Journal of Pharmacognosy and Phytochemistry
Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
https://www.phytojournal.com
JPP 2024; 13(3): 165-178
Received: 05-03-2024
Accepted: 07-04-2024

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An overview of Indian herbs with the potential in the treatment of the Alzheimer's disease

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DOI: https://doi.org/10.22271/phyto.2024.v13.i3c.14955

Abstract
Alzheimer's disease (AD) is a neurodegenerative condition that severely impairs memory and cognitive function. As the illness worsens, it produces verbal and visuospatial difficulties, as well as behavioural issues like rage, sadness, and indifference. The current treatment for Alzheimer's disease has no known cure, symptomatic relief can retard the progression with memory loss and other symptoms. However, natural remedies have a therapeutic effect on several symptoms of this disease, including dementia and Alzheimer's disease. The current review intends to provide an overview of herbs, such as Shankhpushpi, Brahmi, Pumpkin, Ashwagandha, Almond, Kesar, Sage, Amla, Turmeric and many more that have been documented to have CNS activity with respect to AD and could be used to treat symptoms, slow the development of AD.

Keywords: Alzheimer's disease, acetylcholinesterase inhibitors, Indian herbs

Introduction

Alzheimer's Disease

It is a progressive, degenerative disorder mainly affecting brain nerve cells or neurons, particularly in the cerebral cortex, resulting in memory loss, cognitive impairment, and behavioural disorders. It is thought to be a mix of hereditary, environmental, and behavioural variables. Abnormal protein deposits in the brain, such as beta-amyloid plaques and tau tangles, cause nerve cell death and consequent shrinkage of brain tissue [1].

Epidemiology

It is estimated that at least 55 million people worldwide suffer from Alzheimer's disease or other dementias. This figure will roughly double every 20 years, reaching 78 million in 2030 and 139 million in 2050 if no advances are made. In the time it takes to read this line, another person around the world has been diagnosed with dementia. Every three seconds, someone in the world is affected by dementia. One in every three elderly adults dies from Alzheimer's disease or a related dementia [2].

Pathophysiology

Alzheimer's disease (AD) has a complex pathophysiology that includes many neurotransmitter systems and pathophysiologic pathways. The biochemical changes that occurred during Alzheimer's disease are formation of amyloid plaques, neurofibrillary tangles, neuronal cell death, which are well-known and critical components of the disease's pathophysiology [3]. Figure 1shows the metabolic alterations that occur throughout Alzheimer's disease.

Symptoms

The symptoms of Alzheimer's disease typically begin with mild memory problems and gradually progress to more severe cognitive impairments. The disease mainly affects the thinking skills, memory and behavior [4]. Common symptoms of AD are shown in the figure 2.

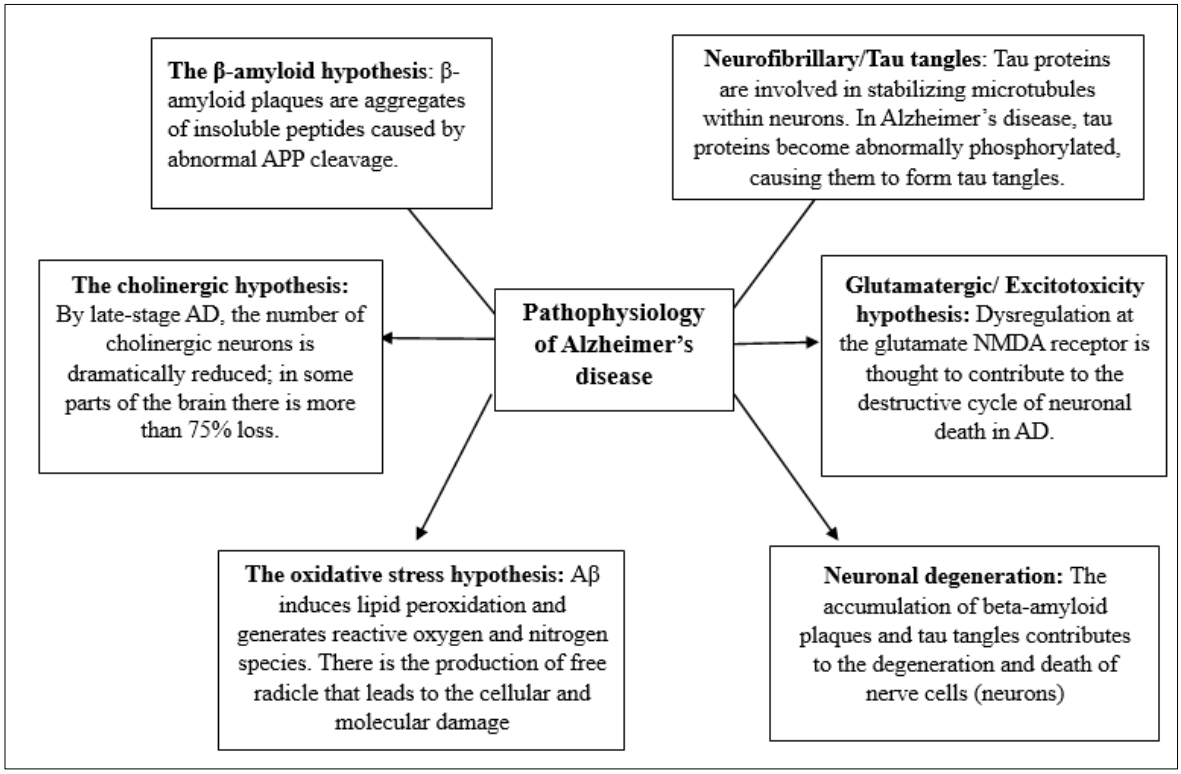

Fig 1: Pathophysiology of the Alzheimer's Disease

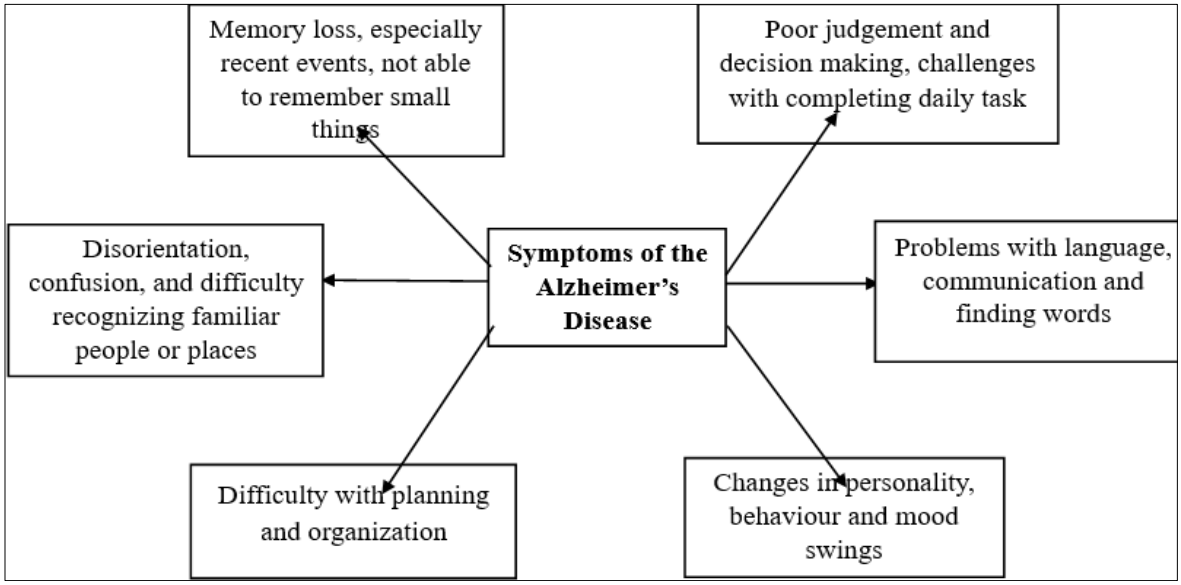

Fig 2: Symptoms of Alzheimer's Disease

Risk Factors

Alzheimer's disease is a complex condition with numerous risk factors that can be broadly classified as modifiable and non-modifiable. Understanding these risk factors can help people make lifestyle decisions that lower their risk or aid in early detection and management. Here are some of the main risk factors.

