



A COMPREHENSIVE REVIEW OF HERBAL REMEDIES IN THE TREATMENT OF ALZHEIMERS DISEASE

P. Madhavi*, D. Niharika, B. Niharika, Marfat Ali, Saidul Islam

Department of Pharmacology, Pulla Reddy Institute of Pharmacy,
Hyderabad - 502313, India.

*Corresponding author E-mail: madhavi.pharma33@gmail.com

ARTICLE INFO

ABSTRACT

Key words:

Alzheimers disease, dementia, memory loss, neurodegenerative diseases, herbal plants.

Access this article online Website:
<https://www.jgtps.com/>
Quick Response Code:



Alzheimer's disease (AD) is a multifaceted, diverse mental health condition that is characterized by a decline in memory that occurs with age and a dysfunction of several cognitive processes. Because of a significant loss of cholinergic neurons in a particular brain region, it is the most prevalent form of dementia among the elderly population. Many herbs have been used to treat cognitive disorders, including neurodegenerative diseases like Alzheimer's disease, in traditional Ayurvedic and Chinese medical traditions. Many herbs have been demonstrated to enhance brain function and may be useful in the treatment of AD. In this paper, we present a comprehensive analysis of the function of drugs and herbs in the management of Alzheimer's disease.

INTRODUCTION

Alzheimer's disease (AD) is a neurological condition characterized by a decrease in memory and cognition that is irreversible. Currently, the most common type of dementia, AD, is thought to be responsible for three-quarters of cases. Additionally, AD ranks fifth among senior patients 65 years of age and above in terms of cause of death. Neurofibrillary tangles (NFTs) and senile plaques are thought to be the primary pathology indicators of AD. Furthermore, there is mounting evidence that A β peptides are essential to the pathophysiology of AD. As of right now, AD cannot be modified by any therapy. It has been established that cholinergic and glutamatergic pathways play simultaneous roles in the development of AD. Acetylcholine is essential for cognitive function, and those with AD have decreased acetylcholine functions and concentrations [1]. Reactive oxygen species have the potential to play a role in amyloid-mediated neuronal

damage and neurofibrillary pathologies. The brains of AD patients show abnormally high levels of oxidatively modified proteins, lipids, and DNA. This type of free radical-mediated molecular damage is especially noticeable in the context of serine plaques and in neurofibrillary tangle-bearing neurons [2]. Pathophysiological factors might involve genetic mutations, aging, and environmental factors; these can include things like smoking, severe head injury, depression, ischemic and neurological illness, greater parental age, and elevated homocysteine levels [3]. An early diagnosis is essential to assessing a treatment's effectiveness. Memory and cognitive ability testing, informant interviews, and clinical evaluations are all part of the diagnosis process for AD. Tests such as blood and imaging can assist identify the dementia-causing disease and help rule out other possible explanations of the symptoms. The existence of plaques and tangles linked to AD can be found via biomarker testing, such as particular kinds of

PET scans and assays that evaluate the levels of tau and amyloid proteins. These biomarkers offer a more reliable way to diagnose the pathology during life^[4]. In addition to treating neurological conditions, herbal remedies have lately been used to cure and avert Alzheimer's disease. Traditionally, medicinal plants have been used to treat Alzheimer's.

2. HERBAL REMEDIES IN THE THERAPY OF ALZHEIMER'S DISEASE:

2.1. Asian ginseng: The scientific name of Asian ginseng is *Panax ginseng*. It belongs to the family Araliaceae. Ginseng, which has a diverse spectrum of pharmacological effects. The primary family of active ingredients in ginseng is called ginsenosides. Their biological activity and medical significance are distinct, exhibiting anti-tumour, anti-inflammatory, antioxidant, and anti-apoptotic effects. The incidence of disorders affecting the neurological system has increased due to higher stress levels in life. The treatment comprising carefully chosen proportions of ginseng's different constituents is probably going to work better than a straightforward extract of the root^[5]. It has been discovered that *Panax ginseng*'s active ingredients, ginsenosides, may also be useful in the treatment of dementia. Ginseng-derived glycolipoprotein, gintonin has the ability to treat Alzheimer's disease (AD) and other disorders associated with intellectual impairment because it contains G-protein-coupled lysophosphatidic acids^[6].

