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Review Article

Potential role of medicinal plants against Alzheimer's disease: An update on therapeutic interventions

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Abstract

Alzheimer's disease (AD) is the dominant source of dementia worldwide among numerous neurodegenerative disorders, with no definitive and enduring cure to date despite prolonged research efforts. AD is believed to be caused due to the accumulation of extracellular Aβ plaques and intracellular neurofibrillary tangles consisting of hyper phosphorylated τ-protein in various parts of the human brain, such as the cortex and limbic system. The development of drugs has been significantly benefited by Ayurveda medicinal plants. Presently, there are more than a hundred new medicines already in clinical development. The primary emphasis of the review is on exploring multiple medicinal plants as a means of preventing symptoms associated with Alzheimer's disease. A study of the phytochemical properties in various parts of plants has revealed several significant chemical compounds, including lignans, flavonoids, tannins, polyphenols, triterpenes, sterols, and alkaloids. These agents exhibit a diverse range of pharmacological functions that can aid in the prevention and treatment of various conditions, such as inflammation, amyloid deposits, cholinesterase inhibition, hyperlipidemia, and oxidative stress.

1. Introduction

Alzheimer disease (AD) is a neurodegenerative disorder of the brain which is mostly affecting old age people. The characteristics of the disorder are memory loss, behavior deterioration, thought slowness and performance impairment [1]. The term Alzheimer Disease was discovered by a German neuropathologist and psychiatrist named Alois Alzheimer in 1906 [2]. Approximately five million people with age 65 years or older and 200000 people younger than 65 years are affected by AD [3]. Alzheimer's disease cannot be cured completely, but symptomatic treatment may improve memory and other problems related with dementia.

Traditional medicine is practiced worldwide as memory enhancer since ancient times. Natural therapy including herbs and medicinal plants has been used in the treatment of memory deficits such as dementia, amnesia, as well as Alzheimer's disease for a long time [4]. Inflammation of brain tissues, increase in the level of free radicals and deficiency of acetylcholine are the major factors responsible for the generation of AD.

1.1 Pathophysiology

The pathology in AD is neuronal degeneration and loss of synapses in the hippocampus, cortex, and subcortical structures [5]. This loss results in gross

atrophy of the affected regions, resulting in loss of memory, inability to learn new information, mood swings, executive dysfunction, etc. [6].

The histopathological characteristic features seen in the brain of patients with AD are:

1. Senile plaques contain extracellular aggregates of amyloid-beta (Aβ), a peptide synthesized by breakage of Aβ precursors (genetic locus 21q21–22). Abnormal deposits of Aβ are also seen in blood vessels.
2. Intracellular aggregations of neurofibrillary tangles (NFTs), dense bundles of abnormal fibres in the cytoplasm of neurons which consist of an altered form of the hyper phosphorylated microtubules associated protein (τ) [7].

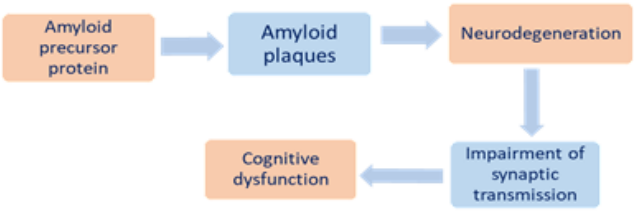

Figure 1. General pathogenesis of Alzheimer's Disease

Aβ plaques develop initially in basal, temporal and orbitofrontal, neocortexregions of the brain and in later stages progress throughout the neocortex, hippocampus, amygdala, diencephalon, and basal ganglia. Aβ is found throughout the mesencephalon, lower brain stem, and cerebellar cortex in critical cases [8].

This concentration of Aβ triggers τ-tangle formation, which is found in the locus coeruleus and transentorhinal and entorhinal areas of the brain. In the critical stage, it spreads to the hippocampus and neocortex**.** For establishing the cause of AD, number of hypotheses is proposed. The cholinergic hypothesis, which is the oldest theory, describes acetylcholine (ACh) deficiency as one of the causative factor for AD. Currently available therapies for AD management are based on this hypothesis. The β-amyloid hypothesis, the most cogent hypothesis provides the basis for the development of new therapeutic strategies for AD treatment [9].

According to (based on) cholinergic hypothesis, acetylcholine deficiency is one of the causative factors for AD [10]. So treatment for AD is done based on this hypothesis**.** Treatment option for AD is mainly targeting the following, cholinergic dysfunction, amyloid β neurotoxicity, oxidative damage and inflammation [11].Various studies showed that non-steroidal anti-inflammatory drugs and antioxidants diminish the development of AD [12]. FDA approved drugs for the treatment and to alleviate the symptoms of AD are donepezil, rivastigmine, galantamine (acetylcholinesterase inhibitors) and memantine (NMDA receptor antagonist).Cholinesterase inhibitors acts by improving cognition in patients with mild to moderate AD while for severe AD cases Memantine is more appropriate [13]. General pathogenesis of Alzheimer's disease presented in Fig 1.

