Exploring the Pharmacological Potential of Herbal Drugs for Managing Alzheimer's Disease: A Review

Jatin Kumar[1], Ankita Lakhanpal[1], Pooja Mathur[1], Ritu[1*]

[1] Department of Pharmacy, School of Medical and Allied Sciences, G.D. Goenka University, Gurugram-122103, India

e-mail ritumalik1989@gmail.com

Abstract

This review explores the pharmacological and therapeutic potential of herbal drugs in the context of managing Alzheimer's disease. Here, diverse array of herbal compounds, their neuroprotective properties, and their impact on key pathways implicated in Alzheimer's pathogenesis are described. Emphasizing the significance of natural products, this review highlights their potential as alternative or adjunctive therapies for Alzheimer's, addressing both symptomatic relief and disease-modifying effects. The exploration of herbal drugs as a promising avenue in Alzheimer's management underscores the need for further research to elucidate mechanisms, optimize formulations, and establish clinical efficacy, ultimately contributing to the development of novel and holistic approaches to address this debilitating neurodegenerative condition.

Keywords: Alzheimer's, herbal drugs, disease, natural products.

1. Introduction

Memory refers to the process of encoding, accumulating, and recalling knowledge and previous experiences. Dementia and Alzheimer's disease (AD) both result in memory loss; together these form the leading form of dementia worldwide with 60% to 80% of cases worldwide[1]. Alzheimer's (AD) Disease is an advanced neurodegenerative condition with both neuropathological and neurochemical symptoms; its exact cause remains unknown[3]. Dementia AD that emerges prior to 65 is typically marked by both rapid deterioration with clear multiple higher cortical function impairments and slower decline[9]. Memory development becomes impaired after this age threshold has passed[2].

- Aging Genetic history
- Down Syndrome
- Head injury
- Head trauma
- Mild Cognitive Impairment.

Alzheimer's (AD) should be distinguished from other types of dementia such as vascular dementia, Parkinson's with dementia, reversible and frontotemporal degeneration or dementia with Lewy bodies[4]. Recent approaches for Alzheimer's disease therapy revolve around targeting its biochemical causes[9]. Current medications available include those which improve cholinergic function and inhibit free radical production; anti-inflammatory compounds; oestrogens; as well as natural remedies and supplements[6]. Fig 1 indicates the pathophysiological mechanism responsible for AD.

2. Herbal drug as a new generation for treating alzheimer disease (AD)

Over 35,000 industrial species are utilized worldwide for medical uses, with 4,200 flavonoid structures (polyphenolic), terpenes, and phytochemicals comparable to alkaloids being utilized as medicine[11]. These medicines offer many health benefits for antipsychotics, antifatigue anxiolytics narcotics antioxidants antidepressants antineoplastics diabetic arthritis antifatigue antilipo genic products which may provide some level of support[10].

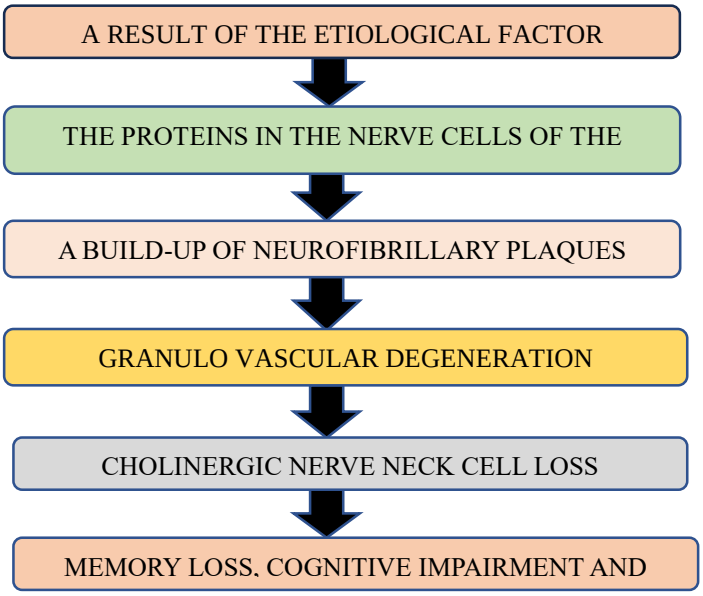

Fig 1 Pathophysiology of Alzheimer Disease (AD)

They may help manage symptoms caused by inflammation oxidation infection which results from late-stage complaints which involve changes within cells due to inflammation oxidation cellular changes which results from inflammation oxidation infection of cells which need medication alongside their general antipsychotic and antioxidant/antidepressant usage[12].

Unfortunately, herbal medications still pose certain challenges, including large variances between batches due to variations in factory-grown terrain that alter bioactivity significantly and as such pharmaceutical corporations have had no choice but to employ synthetic composites in medical curatives instead of herbal medications that offer significant health advantages but exhibit adverse side-effects when used against complex disorders like cancer, osteoporosis or announcement [13]. Although herbal medications offer several health advantages - like providing protection from environmental toxins - pharmaceutical corporations inevitably use single motes of synthetic composites instead[14].

While herbal medicines offer major health advantages but pharmaceutical corporations must employ single motes of synthetic composites in medical curatives treatments; because of this constraint pharmaceutical corporations must use single motes of synthetic composites from synthetic composite manufacturers instead whereas pharmaceutical corporations must use single motes of their medicinals when dealing with complex disorders like cancer, osteoporosis or announcement. Although herbal medications offer numerous health advantages they often exhibit either no real advantage but exhibit excessive adverse health side-effects when used when used against complex disorders including cancer, osteoporosis or announcement[15].

