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Role of Medicinal Plants for the Treatment of Alzheimer's Disease

Ram Babu Sharma [a*], Rajiv Sharma [a] and Kundan Singh Bora [a]

[a] University Institute of Pharma Sciences, Chandigarh University, Ludhiana- Chandigarh Highway, Mohali, 140413, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

In today's era, most of the diseases are treated by allopathic drugs. The reliance on allopathic drugs for the treatment of most diseases is gradually increasing day by day due to their rapid effects and the immediate relief to patients. However, these drugs induce some serious side effects in patients, and in some cases, the patient may die. Thus, the interest of researchers is growing day by day towards medicinal plants for the treatment of diseases. It has also been viewed that some herbal plants have great therapeutic and pharmacological effects in the treatment of Alzheimer's disease. The initial studies, which have been carried out by different researchers, demonstrated very valuable results and enlighten a ray of hope for the treatment of Alzheimer's disease which is associated with CNS disfunction. In this article, the author focused on those plants which are especially used in the treatment of Alzheimer's disease.

Keywords: Allopathic drugs; medicinal plants; alzheimer's disease; neurodegenerative disorder

1. INTRODUCTION

Alzheimer's disease is a neurodegenerative disorder that causes patients to have strange behaviour, changes in personality, a decline in mental ability, and significant memory loss [1-2]. As we know, no permanent treatment for Alzheimer's disease exists; only symptomatic treatment is found in allopathic drugs [3-4]. In the next 50 years, the number of instances of

**Corresponding author: E-mail: sharmaram77@ymail.com;*

Alzheimer's disease is predicted to drop substantially if a treatment intervention can be ignored by researchers [5].

With over a hundred new compounds in clinical trials, it has been found in initial studies that Ayurvedic medicinal plants will have the best option without any adverse effects for the treatment of Alzheimer's illness [6-8]. Several studies have indicated that Ayurvedic medicinal herbs and their components can treat Alzheimer's disease [7]. During the studies, it has also been found that in medicinal plants, several medicinal constituents have been isolated from the plant by the extraction and isolation process, like glycosides, alkaloids, flavonoids, tennis, polyphenols, triterpenes, sterols [8–9]. These compounds are not only used in the treatment of Alzheimer's disease but also have anti-inflammatory, anti-amyloidogenic, anti-cholinesterase, hypolipidemic, and anti-amyloidogenic pharmacological actions [10].

In the preliminary studies and data obtained from various plants, it was found that through the different cellular activities and clinical applications of different plants, it was found that medicinal herbs have the ability to effectively treat Alzheimer's without any negative side effects [11–13].

2. WHAT IS ALZHEIMER'S DISEASE AND HOW DOES IT AFFECT YOU?

Alzheimer's disease is a memory-related degenerative brain disorder that is associated with memory loss in patients. The disease mainly starts in the age group of mid-sixties, where preliminary symptoms have developed [14] It has been found that Alzheimer's disease could persist in the age group between 30 and 60 years. Dementia is the main cause of Alzheimer's disease in the late sixties in human beings [15].

The Alzheimer's disease name comes after the name of Dr. Alois Alzheimer's disease. A lady died of an unusual mental illness in 1906, Dr. Alzheimer detected abnormalities in her brain tissue [16]. Her symptoms included memory loss, language problems, and unpredictable behaviour. After she died, he discovered many aberrant clumps (now known as in her brain, she had amyloid plaques and twisted bundles of fibres (now called neurofibrillary, or tau, tangles) [17].

These plaques and tangles in the brain are still regarded as pathological signs to be observed among Alzheimer's disease patients. Another indication is a condition in which nerve cells (neurons) in the brain lose their connections [18-19] The brain, as well as the nerves, muscles, and organs throughout the body, has a neuronal connection that helps them interact with one another [20]. It might be caused by a variety of additional, more complicated brain alterations that are considered part of Alzheimer's disease [21].

Memory is controlled by the hippocampus, part of the brain formation that appears to be the source of the injury. As neurons die, it affects other parts of the brain, and this damage is widespread and continuous as Alzheimer's disease progresses. The result is that brain tissue will decrease significantly and the patient will slowly lose memory [22-23].