1.2 Herbs/medicinal plants

Traditional medicines have been practiced for treating and curing various diseases and illnesses since ancient times. It is due to the fact that the phytochemicals present in herbs and medicinal plants have significant impact on treating diseases and improves health with the least side effects. The herbs which have been used for the treatment of Alzheimer's disease have the ability to improve brain functions [14]. The exact mechanism of action of medicinal plants against AD is not known, but they exert their protective effects against cognitive impairment through antioxidant and anti-inflammatory activities and specific action on AChE, β-amyloid fibril formation and tau aggregation [15]. The possible mechanism of action of herbal drugs shown in Fig 2.

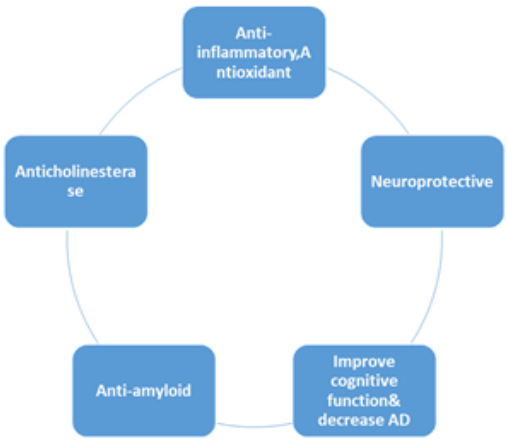

Figure 2. Herbal drugs possible mechanism of action

2. Materials and methods

2.1 Search strategy and selection

The current study was conducted for finding plants that gives anti-Alzheimer's activity. The published studies were searched by using terms like 'anti-Alzheimer's activity of various plants', 'anti-cholinesterase activity', 'evaluation of anti-

Alzheimer's activity', 'neuro-protective herbs', 'Indian medicinal herbs for anti-Alzheimer's activity', 'cholinesterase inhibitory activity', 'medicinal plant with anti-Alzheimer's activity', 'effect of medicinal plants on Alzheimer's disease', and 'anti-Alzheimer's activity of fruit' through Google, Google Scholar, PubMed.

3. Results and discussion

The plants that give anti-Alzheimer's activity were selected and study their phytochemical constituents that give different activity. We have enlisted the selected plants that give anti-Alzheimer's activity below.

3.1 Satureja cuneifolia

3.1.1 General description

*Satureja cuneifolia*is a plant (Fig. 3.) of the *Lamiaceae* family, which is used in Ayurveda and herbal treatment for centuries [16].

3.1.2 Active constituents

The methanolic and water extract of *Satureja cuneifolia* contains both flavonoids and phenolic compounds like rutin, kaempferol-3-Orutinoside and fumaric acid, and the results show that methanolic extract is rich in phenolic compounds, which highlights the anti-oxidant and antiradical property in the plant.

3.1.3 Pharmacological properties

Antioxidant, antidiabetic and anti-Alzheimer's disease activity.

The extracts were analysed by LC-MS/MS method and total phenolic contents were determined. By some enzyme inhibition method as in vitro, it has been found that the methanolic and water extract of *Saturejacuneifolia* enhances the anti-Alzheimer and ant diabetic activity [17]. It has been found that water and methanolic plant extract have the inhibitory property of α-glycosidase and α-amylase enzyme hence shows antidiabetic activity. Also the water and methanolic extract of plant have the inhibitory property on acetylcholinesterase and butyrylcholinesterase enzymes. Also conduct antioxidant potential by DPPH scavenging assay, ABTS scavenging assay, DMPD scavenging assay, FRAP assay, Cu^{2+} reducing assay, Fe^{3+} reducing assay, and LC-MS/MS analysis and instrumentation [18].

3.2 Moringa oleifera

3.2.1 General description

In the family *Moringaceae*, *Moringa oleifera* (Fig. 4.) is the common species amongst the 13 cultivars. It's commonly used in Africa and Asia as a food or food additive, due to its Phytochemical and pharmacological property [19].

3.2.2 Active constituents

The phytochemicals present in the plant are phenolic compounds, carotenoid, polyphenol, flavonoid, saponin, terpene and glycoside compounds [20].

3.2.3 Pharmacological properties

Aqueous, methanol, ethyl acetate and hexane extract of leaf, seed, and root of *Moringa oleifera* shows pancreatic lipase and acetylcholinesterase inhibition properties, as well as it shows antioxidant activity (DMPD+ radical scavenging activity, nitrite scavenging activity and ferric reducing power). Also, it's used to treat asthma, heart disease, anemia, swelling and wounds [82].

The modified method of Ingkaninan et al. was employed for assaying acetylcholinesterase activity and absorbance was taken at 405nm. Aqueous leaf extract (IC50 = 3.26 ± 0.26 mg/ml) and hexane root extract (IC50 = 0.08 ± 0.00 mg/ml) exhibited the highest antilipase and antiacetylcholinesterase activity respectively. The result shows that *Moringa oleifera* shows antilipase, anticholinesterase, and antioxidant properties [21].

Figure 3. *Satureja cuneifolia*

Figure 4. *Moringa oleifera*

3.3 Phyllanthus acidus

3.3.1 General description

Phyllanthus acidus (Fig. 5.), belonging to the family *Euphorbiaceae*, is a tree that has been used in traditional medicine to treat pain, inflammatory, oxidative stress related disorders and is also important to promote intellect and enhance memory.

3.3.2 Active constituents

Phyllanthusacidus contain chemical constituents like phenolic compounds and flavonoids [22].

