RESEARCH PAPER

Multi-Target Therapeutic Potential Of Herbal Medicines In Alzheimer'S Disease: Mechanistic Insights And Translational Challenges

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Abstract

Alzheimer'S disease (ad) is a chronic, progressive neurodegenerative disorder and the leading contributor to dementia worldwide. It is clinically characterized by a gradual decline in memory, impairment of cognitive functions, behavioral abnormalities, and eventual loss of independence in daily activities. Despite extensive advancements in pharmaceutical research, currently available therapeutic agents—including acetylcholinesterase inhibitors and n-methyl-d-aspartate (nmda) receptor antagonists—primarily offer symptomatic relief without significantly altering disease progression. Furthermore, long-term use of these medications is often associated with adverse effects, reduced therapeutic efficacy, and poor patient adherence. In recent years, there has been increasing interest in plant-based therapeutics due to their multi-target pharmacological actions and relatively favorable safety profiles. Herbal medicines, extensively utilized in traditional systems such as ayurveda, traditional chinese medicine, and european phytotherapy, contain diverse bioactive compounds capable of modulating multiple pathological pathways involved in ad. This review provides a comprehensive evaluation of medicinal plants such as curcuma longa, bacopa monnieri, centella asiatica, ginkgo biloba, withania somnifera, tinospora cordifolia, and huperzia serrata, highlighting their neuroprotective, antioxidant, anti-inflammatory, and acetylcholinesterase inhibitory activities. These effects are primarily mediated by phytoconstituents including curcumin, bacosides, ginkgolides, withanolides, alkaloids, and flavonoids. Despite promising preclinical findings, challenges such as lack of standardization, variability in phytochemical composition, limited pharmacokinetic data, and insufficient clinical validation hinder their widespread clinical application. Therefore, further research focusing on mechanistic studies, formulation development, and large-scale clinical trials is essential. Herbal medicines, nonetheless, represent a promising complementary approach for the management of alzheimer'S disease.

Keywords: Alzheimer'S Disease, Dementia, Herbal Drugs, Neuroprotection, Acetylcholinesterase Inhibitors, Antioxidants, Phytochemicals.

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1. INTRODUCTION

Alzheimer's disease is a complex neurodegenerative disorder that significantly affects memory, cognition, and behavior, ultimately impairing an individual's ability to perform routine daily tasks. It is the most common form of dementia and represents a major global health challenge. [1]

The disorder was first described by Alois Alzheimer in the early 20th century, who identified characteristic neuropathological features such as neuronal degeneration, amyloid plaque formation, and neurofibrillary tangles. Since then, extensive research has been conducted to understand its underlying mechanisms and develop effective treatments.

According to global health estimates, approximately 50 million individuals are currently living with dementia, and this number is projected to increase dramatically to over 150 million by 2050. [2–4] This rise is largely attributed to increased life expectancy, demographic transitions, and the growing prevalence of lifestyle-related disorders.

In addition, factors such as obesity, diabetes, and cardiovascular diseases have been linked to an increased risk of cognitive decline and dementia. The burden is expected to be particularly significant in low- and middle-income countries, where healthcare resources are limited and aging populations are expanding rapidly. [5–8]

2. PATHOPHYSIOLOGY OF ALZHEIMER'S DISEASE

The pathogenesis of Alzheimer's disease is multifactorial and involves a complex interaction of genetic, biochemical, and environmental factors. The hallmark pathological features include the accumulation of amyloid-beta (Aβ) plaques and neurofibrillary tangles composed of hyperphosphorylated tau protein.

Amyloid-beta peptides, derived from the cleavage of amyloid precursor protein (APP), aggregate to form extracellular plaques that disrupt neuronal communication and trigger inflammatory responses. Simultaneously, tau protein abnormalities lead to the formation of intracellular tangles, resulting in cytoskeletal destabilization and neuronal death.

Oxidative stress plays a critical role in disease progression by generating reactive oxygen species (ROS), which damage cellular components such as lipids, proteins, and DNA. Neuroinflammation, mediated by activated microglia and astrocytes, further exacerbates neuronal injury.

Additionally, cholinergic dysfunction—characterized by reduced levels of acetylcholine—is strongly associated with cognitive impairment in AD. Other contributing mechanisms include mitochondrial dysfunction, excitotoxicity, insulin resistance, and genetic factors such as ApoE polymorphism. [9–10]

3. CLINICAL FEATURES AND DISEASE PROGRESSION

Alzheimer's disease progresses gradually and is typically categorized into multiple stages, each associated with distinct clinical features.