One of the most frequent early indicators of Alzheimer's disease is memory difficulties. However, the severity of symptoms varies from person to person [24]. Other indications of Alzheimer's disease in its early stages include the inability to recognise the correct texts, eye side and word fixation problems, and developing slow learning capabilities or judgement. MCI is a disorder that can progress to Alzheimer's dementia, however not everyone with MCI develops the illness [25].

Simple chores in daily routine, even not properly preparing meals, making payments, travelling from one to another place, etc., are challenges for Alzheimer's sufferers. Such patients having short memory and repeat the same thing again and again, not properly keep the things at right place moreover, cannot bale to solve the simple and find even simple things perplexing. As the illness will be progressive, the patient getting irritation, and frequent mood swings also occur [26].

3. CAUSES AND RISK FACTORS

The reasons for Alzheimer's disease are being tried by many researchers in various ways. It has been found that a number of genes are being caused by Alzheimer's disease [27]. It has also been studied that, along with hereditary factors, a variety of environmental variables have also been associated with the development of Alzheimer's disease. Other causing factors are also found, like long-term

exposure to metals such as silicon or aluminium, chemicals like free radicals and traumatic events, etc [28]. The origin of Alzheimer's disease is caused by a disruption of bio-metal homeostasis (Cu, Zn, Fe) and oxidative stress in brain cells [29-30]. In the 1960s and 1970s, aluminium was discovered as a possible cause of Alzheimer's disease. Concerns regarding aluminium contamination in everyday products such as cooking pots, foil, beverage cans, antacids, and antiperspirants arose as a result of this assumption [31]. However, various studies have suggested that there is no indication of aluminium as a causative metal in the origin of Alzheimer's disease. However, few experts feel that long-term exposure to aluminium sources poses a serious threat to Alzheimer's disease. Some scientists still believe that some chronic diseases like diabetes, hypertension, high cholesterol, and stroke are all risk factors for Alzheimer's disease and dementia [32].

4. SYMPTOMS AND SIGN OF ALZHEIMER DISEASE

Memory loss is the most common sign of Alzheimer's disease, and it can be characterised by behaviours such as forgetting appointments, being away from home, misplacing belongings, and asking the same questions again and again. In addition to memory difficulties, sleeplessness, anxiety, melancholy, disruptive behaviour, and hallucinations are all symptoms of Alzheimer's disease. Numerous investigations and evidence suggest that the brain metabolic activity reduction is caused or exacerbated by Alzheimer's disease [33–35].

Three steps are most crucial for Alzheimer's disease and may be divided into each with its own set of signs and symptoms [36]. The common symptoms of disease are dilemma, amnesia, disorientation, recent reminiscence harm, and behaviour change. All these symptoms mostly occur in the last two to four years [37]. Loss of recognition, decreased heed span, phantasms, impatience, muscular tremors, reduced explanation ability, high level of anger, and increased difficulty in organising ideas are all common symptoms of the second stage. Stage Three, which lasts one to three years and is linked to risk factors including age and brain damage, self-gratification, difficulties in chewing and swallowing, the development of topical problems related to skin, and seizures are prevalent [38].

5. DIAGNOSIS

There is no early sign of disease at this early stage. Therefore, it is very difficult to recognise Alzheimer's disease at this preliminary stage so that treatment may not begin as soon as possible [39]. To optimise the chances of enjoying a normal and healthy life, these herbal therapies should begin as soon as possible following diagnosis (together with regular brain exercises) [40-41].

A comprehensive examination that includes the following tests can correctly identify Alzheimer's disease:

- ✓ A neurological examination
- ✓ Various tests for anaemia, vitamin deficiencies, and other diseases are so that they rule out the chances of these diseases.
- ✓ Complete medical and psychological history [42].
- ✓ A mental state assessment to assess a person's ability to think and remember things having a conversation with family members or carers [43].
- ✓ Psychiatric Assessment: The following tests are used to diagnose Alzheimer's disease: The Mental Status Examination (MSE), one of the most significant diagnostic tests for dementias like Alzheimer's disease [44].

For Alzheimer's disease, The Mini-Cog test is performed which takes around three minutes and is widely used in emergency departments for individuals [45].

5.1 Urine Analysing Test

To determine whether a patient has Alzheimer's disease or another kind of dementia, the doctor will do a variety of tests, including a urine study. Urinalysis (urine testing) detects abnormalities in the urine. A urine test can identify a variety of illnesses or disorders, including severe renal disease, that have symptoms that are similar to dementia [46].

