INTERNATIONAL JOURNAL OF
Clinical and Pharmaceutical Innovations
An International Peer Reviewed Open Access Journal

Review Article

ISSN (Online): 3142-8665
CODEN (USA): IJCPSM

2026, Volume 1, Issue 8, Page No: 42-56.

ROLE OF NATURAL PRODUCTS IN THE PREVENTION AND TREATMENT OF ALZHEIMER'S DISEASE: A COMPREHENSIVE REVIEW

Tawanda Tasiyana*, Ray Chimango, Ahmad Abdullahi Maikano

Department of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh, India.

Article Info: **Received:** 11 September 2026, **Revised:** 01 October 2026, **Accepted:** 21 October 2026

***Corresponding Author: Tawanda Tasiyana**

Department of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh, India.

DOI: https://doi.org/10.5281/zenodo.23850303

Citation:
Tawanda Tasiyana*, Ray Chimango, Ahmad Abdullahi Maikano. (2026). Role Of Natural Products In The Prevention And Treatment Of Alzheimer's Disease: A Comprehensive Review. International Journal of Clinical and Pharmaceutical Innovations, 1(8), 42-56.

ABSTRACT
Alzheimer's disease is a multifactorial neurodegenerative disorder characterized by progressive cognitive decline, neuronal dysfunction and memory impairment. It predominantly affects older adults and represents one of the leading causes of dementia globally. The clinical manifestation of Alzheimer's disease includes forgetfulness of recent events, difficulty recalling familiar information, impaired concentration and difficulties with planning and problem-solving abilities. The pathogenesis and progression of Alzheimer's disease are associated with several complex interconnected mechanisms, including oxidative stress associated with mitochondrial dysfunction, intracellular accumulation of hyperphosphorylated tau proteins leading to formation of neurofibrillary tangles, extracellular accumulation of β-amyloid plaques and the contribution of genetic and environmental factors. Current pharmacological interventions are largely aimed at alleviating symptoms and slowing cognitive deterioration whilst their ability to modify the underlying pathological processes remains restricted. This clearly shows the need for novel therapeutics strategies that target multiple pathological mechanisms to address this neurodegenerative disorder. This has led to the use of natural products, particularly medicinal plants and their bioactive constituents which have attracted increasing attention from scientific and pharmaceutical communities due to their ability to distort several pathways involved in Alzheimer's disease pathogenesis and alleviate associated symptoms. Various natural products, including flavonoids, gingerols, tannins, anthocyanins, triterpenes and alkaloids have shown potential in the prevention and treatment of several diseases. These compounds possess anti-inflammatory, antioxidant, anti-amyloidogenic and anticholinesterase activities. They function by improving synaptic function, maintaining mitochondrial activity, reducing limiting β-amyloid aggregation, inhibiting tau hyperphosphorylation, reducing oxidative stress and neuroinflammation.

KEYWORDS: Alzheimer's disease, anticholinesterase, anti-amyloidogenic, neuroinflammation, neurodegenerative.

INTRODUCTION

It was discovered by Dr. Alois Alzheimer in 1906 and is currently among the most prevalent chronic neurodegenerative diseases worldwide.[1] Alzheimer's disease is a progressive neuronal damage disorder that commonly affects elderly people. It is associated with

gradual decline in cognitive function, memory loss and sudden mood swings.[2] The major pathological features of the disease include the accumulation of amyloid beta (Aβ) plaque outside neurons and the formation of intracellular neurofibrillary tangles consisting of abnormally hyperphosphorylated tau proteins.[3] These pathological changes interfere with communication between nerve cells resulting in neuroinflammation and promote neuronal cell death. Alzheimer's disease is regarded globally as the main cause of most common neurological disorders and dementia. Its available treatment options are limited and often provide ineffective therapeutic benefits. This has led to increasing in the discovery and application of natural products among the research community and pharmaceutical industry due to their potential neuroprotective effects and ability to target numerous pathological mechanisms. The bioactive compounds in natural products may work together through additive or synergistic effects to provide neuroprotection. Advanced age is considered the strongest and most significant risk factor for Alzheimer's disease. The prevalence of Alzheimer's disease increases substantially with age, affecting an estimated 3% of individuals aged 65-74 years, 17% of those aged 75-84 years and 32% of individuals aged 85 years and older.[4], [5] Currently only few drug have been approved by FDA for the treatment of Alzheimer's disease namely galantamine, donepezil, rivastigmine and memantine. Memantine helps to protect neurons from excessive stimulation by blocking N-methyl D-aspartate (NMDA) receptors, while other medications work by increasing the availability of neurotransmitters in the brain. These drugs mainly provide symptomatic relief without stopping or reversing the damage and loss of neurons. This limited effectiveness of current treatments has led to rapid increase in need for more effective therapies, lured researchers to investigate the underlying mechanisms and develop disease modifying treatments capable of slowing disease progression.[6] Natural products with nootropic properties have shown potential benefits in neuropsychopharmacology and may provide neuroprotective effects by promoting neuronal growth and regeneration. The commonly used medicinal plants include ginkgo biloba, huperzia serrata, curcuma longa (turmeric) and panax ginseng which have shown potential in targeting different mechanisms involved in Alzheimer's disease development. Ginkgo biloba contains flavonoids and terpenoids that may provide neuroprotective effects by reducing amyloid beta accumulation and improving cerebral blood flow. Hurpezia serrata, a natural source of huperzine A, possess acetylcholinesterase inhibitory activity, which help enhance cholinergic function. Curcuma longa which contains curcumin with antioxidant and anti-inflammatory properties that may assist in lowering oxidative stress and neuroinflammation. Similarly, ginsenoside derived from panax ginseng have shown neuroprotective and anti-amyloidogenic activities. This review focuses on the pharmacotherapeutic targets of Alzheimer's disease and evaluates the potential role of natural products crucial in its prevention and treatment.

MATERIALS AND METHODS

A comprehensive literature search was conducted to identify relevant studies investigating the role of natural products and their bioactive constituents in the prevention and treatment of Alzheimer's disease (AD). Relevant data were collected from peer-reviewed online journals, review articles, textbooks, reference books and reports from recognized health organizations. Electronic databases such as PubMed, Google Scholar, ScienceDirect and other academic sources.

RESULTS AND DISCUSSION

Pathophysiology and major hypothesis of Alzheimer's disease

Alzheimer's disease is a multifaceted and progressive neurodegenerative diseases, it is also the major contributing cause of dementia globally.[7] Its pathophysiology involves a complex interplay of molecular, cellular as well as physiological abnormalities. Numerous hypotheses have been suggested to explain the progression and development of Alzheimer's disease such as amyloid cascade, tau cholinergic, oxidative stress, neuroinflammation, mitochondrial dysfunction, vascular and metabolic hypotheses.[8] These interconnected processes have been proposed to contribute to cognitive decline and other characteristic clinical manifestations of the disease. The mentioned mechanisms interact and contribute collectively to Alzheimer's disease pathogenesis. The clear understanding of these mechanisms is vital for identifying therapeutic targets and evaluating the potential of natural products as multitarget agents in the prevention and treatment of Alzheimer's disease.

The amyloid hypothesis

The amyloid cascade hypothesis suggests that the abnormal accumulation and aggregation of amyloid-β (Aβ) peptides in the brain leading to the pathogenesis of AD, initially contributing to the formation of amyloid plaques and subsequently promoting neuroinflammation, oxidative stress, synaptic dysfunction and neuronal injury. These interconnected pathological processes leads to neuronal loss as well as cognitive decline characteristic of AD.[9] Nevertheless, accumulating evidence has led to a re-evaluation of the amyloid hypothesis as the primary drivers of neurodegeneration. Increasing attention has been directed toward soluble Aβ oligomers, which may exert greater neurotoxic effects compared to mature amyloid plaques through disrupting synaptic function and neuronal signaling. Additionally, advances in molecular and imaging studies have upgrade understanding of the pathways involved in Aβ generation, aggregation, transport and clearance, showing additional potential therapeutic targets.[10] Despite being a central theory for a long period of time, the amyloid hypothesis in AD continues to develop as emerging evidence reveals increasingly complex

interactions between Aβ pathology and other disease mechanisms, providing new opportunities for therapeutic intervention.[11]

Tau hypothesis

It proposes that the accumulation and abnormal modification of tau protein in the brain play an essential role in the development and progression of AD. Tau is a microtubule-associated protein that is crucial for maintaining the structure and neuron function. Tau under normal physiological conditions stabilizes microtubule, which serve as intracellular pathways for the transport of nutrients, proteins and other vital molecules within neurons. In AD, abnormal hyperphosphorylation of tau reduces its ability to stabilize microtubules, enhancing tau aggregation and the formation of neurofibrillary tangles. These pathological changes disrupt axonal transport, impair neuronal function and contribute to synaptic dysfunction and neuronal degeneration.[12] The abnormal hyperphosphorylated of tau reduces its ability to stabilize neuronal microtubules, promoting the formation of neurofibrillary tangles. This disrupts axonal transport and neuronal action hence contributing to synaptic dysfunction, neuronal degeneration and cognitive impairment.[13] Recent evidence has provided further support for the role of tau pathology in AD, with studies identifying specific abnormal forms of tau that are associated with disease progression. Consequently, therapeutic strategies targeting pathological tau are being investigated to inhibit its abnormal modification, aggregation and accumulation in the brain. Advances in tau specific imaging techniques have also enabled the visualization and assessment of tau pathology in living patients, providing valuable opportunities for disease diagnosis, monitoring of progression and evaluation of tau targeted therapies.[14], [15]

