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Review paper

Plants from Ayurveda medicine used in treatment of Alzheimer's and other neurodegenerative disorders

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Abstract

Through the evolution, many diseases affected humans and many cures were obtained from nature.

Traditional medicine recommends numerous plants and their constituents to enhance cognitive function as well as relief from depression, memory loss, and other symptoms of Alzheimer's disease.

A common problem in ethnopharmacological studies is identifying diseases from old records, either because the local culture describes the condition differently, or because the disease is unknown at that time. This is especially true at Alzheimer's, which as a disease was identified late, thus relevant symptoms have to be identified when searching the literature like plants used in maintenance of language ability, symptoms of forgetfulness, dementia.

In this manuscript, we review a subset of herbs used traditionally in Ayurveda, that supports traditional use in neurodegenerative or memory related disorders for treatment of Alzheimer's.

Key words: ethnomedicine, Alzheimer's, ayurveda, dementia

Introduction

Although there are treatments available to help manage the symptoms of Alzheimer's, the disease eventually leads to death. Scientists are working hard to better understand this complex disease in order to develop more effective treatments and ultimately find a cure.

There has been an increase in interest in using plants and their phytochemicals to treat dementia in recent years especially due to lower side effects herbal medicine retain. Traditionally divers plants have been used to cure neurocognitive disorders, including Alzheimer's disease (Howes et al., 2003). There is a growing body of evidence that ethnomedicine, or the use of traditional medicine practices from different cultures, can be effective in the management of dementia. It is hypothesized that the phytochemicals of the herbs work synergistically and can also modulate the effects of other constituents within the same plant or from other species. While more research is needed to confirm these findings, they offer hope for those who are looking for alternative treatment options for this debilitating condition.

The aim of this manuscript is to identify prominent single herbs or a mixture of herbs traditionally used especially in Indian Ayurvedic medicine for treatment of Alzheimer's disease and other neurodegenerative symptoms.

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History of Ayurveda

Ayurveda, translated as knowledge of life, is a system of traditional medicine native to the Indian subcontinent with a 6500 years history. It relies on a holistic approach to health and wellbeing, taking into account the body, mind, and spirit. Ayurvedic practitioners use a variety of techniques to promote balance in the body, including diet, lifestyle changes, massage, and herbal remedies. In Ayurvedic medicine, more than 5000 signs and symptoms of different diseases have been described, and there are 700 herbs and 6000 yoga treatments available (Sharma et al., 2021). Treatments in Ayurveda are based on the principle of five elements, earth, water, fire, air and space. Five elements are used to create the human physique, and the first element is, bones & organs that are symbolized by earth (bhumi/prithvi), blood is symbolized by water (varuna/jal), heat of the body symbolized by fire (agni), air (vayu) and astral body symbolized by space (dyaus/akash). A combination of each element results in three humors, or doshas, known as vata (energy of movement symbolized as mixture of air and space), kapha (energy of lubrication and structure symbolized by mixture of water and earth) and pitta (energy of digestion or metabolism symbolized by mixture of fire and water). These doshas are believed to be responsible for a person's, mental, emotional and physiological health and if these three energies are balanced, the body will stay healthy; otherwise, it will get ill in various ways (Sharma et al., 2021). Alzheimer's was not mentioned directly in Ayurvedic literature but, symptoms of amnesia and memory loss are well documented. Branch of Ayurveda, Rasayana or Jara Chikitas, describe diseases that are related to aging, as well as science of longevity and rejuvenation, that is linked with Alzheimer's symptoms. Nervous system disorders, were thought to be when there were imbalances of Vata, and this disorder is associated with weakness distress, or hypersensitivity of the nervous system (Rao et al., 2012). In Ayurveda, herbs with various properties have been used to treat nervous system disorders such as memory loss in the elderly, unconsciousness, and undeveloped brains and, the most popular plants and formulations that are used to delay the aging of the human brain and improve memory.

Below we will present some studies found in literature that supports traditional use plants from Ayurveda in neurodegenerative or memory related disorders for treatment of Alzheimer's.

