

Medicinal plants: Potent effect on memory deficits and Alzheimer's disease

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Abstract

Alzheimer's disease is a neurological illness that causes memory loss and mild cognitive impairment, eventually leading to dementia. It is an age-related condition characterized by memory impairments. To get a therapeutic evaluation for Alzheimer's disease, numerous research has been reported. Currently, no proper medicines are available for Alzheimer's disease, but the symptoms are minimized, improving dementia and memory-related complications. Globally, traditional medicines have been adopted as memory improvement from antique times. Medicinal herbal plants from natural sources are used to cure numerous memory deficits like amnesia, dementia, and Alzheimer's disease. It's used in the Unani and Traditional medical management, and it's shown to have a dynamic aspect in the treatment and management of the neurodegenerative disease. Numerous therapeutic plants and herbs have been synthesized, and their substantial effects have been discovered and demonstrated in clinical experiments. The elemental method of action, on the other hand, is still impending. We investigated the role of various medicinal and herbal plants in the treatment and management of memory impairments and Alzheimer's disease using traditional herbal therapy.

Keywords: Alzheimer's disease; dementia; memory; medicinal plants; neurodegenerative disease.

1. INTRODUCTION

Alzheimer's disease (AD) is a brain disease caused by a neurodegenerative disorder. [1]. Aloes Alzheimer was the name of a German physician. Alzheimer was first mentioned by him in 1906[2]. It is a progressive neurological illness that the senior population above the age of 65 is most affected. Dementia is Alzheimer's disease, is thought to account for 60% of all cases [3]. Alzheimer's disease has a significant economic and societal impact[4]. The prevalence of the disease has been shown to increase with age. Degeneration in the virtual sense, ongoing inattention, confusion, reduced speaking ability, and amnesia are all symptoms of Alzheimer's disease. A reduced ability to believe is all signs and symptoms of this ailment. The amyloid hypothesis was hypothesized as the primary Alzheimer's disease is affected by a multitude of factors. It also produces extracellular amyloid protein aggregation in plaques and the deposition and misfolding of tau protein neurofibrillary tangles, which cause memory loss and cognitive impairment[5]. The main component of senile plaques is aggregated amyloid; This is derived from the precursor protein of amyloid (APP). APP is a glycoprotein that is important for neuronal homeostasis, transport, signalling, and development. [6].

A mix of genetic and environmental variables, as well as ageing, produce neurodegenerative disorders. [7]. The biomarker for Alzheimer's disease detection is amyloid and neuron damage. Alzheimer's disease can take years to manifest, with no apparent symptoms[8]. It begins with normal brain activity, first with a collapse to induce fresh memories to be formed due to the need to focus on new knowledge, and forgetfulness is swiftly manifested. [9]. It is characterized by a lack of cholinergic activity, stress, and the as a result of inflammation, plaques develop. Inflammation in the central nervous system raises the risk of Mutations in microglia cause Alzheimer's disease and cognitive ageing. [10]. The pathogenesis of Alzheimer's disease begins

in the temporal lobes and hippocampus complex of the basal forebrain.[11]. It impacts the patient's quality of life because it is fundamentally linked to feelings[12]. Patients' differences in behaviour (whether unfavourable or favourable) are the most critical indicators of Alzheimer's disease. Dementia and Alzheimer's disease are more likely by smoking, diabetes, and cardiovascular disease[13], [14].

Neurofibrillary tau and extracellular Amyloid are hallmarks of Alzheimer's disease. The function of Amyloid in Neurodegenerative diseases aetiology has gotten the greatest attention. [15]. However, following the failure of a clinical trial to treat Amyloid and the development of other ways in the past, such as the proliferation of unique intracellular proteins, tau has resurfaced as a curative goal in managing Alzheimer's disease[16]. Although the widespread study of therapeutic tau in sick brains has expressed that atypical tau protein in any illness, encouraging the concept that different attributes of tau pathology arise through prion such as seed dependent aggregation, the pathophysiology of tau proteins are identified in the clutter of neurodegeneration. As a result, the changes in tau transfer from cell to cell and conversion of native tau to atypical forms might be the key to delaying Alzheimer's disease and other memory difficulties. [17-18].