Non-modifiable risk factors

1. **Age:** The risk of Alzheimer's disease increases with age. It is most common in individuals over the age of 65, and the risk continues to rise with advancing age [5].
2. **Genetics:** Family history plays a role in Alzheimer's risk. Individuals who have a first-degree relative (parent or sibling) with Alzheimer's may have a higher risk. Specific genetic mutations, such as the APO ε4 gene, amyloid precursor protein (APP) gene, presenilin 1 (PSEN1) gene, and presenilin 2 (PSEN2) gene, are associated with an increased risk of developing the disease [5].
3. **Gender:** Alzheimer's disease is more common in women than men. This difference may be due to hormonal changes associated with menopause [5].
4. **Down syndrome:** Individuals with Down Syndrome are at a higher risk of developing Alzheimer's disease because Because chromosome 21 contains a gene that makes amyloid protein, one of the essential proteins linked to the alterations in the brain linked to Alzheimer's disease, it is important in understanding the connection between Down syndrome and the disease [5].

Modifiable risk factors

1. **Obesity and smoking:** Studies have revealed that obesity causes the same regions of the brain to shrink as the brain does when an individual has Alzheimer's disease. In addition to being a risk factor in and of itself, smoking raises the chance of developing other risk factors for vascular dementia and Alzheimer's disease, such as stroke and high blood pressure [6].
2. **Head trauma and depression:** People who have experienced a traumatic brain injury (TBI) who are 50 years of age or older are more likely to develop dementia and Alzheimer's disease, according to several big studies. Those with more severe and multiple TBIs are at significantly higher risk [6].
3. **Cardiovascular health:** Hypertension, which encourages the buildup of amyloid, the pathogenic misfolded protein that characterizes Alzheimer's disease patients' brains [6].
4. **Diabetes:** Insulin resistance is linked to Alzheimer's disease and type 2 diabetes. Elevated blood sugar levels are caused by cells that develop resistance to the actions of insulin in type 2 diabetes. In a similar vein, insulin resistance has been linked to Alzheimer's disease and has been shown to impair brain function as well as contribute to the disease's progression [6].

Treatment of AD

Currently, there is no cure for AD, but various drugs can help to manage symptoms and improve the quality of life for individuals with the condition. Synthetic drugs given in the treatment of Alzheimer's disease are mainly focusing on the inhibition of Acetylcholinesterase enzyme. Table no. 1 enlists the U. S. FDA approved Acetylcholinesterase Inhibitors in the Treatment of Alzheimer's disease [7].

Table 1: Acetylcholinesterase Inhibitors in the Treatment of Alzheimer's disease

Sr. No.	Drug name	Brand name	Mode of action
1.	Donepezil	Aricept	Reversible, non-competitive and acetylcholinesterase inhibitor
2.	Rivastigmine	Exelon	Acetylcholinesterase and butylcholinesterase inhibitor
3.	Galantamine	Razadyne	Reversible, competitive and acetylcholinesterase inhibitor and modulator
4.	Memantine	Namenda	Non-competitive NMDA antagonist

Due to the numerous adverse drug effects of these approved medications such as bradycardia from donepezil, hepatotoxicity from the rivastigmine and hallucinations from memantine, the use of Indian herbal remedies for AD has emerged in recent years.

The Indian medical system, which includes Ayurveda and traditional herbal therapy, has a long history of using natural medicines to improve health and treat various maladies. While there are no known therapies for Alzheimer's disease in Ayurveda or traditional Indian medicine, several herbs are thought to promote brain health and cognitive function. It is crucial to emphasize that the efficacy of these herbs have been investigated. These herbs which are promoting brain health and cognition are reviewed here and their proposed mechanism of action along with their traditional functional features, and bioactive constituents is discussed below:

Indian herbs used to cure Alzheimer's disease

Shankhpushpi (*Convolvulus pleuricaulis*)

Traditional functional feature: Sankhpushpi (*Convolvulus pleuricaulis*) is a member of the Convolvulaceae family. It is called as a brain tonic and is used to promote overall brain health. Shankhpushpi is said to support the nervous system and help reduce mental fatigue and stress. Conventionally, *C. pluricaulis* has been used to treat bacterial infections, viral disorders, epilepsy, liver disorder, and cytotoxicity [8].

MOA of the extract: Deore investigated cognitive property of Shankpushpin by using two hydroalcoholic extract: South shankhpushpi (CPE) and North shankhpushpi (CTE)

1. ***In vitro* evaluation of acetylcholinesterase inhibition by both extracts:** This evaluation was done by Ellmans's colorimetric method. Both hydroalcoholic extracts of North Indian Shankhpushpi and South shankhpushpi inhibited anticholinesterase enzyme to a certain extent. It is observed that, CPE inhibited Anticholinesterase enzyme (52.14±1.19%) significantly than that of CTE (46.14±2.31%) [9].
2. ***In vitro* evaluation of effect of extract on LOX enzyme activity:** salicylic acid was used as standard drug for determining activity. Both hydroalcoholic extract reduced (CPE and CTE) the LOX level *in vitro*.but when compared with each other, CPE reduced the LOX level l (15.20±2.06 4.4 δ234/mg protein/min) with slightly higher rate than that of CTE (11.03±5.10 δ234/mg protein/min) but lesser than that of salicylic acid (42.08±3.12 δ234/mg protein/min) [10].

Bioactive component

Scopoletin and Scopolin: Show the Acetylcholinesterase inhibitory activity. Rollingergenerated structure-based pharmacophore model utilizing an *in silico* filtering experiment to prove the acetylcholinesterase activity [11].

Shankhpushpine: This alkaloid is known as a chemotaxonomic marker for this species.

Convolvulus pleuricaulis also contains convolamine, convoline, beta-sitosterol, kaempferol, phytosterols. Papilionaceae, taraxerol, taraxerone, beta-sitisterol, kaempferol, anthocyanins and flavoniods

Pumpkin (*Cucurbita pepo* L.)

Traditional functional feature: *Cucurbita pepo L.* belongs to the family Cucurbitaceae popularly known as guard family. It is good supplement of carbohydrate, minerals, proteins, and fat coupled with high mineral content. Also it is good source of vitamin A, iron, phosphorus, and calcium. It is emerged as medicinal agent [12].

MOA of extract: Oxidative stress has been identified as a hallmark of several chronic diseases and associated consequences, including diabetes, neurodegenerative disorders, and cancer. Pepo seeds contain a high concentration of Vitamin E (Tocopherol, an antioxidant), and pumpkin seed oil is thought to be a substantial source of vitamin E. Pumpkin extract supplementation significantly raised the serum and liver activity of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH) in mice [13].