Pharmacological and clinical studies on Ayurveda herbs and polyherbal formulation for treatment of Alzheimer's

Acorus calamus

The ayurvedic medicine *Acorus calamus* or Vacha sometimes known as "sweet flag," has long been utilized for its sedative, laxative, diuretic, and carminative effects. The rhizome has been used to treat memory loss in Ayurvedic medicine. *In vivo*, ethanolic and hydroethanolic rhizome extracts both had sedative and neuroprotective properties, especially due to presence of β-asarone. *A. calamus* was discovered to have anti-oxidant action and to be effective at scavenging excess oxygen free radical generation.

In mouse cells and human peripheral blood leukocytes, it also plays protective roles against radiation-induced DNA and membrane damage.

The essential oil of *A. calamus* and its component, β-asarone, have been proven in numerous investigations to have acetyl cholinesterase (AChE) inhibiting capability (Ajmalhussain, 2019).

Bacopa monnieri

Bacopa monnieri or Brahmi is advised for mental stress, memory loss, epilepsy, sleeplessness, and asthma in the Ayurvedic medical system. *Bacopa monnnieri* is widely studied and it is found in many formulations for intellect promoting. Saponins, bacopasides III, IV, V, bacosides A and B, bacosaponins A, B, C, D, E, and F, alkaloids, sterols, betulic acid, polyphenols, and sulfhydryl compounds are among the bioactive phytochemicals found in this plant and may be the reason for the plant's neuroprotective properties.

Phytochemicals found in Brahmi have been shown in both *in vitro* and *in vivo* investigations to have an antioxidant and free radical scavenging effect by preventing lipid peroxidation in several brain regions. Brahmi works by suppressing lipoxygenase activity, lowering divalent metals, scavenging reactive oxygen species, and limiting the generation of lipid peroxides (Gregory et al., 2021).

A phase 2b randomized double-blind study with *Bacopa monnieri's* in human clinical trials, was done to evaluate the efficacy of Donepezil, the gold standard drug, and *Bacopa monnieri*.

A group of 48 individuals participated in the trial, which involved the administration of 10 mg of Donepezil and 300 mg of *Bacopa monnieri* extract. Results were analyzed using the Postgraduate Institute (PGI) memory scale and the Alzheimer's Disease Assessment Scale (ADAS-cog). Studies comparing *Bacopa monnieri* to dopenzil have not found any appreciable differences between the two, those *Bacopa monnieri* can be consider a potent anti-Alzheimer drug (Chinnathamb and Dubey, 2019).

Baliospermum montanum

The Euphorbiaceae family includes the aromatic medicinal herb *Baliospermum montanum* known as Danti in Hindi and Sanskrit. It is mentioned in Ayurveda as is one of Rasayana plant.

It is one of the plants found in Brahmarasayana formulation that it is believed to increase focus, promote life expectancy, slow down the aging process, and prevent fatigue and drowsiness.

B. montanum in a study showed considerable inhibition activity with IC_{50} 137.5 μg/ml indicating the possibility of application of *B. montanum* for the treatment of cognitive diseases such as Alzheimer, since they may contribute to increase acetylcholine in cholinergic neurons (John et al., 2013) (Manyam, 1999).

Benincasa hispida

Benincasa hispida, also known as Kushmanda, is an herb belonging to the Cucurbitaceae family that is also known by the common names "White Pumpkin" and "Wax Gourd.". It is described in Ayurveda as brain tonic, memory-enhancing, refrigerant, restorative, rejuvenator, and vitalizer. Its fruits, seeds, and leaves are key ingredients in various Ayurvedic medicines, including "Kushmandpak," "Kushmandkhand," "Kushmand Churna," "Kushmandgud," "Kushmandaka Rasayana," and "Kushmandadi Ghrita," which are used to treat generalized weakness and incapacity.

Triterpenoids, flavonoids, glycosides, saccharides, carotenes, vitamins, sitosterin, and uronic acid are the main compounds.

In some studies, the therapy with continuous administration of aqueous extract of *Benincasa hispida* pulp (400 mg/kg bw) at the colchicine-induced rat model of Alzheimer's disease, appeared to be effective antioxidant. Additionally, it improved the frequency of accurate decisions made out of ten trials per day, boosted antioxidant levels in several brain regions, and reduced latency time dosage dependently (Al-Snafi, 2013; Shakya et al., 2019).