Mild Cognitive Impairment (MCI) is a condition in which a person's capacity to think and remember things is impaired (MCI): -People may dread the beginning of dementia while, in reality, they are suffering from moderate cognitive impairment. People may dread the beginning of dementia when, in reality, they are

suffering from moderate cognitive impairment [47].

5.2 Dementia Diagnosis Visual Cues

There are several visible indicators that someone is suffering from Alzheimer's disease, is a kind of dementia. It's conceivable that patient personal hygiene, clothes, and look will deteriorate. Although visual clues are helpful, they only disclose one element of human behaviour and appearance that might lead to a diagnosis. The Mini Mental State Examination (MMSE) is the most common memory test, and it can assist in dementia diagnosis [48]

5.3 Lumbar Puncture Test

Although lumbar puncture is not commonly used in dementia testing, it might identify unusual illnesses that resemble dementia symptoms. The Mini Mental State Examination (MMSE) is the most frequent memory test, and it can help in dementia diagnosis.

The electroencephalogram (EEG) is a valuable tool for Alzheimer's disease diagnosis. The EEG shows a widespread and symmetrical slowing of the brain waves in those who have the illness [49].

Allopathic drugs have side effects in Alzheimer's disease.

In allopathic treatment, lots of options are there for the treatment of Alzheimer's disease, but these drugs do have some serious side effects. Therefore, recently, the belief of people is shifting towards herbal drugs [50].

6. ALZHEIMER'S DISEASE AND MEDICINAL HERBS

A wide range of phytocompounds found in medicinal plants can be isolated and utilised as raw materials in various scientific approaches. In the pharmaceutical field, secondary metabolites from plants are also significant commercially and are utilised. Medicinal plants have recently acquired widespread popularity as a result of their fewer negative effects as compared to manufactured medications and the need to satisfy the medical needs of an ever-increasing human population [51]. Due to a number of circumstances, maintaining a steady supply of source material is challenging, such as geographical dispersion, climate variations, cultural traditions, labour costs, the overexploitation of pharmaceutical firms and the selection of better plant stock [52] *Centella asiatica*, *Ginkgo biloba, Withania somnifera, Bacopa monnieri, Salvia officinalis, Melissa officinalis, Tinospora cordifolia, Glycyrrhiza glabra, Centella asiatica, Ginkgo biloba, Withania somnifera, Bacopa monnieri, Salvia officinalis, Melissa officinalis, Tinospora cordifolia, Glycyrrhiza glabra*, and other medicinal herbs can help to treat Alzheimer's disease [53].

6.1 *Withania somnifera* (Ashwagandha)

Nerve tonic *Withania somnifera* is a renowned ayurvedic herb helpful to overcome or adjust to stress of body. It is a member of the Solanaceae family. The root part of plant is frequently utilised for medicinal purpose in the treatment of Alzheimer's disease. It has scavenging free radicals, antioxidants, and the immune system boosting properties.*W. somnifera* has a calming effect, whilst other adaptogens have a stimulating effect, hence has beneficial for patients.
A recent research of *W. somnifera* is used to reduced tension and difficulty to focus, as well as corrected amnesia in a dose-dependent way with no side effects [10]. The phytocompounds discovered in *W. somnifera* are withanolides A to Y, withasomidienone, withasomniferin A. dehydro withanolide R. withaferin A. withasomniferols A to C, and withanone, phytosterols sitoindosides VII to X, beta-sitosterol, alkaloids, amino acids, and substantial amounts of iron, phytosterols sitoindosides VII to X, phytosterol [54].

Free radicals produced at the start and throughout the process of Alzheimer's disease have been discovered to be scavenged by withanamides. It reduced amyloid plaque-induced neuronal cell death. According to molecular modelling studies [55], the -amyloid (A 25–35) active motif is bound by withanamides A and C, in particular, inhibiting fibril formation.

Acetylcholine content and choline acetyl transferase activity will be enhanced while aqueous extracts of *W. somnifera* are being used, and it also enhances cognition and memory in rats. Furthermore, *W. somnifera* methanol extracts restored amyloid peptide-induced memory loss by restoring pre- and post-synapses in neurons. It has also been seen that in vivo effects last long after the drug is withdrawn [56].