The risk of Alzheimer's disease was dramatically lowered when cardiovascular problems, such as blood pressure, stroke, and other symptoms, were managed and monitored[13]. Chemicals, physical exposure, and the workplace environment have little bearing on the development of Alzheimer's disease. Simple intellectual activities like watching TV, playing games, and reading newspapers/books can help people with dementia and Alzheimer's disease. By interfering with neurotransmitter function, antihistamines, non-psychoactive medications, and cardiac treatments can all induce memory deficits [19].

Butyrylcholinesterase (BchE), acetylcholinesterase (AChE), and -amyloid secretase-1 (BACE-1) are all involved in amyloid plaque accumulation and aggregation in Alzheimer's sufferers' brains[20]. Alzheimer's patients' brains show a cluster of hyperphosphorylated tau protein, which is a crucial indication of the disease and amyloid accumulation in the grey matter of the brain and, eventually, neuron loss, resulting in intellectual disability. Amyloid accumulation causes inflammation, which leads to necrobiosis and intellectual disability[21] due to the activation of immune cell aggregation. Alzheimer's disease's pathology is shown in **Figure 1**.

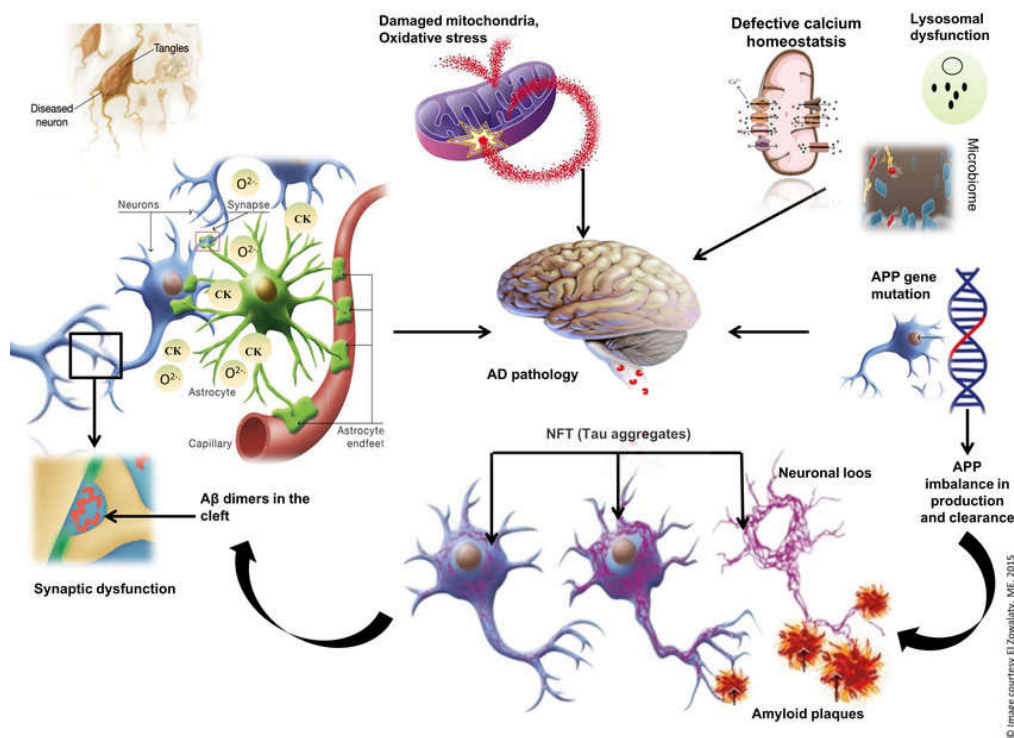


Figure 1. The pathophysiology of Alzheimer's disease is depicted in this diagram. [22]

The main inherited risk factors include genetic elements and apolipoprotein E (APOE) genes. When Alzheimer's disease is in its early stages, genes including APP and presenilins (PSEN I, PSEN II) are changed. Because of its increased expression, the APOE gene may cause amyloid to accumulate[23]. Redox-active metals interact with oxidative components in the mitochondria,

causing a large amount of hydrogen peroxide to be produced, causing oxidative damage[24,25]. Degradation of tau protein and amyloid compensate for this damage while also cascading it. The quantity of acetylcholinesterase is reduced when large amounts of amyloid and tau protein are removed[26].