2.2. Ashwagandha: The scientific name of ashwagandha is *Withania somnifera*, commonly known as winter cherry belonging to the family Solanaceae. The active constituents of ashwagandha include alkaloids (isopelletierine, anafierine, cuseohygrine, anahygrine), steroidal lactones (withanolide-D, withaferin-A) and saponins^[7]. Pharmacological activities of *Withania somnifera* include anti-inflammatory, anti-stress, anti-aging activities and exhibit its effect on central nervous system. Sitoindosides VII– X and Withaferin, which were separated from the aqueous methanol extract of *Withania*

somnifera roots, has shown their actions on GABAergic, glutamatergic, and cholinergic receptors in the brain. The cortical muscarinic acetylcholine receptors can react to medications, it could be the reason why *Withania somnifera* extracts enhance memory and cognition in both humans and animals^[8].

2.3. Indian saffron: The scientific name of Indian saffron is *Crocus sativus*, commonly known as saffron crocus or autumn crocus. It belongs to the family of Iridaceae. The active constituents of saffron include crocin, crocetin, picrocrocin, safranin^[9]. The pharmacological activities of saffron includes anti-oxidant, anti-tumour, anti-diabetic, and also has cognition enhancing effects^[9]. It is believed that *C. sativus* and its components boost cognitive functioning and target AD-related pathways, inhibiting A β fibrillogenesis and promoting A β 42 breakdown and clearance. Herbal medications not only stop oxidative damage brought on by A β aggregation, but also decrease neuroinflammation after microglia activity is modulated^[10].

2.4. Ginkgo: The scientific name of ginkgo is *Ginkgo biloba*, commonly known as white fruit or maidenhair tree. It belongs to the family Ginkgoaceae. The active constituents present in ginkgo are phenolic acids, proanthocyanidins, flavonoid glycosides, such as myricetin, kaempferol, isorhamnetin, and quercetin, and the terpene ginkgolides and bilobalides. The pharmacological activities include anti-oxidant, anti-dementia, anti-cancer, anti-diabetic, anti-microbial^[11]. *G. biloba* has been shown to improve memory and cognitive functions by increasing blood flow in the brain, protecting brain lipids from peroxidation, facilitating oxygen and glucose utilization by brain cells, reducing amyloid plaque deposition (Wan et al., 2016), and lowering A β oligomer and APP levels (Tchantchou et al., 2007; Augustin et al., 2009)^[12].

2.5. Brahmi: The scientific name of Brahmi is *Bacopa monnieri*, commonly known as water hyssop. It belongs to the family of Scrophulariaceae. The active constituents

present in brahmi are alkaloids such as brahmine, herpestine, and nicotine, as well as saponins such d-mannitol and hersaponin, acid A, and monnierin. The other pharmacological activities of Brahmi include anti-oxidant, neuroprotective, anti-inflammatory, anti-convulsant. Bacoside A has an increased antioxidant defence system memory-enhancement action, and could be used as a nootropic. These herbs function by activating numerous pathways to improve memory and learning capacities, which may provide some symptomatic relief to Alzheimer's patients who have dementia in its early stages^[13]. The saponins in Bacopa regulate hypothalamic-pituitary-adrenal (HPA) axis output and preserve the hippocampus. Bacopa has an anti-inflammatory impact in activated microglial cell cultures. Microglial cells respond to injury by changing into a neuroprotective or neurotoxic phenotype, releasing pro-inflammatory cytokines^[14].