People turn to sauces for comfort. People believe flavors to be safer and natural alternatives than medications; complex mixtures may even prove effective against complex diseases - which might explain the exponential rise of herbal products over the last decade in America - now accounting for seven billion in annual demand while pharmaceutical sales, including precursor sales, in 2002 totaled an estimated 30 billion! Almost one out of every three Americans currently take herbal supplementation regularly while one third or less do so when considering female usage or surgery as the driving factors of usage rates differ by gender and elderly status or general ageing populations[15].

Herbal Medicine for Alzheimer's Treatment Options Available to Help Combat its Impact

Recently there has been an upsurge of interest in plants as treatments in Western societies. This enthusiasm can be found both within pharmaceutical firms searching for novel physiologically active compounds as well as consumer self-medication with crude plant extracts. Plants remain one of the primary sources for medicine with Reserpine having originated from Roulphia serpentina while Ashwagandha comes from Withania somnifer containing Withani somnifer as its parent plant species[16].

Secondary metabolites and essential oils with therapeutic value can be found abundantly in medicinal plants, making these natural sources an attractive target for drug discovery and development researchers[17][19]. Table 1 describe the plants used in AD with their possible mechanism of action[18][20].

Table 1 Natural plants with their mechanism of action in AD

S.No	Drug/family	Phytoconstituent	Mechanism of action
1	**Withania somnifer**	The dehydrowithanolide, the withasomniferin, the with asomidienones, as well as somniferous C and A.	Neuronal cell death started by amyloid plaques is blocked.
2	**Ginkgo Biloba**	Terpene tri lactones, ginkgolides A, B, C, J, and bilobalide, polyprenols flavones, proanthocyanidins, alkylphenols	In Alzheimer's, the membranes become less fluid due to cell damage.
3	**Salvia officinalis**	Cineole, cineol, fumaric, chlorogenic, acid thujone tannic, oleic, ursolic, cornsole caffeic,	Inhibition of acetylcholinesterase
4	**Curcuma longa**	Curcumin and polyphenol	This involves inhibition of the articular transcription factor NF-B.
5	**Urtica dioica**	Acetylcholine, histamine, 5-hydroxy tryptamine, protein, fat, fiber	Boosting up the cholinergic system in the brain
6	**Huperzia serrata**	Lycoposerramine-H, serratidine, obscurumine A, 11α-O-acetyllycopodine, huperzine A, huperzine B, huperzinine, lycodine	Acetylcholinesterase (AChE), inhibitory activity
7	**Lepidium meyenii**	Alkaloids, amino acids, arginine, histidine, phenylalanine, threonine, tyrosine	It provides its antioxidant and AChE inhibitory activities 82

NF-κB-Nuclear factor kappa B , AChE- Acetylcholinesterase.

Detailed description of natural plants with their pharmacognostical characteristics and possible mechanism of action

It has been reported that the following natural plants have been extensively used in the management and treatment of AD. These are having good antioxidant and anti acetycholinestrase activity.

Withania somniferous, also called ashwagandha or Indian ginseng and winter cherry for almost three thousand years, is an important plant used in Ayurvedic medicine and other traditional systems[21]. Its roots, known as rasayanas are believed to be beneficial for health, longevity, and a slowing of the aging processes. They also revitalize the body when it is in weakened conditions.

The plant was historically used as a remedy for ulcers, bacterial infections, poisonous venoms and senile degeneration. It is also an adaptogen, antioxidant, aphrodisiac and liver tonic. Clinical studies and animal experiments support the use of WS to treat anxiety, neurological and cognitive diseases, inflammation and hyperlipidaemia as well Parkinson's [22]. Due to its anti-chemo preventive properties, WS may be an effective adjuvant in patients undergoing radiation or chemotherapy. Recent studies have shown that WS can be used to reduce the likelihood of developing tolerance or dependence on certain psychotropic medications when given chronically[22-23].

Phytochemistry

The chemical constituents of WSA are of great interest to researchers. Alkaloids are biologically active chemicals (ashwagandha cuscohygrine anhydride tropine etc.). Withaferin, a withanolides, A-y withasomniferin, A withasomidienone and somniferous, A-C are some of the steroidal substances[25]. Saponins with an extra acyl group are also present (sitoindosides VII and VIII), as well withanolides containing glucose on carbon 27 (sitoindosides IX andX)[25].

Mechanism Of Action

Withania somnifera is regarded as a memory booster and nerve tonic in Indian medicine. It has also shown promising results in preclinical Alzheimer's studies[26][27]. PC-12 cells can be rescued from H2O2 toxicity and Ab(1-42) induced by Withanamides or aqueous extracts of Withania somnifera[31].Withania somnifera extract (L.), has shown to reverse Alzheimer's disease by increasing the flow of Ab out of the brain and into the blood. This is done by activating the liver's low-density-lipoprotein receptor related protein (LRP1)[29-30]. The aqueous Withania somnifera L. extract improved the cognitive and psychomotor abilities of healthy participants[30].