Bioactive component

Carotenoids: Alpha carotene, beta carotene, lutein, zeaxanthin, and retinol. They serve as an antioxidant and scavenge reactive oxygen species (ROS). ROS can activate

both death receptor and mitochondria-mediated apoptotic pathways. Carotenoids act as antioxidants, scavenging ROS and preventing ROS-induced apoptosis. Carotenoids activate cell-signalling pathways such as Erk, Akt, and NF- to promote antioxidant defense, anti-inflammation, and anti-apoptosis. Illustration created with BioRender [14].

Other active constituents present are Flavonoids, alkaloids, polyphenols, triterpenoids, phytosterols, fatty acid components (Palmitic, palmitoleic, stearic, oleic, linolenic, gadoleic acid).

Ashwagandha (*Withania somnifera*)

Tradional functional feature: *Withania somnifera***,** a member of the Solanaceae family and sometimes known as Ashwgandha or Indian ginseng, is extensively spread in India, Nepal, China, and Yemen. The planthas positive effects in a variety of neurological illnesses, including stress, Parkinson's disease, Huntington's disease, and Alzheimer's disease [15].

MOA of extract

Regulation of opioid receptors (Mu-opioid (MOP) and nociceptin (NOP)) gene expression in SH-SY5Y cells [16].

Inhibited the caspase independent mechanism of apoptosis by the inhibition of poly (ADP-ribose) polymerase-1 and improve anti-oxidant enzyme hemoxygenase-1(HO-1) [17].

Bioactive components

Withanone: Shows considerable efficacy by inhibiting amyloid β-42. It enhances the activity of acetyl choline, glutathione, and secretase enzymes (β and γ), and reduces pro-inflammatory cytokine levels.

Withanolide-A: It inhibits the human acetyl cholinesterase by high binding affinity, predicted by docking simulation studies.

Withanolides and withanosides: Up-regulation of lipoprotein receptor-related protein in the liver led to neuroprotective effects against $H_2O_2$and β-Amyloid cytotoxicity in APP/PS1 transgenic mice with Alzheimer's disease.

Other constituents present are Glycowithanolides (Sitoindoside IX and sitoindoside X), Stigmasterol, Withaferin A and withanolide (G and B) [18].

Brhami (*Bacopa monnieri*)

Tradional functional feature: *Bacopa monnieri* is a nootropic ayurvedic plant that has been used for centuries to treat neurological diseases. It belonged to the Scrophulariaceae family. Most ancient Indian physicians and Ayurvedic practitioners used herbs to treat dermatitis, anemia, and diabetes. It also serves as a safe heart tonic. It is well recognized for its ability to improve memory and cognitive function. It is frequently used to enhance learning and retention of information. It is thought to accomplish this by supporting the nerve system [19].

MOA of extract

Brhami has been shown to boost the numerous antioxidant molecules, including GSH and SOD. Additionally, it increases oxidative damage caused by H_2O_2. According to research, Brahmi inhibits lipoxygenase activity in mice's brains. It turns out to be a case of free radical scavenging. Brhami decreases neuroinflammation by lowering the quantity of caspase-10 in cells. Caspases are cysteine aspartate proteases and they are mainly involved in inflammatory processes and death. The interleukin converting enzyme caspase-10 is causes proteolytic cleavage of interleukin precursor protein [20].

Bioactive components

Bacoside A: The bioactive component of Brahmi, Bacoside A showed neuroprotective activity against Amyloid-β-induced cytotoxicity in SH-SY5Y cells. They dissolve the matured aggregates of amyloid β.

Betulinic acid: induces the rapid fibrilization of Amyloid-β and reduces the oligomer formation of Amyloid-β [21].

Bacoside A3: This triterpenoid saponin is the promising target for the treatment of Alzheimer's disease by inhibition of the Acetylcholinesterase [22].

Hesperetin: Hesperidin, a bioactive flavonoid, dramatically reduced oxidative stress, apoptosis, and neurodegeneration in mice who had received an i.c.v. injection of Aβ 24 hours earlier. The dose was 50 mg/kg. *In vitro*, hesperetin doses of 10, 20, or 50 μM reduced ROS levels, lipid peroxidation, and increased NRF2/HO-1 expression in Aβ-challenged HT22 and BV-2 cells [23].

Brhami also contains alkaloids brahmin, nicotine, bacosides B, saponins A, B and C, stigmastanol, β-stigasterol, α-alanine, aspartic acid, glutamic acid, and serine and pseudojumbogenin glycosides

Turmeric (*Curcuma longa*)

Traditional functionalfeature: *Curcuma longa* belongs to the Zingiberaceae, or ginger family. The plant is sterile and does not generate seeds. Nowadays, curcumin is utilized to treat cardiovascular disease, arthritis, and Crohn's disease. It is also called as an anti-inflammatory agent [24].

MOA of extract

1. *Curcuma longa* inhibits cyclooxygenases and phospholipase. It also lowers ROS production by activated neutrophils, while inhibiting AP-1 and NF-Kappa B inhibits the activation of the pro-inflammatory cytokines TNF (Tumour necrosis factor)-alpha and IL-1 beta.
2. It serves as an antioxidant by enhancing superoxide dismutase activity, reducing lipid peroxidation and free radical production. And it boosts haemooxygenase.
3. Reduces neuroglial cell proliferation while increasing oligodendrocyte activity by effect on clial cells.
4. Prevents neurotoxicity induced by heavy metals like cadmium and lead. It is claimed that curcumin lowers inflammatory damage by inhibiting metal-induced NF-kappa [25].

Bioactive component

Curcumin prevents the generation and accumulation of Aβ. Administering intragastric curcumin to a mouse model of Alzheimer's disease decreased A production via inhibiting BACE1 expression, which cleaves APP into Aβ. Rats given curcumin showed enhanced spatial learning and memory outcomes and were less prone to synapse degradation [26].

Ginkgo (*Ginkgo biloba*)

Traditional functionalfeature: *Ginkgo biloba*, a member of the Coniferae family, has long been utilized in traditional

medicine. One of its most well-known non-traditional functional characteristics is its ability to support cognitive function and memory. It is used to treat age-related memory loss and cognitive diseases such as dementia and Alzheimer's disease. Ginkgo is known to have vasodilatory properties, which means it can help widen blood vessels and increase blood circulation [27].

MOA of extract

1. Ginkgo provides antioxidant action by scavenging free radicals. The flavonoid part of the extract is hypothesized to have antioxidant properties via directly scavenging ROS, chelating prooxidant transitional metal ions, and boosting antioxidant protein levels such as SOD and GSH.
2. Anti-inflammatory action: The anti-inflammatory properties may be ascribed to the combination of ginkgolide and flavonoid components. It acts as an antagonist to platelet activation factor (PAF).
3. It effectively prevents amyloidogenesis and Aβ aggregation. It protects against Aβ-induced neurotoxicity by reducing ROS accumulation, glucose absorption, mitochondrial dysfunction, activation of the AKT, JNK, and ERK 1/2 pathways, and apoptosis [28].

Bioactive components

Quercetin and Myricetin: Two flavonoid components with this structure are particularly effective at inhibiting the oxidation of tert-butylhydroperoxide. The flavonoid fraction is thought to be primarily responsible for the antioxidant effects of EGb761[29].