2.6.Fenugreek: The scientific name of fenugreek is *Trigonella foenum graecum*, commonly known as methi belonging to the family Fabaceae. The active constituents of fenugreek include trigonelline, diosgenin, 4-Hydroxyisoleucine. The pharmacological activities of fenugreek include anti-inflammatory, anti-diabetic, anti-cancer, analgesic, gastroprotective. Fenugreek provides neuroprotection against amyloid-beta-induced mitochondrial dysfunction and ameliorates cognitive impairments through the Nrf2-mediated antioxidative pathway. To shield the cellular organelle from oxidative stress, it increases the activities of SOD and catalase and scavenges reactive oxygen species^[15]. Supplementing AD patients with fenugreek seed extract has favourable and potentially significant impacts on their BP, memory, quality of life, and levels of selective oxidative markers^[16].

2.7.Sage: The scientific name of sage is *Salvia officinalis*, commonly known as commonly known as sage, garden sage, belonging to the family Lamiaceae. The active constituents of sage include carbohydrates, alkaloids, fatty

acids, glycosidic derivatives, phenolic compounds, poly acetylenes, steroids, terpenoids and waxes. The pharmacological activities include anti-cancer, anti-mutagenic, anti-oxidant, anti-inflammatory, anti-nociceptive, cognitive and memory enhancing effects^[17]. The primary flavonoid in the hydroalcoholic extract of *S. officinalis*, rosmarinic acid, enhances cognition in healthy rats and prevents diabetes-induced impairments in learning and memory. Moreover, the hydroalcoholic extract of *S. officinalis* lowers the memory impairment caused by morphine^[18].

2.8.Liquorice: The scientific name of liquorice is *Glycyrrhiza glabra*, commonly known as mulaithi belonging to the family Fabaceae. The active constituents of liquorice are triterpene, saponin, flavonoids, polysaccharides, pectin's, simple sugars, amino acids^[19]. The pharmacological activities of liquorice include anti-oxidant, anti-inflammatory, anti-carcinogenic, anti-mutagenic, neuroprotective and anti-depressant activity. Anti-oxidant qualities of liquorice extract may have a defensive impact in the body by reducing brain damage and enhancing memory and neuronal function. Memory-enhancing benefits may result from the combination of neuroprotective and anti-inflammatory antioxidant actions^[20].

2.9. Green tea:

The scientific name of green tea is *Camellia sinensis* commonly known as tea plant, belonging to the family Theaceae. The active constituents are flavonoids, catechins, phenolic acids, alkaloids, amino acids and carbohydrates. The pharmacological activities include anti-oxidant, anti-diabetic, anti-cancer and neuroprotective activities^[21].

In the Alzheimer-like rat model, green tea has the highest concentration of epigallocatechin gallate (EGCG) and a higher neuroprotective effect, preventing memory impairments and Elevating levels of reactive oxygen species (ROS) and thio-barbituric acid reactive substances (TBARS) in the hippocampal region^[22].

