JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2022/29277

SHORT REVIEW

# A Review on Herbal Remedies for Alzheimer's Disease

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## Abstract

Among the neurodegenerative disorders, Alzheimer's disease is the most common type where the individual suffers from dementia. It usually affects citizens aged 65 and above. Its high prevalence and debilitating effects call for the need of effective therapeutic interventions to deal with this grave disease. The inefficiency of currently available therapeutic options pushes our attention towards finding effective alternative therapeutic options to either successfully prevent or treat AD. Herbal remedies are a potential gold mine that offer hope against this crippling disease. The aim of this review is to throw a light on the potential of a few potential and promising herbal which can provide an alternative therapeutic intervention for the prevention and management of AD amongst a plethora of herbal drugs.

**Keywords:** Alzheimer's Disease, Cognitive Function, Disorder, Beta-Amyloid Plaques, Herbal Drugs, Memory, Neurodegenerative Tau Protein

## 1. Introduction

Alzheimer's Disease (AD) is the most common form of dementia and the biggest unmet need in neurology. Commonly, people over the age of 65 are affected with AD. Early onset is a possibility but is rather uncommon[1]. It has been found that around 6.2 million Americans aged 65 and above were suffering from Alzheimer's dementia in 2021. Fatalities due to Alzheimer's and dementia have increased by 16 % during the Covid-19 pandemic in the United States alone. In the year 2021, the economic burden of Alzheimer's and other common forms of dementia was estimated to be around $355 billion and it is estimated to increase to around $1.1 trillion by 2050[3].

AD is a neurodegenerative disorder with a slow progression which is distinguished by loss of memory and ultimately by impairment in planning, language, perception and reasoning. The etiology of AD is not yet completely understood. Suggested reasons for initiation of AD may be related to environmental, lifestyle and genetic predisposition. It is proposed that reduced synthesis of acetylcholine (ACh) is one of the main causative factors for AD[1,2].

## 2. Pathology of Alzheimer's Disease

Identification of AD as a proteopathy is because of the aggregation of abnormal folds of beta amyloid and tau proteins. Build-up of proteins in the brain is a distinctive occurring in AD. This build-up is of two types:

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Article Received on: 06.01.2022 Revised on: 03.03.2022 Accepted on: 06.03.2022

**Plaques:** These are beta-amyloid protein aggregates which occupy the spaces between the nerve cells.

**Tangles:** Aggregates of tau protein which have been found to accumulate inside the cells.

In the cerebral cortex and certain subcortical regions there is notable loss of neurons and synapses. This results in degeneration of the affected regions as well as degradation in the parietal and temporal lobe and also parts of the frontal cortex and cingulate gyrus. It has been found that the concentration of neurofibrillary tangles (NFTs) in many older individuals is higher in the temporal lobe. This is subject to ageing[1,2].

**Mechanism**: The exact mechanism of AD is not known but current research findings point to the aggregation of beta-amyloid protein as the exceptional occurrence which triggers neuronal deterioration. The amyloid fibrils have been found to be responsible for inducing programmed cell death (apoptosis) by creating an imbalance in the calcium ion homeostasis of the cell. Furthermore, the build-up of beta-amyloid protein in the mitochondria of brain cells inhibits certain enzymes and also the uptake of glucose by neurons. The abnormal aggregation of tau protein results in tauopathy. In AD, tau is subject to hyperphosphorylation subsequent to which there is pairing with other threads forming NFTs which causes disruption of the neuron's transport mechanism. It is believed that various cytokines and some inflammatory markers may have a role in the pathogenesis of AD. Inflammation may either be a sign of an immunological response or be secondary to tissue damage in AD[1,2].

**Types of Alzheimer's Disease**

1. **Early onset AD:** In this, the onset is before the age of 60. It is uncommon. It has been found to have a genetic basis. Condition of the patient deteriorates quickly.
2. **Late onset AD:** It occurs after the age of 60. It is believed to be the most prevalent type of AD[1,2].

**Stages of Alzheimer's**

1. **Early stage:** It is also known as the mild stage and it lasts for about 2–4 years and is distinguished by frequent memory loss of recent events. The patient often tends to forget recent events and conversations.
2. **Second stage:** The duration of this stage maybe 2-10 years. This stage is marked by notable memory loss that impacts life across settings.
3. **Moderate stage:** In this stage patients experience problems in learning new things. They often fail in recognizing friends and family. They experience difficulty in carrying out basic activities like getting dressed. Delusions, paranoia and impulsive behavior is common.
4. **Last stage:** It may have a time period of about 1-3 years. This stage involves severe to total loss of verbal skills. Falls and immobility are likely. Extreme behavioral problems, hallucination and delirium are observed[1,2].