Amla (*Emblica officinalis*)

Traditional functional feature: *Emblica officinalis* is described as a maharasayana in several Ayurvedic literature, and it enhances intelligence, memory, illness resistance, longevity, and sensory power. It belonged to the Euphorbiaceae family. This fruit is believed to have powerful antioxidant, analgesic, antipyretic, adaptogenic, immunomodulatory, and antiulcerogenic properties [30].

MOA of extract: The EO (*Emblica officinalis*) extract at 300, 450, and 600 mg kg-1, i.p. substantially and dose-dependently reduced the scopolamine-induced increase in mouse brain AchE levels. At doses of 300, 450, and 600 mg kg-1 of EO extract, cholinesterase activity decreased by 24.34, 35.19, and 53.64 percentage points ($p<0.001$). Emblica officinalis extract has the ability to improve or alleviate spatial long-term memory and short-term memory through mechanisms such as antioxidant, anti-inflammatory, AchE inhibitory, hypolipidemic, and neuroprotective activities [30].

Bioactive component

Pyrogallol: Pyrogallol is a bioactive compound of *Emblica officinalis* that possess both antioxidant as well as prooxidant properties, i.e. the ability to generate reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2) [31].

Pepper (*Piper nigrum*)

Traditional functional feature: *Piper nigrum L.* (Piperaceae) is used in traditional medicine in many countries as a pain reliever, anti-inflammatory, anticonvulsant, antioxidant, antidepressant, and cognitive enhancer. In India, it has long been used to treat malaria and epilepsy in China [32].

MOA of extract: Action on the brain. Cholinesterase levels: Piper nigrum at 20mg/kg body weight had 24.69% lower cholinesterase levels than the AD control group and 11.58% higher cholinesterase than the control group. In contrast, the test group with 200 mg/kg body weight exhibited 25.69% less cholinesterase than the AD control group and 10.29% more than the control.

Action of extract in cognition and memory: In the Morris water maze test, the escape latency time (ELT) was significantly lower in the T 20 group, at 56% less than the AD control, and 22% higher than the control group. T 200 group likewise showed 67% less than AD control, all results are significant at 0.001. On the other hand, all the groups except AD groups spent more time in the fourth quadrant (where the previous platform was kept [33].

Bioactive component

Piperine: Piperine inhibited activation of protein kinase B and glycogen synthase kinase 3β. GSK-3β has been shown to influence cholinergic dysfunction, oxidative stress, and neuroinflammation. Since then, it has been considered a potential biological target for dementia therapy [34].

Neem (*Azadirchta indica*)

Traditional functional feature: *Azadirachta indica*, also known as neem, is a tree endemic to the Indian subcontinent. It belonged to the Meliaceae family. It has long been utilized in Ayurvedic medicine for a variety of health benefits. Azadirachta indica includes a variety of bioactive components, including triterpenoids, flavonoids, and alkaloids, which have demonstrated antioxidant, neuroprotective properties and ant-inflammatory properties in some studies [35].

MOA of extract: *Azadirachta indica* demonstrated anxiolytic efficacy in Colchicine-treated animals in the open field test. It significantly reduced the anxiety generated by IB (ibotenic acid) and Colchicine during the Elevated plus Maze test. A. indica decreased the depression caused by Ibotenic acid and Colchicine, and the effects were comparable to those of impiramine. Morris' water maze test revealed that pre-treatment with *A. indica* enhanced spatial learning, working memory, and reference memory to a level comparable to donepezil. *A. indica* considerably improved deficiencies in active avoidance learning and retention of learnt behavior that were brought on by ibotenic acid and colchicine. *A. indica* substantially decreased the quantity of malondialdehyde after Ibotenic acid and colchicine improved lipid peroxidase activity. *A. indica* stabilized rise in superoxide dismutase and a decreasing trend in acetylcholine-esterase (AChE) activity was seen with Ibotenic acid and Colchicine lesions. *A. indica* had no effect over the AChE activity [36].

Bioactive component: Limonoids, this tetranortriterpenoid class of molecules is having number of biological activity that includes, anti-fungal, anti-bacterial, anti-inflammatory, anticancer, and anti-feedant and it also inhibits Tau mediated toxicity [36].

Tulsi (*Ocimum sanctum*)

Traditional functional feature: It belongs to the labiatae family. It has been shown to possess anti-antioxidant and anti-stress properties. *Ocimum sanctum* has also been suggested to possess anticancer, antimicrobial, antidiabetic,

hepatoprotective, adaptogenic, antiemetic and also as an analgesic [37].

MOA of extract: Raghavendra demonstrated Acetylcholinesterase inhibitory activity by using two types of Alzheimer models -1) colchicine induced Alzheimer disease rat models and 2) Ibotenic acid induced Alzheimer disease induced rat models [38].
Four types of behavioural procedures were performed: 1) Open field test 2) Elevated plus maze test 3) Porsolt's swim test 4) Learned helplessness test 5) Morris' water maze test.
The current investigation indicates the positive benefits of a standardized extract of O. sanctum on IB and Col-induced AD in rats. OS greatly reduced the cognitive loss caused by some neurotoxins in rats. Rats treated with OS had shorter swimming latencies to the goal platform than the placebo groups, indicating superior reference, or spatial memory performance. OS-treated rats also showed increased working memory in probing trials, indicating consolidation of memory.
Effect on Acetylcholinesterase: Anti-cholinesterase activity was assessed on the seventh, fourteenth, and twenty-eighth days after AD was induced with ibotenic acid and colchine. Rat brains were homogenized with a Teflon homogenizer in an M/15 ice-cold phosphate buffer (pH 7.2), and 10 mL of the homogenate was utilized for the subsequent experiment. The color created was measured at 540 nm and represented as mmol of ACh hydrolysed/g of brain tissue [38].

Bioactive component: Eugenol, Reduces the excessive influx of calcium ions into neurons caused by Aβ, preventing neurodegeneration. Moreover, eugenol has antidepressant-like effects. Eugenol, like other antidepressants, stimulates the expression of the brain-derived neurotrophic factor (BDNF) gene in the hippocampus, which is required for antidepressant effect. Furthermore, eugenol inhibits monoamine oxidase A (MAO-A) and may restore monoamines that are reduced in the brain of people with depression [39].

Saffron (*Crocus sativus*)
Traditional Functional Features: *Crocus sativus* L., a stemless herb from the Iridaceae family with blood-activating and menstruation-regulating properties, has been used as a food source since antiquity. It is primarily used to relax nerves, reduce blood toxicity, improve blood circulation, and eliminate blood stasis [40].

MOAs of the Extract: Recent studies have revealed that *Crocus sativus* L. possesses a number of beneficial pharmacological qualities, including anticonvulsant, antidepressant, anti-inflammatory, anticancer, and actions that improve learning and memory [40]. Soeda *et al*., created an experiment to study the neuroprotective processes of *Crocus sativus* L. It was discovered that *Crocus sativus* L. reduced ethanol-induced impairment of learning and memory by significantly reducing the release of cytochrome c from the mitochondria caused by caspase-3 and TNFalpha in PC-12 cells [42].

Bioactive component: Crocinand Crocetin, effectively increased gamma-glutamylcysteinyl synthase mRNA expression in mice, contributing to GSH synthesis and reducing neutral sphingomyelinase activity and ceramide generation. Another study found that these drugs decreased GSK3β and ERK1/2 kinases, as well as greatly reduced total tau and tau phosphorylation, making them potential options for AD prevention and treatment [43].