3.3.3 Pharmacological properties

The in vitro study of methanolic fruit extract of *Phyllanthus acidus* shows it has a considerable amount of antioxidant activity as well as anti-

acetylcholinesterase and anti-butyrylcholinesterase activity, so it shows its effectiveness against Alzheimer's disease and other neurodegenerative disorders [23]. Anti-diabetic activity, burning micturition, enhancing immunity and to treat anemia are the other uses [82].

Antioxidant potential and neuroprotective activities were evaluated by assessing total phenol content (FCR assay), total flavonoid content, total antioxidant capacity, Fe^{3+} reducing power capacity, DPPH (2, 2-diphenyl-1-picrylhydrazyl) and hydroxyl radical scavenging capacity, lipid peroxidation inhibition activity & metal chelating activity, acetylcholinestrase (AChE) and butyrylcholinestrase (BChE) inhibitory activities were performed using Ellman's method [24].

3.4 Clitoria ternatea

3.4.1 General description

Clitoria ternatea (Fig. 6.) belongs to the family *fabaceae*, have been widely used as a brain tonic and is believed to promote memory and intelligence [25]. Hence the present study was conducted to determine the Alzheimer's activity of *Clitoria ternatea*.

3.4.2 Active constituents

The alcoholic extract of *Clitoria ternatea* contains phytochemicals like flavonoids, alkaloids, tannins, phytosterol, phenol and saponins [26].

3.4.3 Pharmacological activities

The test for determining the activity of acetyl cholinesterase was done by Ellmann's method; used for monitoring cholinesterase activity and also Ach hydrolysis by acetyl cholinesterase. From the study, it was found that aqueous extract of *Clitoria ternatea* has a higher activity when compared to neostigmine standard. So the aqueous extract of *Clitoria ternatea* can be used for Alzheimer's disease.

3.5. Crocus sativus

3.5.1 General description

Crocus sativus (Fig. 7.) also called saffron belongs to the family *Iridaceae*, having great properties on memory and cognitive deficiency [27].

Figure 5. *Phyllanthus acidus*

Figure 6. *Clitoria ternatea*

3.5.2 Active constituents

The Phytochemicalconstituents present in the *Crocus sativus* are picrocrocin, kaempferol, safranal, phenol, flavonoids and crocetin. These phytochemicals have the capacity to elucidate anti-Alzheimer's and memory enhancer properties [28].

3.5.3 Pharmacological activities

C.sativus possess Nerve sedative, analgesic, anti-Alzheimer's activity. Also saffron has the ability to cross the blood brain barrier, so it can be considered in therapeutic approaches of other neurological disorders.

From the study, it has been shown that the *Crocus sativus* has the greater effect on Alzheimer's disease and also other neurological effects. The phytochemical constituents and pharmacological property it has a greater value in the treatment of Alzheimer's disease [29].

3.6 Annona squamosa

3.6.1 General description

The plant *Annona squamosa* Linn (Fig. 8.) belongs to the family *Annonaceae*.

Figure 7. *Crocus sativus*

Figure 8. *Annona squamosa*

3.6.2 Active constituents

The secondary metabolites present in the plants were anthocyanidins, flavones, flavonols, and alkaloids [30]. Among phenolic compounds, flavonoids enhance antioxidant properties in plant extracts. Vitamin C is considered a powerful antioxidant which eliminates non-radical reactive species. Carotenoids, found in the pulp and seed of *A. squamosa* shows antioxidant activity by suppression of superoxide O2 which can result in cell damage. Carotenoid consumption provides prevention of degenerative diseases.

3.6.3 Pharmacological activities

Antioxidant, anti-inflammatory, antidiabetic and anti-acetylcholinesterase activity. Fruit is sweet, flavorous, enriches the blood, increases muscular strength, cooling, sedative to heart and relieve vomiting. Root cathartic, drastic purgative. Astringent bark is used as

an antidiarrhoeic cure in Cambodia. Leaves are used as insecticide. The total phenolic, flavonoids and vitamin C content of methanolic extracts of pulp and seed of *Annona squamosal* L was determined by the Folin–Ciocalteu method, aluminium chloride colorimetric method, 2,6-dichlorophenol-indofenol titration method respectively. Evaluation of antioxidants was conducted by using the ABTS, Fe3+ reduction, β-carotene protection, DPPH and 2-DR protection methods. The assay for inhibition of acetylcholinesterase activity was determined using the method described by Ellman [31].

3.7 Glycyrrhiza glabra

3.7.1 General description

Glycyrrhiza glabra a plant (Fig. 9.) of the *Leguminosae* family which is used in Ayurveda and herbal treatment for centuries [32].

3.7.2 Active constituents

The aqueous root extract of *Glycyrrhiz aglabra* contains triterpene, saponins, polysaccharides, flavono-ids, mineral salts, amino acids, pectins, simple sugars and various other substances.

3.7.3 Pharmacological properties

It has antimalarial, expectorant, diuretic, laxative, antispasmodic, anti-inflammatory, antioxidant, anti-ulcer and sedative properties. Glycyrrhizin and its aglycone, glycyrrhetinic acid, enhance anti-inflammatory activity [33].