## 3. Diagnosis of Alzheimer's Disease

It can be done with the help of patient's history. Detailed information obtained from close ones such as from friends and family plays an important role in the diagnosis. Clinical findings confirming the presence of characteristic features may act as the final confirmatory test. As other disorders have symptoms resembling those of AD, it is also important to rule out the possibility of alternative conditions.

Technologically advanced tests like Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Single Photon Emission Computer Tomography (SPECT) or Positron Emission Tomography (PET) can be used to confirm the diagnosis of AD. In patients already suffering from dementia, SPECT acts as the main differentiating test. Apart from imaging tools, other tests are useful in assessing parameters like cognitive impairment which aid the diagnosis. For example, Mini-Mental State Examination (MMSE). As depression can be a cause, an early sign or can even be concurrent with AD, it is very important to diagnose the patient for the same[1,2].

## 4. Current Scenario

The two characteristic pathological features of AD are extracellular deposits of beta-amyloid deposits and intracellular neurofibrillary tangles (NFT)[1,2]. Many of

the drugs currently used for treatment targeting these two pathways have failed to give promising results. Therefore, there is a need to throw a light on other remedies which consider other pathophysiological pathways like neuroinflammation, oxidative stress, autophagy, neurotransmitter excitotoxicity and other possible pathways underlying AD[4,5]. While focus till now has been more on allopathic medicines, the use of herbal drugs dates back to thousands of years and has held importance in many cultures across the globe as a traditional way of medicine. They appear to be safe and effective but have not received much scientific attention unfortunately. In traditional practices of medicine, various herbs and their constituents have been shown to improve symptoms of AD such as deterioration in cognitive function, memory loss and even depression. Treatment involves use of either a single herb or a mixture subject to severity of the illness. This type of an approach has been made use of in Traditional Chinese Medicine (TCM), Ayurveda and Native Americans' system of medicine[6–10]. In this review, we throw a light on a few herbs that could be useful in AD.

## 5. Herbal Drugs used in the Treatment of AD

### *Ashwagandha (Withania somnifera)*

It is an age-old herb which is used widely in the Ayurvedic system. "Indian Winter cherry" or "Indian Ginseng" are its alternative names. Ashwagandha is an herb belonging to the family Solanaceae and is used as a Rasayana for its multiple health benefits. Its constituents include withanolides A to Y, withasomniferin A, withasomnidienone, withasomniferols A-C, withaferin, withanone and others[11].

Various studies based on molecular modelling have shown that withanamide components of Ashwagandha help in preventing the formation of amyloid fibrils. They also protect the adrenal phaeochromocytoma cell line and neuronal cells in rats from beta-amyloid precipitated cell death[12–14]. In another study, cultured neurons from rats were first treated with beta-amyloid peptides which caused neuronal atrophy and loss of stimuli both pre- and post synaptically. These changes were reversed to a notable extent when treated with withanolide A[15].

Studies done on effects of aqueous extracts of ashwagandha in rats showed that there was an increase in acetylcholine concentration and also in the activity of the enzyme choline acetyl transferase[16-18]. In a different study conducted on human neuroblastoma cells, dose and time dependent growth of the neuronal process was observed post treatment with methanol extract of ashwagandha[16]. In a study based on an AD model of fruit fly (*D. melanogaster*), it was observed that treatment with *W. somnifera* decreased beta-amyloid toxicity[19].

A pilot study involving 50 subjects with mild cognitive impairment included two groups, one was treated with *W. somnifera* (300 mg two times a day) and the other received a placebo for eight weeks. The results showed that the test group showed significant improvement in memory tests as compared to the placebo group. The test group also showed significant improvement in information processing speed, sustained attention and executive function[20]. Even though a decent amount of literature exists on the beneficial effects of *W. somnifera* in grave diseases like AD but we believe more human centric studies or trials are needed to unveil the true potential of this powerful herb.