Ginkgo Biloba

Ginkgo Biloba is considered a living fossil and has been a recognized plant in human history for more than 2000 years. Although it is found in China, Japan and Korea in its natural habitat, the origin of this plant can be traced to isolated valleys in Zhejiang Province in east China[32]. G. biloba has no close relatives within the kingdom of plants. It is classified as a separate division. The Ginkgophyta Ginkgo has a dioecious specie, where male and female flowers appear in roughly equal numbers, although monoecious plants are reported in rare cases. The deciduous leaves alternate or are grouped in groups of 3 or 5 on shorter branches. They can be petiolate or fan-shaped or Adiantum-shaped[35].

Description of the plant

Ginkgo Biloba The oldest tree species is Ginkgo Biloba One tree may live up to 1,000 years, and reach a height 120 feet. The tree has short, fan-shaped branches and smelly fruits. It has an interior seed that may be toxic[32]. Ginkgos, which are hardy and tough trees, are often planted in urban areas of the United States. Fall leaves are a brilliant color.

It was once thought that the tree had disappeared from nature, but it is now widely cultivated in eastern China, Korea and Japan.

Part used leaf, seeds, root, bark

Phytochemistry

- Ginkgo Evaluation of Memory Study (GEM), extract of Ginkgo.
- It is standardised to have two main constituents, namely flavonoids (between 22 and 27%) and terpene-lactones (5 to 7%) (bilobalide and ginkgolides). Terpene lactones are unique to G biloba, and consist of ginkgolides or bilobalides[32].
- In preclinical studies, the flavonoids (and ginkgolides) have a wide range of biological activities[33].

Mechanism of Action

The flavonoids are active as antioxidants and appear neuroprotective. Ginkgolide B is a potent antagonist of the platelet-activating factor receptor. Ginkgolides A and J variously inhibit hippocampal neuron dysfunction and neuronal cell death caused by amyloid beta protein-42 (Aβ42). Ginkgolides A and J decrease Aβ42-induced pathological behaviors, enhance neurogenesis in animal models of Alzheimer's disease, nine and inhibit Aβ aggregation, providing a substantial rationale for G Biloba extracts to be used as possible treatments for Alzheimer's [34-37].

Salvia officinalis

Salvia officinalis L. is a Labiatae/Lamiaceae round perennial shrub. Salvia, which has around 900 different species, is the largest genus within this family. The plants of this genus can be found in many parts of the world. S. officinalis is endemic to Middle East and Mediterranean areas. S. officinalis aerial parts have been used in traditional medicine and cooking for a very long time[40]. The flavor and seasoning abilities of this plant have been used in many cuisines. In Asia and Latin America, it has been used to treat a wide range of ailments, including seizures, ulcers and gout. It also helps with inflammation and dizziness.

The Lamiaceae is native to Europe and the surrounding Mediterranean region, Southeast Asia and Central and South America. The Middle East, the Mediterranean and Central America are its native regions. It has spread to other parts of the globe. S. The term "sage", which is often used to describe a wide range of species, both related and not, can be confusing. Officinalis is traditionally used as a conception aid[40].

Botanical Description

Simple opposite leaves with greenish-grey or white hairs at the base and on top. Stems can be upright or procumbent with hairy branches of dark green [45]. Petiolate, long, elongated leaves with serrated edges, rugose surfaces, and basal lobes. Blooms can be 2-4mm in length and are false spikes that have 5-10 violet blue flowers. They bloom between March and July, depending on their environment [41].

Parts used - the flowers, leaves and stem of S. Officinalis can be identified.

Phytochemistry Major phytochemicals found in the flowers, leaves and stems are identified. Alkaloids are among the constituents. Other components include carbohydrates, fatty acid, glycosidic compounds (e.g. flavonoids and tannins), phenolics (e.g. coumarins), steroids, polyacetylenes as well as terpenes/terpenoids[42].The essential oil prepared by aerial parts of S.officinalis contains more than 120 different components. Oils containing borneol and camphor are the main constituents[43-45]. When comparing the levels of phytochemicals present in S. Officinalis's flowers, leaves and stem, the highest concentrations are found in a-pinene and cineole in the stem. In the leaves, the strongest phytochemicals present include bornyl, camphor and camphene. It is important to remember that the composition of S. officinalis, just like any other herb, can change depending on altitude, water availability, and climate [43].

Mechanism of Action

This study assessed the efficacy and safety of Salvia officinalis in patients with mild to moderate Alzheimer's disease over a period of four months. The study showed that S.officinalis was effective

Curcuma longa

Curcuma Longa (also known as Turmeric) is a perennial herb that is part of the Zingiberaceae family. It is widely cultivated in Asia, mainly in India and China. A yellow powder is produced by the rhizome or medical component of this plant. The dried Curcuma longa is used to produce turmeric, which gives curry powder a distinctive yellow colour. It is also known as Indian saffron in Arabic, yellow ginger in Chinese, and Kyoo (or Ukon) in Japanese[54].

Turmeric is used for centuries in Asian cooking for its color and flavor. It's also used by Chinese and Ayurvedic medicine as an anti-inflammatory and for jaundice and other bleeding problems. The Chinese Pharmacopoeia, as well as nations like Japan and Korea recognize its use for many medical purposes. It is used topically and orally in China to treat viral hepatitis and urticaria, as well as joint inflammation, sores throat, and other wounds[48,54].

Turmeric is found in all tropical and subtropical regions of the globe. It is not known where the plant originated, but it's assumed that they came from southeast Asia and most likely India. In India, the plant grows in all corners. Turmeric is grown throughout Africa, including in Burma and Indonesia. Although India produces the largest amount of turmeric, it's also found in Taiwan, Japan. The use of turmeric in Brazil has been increasing, mostly due to its ability to improve food smell and color [52].