In the early stage, patients experience mild memory loss, difficulty in recalling recent events, and subtle changes in mood or behavior. As the disease advances, cognitive impairment becomes more pronounced, affecting language, reasoning, and problem-solving abilities.

In the moderate stage, individuals may exhibit confusion, disorientation, impaired judgment, and difficulty performing complex tasks. Behavioral symptoms such as agitation, anxiety, and depression are also common.

The advanced stage is characterized by severe cognitive decline, loss of communication abilities, and complete dependence on caregivers. Patients may also experience hallucinations, motor dysfunction, and increased vulnerability to infections. [9]

4. LIMITATIONS OF CURRENT PHARMACOTHERAPY

Although several drugs have been approved for the management of Alzheimer's disease, their therapeutic benefits are limited. Acetylcholinesterase inhibitors such as donepezil, rivastigmine, and galantamine aim to enhance cholinergic transmission, while memantine acts by modulating glutamatergic activity.

However, these medications primarily provide symptomatic relief and do not address the underlying causes of the disease. Their effectiveness tends to decline over time, particularly in advanced stages.

Moreover, these drugs are associated with various adverse effects, including gastrointestinal disturbances, dizziness, cardiovascular complications, and sleep disorders. Long-term treatment also imposes a significant economic burden on patients and healthcare systems. [10–11]

5. ROLE OF HERBAL MEDICINES IN ALZHEIMER'S DISEASE

Herbal medicines have emerged as a promising alternative due to their ability to target multiple pathways involved in Alzheimer's disease. Unlike synthetic drugs, which typically act on a single molecular target, phytochemicals exhibit diverse pharmacological activities.

Medicinal plants used in traditional systems of medicine contain bioactive compounds that possess antioxidant, anti-inflammatory, neuroprotective, and cholinesterase inhibitory properties. These effects contribute to the preservation of neuronal integrity and improvement of cognitive function.

Furthermore, herbal formulations are generally well tolerated and suitable for long-term use. Their accessibility

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and cost-effectiveness make them particularly valuable in resource-limited settings. [12–14]

Neuropharmacological Basis and Herbal Evidence

A growing body of experimental and clinical evidence supports the neuroprotective role of plant-derived compounds in cognitive disorders. Studies have demonstrated that several phytochemicals can modulate neurotransmitter systems, particularly the cholinergic pathway, which plays a central role in memory and learning. [14]

Herbal extracts such as *Bacopa monnieri* have shown the ability to enhance synaptic transmission and improve cognitive performance by regulating acetylcholine levels and promoting dendritic growth. Similarly, *Withania somnifera* has been reported to exert neuroregenerative effects by stimulating axonal and dendritic outgrowth, thereby contributing to improved neuronal connectivity. [13–14]

Oxidative stress is another critical factor implicated in neurodegeneration. Natural antioxidants such as vitamin E, vitamin C, and carotenoids have demonstrated protective effects against free radical-induced neuronal damage. These compounds help stabilize cellular membranes and prevent lipid peroxidation, thereby preserving neuronal integrity. [15-17]

In addition, acetylcholinesterase inhibition remains one of the most effective strategies for improving cognitive function in Alzheimer's disease. Several plant-derived alkaloids and flavonoids have been identified as potent inhibitors of this enzyme, supporting their therapeutic relevance. [18]

Types of Dementia and Overlapping Pathologies

Dementia encompasses a range of neurodegenerative conditions, of which Alzheimer's disease accounts for the majority of cases. However, other forms such as vascular dementia, Lewy body dementia, and frontotemporal dementia also contribute significantly to the overall disease burden. [19]

Vascular dementia arises primarily due to impaired cerebral blood flow, often resulting from stroke or chronic vascular insufficiency. The clinical presentation may resemble Alzheimer's disease, although the progression is typically more abrupt or stepwise in nature. [20]

Mixed dementia, characterized by the coexistence of Alzheimer's pathology and vascular abnormalities, is increasingly recognized as a common clinical entity. This overlap complicates diagnosis and therapeutic management. [21]

Neurodegenerative disorders such as Parkinson's disease frequently progress to dementia in later stages, highlighting shared pathological mechanisms such as protein aggregation and neuronal loss. Lewy body dementia, in particular, is associated with abnormal deposition of alpha-synuclein and presents with fluctuating cognition, hallucinations, and motor symptoms. [22]