Neuroinflammation hypothesis

It is recognized as a vital contributor to the progression and development of Alzheimer's disease. This hypothesis highlights negativity of persistent inflammatory actions within the brain. This persistent inflammatory activity promotes neuronal damage and cognitive decline in individuals. The neurodegenerative processes in individuals is due to the increased levels of inflammatory mediators such as cytokines and chemokines.[16] Microglia which are known as principal resident immune cells of the central nervous system poses a complex and context-dependent role in AD. microglia continues to monitor the CNS under physiological conditions in order to eradicate cellular debris and also contribute to the removal of abnormal proteins. During the early stages of AD, their activity may be beneficial through facilitating the clearance of amyloid-beta (Aβ) as well as abnormal tau proteins. Microglial phagocytosis of amyloid-beta aggregates is essential in reduction of plaque accumulation and provides neuroprotective effects.[17] Nevertheless, continuous exposure to elevated amyloid-beta, hyperphosphorylated tau and other known damage associated molecular patterns (DAMPs) can cause excessive microglial activation as the disease advances.[18] Increased amounts of pro-inflammatory cytokines, chemokines and reactive oxygen species are produced by activated microglia. These mediators facilitate neuronal damage and promote the progression of neurodegenerative pathways.[19]

Mitochondrial dysfunction hypothesis

Mitochondria is a membrane bound organelle essential for the production of energy and other metabolic processes.[20] Multiple evidence suggests that impaired mitochondrial function is associated with the pathogenesis of AD. Numerous mitochondrial abnormities have been reported in the brains of individuals with AD, including reduced mitochondrial mass, structural alterations and impaired respiratory activity.[21] These abnormalities causes oxidative stress, inflammation, apoptosis and several cellular disturbances involved in neurodegeneration.[22] AD progression is associated with oxidative stress, mitochondrial impairment and disrupted copper homeostasis. Accumulation of excess copper may contribute to mitochondrial injury by interfering with electron transport, promoting the generation of reactive oxygen species (ROS) and disrupting cellular energy metabolism. These processes can intensify oxidative damage and promote the aggregation of amyloid-beta and tau proteins hence contributing to neurodegenerative progression.[23] Several therapeutic strategies have been proposed with the aim to lower copper related toxicity and protecting mitochondrial function thereby slowing AD progression. These strategies include the application of antioxidants, agents that stimulate mitochondrial biogenesis and compounds that enhance mitophagy. For instance, activation of mitochondrial biogenesis through the PGC-1α pathway has been associated with improved mitochondrial activity and reduced Aβ related pathology in animal models of AD.[23]

© 2026 Author(s) | Published by IJCPI | Open Access under CC BY 4.0 License |

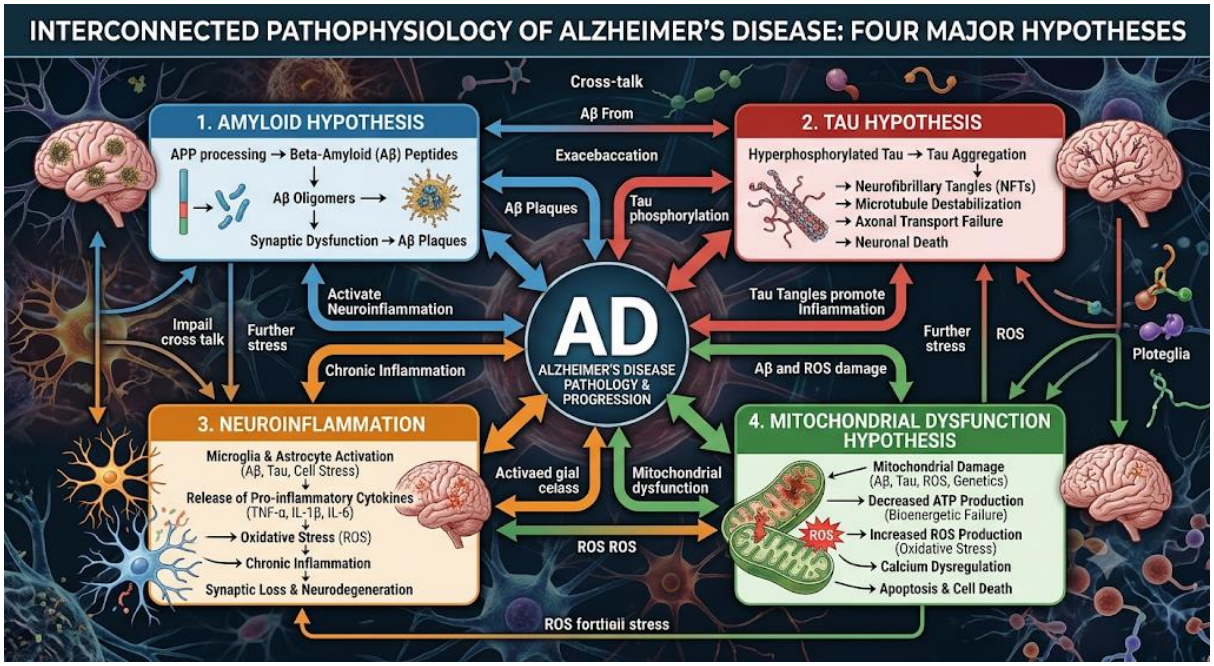

Fig 1: interconnected pathophysiological mechanisms and major hypotheses of Alzheimer's Disease.

Major therapeutic targets in Alzheimer's disease research

Recent advances in AD research have improved understanding of the molecular mechanisms involved in disease development and have revealed numerous potential therapeutic targets. Although amyloid-beta and tau remain major areas of investigation, increasing attention has also been directed towards neuroinflammation and mitochondrial dysfunction as important contributors to AD pathogenesis.[24] Research investigating Aβ and tau has identified multiple possible approaches for disease modifying therapy. Aβ and tau constitute the major pathological components of amyloid plaques and neurofibrillary tangles, respectively. Current strategies include reducing the formation or accumulation of these abnormal proteins in the brain.[25] Enzymes involved in Aβ production, for example β-secretase and ϒ-secretase, have therefore been investigated as potential drug targets with multiple inhibitors progressing to clinical evaluation.[26] Likewise, inhibition of tau associated kinases including glycogen synthase kinase-3 (GSK-3) has shown potential for lowering tau pathology in AD models.[27] Another therapeutic strategy applied involves promoting the removal of pathological proteins from brain. Microglia which act as resident immune cells within the CNS, involved in eradication of Aβ and tau. Nonetheless, their removal may become impaired during AD progression as a result therapeutic strategies are designed to regulate microglial activity and restore their ability to remove pathological proteins.[28]

Neuroinflammation as a therapeutic target

Inflammation function as first line defense mechanism hence an important component of the immune response to injury or infection. However, persistent neuroinflammation may contribute to neuronal damage and neurodegeneration in AD. Increasing evidence indicates that neuroinflammatory processes are significant features of Alzheimer's pathology.[29] Immune cells within the CNS, particularly microglia and astrocytes control inflammatory responses in the brain. Dysregulated activation of these calls may enhance sustained neuroinflammation and contribute to disease progression.[30] Alzheimer's disease also occurs due to chronic inflammation interacting with the accumulation of Aβ plaques as well as tau neurofibrillary tangles.[31] Another potential therapeutic strategy that has emerged is the modulation of neuroinflammation. Non-steroidal anti-inflammatory drugs (NSAIDs) which are classified under anti-inflammatory agents and minocycline have been examined for their potential effects on disease progression. Nevertheless, limitations such as adverse effects and insufficient specifically for inflammation within the brain have restricted their therapeutic application.[32]

Mitochondrial dysfunction as a therapeutic target

Mitochondrial dysfunction has emerged as a potential therapeutic target for AD research besides amyloid, tau and inflammatory mechanisms.[33] Mitochondrial are regarded as power house cells because of their ability to produce cellular energy and helps in neuronal functioning. Its impairment can contribute to cellular injury and also causes death. Accumulated evidence suggests that mitochondrial abnormalities may lead to the pathogenesis of AD.[34] Dysfunction mitochondria produce less cellular energy while generating excess reactive oxygen species as well as disrupting calcium homeostasis thereby contributing to neuronal injury and death. Additionally, tau and amyloid-beta pathology may contribute to mitochondrial impairment.[35] Newer therapeutic strategies aimed at preserving mitochondrial function are being examined such as mitochondria-

targeted antioxidants and compounds capable of enhancing mitochondrial activity. Metformin, an activator of AMP-activated protein kinase (AMPK), has emerged due to its potential effects on mitochondrial function.[36]