The aqueous extract of the root of *Glycyrrhiza glabra* was administered orally in 1-month-old male Wistar albino rats for six successive weeks by Four doses (75, 150, 225, and 300 mg/kg). The antioxidant and anti-inflammatory activities of *Glycyrrhiza glabra* exhibit memory enhancement effect. It concluded that the aqueous root extract of *Glycyrrhiza glabra* reveals memory enhancement effects in the management of impaired learning, dementia, Alzheimer's disease, and other neurodegenerative disorders [34].

3.8 Withania somnifera

3.8.1 General description

Ashwagandha, or Withania somnifera, (Fig. 10), is a *Solanaceae* family herb, often called Indian winter cherry or Indian ginseng, and has been used for thousands of years in India to benefit health [35].

3.8.2 Active constituents

Withasomniferin A, withasomidienone, withasomni-ferols A to C,withaferin A, and withanone are among the most interesting steroidal compounds in Ashwagandha. withanamides antagonise neuronal cell death triggered by amyloid plaques. It also contains alkaloids, high amounts of iron and amino acids including tryptophan, also contain lignans, tannins, polyphenols, sterols and flavanoids.

3.8.3 Pharmacological properties

So it has antioxidant activity, free radical scavenging activity, anti-inflammatory, ant-amyloidogenic, anti-cholinesterase and hypolipidemic activities [36]. Also used to anxiety, depression, and fatigue [82].

Aqueous extracts of this herb have been found to increase cognition-enhancing and memory-improving effects. Methanolic extracts of *Withania somnifera* reversed amyloid peptide-induced memory deficit in mice. So*Withania somnifera* is used in the treatment of Alzheimer's disease [37].

Figure 9. *Glycyrrhiza glabra*

Figure 10. *Withania somnifera*

3.9 Celastrus paniculatus

3.9.1 General description

Celastrus paniculatus (Fig. 11.) is a woody liana commonly known as black oil plant. it is found in Maldives, Australia, China, Cambodia, Malaysia, Taiwan, Nepal, Thailand and in the Pacific Islands. *Celastrus paniculatus* is plant belonging to the family *Celastraceae* [38].

3.9.2 Active constituents

The seed of *C. paniculatus* contains sesquiterpene alkaloids, monounsaturated and polyunsaturated fats, sesquiterpene ester triterpenoids, volatile oil, polyalcohol esters, sterols and fatty acids.

3.9.3 Pharmacological properties

The oil obtained from the seed of *Celastrus paniculatus* enhances sedative and anticonvulsant properties.

The methanolic extract of *Celastrus paniculatus* seed exhibited analgesic and anti-inflammatory properties in mice and rats [39]. *Celastrus paniculatus* seed oil enhances memory processes in rats. A methanolic extract of *Celastrus paniculatus* seed oil enhances the free radical scavenging effects. *Invitro* cholinesterase enzyme inhibition assay and scavenging of DPPH, ONOO-, reducing power and

inhibition of total ROS generation assay were used for studying anti-Alzheimer's disease and antioxidant effect of crude methanolic extract various organic soluble fractions of *Celastrus paniculatus* seed. The EtOAc fraction had major (pp0.001) inhibitory effects on cholinesterases [40].

3.10 Ginkgo biloba

3.10.1 General description

Ginkgo biloba (Fig. 12.) is a living fossil that belongs to the family *Ginkgoaceae*, widely cultivated in China and Japan. It's herbal medicine that has been used in China since ancient times. *Ginkgo biloba* extract (GBE) has been widely used to treat Alzheimer's disease.

3.10.2 Active constituents

The various phytochemical constituents present in the extract are ginkgo flavonoids, including quercetin, kaempferol, and isorhamnetin, terpene lactones, consisting of ginkgolides A, B, and C and bilobalide, and ginkgolic acids [41].

Figure 11. *Celastrus paniculatus*

Figure 12. *Ginkgo biloba*

3.10.3 Pharmacological properties

Flavonoids enhance the antioxidant effects. The flavonoids and terpenoids present in the extract of *Ginkgo biloba* are responsible for anti-oxidation, anti-inflammation, and anti-apoptosis; protection against mitochondrial dysfunction, amyloidogenesis, and Aβ aggregation which exhibit anti Alzheimer'seffect [42].

3.11 *Coriandrum sativum*

3.11.1 General description

Coriander (*Coriandrum sativum)* (Fig. 13.) is an aromatic plant of *Umbellifera* or *Apiaceae*. [43]. Green coriander contains high level of water, thiamine, zinc and dietary fibres and fewer amounts of saturated fats, and cholesterol. Seeds are rich in vitamins, lipids and minerals, such as calcium, phosphorus, sodium, zinc, potassium and magnesium. The fresh leaves can be used for garnishing but also used in many foods.

3.11.2 Active constituents

The main components of essential oil are linoleic and linolenic acids. The phenolic compounds provide antioxidant activity for *C. sativum* exhibit hepatoprotectiveactivity [44]. *C. sativum*'s hepatoprotective activity is attributed to its phenolic compounds, which possess antioxidant properties.

3.11.3 Pharmacological properties

The seeds and leaves of the plant have been reported to possess a range of beneficial properties such as antioxidant, diuretic, cholesterol lowering, anxiolytic, sedative-hypnotic and anticonvulsant activities.