Boerhavia diffusa

Boerhavia diffusa, Punarnava, has been categorized as a "rasayana" herb, which is said to have properties like antiaging, reestablishing youth, strengthening life and brain power, and disease prevention. All of these properties imply that they increase the body's resistance to any onslaught, or in other words, that they provide hepatoprotection and immunomodulation. Studies has shown that *B. diffusa* has strong anti-inflammatory due to compounds like eupalitin, eupalitin-3-O-D-galactopyranoside, sitosterol, liriodendrin, boerhavinone B, and punarnavine were selected and shortlisted from reviews of research articles. Also, a methanol extract exhibited stronger antioxidant abilities with a high level of phenolics and flavonoids (Mishra et al., 2014), (Kumar and Varadaraju, 2021; Sinan et al., 2021).

Convolvulus pluricaulis

Convolvulus pluricaulis, traditionally referred to as Shankhapushpi (Family: Convolvulaceae) according to Ayurveda is one of the best nerve tonics for treating aging and neural illnesses. The nerve tonic also has anti-stress, adaptogenic, and memory-enhancing effects in addition to delaying brain aging and assisting in neural tissue regeneration. It contains volatile oils, the alkaloids shankhpushpine and convolamine, the flavanoid kampferol, phytosterol, amino acids, fatty acids, scopoletin, and β-sitosterol, as well as other compounds (Yoggeta et al., 2021). In one study supplementation with aqueous extract of *C. pluricaulis* reduced the quantity of tau protein in the *Drosophila* Alzheimer's model, with the ordinary standard meal extends longevity and improves locomotor impairments. In the fly model, *C. pluricaulis* ameliorates the effects of induced oxidative stress and restores the depletion of AChE activity by acting as an endogenous activator of the cellular antioxidant defenses (Kizhakke et al., 2019).

Convolvulus pluricaulis is also known to have anti-AChE activity. In the brain and hippocampus of male Wistar rats with scopolamine-induced cognitive impairment, aqueous *Convolvulus pluricaulis* extract significantly inhibited AChE. Scopoletin and scopolin, two of the *Convolvulus pluricaulis* 's active ingredients, have significantly and dose-dependently lessened scopolamine-induced amnesia in mice. Combining *C. pluricaulis* and rivastigmine prevented rats AChE activity from increasing due to aluminum exposure.

Humans may benefit therapeutically from consuming *C. pluricaulis* extract if they want to stop or slow the advancement of an oxidative stress-mediated neurodegenerative illness. This study reveals that C. *pluricaulis* has neuroprotective properties that can help reduce Alzheimer's-induced neurotoxicity (Karunakaran et al., 2022).

Centella asiatica

Centella asiatica, is known by a variety of names, including "gotu kola," "Indian pennywort," "Asiatic pennywort," and "tiger herb" and belongs to the Apiaceae family.

Centella asiatica is one of the key revitalizing herbs for nerve and brain cells in the Ayurvedic school of medicine and is thought to be able to increase intellect, lifespan, and memory (Rao et al., 2012).

Highly variable triterpenoid saponins, such as asiaticoside, oxyasiaticoside, centelloside, brahmoside, brahminoside, thankunoside, isothankunoside, and related sapogenins, comprise the majority of this plant's bioactive components. Additionally, it contains triterpenoid acids such as betulic acid, asiatic acid, madecassic acid, brahmic acid, and isobrahmic acid (Khanum and Kumar, 2012).

Asiaticoside derivatives, such as asiatic acid and asiaticoside, found in Gotu Kola have been demonstrated to suppress β-amyloid, lower levels of free radicals, and lessen hydrogen peroxide-induced cell death, decreases hippocampus Aβ levels and apoptosis both *in vitro* and *in vivo*, improves learning and memory in Alzheimer's mouse models. Potential application in the management of Alzheimer's and β-amyloid toxicity (Kalász et al., 2018).