Gut microbiome and other emerging target

The gut microbiome has emerged as a potential therapeutic strategy in AD research. The change in the composition of intestinal microbiota may impact biological processes related with cognitive impairment and dementia. Additionally the immune regulation in AD is influenced by the gut microbiome therefore resulting in modulation of the microbiome.[37] Other emerging targets such dietary modification and regular physical activity have been investigated for their potential role in reducing the risk of disease development. This development is crucial since it facilitate the identification of novel targets necessary for treatment and prevention of AD.[38] Numerous evidence and current models of AD pathogenesis emphasize that the disease is unlikely to evolve from a single pathological mechanism. Several interconnected pathological pathways such as amyloid accumulation, tau abnormalities, neuroinflammation, mitochondrial dysfunction and oxidative stress may interact resulting in progression of AD. These interactions may also support the development of crucial therapeutic strategies capable of addressing various disease mechanisms. Evidence also suggests that modulation of inflammatory activity may affect mitochondrial physiological activity and conserve neuronal integrity.[39]

Medicinal plants and natural products as multitarget neuroprotective agents in Alzheimer's disease

Medicinal plants and their bioactive constituents have demonstrated promising potential in reducing the progression and symptoms of Alzheimer's disease.[40] Natural products such as phenolic compounds, lignans, flavonoids, tannins, polyphenols, triterpenoids, sterols, and alkaloids produce diverse neuroprotective activities through antioxidant, anti-inflammatory, anti-amyloidogenic, anti-tau aggregation as well as anticholinesterase activities.[41] They have gained global recognition in healthcare sector due to their ability to act on multiple pathological pathways. Natural products extracts and mixtures may contain numerous active compounds that act synergistically, potentially exhibiting greater neuroprotective effects than single compounds.[42] Additionally, some extracts may provide affordable therapeutic options but their safety and efficacy require maximum evaluation to prevent toxicity. However, certain individual compounds such as curcumin, resveratrol, melatonin and vitamins C and E as well as herbal extracts such as ginkgo biloba, green tea as well as other standardized plant extract.[43] For instance, resveratrol may exert neuroprotective effects by reducing oxidative stress and inflammation, promoting Aβ clearance, inhibiting GSK3β, reducing tau phosphorylation and enhancing cholinergic neurotransmission and BDNF expression.[44] [45] [46] [47] [48]

Neuroprotective natural products from medicinal plants and food for AD

Several medicinal plants have been identified with emerging biological compounds designed to target the cellular aging pathways of the brain hence delaying or reversing cognitive decline.[49] This is expressed in both the extracts and the active individual compounds derived from various medicinal plants that have been evaluated for their ability to modulate AD pathology.[50] The phytoconstituents present in medicinal plants such as phenolic lignans, flavonoids, tannins, polyphenols, alkaloids, triterpenes as well as sterols elicit multiple beneficial neuroprotective physiological activities which include antioxidant, anti-neuroinflammatory, anti-amyloidogenic, anti-tau aggregation and anticholinesterase activities.[51] Numerous bioactive compounds, including curcumin, melatonin, resveratrol together with vitamin C and E, herbal preparations such as garlic extract, gingko biloba extract and green tea have been evaluated for their potential therapeutic effects in patients with AD, with promising outcomes been obtained from various studies.[52] Several neuroprotective natural compounds especially those with antioxidant properties are naturally present in the human diet. These compounds can be obtained from various dietary sources such as fruit, vegetables, flowers and certain herbal beverages. Their presence in commonly consumed foods has generated considerable interest in their potential neuroprotective effects. The following subsections summarize medicinal plants, their herbal extract and food derived natural products that have demonstrated potential neuroprotective effects against AD.

Panax ginseng

It has been widely used as one of the main traditional medicine in eastern countries because it possesses various pharmacological actions. Studies have demonstrated its inhibitory action against the neurotoxicity induced by Aβ in vitro and attenuates Aβ accumulation in vivo in the brain of AD animal models.[53] Studies in mouse models of AD have shown that fermented ginseng extract may reduce brain Aβ formation and improve memory function.[54] Its extract has demonstrated potential neuroprotective effects in models of AD. Ginseng extract has been orally administered to mice injected with Aβ oligomers restored the reduced level of synaptophysin and choline acetyltransferase (ChAT) activity.[55] Its extract has been investigated in numerous clinical studies conducted in patients with AD. Prolonged administration of red ginseng together with convectional AD medications was associated with noticeable positive changes in cognitive function and elicit minor adverse effects on AD patients.[56] Moreover, treatment with red ginseng for a period more than 12 weeks was reported to improve frontal cortical activity in elderly patients with AD.[57] Multiple studies and experiments have examined and

demonstrated the functions of various forms of ginseng which include white ginseng, red ginseng and fermented ginseng on AD patients. Accumulated evidence indicates that biologically active components available in ginseng may assist in preventing cognitive impairment by lowering Aβ production and aggregation. The major bioactive phytochemicals such as ginsenosides and gintonin, have been reported to protect the neurons against Aβ-induced neurotoxicity and oxidative stress. Researhes indicate that ginseng constituents may also facilitate the production of soluble amyloid precursor protein-α (sAPPα) rather than Aβ, exert anti-inflammatory effects, promote cholinergic actions, stimulate hippocampal neurogenesis and enhance cognitive performance.[58] Overall, these neuroprotective activities suggest that ginseng may possess potential in the prevention and management of AD, although further clinical evaluation is recommended.

Gingko biloba L (Ginkgoaceae)

Gingko biloba leaf extract is widely recognized for its potential to enhance memory and reduce age related cognitive decline in individuals, which has contributed to its usage globally in dietary supplements. Its neuroprotective functions may be attributed to numerous mechanisms such as scavenging of free radicals, prevention of mitochondrial dysfunction, activation of JNK (c-Jun N-terminal kinase) and ERK (Extracellular Signal-Regulated Kinase) signaling pathways and inhibition of neuronal apoptosis.[59] Multiple clinical and preclinical trials have been investigated using both single-dose and long-term treatment protocols, although the outcomes were inconsistent. Evaluation of both obtained outcomes indicated that gingko biloba may improve cognitive function in AD and dementia patients when administered for a prolonged period at an appropriate dose.[60] The neuroprotective activities of gingko biloba are mainly attributed to its phytochemical constituents such as flavonoids, organic acids and terpenoids. Overall, gingko biloba is considered to possess neuroprotective properties that may provide both preventive and therapeutic benefits in the management of AD.

Curcuma longa L (Zingiberaceae)

The bioactive constituents available in this spice are curcuminoids such as curcumin and other compounds.[61] It has been reported that curcumin possess various activities such as anti-inflammatory, antioxidant, antitumor and antibacterial functions.[62] It has also demonstrated considerable potential in the prevention and treatment of Alzheimer's disease. The ethanolic extract of turmeric has been reported to exhibit neuroprotective activity through its antioxidant effects.[63] Regular consumption of turmeric has also been associated with a potentially reduced incidence of AD hence suggesting a possible preventive role.[64] Importantly, studies have reported that frequent turmeric consumption improves the cognitive performance in older adults.[65] In patients with AD, turmeric supplementation has been reported to improve certain behavioral symptoms, further supporting its potential therapeutic value in AD management.[66]

Zingiber officinale R (Zingiberaceae)

Commonly used as extracts or as ingredients of ginger tea in food supplements due to its ability to decrease acetylcholinesterase (AChE) activity. It also inhibits lipid peroxidation and exerts a neuroprotective effect against AD. The neuroprotective effects of Z. officinale may be due to its ability to regulate excessive N-methyl-D-aspartate (NMDA) receptor activity and inhibit free radical generation.[67] Current research suggests that Zingiber officinale may possess both preventive and therapeutic potential against AD. The main chemical constituents present in zingiber officinal include gingerols, shogaols, bisabolene, zingiberene and monoterpenes.[68]

Punica granatum (pomegranate)

Pomegranate extracts and juice have been reported to exhibit neuroprotective effects against the progression and development of AD in various animal models.[69], [70], [71] These neuroprotective actions may be mediated through numerous mechanisms such as the reduction of oxidative stress, suppression of oxidative stress, suppression of neuroinflammation and inhibition of soluble Aβ accumulation and amyloid deposition in the hippocampus. Accumulating evidence indicates that the bioactive constituents of pomegranate has suggested that urolithins, which are capable of reaching the brain may contribute to its anti-Alzheimer's disease effects. Its major phytoconstituents have demonstrated protective effects against Aβ-induced neurotoxicity and paralysis.[72] Overall, the neuroprotective properties of pomegranate indicate its potential preventive and therapeutic applications in AD.