Gotu kola (*Centella asiatica*)
Traditional functional feature: *Centella asiatica*, popularly known as Indian pennywort, belongs to the Apiaceae family of plants. This herb has been utilized for hundreds of years in both folk and scientific medicine [44]. *Centella asiatica* is useful for treating minor wounds, hypertrophic wounds, burns, and psoriasis. This is also indicated as an antipyretic, diuretic, rheumatic, antibacterial, antiviral medicine, in the treatment of venous insufficiency, and to improve cognition, relieve anxiety, and as an anti-cancer agent [45].

MOA of the extract: The extract inhibited AChE with 50% inhibition rate at 150 μg/mL concentration, according to the spectrophotometric technique (45). The *Centella asiatica* extract inhibited acetylcholinesterase enzyme with an IC50 of 106.55±9.96 μg/mL *Centella asiatica* (Umbelliferae) extract shown CNS depressive action. The mechanism of action includes promoting fibroblast proliferation and increasing the synthesis of collagen and acidic mucopolysaccharides, increasing intracellular fibronectin content and mitotic activity in the germ layer, significantly improving the tensile strength of newly formed skin, and inhibiting the inflammatory phase of hypertrophic scars and keloids [45].

Bioactive component
Triterpene acid: Asiatic, madecassic, termenolic, centic, centellic, centoic, indocentoic, betulic, and madasiatic acids. Pretreatment of SH-SY5Y cells with Asiatic acid (0.1-100 nmol/L) reduced the toxicity caused by 10 mmol/L glutamate in a concentration-dependent manner. Asiatic acid (10 nmol/L) reduced apoptotic cell death and ROS, maintained mitochondrial membrane potential (MMP), and increased production of PGC-1α and Sirt1 [46].
Glycosides- Asiaticoside A and asiaticoside B. Asiaticoside at doses of 5 or 10 mg/kg produced anxiolytic effects in mice 46. Total triterpenes extracted from *C. asiatica* reduced immobility duration, corrected amino acid imbalance in forced swimming mice, and shown antidepressant activity[48].
Flavonoids such glucosylquercetin, 3-glucosylkaempferol, 7-glucosylkaempferol, and the alkaloid hydrocotylin are also presentin*Centella asiatica*.

Sage (*Salvia officinalis*)
Traditional functional feature: Common sage (*Salvia officinalis* L.) is a fragrant and medicinal herb that is well-known for its pharmaceutical capabilities. It belongs to the Lamiaceae family. Sage has been used medicinally in the past, and it may provide health advantages. Some traditional applications of sage include healing sore throats, relieving digestive difficulties, and boosting memory and cognitive function. It can also be used in herbal drinks and as an essential oil. The essential oils of both species showed outstanding bacteriostatic and bactericidal activity against *Bacillus cereus, Bacillus megatherium, Bacillus subtilis, Aeromonas hydrophila, Aeromonas sobria*, and *Klebsiella oxytoca* [49].

MOA of extract: It protects hepatocytes against dimethoxy naphthoquinone- and hydrogen peroxide-induced DNA damage through elevation of glutathione peroxidase activity [49].

Bioactive components: The primary phytochemicals found in *Salvia officinalis* L. flowers, leaves, and stem have been identified. Alkaloids, carbohydrates, fatty acids, glycosidic derivatives (e.g., cardiac glycosides, flavonoid glycosides, saponins), phenolic compounds (e.g., coumarins, flavonoids, tannins), polyacetylenes, steroids, and terpenes/terpenoids (e.g., monoterpenoid6-shogaol, Zingiber's principal bioactive ingredient, has significant neuroprotective effects in LPS-treated astrocytes and animal models of Parkinson's disease, as well as in transient global ischemia and LPS-mediated neuroinflammation. It reduced inflammatory glial cell reactivation in mice with intrahippocampal Aβ injections and improved memory impairments caused by Aβ or scopolamine [49].

Jatamansi (*Nardostachys jatamansi*)

Traditional functional feature: *Nardostachys jatamansi* (Family Valerianaceae), also known as Bhut jata, Nalada, or Spikenard, is a well-known medhya (intellect-promoting) herb having numerous therapeutic effects, particularly those affecting the central nervous system [51]. Jatamansi has long been utilized in the treatment of a wide range of ailments, including digestive, circulatory, neurological, pulmonary, urinary, reproductive, and skin diseases [50].

MOA of extract: *Nardostachys jatamansi* roots have been used in Ayurvedic medicine for their anti-ischemic, antioxidant, anticonvulsant, and neuroprotective properties. The current study sought to determine the potential of *Nardostachys jatamansi* as a memory booster. The raised plus maze and passive avoidance paradigms were used to assess learning and memory parameters. An ethanolic extract of *Nardostachys jatamansi* was administered to both young and old mice in three doses (50, 100, and 200 mg/kg, p.o.) over eight days. The 200 mg/kg dose of *Nardostachys jatamansi* ethanolic extract greatly improved learning and memory in young mice and corrected the amnesia caused by diazepam (1 mg/kg, i.p.) and scopolamine (0.4 mg/kg, i.p.). Furthermore, it corrected age-induced forgetfulness caused by mice's natural aging. Because scopolamine-induced amnesia was reversed, the memory improvement could be due to stimulation of cholinergic transmission in the brain. As a result, *Nardostachys jatamansi*may show to be an effective memory-restorative agent in treating dementia in the elderly [52].

Bioactive component: Jatamansinol, improves locomotor activity and it also improves learning and memory. It boosts antioxidant defense system [51].

Sesquiterpenoids are a group of various natural compounds and are the derivatives of a 15-C precursor called farnesyl pyrophosphate (FPP). This diverse group is considered vital for the identity and protection of plants (Response to allopathic stimulation) and imparts various biological activities such as antimicrobial and anti-inflammatory effects. Moreover, these compounds (Figure 1) can be used to hit pharmacological targets in managing the condition of AD [53].

Chandan (*Santalum album*)

Traditional functional feature: *Santalum album* L. (Santalaceae), sometimes known as Indian Sandalwood, is one of the oldest and most valuable sources of natural smell, with enormous therapeutic and commercial significance [54]. *Santalum album* L. is a semi-parasitic tree from the Santalaceae family. It has a high economic value, which is primarily reflected in its heartwood, which is frequently used as a raw material for carving crafts, as well as incense commonly used in perfume, while sandal essential oil extracted from its heartwood has anti-cancer, antioxidant, anti-inflammatory, and analgesic properties and has been used in the treatment of skin diseases [55].

Mode of action

In human neuroblastoma cells, *Santalum album* modifies the neuroinflammatory response induced by the TLR3 agonist polyinosnic-polycytidylic acid (PolyI: C). *Santalum album* extract modulated the TLR3-mediated immunological response in SH-SY5Y cells. The CM of *Santalum album* extract significantly increased the mRNA levels of IFN-β, IFN-α, MxA, and OAS-1 while lowering IL-6, CXCL8, CCL2, and IP-10. S. album extract exhibited an indirect influence on IFNs and inflammatory cytokines in SH-SY5Y cells [56].

Bioactive conmponnet

α-santalol and β-santalol: These sesquiterpenoids slow aging by reducing oxidative stress and protein aggregation [57]. These bioactives contribute significantly to biological activity and health-promoting effects in humans. Preclinical and clinical research have demonstrated that these bioactive components have antioxidant, anti-inflammatory, antibacterial, antifungal, antiviral, neuroleptic, antihyperglycemic, antihyperlipidemic, and anticancer properties [58].