S. No	Plantname	Family	Phytoconstituents	Pharmacological Activities.
1.	<i>Panax ginseng</i>	Araliaceae	Ginsenosides, steroidal saponins, Protopanaxadiols, Protopanaxatriols.	anti-tumour, anti-inflammatory, antioxidant, and anti-apoptotic effects.
2.	<i>Withania somnifera</i>	Solanaceae	Alkaloids, Steroidal lactones and saponins.	anti-tumour, anti-inflammatory, antioxidant, and anti-apoptotic effects.
3.	<i>Crocus sativus</i>	Iridaceae	Crocin, crocetin, picrocrocine, safranin.	anti-oxidant, anti-tumour, anti-diabetic, and also has cognition enhancing effects.
4.	<i>Ginkgo biloba</i>	Ginkgoaceae	Phenolic acids, proanthocyanidins, flavonoid glycosides.	anti-oxidant, anti-dementia, anti-cancer, anti-diabetic, anti-microbial.
5.	<i>Bacopa monnieri</i>	Scrophulariaceae	Alkaloids, saponins.	anti-oxidant, neuroprotective, anti-inflammatory, anti-convulsant.
6.	<i>Trigonella foenum graecum</i>	Fabaceae	Trigonelline, diosgenin, 4-Hydroxyisoleucine.	anti-inflammatory, anti-diabetic, anti-cancer, analgesic, gastroprotective.
7.	<i>Salvia officinalis</i>	Lamiaceae	Carbohydrates, alkaloids, fatty acids, glycosidic derivatives, phenolic compounds, polyacetylenes, steroids, terpenoids and waxes	anti-cancer, anti-mutagenic, anti-oxidant, anti-inflammatory, anti-nociceptive, cognitive and memory enhancing effects
8.	<i>Glycyrrhiza glabra</i>	Fabaceae	Triterpene, saponin, flavonoids, polysaccharides, pectins, simple sugars, amino acids	anti-oxidant, anti-inflammatory, anti-carcinogenic, anti-mutagenic, neuroprotective and anti-depressant activity
9.	<i>Camellia sinensis</i>	Theaceae	Flavonoids, catechins, phenolic acids, alkaloids, amino acids and carbohydrates	anti-oxidant, anti-diabetic, anti-cancer and neuroprotective
10.	<i>Phyllanthus acidus</i>	Phyllanthaceae	Terpenoids, sterols, tannins, flavonoids, glycosides, alkaloids and phenolic compounds.	antioxidant, hepatoprotective, hypoglycaemic and antimicrobial.

2.10. Amla: The scientific name of amla is *Phyllanthus acidus* commonly known as goose berry belonging to the family Phyllanthaceae. The active constituents of amla are terpenoids, sterols, tannins, flavonoids, glycosides, alkaloids and phenolic compounds.

The pharmacological activities include antioxidant, hepatoprotective, hypoglycaemic and antimicrobial. Given that the plant extract reduces oxidative stress, lipid peroxidation, and AChE activity while raising brain antioxidant enzyme levels and improving cognitive abilities, it is employed in the treatment of Alzheimer's patients^[23].

CONCLUSION:

In conclusion, there indicates positive potential for the use of medicinal plants in the treatment of Alzheimer's disease. Preclinical investigations have shown that a variety of plant materials have neuroprotective and cognitive benefits. However, more thorough investigation is necessary to confirm the safety and efficacy of these plant-based treatments for Alzheimer's patients. Combining conventional knowledge with innovative scientific methods could offer new possibilities in the search for effective treatment remedies for the challenging neurological condition.

REFERENCES:

1. John OO, Amarachi IS, Chinazom AP, Adaeze E, Kale MB, Umare MD, Upaganlawar AB. Phytotherapy: A promising approach for the treatment of Alzheimer's disease. *Pharmacological Research-Modern Chinese Medicine*. 2022 Mar 1;2:100030.
2. Singh AK, Gupta A, Mishra AK, Gupta V, Bansal P, Kumar S. Medicinal plant for curing Alzheimer's disease. *International Journal of Pharmaceutical & Biological Archive*. 2010;1(2):108-14.
3. Ormsby M. Herbs for Alzheimer's disease: A review of neuroprotective properties of *Panax ginseng*.
4. Olloquequi J, Ettcheto M, Cano A, Fortuna A, Bicker J, Sánchez-Lopez E, Paz C, Ureña J, Verdaguer E, Auladell C, Camins A. Licochalcone A: A Potential Multitarget Drug for Alzheimer's Disease Treatment. *International journal of molecular sciences*. 2023 Sep 16;24(18):14177.
5. Razgonova MP, Veselov VV, Zakharenko AM, Golokhvast KS, Nosyrev AE, Cravotto G, Tsatsakis A, Spandidos DA. *Panax ginseng* components and the pathogenesis of Alzheimer's disease. *Molecular Medicine Reports*. 2019 Apr 1;19(4):2975-98.
6. Zhang Z, Liu J, Guo M, Li H. *Panax Ginseng* in the treatment of Alzheimer's disease and vascular dementia. *Journal of Ginseng Research*. 2023 Mar 21.
7. Singh N, Bhalla M, de Jager P, Gilca M. An overview on ashwagandha: a Rasayana (rejuvenator) of Ayurveda. *African journal of traditional, complementary and alternative medicines*. 2011;8(5S).
8. Parihar S. A literature review on pharmacological activities of *Withania somnifera*. *Biological Sciences*. 2022 Mar 7;2(1):147-54.
9. Hosseini A, Razavi BM, Hosseinzadeh H. Pharmacokinetic properties of saffron and its active components. *European Journal of Drug Metabolism and Pharmacokinetics*. 2018 Aug; 43:383-90.
10. Rajabian A, Hosseini A, Hosseini M, Sadeghnia HR. A review of potential efficacy of Saffron (*Crocus sativus* L.) in cognitive dysfunction and seizures. *Preventive Nutrition and Food Science*. 2019 Dec;24(4):363.
11. Biernacka P, Adamska I, Felisiak K. The Potential of *Ginkgo biloba* as a Source of Biologically Active Compounds—A