Oryza sativa (rice berry)

Research has shown that oxidative stress is associated with the pathogenesis of AD. Evidence suggests that rice berry contain antioxidant compounds hence provides protective effects against memory impairment and hippocampal neurodegeneration. Its bioactive constituents also reduce hippocampal acetylcholinesterase (AChE) activity and lipid peroxidation products. Accumulating evidence suggests that rice berry may have potential as a beneficial agent for the prevention and management of AD.[73]

Centella asiatica L (Apiaceae)

It is a herbal medicine which has been traditionally used due to its ability to support the neuronal cells and improving cognitive functions such as memory and learning.[74] The extract of C. asiatica were shown to reduce β-amyloid pathology and oxidative stress in the brain of a mouse with AD.[75] Its ethanolic extracts have also demonstrated neuroprotective effects against Aβ-induced neurotoxicity by reducing the availability of reactive oxygen species (ROS) production and

improving its antioxidant defense system through increased activities of antioxidant enzymes and elevated levels of glutathione and glutathione disulfide.[76] This findings highlights the potential of C. asiatica as a traditional medicinal agent for the prevention and management of AD.[77] The main chemical constituents which exhibit antioxidant activity are Asiatic acid and asiaticoside and they lower free radical levels and shields the neuronal cells from damage associated with β-amyloid accumulation.[78]

Glycyrrhiza inflata B (Fabaceae)

It is widely known for its ability to enhance mitochondrial biogenesis and reduce oxidative stress.[79] Its aqueous extract demonstrated anti-apoptosis effects together with reductions in reactive oxygen species production and tau misfolding while exhibiting low cytotoxicity in cellular models of AD.[80] Further studies demonstrated that glycyrrhiza inflata extract and its main constituents licochalcone A and liquiritigenin exhibited potent anti-Aβ aggregation and free radical scavenging actions. Research suggests that both the extract and its individual bioactive phytoconstituents suppressed the production of nitric oxide (NO), tumor necrosis factor-alpha (TNF-α), interleukin-1β (1L-1β), prostaglandin E_2 (PGE_2) and interleukin-6 (1L-6) in lipopolysaccharide (LPS) stimulated RAW 264.7 and BV-2 cells hence providing protection against cell death.

Uncaria rhynchophylla M (Rubiaceae)

It is a medicinal herb, traditionally used in Chinese medicine which has demonstrated potential neuroprotective against AD. Its extract has shown free radical scavenging functions and the ability to inhibit lipid peroxidation.[81] It has also been reported to protect neurons from damage by suppressing microglial activation, nitric oxide synthase, inducible nitric oxide synthase and apoptosis.[82] The extract contains several bioactive alkaloids such as rhynchophylline, isorhynchophylline, hirsutine, hirusteine, corynantheine, corynoxine and dihydrocorynantheine.[83], [84] Overall, these findings indicate that uncaria rhynchophylla may have potential applications in the prevention and treatment of AD.

Neuroprotective natural products from marine sources for AD

Marine derived natural products which develop under diverse and challenging environmental conditions possess unique chemical structures and have emerged as promising sources for the discovery of therapeutic agents against multiple disease such as AD. Several marine derived compounds and their synthetic analogues have demonstrated potential in combating AD related pathological processes.[85] As a result, natural products are being investigated for their neuroprotective properties and potential applications in the prevention and treatment of AD.

Marine macroalgae (seaweeds)

They are regarded as plant-like organisms commonly found in coastal environments and contain a wide range of bioactive compounds such as polyphenols, polysaccharides, pigments, amino acids, peptides and proteins. These phytochemicals have demonstrated numerous health-promoting and neuroprotective properties globally. The methanolic extract of Eisenia bicyclis setchell, a perennial brown seaweed, along with ethyl acetate and n-butanol fractions exert neuroprotective activity by reducing intracellular reactive oxygen species production in cells exposed to Aβ. The neuroprotective effects were mainly linked with phlorotannins such as eckol, phlorofucofuroeckol A and 7-phloreckol.[86] Likewise, ishige foliacea, another brown seaweed, contains a phlorotannin-rich fraction that has shown to enhance memory impairment in experimental models. Its effects were linked with several complementary mechanisms such as reduction of brain acetylcholinesterase (AChE) action, suppression of oxidative stress and activation of the extracellular signal-regulated kinase (ERK)-brain-derived neurotrophic factor (BDNF)-cAMP response element-binding protein (CREB) signaling pathway.[87] Collectively, these research findings indicate that marine macroalgae may serve as a promising sources of natural agents for the prevention and potential treatment of AD. Their neuroprotective effects may involve multiple pathways such as protection against neuronal damage, reduction of oxidative stress, inhibition of AChE activity and improvement of memory impairment.

Spirulina cyanobacteria

Cyanobacteria, commonly referred to as blue-green algae, are prokaryotic organisms closely related to bacteria and possess diverse biological properties.[88] Spirulina platensis is a nutrient-rich cyanobacterium containing carotenoids, polysaccharides, polyunsaturated fatty acids, vitamins, minerals and proteins.[89] Its protein extract has demonstrated potent antioxidant activity by scavenging free radicals and preventing radical-mediated cell death in vitro.[90] Additionally, aqueous extracts of S. platensis and its active components were reported to reduce cytotoxicity and suppress the expression of inflammation related genes such as cyclooxygenase-2 (COX-2), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) and inducible nitric oxide synthase (iNOS), suggesting potential neuroprotective and AD preventive effects. Similarly, spirulina maxima contains various biologically active constituents such as carotenoids, polysaccharides, chlorophylls and vitamins.[91] Its extract was shown to improve learning and memory impairment in an AD mouse model. These neuroprotective effects were associated with reduced hippocampal expression of Aβ, amyloid precursor protein (APP), beta-site amyloid precursor protein cleaving enzyme-1 (BACE-1), decreased AChE activity, suppression of hippocampal oxidative stress, increased brain derived neurotrophic factor (BDNF) levels and activation of the brain derived neurotrophic factor (BDNF)/ phosphoinositide 3-kinase

(PI3K)/ protein kinase B (PKB) signaling pathway.[92] These findings suggest that spirulina species may have promising neuroprotective potential against AD through multiple mechanisms such as antioxidant, anti-inflammatory, anti-AChE, anti-amyloid and BDNF mediated signaling pathways.

Table 1: neuroprotective natural products extracts and mixtures from marine source, medicinal plants and food for Alzheimer's disease.

S.no	Source	Natural product	Scientific name	Key neuroprotective effects	Research status	Reference
Neuroprotective natural products from marine source						
1	Marine macroalgae (seaweed)	Phlorotannins (eckol, phlorofucofuroeckol A, 7-phloreckol) Phlorotannin-rich fraction	Eisenia bicyclis (Kjellman) setchell Ishige foliacea	Reduced intracellular ROS production, neuroprotective against Aβ induced toxicity, improved memory impairment, reduced AChE activity, suppressed oxidative stress, activated ERK-BDNF-CREB pathway	In vitro and in vivo	[93], [94]
2	Spirulina cyanobacteria	C-phycocyanin and other bioactives	Spirulina platensis and spirulina maxima	Antioxidant, anti-inflammatory effects, reduced AChE activity, inhibited amyloid related genes (APP, BACE-1), increased BDNF and activated BDNF/PI3K/Akt signaling pathway	In vitro and in vivo	[95], [96], [97]
Neuroprotective natural products for medicinal plants and food for Alzheimer's disease						
3	Panax ginseng	ginsenosides	Panax ginseng	Antioxidant, anti-inflammatory, inhibits Aβ aggregation, enhances memory and cognitive	Invitro and in vivo	[98], [99]
4	Ginkgo biloba	Flavonoids, terpenoids	Ginkgo biloba	Antioxidant, anti-inflammatory, improves cerebral blood flow, inhibits AChE	In vitro and in vivo	[100], [101]
5	Curcuma longa	curcumin	Curcuma longa	Anti-inflammatory, antioxidant, inhibits amyloid and tau pathology, enhance BDNF signaling	In vitro and in vivo	[102], [103]
6	Zingiber officinale	Gingerols, shogaols	Zingiber officinale	Antioxidant, anti-inflammatory, protect neurons from oxidative stress, inhibits AChE	In vitro and in vivo	[104], [105]
7	Punica granatum	Ellagitannins, punicalagins	Punica granatum	Inhibits Aβ aggregation, antioxidant, anti-inflammatory, improves cognitive function	In vitro and in vivo	[106], [107]
8	Rice berry	Anthocyanins, polyphenols	Oryza sativa	Antioxidant, anti-inflammatory, improves learning and memory	in vivo	[108]
9	Centella asiatica	Asiatic acid, asiaticoside	Centella asiatica	Reduces Aβ related neurotoxicity and oxidative stress, enhances antioxidant defense, support neuronal protection	In vitro and in vivo	[109], [110]
10	Uncaria	Rhynchophylline,	Uncaria	Scavenges free radicals,	In vitro	[111], [112]

	rhynchophylla	isorhynchophylline	rhynchophylla	inhibits lipid peroxidation and microglial activation, reduces neuroinflammation	and in vivo	
11	Glycyrrhiza inflata	Licochalcone A, flavonoids, liquiritigenin	Glycyrrhiza inflata	Reduces oxidative stress, tau misfolding, suppresses inflammatory mediators, protect neuronal cells, inhibits Aβ aggregation	In vitro and in vivo	[113], [114]

Challenges and limitations of natural products in Alzheimer's disease

Natural products and their bioactive constituents have attracted considerable attention as potential neuroprotective agents for the prevention and treatment of AD. This is achieved because they exhibit antioxidant, anti-inflammatory and neuroprotective properties. Accumulated evidence suggests that these properties influence several pathological mechanisms associated with progression and development of AD such as amyloid-beta accumulation, tau protein abnormalities, oxidative stress and neuroinflammation. Despite these promising findings, the clinical applications of natural products in AD remains challenging because of their limited bioavailability, poor solubility and inadequate penetration of the blood brain barrier (BBB).[115], [116] For instance tea catechins[117], resveratrol[118] and curcumin[119] have been reported to exhibit limited bioavailability and stability because of their susceptibility to degradation into inactive metabolites.[120] These limitations may reduce the concentration of active compounds reaching the brain hence diminishing their therapeutic effects. Additionally, the BBB restricts the entry of many bioactive compounds into the brain tissues, limiting their distribution to the intended sites of action. Additional challenges such as variations in the chemical composition of natural extracts, difficulties in standardizing formulations, uncertainties regarding optimal dosage and potential interactions with convectional medications. Therefore, these limitations must be addressed before natural products can be reliably translated into clinically effective interventions for AD.