Rare conditions such as Huntington's disease and Creutzfeldt–Jakob disease also contribute to cognitive decline, although their etiology differs significantly. Additionally, traumatic brain injury and conditions like normal pressure hydrocephalus can mimic dementia-like symptoms, necessitating careful differential diagnosis. [23–24]

Disease Progression and Clinical Staging

The progression of Alzheimer's disease follows a gradual and predictable pattern, typically categorized into multiple stages based on the severity of cognitive and functional impairment. [25]

In the early stages, individuals may experience subtle memory lapses, difficulty recalling recent events, and mild cognitive disturbances. These symptoms often go unnoticed or are attributed to normal aging. [26]

As the disease advances, cognitive impairment becomes more pronounced, affecting language, reasoning, and decision-making abilities. Patients may exhibit confusion, disorientation, and difficulty performing routine tasks. Behavioral and psychological symptoms such as anxiety, depression, and irritability are also common. [27]

In the advanced stages, patients experience severe memory loss, inability to recognize familiar individuals, and complete dependence on caregivers. Motor dysfunction, impaired communication, and increased susceptibility to infections are frequently observed. [28-29]

Understanding these stages is essential for early diagnosis, appropriate therapeutic intervention, and effective patient management.

Etiology and Risk Factors

The development of Alzheimer's disease is influenced by a combination of genetic, environmental, and lifestyle factors. Genetic predisposition, particularly involving the ApoE gene, is considered a major risk factor. [30]

Environmental factors such as exposure to heavy metals, toxins, and pollutants have also been investigated for their potential role in neurodegeneration. Although aluminium exposure was previously suspected to contribute to Alzheimer's pathology, current evidence remains inconclusive. [31]

Metabolic disorders, including diabetes mellitus, hypertension, and hypercholesterolemia, are increasingly recognized as significant contributors to cognitive decline. These conditions may promote vascular damage, oxidative stress, and inflammation, thereby accelerating disease progression.

Clinical Manifestations and Disease Course

Alzheimer's disease is characterized by progressive cognitive and behavioral changes that worsen over time. Early symptoms typically include memory impairment,

difficulty concentrating, and reduced problem-solving ability. [32]

As the disease progresses, patients may develop behavioral disturbances such as agitation, sleep disorders, hallucinations, and emotional instability. These symptoms significantly impact the quality of life of both patients and caregivers.

The disease course is generally divided into three phases: early, moderate, and severe. The duration of each phase varies among individuals but is influenced by factors such as age, comorbidities, and genetic predisposition. [33]

Diagnostic Approaches

Accurate diagnosis of Alzheimer's disease requires a comprehensive evaluation combining clinical, cognitive, and laboratory assessments. [34]

Cognitive screening tools such as the Mini-Mental State Examination (MMSE) and Mini-Cog test are widely used for initial assessment. Neuroimaging techniques, including MRI and CT scans, help identify structural brain changes such as atrophy.

Laboratory investigations are essential to exclude other conditions that may mimic dementia, such as vitamin deficiencies, thyroid disorders, and infections. In certain cases, cerebrospinal fluid analysis and advanced biomarkers may be utilized for more precise diagnosis.

Early detection is crucial, as it allows timely intervention and may help slow disease progression.

6. NEUROPROTECTIVE MECHANISMS OF HERBAL COMPOUNDS

The therapeutic potential of herbal medicines in Alzheimer's disease is primarily attributed to their ability to modulate multiple pathological mechanisms:

- **Antioxidant activity:** Neutralization of free radicals and reduction of oxidative stress
- **Anti-inflammatory effects:** Suppression of neuroinflammatory pathways
- **Cholinesterase inhibition:** Enhancement of acetylcholine levels
- **Anti-amyloidogenic effects:** Prevention of amyloid-beta aggregation
- **Neurogenesis stimulation:** Promotion of neuronal growth and synaptic plasticity

Phytochemicals such as flavonoids, alkaloids, terpenoids, and polyphenols play a crucial role in these mechanisms.

7. DIAGNOSIS OF ALZHEIMER'S DISEASE

The diagnosis of Alzheimer's disease requires a comprehensive and multidisciplinary approach. Clinical evaluation includes detailed medical history, cognitive assessment, and neurological examination.