6.2 *Bacopa monnieri* (Brahmi)

The Scrophulariaceae family includes *Bacopa monnieri*. This plant grows in wet, marshy areas. It is commonly used as a nerve tonic in Ayurvedic medicine. Apart from this activity, it also exhibits other activities like cardiotonic, diuretic, anti-asthma, sleeplessness, epilepsy, and rheumatism treatment. Butyric acid, sterols, alkaloids, polyphenols, and sulfhydryl compounds, butyric acid, sterols, alkaloids, polyphenols, and sulfhydryl compounds, butyric acid, sterols, alkaloids, polyphenols, and sulfhydryl compounds, butyric acid, sterols, alkaloids, polyphenols, and sulfhydryl compounds, as well as sterols, alkaloids, polyphenols, and sulfhydryl compounds, all. *B. monnieri* has traditionally been Memory and cognitive function are aided by this supplement. The neuropharmacological and nootropic effects of *B. monnieri* extracts have been widely researched. monnieri increases activity of protein kinases in the hippocampus, which contributes to its memory-enhancing effects. The rat models revels that, *B. monnieriis* very effective for prevention of cholinergic degradation and improved cognition [57].

A standardised *B. monnieri* extract was shown to restore cognitive impairments caused by intra-cerebroventricular administration of Ibotenic acid and colchicines when injected into the basalis magnocellular nucleus. In the frontal cortex of the hippocampus, *B. monnieri* restored acetylcholine depletion, decreased choline acetyltransferase activity, and reduced muscarinic cholinergic receptor binding. In the same research, by reducing cellular acetylcholinesterase activity, *B. monnieri* extracts protected neurons against amyloid-induced cell death. The presence of reactive oxygen species was decreased in neurons treated with *B. monnieri* extract, suggesting that it suppressed oxidative stress within the cell [58].

6.3 *Centella asiatica* (Gotu Kola)

Centella asiatica is a plant that may be found in India, Sri Lanka, and Bangladesh and belongs to the *Apiaceae* family. Triterpenes, asiatic acid, asiaticoside, adecassoside, sapogenins, glycosides, madecassic acid, vellarin, and centelloside are among the bioactive chemicals identified in the Centella asiatica plant. In vitro, asiatic acid and asiaticoside reduced hydrogen peroxide-induced cell death, free radical concentrations, and prevented amyloid cell death, suggesting that they may have a role in Alzheimer's disease therapy and toxicity prevention. In mouse brains, Centella asiatica extracts decreased amyloid disease and changed oxidative stress response components. It is a necessary plant for nerve brain cells for proper functioning, improving intelligence, enhancing memory, and increasing the lifespan of nerve cells [59].

6.4 *Ginkgo biloba*

Ginkgo biloba is a kind of plant that belongs to the Ginkgoaceae family and is abundantly found in China. Blood circulation issues, awareness loss, depression, and headaches are all treated with *ginkgo biloba* extract. According to the researchers, this extract contained approximately 24% flavonoid, accounting for 24% of the total, with terpene lactones accounting for 6%. Apoptosis inhibition, preventing membrane lipid peroxidation, anti-inflammatory actions, and lowering amyloid aggregation are only a few of the benefits. All the molecular and cellular neuroprotective mechanisms that standardised ginkgo extract has been shown to engage. There have been a lot of clinical studies done on its possible involvement in cognitive problems [60]. Ginkgo biloba treatment enhanced the acquisition, storing, and recall of a two-response food reward sequence in mice. Ginkgo biloba improves cognitive performance without affecting the histopathological implications of overexpression in an Alzheimer's disease animal model of amyloid precursor protein. Ach inhibition alleviated scopolamine-induced passive avoidance deficits, and *ginkgo biloba* extract decreased the acetylcholinesterase activity in the brain significantly. Increased baseline acetylcholine levels are associated with decreased acetylcholinesterase activity.

6.5 *Curcuma longa* (Turmeric)

Curcuma longa, a Zingiberaceae plant prominently known for its anti-inflammatory property, has been linked to a lower risk of Alzheimer's disease. *Curcumin longa* inhibits plaque formation as a result, oxidative stress and amyloid disease develop in the brain. are reduced at significant extant. In Southeast Asian nations, usually people used turmeric regularly thus, it has found that these people have a 4.4-fold decreased risk of Alzheimer's disease [61].