The present study evaluated the impact of inhaling volatile oil (at concentrations of 1% and 3% per day) over the course of 21 days, on spatial memory performance in a rat model of Alzheimer's disease induced by Aβ1-40. In comparison to the control group, the results of the step down inhibitory avoidance test indicated that inhalation of linalool at a concentration of 1% improved acquisition memory, reduced aggressive behaviour, increased social interaction and exhibited anxiolytic properties in mice. Moreover, coriander's primary constituent's linalool exhibits diverse neuro-pharmacological effects include anti-anxiety, sedative, anticonvulsant, and anti-Alzheimer's disease activities [45].

3.12 Bacopa monnieri

3.12.1 General description

Bacopa monnieri (Fig. 14.), also known as Brahmi, is an herb from the *Scorophulariacae* plant family that has been mentioned in the Indian traditional medicine (ayurveda) literature for it's medicinal properties in treating anxiety, intellect and memory disorders [46].

Figure 13. *Coriandrum sativum*

Figure 14. *Bacopa monnieri*

3.12.2 Active constituents

It contains alkaloids, glycosides, sapogenin, saponins and flavonoids.

3.12.3 Pharmacological properties

Antioxidant, free radical scavenging, anti-Alzheimer's activity. Also used to control mental stress, anxiety, lower blood pressure, and anti-epilepsy activity [82].

Research has demonstrated that EBm promotes mechanisms for scavenging free radicals and safeguards cells in the pre-frontal cortex,

hippocampus and striatum against cytotoxicity and DNA damage associated with Alzheimer's disease. Several animals and in vitro studies have revealed that EBm exhibits antioxidant and free radical scavenging properties [47].

3.13 Peruvian maca

3.13.1 General description

Peruvian maca (lepidiummeyenii) (Fig. 15.) belongs to the family *Brassicaceae* is a root native to the Andean region known for its high fibre and nutrient content including vitamin C, copper, and iron [48]. Additionally, this fruit contains bioactive compounds that provide numerous benefits to individuals seeking a healthy diet.

3.13.2 Active constituents

Maca root is abundant in essential amino acids, fatty acids and minerals especially iron, calcium and copper.

3.13.3 Pharmacological properties

Anti-oxidant, anti-cancer, anti-inflammatory and antidepressant.

Maca has been shown to provide a wide range of health benefits, including but not limited to regulation of sexual dysfunction, neuroprotection, memory enhancement, anti-depressant effect, antioxidant properties, anti- cancer properties, anti-inflammatory properties and skin protection. Maca extract contains Macamides which are considered to be the active compounds responsible for nuro-protective effect by inhibiting FAAH [49, 50].

Figure 15. *Peruvian maca*

Figure 16. *Phyllanthus emblica*

3.14. Phyllanthus emblica

3.14.1 General description

Phyllanthus emblica Linn (Fig. 16.) or *Emblica officinalis* Gaertn, commonly referred to as amla or Indian gooseberry, [51] is considered the most significant medicinal plant in the Ayurvedic traditional system of medicine. The Indian gooseberry belongs to the family *Phyllanthaceae*.

3.14.2 Active constituents

Compounds such as tannoids, tannins, vitamin C, and flavonoids.

3.14.3 Pharmacological properties

Amla has been reported to exhibit various activities such as radiomodulatory, chemomodulatory, chemopreventive, free radical scavenging, antioxidant, anti-inflammatory, antimutagenic, and immune modulatory effects [52]. The fruit of this plant is known to exhibit strong antioxidant properties.

Amnesia was induced by administering Scopolamine (1 mg kg-1, IP), and the memory was assessed through the elevated plus-maze and passive avoidance tests. Piracetam (200 mg kg-1, IP) was used as a reference nootropic agent. The findings of the study revealed that the EO extract was effective in reversing the amnesia induced by scopolamine, indicating its potential as a memory enhancer with anti-oxidant and anti-cholinesterase activity. The study suggests that EO extract could be useful in the treatment of cognitive impairments induced by cholinergic dysfunction [53].

3.15. Acorus calamus

3.15.1 General description

Acorus calamus Linn (Acoraceae) (Fig. 17.), commonly known as Vacha, is a herb used in traditional Indian medicine to treat a variety of health conditions. *Acorus calamus* L. is a perennial monocot plant from [54] the *Acoraceae* family, and its rhizomes have been extensively used in traditional medicine to treat various ailments, including mental ailments, chronic diarrhoea, and fever, among others.

3.15.2 Active constituents

Volatile oil (1.5-3.5%), starch, resin, and tannin, eugenol and asarone. Volatile oil contains asaraldehyde [83].

3.15.3 Pharmacological properties

Acorus calamus leaves, rhizomes, and essential oil have been found to possess several biological activities, such as antispasmodic and carminative properties [54]. The extract of *Acorus calamus* Linn (Acoraceae), commonly known as calamus, and its constituent α-asarone have demonstrated significant reduction in the production of reactive oxygen species (ROS) induced by l-glutamate. Additionally, the extract and α-asarone were able to suppress the phosphorylation of protein kinase RNA-like ER kinase (PERK) induced by tunicamycin [55].

