tea catechins as a disease-modifying AD therapy. Recent clinical-trial reviews emphasize that outcomes of natural compounds differ considerably according to formulation, dose, population and disease stage.[50]

7. Proposed Mechanisms of Herbal Drugs in Alzheimer's Disease

The principal advantage proposed for herbal medicines is their multi-target pharmacological activity.

7.2. Cholinesterase inhibition

Several plants and phytochemicals can inhibit acetylcholinesterase or butyrylcholinesterase, potentially increasing acetylcholine availability and improving cholinergic neurotransmission.

7.2. Anti-amyloid activity

Certain phytochemicals have been investigated for reducing amyloid-β aggregation, promoting amyloid clearance or modifying amyloid-associated toxicity.[51]

7.3. Anti-tau activity

Curcumin and several other phytochemicals have demonstrated experimental effects on tau phosphorylation or aggregation, although clinical evidence remains limited.

7.4. Antioxidant activity

Flavonoids and polyphenols can scavenge reactive oxygen species and/or activate endogenous antioxidant systems such as Nrf2-associated pathways.

7.5. Anti-inflammatory activity

Several phytochemicals suppress inflammatory signaling pathways such as NF-κB and reduce the production of inflammatory mediators. Chronic neuroinflammation is increasingly recognized as an important component of AD pathogenesis.[52]

7.6. Mitochondrial protection

Some phytochemicals may preserve mitochondrial membrane potential, reduce oxidative injury and improve cellular energy metabolism.

7.7. Neurotrophic signaling

Certain plant-derived compounds may activate pathways involving BDNF, TrkB and related mechanisms that support neuronal survival and synaptic plasticity.[53]

7.8. Gut-brain axis modulation

Herbal preparations may influence intestinal microbial composition and microbial metabolites, providing another potential mechanism through which phytochemicals could influence neuroinflammation and cognitive function.[54]

8. Advantages of Herbal Approaches

Herbal medicines offer several scientifically interesting characteristics:

8.1. Multi-target activity: A single extract may affect oxidative stress, inflammation, neurotransmission and protein aggregation simultaneously.[55]

8.2. Chemical diversity: Plants provide structurally diverse molecules that can serve as lead compounds for drug discovery.

8.3. Potential antioxidant activity: Many polyphenols and flavonoids can modulate oxidative pathways.

Traditional knowledge: Long-standing use of several medicinal plants provides a basis for pharmacological investigation.

8.4. Potential for combination therapy: Herbal compounds may theoretically complement conventional therapies, although clinical interaction studies are required.

8.5. Drug-delivery opportunities: Modern pharmaceutical technologies can improve the solubility, stability and bioavailability of poorly absorbed phytochemicals.

These potential advantages should not be interpreted as evidence that herbal products are inherently safer than conventional drugs. Herbal products can produce adverse effects and clinically relevant drug interactions, and their quality may vary substantially.[55]

9. Limitations and Safety Concerns of Herbal Medicines

Despite their promise, several challenges restrict the clinical application of herbal drugs in AD.

9.1. Lack of standardization

The concentration of active constituents may vary with species, geographical origin, cultivation conditions, harvesting, extraction and storage.

9.2. Poor bioavailability

Many promising phytochemicals, particularly curcumin, exhibit poor aqueous solubility, rapid metabolism and limited systemic or brain exposure.[56]

9.3. Inadequate clinical evidence

Preclinical activity does not necessarily translate into clinical efficacy. Recent systematic reviews emphasize heterogeneity and methodological limitations in human herbal studies.[57]

9.4. Herb-drug interactions

Herbal products may affect cytochrome P450 enzymes, transporters, platelet function, blood pressure or other physiological pathways. Consequently, concurrent use with conventional medications requires professional supervision.

9.5. Contamination and adulteration

Poor-quality products may contain contaminants, incorrect plant species or undeclared pharmaceutical substances.[58]

9.6. Inconsistent formulations

Different studies may use different extracts and concentrations, making direct comparison difficult.