- Review of the Recent Literature and Patents. *Molecules*. 2023 May 9;28(10):3993.
12. Nowak A, Kojder K, Zielonka-Brzezicka J, Wróbel J, Bosiacki M, Fabiańska M, Wróbel M, Sołek-Pastuszka J, Klimowicz A. The use of Ginkgo biloba L. as a neuroprotective agent in the Alzheimer's disease. *Frontiers in pharmacology*. 2021 Nov 4; 12:775034.
 13. Walker EA, Pellegrini MV. Bacopa Monnieri. InStatPearls [Internet] 2023 Mar 17. StatPearls Publishing.
 14. Sendri N, Bhandari P. Bacopa monnieri. InHerbs, Spices and their Roles in Nutraceuticals and Functional Foods 2023 Jan 1 (pp. 111-131). Academic Press.
 15. Varshney H, Siddique YH. Pharmacological Attributes of Fenugreek with Special Reference to Alzheimer's Disease. *Current Alzheimer Research*. 2022.
 16. Foroumandi E, Javan R, Moayed L, Fahimi H, Kheirabadi F, Neamatshahi M, Shogofteh F, Zarghi A. The effects of fenugreek seed extract supplementation in patients with Alzheimer's disease: A randomized, double-blind, placebo-controlled trial. *Phytotherapy Research*. 2023 Jan;37(1):285-94.
 17. Ertas A, Yigitkan S, Orhan IE. A focused review on cognitive improvement by the genus *Salvia* L.(Sage)—From ethnopharmacology to clinical evidence. *Pharmaceuticals*. 2023 Jan 23;16(2):171.
 18. Ghorbani A, Esmaeilzadeh M. Pharmacological properties of *Salvia officinalis* and its components. *Journal of traditional and complementary medicine*. 2017 Oct 1;7(4):433-40.
 19. Sharma V, Katiyar A, Agrawal RC. *Glycyrrhiza glabra*: chemistry and pharmacological activity. *Sweeteners*. 2018:87.
 20. Pastorino G, Cornara L, Soares S, Rodrigues F, Oliveira MB. Liquorice (*Glycyrrhiza glabra*): A phytochemical and pharmacological review. *Phytotherapy research*. 2018 Dec;32(12):2323-39.
 21. Zhao T, Li C, Wang S, Song X. Green tea (*Camellia sinensis*): A review of its phytochemistry, pharmacology, and toxicology. *Molecules*. 2022 Jun 18;27(12):3909.
 22. Schimidt HL, Garcia A, Martins A, Mello-Carpes PB, Carpes FP. Green tea supplementation produces better neuroprotective effects than red and black tea in Alzheimer-like rat model. *Food Research International*. 2017 Oct 1;100:442-8.
 23. John OO, Amarachi IS, Chinazom AP, Adaeze E, Kale MB, Umare MD, Upanlawar AB. Phytotherapy: A promising approach for the treatment of Alzheimer's disease. *Pharmacological Research-Modern Chinese Medicine*. 2022 Mar 1;2:100030.