Clove (*Syzygium aromaticum*)

Traditional functional feature: *Syzygium (S.) aromaticum*, often known as clove, is a dried flower bud from the Myrtaceae family [59]. Interestingly, they are widely employed for a variety of therapeutic uses and in the perfume industry, with clove being one of the spices that may be used as a preservative [60]. Clove's effectiveness in inhibiting numerous degenerative diseases is linked to the presence of various chemical components in high concentrations that have antioxidant activity [59].

Mode of action: *Syzygium aromaticum* is capable of scavenging ROS and increasing the percentage of anti-oxidant enzymes. It also increased SIRT1 activity and decreased γ-secretase levels. It lowers the oxidative equilibrium in amyloid beta-induced toxicity [61].

Bioactive component: Eugenol: It inhibits the enzymes acetylcholinestrase and butyrylcholinesterase and has several medical benefits in traditional medicine as an antibacterial, antioxidant, analgesic, and neuroprotective [62]. Eugenol prevents neurons from dying due to excessive calcium ion influx caused by Aβ. Moreover, eugenol has antidepressant-like effects. Eugenol, like other antidepressants, stimulates expression of the brain-derived neurotrophic factor (BDNF) gene in the hippocampus, which is required for an antidepressant to be effective [63].

Jyotishmati (*Celastrus paniculatus*)

Traditional functional feature: *Celastrus paniculatus*, often known as Malkangani or Jyotishmati, belongs to the Celastraceae family. Celastrus paniculatus is used in Ayurvedic medicine as a nervine tonic, tranquilizer, and diuretic, as well as to treat rheumatism, gout, leprosy, and asthma [64]. It is an Indian medicinal plant that plays an important role in the Ayurvedic medical system. It has been

used to cure a variety of ailments for millennia. It is considered a blessing for students because of its proven function of memory sharpening [65].

Mode of action: Celastrus paniculatus has high DPPH free radical scavenging activity, inhibits the activity of authentic peroxynitrite (ONOO-), and inhibits the formation of total reactive oxygen species (ROS) [66].

Bioactive component

Pristemerin: Pristimerin decreased the expression and interaction of TNF Receptor-Associated Factor 6 (TRAF6) and Interleukin-1 Receptor-Associated Kinases (IRAK1), which limited TGF-beta activating kinase 1 (TAK1) activation. Pristimerin also dramatically slowed BV-2 microglial migration and reduced neuron-like PC cell death [67].

Giloy (*Tinospora cordifolia*)

Traditional functional feature: *Tinospora cordifolia* (Giloy) is a well-known medicinal plant in the Menispermaceae family, and it is a key source of innovative medications and healthcare products. Giloy's extensive medical properties and therapeutic applications, as well as phytochemical study, highlight its importance as a wonderful medicinal plant. Anti-inflammatory, anti-spasmodic, antioxidant, anti-allergic, and anti-cancer activities have been demonstrated. The plant's primary stem is bitter, stomachic, diuretic, promotes bile output, and treats jaundice [68].

Mode of action: This property, when examined in a rat model of 6-hydroxy dopamine-induced Parkinson's disease, provided protection by increasing dopamine levels and decreasing iron accumulation [69]. Its aqueous ethanolic extract has an antipsychotic effect on rats given amphetamines, lowering hyperactivity and locomotor activity. This mode of action is most likely the result of extract binding to the dopaminergic D2 (DAD2) receptor [70]. It benefits youngsters with behavioural issues and mental deficiencies by enhancing memory and learning [71]. Furthermore, it has been shown to be useful in treating depression [72]. 6- Hydroxy dopamine (6-OHDA) was given intracerebrally to generate Parkinson's disease in a lab animal model, and the ethanolic extract provided significant neuroprotection by increasing dopamine levels and recovering locomotor activity [73].

Bioactive components

Alkaloid (Palmetine, Berberine and Mangoflorine): This alkaloids present in the *Tinospora cordifolia* shows anti-inflammatory, anti-cancer and neuroprotective activity [74].

Garlic (*Allium satium*)

Traditional functional feature: Garlic (*Allium sativum* Linn., Alliaceae) has long been used as both a food ingredient and a herbal remedy. Previous research on garlic focused its antioxidant benefits against atherosclerosis and cancer [75]. Aged garlic extract has high antioxidant activity as well as other bio-activities, providing people with a variety of health benefits. Garlic is a top choice for illness prevention due to its high concentration of organosulfur compounds and antioxidant activity [76].

Mode of action: Previous studies have shown that AGE can reduce neurotoxicity and cognitive impairment caused by Aβ. The ethyl acetate portion of AGE reduces cellular oxidative stress, enhances viability, and decreases death in PC12 cells exposed to Aβ-induced cytotoxicity. Pre-treatment with AGE reduces Aβ-induced learning and memory deficits in mice, as evidenced by the Y-maze and passive avoidance tests [77].

Bioactive component

S-allyl Cysteine (SAC): SAC has excellent antioxidant properties [78]. SAC has been shown to disrupt Aβ fibrils *in vitro*. SAC therapy can inhibit Aβ-induced hippocampal neurodegeneration and neuronal cell death via the caspase-12-dependent pathway. Additionally, SAC can reduce endoplasmic reticulum stress [79].

Almond (*Prunus amygdalus*)

Traditional functional feature: *Prunus amygdalus* (Rosaceae; PA) is a little tree native to the Mediterranean Sea. PA's edible part comprises of almonds or badam nuts, a popular healthy snack.PA nuts offer pharmacological actions such as stress relief, antioxidants, immunostimulants, cholesterol reduction, and laxative properties [80]. PA nuts are known as medhyarasayana, a nootropic medicine, in Ayurvedic texts and mythology [81].

Mode of action: According to Kulkarni *et al*'s study, PA at the above-mentioned doses after 7 and 14 days of administration in the respective groups significantly reversed scopolamine (1 mg/kg i.p.)-induced amnesia, as evidenced by a decrease in transfer latency in the EPM (Elevated Plus Maze) task and step-down latency in the passive avoidance task. *Prunus amygdalus* lowered brain ChE activity in rats. PA also shown amazing cholesterol and triglyceride-lowering properties, as well as a small increase in glucose levels [82].

Bioactive component: Morin Morin enhances learning and memory in the Aβ1-42-induced rat model of Alzheimer's disease by reducing oxidative stress, neuroinflammation, and neuronal death in the hippocampus. This natural flavonoid drug protects AD model rats by decreasing the expression of BDNF, NMDA receptor, and α7 nACh receptors in the hippocampus [83].

Kesar (*Crocus sativus*)

Traditional functional feature: *Crocus sativus*, often known as saffron or Kesar, is utilized in Ayurveda and other traditional remedies for aphrodisiac, antispasmodic, and expectorant properties. Modern pharmacological research has shown that *Crocus sativus* extracts have antinociceptive, anti-inflammatory, anticancer radical scavenger, and neuroprotective properties [84].

Mode of action: *In vivo* investigations demonstrated the effect of *Crocus sativus* extract (50 mg/kg/day, added to mice food) on the BBB tightness and function. This was connected with lower Aβ burden and related pathological alterations in 5XFAD mice used as an AD model. *Crocus sativus* extract enhances Aβ clearance mechanisms, including BBB clearance, enzymatic degradation, and ApoE clearance [85].