Botanical description

Turmeric is not a seed-producing plant. Turmeric's rhizome, which is a thick, fleshy underground stem ringed by the bases of old leaf bases, is a part that has medicinal properties. The rhizomes are boiled, dried, and ground into the bright yellow spice[48].

Part used roots

Phytochemistry

Curcuminoids are the active components of turmeric, which is a mixture of curcumin (diferuloylmethane), monodexmethoxycurcumin, and bisdemethoxycurcumin. Sugars, proteins, and resins are also constituents. Curcumin, which is found in raw turmeric and comprises 0.3-5% of its active component, has been the subject of extensive research[50]. Turmeric is comprised of a group of three curcuminoids curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (tumerone, atlantone, and zingiberone), sugars, proteins, and resins. Curcumin is a lipophilic, or phenolic, compound that's almost impossible to dissolve in water. It is however stable in stomach acid[52,54].

Mechanism of action

Alzheimer's disease is characterized by chronic inflammation of neurons. Many studies have demonstrated the associated inflammation modifications, such as Microgliosis or Astrocytosis. The studies also revealed the presence of proinflammatory compounds that accompany amyloid-b deposition[49]. Chronic use of NSAIDs may have toxic effects on kidneys and GI system. Curcumin has powerful anti-inflammatory properties. Through its anti-inflammatory effects, it may be able to play a part in the treatment of AD.

Curcumin inhibits Ab induced expression of Egr-1, and Egr-1 DNA-binding activities[51,53]. Egr-1 is involved in the expression of cytochemokines in response to amyloid-peptides in monocytes. Curcumin inhibits Egr-1's DNA-binding activities, which reduce inflammation. Curcumin can reduce the chemotaxis that occurs when monocytes are activated by chemokines released from microglia or astrocytes[53].

Urtica dioica

Urtica dioica L. is also known as the stinging-nettle. It belongs to the Urticaceae. The plant is widely distributed throughout temperate and tropical regions of the globe. In the Himalayas, it can be found at altitudes between 2,100 and 3,200 meters. Urtica comes from the word 'uro,' which means to burn. Or 'urere,' meaning to sting. Bichu Butti in Hindi, Punjabi and Unani is its vernacular term[57]. Urtication is a traditional treatment that has been used since ancient times to stimulate circulation, warm joints, and limbs.

Urtica dioica has been the subject of numerous studies around the globe. Understanding molecular mechanisms that cause favourable effects may pave the path for new treatment methods. The active ingredients of Urtica extracts are separated to maximize therapeutic effects[57].

Distribution of Urtica species Urtica dioica L., the most common and largest Urtica species. The nettle grows in humus or light soils. The soil should be light, sandy and fresh. All soils, but especially those with new organic material are supported by it. The nettle grows in masses, not alone. It is always near the movement of insects[57].

Phytochemistry

Urtica dioica is a plant that contains mainly flavonoids and tannins. It also has volatile and fatty compounds, polysaccharides and polysaccharides. Terpenes and isolectins are other chemical components[58-59].

Flavonoids kaempferol isorhamnetin quercetin astragalin rutin

Phenolics Caffeic acid (HTML0), scopoletin, and phenylpropanes.

Carotenes b-carotene, hydroxy-carotene, lutein, epoxide of lutein, and violaxanthin.

Essential oil esters, free alcohols, and ketones identified as 2-methyl-2-hapten-2-one, acetophenone, ethyl ketone, traces of nitrogenous substances, phenols, and aldehydes Fatty AcidsPalmitic stearic linolenic linolenic Other constituents Minerals, such as iron and calcium, and vitamins B, C and K

Mechanism of action

This plant is used to treat Alzheimer's Disease (AD), a neurodegenerative disease that causes memory loss, cognitive decline, and behavioral changes. The main causes are oxidative stress and inflammation cascades. Other mechanisms include senile plaques and neurofibrillary knots[56,60].

U. dioica is a good choice for treating and managing AD, because it has been shown to have high anti-inflammatory and antioxidant activity. Several experimental studies have confirmed the importance and benefits of U. dioica in the treatment of AD. To understand how this herbal remedy is effective, it's important to have a good understanding of OS, and the inflammatory cascade[56,62].

Huperzia Serrata

It is a plant species in the Lycopodiaceae family that is often known as Chinese club moss. This herbaceous perennial plant is endemic to Southeast Asia, specifically China and India. It has a long history of usage in Chinese medicine, where it goes by several names, including Quin Ceng Ta and Jin Bu Huan[66].

It grows well in moist woodland regions and on rocks. Huperzia Serrata is cultivated in many places for its traditional medicinal applications and for the extraction of chemicals such as Huperzine A, which has received interest for its possible cognitive advantages. Huperzia serrata is grown in different places where the climate and environmental circumstances are favourable[66].

Rheumatism, cold, fever, bruises, discomfort, strains, contusion, stasis swelling, bleeding throat, carbuncle swelling, bleeding injuries, snake bites, burns, and inflammation are all treated with Huperzia serrata. It can also be used to increase blood flow and relax muscles[68].

Botanical Distribution

- Huperzia serrata is a small, evergreen plant that typically grows in damp, forested areas and on rocks.
- It has needle-like leaves arranged in whorls along its stem, giving it a distinctive appearance.
- The plant produces spore cones at the tips of its branches, contributing to its classification as a club moss.