These findings suggest that *A. calamus* extract and α-asarone may offer protection to hippocampal cells against oxidative and ER stress by reducing ROS production and suppressing PERK signaling, respectively. α-Asarone shows promise as a potential therapeutic agent for treating neurodegenerative disorders, such as Alzheimer's disease [56].

3.16 Panax ginseng

3.16.1 General description

Panax Ginseng (Fig. 18.) belongs to the family *Araliaceae*. Ginseng is a memory boosting herb which is commonly used in China, Japan and Korea.

3.16.2 Pharmacological properties

The beneficial pharmacological effects of ginseng include antioxidant, anti-inflammatory, anticancer and vasorelaxative effects [57].

3.16.3 Active constituents

The key components present in ginseng extract are Ginsenosides and gintonin, they possess anti-AD effects. Ginsenosides (a derivative of triterpenoid) are the first isolated chemical from ginseng which inhibits aggregation of amyloid β (Aβ) and removes Amyloid-β from neurons. It reduces the symptoms of AD by inhibiting the activity of Anticholinesterase [58].

Figure 17. *Acorus calamus*

Figure 18. *Panax ginseng*

According to recent reports, ginsenosides and gintonin are responsible for anti-AD activity via inhibition of Aβ-induced neurotoxicity and reactive oxidative stress, stimulation of soluble amyloid precursor protein α (sAPPα) formation (but not Aβ), anti-inflammatory effects, and enhancement of cholinergic systems, hippocampal neurogenesis, and cognitive functions by conducting in vitro and in vivo studies. Further study should be needed to explore the benefits of ginseng extract [59].

3.17 Uncaria tomentosa

3.17.1 General description

Uncaria tomentosa (Fig. 19.) known as Cat's claw belongs to the family *Rubiaceae*. It is preferred as raw material for cat's claw.

3.17.2 Active constituents

Alkaloids are the major constituent responsible for pharmacological activities. The primary chemical constituents found in Cortex Uncariae are tetracyclic indole alkaloids such isorhynchophylline and rhynchophylline, along with indole alkaloids like speciophylline, mitraphylline, pteropodine, uncarine F, and isomitraphylline.

3.17.3 Pharmacological properties

The known pharmacological activities of *U.tomentosa* are anti-inflammatory, antioxidant, immune modulator, antitumor, antidepressant and neuroprotective activity.

It has been reported that *uncaria tomentosa* can alleviate cognitive impairments in AD [60]. A similar plant of the family known as uncariarhynchophylla also possess the same activity since both contain similar chemical constituents. A study was conducted to compare the anti-AD activities of methanolic extracts of these plants and it has proved that they significantly improved the learning and memory impairments in STZ-induced rats [61]. A study was carried out for evaluating the anticholinesterase activity of the aqueous extract of *Uncaria tomentosa*. The extract showed maximum inhibition of the enzyme. So it reveals that *U. tomentosa* possessespotent anti-AChE activity. Oxindole alkaloids present in aqueous extract are responsible for anti-AChE activity [62].

Figure 19. *Uncaria tomentosa*

Figure 20. *Curcuma longa*

3.18 Curcuma longa

3.18.1 *General description*

Curcuma longa (Fig. 20.) belongs to the family *Zingiberaceae*. It consists of dried as well as fresh rhizomes and is a common spice in South Asia

3.18.2 Active constituents

Turmeric contains about 5 per cent of volatile oil, resin, abundant zingiberaceous starch grains and curcuminoids [83].

The active constituent present in *Curcuma Longa* is Curcumin (difeuloylmethane) [63].

3.18.3 Pharmacological properties

Curcumin is a powerful anti-inflammatory agent and antioxidant so it has been used to treat inflammation of skin and muscles in the Indian and Chinese systems of medicine. Curcumin can penetrate blood-brain barrier as it is a small molecule. Curcumin inhibits the production and accumulation of Aβ polypeptide. A diet containing significant amounts of curcumin may be the reason for the lower risk of AD in older Indians, since it was revealed that the prevalence of AD in adults aged 70 to 79 in India is 4.4 times lower than that in the United States [64].

Studies showed that curcumin protects neurons from degeneration. Curcumin is incorporated with PLGA-PEG-PLGA thermo-sensitive hydrogel and given as an intramuscular injection in aluminium chloride induced rat model, the system sustained the release of curcumin loaded micelle for 20 days and showed good biocompatibility and biodegradability which effectively prevent development and progression of AD. No significant toxicity has been reported [65]

3.19 Centella asiatica

3.19.1 General description

Centella asiatica (Fig. 21.) also known as Jalbrahmi or Mandukparni belongs to the family *Apiaceae* [66]. In the Ayurvedic system of medicine, the leaves of Centella have been used as a memory enhancer. It has a potential to prevent various memory-related disorders and also practiced in African and Chinese system of medicine.

3.19.2 Active constituents

Asiatic acid, asiaticosides, madasiatic acid, madecassoside, (main constituents) brahmoside, brahminoside, isothankuniside, thankuniside and centelloside are the important phytochemicals present *Centella asiatica* [68]. Ethanolic extract of *C. Asiatica* has been shown to have antioxidant, AChE inhibitory and anti-diabetic activity which may lead to the finding of a more effective agent for the treatment and management of AD and Diabetes and related other disorders. The enzymes acetyl cholinesterase (AChE) and butyryl cholinesterase (BChE) were measured to determine the anti-Alzheimer activity [69].