Standard diagnostic tools include:

- Mini-Mental State Examination (MMSE)
- Mini-Cog test
- Neuroimaging techniques (MRI, CT scan)
- Electroencephalography (EEG)
- Laboratory investigations

Early diagnosis is essential for effective management and may help delay disease progression through timely intervention. [34]

8. DISADVANTAGES OF CONVENTIONAL DRUGS

Despite their widespread use, conventional drugs for Alzheimer's disease have several limitations:

- Inability to cure or reverse disease progression
- Adverse side effects affecting patient compliance
- Reduced efficacy in advanced stages
- High cost of long-term therapy
- Risk of drug interactions in elderly patients

These challenges emphasize the need for safer and more effective therapeutic options. [35]

9. THERAPEUTIC IMPORTANCE OF HERBAL MEDICINES

Herbal medicines offer a holistic approach to the management of Alzheimer's disease by addressing multiple pathological pathways simultaneously. Their benefits include:

- Enhancement of memory and cognitive function
- Protection against neuronal damage
- Reduction of oxidative stress and inflammation
- Improved safety profile compared to synthetic drugs

These properties make them suitable as both preventive and therapeutic agents in neurodegenerative disorders. [36]

List of Herbal plants used having Anti-Oxidant (Anti-Alzheimer) activity:

Sr. No.	Plant	Synonym (CommonName)	PartOfPlant	Therapeutic Activity	Extract	Active Phytochemical Constituents
1.	*CurcumaLongaL.* (Zingiberaceae)	Turmeric /Harida	Rhizome	Anti-inflammatory Anti-oxidant	Aqueous Ethanolic, Methanolic,Hydroalcoholic	Diferuloylmethane (Curcumin)
2	*BaccopamonnieraWettst*(Scrophulariaceae)	*Herpestismonnieria* (L.)Kunth, Brahmi	Whole plant (especiallyleaves and stems)	Memory-enhancing (nootropic), Neuroprotective, Anti-Alzheimer's, Antioxidant, Anxiolytic, Antidepressant,and Anti-inflammatory Activities.	Aqueous Ethanolic, Methanolic, Hydroalcoholic	Bacosides(BacosideAand BacosideB) Bacopasaponins, Alkaloids (brahmine, herpestine),Flavonoids,Triterpenoid ,saponins,Sterols
3	*CentellaasiaticaL.* (Umbelliferae)	*Hydrocotyleasiatica*L., GotuKola	leaves	Anti-Oxidant	Ethanolic, Methanolic,Hydroalcoholic, Aqueous Extract	Triterpenoids saponins
4.	*GinkgobilobaL.* (Ginkgoaceae)	*Salisburiaadiantifolia*Sm., Maidenhair tree	Leaves, Seeds	Neuroprotective, Anti-oxidant	Ethanolic, Methanolic,Hydroalcoholic, Aqueous Extract	Gingkolides, Flavonoids, Saponins.
5.	*Salvia officinalis* (Lamiaceae)	*Salvia lavandulifolia*Vahl., Sage.	Leaves	antioxidants	Ethanolic, Methanolic,Hydroalcoholic, Aqueous	Phenolicacid
6.	*Rosmarinus officinalis* (Lamiaceae)	*Salvia rosmarinus* Spenn. Rosemary (Satapatrika)	Leaves	Anti-oxidants	Ethanolic, Methanolic,Hydroalcoholic, Aqueous	Phenolic Acid
7.	*Matricariarecutita* (Asteraceae)	*Matricariachamomilla* L. GermanChamomile	Flowerhead	Anti-oxidant	Ethanolic, Methanolic,Hydroalcoholic, Aqueous.	Phenolic Acid