### *Brahmi (Bacopa monnieri)*

It is a medicinal herb used widely by the traditional Ayurvedic practitioners in India. Water hyssop, thyme leafed gratiola, herb of grace and Indian pennywort are a few other common names for this herb. Its active constituents are bacoside A and B, betulinic acid, D-mannitol, stigmastanol, b- sitosterol, stigmasterol and others[21]. Several in vitro as well as *in vivo* research studies have shown that brahmi has an inhibitory action on reactive oxygen species. This is because of blockade of an important step in the oxidation of lipids in several areas of the brain by its active constituents[22–26].

In a research work performed to test the neuroprotective effect of brahmi in rats with AD, an alcoholic extract of brahmi was used at the doses of 20, 40 and 80 mg/kg for a duration of 14 days before and 7 days after the intracerebroventricular (icv)

administration of ethylcholine aziridinium ion (AF64A). At the end, spatial memory was tested using Morris Water Maze (MWM) and the cholinergic neuron density was also analyzed. In the results it was found that brahmi extract improved the escape latency time. The reduction of cholinergic neuron densities was found to be blocked as well[27]. Many studies have been done to show brahmi's role in memory and intellect[23,28–32]. A study was conducted on 10 subjects in which they were given 500 mg of Sideritis extract, 320 mg brahmi extract or a combination of both. This was followed by conducting an Attention d2 Test which is a neuropsychological measure of selective and sustained attention and visual scanning speed. In the tests it was observed that a combination of Sideritis extract with a low dose Brahmi extract resulted in improvement of the d2 concentration test score[33,34].

In a multicenter clinical trial, 104 patients with MCI were given Brahmi along with astaxanthin, phosphatidylserine and tocopherol for sixty days. At the end of the study, the cognitive and mnemonic performance was tested with validated instruments like the Alzheimer's Disease Assessment Scale-Cognitive (ADAS-cog) and Clock-Drawing Test (CDT). It was found that the improvement in the scores observed after 60 days were statistically significant when compared to the scores noted at the beginning of the study[35].

A clinical trial involving 35 enrollments with the age over 55 years was conducted over a duration of 16 weeks. The patients received either 125 mg of *B. monnieri* extract or a placebo two times a day for the first 12 weeks followed by a placebo for 28 days. At the end of the study there was notable improvement in paired association learning, mental control and logical memory in the test group compared to the control group (placebo group)[36].

At present, decent amount of literature is present supporting the claim that Brahmi could prove to be a groundbreaking alternative therapeutic herb for terminal illnesses like AD but we believe there is a need for more human based trials which could help make an unassailable case for the use Brahmi in diseases like AD.

### Cat's Claw (Uncaria tomentosa)

This tropical vine also commonly known as Life-giving Vine of Peru is from the Rubiaceae family. It is found mainly in the Amazon rainforest and in the tropical lands of Central and South America. It gets its name due to the resemblance of its hooked thorns with a cat's claw. Its main phytoconstituents are oxindole and indole alkaloids, glycosides, organic acids, proathocyanidins, sterols and triterpenes[37,38]. In a study on genetically-modified mice having AD, treatment with Cat claw's extract for 14 days led to notable reduction in the beta-amyloid (by 59%) and plaque number (by 78%) in the hippocampus and cortex[39].

Pre-clinical studies performed on mouse models of AD showed that Cat claw's extract improved memory, inhibited the formation of plaques and tangles and also reduced astrocytosis and microgliosis[39,40]. It was observed that it not only impedes the formation of fibrils and tau protein tangles but also breaks down the already formed fibrils and tau protein tangles[39,40]. Even though fewer studies have been done to assess the potency of this tropical herb, the currently available studies do make a strong case for the need of further research to evaluate the true potential of this herb in treating diseases like AD.

### Chinese Club Moss (Huperzia serrata)

An herb used for AD and general memory disorders. It contains serratidine, lycodine, huperzinine, huperzine A and huperzine B[41]. Huperzine A is the main substance that acts an acetylcholine esterase inhibitor and gives beneficial effect in AD[42]. Various studies conducted to test the safety and efficacy of of huperzine A have shown that it is effective in the treatment of AD[43]. We believe *H. serrata* is a very scarcely studied herb which if studied more could possibly prove to be a useful herbal drug for AD.