Part used whole aerial plant, including stems and leaves

Phytochemistry

Huperzia serrata contains four classes of Lycopodium alkaloids, including lycodine, Lycopodine, fawcettimine, and miscellaneous types.

Lycodine alkaloid HuperzineA, NN-DimethylhuperzineA, 6αHydroxyhuperzineA, 6β-HydroxyhuperzineA, 6βHydeoxyhuperzineA, PhlegmariurineM, HuperzineU, HuperzineC, HuperzineD, Huperzinine, Isofordine, HuperzineB, N-MethylhuperzineB, De-N-methyl-βobscurine[65][67].

Mechanism of Action

Acetylcholinesterase Inhibition

- Huperzine A inhibits acetylcholinesterase, an enzyme in the brain that breaks down acetylcholine.
- Alzheimer's is caused by a lack of acetylcholine and is a condition that occurs when cholinergic neurons degenerate.
- Which occurs due to the degeneration of cholinergic neurons. Huperzine A, by inhibiting AChE, increases the levels of acetylcholine. This could improve cholinergic neurotransmission and cognitive functions[69].

Beta-Amyloid Regulation

The accumulation is the hallmark of Alzheimer's.

Beta-amyloid plaques in the brain. Some studies propose that Huperzine A may influence the metabolism of beta-amyloid and potentially reduce its aggregation [64].

Antioxidant properties

The accumulation is the hallmark of Alzheimer's. Huperzine A has been reported to have antioxidant properties, which could help counteract oxidative damage to neurons[64].

Lepidium meyenii (Maca)

Lepidium meyenii Walp. Maca is an annual or biennial Brassicaceae plant that has a history of being grown in South America's Andes at 3,500-4,001 m. China was the first country to domesticate Maca. The plant is now cultivated in China, specifically Yunnan and Xinjiang. Maca, which is used as food and medicine in Peruvian tradition, has been dubbed "Peruvian Ginseng". Natives from the Central Andes consider Maca's fresh hypocotyl poisonous[69].

Maca tubers are classified into different ecotypes in Peru based on their color. In particular, the active ingredients and pharmacological values of Maca in yellow, black, and red have been well-studied. Findings revealed some variations in the active components and nutritional content of each ecotype [69].

Botanical Distribution

Maca is our latively small plant, usually reaching A height between 8 and 12 inches(20-30 cm). It has a rosette of leaves that form at ground level. The plant produces a central stalk with small, off-white flowers. The leaves of the Maca are basal and form a rosette. They are green and slightly lobed, resembling those of radishes[69-70].

Maca hypocotyl contains a variety of nutrients, including amino acids. Vitamins, carbohydrates and other trace elements are essential, but so too is lipids. Active components, such as alkaloids and glucosinolates. Polysaccharides, polyphenols, sterols [70]. Maca has antioxidant, antifatigue, and neuroprotective properties. Treatment of Diabetes, Prostatic Hyperplasia and Menopausal Symptoms osteoporosis[70].

Phytochemistry

Alkaloids, polysaccharides and isothiocyanates are among the rich constituents. The Maca plant contains polyphenols and sterols. Maca's hypocotyl contains secondary antioxidants[71]. Maca contains metabolites like flavonoids, natural phenols and other phenols. Maca has various biological Antioxidants, cancer-fighting, fatigue-fighting, and neuroprotective activities are all examples of this. Anti-osteoporosis treatment, menopausal symptoms relief, and improved sexual performance Function and fertility[71].

Mechanism of Action

Macas are available in different colors. The color of maca’s can be different. Yellow, red and black maca’s have been described as having biological effects. Progressive Memory deficits are caused by central cholinergic system degeneration and excessive ,oxidative stress, and differentiation/apoptosis imbalance characterize, ovariectomy. The model is used widely to simulate the effects of menopause in women[75]. Women's Memory and Learning. This mimics brain oxidative stress. Functions of monoaminergic and cholinergic systems. The present study examined the effects of ovariectomy[72]. As observed by the Water Morris Maze, impaired memory functions were caused. Step-down avoidance test. Spatial memory is affected by ovariectomy. It is vital to understand that memory deficits can be influenced by the estrous cycle.

Test performance is a measure of the test's effectiveness[73]. Black Maca, when used in the Water Morris Maze was able alleviate effects of ovariectomy. Water Morris's maze is an important thing to remember. Black maca may improve memory and spatial learning Ovariectomy can cause spatial memory and learning deficits. Antioxidants play a crucial role in treating or preventing chronic disease or prevention of chronic disease. The antioxidants reduce the damage that reactive oxygen species can cause to cell components. Polyphenolic compounds found in nature are potent antioxidants [74].

Conclusion

In conclusion, the exploration of the pharmacological and therapeutic potential of herbal drugs for managing Alzheimer's Disease (AD) holds promise as a valuable avenue in the quest for effective treatments. The multifaceted nature of (AD), involving complex mechanism such as oxidative stress, neuroinflammation, and amyloid beta accumulation, requires a comprehensive approach. Herbal drugs, with their diverse bioactive compounds, demonstrate the potential to modulate these pathways and provide neuroprotective effects.

However, it is crucial to acknowledge the need for rigorous scientific research and clinical trials to validate the efficacy, safety, and optimal dosage of herbal drugs in the context of AD management. Standardization of herbal extracts, identification of active compounds, and understanding their mechanism of action are essential steps in advancing their integration into mainstream medical practices.

