

A REVIEW: NATURAL PLANTS AND ALZHEIMER'S DISEASE

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Received: 14 July 2025 | **Revised & Accepted:** 1 October 2025

Keywords: Alzheimer's disease, cognition, neurodegenerative disorders, acetylcholine, herbal formulations, neurotransmitters, Plant products.

ABSTRACT

Alzheimer's disease is a progressive neurodegenerative disease that is characterized by severe memory loss, unusual behaviour and a decline in cognitive function. It is the most common form of dementia, affecting more than 5.4 million people in the USA. Alzheimer's disease is characterized by the low levels in the brain of the neurotransmitters of acetylcholine. The major advances in the treatment of AD have been the use of acetylcholinesterase inhibitors such as galantamine, huperzine A, physostigmine and its derivatives to increase the levels of ACh rather than the use of cholinergic compounds, although compounds with nicotinic properties have attracted some interest. Some of the plants secondary metabolites have also shown to possess antioxidant, anti-inflammatory, neuroprotective and cognition enhancing effects. Presently according to WHO, around more than 80% world population rely on natural remedies to cure their health-related issues. A significant shift of drug discovery is being witnessed from synthetic moieties to herbal formulation.

INTRODUCTION

Globally, Alzheimer's disease causes dementia in about 80% of persons. Programmed cell death in Alzheimer's disease is the result of complex biochemical alterations in cells, such as oxidative stress, disruption of Ca^{2+} homeostasis, inflammation, metabolic abnormalities, and the buildup of unfolded or misfolded proteins (1). Alzheimer's disease advances from minor symptoms like mood swings and memory loss to severe incapacity, necessitating all-encompassing care and frequently placement in a nursing facility (2). Offering insights into the ancient understanding of neurological

conditions, including age-associated memory loss, the Ayurvedic concept of Vata, Vyadhi, which includes disorders of the nervous system caused by imbalances of the biological air humor, also emphasizes the potential therapeutic benefits of herbal remedies (3). Higher acetylcholinesterase activity and the generation of free radicals have been connected to microglia activation, which causes neuroinflammation and contributes to the pathophysiology of Alzheimer's disease (4). As a result of the increasing trend of creating medications from medicinal plants, standardized, safe, and effective plant-derived medicines have been developed to alter the course and symptoms of Alzheimer's disease.

Blueberry extract treatment has been demonstrated to have an inverse relationship with oxidative stress in vitro, reducing stress signaling in cell lines exposed to substances that induce oxidative stress (5). Natural foods like fruits, vegetables, nuts, herbs, and marine substances are being investigated for their potential as a treatment for Alzheimer's disease prevention due to the shortcomings of current preventive measures. Preclinical and clinical research has been conducted on natural compounds rich in antioxidants and flavonoids to examine their neuroprotective properties. Genetic abnormalities in presenilin and amyloid precursor protein (APP) contribute to the development of Alzheimer's disease by interfering with normal APP processing, which increases the creation of Ab peptide and causes neuronal death (6). Numerous pharmacological activities, including anti-inflammatory, anti-amyloidogenic, and antioxidant properties, are displayed by the vast array of phytochemicals, which include lignans, flavonoids, and triterpenes. (7)

WITHANIA SOMNIFERA (SOLANACEAE)

Indian ginseng, or ashwagandha, is a medicinal plant whose roots are used for their therapeutic qualities. This plant, especially its root, which is thought to have restorative qualities, has a long history of use in traditional medicine. Also known as Indian winter cherry, it is a medicinal herb prized for the healing properties of its roots. Ashwagandha's pharmacological actions are attributed to its rich and varied phytochemical composition, which includes alkaloids and withanolides. The medicinal qualities of ashwagandha are attributed to its bioactive components, which include

alkaloids (like withanine) and withanolides (like withaferin A). A neuroinflammatory response is triggered by the buildup of beta amyloid protein and hyperphosphorylated proteins, which eventually causes irreparable damage to the central nervous system and advances Alzheimer's disease. The microglia that accompany accumulating senile plaques try to break down and eliminate both the senile plaques and damaged and dead neurons. Ashwagandha displays promise in the treatment of Alzheimer's disease by lowering inflammation and beta amyloid aggregation. Significant neuroprotective benefits, such as decreased cerebral infarction and edema, enhanced blood-brain barrier function, and normalized metabolic parameters, were observed in mice fed withanolide A intranasally (8).