Research was conducted on mice, with modest dosages of Curcumin administered and it was found that, a level of 40% in Alzheimer's disease decreased when animals were kept on a control

medication. Curcumin caused a 43 % reduction in plaque load when administered at a lower dose, in the brains of animals with Alzheimer's illness. Another study was also suggested that the property of anti-inflammatory of turmeric one of the reasons to lower incidence of disease [62].

6.6 *Glycyrrhiza glabra*

This plant, in scopolamine-induced dementia, it has been found to enhance memory. Linalool oxide, geraniol, glycyrrhizin, tannin, trimethyl pyrazine, trimethyl are the content which are responsible for given the Anti- Alzheimer effect. During the study it has also been found that *Glycyrrhiza glabra* improves the memory in mice. While study three dosage of extract were given in the levels of 75, 150, and 300mg/kg, for the seven days, among all doses, the 150mg/kg dose was proved to be the most effective Therefore, appropriate quantity of dose could be beneficial in Alzheimer's disease treatment [63].

6.7 *Lepidium meyenii*

It is a member of the *Brassicaceae* family and is renowned for enhancing memory and learning ability. It was found to improve cognition in Alzheimer's sufferers. It improves memory by raising acetylcholine levels in the brain. Because of its acetylcholinesterase inhibitory and antioxidant properties, it improves memory impairment caused by ovariectomy [64].

6.8 *Magnolia officinalis*

It comes from the *Magnoliaceae* family and helps with scopolamine-induced memory loss. It suppresses the action of acetyl cholinesterase. Magnolol and honokiol, both produced from *Magnolia officinalis*, boost the choline acetyltransferase activity. They also inhibit the uptake of acetylcholine and increase the release of acetylcholine from the hippocampus to nerve cells to counter the Alzheimer's disease. Honokiol also play the role of preventing the formation of reactive oxygen species (ROS) hence, exhibits the anti-inflammatory properties. Therefore, *Magnolia officinalis* exhibiting antioxidant and anti-inflammatory properties are very important in the treatment of Alzheimer's disease [65].

6.9 *Tinospora cordifolia* (Giloy)

Tinospora cordifolia is a member of the *Menispermaceae* family. It has shown to improve memory in both normal and memory-impaired animals. It is a choline supplement which improves cognitive performance by stimulating the immune system and boosting acetylcholine production. *Tinospora cordifolia is a learning and memory booster according to Ayurveda* and aqueous extract plant roots enhanced logical memory and verbal learning [62-63].

6.10 *Convolvulus pluricaulis* (Shankhpushpi)

*Convolvulus pluricaulis*is is the member of is a memory booster that belongs to the *Convolvulaceae family.* According to a research*, Convolvulus pluricaulis* aqueous extract and ethyl acetate improve memory and enhance the learning capacities. The use of this plant is found to maintain the calmness by regulating the level of stress hormone like cortisol and adrenaline in the body. During the studies, it was observed that it enhances the level of learning and memory in rats while giving ethanolic extract to them. *Convolvulus pluricaulis* administration enhanced acetylcholinesterase activity in hippocampal CA_1 and CA_3 areas linked to memory and learning skills [64].

7. CONCLUSION

Due to the various serious side effect of allopathic drugs, ayurvedic medicines drown the attention of patients. The herbal medicines becoming more popular day by day due to more effectiveness and less side effects. Medicinal plants have a wide range of potentially bioactive chemicals which is possible to utilise them in the treatment of Alzheimer's disease. Therefore, there is an alternative for patients to opt the herbal medicines instead of synthetic product in order to treat Alzheimer's disease. The main aim of this article is to discuss the use and scope of many medicinal plants which can be frequently used in Alzheimer's disease treatment. In today's era a big challenge in front of scientist to discover the specific mechanisms of action of herbal plant so that the representation of effectiveness on plant medicines can be placed in a concrete manner. Although, the preliminary studies have been carried out only on small animals but it has to be elaborated and further studies must be conducted in a broad prospective on larger population for establishing the medicinal plants as a source of drugs for the management of Alzheimer's disease.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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