### Ginkgo (Ginkgo biloba)

Commonly called as the maidenhair tree, fossil tree, knew tree or the Japanese silver apricot, this plant belongs to the family Ginkgoaceae. It contains terpene,

trilactones, ginkgolides A, B, C, J, bilobalide, biflavones, alkylphenols, polyprenols and other substances44. It cleans up free radicals which in turn reduces lipid peroxidation. It also blocks the decline of membrane fluidity and cell damage observed in AD45. G. biloba is commonly used for treating early-stage AD and vascular dementia. In vitro studies have shown that *G. biloba* reverses beta-amyloid and NO-induced toxicity. It also reduces programmed cell death46–48. Multiple randomized controlled trials, have shown that there is betterment of cognitive ability in AD patients on treatment with *G. biloba*[49–51]. Its extract has been shown to be useful in therapy of patients suffering from various types of dementia in European countries[52,53]. In a study based on nanosized extract of *G. biloba*, it was observed that the group of animals treated with the extract showed improved acetylcholine neurotransmitter discharge from several sections of the brain compared to the control group[54].

*G. biloba* is a very potent herb which has positive effect on symptoms in AD patients but its use is undermined by the limited data available. Most studies carried out till date are focused on animal-based models and hence there is a need of large-scale clinical trials to discover more about the potential of this herb to help patients suffering from AD.

### Ginseng (Panax ginseng)

An herb belonging to Araliaceae family has long been valued in Chinese medicine for its antioxidant and anti-inflammatory effects. It contains ginsenosides, 20(S)-protopanaxadiol (PPD) and 20(S)-protopanaxatriol (PPT)[55]. Studies have shown that it can be useful in treating grave disorders like AD and Parkinson's disease as it inhibits generation or aggregation of beta-amyloid proteins, increases removal of beta-amyloid from the neurons and interrupts tau hyperphosphorylation[56,57]. Large portion of the literature available on the effect of *P. ginseng* in treating AD is focused on animal studies. Hence, it is imperative that more studies are carried out in the form of both animal-based studies as well as clinical trials.

### Gotu Kola (Centella asiatica)

This tropical medicinal plant is also commonly known as Indian pennywort, Asiatic pennywort and kodavan. It belongs to the Apiaceae family. Its main constituents are Asiatic acid and asiaticoside[58]. In vitro study shows that it inhibits beta-amyloid cell death and toxicity and hence it could play an important role in prevention and treatment of AD. Furthermore, other in vitro studies have also shown that *C. asiatica* plant derivatives had free radical scavenging capability and also blocked $H_2O_2$ induced cell death[58–62].

Study conducted to assess the effect of ethanolic extract of *C. asiatica* in human SH-SY5Y cells showed that in presence of nerve growth factor (NGF) it had a positive effect on the outgrowth of neural processes in the cells and also increased the rate of axonal regeneration in rats[63]. A randomized clinical trial on 28 healthy enrollments was carried out using *C. asiatica* extract at varying doses (250, 500 and 750 mg) once daily for 60 days. Cognitive performance and mood were assessed before and after the administration of *C. asiatica* extract. The results showed that *C. asiatica* at high dose enhanced working memory of the subjects. The subjects also reported improvement in mood following treatment with *C. asiatica*[64].

Not much literature of research conducted on humans is available on the effect of *C. asiatica* in patients suffering from AD. Hence, it is important that more focus is put on carrying out human centric trials to evaluate the pros and cons of this herb when used to treat patients with AD.

### Guggulu (Commiohora wightii)

A flowering plant native to the Burseraceae family, Guggulu also called as Indian bdellium—tree, gugal, guggul or mukul myrrh tree is one of the most widely used ayurvedic herbs. It is often used as a binding agent in many tablets due to its oleogum resin. Its main constituents are cuminic aldehyde, eugenol, terpenes, guggulsterone and guggulsterols I, II and III[65].

A study has shown that it reduces neuronal cholesterol levels and inhibits the beta-amyloid forming amyloidogenic pathway[66]. It has an inhibitory action towards the reactive oxygen species. This is due to the presence of ferulic acid, phenols and nonphenolic aromatic acids and is considered valuable for its use in AD[67–69]. The literature available on the effect of *C. wightii* in therapy of AD is scarce but even with limited research *C. wightii* has shown good promise

to be beneficial in treating AD. This calls for the need of further research on animal-based models as well as clinical trials in order to further evaluate the effect of *C. wightii* in treating AD.