CLITORIA TERNATEA L. (LEGUMINOSAE)

Extracts from *Clitoria ternatea* have long been used to increase longevity and memory; research indicates that they can facilitate the formation of neural stem cells and boost cognitive function. The aqueous root extract of *C. ternatea* has been shown in vitro to promote the development, differentiation, and proliferation of neural precursor cells, displaying neurotrophic effects akin to those of BDNF, FGF-2, and Neuregulin 1. Its potential therapeutic effects for neurological diseases are suggested by the fact that *Clitoria ternatea* aqueous root extract has been demonstrated to improve learning and memory in rats as well as to stimulate the proliferation and differentiation of neural stem cells (9). Studies on the effectiveness of *Clitoria ternatea* in Alzheimer's disease have shown that it may be beneficial in several ways, with its bioactive

components serving as possible building blocks for the creation of novel memory-improving treatments (10).

GINKGO BILOBA L. (GINKGOACEAE)

As a potential treatment for diseases including Alzheimer's and tinnitus, ginkgo may improve circulation, reduce neurological symptoms, and improve cognitive performance. Because of its blood-thinning qualities, possible adverse effects, and contraindications in specific populations, including pregnant women and those using anti-clotting drugs, ginkgo biloba should be used with caution even if it is normally well tolerated. It has been demonstrated in numerous research that ginkgo biloba can scavenge free radicals. Unsaturated phospholipids, which are widely present in brain cell membranes, can be harmed by free radicals, especially reactive oxygen species like nitric oxide. The brain is particularly susceptible to oxidative stress because it contains a lot of these lipids.

According to this study, the flavonoids in ginkgo biloba can counteract nitric oxide, protecting hippocampus neurons in the process. These results lend credence to the use of ginkgo extract in the treatment of cerebral insufficiency (11).

PANAX GINSENG (ARALIACEAE)

Panax ginseng, also referred to as "The Lord of Herbs," is a perennial herb that has been utilized for more than 4,000 years in China, Korea, and Japan. It belongs to the Araliaceae family. It was originally documented in "Sheng Nong's Herbal Classic," one of China's earliest pharmacological texts. Traditionally, it has been valued for its

ability to soothe the mind, uplift mood, enhance cognitive function, and has shown promise in the treatment of dementia. The glycolipoprotein ginsengin, which contains G-protein-coupled lysophosphatidic acids, has potential use in the management of Alzheimer's disease (AD) and other cognitive impairments. Gintonin may function through several pathways, according to research, including lowering acetylcholine (ACh) levels and choline acetyltransferase (ChAT) activity, increasing acetylcholinesterase (AChE) activity, reducing β -amyloid accumulation, protecting the blood-brain barrier (BBB), promoting hippocampus neurogenesis, and modulating synaptic function (12).

MELLISA OFFICINALIS L. (LAMIACEAE)

In Iranian traditional medicine, *Melissa officinalis* L. (of the Labiatae family) has long been used to treat neurological disorders like sadness and anxiety. It is also known to improve memory. Strong anti-inflammatory and antioxidant qualities are displayed by the plant. The extract of *M. officinalis* also has neurotropic properties and cholinergic action. Its capacity to shield PC12 cells against beta-amyloid-induced damage was shown in earlier studies. The goal of the current study is to evaluate how the cholinergic system influences the effects of *M. officinalis* extract on memory and learning (13).

CURCUMA LONGA L. (ZINGEBERACEAE)

Turmeric's curcumin, a substance with anti-inflammatory and antioxidant qualities as well as the capacity to bind to amyloid plaques, suggests promise in the treatment of Alzheimer's disease. Low

bioavailability, however, limits its efficacy. Enhancing distribution and efficacy using nanotechnology could provide a solution, making curcumin an attractive study topic for Alzheimer's disease treatment (14). Curcumin may help Alzheimer's disease by lowering inflammation and oxidative stress while also preventing the development of amyloid plaque. Nanotechnology may improve curcumin's therapeutic benefits and bioavailability, opening new avenues for the treatment of Alzheimer's disease. Curcumin is a viable option for Alzheimer's disease study and possible treatment because of its many different qualities. According to research, curcumin may help reduce the symptoms of Alzheimer's by focusing on several disease processes, such as oxidative stress and inflammation (15).