Bioactive component

Crocin Reduced malathion-induced neurological changes and cognitive impairment by lowering oxidative stress and inflammation, decreasing TAU protein hyperphosphorylation, and exerting antiapoptotic actions [86].

Shatavari (*Asparagus racemosus*)

Traditional fucntional feature: Shatavari (*Asparagus racemosus*) is a valuable plant from the Asparagaceae family with enormous therapeutic potential. It is a climbing shrub native to India's low forests [87]. It is utilized in ancient and traditional Ayurvedic medicine to treat a number of conditions, including immunological problems, cancer, and female reproductive health [88].

Mode of action: J. Meena *et al*. found that the methanolic extract of *Asparagus racemosus* is a non-selective competitive inhibitor of both cholinesterase and monoamine oxidase enzymes. MAR (Methanolic extract of *Asparagus racemosus*) significantly reduced mitochondrial MAO-A and B levels in a dose-dependent manner. Similar to cholinesterase inhibition, only MAR inhibited enzymes with IC50 levels. MAR demonstrated a 75-fold higher IC50 value for MAO-A activity than the standard drug moclobimide. In compared to moclobimide, MAR exhibited a much lower Imax. The potency of MAR in terms of Ki values was 44 times lower than that of moclobimide. MAR's IC50 value for MAOB inhibition was roughly 245 times greater than that of selegeline. The Imax for MAR was substantially lower than that of selegiline. Potency of MAR to inhibit MAO-B was 87 times lower than that of selegiline [89].

Bioactive component

Shatavarin IV: This bioactive component of Shatavarin IV exhibits neuromodulatory properties via boosting synaptic acetylcholine levels and nACHR (Nicotinic Acetylcholine Receptor) activity [90].

Bringraj (*Eclipta alba*)

Traditional functional feature: *E. alba*, sometimes called Bhringraj, is a tiny, branching perennial herbaceous plant. It belongs to the Asteraceae family. Traditionally, it has been used to treat jaundice, night blindness, headaches, and hair-related disorders. It is also regarded as a rejuvenator. According to the Ayurvedic Pharmacopoeia of India, this herb is considered hepatoprotective [91].

Mode of action: According to Singh *et al*., EA (300 and 600 mg/kg, oral) effectively reduced scopolamine-induced learning and memory losses while also decreasing scopolamine-induced increases in brain AChE activity and oxidative stress levels. It may be concluded that *Eclipta alba* has a considerable protective effect against scopolamine-induced memory losses in mice, which can be linked to its anti-AChE and anti-oxidant properties [92].

Bioactive component

Wedelolactone: This bioactive component of *Eclipta alba* demonstrates good radicle scavenging action. Protection of neuropharmacological functions [93]. It inhibits N-methyl-N-nitrosourea-induced retinal neurodegeneration by suppressing the AIM2/CASP11 pathway [94].

Lemon balm (*Mellisa officinalis*)

Traditional functional feature: *Melissa officinalis*, or lemon balm, belongs to the Lamiaceae family. This plant produces little white flowers in the summer and leaves with a slight lemon aroma. This phytomedicine is used to improve the motivation and behavior of dementia sufferers[95]. This plant is said to have antioxidant, antidepressant, anxiolytic, and anti-inflammatory properties [96]. This herbal medicine's therapeutic properties are attributed to its three primary active constituents: triterpenes, phenolic acids, and flavonoids [97].

Mode of action: Soodi *et al*. demonstated that the ethanol extract of M. officinalis improves learning and memory in the scopolamine model of dementia. They attributed this cognitive-supportive effects to the inhibitory effect on AChE activity [98]. According to research, M. officinalis relieves several symptoms in Alzheimer's patients via altering the serotonergic system as well as ligand-gated and ion channels [99].

Bioactive constituent

Gallic acid: Gallic acid, an important ingredient of *M. officinalis*, has been shown in studies to inhibit matrix metalloproteinase-2 activity, which is associated with Alzheimer's disease. The medicinal herb reduces Aβ-induced neurotoxicity, demonstrating neuroprotective properties [100].

Red sage (*Salvia miltiorrhiza*)

Traditional functional feature: *Salvia miltiorrhiza*, a member of the Lamiaceae family, with spreading stems and widely spaced leaves. It has been widely utilized to treat a variety of disorders [101]. *Salvia miltiorrhiza* is a well-known traditional Chinese herb from the Labiatae family that is used in many parts of the world to cure a variety of ailments due to its great medicinal properties have useful pharmacological activities. Antioxidant, antimicrobial, and antiviral action, as well as anti-cancer, anti-inflammatory, and cardiovascular disease, have all received special study [102].

Mode of action: It protects the PC12 cell line against neurotoxicity caused by H_2O_2, lowers lipid peroxidation, and maintains anti-oxidant enzymes, intracellular Ca2+ levels, and the caspase-3 enzyme in an active condition [105].

Bioactive component

Cryptotanshinone: It reduces Aβ plaque formation and glutamate-induced neuronal damage by targeting the gamma-secretase pathway [103]. Cryptotanshinone has been shown to improve cognitive function and have a strong effect on amnesia [104].

Tanshinone: It has antioxidant action. It can chelate metal ions that promote Aβ plaque development while also inhibiting ROS production [106].

Table 2: List of herbal drugs used in relieving the symptoms in Alzheimer's disease along with their biological source, mechanism of action and bioactive components.

Sr. No	Herbal drug	Biological source and family	Mechanism of action	Bioactive components	References
1.	Shankhpushpi	*Convolvulus pleuricaulis* belongs to Convolvulaceae family.	Show anti-alzheimers activity by acetylcholinesterase and lipoxygenase inhibition by	Scopoletin, Scopolin, Shankhpushpine	[8, 9, 10, 11]
2.	Pumpkin	*Cucurbita pepo* belongs to	By increasing serum and liver activity of	Carotenoids: (Alpha carotene, beta	[12, 13, 14]