In various rodent investigations, the cognitive effects of the aqueous extract of *Centella asiatica* (100–300

mg/kg/day) have been assessed using common tests like the shuttle box, step-through paradigm, elevated plus maze, and passive avoidance tests. *Centella asiatica* extract significantly enhanced learning and memory in wild-type rats, rats exposed to CNS toxicity (intracerebroventricular streptozotocin), and pentylenetetrazole (PTZ)-kindled animals. The extract significantly improved learning effectiveness and spatial memory in neonatal mice when given to them between days 15 and 30 postpartum, with no adverse effects on locomotor function. There have also been reports of *Centella asiatica* 's direct neurotropic effects. In hippocampus neurons of both adult and neonatal rats, *Centella asiatica* aqueous extract significantly increased dendritic number of nodes of apical and basal dendrites (Soumyanath et al., 2021).

Celastrus paniculats

Jyotishmati, *Celastrus paniculats*, is a prized medicinal herb that has been used for ages in Ayurveda to improve memory and focus. It is renowned for its beneficial effects on the brain, both mental focus and cognitive ability (Rao et al., 2012).

Numerous fatty acids, including oleic, palmitic, linoleic, stearic, lignoceric, linolenic acid, acetic acid, and benzoic acid, are included in the chemical components of *Celastrus paniculats*. Research at several seed extracts, found that the aqueous extract of *Celastrus paniculats* contained sugars, tannins. Stearic acids and palmitic acids are found in ether extract. Malkanguniol was found to be the main sesquiterpene polyalcohol in methanolic extract, which also contains other sesquiterpene polyalcohols. From the seed oil of *Celastrus paniculats*, paraffinic hydrocarbons, amyrin, sitosterol, and pentacyclic triterpene diol paniculatadiol were identified (Pai et al., 2016).

The potential antioxidant and anti-alzheirmer activity of the crude methanolic extract of *Celastrus paniculatus* seeds and its organic soluble components were investigated. The extracts had a strong ability to scavenge DPPH free radicals and moderate anticholinesterase activity (Badrul and Ekramul, 2011).

Curcuma longa

Curcuma longa, Turmeric, is a member of ginger family (Zingiberaceae). Since ancient times, it has been widely utilized in Ayurveda as a painkilling and anti-inflammatory substance to treat pain and inflammation in the muscles and skin (Mishra and Palanivelu, 2008).

Curcuma has large levels of flavonoids, sesquiterpenoids of the bisabolane type, and polyphenols. The primary polyphenol in turmeric is called curcumin (Rao et al.,2012; Wu et al., 2020).

Through mechanisms of suppression of apoptosis by inhibition of ROS, curcumin attenuates β-amyloid-induced PC12 cell neurotoxicity through inhibition of oxidative stress, intracellular calcium levels, and hyperphosphorylation of tau protein, oxidative damage, and inhibition of Aβ, thereby reducing the cytotoxicity caused by this protein. Curcumin on SH-SY5Y cells, protects against the decline in Aβ production by inhibiting the GSK-3-mediated activation of PS1 (da Costa et al., 2019).

When curcumin was given to elderly mice with advanced plaque deposits like those of Alzheimer's disease, the amount of plaque formation was reduced. It lessened oxidative harm and corrected the amyloid pathology in a transgenic mice model of Alzheimer's disease. Curcumin's potent antioxidant and anti-inflammatory capabilities also reduced the oxidative and inflammatory signs of Alzheimer's disease (Krup et al., 2013).

Cuscuta reflexa

Cuscuta reflexa, Amarbail, Akashbail, belongs to family Cuscutaceae and according to Ayurveda suggestion, its juice was mixed with water and was used to treat brain problems (Sharma et al., 2021). Numerous phytochemicals have been identified from *C. reflexa*, including cuscutine, stigmasterol, kaempferol, dulcitol, myricetin, and coumarin (Raza et al., 2015).

When compared to ascorbic acid, methanolic extract of *C. reflexa* demonstrated significantly stronger antioxidant activity by suppressing DPPH. The outcome of this investigation demonstrates that extract may be used as a readily available natural antioxidant source (Haq et al., 2019).

In Scopolamine induced amnesic albino Wistar rats, in one study it was administrated oral, 200 mg kg^{-1} day^{-1}, 14 days of methanolic extract of plant and the result showed memory enhancing activity by decreasing transfer latency during the acquisition phase and retrieval phase and decreased in AChE and lipid peroxidation (Chen et al., 2018).