Using preventative, preventive, and appropriate curative measures, Alzheimer's disease can be slowed[27]. Physical activity and lifestyle changes may assist in lowering Alzheimer's disease prevalence[28]. Minor metabolites produced from medicinal and herbal plants have significant effects on treating Alzheimer's and dementia.[29]. Numerous natural compounds occur naturally and have anti-Alzheimer activity. Antioxidant, AchE action, suppression of amyloid buildup, hyperphosphorylated tau protein, and neuroprotective activity are all properties of medicinal and herbal plants[30].

For the time being, there are no drugs available to treat Alzheimer's disease. Medicines are quite expensive and have various side effects that are accessible on the market, but individuals cannot purchase them due to financial constraints. Natural products could be crucial in the medical and pharmaceutical industries. Natural products are effective, have fewer side effects, and are also cost-effective. Natural products are being studied by researchers and scientists all around the world. Herbal and medicinal plants include a variety of natural and vital pharmacological compounds, some of which are extremely important and potent for various pharmacological actions, as shown in **Figure 2**. As a result, the primary objective of this study is to use a literature

review to examine the anti-Alzheimer activity of medicinal and herbal plants.

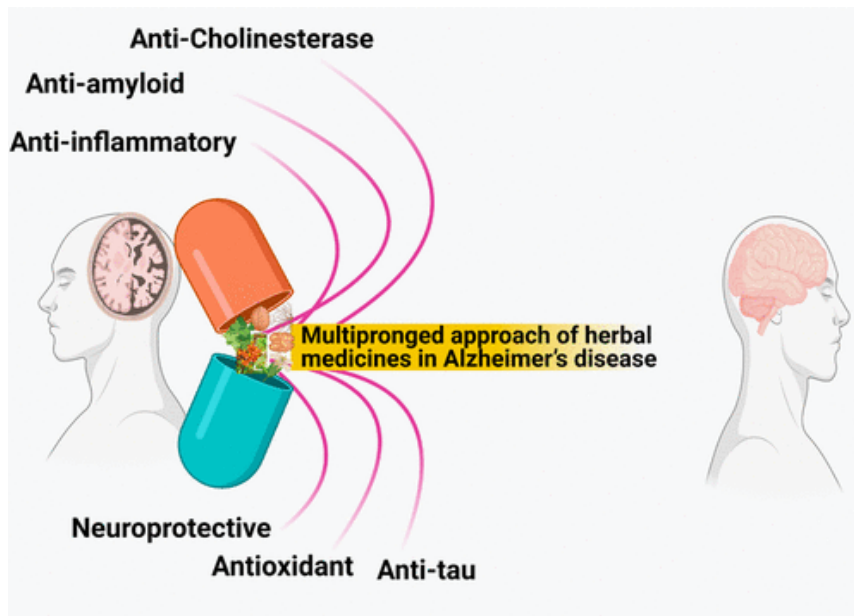


Figure 2. The mechanism of herbal therapies in the management of Alzheimer's [31].

MATERIAL AND METHODS

Overall, this review's work is accomplished by exploring different study and research papers from PubMed, Science direct, Research gate, Google scholar, and various types of journals. The anti-Alzheimer activity of medicinal plants is explored through this review.

Bacopamonnieri

Bacopamonnieri (also known as Brahmi, water hyssop, *Bacopamonniera*, and *Herpestismonniera*) is a creeping perennial with tiny rectangular leaves and purple blooms native to Australia and India. BM is a weed that grows in rice fields in East Asia and the United States.