		the family Cucurbitaceae	superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH)	carotene, lutein, zeaxanthin, and retinol)	
3.	Ashwagandha	*Withania somnifera* belongs to the Solanaceae family	Regulation of opioid receptors (Mu-opioid (MOP) and nociceptin (NOP)) gene expression in SH-SY5Y cells	Withanone, Withanolide-A, Withanolides, withanosides	[15, 16, 17, 18]
4.	Brhami	*Bacopa monnieri* belongs to the Scrophulariaceae family.	Inhibits lipoxygenase activity.It also decreases neuroinflammation by lowering the quantity of caspase-10	Bacoside A, Betulinic acid, Bacoside A3. Hesperetin	[19, 20, 21, 22, 23]
5.	Turmeric	*Curcuma longa* belongs to the family of Zingiberaceae.	Inhibits cyclooxygenases and phospholipase. serves as an antioxidant by enhancing superoxide dismutase activity.	Curcumin	[24, 25, 26]
6.	Ginkgo	*Ginkgo biloba* belongs to the Coniferae family,	Provides antioxidant action by scavenging free radicals and also effectively prevents amyloidogenesis and Aβ aggregation.	Quercetin and Myricetin	[27, 28, 29]
7.	Amla	*Emblica officinalis* belonged to the Euphorbiaceae family.	Improve or alleviate spatial long-term memory and short-term memory through mechanisms such as antioxidant, anti-inflammatory, AchE inhibitory, hypolipidemic, and neuroprotective activities	Pyrogallol	[30, 31]
8.	Pepper	*Piper nigrum* belongs to the Piperaceae family.	Inhibited activation of protein kinase B and glycogen synthase kinase 3β(GSK-3β)	Piperine	[32, 33, 34]
9.	Neem	*Azadirachta indica* belongs to the Meliaceae family.		Limonoids,	[35, 36]
10.	*Tulsi*	*Ocimum sanctum* belongs to the family labiatae		Eugenol	[37, 38, 39]
11.	Safron	*Crocus satius* belongs to the Iridaceae family	Reduced impairment of learning and memory by significantly reducing the release of cytochrome c from the mitochondria caused by caspase-3 and TNFalpha in PC-12 cells.	Crocin Crocetin	[40, 41, 42, 43]
12.	Gotu kola	*Centella asiatica*belongs to the Apiaceae family	Causes CNS depression by promoting fibroblast proliferation and increasing the synthesis of collagen and acidic mucopolysaccharides, increasing intracellular fibronectin	Triterpene acid-Asiaticoside A and asiaticoside B	[44, 45, 46, 47, 48]
13.	Sage	*Salvia officinalis* belongs to the Lamiaceae family.	protects hepatocytes against dimethoxy naphthoquinone- and hydrogen peroxide-induced DNA damage through elevation of glutathione peroxidase activity.	cardiac glycosides, flavonoid glycosides, saponins), phenolic compounds (e.g., coumarins, flavonoids, tannins),	[49]
14.	Jatamansi	*Nardostachys jatamansi* belongs to the family Valerianaceae	An effective memory-restorative agent in treating dementia by causing stimulation of cholinergic transmission	Jatamansinol, Sesquiterpenoids	[50, 51, 52, 53]
15.	Chandan	*Santalum album* belongs to the family Santalaceae	Slow aging by reducing oxidative stress and protein aggregation	α-santalol and β-santalol:	[54, 55, 56, 57, 58]
16.	Clove	*Syzygium aromaticum* belongs to the family Myrtaceae	Capable of scavenging ROS and increasing the percentage of anti-oxidant enzymes. It also increased SIRT1 activity and decreased γ-secretase levels. It lowers the oxidative equilibrium in amyloid beta-induced toxicity 61.	Eugenol	[59, 60, 61, 62, 62]
17.	Jyotishmathi	*Celastrus paniculatus* belongs to the Celastraceae family.	radical scavenging activity, inhibits the activity of authentic peroxynitrite (ONOO-), and inhibits the formation of total reactive oxygen species (ROS).	Pristemerin	[64, 65, 66, 67]
18.	Giloy	*Tinospora cordifolia* belongs to the Menispermaceae family,	Lowering hyperactivity and locomotor activity. This mode of action is most likely the result of extract binding to the dopaminergic D2 (DAD2) receptor	Alkaloid(Palmetine, Berberine and Mangoflorine)	[68, 69, 70, 71, 72, 73, 74]
19.	Garlic	*Allium sativum* belongs to the *Alliaceae* family	Inhibit Aβ-induced hippocampal neurodegeneration and neuronal cell death via the caspase-12-dependent pathway.	S-allyl Cysteine(SAC):	[75, 76, 77, 78, 79]
20.	Almond	*Prunus amygdalus* belongs to the family *Rosaceae;*	lowered brain ChE activity in rats. PA also shown amazing cholesterol and triglyceride-lowering properties, as well as a small increase in glucose levels 82.	Morin	[80, 81, 82, 83]
21.	Kesar	*Crocus sativus* belongs to the Iridaceae family	cognitive impairment by lowering oxidative stress and inflammation, decreasing TAU protein hyperphosphorylation, and exerting antiapoptotic actions 86	crocin	[84, 85, 86]
22.	Shatavari	*Asparagus racemosus* belongs to the Asparagaceaefamily	Non-selective competitive inhibitor of both cholinesterase and monoamine oxidase enzymes reduced mitochondrial MAO-A and B levels in a	Shatavarin IV	[87, 88, 89, 90]

			dose-dependent manner.		
23.	Bringraj	*Eclipta alba* belongs to the Asteraceaefamily.	Inhibits N-methyl-N-nitrosourea-induced retinal neurodegeneration by suppressing the AIM2/CASP11 pathway	Wedelolactone	[91, 92, 93, 94]
24.	Lemon	*Mellisa officinalis* belongs to the family Rutaceae	Shows anti-Alzheimer's activity by inhibit matrix metalloproteinase-2	Gallic acid	[95, 96, 97, 98, 99, 100]
25.	Red sage	*Salvia miltiorrhiza*, a member of the Lamiaceae family,	protects the PC12 cell line against neurotoxicity caused by H_2O_2, lowers lipid peroxidation, and maintains anti-oxidant enzymes, intracellular Ca2+ levels	Cryptotanshinone and Tanshinone	[101, 102, 103, 104, 105, 106]

List of abbreviations

1. **AD:** Alzheimer's disease
2. **AchE:** Acetylcholinesterase
3. **ROS:** Reactive Oxygen Species
4. **PSEN:** Presenilin
5. **APP:** Amyloid Precursor Protein
6. **LOX:** Lipoxygenase
7. **SOD:** Superoxide dismutase
8. **CAT:** Catalase
9. **GSH:** Glutathione
10. **ERK:** Extracellular signal-regulated kinase.
11. **AKT:** Protein kinase B
12. **NF-κB:** Nuclear factor kappa-light-chain-enhancer of activated B cells
13. **MOP:** Mu-Opoid
14. **NOP:** Nociceptin
15. **NRF:** Transcription factor
16. **BACE:** Beta-site APP cleaving enzyme
17. **PAF:** Platelet Activation Factor
18. **JNK:** c-Jun N-terminal kinases
19. **Egb:** Ginkgo biloba extract
20. **BDNF:** Brain Derived Neurotrophic Factor
21. **MAO-A:** Monoamine oxidase
22. **TNF:** Tissue Necrosis Factor
23. **PC:** Phosphatidylcholine
24. **GSK:** Glycogen Synthase Kinase
25. **MMP:** Mitochondial Membrane Potential
26. **PGC:** Primordial germ cells
27. **LPS:** Lipopolysaccharides
28. **FPP:** Farnesyl Pyrophosphate
29. **IFN:** Interferon
30. **MxA:** Myxovirus
31. **OAS:** Oligoadenylate synthetase
32. **SIRT:** Sirtuin
33. **IRAK:** Interleukin-1 Receptor Association Kinases
34. **BV:** Biological value
35. **DAD:** Diketopyrrolopyrrole
36. **6-OHDA:** 6-Hydroxy dopamine
37. **AGE:** Advanced glycation endproduct
38. **SAC:** S-allyl Cysteine
39. **EPM:** Elevated Plus Maze
40. **FAD:** Flavin Adenine Dinucleotide

Conclusion

As Alzheimer's disease affects a person's cognitive, emotional, and physical aspects, a multifaceted approach to prevention and treatment is appealing. After doing thorough sceintific research, we conclude that herbal drugs can be preferred more over synthetic drugs because herbal medications are generally considered as more natural and safer than synthetic drugs because they are produced from plants and have been used for ages in traditional health system such as Ayurveda. This article provides a clear understanding of the Indian medicines used to manage the symptoms of Alzheimer's disease.

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