Commiphora mukul

Commiphora mukul belongs to Burseraceae family and it is one of the constituents of Guggul, which is one of the most valuable remedies in Ayurveda medicine used to treat arthritis, inflammation (Salehi et al., 2015). Oleogum resin, *guggulu*, is produced by a number of different plant species including *Commiphora mukul*, *C. molmol*, *C. abyssinica*, *C. Burseraceae*, and *C. whighitii*, exudes through fissures and crevices in the bark. A blend of 30% to 60% water-soluble gum, 20% to 40% alcohol-soluble resins, and roughly 8% volatile oils make up the oleogum resin found in guggulu. Mucilage, carbohydrates, and proteins are examples of components that are water soluble. The heerabomyrrhols, commiphoric acids, and commiphorinic acid are components that are soluble in alcohol. Terpenes, sesquiterpenoids, cuminic aldehyde, eugenol, the ketone steroids Z and E-guggulsterone, and guggulsterols are some of the volatile components. Additionally, ferulic acids, phenols, and other non-phenolic aromatic acids found in guggulu are strong superoxide radical scavengers and may be useful in the treatment of Alzheimer’s (Rao et al.,2012).

It's possible that *C. mukul's* capacity to reduce hyperglycemia is at least partially responsible for the improvement in cognitive function shown in the diabetic rats. Due to guggul's reduction of serum LDL cholesterol and triglyceride levels in both human and animal studies. Studies showed a connection between cholesterol, the production of amyloid precursor proteins, and Alzheimer's disease. The β amyloid-forming amyloidogenic pathway is inhibited by cholesterol-reducing medications by lowering neuronal cholesterol levels, which may be accomplished by separating cholesterol from the amyloid precursor protein. These findings suggest that the use of cholesterol-lowering medications is linked to a decline in Alzheimer's prevalence. The results of this investigation suggest that *C. mukul* can alleviate diabetic rats' cognitive impairment (Salehi et al., 2015).

Cynodon dactylon

Since ancient times, numerous medical treatments have been employed to treat neurological problems. The Poaceae family contains *Cynodon dactylon*, known as doob, in Ayurveda is reported as the heart and brain tonic (Pattanashetti et al., 2021).

Active substances such flavonoids, tannins, alkaloids, phytosterols, saponins, glycosides, phenols, proteins, and carbohydrates were present in the hydro-alcoholic extract of *C. dactylon*.

The *in vitro* study revealed scavenges activity of free radical by inhibition of DPPH by hydro-alcoholic extract of *C. dactylon* and *in vivo* study has shown anti-amnesic action due to decrease AChE enzyme levels and increase antioxidant levels in amnesia by scopolamine in rats (Pattanashetti et al., 2021).

Aqueous extract of *C. dactylon* has potential to prevent aluminium-induced neurotoxicity in brain regions like the cerebral cortex, hippocampus and cerebellum. The extract's flavonoid glycosides and phenolic content may help either directly by scavenging free radicals or indirectly by safeguarding the activities of antioxidant enzymes (Sumathi et al., 2021).

Desmodium triquetrum

Desmodium triquetrum belongs to family Leguminosae, and in Ayurveda, *Desmodium triquetrum* is frequently used to treat a variety of neurological conditions.

The extract's preliminary phytochemical study indicated the presence of amino acids, steroids, phenolic compounds, saponins, glycosides, and flavonoids. The roots, fruits, and leaves of this plant all include tannins, alkaloids, hipaforin, trigonelin, tanning material, and silicic, while the roots also contain saponins, flavonoids, and tannins (Linn et al., 2016).

The usefulness of an aqueous extract of *D. triquetrum* roots in reducing scopolamine-induced amnesia in mice was studied. Long-term memory was evaluated using the passive avoidance paradigm. By assessing the total amount of acetylcholine in the brain and the amount of acetylcholinesterase activity in various mouse brain regions, we have been able to pinpoint the potential mechanism by which *D. triquetrum* causes the antiamnesic effects. Mice with scopolamine-induced amnesia were treated with *D. triquetrum* (50, 100, and 200 mg/kg, p.o.) for seven days in a row. Similar to the common cerebro-protective medication piracetam, *D. triquetrum* boosted the amount of acetylcholine in mice brains and inhibited the activity of acetylcholinesterase.