ACORUS CALAMUS (ACORACEAE)

The tall, wetland herb known as sweet flag (*Acorus calamus*) has ancient medicinal uses. It is prized for the spicy scent of its leaves and rhizomes, which are frequently utilized as cinnamon or ginger. Since the plant rarely produces seeds, it is primarily propagated vegetatively by cutting off its components (16). It can be preserved and its medical needs met by growing it in a lab (in vitro). Its rhizomes have been used for its therapeutic oil since ancient times and can be found up to 6000 feet in the Himalayas. Along with their relaxing, digestive, and restorative qualities, they aid in the treatment of epilepsy, mental disease, diarrhoea, and stomach pain. The majority of *Acorus calamus*'s experimental research has concentrated on its stem, roots, and leaves. Calamus oil is a yellow aromatic oil found in the dried rhizome that gives the plant its insecticidal and therapeutic qualities. To

find the active ingredients and comprehend their potential medicinal benefits, researchers have also investigated the rhizome and its oil (17). The antispasmodic, antibacterial, antifungal, antioxidant, neuroprotective, and anti-diabetic properties of its leaves, rhizomes, and oils are evident. In addition to protecting the brain from harm, it promotes mental health and memory. It is prized in Chinese, Pakistani, and Ayurvedic medicine for neurological and digestive health, and is frequently mixed with other medicines.

MORINGA

(MORINGACEAE)

Rats' ketamine-induced memory impairment may be lessened by *Moringa oleifera*, according to the study, especially its flavonoid quercetin, which altered NMDA receptors. NMDA receptors and male Wistar rats with ketamine-induced memory impairments are affected by *M. oleifera*. To observe the effects of the medicinal herb on WM, male Wistar rats with ketamine-induced memory impairment were used. One kind of flavonoid present in *M. Oleifera*, quercetin, was shown to significantly boost the expression of the NMDAR NR2A and NR2B subunits.

According to one study, MO leaves' omega-3 polyunsaturated fatty acid raised the NR2B subunit in the hippocampus and prefrontal brain. Omega-3 polyunsaturated fatty acids, which are contained in *M. oleifera* leaves, were found to improve the NR2B subunit in the prefrontal cortex and hippocampus. In the hippocampus, dietary polyunsaturated fatty acids from *M. oleifera* increased the expression of NR2A and NR2B subunits (18).

LIQUORICE (FABACEAE)

Glycyrrhiza glabra, a well-known medicinal herb used in Ayurveda, belongs to the Leguminosae family. Originating in Iraq, it is widespread throughout Asia and Europe, particularly in China, Italy, Spain, Turkey, and Central Asia. Another species, *G. uralensis*, is primarily found in Mongolia and China (19). India, Iran, the United States, and the United Kingdom are among the more than a dozen nations that commercially grow liquorice. It has substantial economic importance because of its use in medications, cosmetics, food goods, and tobacco. Its medicinal benefits and chemical makeup have been well studied.

ALLIUM SATIVUM (AMARYLLIDACEAE)

Raw garlic contains allicin, which lowers oxidative stress and inflammation and may help reduce the symptoms of Alzheimer's disease. Allicin may be useful in managing the pathophysiology of Alzheimer's disease due to its neuroprotective properties, which are mediated by APP metabolic modulation and oxidative stress reduction. A human double mutant APP and PS1 gene-expressing animal model of AD has been used to study the neuroprotective effects of allicin. Through its effects on APP metabolism, Allicin improved memory by reducing the production of A β peptide, which was mediated by PS1, PS2, BACE1, and nicastrin (20,21).

PUNICA GRANATUM (PUNICACEAE)

The intricacy of Alzheimer's disease, which is characterized by memory loss, cognitive decline, and synapse dysfunction with few available treatments, is highlighted by research

(23,24). A study looked at how rosuvastatin and pomegranate juice affected the cognitive deficits caused by scopolamine in rats. The results demonstrated that the juice of *Punica granatum* efficiently counteracted cognitive impairment, was on par with the usual treatment, donepezil, and had superior neuroprotective effects compared to rosuvastatin. This raises the possibility that *Punica granatum* could slow the progression of Alzheimer's disease. There are contradictory reports regarding statins' neuroprotective properties (25). Because of this discrepancy, we investigated how Rosuvastatin affected memory. Additionally, the test agents were contrasted with the acetylcholinesterase inhibitor, donepezil, used in the standard therapy group (26).

CONCLUSION

The presence of anthraquinone glycosides, dimeric anthraquinone derivatives, bacosides, curcuminoids, triterpenoid saponins, zeatin, crocin, flavonoids, cinnamic acid derivatives, naphthalene glucosides, and stilbenes is what causes the actions. Certain standardized extracts have shown promise in clinical trials, and their pharmacological and pharmacokinetic characteristics are presently being studied. Hypericum extract and Ginkgo biloba extract EGB 761 are two examples. According to pharmacological and phytochemical research, several phytoconstituents may be viable therapeutic targets for the treatment of AD. The pharmacological effects of medicinal plant extracts with a broad range of polarity and several classes of phytochemical compounds have therefore been shown to be

important to the treatment of AD.

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