Future perspectives

Nanotechnology based drug delivery systems represent a promising approach for addressing some of the pharmacokinetic limitations linked with the application of natural products. Nanocarriers may enhance the solubility, stability, bioavailability and delivery of selected bioactive compounds to the brain thereby potentially improving their therapeutic effectiveness.[121],[122] Healthcare professionals are now focused on investigating systems such as polymeric nanoparticles, nanogels, solid lipid nanoparticles, crystalline nanoparticles, liposomes, micelles and dendrimer-based complexes. These systems are believed to protect active compounds from degrading and depending on their formulation, promote transport across the blood brain barrier. Prior investigations have examined the use of nanocarriers to improve epigallocatechin-3-gallate (EGCG), which is a major polyphenolic compound found in green tea, delivery in the context of AD[123], rosmarinic acid for huntington's disease[124] and curcumin for brain disorders.[125] These examples demonstrate the broader potential of nanotechnology in neurological conditions should not be interpreted as direct evidence of efficacy in AD. Additional studies are required to establish the safety, effectiveness and clinical applicability of these formulations. Future investigations are necessary to establish the standardization of natural product extracts, identification of active constituents, optimization of dosage regimes and evaluation of long-term toxicity and drug interactions. Furthermore, research should explore multi-target therapeutic strategies that address numerous pathological processes involved in AD progression and development.

CONCLUSION

Natural products and their bioactive constituents have demonstrated promising neuroprotective potential in experimental studies investigating Alzheimer's disease. Their ability to elicit antioxidant, anti-inflammatory and other vital pharmacological activities suggest that they may influence multiple pathological mechanisms involved in AD. The numerous pathological mechanisms which lead to the development and progression of AD include amyloid-beta accumulation, tau protein abnormalities, oxidative stress and neuroinflammation. The ability of certain natural compounds to act on multiple biological targets makes them attractive candidates for the development of therapeutic strategies. Nevertheless, despite encouraging preclinical findings, their clinical application remains restricted by challenges such as poor bioavailability, inadequate blood brain barrier penetration, chemical instability and insufficient clinical evidence. Future studies should aim at identifying active constituents, standardizing natural products formulations, enhancing pharmacokinetic properties and conducting well-designed clinical trials to establish their therapeutic efficacy and long-term safety. Nanotechnology based drug delivery systems may offer opportunities to improve stability, bioavailability and brain delivery of selected neuroprotective compounds. Overall, natural products represent a promising

foundation for the research necessary for the prevention and management of AD.

ACKNOWLEDGEMENT
The author sincerely thanks Kalinga University, Naya Raipur for providing the necessary facilities. The author also acknowledges the use of Google Gemini, an artificial intelligence (AI) tool, to assist in generating illustrative images incorporated into this review article. The generated images were reviewed and selected by authors to support the visual presentation of concepts discussed in the manuscript.

Conflict of interest
The authors have no conflicts of interest.

REFERENCE
1. M. Weinstock, "Therapeutic agents for Alzheimer's disease: a critical appraisal," *Front. Aging Neurosci.*, Dec. 2024; 16: 1484615, doi: 10.3389/fnagi.2024.1484615.
2. P. N. Tripathi *et al.*, "Review of Pharmacotherapeutic Targets in Alzheimer's Disease and Its Management Using Traditional Medicinal Plants," *Degener. Neurol. Neuromuscul. Dis.*, 2024; 14: 47–74, doi: 10.2147/DNND.S452009.
3. M. V. F. Silva, C. de M. G. Loures, L. C. V. Alves, L. C. de Souza, K. B. G. Borges, and M. das G. Carvalho, "Alzheimer's disease: risk factors and potentially protective measures," *J. Biomed. Sci.*, May 2019; 26(1): 33, doi: 10.1186/s12929-019-0524-y.
4. L. A. Farrer *et al.*, "Effects of age, sex, and ethnicity on the association between apolipoprotein E genotype and Alzheimer disease. A meta-analysis. APOE and Alzheimer Disease Meta Analysis Consortium," *JAMA*, Oct. 1997; 278(16): 1349–1356.
5. L. E. Hebert, J. Weuve, P. A. Scherr, and D. A. Evans, "Alzheimer disease in the United States (2010-2050) estimated using the 2010 census," *Neurology*, May 2013; 80(19): 1778–1783. doi: 10.1212/WNL.0b013e31828726f5.
6. J. M. Long and D. M. Holtzman, "Alzheimer Disease: An Update on Pathobiology and Treatment Strategies," *Cell*, Oct. 2019; 179(2): 312–339, doi: 10.1016/j.cell.2019.09.001.
7. "Alzheimer's Disease: Exploring Pathophysiological Hypotheses and the Role of Machine Learning in Drug Discovery - PMC." Accessed: Sep. 25, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC11816687/
8. K. A. T. Baldo *et al.*, "Human Microglial Molecular Alterations in Aging and Alzheimer's Disease," *Cells*, Jun. 2026; 15(13): 1159, doi: 10.3390/cells15131159.
9. R. I. Mehta and R. I. Mehta, "The Vascular-Immune Hypothesis of Alzheimer's Disease," *Biomedicines*, Jan. 2023; 11(2): 408, doi: 10.3390/biomedicines11020408.
10. "New Insights into Alzheimer's Drug Discovery Targeting NF-κB," *Biointerface Res. Appl. Chem.*, Feb. 2024; 14(1): 18, doi: 10.33263/BRIAC141.018.
11. "Alzheimer's Disease: Exploring Pathophysiological Hypotheses and the Role of Machine Learning in Drug Discovery - PMC." Accessed: Sep. 26, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC11816687/
12. H. Wang, M. Sun, W. Li, X. Liu, M. Zhu, and H. Qin, "Biomarkers associated with the pathogenesis of Alzheimer's disease," *Front. Cell. Neurosci.*, 2023; 17: 1279046, doi: 10.3389/fncel.2023.1279046.
13. A. V. Atoki, P. M. Aja, E. N. Ondari, and T. S. Shinkafi, "Advances in Alzheimer's disease therapeutics: biochemistry, exploring bioactive compounds and novel approaches," *Int. J. Food Prop.*, Sep. 2023; 26(1): 2091–2127, doi: 10.1080/10942912.2023.2243050.
14. L. Fang *et al.*, "Specific serum autoantibodies predict the development and progression of Alzheimer's disease with high accuracy," *Brain. Behav. Immun.*, Jan. 2024; 115: 543–554, doi: 10.1016/j.bbi.2023.11.018.
15. I. Ozsahin, E. P. Onakpojeruo, B. Uzun, D. Uzun Ozsahin, and T. A. Butler, "A Multi-Criteria Decision Aid Tool for Radiopharmaceutical Selection in Tau PET Imaging," *Pharmaceutics*, Apr. 2023; 15(4): 1304, doi: 10.3390/pharmaceutics15041304.
16. "Frontiers | Revisiting the neuroinflammation hypothesis in Alzheimer's disease: a focus on the druggability of current targets." Accessed: Sep. 29, 2026. [Online]. Available: https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2023.1161850/full
17. "Microglia and Alzheimer's Disease - PubMed." Accessed: Sep. 29, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/36361780/
18. T. Li, L. Lu, E. Pember, X. Li, B. Zhang, and Z. Zhu, "New Insights into Neuroinflammation Involved in Pathogenic Mechanism of Alzheimer's Disease and Its Potential for Therapeutic Intervention," *Cells*, Jun. 2022; 11(12): 1925, doi: 10.3390/cells11121925.
19. O. M. Obukohwo, O. A. Oreoluwa, U. O. Andrew, and U. E. Williams, "Microglia-mediated neuroinflammation in traumatic brain injury: a review," *Mol. Biol. Rep.*, Oct. 2024; 51(1): 1073, doi: 10.1007/s11033-024-09995-4.
20. "The Key Role of Mitochondrial Function in Health and Disease - PubMed." Accessed: Sep. 29, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/37107158/
21. "Peripheral Mitochondrial Dysfunction: A Potential Contributor to the Development of Metabolic Disorders and Alzheimer's Disease - PubMed."