REFERENCE

1. Castellani, R. J., Rolston, R. K., & Smith, M. A. (2010). Alzheimer disease. Disease-a-month DM, 56(9), 484.
2. Knopman, D. S., Amieva, H., Petersen, R. C., Chetelat, G., Holtzman, D. M., Hyman, B. T., ... & Jones, D. T. (2021). Alzheimer disease. Nature Reviews Disease primers 7(1), 33.
3. Cummings, J. L., & Cole, G. (2002). Alzheimer disease. Jama, 287(18), 2335-2338.S
4. Apostolova, L. G. (2016). Alzheimer disease. Continuum Lifelong Learning in neurology, 22(2 dementia), 419.
5. ariot, P. N., & Federoff, H. J. (2003). Current treatment of Alzheimer disease and future perspectives Alzheimer disease and associated disorders, 17, S105 - S113.
6. Small, G. W., & Greenfield, S. (2015). Current and future treatment options for Alzheimer's disease. The American Journal of Geriatric Psychiatry 23(11), 1101-110
7. Kumar, A., & Singh, A. (2015). Update on Alzheimer's Disease Pathophysiology and Management. The Pharmacological Reports, 67(2) 195-203.
8. Imbimbo, B. P., Lombard, J., & Pomara, N. (2005). Pathophysiology Alzheimer's Disease Neuroimaging Clinics, 15(4), 727-753.
9. Thakur, A. K., Kamboj, P., Goswami, K., & Ahuja, K. J. J. A. P. R. (2018). A review of the pathophysiology and treatment of Alzheimer's Disease. J anal pharm Res. 9(2) 226-35.
10. Santos-Neto, L. L. D., de Vilhena Toledo, M. A., Medeiros-Souza, P., & de Souza, G. A. (2006). The use of herb medicine in Alzheimer's--a systematic overview Evidence-based complementary alternative medicine 3, 441-445.

11. Jadhav, R. P., Kengar, M. D., Narule, O. V., Koli, V. W., & Kumbhar, S. B. (2019). A review on Alzheimer's Disease (AD) and its herbal treatment of Alzheimer's Disease. *Asian Journal of Research in Pharmaceutical Science*, *9*(2), 112-122.
12. Soheili, M., Karimian, M., Hamidi, G., & Salami, M. (2021). Alzheimer's disease treatment The share of herbal medicines. *Iranian journal of basic medical sciences*, *24*(2), 123.
13. Singhal, A. K., Naithani, V., & Bangar, O. P. (2012). Medicinal plants with a potential to treat Alzheimer and associated symptoms. *International Journal of Nutrition, Pharmacology, Neurological Diseases*, *2*(2), 84-91.
14. Akram, M., & Nawaz, A. (2017). Effects of medicinal plants on Alzheimer's disease and memory deficits. *Neural regeneration research*, *12*(4), 660.
15. Rao, R. V., Descamps, O., John, V., & Bredesen, D. E. (2012). Ayurvedic medicinal plants for Alzheimer's disease a review. *Alzheimer's research & therapy*, *4*, 1-9.
16. Anekonda, T. S., & Reddy, P. H. (2005). Can herbs be used to treat Alzheimer's? Brain research reviews 50(2), 361-376.
17. Lee, J., Jin, C., Cho, S. Y., Park, S. U., Jung, W. S., Moon, S. K., ... & Kwon, S. (2020). Herbal medicine for Alzheimer's disease A protocol of a systematic review, meta-analysis and protocol. Medicine, 99(33)
18. Geun Kim, H., & Sook Oh, M. (2012). Herbal medicine for the treatment and prevention of Alzheimer's. Current pharmaceutical design, 18(1), 57-75.
19. Ghai, R., Nagarajan, K., Arora, M., Grover, P., Ali, N., & Kapoor, G. (2020). Current strategies and novel approaches to Alzheimer disease. CNS and Neurological Disorders - Drug Targets, 19(9). 676-690.
20. Soheili, M., Karimian, M., Hamidi, G., & Salami, M. (2021). Alzheimer's Disease Treatment The Share of Herbal Medicines. Iranian Journal of Basic Medical Sciences, 24(2) 123.
21. Gupta, G. L., & Rana, A. C. (2007). Withania somnifera a review. Pharmacognosy Review, 1(1).
22. Gupta, G. L., & Rana, A. C. (2007). PHCOG Magazine. Review of the plant Withania somnifera, also known as Ashwagandha. Pharmacognosy Reviews 1(1) 129-136.
23. Mishra, L. C., Singh, B. B., & Dagenais, S. (2000). Review of the scientific basis for therapeutic use withania somnifera. Alternative medicine review, 5(4), 334-346.
24. M.A. Weiner, J. Weiner. Ashwagandha (India ginseng). In Herbs That Heal. Quantum Books, Mill Valley CA, 70-72 (1994).
25. N.P. Visavadiya, A.V. Narasimhacharya. Withania somnifera Dunal has antioxidant and hypocholesteremic effects in hypercholesteremic rat. Phytomedicine 2006 (In Press)
26. I. Ilayperuma, W.D. Ratnasooriya, T.R. Weerasooriya. Effect of Withania somnifera extract on male rats' sexual behavior. Asian J. Androl. 4(4) 295-298 (2002).
27. Kulkarni, S. K., & Dhir, A. (2008). Withania somnifera an Indian ginseng. Progress in neuro-psychopharmacology and biological psychiatry, 32(5), 1093-1105.
28. Mishra, L. C., Singh, B. B., & Dagenais, S. (2000). Scientific basis for the therapeutic use of Withania somnifera (ashwagandha) a review. Alternative medicine review, *5*(4), 334-346.
29. Singh, G., Sharma, P. K., Dudhe, R., & Singh, S. (2010). Biological activities of Withania somnifera. Ann Biol Res, *1*(3), 56-63.