10. Current Clinical Evidence: What Does the Literature Show?

The most recent evidence indicates that herbal medicine research in dementia is progressing but remains clinically heterogeneous. A 2026 systematic review identified 48 human studies investigating herbal treatments for dementia, with 27 contributing to quantitative analysis. Encouraging findings were particularly reported for Ginkgo biloba, Crocus sativus, Salvia officinalis and Melissa officinalis. However, the review emphasized that many studies were small and short in duration, and that evidence was insufficient to establish equivalence or superiority to standard treatments.[59]

A 2025 systematic review of 31 clinical-trial articles involving 3,582 participants similarly found variable results across natural products. The review reported potential benefits for several herbal extracts but emphasized differences in study design, intervention and outcome assessment.[60]

These findings support continued investigation but do not support the conclusion that herbal medicines should replace approved pharmacological treatment.

11. Future Perspectives

The future of herbal therapy for AD is likely to depend on the integration of traditional medicinal knowledge, modern pharmacology, nanotechnology, biomarker science and precision medicine.

11.1 Standardized phytopharmaceuticals

Future studies should use chemically standardized extracts with clearly defined concentrations of active constituents. Batch-to-batch reproducibility should be demonstrated using HPLC, LC-MS/MS, GC-MS or other validated analytical methods.[61]

11.2 Nanotechnology-based delivery systems

Many phytochemicals suffer from poor solubility and bioavailability. Nanoparticles, nanoemulsions, liposomes, phytosomes, polymeric nanoparticles, solid lipid nanoparticles and nanostructured lipid carriers may improve stability, absorption and brain delivery.[62]

11.3 Blood-brain barrier targeting

Future research should investigate ligand-mediated and receptor-mediated delivery systems designed to improve transport across the blood-brain barrier.[63]

11.4 Combination therapy

Because AD involves multiple interacting mechanisms, rational combinations of phytochemicals with conventional therapies may be investigated. Such approaches must be evaluated in controlled clinical trials for efficacy, safety and pharmacokinetic interactions.[64]

11.5 Biomarker-guided clinical trials

Future trials should incorporate biomarkers such as amyloid and tau PET imaging, cerebrospinal-fluid biomarkers, plasma phosphorylated tau, neurofilament light chain and inflammatory markers where appropriate.[65]

11.6 Earlier intervention

Because substantial neuronal and synaptic damage occurs before clinical dementia becomes advanced, future trials may need to investigate phytotherapeutics during preclinical AD or mild cognitive impairment rather than only established dementia.[66]

11.7 Gut-brain axis

The relationship between herbal medicines, microbiota, microbial metabolites and neuroinflammation represents an emerging research direction.[67]

11.8 Artificial intelligence and systems pharmacology

Network pharmacology, molecular docking, artificial intelligence and multi-omics approaches may help identify interactions between plant compounds and multiple AD-associated molecular targets.[68]

12. Conclusion

Alzheimer's disease is a multifactorial neurodegenerative disorder involving amyloid-β accumulation, tau pathology, cholinergic dysfunction, oxidative stress, mitochondrial impairment, neuroinflammation, synaptic dysfunction and neuronal loss. Conventional medicines provide important symptomatic benefits, while anti-amyloid therapies have introduced disease-modifying treatment for selected patients with early disease. Nevertheless, limitations related to efficacy, safety, accessibility, monitoring and disease complexity continue to drive the search for complementary therapeutic approaches.

Medicinal plants including Ginkgo biloba, Bacopa monnieri, Withania somnifera, Curcuma longa, Crocus sativus, Salvia officinalis, Melissa officinalis, Panax ginseng, Centella asiatica and Huperzia serrata contain bioactive compounds capable of influencing multiple AD-related pathways. Recent clinical and systematic-review evidence is particularly encouraging for some standardized herbal preparations, but the evidence remains heterogeneous and insufficient to establish herbal medicines as replacements for approved AD treatments.

The future of phytotherapeutic research should therefore focus on standardized extracts, mechanism-based drug development, and improved bioavailability, targeted delivery systems, biomarker-guided trials and adequately powered randomized clinical studies. A scientifically validated integration of herbal bioactives with modern pharmaceutical technologies may provide new therapeutic candidates for the complex and multifactorial nature of Alzheimer's disease.

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