Accessed: Sep. 29, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/37508448/
22. "The Role of Mitochondria in Neurodegenerative Diseases: the Lesson from Alzheimer's Disease and Parkinson's Disease - PubMed." Accessed: Sep. 29, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/32445085/
23. "Dynamic Interplay between Copper Toxicity and Mitochondrial Dysfunction in Alzheimer's Disease - PubMed." Accessed: Sep. 29, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/33923275/
24. M. U. Rehman *et al.*, "Mitochondrial dysfunctions, oxidative stress and neuroinflammation as therapeutic targets for neurodegenerative diseases: An update on current advances and impediments," *Neurosci. Biobehav. Rev.*, Jan. 2023; 144: 104961, doi: 10.1016/j.neubiorev.2022.104961.
25. "Amyloid-β-independent regulators of tau pathology in Alzheimer disease - PubMed." Accessed: Sep. 29, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/31780819/
26. B. P. Imbimbo, S. Ippati, M. Watling, and C. Imbimbo, "Role of monomeric amyloid-β in cognitive performance in Alzheimer's disease: Insights from clinical trials with secretase inhibitors and monoclonal antibodies," *Pharmacol. Res.*, Jan. 2023; 187: 106631, doi: 10.1016/j.phrs.2022.106631.
27. "Isoorientin, a GSK-3β inhibitor, rescues synaptic dysfunction, spatial memory deficits and attenuates pathological progression in APP/PS1 model mice - PubMed." Accessed: Sep. 29, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/33069740/
28. E. Medrano-Jiménez, K. F. Meza-Sosa, J. A. Urbán-Aragón, I. Secundino, G. Pedraza-Alva, and L. Pérez-Martínez, "Microglial activation in Alzheimer's disease: The role of flavonoids and microRNAs," *J. Leukoc. Biol.*, Jul. 2022; 112(1): 47–77, doi: 10.1002/JLB.3MR1021-531R.
29. T. Ozben and S. Ozben, "Neuro-inflammation and anti-inflammatory treatment options for Alzheimer's disease," *Clin. Biochem.*, Oct. 2019; 72: 87–89, doi: 10.1016/j.clinbiochem.2019.04.001.
30. "Immune cell regulation of glia during CNS injury and disease - PubMed." Accessed: Sep. 29, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/32042145/
31. K. A. Walker, L. M. Le Page, N. Terrando, M. R. Duggan, M. T. Heneka, and B. M. Bettcher, "The role of peripheral inflammatory insults in Alzheimer's disease: a review and research roadmap," *Mol. Neurodegener.*, Jun. 2023; 18(1): 37, doi: 10.1186/s13024-023-00627-2.
32. H. G. Dailah, "Potential of Therapeutic Small Molecules in Apoptosis Regulation in the Treatment of Neurodegenerative Diseases: An Updated Review," *Molecules*, Oct. 2022; 27(21): 7207, doi: 10.3390/molecules27217207.
33. A. B. Reiss *et al.*, "Mitochondria in Alzheimer's Disease Pathogenesis," *Life*, Jan. 2024; 14(2): 196, doi: 10.3390/life14020196.
34. "Mitochondrial Dysfunction and Oxidative Stress in Alzheimer's Disease - PMC." Accessed: Sep. 29, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC7930231/
35. C. Peggion, T. Calì, and M. Brini, "Mitochondria Dysfunction and Neuroinflammation in Neurodegeneration: Who Comes First?," *Antioxidants*, Feb. 2024; 13(2): 240, doi: 10.3390/antiox13020240.
36. G. Galizzi and M. Di Carlo, "Mitochondrial DNA and Inflammation in Alzheimer's Disease," *Curr. Issues Mol. Biol.*, Oct. 2023; 45(11): 8586–8606, doi: 10.3390/cimb45110540.
37. "Current understanding of the Alzheimer's disease-associated microbiome and therapeutic strategies - PubMed." Accessed: Oct. 03, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/38172602/
38. D.-O. Seo and D. M. Holtzman, "Current understanding of the Alzheimer's disease-associated microbiome and therapeutic strategies," *Exp. Mol. Med.*, Feb. 2024; 56(1): 86–94, doi: 10.1038/s12276-023-01146-2.
39. "Dysregulated Neurotransmission induces Trans-synaptic degeneration in reconstructed Neuronal Networks - PubMed." Accessed: Oct. 03, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/30072750/
40. M.-J. R. Howes, N. S. L. Perry, and P. J. Houghton, "Plants with traditional uses and activities, relevant to the management of Alzheimer's disease and other cognitive disorders," *Phytother. Res. PTR*, Jan. 2003; 17(1): 1–18, doi: 10.1002/ptr.1280.
41. "Traditional used Plants against Cognitive Decline and Alzheimer Disease - PMC." Accessed: Aug. 29, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC3153012/
42. D. Kaufmann, A. Kaur Dogra, A. Tahrani, F. Herrmann, and M. Wink, "Extracts from Traditional Chinese Medicinal Plants Inhibit Acetylcholinesterase, a Known Alzheimer's Disease Target," *Molecules*, Aug. 2016; 21(9): 1161, doi: 10.3390/molecules21091161.
43. G. D'Onofrio *et al.*, "Phytochemicals in the Treatment of Alzheimer's Disease: A Systematic Review," *Curr. Drug Targets*, 2017; 18(13): 1487–1498, doi: 10.2174/1389450117666161102121553.
44. X. Ma, Z. Sun, Y. Liu, Y. Jia, B. Zhang, and J. Zhang, "Resveratrol improves cognition and reduces oxidative stress in rats with vascular dementia," *Neural Regen. Res.*, Aug. 2013; 8(22): 2050–2059, doi: 10.3969/j.issn.1673-5374.2013.22.004.
45. H. F. Zhao, N. Li, Q. Wang, X. J. Cheng, X. M. Li, and T. T. Liu, "Resveratrol decreases the insoluble Aβ1-42 level in hippocampus and protects the integrity of the blood-brain barrier in AD rats,"

Neuroscience, Dec. 2015; 310: 641–649, doi: 10.1016/j.neuroscience.2015.10.006.
46. X. He *et al.*, "Resveratrol Attenuates Formaldehyde Induced Hyperphosphorylation of Tau Protein and Cytotoxicity in N2a Cells," *Front. Neurosci.*, Jan. 2017; 10: 598, doi: 10.3389/fnins.2016.00598.
47. R. Schmatz *et al.*, "Resveratrol prevents memory deficits and the increase in acetylcholinesterase activity in streptozotocin-induced diabetic rats," *Eur. J. Pharmacol.*, May 2009; 610: 1–3, pp. 42–48, doi: 10.1016/j.ejphar.2009.03.032.
48. "Effect of oral resveratrol on the BDNF gene expression in the hippocampus of the rat brain - PubMed." Accessed: Aug. 29, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/21221775/
49. M.-J. R. Howes, N. S. L. Perry, and P. J. Houghton, "Plants with traditional uses and activities, relevant to the management of Alzheimer's disease and other cognitive disorders," *Phytother. Res. PTR*, Jan. 2003; 17(1): 1–18, doi: 10.1002/ptr.1280.
50. "Natural products as promising drug candidates for the treatment of Alzheimer's disease: molecular mechanism aspect - PubMed." Accessed: Oct. 03, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/24381531/
51. "Plants with traditional uses and activities, relevant to the management of Alzheimer's disease and other cognitive disorders - PubMed." Accessed: Oct. 03, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/12557240/
52. G. D'Onofrio *et al.*, "Phytochemicals in the Treatment of Alzheimer's Disease: A Systematic Review," *Curr. Drug Targets*, 2017; 18(13): 1487–1498, doi: 10.2174/1389450117666161102121553.
53. "Oriental medicine Jangwonhwan reduces Abeta(1-42) level and beta-amyloid deposition in the brain of Tg-APPswe/PS1dE9 mouse model of Alzheimer disease - PubMed." Accessed: Oct. 03, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/20079417/
54. "Bioactive Compounds and Their Derivatives: An Insight into Prospective Phytotherapeutic Approach against Alzheimer's Disease - Islam - 2022 - Oxidative Medicine and Cellular Longevity - Wiley Online Library." Accessed: Oct. 03, 2026. [Online]. Available: https://onlinelibrary.wiley.com/doi/10.1155/2022/5100904
55. J. G. Choi *et al.*, "White Ginseng Protects Mouse Hippocampal Cells Against Amyloid-Beta Oligomer Toxicity," *Phytother. Res. PTR*, Mar. 2017; 31(3): 497–506, doi: 10.1002/ptr.5776.
56. J.-H. Heo *et al.*, "Improvement of Cognitive Deficit in Alzheimer's Disease Patients by Long Term Treatment with Korean Red Ginseng," *J. Ginseng Res.*, Nov. 2011; 35(4): 457–461, doi: 10.5142/jgr.2011.35.4.457.
57. J.-H. Heo, M.-H. Park, and J.-H. Lee, "Effect of Korean Red Ginseng on Cognitive Function and Quantitative EEG in Patients with Alzheimer's Disease: A Preliminary Study," *J. Altern. Complement. Med.*, Apr. 2016; 22(4): 280–285, doi: 10.1089/acm.2015.0265.
58. H.-J. Kim *et al.*, "Panax ginseng as an adjuvant treatment for Alzheimer's disease," *J. Ginseng Res.*, Oct. 2018; 42(4): 401–411, doi: 10.1016/j.jgr.2017.12.008.
59. "Neuroprotective and Antioxidant Effect of Ginkgo biloba Extract Against AD and Other Neurological Disorders - PubMed." Accessed: Oct. 05, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/31376068/
60. "An Updated Review of Randomized Clinical Trials Testing the Improvement of Cognitive Function of Ginkgo biloba Extract in Healthy People and Alzheimer's Patients - PubMed." Accessed: Oct. 05, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/32153388/
61. M. Di Paolo, L. Papi, F. Gori, and E. Turillazzi, "Natural Products in Neurodegenerative Diseases: A Great Promise but an Ethical Challenge," *Int. J. Mol. Sci.*, Oct. 2019; 20(20): 5170, doi: 10.3390/ijms20205170.
62. M. Pulido-Moran, J. Moreno-Fernandez, C. Ramirez-Tortosa, and M. Ramirez-Tortosa, "Curcumin and Health," *Molecules*, Feb. 2016; 21(3): 264, doi: 10.3390/molecules21030264.
63. S. Yuliani, null Mustofa, and G. Partadiredja, "The neuroprotective effects of anethanolic turmeric (Curcuma longa L.) extract against trimethyltin-induced oxidative stress in rats," *Nutr. Neurosci.*, Nov. 2019; 22(11): 797–804, doi: 10.1080/1028415X.2018.1447267.
64. M. Ganguli *et al.*, "Apolipoprotein E polymorphism and Alzheimer disease: The Indo-US Cross-National Dementia Study," *Arch. Neurol.*, Jun. 2000; 57(6): 824–830, doi: 10.1001/archneur.57.6.824.
65. T.-P. Ng, P.-C. Chiam, T. Lee, H.-C. Chua, L. Lim, and E.-H. Kua, "Curry consumption and cognitive function in the elderly," *Am. J. Epidemiol.*, Nov. 2006; 164(9): 898–906, doi: 10.1093/aje/kwj267.
66. "Effects of turmeric on Alzheimer's disease with behavioral and psychological symptoms of dementia - PubMed." Accessed: Oct. 05, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/23723666/
67. G. Oboh, A. O. Ademiluyi, and A. J. Akinyemi, "Inhibition of acetylcholinesterase activities and some pro-oxidant induced lipid peroxidation in rat brain by two varieties of ginger (Zingiber officinale)," *Exp. Toxicol. Pathol. Off. J. Ges. Toxikol. Pathol.*, May 2012; 64(4): 315–319, doi: 10.1016/j.etp.2010.09.004.
68. B. H. Ali, G. Blunden, M. O. Tanira, and A. Nemmar, "Some phytochemical, pharmacological and toxicological properties of ginger (Zingiber officinale Roscoe): a review of recent research,"