In animal models and in vitro, BM has been widely researched. Although BM has been linked to The focus of this review will be on cognition, learning, and memory in treating anxiety, epilepsy, and other neurological diseases. Memory emphasizes the clinical studies referenced, with other

aspects of awareness such as fluid intelligence and creativity being overlooked. Clinical studies used to be short and sweet, generally lasting only 12 weeks. Although the long-term effects of BM on humans are unknown, animal studies suggest that it protects against age-related neurodegeneration rather than gradual toxicity or tolerance development.

Lopresti et.al was reported in a 28-day, randomized, double-blind, placebo-controlled study, 100 people with self-reported poor sleep received either a placebo or a standardized *Bacopamonnieri* extract (150 mg twice daily). The Bergen Insomnia Scale (primary outcome measure), the Functional Outcomes of Sleep Questionnaire, the Pittsburgh Sleep Diary, the Short Form-36 Health Survey, and the Depression, Phobia, and Sleep Apnea Questionnaire were all used in this study. Anxiety, and Stress Scale were among the outcome measures used. In addition, salivary cortisol, dehydroepiandrosterone sulphate, immunoglobulin A (sIgA), -amylase (sAA), C-reactive protein, melatonin, and the tiredness biomarker score were evaluated. According to the Bergen Insomnia Scale, *Bacopamonnieri* did not improve sleep patterns [32].

Withania somnifera (Solanaceae)

Ashwagandha (*WithaniaSomnifera*, *WS*), an Ayurvedic herb known as Indian winter cherry and Indian ginseng and belongs to the *Solanaceae* family, has been used in India for its various health benefits since ancient times.

WS is one of Ayurveda's most effective herbs, having been utilized for over 3000 years in stress management, energy enhancement, and promoting health. [33,34][35].

Zahiruddin concentrated on the documented neuroactive phytoconstituents, commercially accessible products, pharmacological investigations, mechanism of action, and recently published patents linked to Ashwagandha's neuroprotective benefits in brain diseases.[36].

Kaur et al. [37] examined *Withania somnifera* (L.) (*W. somnifera*) as a vital medicinal plant because of its great therapeutic potential. It has garnered a lot of interest since ancient times. Scientific confirmations of its medicinal potential for various illnesses have raised demand in both local and international markets. As a result, farming is necessary for new alternatives to conventional to address the huge gap between demand and supply. An in vitro growth method enables the creation of large-scale healthy, genetically, and phytochemically compatible *Withania somnifera* plants, promoting the herbal sector and allowing pre-clinical research. However, one of the most challenging parts of *W. somnifera* is in vitro propagation. For a long time on cytokinin-containing MS medium, *somnifera* must sustain a high shoot multiplication rate. The current work established a multi-step method for the prolonged maintenance of in vitro shoots that included rotational cultures of *Withania* shoots in auxin-cytokinin containing culture medium to minimize the detrimental effects of cytokinin. In vitro shoots were evaluated for genetic homogeneity and stable pharmaceutically important components after a lengthy time of growth [38].

***Curcuma longa* (Zingiberaceae)**

Curcumin is the primary polyphenol found in turmeric curry (*Curcuma longa*), a *Zingiberaceae* plant that thrives in tropical areas and is native to South Asia.

This molecule contains properties that can help prevent or alleviate pathological processes linked to neurodegenerative diseases like cognitive decline, mood disorders, and dementia. [39].

The derivative of Glycyrrhizainflata, a multifunctional drug for Alzheimer's disease treatment, was reported by Cao et al. *Curcumin* (*Cur*), an anti-disease Alzheimer's (AD) medicine that shares the same caffeic acid scaffold as Licochalcone B (LCB), a Glycyrrhizaindica root extract.