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8.	*Melissa officinalis L.*(Lamiaceae)	*Melissa romana* Mill.,LemonBalm,	Leaves Aerial-Part	Anti-oxidant	Aqueous, EthanolicMethanolic,	Phenolic acids (rosmarinicacid, caffeic acid)/Flavonoids (quercetin, luteolin)/Volatile oils(citral, citronellal, geraniol)/Triterpenes (ursolic acid)
9.	*Glycyrrhizaglabra* (Fabaceae)	*Liquiritia glabra (L.), Licorice* /Yashtimadhu	Roots And Stolons	Anti-oxidant	Methanolic,Hydroalcoho-lic, Ethanolic,	Triterpenoids/Flavonoids/ polysaccharide
10.	*GalanthusnivalisL.* (Amaryllidaceae)	Snowdrop	Bulbs/ Aerialparts	Neuroprotective Anti-oxidant	Ethonolic, Methanolic extract	Alkaloids(Galantamine)/Flavonoids
11.	*Huperzia serrata* (Lycopodiaceae)	*Lycopodium serratum*, Thunb/ Chinese club moss	WholePlant	Neuroprotective Anti-oxidant	Methanolic, Ethanolic, Alkoloids extract	Flavonoids, Phenolic compound
12.	*Commiphorawhighitti*(Burseraceae)	*Commiphoramukul*(Hook. ex Stocks) Engl	Oleo-gum-resin	Neuroprotective Anti-oxidant	Methanolic, Ethanolic	Guggulsterones(E- and Z-guggulsterone) Sesquiterpenoids, Diterpenoids, Steroids
13.	*Lipidium Meyenii Walp*(Brassicaceae)	*Lepidiumperuvianum* Chacon,C.M-Maca	Hypocotyl (tuberousroot)	Antioxidant, AChEInhibit	Ethanolic, Methanolic, Hydroalcoholic, Aqueous Extract	Macamides, Macaenes, Glucosinolates, Sterols
14.	*Panax Ginseng* (Araliaceae)	*Panax schinseng* Nees, C.M- Korean Ginseng	Root	Antioxidant, Anti-Alzheimer's, Anti-Inflammatory	Ethanolic, Methanolic, Hydroalcoholic.	Ginsenosides, Saponins, Polysaccharide, Peptides
15.	*AcoruscalamusL.* (Araceae)	*Acorus odoratus* Aiton, Sweet flag/vacha	Rhizomes	Neuroprotective, Memoryenhancer, Anti-Alzheimer's	Ethanolic, Methanolic, Essential oil, Aqueousextract	Phenylpropanoid (α-asarone, β-asarone), Volatile oils,Flavonoids, Tannins.
16.	*Angelica archangelica L.(*umbelliferae)	*Archangelicaofficinalis*Hoffm., Gardenangelica	Root and Rhizomes, Stems, Seed.	Carmenative, Antioxidant,Anti-Alzheimers, Anti-Inflammatory	Aqueous, Ethanolic, Methanolic,Essential oils Extract	Coumarins, Volatile oils, Flavonoids, Phenolic Compounds.

17.	*Tinosporacordifolia*(Menispermaceae)	*Tinospora sinensis* (Lour.) Merr. , Guduchi/Giloy	Stems, Roots and Leaves	Neuroprotective, Anti-Alzheimer, Antioxidant, Anti-inflammatory.	Aqueous, Methanolic,Ethanolic, Hydroalcoholic Extract.	Alkaloids, glacosids, steroids, Polysaccharides, Diterpenoids lactones.
18.	*Magnoliaofficinalis* (Magnoliaceae)	*Magnolia obovataThunb,* Houpomangnolia	StemandRoot bark	Neuroprotective, Memory enhancer Anti-Alzheimers,	Ethanolic, Methanolic,Aqueous,Hydroalcoholic extract	Biphenolic compounds, Alkoloids, Essential oils, Neolignanes
19.	*Collinsoniacanadensis* (Lamiaceae)	*Collinsoniaborealis* Raf,.Stoneroot	Root,Rhizomes and Leaves	Neuroprotective, Antioxidant, Mild anxiolytic,	Ethanolic, Methanolic,Aq	Phenolic compounds, Volatile oils,
20.	*Bertholettiaexcelsa* (Lecythidaceae)	Brazilnuttree	Seeds	Neuroprotective, Antioxidant, Cardioprotective.Anti- Inflammatory.	Ethanolic, Methanolic,Aqueous, Oil extract	Selenium,Phenolic compounds, Flavonoids, Tocopherol (vitamin E), Unsaturatedfatty acid.
21	*Urtica dioica L.* (Clusiaceae)	*Urticamajor*DC, Stinging nettle.	Leaves, Roots,Aerial parts	Neuroprotective, Anti-Alzheimer, Antioxidant,Anti-inflammatory.	Ethanolic, Methanolic,Aqueous,Hydroalcoholic extract	Flavonoids, Phenolic acid, Lignans,Sterols, Vitamin and Minerals
22.	*Physalissomnifera* L.(Solanaceae)	*Physalissomnifera* L. Ashwagandha/ Indian ginseng	Roots and Leaves.	Neuroprotective, Anti-Alzheimer, Antioxidant,Anti-inflammatory	Ethanolic, Methanolic,Aqueous,Hydroalcoholic extract	Withanolides, Alkaloids, Saponins, Flavonoids. Steriodallactones.
23.	*BucananiaLanzan* (Anacardiaceae)	*Buchananialatifolia* Roxb. ,Chironji/ Charoli	Seeds, Bark, Leaves.	Neuroprotective, Anti-Alzheimer, Antioxidant,Anti-inflammatory	Ethanolic, Methanolic,Aqueous,Hydroalcoholic extract	Phenolic compounds, Flavonoids,Fatty acid, Sterols, Triterpenoids.