Food Chem. Toxicol. Int. J. Publ. Br. Ind. Biol. Res. Assoc., Feb. 2008; 46(2): 409–420, doi: 10.1016/j.fct.2007.09.085.
69. R. E. Hartman *et al.*, "Pomegranate juice decreases amyloid load and improves behavior in a mouse model of Alzheimer's disease," *Neurobiol. Dis.*, Dec. 2006; 24(3): 506–515, doi: 10.1016/j.nbd.2006.08.006.
70. L. Rojanathammanee, K. L. Puig, and C. K. Combs, "Pomegranate polyphenols and extract inhibit nuclear factor of activated T-cell activity and microglial activation in vitro and in a transgenic mouse model of Alzheimer disease," *J. Nutr.*, May 2013; 143(5): 597–605, doi: 10.3945/jn.112.169516.
71. "Pomegranate from Oman Alleviates the Brain Oxidative Damage in Transgenic Mouse Model of Alzheimer's disease - PMC." Accessed: Oct. 05, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC4220500/
72. T. Yuan *et al.*, "Pomegranate's Neuroprotective Effects against Alzheimer's Disease Are Mediated by Urolithins, Its Ellagitannin-Gut Microbial Derived Metabolites," *ACS Chem. Neurosci.*, Jan. 2016; 7(1): 26–33, doi: 10.1021/acschemneuro.5b00260.
73. W. Pannangrong, J. Wattanathorn, S. Muchimapura, S. Tiamkao, and T. Tong-Un, "Purple rice berry is neuroprotective and enhances cognition in a rat model of Alzheimer's disease," *J. Med. Food*, 2011; 14: 7–8, 688–694, doi: 10.1089/jmf.2010.1312.
74. "Neuroprotective Herbs for the Management of Alzheimer's Disease - PMC." Accessed: Oct. 06, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC8068256/
75. "Centella Asiatica Improves Memory and Promotes Antioxidative Signaling in 5XFAD Mice - PMC." Accessed: Oct. 06, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC6943631/
76. C.-L. Chen, W.-H. Tsai, C.-J. Chen, and T.-M. Pan, "Centella asiatica extract protects against amyloid β1-40-induced neurotoxicity in neuronal cells by activating the antioxidative defence system," *J. Tradit. Complement. Med.*, Oct. 2016; 6(4): 362–369, doi: 10.1016/j.jtcme.2015.07.002.
77. "Indian Medicinal Herbs and Formulations for Alzheimer's Disease, from Traditional Knowledge to Scientific Assessment - PMC." Accessed: Oct. 06, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC7764187/
78. "Neuroprotective Natural Products for Alzheimer's Disease - PMC." Accessed: Oct. 06, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC8225186/
79. C. M. Chen *et al.*, "Aqueous extract of Glycyrrhiza inflata inhibits aggregation by upregulating PPARGC1A and NFE2L2-ARE pathways in cell models of spinocerebellar ataxia 3," *Free Radic. Biol. Med.*, Jun. 2014; 71: 339–350, doi: 10.1016/j.freeradbiomed.2014.03.023.
80. Y.-J. Chiu *et al.*, "Chinese Herbal Medicine Glycyrrhiza inflataReduces Aβ Aggregation and Exerts Neuroprotection through Anti-Oxidation and Anti-Inflammation," *Am. J. Chin. Med.*, Oct. 2018; 1–25, doi: 10.1142/S0192415X18500799.
81. C. L. Hsieh, N. Y. Tang, S. Y. Chiang, C. T. Hsieh, and J. G. Lin, "Anticonvulsive and free radical scavenging actions of two herbs, Uncaria rhynchophylla (MIQ) Jack and Gastrodia elata Bl., in kainic acid-treated rats," *Life Sci.*, 1999; 65(20): 2071–2082, doi: 10.1016/s0024-3205(99)00473-7.
82. N.-Y. Tang *et al.*, "Uncaria rhynchophylla (miq) Jack plays a role in neuronal protection in kainic acid-treated rats," *Am. J. Chin. Med.*, 2010; 38(2): 251–263, doi: 10.1142/S0192415X10007828.
83. J.-S. Shi, J.-X. Yu, X.-P. Chen, and R.-X. Xu, "Pharmacological actions of Uncaria alkaloids, rhynchophylline and isorhynchophylline," *Acta Pharmacol. Sin.*, Feb. 2003; 24(2): 97–101.
84. Y.-F. Xian *et al.*, "Bioassay-Guided Isolation of Neuroprotective Compounds from Uncaria rhynchophylla against Beta-Amyloid-Induced Neurotoxicity," *Evid.-Based Complement. Altern. Med. ECAM*, 2012; 2012: 802625, doi: 10.1155/2012/802625.
85. "Marine Natural Products, Multitarget Therapy and Repurposed Agents in Alzheimer's Disease - PubMed." Accessed: Oct. 06, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/32933034/
86. B. R. Ahn, H. E. Moon, H. R. Kim, H. A. Jung, and J. S. Choi, "Neuroprotective effect of edible brown alga Eisenia bicyclis on amyloid beta peptide-induced toxicity in PC12 cells," *Arch. Pharm. Res.*, Nov. 2012; 35(11): 1989–1998, doi: 10.1007/s12272-012-1116-5.
87. "cabidigitallibrary.org/doi/full/10.5555/20183263209." Accessed: Oct. 07, 2026. [Online]. Available: https://www.cabidigitallibrary.org/doi/full/10.5555/20183263209
88. R. Singh *et al.*, "Uncovering Potential Applications of Cyanobacteria and Algal Metabolites in Biology, Agriculture and Medicine: Current Status and Future Prospects," *Front. Microbiol.*, 2017; 8: 515, doi: 10.3389/fmicb.2017.00515.
89. "Natural Products and Their Bioactive Compounds: Neuroprotective Potentials against Neurodegenerative Diseases - PMC." Accessed: Oct. 07, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC7042511/
90. P. Bermejo-Bescós, E. Piñero-Estrada, and A. M. Villar del Fresno, "Neuroprotection by Spirulina platensis protean extract and phycocyanin against iron-induced toxicity in SH-SY5Y neuroblastoma cells," *Toxicol. Vitro Int. J. Publ. Assoc. BIBRA*, Sep. 2008; 22(6): 1496–1502, doi: 10.1016/j.tiv.2008.05.004.
91. J.-C. Lee *et al.*, "Marine algal natural products with anti-oxidative, anti-inflammatory, and anti-cancer