There is, however, no proof that LCB possesses anti-AD properties. This research looked into the anti-AD properties of LCB. LCB prevented self-aggregation of amyloid-beta (A42) and disaggregated pre-formed A42 fibrils (IC50 = 2.16 0.24 M), as well as chelating metal ions to reduce metal-induced A42 aggregation. Molecular docking further demonstrated that LCB prevented A42 self-aggregation by inhibiting its shape for AD[40].

Lepidiummeyanii

For almost 2,000 years, the Andean area has employed *Lepidiummeyanii* (maca) as a food and traditional medicine[41]. *Lepidium meyenii*, sometimes known as Maca, is a herbaceous living form that belongs to the Brassicaceae family and maybe grown up to 4500 metres above sea level. Starch, polyphenolics, dietary fibre, alkaloids, protein, macamides, gingerol (phenol), ergosterol peroxide (steroid), and tanshinone I, panaxytriol, macaene, and macamides are all-natural sources of health-promoting chemicals.campesterol, etc. Based on the available information and review of literature, maca also help to improve reproductive health, has better antioxidant activity, anticancer, hepatoprotective and immunomodulatory activity, which announce it as a superfood to reduce ageing.

According to an article published in 2021 by Talia et al., *Lepidiummeyanii* is a promising anti-AD drug. It could become pharmacological candidates to prevent Alzheimer's disease due to its various actions as potent inhibitors of AChE, BuChE, BACE, and MAGL.

The current study looked at the anticholinesterase effects of total alkaloids from *L. sativum* seeds and other plants and the ability of *Lepidine B* and *E* to inhibit AChE, BuChE, BACE, and MAGL. As a result, the critical interactions of the inhibitor enzyme complex must be determined.

Alkaloidal extracts of *Lepidium sativum* and ethyl acetate extracts of *Juniperus phoenicea* and *Juniperus oxycedrus* had substantial acetylcholinesterase inhibitory action, with IC_{50} values of 0.59 [42].

Magnolia officinalis

The anti-inflammatory, antioxidant, and neuroprotective effects of *Magnolia officinalis* are well-known. Many nutritional supplements made from *Magnolia officinalis* bark have been sold containing these efficacies. To analyze and compare neuroprotective benefits in the nutritional supplement (Magnolia Extract(TM), Health Freedom Nutrition LLC, USA) and our ethanol extract of *Magnolia officinalis*, we investigated memorial improving and anti-disease Alzheimer's effects of extract products of *Magnolia officinalis* (BioLand LTD, Korea).

Magnolia officinalis extracts helped prevent and treat Alzheimer's disease by increasing memory and reducing amyloidogenic effects by inhibiting β -secretase activity. Magnolia extracts' neuroprotective performance varied depending on cultivating location and manufacturing processes.

Soheili was looked at a *Magnolia officinalis* extract. According to a study released in February 2021 and evaluated in this publication, certain herbal plants have potential therapeutic effects on AD-related symptoms. Despite numerous preclinical studies demonstrating the efficiency of medicinal plants in treating neurodegenerative disorders, such as Alzheimer's disease, clinical research is needed to support the use of herbal medicine in the treatment of AD symptoms. Many herbal plants may help with the symptoms of Alzheimer's disease. Despite a profusion of preclinical studies on the use of medicinal plants to treat neurodegenerative disorders like Alzheimer's disease, clinical research is needed to back up herbal medicine's service in treating AD symptoms. One of the most common types of mental illnesses is schizophrenia.[43].

Convolvulus pluricaulis (Shankhpushpi)

Convolvulus pluricaulis (also known as Shankhpushpi in Hindi) is a herb whose pharmacological and therapeutic benefits have been extensively studied. Shankhpushpine, volatile oil, flavonoids (kempferol derivatives), phytosterol (beta-sitosterol), carbohydrates (glucose, rhamnose, and starch), ceryl alcohol, and scopoletin are all found in the plant[44].

The herb is most typically utilized in the form of a rasayana, which is a rejuvenation therapy. *C. pluricaulis* has been shown to increase both cognitive function and memory in several behavioural tests. [45–47].