10. Description of Medicinal Plants with Antioxidant and Anti-Alzheimer's Potential

1. **Curcuma longa L. (Zingiberaceae)**
   Curcuma longa, commonly known as turmeric, is a well-established medicinal plant from the Zingiberaceae family. Its rhizome is the primary part used for therapeutic purposes. Turmeric is widely recognized for its strong anti-inflammatory and antioxidant effects. These properties are mainly attributed to curcumin (diferuloylmethane), the principal active compound responsible for its pharmacological activity. [37-38]

2. **Bacopa monnieri Wettst. (Scrophulariaceae)**

   Bacopa monnieri (Brahmi) is a prominent herb in traditional medicine systems. The entire plant, especially its aerial parts, is utilized for therapeutic applications. It is known for enhancing memory and cognitive function and exhibits neuroprotective, antioxidant, anxiolytic, antidepressant, and anti-inflammatory effects. Its activity is mainly due to bacosides, along with alkaloids, flavonoids, and triterpenoid saponins. [39]

3. **Centella asiatica L. (Umbelliferae)**
   Centella asiatica, commonly referred to as Gotu kola, is widely used for improving cognitive performance. The leaves are primarily employed

in herbal preparations. The plant shows strong antioxidant activity, mainly due to triterpenoid compounds, which contribute to its neuroprotective properties. [40]

4. **Ginkgo biloba L. (Ginkgoaceae)**
   Ginkgo biloba, often called the maidenhair tree, is extensively studied for its effects on cognitive disorders. The leaves are commonly used to prepare standardized extracts rich in ginkgolides. It exhibits antioxidant and neuroprotective actions and has been reported to show effects comparable to conventional drugs used in Alzheimer's disease management. [41]

5. **Salvia officinalis (Lamiaceae)**
   Salvia officinalis (sage) is a medicinal herb valued for its cognitive-enhancing and antioxidant properties. The leaves are the main part used, and its activity is primarily linked to phenolic compounds that support neurological health. [42]

6. **Rosmarinus officinalis (Lamiaceae)**
   Rosmarinus officinalis (rosemary) is another herb from the Lamiaceae family known for its neuroprotective and antioxidant potential. Its leaves contain phenolic acids that contribute significantly to its therapeutic effects. [43]

7. **Matricaria recutita (Asteraceae)**
   Commonly known as German chamomile, *Matricaria recutita* uses its flower heads for medicinal purposes. It demonstrates calming, antioxidant, and neuroprotective properties, mainly due to its phenolic constituents. [44]

8. **Melissa officinalis L. (Lamiaceae)**
   Melissa officinalis (lemon balm) is widely used for its calming and cognitive-enhancing effects. Leaves and aerial parts are utilized, and its pharmacological activity is attributed to phenolic acids, flavonoids, volatile oils, and triterpenes. [45]

9. **Glycyrrhiza glabra (Fabaceae)**
   Glycyrrhiza glabra (licorice) is known for its antioxidant and neuroprotective properties. The roots and stolons are commonly used, containing active compounds such as flavonoids, triterpenoids, and polysaccharides. [46]

10. **Galanthus nivalis L. (Amaryllidaceae)**
    Galanthus nivalis (snowdrop) is recognized for its neuroprotective effects. Its bulbs and aerial parts contain alkaloids such as galantamine, which play a key role in Alzheimer's disease management. [47]

11. **Huperzia serrata (Lycopodiaceae)**
    Huperzia serrata, commonly called Chinese club moss, is used in its whole form. It exhibits strong antioxidant and neuroprotective activities due to the presence of flavonoids and phenolic compounds. [48]

12. **Commiphora wightii (Burseraceae)**
    Commiphora wightii (guggul) produces an oleo-gum-resin that is widely used for its anti-inflammatory, antioxidant, and neuroprotective effects. Its activity is mainly attributed to guggulsterones and related compounds. [49]