### Jyotishmati (Celastrus paniculatus)

An herb belonging to the family Celastraceae, it holds great value in the Ayurvedic medicine. It contains free fatty acids (FFA), triacylglycerol (TAG), diacylglycerol (DAG), esterified sterols and mono acylglycerol (MAG)[70]. Study done on the aqueous extracts of *C. paniculatus* seed have shown that it has a dose-dependent cholinergic activity which in turn improves memory performance[71]. This herb is still under the microscope for its potential ability to treat patients with AD. Intensive research on both animal-based model as well as clinical trials should be encouraged to make a strong case for its use in the therapy of AD.

### Lemon Balm (Melissa officinalis)

An herb native to the mint family Lamiaceae. It is commonly called as bee balm, honey plant, cure-all or sweet balm also. Its main constituents are rosmarinic acid, oleanolic acid, ursolic acid, caffeic acid, ferulic acid and others[72]. In a study involving AD patients, it was observed that patients who were treated with *M. officinalis* extract orally daily for 120 days showed notable reduction in Alzheimer's symptoms[73].

A clinical trial was conducted over 120 days. It involved subjects with mild to moderate AD. Patients were randomly given either *M. officinalis* or a placebo. At the end the results showed that patients treated with *M. officinalis* had notable improvement in their cognitive function as compared to those who received a placebo[74]. In a clinical trial conducted over 24 weeks on patients with mild dementia due to AD, it was observed that patients that received *M. officinalis* showed a notable improvement in the Neuropsychiatric Inventory Questionnaire (NPI-Q) score by 0.5 points, on the other hand, the group that received a placebo showed worsening of the score by 0.7 points[75].

Among the herbs reviewed in this study, *M. officinalis* presents itself as one of the most promising herbs to alleviate symptoms in patients with AD. Further clinical trials would only strengthen its case to be considered as one of the alternative therapeutic options for treatment of patients with AD.

### Lion's Mane (Hericium erinaceus)

This large shaggy mushroom gets its name because of its resemblance with a lion's mane. It is also called as hou tou gu or yahambushitake. It is highly valued in traditional Chinese medicine and has long been used because of its anti-neoplastic, anti-inflammatory and neuroprotective characteristics[76]. Its main active constituents are erinacines and hericenones[77,78].

A research work conducted to test the effect of *H. erinaceus* extract on cell lines and cultured neurons showed that the *H. erinaceus* extract in presence of NGF stimulates neurite length[79]. In a study conducted on old mice, they were fed *H. erinaceus* extract for 2 months and it was observed that the extract stimulated hippocampal neurogenesis and improved cognitive performance. In another study carried out on mice with AD, it was observed that treatment with *H. erinaceus* extract reduced beta-amyloid plaques and led to increased NGF levels[80,81].

In a small randomized study conducted over 49 weeks on patients with mild AD, it was observed that treatment with *H. erinaceus* extract improved scores related to activities of daily living (dressing, bathing, cooking, etc.)[82]. This medicinal mushroom has good therapeutic potential to treat AD but currently not much research work has been conducted to justify its use as an alternative therapeutic option in patients with AD. Hence, large scale research work could aid in understanding its effect on patients with AD.

### Saffron (Crocus sativus)

It is the reddish-orange dried stigma of the purple crocus flower. It is the costliest spice in the world. Its constituents are gentisic, gallic acids, lycopene, picrocrocin, safranal, crocin, zeaxanthin and beta-carotenes[83]. Research work shows that the chemical constituents present in saffron possess anti-inflammatory and anti-amyloidogenic properties. It also has an inhibitory action towards reactive oxygen species[84–86].

A clinical trial involving 46 patients with mild to moderate AD the patients were randomly either given

saffron 30 mg/day or a placebo for 16 weeks. The end result showed that cognitive performance scores (ADAS-cog and CDR scores) of the test group were notably better than those which received the placebo[87]. A clinical trial involving 68 patients with moderate to severe AD was conducted in which the subjects were either given memantine (20 mg/day) or saffron extract (30 mg/day) for 12 months. The results showed that the saffron extract was as effective as memantine in reducing cognitive deterioration in the patients and it also had fewer side effects[88].

In another clinical trial involving 54 subjects with AD over 22 weeks, the patients were either administered 30 mg/day capsule of saffron or 10 mg/day donepezil. The results showed that both saffron and donepezil had similar effects in improving cognitive function with saffron having fewer side effects as compared to donepezil[89]. Currently available research work has shown that this household spice has the potential to improve cognitive function in patients with AD. Further research focusing more on clinical trials would lead to a better understanding of its potential to alleviate symptoms in patients suffering from AD and would help make a strong case for its use as an alternative therapeutic option in the treatment of AD.