3.19.3 Pharmacological properties

Pharmacological activities of the plant include antioxidant, anti-inflammatory, neuroprotective, antidepressant, nootropic, anticonvulsant, sedative and immune stimulant activity [67]. The results of the present research revealed that the *C. Asiatica* extract might have a substantial inhibitory effect on ChEs. *C. Asiatica* may be able to boost levels of the neurotransmitter acetylcholine and hence enhance synaptic transmission in the AD brain by blocking the enzymes AChEs and BChEs. Through the scavenging of reactive free radicals and ROS, which would otherwise play a significant role in the production of neurofibrillary tangles and neurotic plaques, the plant extract's anti-oxidant activity also, suggested that it has neuro protective effects in AD. A recent study revealed that extract of *Centellaasiatica* selectively decreased the levels of amyloid beta in the hippocampus of animal models with Alzheimer disease [70].

3.20 Convolvulus pluricaulis

3.20.1 General description

*Convolvulus pluricaulis*is (Fig. 22.) is a perennial herb belongs to the family *convolvulaceae*. It is also known as Shankpushpi [71]. It has been used traditionally for curing variety of disorders like nausea, bed urination, ulcers, hypertension, hyperthyroidism, convulsions and neurodegenerative disorders [72].

3.20.2 Active constituents

C.pluricaulis contains bioactive compounds such as cinnamic acid, pentanoic acid, ascorbic acid, vitamin E, phthalic acid, squalene, silane, decanoic acid, linoleic acid, b-sitosterol, tropane alkaloids, and kaempferol [73].

Figure 21. *Centella asiatica* *Figure* **22.** *Convolvulus pluricaulis*

3.20.3 Pharmacological properties

Shankpushpi is a powerful anti-inflammatory, anticonvulsant, anxiolytic, and antioxidant.

Convolvulus pluricaulis has been shown to have a variety of pharmacological actions, including the improvement of learning and memory in both young and old rats in recent studies. Chronic unpredictable mild stress induced rat when exposed to methanolic extract of *C.pluricaulis* resulted in remarkable changes in inflammatory cytokines, liver enzymes, serotonin,

and noradrenaline levels. Hence *C.pluricaulis* may turn out to be an efficacious medication for depression and neuroinflammation [74.]. In a Drosophila model of Alzheimer's disease, *Convolvulus Pluricaulis* alleviated human microtubule-associated protein tau-induced neurotoxicity.

Figure 23. *Eclipta alba*

Figure 24. *Salvia officinalis*

3.21 Eclipta alba

3.21.1 Gneral description

Eclipta alba/false daisy (Fig. 23.) is an annual herbaceous plant belonging to the family *Asteraceae*. It is found throughout India, abundant in marshy places and available in all seasons [83].

Synonyms- Bhringraj and Karisilakanni [75].

3.21.2 Active constituents

The major chemical constituents present in E.alba are alkaloids, flavonoids, glycosides, triterpenoides, polyacetylenes, coumestrans, sigmasterols, etc [76].

3.21.3 Pharmacological properties

Anti-inflammatory, antidiabetic, antiproliferative, hypolipedemic

Clinical studies on pharmacological actions such hepatotoxicity, proliferative, diabetic, hypolipedemic, etc. have been conducted. To investigate the anti-inflammatory effects of an oral methanolic extract, albino Wistar rats have been used [77]. Studies proved that methanolic extract of *E. alba* ameliorates mitochondrial dysfunction and oxidative stress by employing DPPH and ABTS radical scavenging assays for evaluating in vitro antioxidant activity. According to this study, *Ecliptaalba* reduces scopolamine-induced lipid peroxidation, the total neuroprotective effect of the extract was found to be more than 50%, showing the potential advantages of indigenous plants in ameliorating oxidative stress-induced mitochondrial dysfunction and enhances mitochondrial activity in the rat brain [78].

3.22 Salvia officinalis

3.22.1 General description

Salvia officinalis L. (Fig. 24.) belongs to the family *Lamiaceae/Labiatae*. The genus Salvia includes around 900 species and is one of the largest Genus of *Lamiaceae* family. *S.officinalis* is native to Middle East and Mediterraneanareas.

3.22.2 Active constituents

1,8cineole, camphor, α- andβ -thujone, vridiflorol, and α-pinene are among the major chemical constituents found in *S. officinalis.*

3.22.3 Pharmacological properties

It has been used for the treatment of various disorders like inflammation, hyperglycemia, gout, rheumatism, diarrhea, ulcer, seizures, dizziness and paralysis in the folk medicine of Asia and Latin America [79].

Many studies have been undertaken in recent years to examine the pharmacological activities of *S. officinalis*, and it has been reported that it possesses anti-inflammatory, antibacterial, antioxidant hypoglycemia and hypolipidaemic, anti-nociceptive, antimutagenic, and antidementia activities [80]. The pharmacological actions of *S. officinalis* are speculated to include effects that are anti-mutagenic, anti-cancer, anti-inflammatory, and that improve memory and cognition. Essential oils obtained from *S. officinalis* and other species of salvia is known to have anticholinesterase activity and improves mood and cognitive performance [81].