30. Kuboyama, T., Tohda, C., & Komatsu, K. (2014). Effects of Ashwagandha (roots of Withania somnifera) on neurodegenerative diseases. Biological and Pharmaceutical Bulletin, 37(6), 892-897.
31. Jayaprakasam, B., Padmanabhan, K., & Nair, M. G. (2010). Withanamides in Withania somnifera fruit protect PC-12 cells from β-amyloid responsible for Alzheimer's disease. Phytotherapy Research, 24(6), 859-863.
32. Singh, B., Kaur, P., Singh, R. D., & Ahuja, P. S. (2008). Ginkgo Biloba Biology and Chemistry. Fitoterapia, 79(6), 401-418.
33. More, M. P., Motule, A. S., Dongare, P. N., Patinge, P. A., Jawarkar, R. D., Bakal, R. L., & Manwar, J. V. (2021). Ginkgo biloba Pharmacognosy and phytochemistry. Pharmacology, clinical application, and pharmacology. GSC Biological and Pharmaceutical Sciences 16(2) 229-240.
34. Schneider, L. S. (2008). Ginkgo biloba and Alzheimer disease prevention. JAMA, 300(19), 2306-2308.
35. Diamond, B. J., Shiflett, S. C., Feiwel, N., Matheis, R. J., Noskin, O., Richards, J. A., & Schoenberger, N. E. (2000). Ginkgo biloba extract mechanisms and clinical indications. Archives of physical medicine and rehabilitation, 81(5), 668-678.
36. DeKosky, S. T., Williamson, J. D., Fitzpatrick, A. L., Kronmal, R. A., Ives, D. G., Saxton, J. A., ... & Ginkgo Evaluation of Memory (GEM) Study Investigators. (2008). Ginkgo biloba for prevention of dementia a randomized controlled trial. *Jama*, *300*(19), 2253-2262.
37. Birks, J., & Evans, J. G. (2009). Ginkgo biloba for cognitive impairment and dementia. Cochrane Database of systematic reviews, (1).
38. Mahadevan, S., & Park, Y. (2008). Multifaceted therapeutic benefits of Ginkgo biloba L. chemistry, efficacy, safety, and uses. Journal of food science, 73(1), R14-R19
39. Ude, C., Schubert-Zsilavecz, M., & Wurglics, M. (2013). Ginkgo extracts review of the pharmacokinetics. Clinical pharmacokinetics 52, 727-749.
40. Ghorbani, A., & Esmaeilizadeh, M. (2017). Salvia officinalis, its components and their pharmacological properties. Journal of Traditional and Complementary Medicine, 7(4) 433-444.
41. Miraj, S., & Kiani, S. (2016). A review of the therapeutic effects of Salvia offficinalis L. Der Pharmacia Lettre 8(6) 299-303.
42. Cuvelier, M. E., Berset, C., & Richard, H. (1994). Antioxidant constituents in sage (Salvia officinalis). Journal of Agricultural and food chemistry, 42(3), 665-669.
43. Raal, A., Orav, A., & Arak, E. (2007). Composition of the essential oil of Salvia officinalis L. from various European countries. Natural product research, 21(5), 406-411.
44. Zalyhina, Y. V. (2022). Relevance of research of the pharmacological properties of salvia (Salvia officinalis)(literature review). Medicni Perspektivi, 27(2), 44.
45. Daniela, T. (1993). Salvia officinalis l. I. Botanic characteristics, composition, use and cultivation. Ceskoslovenská farmacie, 42(3), 111-116.
46. Imanshahidi, M., & Hosseinzadeh, H. (2006). The pharmacological effect of Salvia species in the central nervous systems. Phytotherapy An International Journal Devoted To Pharmacological And Toxicological Assessment of Natural Product Derivatives. 20(6). 427-437.