### *Shankhpushpi (Convolvulus pluricaulis)*

An herb valued highly in the Ayurvedic system, is commonly known as Butterfly pea. Its active constituents are, convolvine, confoline, convosine, convolidine, kampferol and steroids phytosterol. These contituents give *C. pluricaulis* its medicinal properties[90]. Several studies have shown that *C. pluricaulis* has the ability to relieve mental stress and fatigue. It has also proved to be beneficial in patients with anxiety, mental fatigue and insomnia[22,32,91].

In vitro studies carried out in rats showed that an ethanolic extract of *C. pluricaulis* inhibits reactive oxygen species and notably improves learning and memory in rats[14,92,93]. In another study, aqueous root extract of shankhpushpi was given to neonatal rats. It was found that there was notable improvement in retention and spatial learning performance. A notable increase in ACh concentration and activity was observed[94-96].

Similarly, in a study conducted on mice it was observed that when treated with shankhpushpi there was notable increase in dendritic branching and processes as compared to age-matched saline controls[97]. In another study conducted on old and young mice, it was observed that the *C. pluricaulis* showed an increase in memory retention which was directly proportional to the dose administered. The memory retention was observed to be better in young mice[98].

Currently, research work on animal-based models testing the effect of *C. pluricaulis* have shown promise but there is a lack of research work based on clinical trials. Large scale clinical trials assessing the effect of *C. pluricaulis* in diseases like AD are needed.

### *Turmeric (Curcuma longa)*

This rhizome is native to the ginger family Zingiberaceae. Commonly used as a household spice but it is also widely known for its medicinal characteristics. It gets its yellow colour from a substance named curcumin. It is also known as curcuma, curcuma aromatica and curcumin. It contains essential oils, curcumin and polyphenol with curcumin being the principal active constituent whose anti-inflammatory property has shown to reduce the risk of AD[99,100]. Other curcuminoids include demethoxycurcumin (DMC), bisdemethoxycurcumin (BDMC) and cyclocurcumin[100].

Studies carried out on aged mice with high plaque deposits have shown that oral administration of curcumin significantly reduces the plaque load[101–104]. Research work done in mouse having AD have shown that curcumin reduced inflammation, oxidative damage and amyloid pathology[102,104]. Several studies based on animal models of AD have shown that there is improvement in cognitive function when treated with curcumin. This is believed to be due to curcumin's property to reduce beta-amyloid plaque levels and it's anti-inflammatory and antioxidant action[105–107].

In a study involving 3 human subjects with AD, it was observed that their behavioral symptoms improved significantly after treatment with turmeric for 12 weeks. There was a notable decrease in the Neuro-psychiatric Inventory-brief questionnaire score in all 3 patients and the Mini-Mental State Examination (MMSE) score had increased by 5 points in one patient[108]. Even though

many studies have been performed to test the effect of curcumin on animals, very few human based trials have been performed. Hence, intense research should be encouraged in the form of clinical trials to evaluate the potential of *C. longa* as a therapeutic option for AD.

## 6. Conclusion

In the absence of a medical breakthrough to prevent, slow or cure AD, it is estimated that around 12.7 million people aged 65 and above may suffer from AD by 2050 in the United States alone. These numbers along with the inefficiency of current pharmacological treatment options makes a big case for pharmaceutical companies, research scientists and healthcare professionals to explore other alternative therapies for the prevention and treatment of AD. While many novel therapies are currently under development, their final outcomes are still uncertain and they require more research to truly unveil the hidden potential in these alternative treatment options.

We believe that herbal drugs are one such hidden gem which has a broad scope to deliver promising results in providing better alternatives for prevention and management of AD. In this review we have highlighted how herbal drugs have an extensive range of physiological actions that ultimately enhance memory and restore normal cognitive function. Herbal drugs are generally prescribed as an herbal extract, isolated herb or a mixture of herbs. An increase in efficacy and a decrease in non-specific toxicity has been observed when herbs are used in isolation or as a mixture.

The evidence gathered in this review to support the huge potential of herbal drugs is just the tip of the iceberg and there is still a large amount of unexplored potential which needs to be discovered. Hence, large multicenter clinical trials along with deeper investigations into studying the safety and efficacy along with their mechanism of action is needed to substantiate the claim that herbal drugs can provide a valuable alternative in prevention and management of AD.

## 7. Conflicts of Interest

No conflict of interest.

## 8. References


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