The herbal drugs and their activities are shown in Table 1.

4. Conclusions

The management of Alzheimer's disease is a big challenge for the medical science, because there are few choices and only a few drugs are approved by the US FDA. Since ancient times traditional medicines are practiced for memory loss worldwide. Based on that the plants that give anti-Alzheimer's activity was selected and study their phytochemical constituents that give the different activity. We have enlisted the selected plants that give anti-Alzheimer's activity. Due to the limited availability of journals, libraries, and recent research papers after 2022, the current study was unable to gather a significant amount of information about herbs for the treatment of Alzheimer's disease.

Authors' contributions

Collect literature, J.A.; A.K.P.; S.K.; G.S. and J.J.N.; Materialize and typed the review, M.M.; A.A.G. and S.E.N

Table 1. Herbal drugs and activity

Herbs	Family	Chemical composition	Pharmacological activity
Saturejacuneifolia	Lamiaceae	Flavonoids, phenolic compounds	Anti-Alzheimers, antidiabetic.
Moringaoleifera	Moringaceae	phenolic compounds, carotenoid, polyphenol, flavonoid, saponin, terpene and glycoside	antilipase, anticholinesterase, and antioxidant, Anti-Alzheimers activity.
Phyllanthusacidus	Euphorbiaceae	Phenolic compounds, flavonoids.	Antioxidant, acetylcholinesterase and anti-butyrylcholinesterase.
Clitoriaternatea	Fabaceae	Flavonoids, alkaloids, tannins, phytosterol, phenol and saponins.	Anxiolytic, anti-inflammatory, anti-microbial, anti-cholineseterase.
Crocus sativus	Iridaceae	Crocetin, flavonoids, phenol, picrocrocin, kaempferol.	Nerve sedative, analgesic, anti-Alzheimer's activity.
Annonasquamosa	Annonaceae	Phenolic compounds, flavonoids, carotenoids.	Antioxidant, anti-inflammatory, anti-acetylcholinesterase.
Glycyrrhizaglabra	Leguminosae	Triterpene, saponins, flavonoids, pectins, amino acids.	Antimalarial, antispasmodic, anti-inflammatory, anti-oxidant, anti-Alzheimer's activity.
Withaniasomnifera	Solanaceae	Alkaloids, Iron, Amino acids.	Antioxidant, free radical scavenging, anti-Alzheimer's activity.
Celastruspaniculatus	Celastraceae	Alkaloids, volatile oil, sterol, fatty acids, triterpenoids.	Antioxidant, anti-Alzheimers.
Ginkgo biloba	Ginkgoaceae	Flavonoids, terpenoids, ginkgolic acids.	Anti-free radical, antioxidant, anti-inflammation, anti-apoptosis, anti-Alzheimer's activity.
Coriander sativum	Apiaceae	Phenolic compounds, essential oil.	Antioxidants, anti-anxiety, anticonvulsant, anti-Alzheimer's.
Bacopamonnieri	Scrophulariaceae	Alkaloids, glycosides, flavonoids, saponins.	Antioxidant, free radical scavenging, anti-Alzheimer's activity
Peruvian maca	Brassicaceae	Amino acids, fatty acids, minerals.	Anti-oxidant, anti-cancer, anti-inflammatory, antidepressant, Anti-Alzheimers.
Phyllanthusemblica	Phyllanthaceae	Flavonoids, tannins, vitamin C, tannoids.	Antioxidant, anti-inflammatory, anti-cholinesterase.
Acoruscalamus	Acoraceae	Asarone, shyobunone.	Antispasmodic, carminative, anti-Alzheimer's.
Panax ginseng	Araliaceae	Ginsenosides, gintonin.	Antioxidant, anti-inflammatory, anticancer, Anti-Alzheimers.
Uncariatomentosa	Rubiaceae	Tetracyclic indole alkaloids, indole alkaloids, oxindole alkaloids.	Anti-oxidant, antitumor, neuro protective, antidepressant.
Curcuma longa	Zingiberaceae	Curcumin	Anti-inflammatory, antioxidant, anti-Alzheimer's.
Centellaasiatica	Apiaceae	Asiaticoside, madasiatic acid, brahmoside, thankuniside, centelloside.	Antioxidant, anti-inflammatory, neuroprotective, antidepressant, anticonvulsant.
Convolvulus pluricaulis	Convolvulaceae	Ascorbic acid, vitamin E, linoleic acid, b-sitosterol, tropane alkaloids.	Anti-inflammatory, anticonvulsant, anxiolytic, antioxidant, Anti-Alzheimers.
Ecliptaalpa	Asteraceae	Alkaloids, flavonoids, glycosides, triterpenoids, coumestrans, sigmasterols.	Anti-inflammatory, antidiabetic, antiproliferative, hypolipedemic, Anti-Alzheimers.
Salvia officinalis	Lamiaceae	1,8 cineole, camphor, α,β-thujone, bridiflorol,pinene.	Anti-inflammatory, antioxidant, antidementia, anti-cociceptive, hypolipedemic, Anti-Alzheimers.

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Availability of data and materials

All relevant data are within the paper and its supporting information files. Additional data will be

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Conflicts of interest

Authors have declared that no competing interests exist.

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