Kizhakee Convolvuluspluricaulis (Shankhpushpi) Supplementing with *C. pluricaulis* in addition to a regular diet reduces the neurotoxic effects of hMAP in an AD Drosophila model and shows that it is a robust neuroprotective agent. *Convolvulus pluricaulis* (Shankhpushpi) has long been used as a nerve tonic in traditional Indian herbal medicine. The neuroprotective activities of *C. pluricaulis* extract (aqueous) against human microtubule-associated protein tau (hMAP) produced neurotoxicity were examined in a Drosophila model of Alzheimer's disease (AD). The longevity, locomotor activity, protein level, reactive oxygen species (ROS), lipid peroxidation (LPO), catalase (CAT), and superoxide dismutase (SOD) were all investigatedmodel[48].

Paeoniasuffruticosa

In vitro and in vivo, PGG alone reduced A fibril production and destabilized pre-formed A fibrils, similar to *Paeoniasuffruticosa*. According to our findings, both *Paeoniasuffruticosa* and its active component PGG have considerable inhibitory effects on the development of A fibrils in vitro and in vivo. PGG is a safe and promising lead molecule for developing disease-modifying medications to prevent and treat Alzheimer's disease.

Clinical research in Alzheimer's patients recently indicated that several of these traditional medications enhanced Mini-Mental State Examination scores, P300 latency, and cerebral blood flow, according to Fujiwara *Paeoniasuffruticosa*. Blocking Abeta fibril formation and destabilizing pre-formed Abeta fibrils is an appealing therapeutic and preventive strategy in developing disease-modifying drugs for Alzheimer's disease (AD) because amyloid-beta (Abeta) protein deposition is a consistent pathological hallmark of AD brains. *Paeoniasuffruticosa*, a traditional medicinal herb, was found to suppress fibril production in both Abeta(1-40) and Abeta(1-42) b cells in this investigation[49,50].

Yokukansan

Yokukansan (YKS) is a traditional Japanese herbal medication that has been used to treat a variety of neurological diseases in humans, including age-related anxiety and behavioural and psychological symptoms (BPSD) associated with various forms of dementia, including Alzheimer's disease (AD). However, the cellular and molecular pathways that YKS targets in the brain are still unknown.[51].

Natural herbal medicines containing various physiologically active ingredients have been used for generations and hence have apparent therapeutic promise [52].

The accumulation of amyloid protein (A) is a constant pathological hallmark of Alzheimer's disease (AD) brains, according to Fujiwara et al. *Yokukansan* in 2011. As a result, inhibiting A aggregation in the brain is a promising therapeutic and preventive method in developing Alzheimer's disease (AD) medications. *Yokukansan (YKS)*, a traditional Japanese medicine, suppressed A aggregation in a concentration-dependent manner, according to in vitro research. YKS and *Uncaria hook (UH)*, a component of YKS, were shown to prevent the accumulation of cerebral A in vivo research. In amyloid precursor protein transgenic mice, YKS reduced memory

disturbance and inappropriate social interaction, such as increased aggressive behaviour and decreased social conduct. These findings imply that YKS could be a potent and innovative therapeutic drug for preventing and treating Alzheimer's disease, which could be due to UH [53].

CONCLUSION

Many plants have been utilized in traditional medicine for many years to treat various types of ailments. Many plants are discussed in this review, and these medicinal plants were discovered after researchers and scientists investigated them for anti-Alzheimer activity. These medicinal plants can suppress the buildup of AchE, BchE, and A and improve learning and memory. We looked at various medicinal plants and articles that have many curative properties for Alzheimer's disease treatment. There are currently no medications available to treat Alzheimer's disease. Herbal medicine is commonly used to control Alzheimer's disease and help reduce the condition's signs and symptoms.

Herbal remedies may help patients with Alzheimer's disease live longer. This study investigates if herbal remedies may be used to treat Alzheimer's disease. Many medicinal plants have been chemically evaluated, and some are currently undergoing clinical trials. The basic mechanisms of action, on the other hand, are still in the works.

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