13. **Lepidium meyenii Walp. (Brassicaceae)**
    Commonly known as maca, *Lepidium meyenii* is valued for its antioxidant and acetylcholinesterase inhibitory activity. The root is used therapeutically, and its effects are linked to compounds such as macamides, glucosinolates, and sterols. [50]

14. **Panax ginseng (Araliaceae)**
    Panax ginseng (Korean ginseng) is widely used for enhancing cognitive function and reducing neurodegeneration. The root contains bioactive compounds such as ginsenosides, saponins, and polysaccharides responsible for its antioxidant and anti-Alzheimer's effects. [51]

15. **Acorus calamus L. (Araceae)**
    Acorus calamus (Vacha) is traditionally used for improving memory and brain function. The rhizome contains active constituents such as α-asarone, β-asarone, flavonoids, and tannins, which contribute to its neuroprotective activity. [52]

16. **Angelica archangelica (Umbelliferae)**
    This plant utilizes roots, stems, and seeds for medicinal purposes. It exhibits antioxidant, anti-inflammatory, and neuroprotective properties, largely due to the presence of coumarins and phenolic compounds. [53]

17. **Tinospora cordifolia (Menispermaceae)**
    Commonly known as Guduchi, *Tinospora cordifolia* is widely recognized for its neuroprotective and antioxidant effects. It contains alkaloids, glycosides, and diterpenoids that contribute to its therapeutic potential. [54]

18. **Magnolia officinalis (Magnoliaceae)**
    The bark of *Magnolia officinalis* is used for its cognitive-enhancing and neuroprotective properties. Its activity is mainly attributed to biphenolic compounds and essential oils. [55]

19. **Collinsonia canadensis (Lamiaceae)**
    Collinsonia canadensis is recognized for its antioxidant and neuroprotective potential, along with mild anxiolytic effects. Its pharmacological activity is primarily attributed to the presence of flavonoids, phenolic compounds, and volatile oils. [56]

20. **Bertholletia excelsa (Lecythidaceae)**
    Commonly known as the Brazil nut tree, *Bertholletia excelsa* produces seeds rich in bioactive nutrients. These seeds demonstrate strong antioxidant and neuroprotective properties, largely due to their high content of selenium, vitamin E, and unsaturated fatty acids. [57]
21. **Urtica dioica (Clusiaceae)**
    Urtica dioica (stinging nettle) is known for its antioxidant, anti-inflammatory, and neuroprotective activities. It contains a variety of beneficial constituents, including flavonoids, essential vitamins, and minerals that contribute to its therapeutic effects. [58]
22. **Withania somnifera (Solanaceae)**
    Withania somnifera (Ashwagandha) is widely used in traditional medicine for its neuroprotective and anti-Alzheimer's properties. Its effects are mainly associated with withanolides and other active phytochemicals that support cognitive function and neuronal health. [59]
23. **Buchanania lanzan (Anacardiaceae)**
    Buchanania lanzan exhibits notable antioxidant and neuroprotective activities. Its phytochemical composition includes flavonoids, fatty acids, and sterols, which contribute to its therapeutic potential. [60]

Several medicinal plants, including *Ginkgo biloba*, *Salvia officinalis*, and *Huperzia serrata*, have been extensively investigated for their role in Alzheimer's disease. Other important herbs such as *Acorus calamus*, *Angelica archangelica*, *Bacopa monnieri*, *Centella asiatica*, *Clitoria ternatea*, *Crocus sativus*, *Curcuma longa*, and *Hypericum perforatum* have also been reported in both traditional and contemporary scientific literature for their neuroprotective and cognitive-enhancing properties.

11. DISCUSSION

Alzheimer's disease (AD) remains a complex and multifactorial neurodegenerative disorder involving interconnected pathological pathways such as oxidative stress, neuroinflammation, amyloid-β accumulation, tau protein hyperphosphorylation, and cholinergic dysfunction. Conventional pharmacotherapy, including acetylcholinesterase inhibitors and NMDA receptor antagonists, primarily offers symptomatic relief without significantly altering disease progression. These limitations have driven increasing interest in alternative therapeutic strategies, particularly plant-based interventions.