47. Ammon, H. P., & Wahl, M. A. (1991). (1991). Planta medica 57(01), 1-6.
48. Labban, L. (2014). Review of the medicinal and pharmacological properties Turmeric (Curcuma Longa). Int J Pharm Biomed Sci, 5(1), 17-23.
49. Krup, V., Prakash, L. H., & Harini, A. (2013). Review of the pharmacological activities (Curcuma Longa Linn). J Homeop Ayurv Med. 2(133), 2167-1206.
50. Chanda, S., & Ramachandra, T. V. (2019). Review of the Phytochemical and Pharmacological Importance of Turmeric (Curcuma longa). Research & Review A Journal of Pharmacology 9(1), 16-23.
51. Araujo, C. A. C., & Leon, L. L. (2001). Biological activities of Curcuma longa L. Memórias do Instituto Oswaldo Cruz, 96, 723-728.
52. Omosa, L. K., Midiwo, J. O., & Kuete, V. (2017). Curcuma longa. In Medicinal spices and vegetables from Africa (pp. 425-435). Academic press.
53. Hamaguchi, T., Ono, K., & Yamada, M. (2010). Curcumin and Alzheimer's disease. CNS neuroscience & therapeutics, 16(5), 285-297.
54. Rezvanirad, A., Mardani, M., Shirzad, H., Ahmadzadeh, S. M., Asgary, S., Naimi, A., & Mahmoudi, G. H. A. (2016). Curcuma longa A review of therapeutic effects in traditional and modern medical references. J Chem Pharmac Sci, 9(4), 3438-3448.
55. Verma, R. K., Kumari, P., Maurya, R. K., Kumar, V., Verma, R. B., & Singh, R. K. (2018). Review of the medicinal properties of Turmeric (Curcuma Longa L.). Int. J. Chem. Stud, 6(4), 1354-1357.
56. Durgapal, S., Jantwal, A., Upadhyay, J., Rana, M., Kumar, A., Joshi, T., & Rana, A. J. (2021). Urtica diocia. In Naturally Occurring chemicals Against Alzheimer's disease (pp. 389-400). Academic Press.
57. Joshi, B. C., Mukhija, M., & Kalia, A. N. (2014). Pharmacognostical Review of Urtica dioica L. International Journal of Green Pharmacy, 8(4).
58. Asgarpanah, J., & Mohajerani, R. (2012). Phytochemistry and pharmacologic properties of Urtica dioica L. Journal of medicinal plants research, 6(46), 5714-5719.
59. Rahmati, M., Keshvari, M., Mirnasouri, R., & Chehelcheraghi, F. (2021). Exercise and Urtica dioica extract ameliorate hippocampal insulin signaling, oxidative stress, neuroinflammation, and cognitive function in STZ-induced diabetic rats. Biomedicine & Pharmacotherapy, 139, 111577.
60. Dhouibi, R., Affes, H., Salem, M. B., Hammami, S., Sahnoun, Z., Zeghal, K. M., & Ksouda, K. (2020). Screening of Urtica dioica pharmacological benefits and other uses. Progress in Biophysics and Molecular Biology, 150, 67 - 77.
61. Dar, S. A., Ganai, F. A., Yousuf, A. R., Balkhi, M. U. H., Bhat, T. M., & Sharma, P. (2013). Urtica dioica Pharmacological and toxiological evaluation. Pharmaceutical Biology, 51(2) 170-180.
62. Gulcin, I., Kufrevioglu, O. I., Oktay, M., & Buyukokuroglu, M. E. (2004). The antioxidant, antimicrobial and antiulcer activities of Urtica dioica L. Journal of ethnopharmacology 90(2-3) 205-215.
63. Kim Thu, D., Vui, D. T., Ngoc Huyen, N. T., Duyen, D. K., & Thanh Tung, B. (2019). The use of Huperzia species for the treatment of Alzheimer’s disease. Journal of Basic and Clinical Physiology and Pharmacology, 31(3), 20190159.

64. Luo, C., Chen, Z., Zhang, W., Li, X., Xu, Q., & Yang, S. (2011). Chemical constituents of Huperzia serrata. Zhongcaoyao= Chinese Traditional and Herbal Drugs, 42(12), 2407-2409.
65. Kumbhar, S. A., Hangargekar, C. B., & Joshi, A. A. (2020). HUPERZINE A FROM HUPERZIA SERRATA-A SYSTEMATIC REVIEW. Journal of Advanced Scientific Research, 11(03), 22-29.
66. Ferreira, A., Rodrigues, M., Fortuna, A., Falcao, A., & Alves, G. (2016). Huperzine-A from Huperzia Serrata A review of its sources and chemistry. Phytochemistry Reviews, 15, 51-85.
67. Ma, X., Tan, C., Zhu, D., Gang, D. R., & Xiao, P. (2007). Huperzine A from Huperzia species--An ethnopharmacolgical review. Journal of ethnopharmacology 113(1) 15-34.
68. Kim Thu, D., Vui, D. T., Ngoc Huyen, N. T., Duyen, D. K., & Thanh Tung, B. (2019). The use of Huperzia for Alzheimer's treatment. Journal of Basic and Clinical Physiology and Pharmacology 31(3), 2019.0159.
69. León, J. (1964). The" Maca"(Lepidium meyenii), a little-known food Plant of Peru. Economic botany, 18(2), 122-127
70. Chen, R., Wei, J., & Gao, Y. (2021). Review of the study on active components in Lepidium myyenii (Maca) and their pharmacology. Phytotherapy Research 35(12), 6706 - 6719.
71. Dini, A., Migliuolo, G., Rastrelli, L., Saturnino, P., & Schettino, O. (1994). Chemical composition of Lepidium meyenii. Food chemistry, 49(4), 347-349.
72. Pino-Figueroa, A., Vu, H., Kelley, C. J., & Maher, T. J. (2011). Mechanism of Lepidium Meyenii (Maca), an explanation of its neuroprotective properties. American Journal of Neuroprotection and Neuroregeneration 3(1) 87-92.
73. Pino-Figueroa, A., Nguyen, D., & Maher, T. J. (2010). Neuroprotective effects from Lepidium Meyenii (Maca). Annals of the New York Academy of Sciences 1199(1) 77-85.
74. Wang, S., & Zhu, F. (2019). Chemical composition and health effects of maca (Lepidium meyenii). Food chemistry, 288, 422-443.
75. Bahukhandi, A., Joshi, T., & Kumar, A. (2021). Lepidium meyenii. In Naturally Occurring Chemicals Against Alzheimer's disease (pp. 329-335). Academic Press.