properties," *Cancer Cell Int.*, Jun. 2013; 13(1): 55, doi: 10.1186/1475-2867-13-55.
92. E.-J. Koh *et al.*, "Spirulina maxima Extract Ameliorates Learning and Memory Impairments via Inhibiting GSK-3β Phosphorylation Induced by Intracerebroventricular Injection of Amyloid-β 1-42 in Mice," *Int. J. Mol. Sci.*, Nov. 2017; 18(11): 2401, doi: 10.3390/ijms18112401.
93. B. R. Ahn, H. E. Moon, H. R. Kim, H. A. Jung, and J. S. Choi, "Neuroprotective effect of edible brown alga Eisenia bicyclis on amyloid beta peptide-induced toxicity in PC12 cells," *Arch. Pharm. Res.*, Nov. 2012; 35(11): 1989–1998, doi: 10.1007/s12272-012-1116-5.
94. "Phlorotannin-rich fraction from Ishige foliacea brown seaweed prevents the scopolamine-induced memory impairment via regulation of ERK-CREB-BDNF pathway.," CABI Databases. Accessed: Oct. 07, 2026. [Online]. Available: https://www.cabidigitallibrary.org/doi/full/10.5555/20183263209
95. "Natural Products and Their Bioactive Compounds: Neuroprotective Potentials against Neurodegenerative Diseases - PMC." Accessed: Oct. 07, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC7042511/
96. J.-C. Chen, K. S. Liu, T.-J. Yang, J.-H. Hwang, Y.-C. Chan, and I.-T. Lee, "Spirulina and C-phycocyanin reduce cytotoxicity and inflammation-related genes expression of microglial cells," *Nutr. Neurosci.*, Nov. 2012; 15(6): 252–256, doi: 10.1179/1476830512Y.0000000020.
97. E.-J. Koh, K.-J. Kim, J. Choi, D.-H. Kang, and B.-Y. Lee, "Spirulina maxima extract prevents cell death through BDNF activation against amyloid beta 1-42 (Aβ1-42) induced neurotoxicity in PC12 cells," *Neurosci. Lett.*, Apr. 2018; 673: 33–38, doi: 10.1016/j.neulet.2018.02.057.
98. "Panax ginseng as an adjuvant treatment for Alzheimer's disease - PMC." Accessed: Oct. 07, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC6190533/
99. J.-H. Heo, M.-H. Park, and J.-H. Lee, "Effect of Korean Red Ginseng on Cognitive Function and Quantitative EEG in Patients with Alzheimer's Disease: A Preliminary Study," *J. Altern. Complement. Med.*, Apr. 2016; 22(4): 280–285, doi: 10.1089/acm.2015.0265.
100. H. Liu, M. Ye, and H. Guo, "An Updated Review of Randomized Clinical Trials Testing the Improvement of Cognitive Function of Ginkgo biloba Extract in Healthy People and Alzheimer's Patients," *Front. Pharmacol.*, 2019; 10: 1688, doi: 10.3389/fphar.2019.01688.
101. J. Zhao *et al.*, "Enhanced anti-amnestic effect of donepezil by Ginkgo biloba extract (EGb 761) via further improvement in pro-cholinergic and antioxidative activities," *J. Ethnopharmacol.*, Apr. 2021; 269: 113711, doi: 10.1016/j.jep.2020.113711.
102. N. Hishikawa *et al.*, "Effects of turmeric on Alzheimer's disease with behavioral and psychological symptoms of dementia," *Ayu*, Oct. 2012; 33(4): 499–504, doi: 10.4103/0974-8520.110524.
103. "Apolipoprotein E polymorphism and Alzheimer disease: The Indo-US Cross-National Dementia Study - PubMed." Accessed: Oct. 07, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/10867779/
104. B. H. Ali, G. Blunden, M. O. Tanira, and A. Nemmar, "Some phytochemical, pharmacological and toxicological properties of ginger (Zingiber officinale Roscoe): a review of recent research," *Food Chem. Toxicol. Int. J. Publ. Br. Ind. Biol. Res. Assoc.*, Feb. 2008; 46(2): 409–420, doi: 10.1016/j.fct.2007.09.085.
105. G. Oboh, A. O. Ademiluyi, and A. J. Akinyemi, "Inhibition of acetylcholinesterase activities and some pro-oxidant induced lipid peroxidation in rat brain by two varieties of ginger (Zingiber officinale)," *Exp. Toxicol. Pathol. Off. J. Ges. Toxikol. Pathol.*, May 2012; 64(4): 315–319, doi: 10.1016/j.etp.2010.09.004.
106. T. Yuan *et al.*, "Pomegranate's Neuroprotective Effects against Alzheimer's Disease Are Mediated by Urolithins, Its Ellagitannin-Gut Microbial Derived Metabolites," *ACS Chem. Neurosci.*, Jan. 2016; 7(1): 26–33, doi: 10.1021/acschemneuro.5b00260.
107. L. Rojanathammanee, K. L. Puig, and C. K. Combs, "Pomegranate polyphenols and extract inhibit nuclear factor of activated T-cell activity and microglial activation in vitro and in a transgenic mouse model of Alzheimer disease," *J. Nutr.*, May 2013; 143(5): 597–605, doi: 10.3945/jn.112.169516.
108. "Purple rice berry is neuroprotective and enhances cognition in a rat model of Alzheimer's disease - PubMed." Accessed: Oct. 08, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/21510741/
109. "Indian Medicinal Herbs and Formulations for Alzheimer's Disease, from Traditional Knowledge to Scientific Assessment - PMC." Accessed: Oct. 08, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC7764187/
110. "Centella Asiatica Improves Memory and Promotes Antioxidative Signaling in 5XFAD Mice - PMC." Accessed: Oct. 08, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC6943631/
111. T.-H. Kang *et al.*, "Rhynchophylline and isorhynchophylline inhibit NMDA receptors expressed in Xenopus oocytes," *Eur. J. Pharmacol.*, Nov. 2002; 455(1): 27–34, doi: 10.1016/s0014-2999(02)02581-5.
112. "Uncaria rhynchophylla, a Chinese medicinal herb, has potent antiaggregation effects on Alzheimer's beta-amyloid proteins - PubMed." Accessed: Oct. 08, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/16676329/

113. "Chinese Herbal Medicine Glycyrrhiza inflataReduces Aβ Aggregation and Exerts Neuroprotection through Anti-Oxidation and Anti-Inflammation - PubMed." Accessed: Oct. 08, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/30284464/
114. K. H. Chang *et al.*, "The aqueous extract of Glycyrrhiza inflata can upregulate unfolded protein response-mediated chaperones to reduce tau misfolding in cell models of Alzheimer's disease," *Drug Des. Devel. Ther.*, Feb. 2016; 10: 885–896, doi: 10.2147/DDDT.S96454.
115. S. Hu *et al.*, "Clinical development of curcumin in neurodegenerative disease," *Expert Rev. Neurother.*, Jun. 2015; 15(6): 629–637, doi: 10.1586/14737175.2015.1044981.
116. "Bioavailability of bioactive food compounds: a challenging journey to bioefficacy - PubMed." Accessed: Oct. 13, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/22897361/
117. M. Cascella, S. Bimonte, M. R. Muzio, V. Schiavone, and A. Cuomo, "The efficacy of Epigallocatechin-3-gallate (green tea) in the treatment of Alzheimer's disease: an overview of pre-clinical studies and translational perspectives in clinical practice," *Infect. Agent. Cancer*, 2017; 12: 36, doi: 10.1186/s13027-017-0145-6.
118. J. Renaud and M.-G. Martinoli, "Considerations for the Use of Polyphenols as Therapies in Neurodegenerative Diseases," *Int. J. Mol. Sci.*, Apr. 2019; 20(8): 1883, doi: 10.3390/ijms20081883.
119. "Amphiphilic Nanocarrier Systems for Curcumin Delivery in Neurodegenerative Disorders - PMC." Accessed: Oct. 13, 2026. [Online]. Available: https://pmc.ncbi.nlm.nih.gov/articles/PMC6313553/
120. "Improving solubility and chemical stability of natural compounds for medicinal use by incorporation into liposomes - PubMed." Accessed: Oct. 18, 2026. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/21291975/
121. A. Smith, B. Giunta, P. C. Bickford, M. Fountain, J. Tan, and R. D. Shytle, "Nanolipidic particles improve the bioavailability and alpha-secretase inducing ability of epigallocatechin-3-gallate (EGCG) for the treatment of Alzheimer's disease," *Int. J. Pharm.*, Apr. 2010; 389: 1–2, 207–212, doi: 10.1016/j.ijpharm.2010.01.012.
122. M. Ovais *et al.*, "Phyto-Therapeutic and Nanomedicinal Approaches to Cure Alzheimer's Disease: Present Status and Future Opportunities," *Front. Aging Neurosci.*, vol. 10, Oct. 2018, doi: 10.3389/fnagi.2018.00284.
123. A. Smith, B. Giunta, P. C. Bickford, M. Fountain, J. Tan, and R. D. Shytle, "Nanolipidic particles improve the bioavailability and alpha-secretase inducing ability of epigallocatechin-3-gallate (EGCG) for the treatment of Alzheimer's disease," *Int. J. Pharm.*, Apr. 2010; 389: 1–2, 207–212, doi: 10.1016/j.ijpharm.2010.01.012.
124. R. Bhatt, D. Singh, A. Prakash, and N. Mishra, "Development, characterization and nasal delivery of rosmarinic acid-loaded solid lipid nanoparticles for the effective management of Huntington's disease," *Drug Deliv.*, 2015; 22(7): 931–939, doi: 10.3109/10717544.2014.880860.
125. M. L. Del Prado-Audelo *et al.*, "Formulations of Curcumin Nanoparticles for Brain Diseases," *Biomolecules*, Feb. 2019; 9(20: 56, doi: 10.3390/biom9020056.