The present review highlights the therapeutic potential of various medicinal plants possessing antioxidant, anti-inflammatory, and neuroprotective properties. Phytoconstituents such as curcumin, bacosides, ginsenosides, withanolides, and galantamine have demonstrated promising effects in modulating multiple pathological targets associated with AD. Unlike single-target synthetic drugs, herbal compounds often exhibit a multitarget mechanism of action, which is advantageous in managing a multifactorial disease like Alzheimer's.

Several preclinical and limited clinical studies suggest that these herbal agents may improve cognitive function, reduce oxidative damage, and enhance cholinergic neurotransmission. Additionally, many of these plants have a long history of use in traditional systems such as Ayurveda and Traditional Chinese Medicine, supporting their safety and tolerability. The synergistic effects of combined herbal formulations further enhance their therapeutic potential.

However, despite encouraging findings, the translation of these results into clinical practice remains limited. Variability in plant sources, extraction methods, dosage forms, and lack of standardization pose significant challenges. Furthermore, inconsistencies in clinical trial design and small sample sizes hinder the establishment of conclusive evidence. Therefore, while herbal medicines offer a promising complementary approach, their integration into mainstream therapy requires rigorous scientific validation.

12. LIMITATIONS

Although herbal medicines demonstrate considerable potential in the management of Alzheimer's disease, several limitations must be acknowledged:

- **Lack of standardization:** Variability in plant composition, geographical origin, and extraction techniques leads to inconsistent therapeutic outcomes.
- **Insufficient clinical evidence:** Most data are derived from in vitro and animal studies, with limited large-scale human clinical trials.
- **Poor bioavailability:** Many phytoconstituents, such as curcumin, exhibit low absorption and rapid metabolism, reducing their therapeutic effectiveness.
- **Dose optimization challenges:** Standard dosing guidelines are not well established for many herbal formulations.
- **Potential herb–drug interactions:** Concurrent use with conventional medications may lead to pharmacokinetic or pharmacodynamic interactions.
- **Regulatory issues:** Lack of strict regulatory frameworks for herbal products affects quality control, safety, and efficacy.
- **Limited mechanistic clarity:** Although multiple pathways are suggested, precise molecular mechanisms are not fully understood for many herbs.

These limitations highlight the need for more robust scientific investigation before widespread clinical application.

13. FUTURE SCOPE

The future of herbal medicine in Alzheimer's disease management appears promising, particularly with advancements in pharmaceutical and biomedical research:

- **Development of standardized formulations:** Establishing quality control measures and standardized extracts to ensure reproducibility and efficacy.
- **Advanced drug delivery systems:** Incorporation of nanotechnology-based carriers (e.g., nanoparticles, liposomes, nanoemulsions) to enhance bioavailability and targeted brain delivery.
- **Combination therapy approaches:** Exploring synergistic effects of herbal compounds with conventional drugs for improved therapeutic outcomes.
- **Molecular and mechanistic studies:** Elucidating detailed pathways involved in neuroprotection and disease modification.
- **Large-scale clinical trials:** Conducting multicenter, randomized controlled trials to validate safety and efficacy in human populations.
- **Personalized medicine approaches:** Tailoring herbal treatments based on genetic, metabolic, and lifestyle factors.
- **Integration with modern healthcare systems:** Bridging traditional knowledge with evidence-based medicine for holistic management of AD.
- **Exploration of novel phytoconstituents:** Identification and isolation of new bioactive compounds with potential anti-Alzheimer's activity.

With continued research and technological advancements, herbal medicines may play a significant role as both preventive and therapeutic agents in Alzheimer's disease.

14. CONCLUSION

The increasing prevalence of Alzheimer's disease and the limitations of current pharmacological treatments highlight the urgent need for alternative therapeutic strategies. Herbal medicines, with their multi-target mechanisms and favorable safety profiles, offer a promising approach for the management of this complex disorder.

Preclinical studies have demonstrated significant neuroprotective effects of various medicinal plants, supporting their potential role in slowing disease progression. However, the translation of these findings into clinical practice remains a major challenge due to issues such as lack of standardization, variability in bioactive compounds, and insufficient clinical evidence.

Future research should focus on the identification of active phytoconstituents, development of standardized formulations, and conduction of well-designed clinical trials. Integration of traditional knowledge with modern scientific approaches may pave the way for the development of effective and safe therapeutic agents for Alzheimer's disease.

In conclusion, herbal medicines represent a valuable complementary strategy with the potential to improve patient outcomes and quality of life, provided that rigorous scientific validation is achieved.

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