It is feasible to use the aqueous extract of *D. triquetrum* roots to postpone the onset and lessen the severity of dementia and Alzheimer's disease symptoms (Hanumanthacharjoshi et al., 2018).

In another study in mice models of dementia, the neuroprotective potentials of a methanol extract of *Desmodium triquetrum* dried roots were examined. Mice's learning and memory were evaluated using exteroceptive behavioral models including the Morris water maze and Elevated plus maze. The interoceptive behavioral models were diazepam (1 mg/kg, i.p.) and scopolamine (0.4 mg/kg, i.p.) induced amnesia. In scopolamine, diazepam, and naturally occurring aging amnesic models, *D. triquetrum* (50 and 100 mg/kg, p.o.) dramatically reduced amnesic deficits. *D. triquetrum* was helpful in treating amnesia caused on by aging.

In mice, *D. triquetrum* boosted acetylcholinesterase inhibition activity throughout the brain. As a result, *D. triquetrum* may be utilized as a memory booster and maybe as a treatment for dementia and other neurodegenerative diseases. Its potential for neuroprotection and acetylcholinesterase inhibition may be the mechanism of action (Joshi et al., 2018).

Desmodium gangeticum

Desmodium gangeticum (Fabaceae), also known as Shalparni in Sanskri, has been widely utilized in Ayurveda to treat neurological disorders.

Desmodium gangeticum holds a variety of flavonoids, alkaloids, steroids, terpenoids, phenylpropanoids, pterocarpans, coumarins, saponins and volatile oils. The main bio-active components of the isolated phytochemicals are flavonoids, alkaloids, and pterocarpans. From the plant's aerial sections, alkaloids such 5-methoxy N, N-dimethyl tryptamine, N-methyl-H4-Harman, carboliniumcation, and indole-3-alkyl-amines have been identified. It has been reported that roots contain pterocarpans like gangetin, gangetinin, desmodin, gangetial, and desmocarpin and flavones such as quercetin and rutin were mostly found in aerial part (Linn et al., 2016).

It is reported that *Desmodium gangeticum* extracts were tested in mice for its effectiveness in reducing Alzheimer's symptoms through nootropic action and improving AChE activity, and the results were significant. *Desmodium gangeticum* also has shown to have antioxidant properties (Obulesu and Rao, 2011).

Various extracts from *D. gangeticum's* roots and aerial parts have been shown to be able to cure mice of acute amnesia by scopolamine. In a different study, it was discovered that *D. gangeticum* leaf and root aqueous extract inhibited whole brain AChE activity and raised the amount of acetylcholine in the same experimental paradigm, which eventually improved cholinergic transmission in the brain (Changdar et al., 2019).

Embelia ribes

Embelia ribes (Myrsinaceae), also known as Vidanga in Ayurveda, has been used in traditional medicine to treat a variety of conditions including mental disorders and as a brain tonic. Additionally, embelin has demonstrated anti-inflammatory, antioxidant, analgesic, anticancer, wound healing, hepatoprotective, and antibacterial properties (Bhuvanendran et al., 2018).

Embelin is the main and most important phytochemical found in *Embelia ribes* some of other compounds that were isolated according to the scientific literature are: alkaloid (i.e., christembine), essential oils, saponins, phytosterols (sitosterol and daucosterol), flavonoids (embelia flavosides A-C), vilangin (synthesized from embelin), phenolic components (i.e., virenol A, embeliphenol A) (Sharma et al., 2022).

Embelin has resulted as a multi-targeted agent showing activity against all three enzymes AChE, BChE, and BACE-1 enzymes making it a potential lead for developing as a multifunctional candidate for therapeutic targets of both amyloid and cholinergic hypotheses (Nuthakki et al., 2019).

Embelin exhibits nootropic and neuroprotective properties in scopolamine-induced amnesia in rats, according to another study. The novel object recognition test and the elevated plus maze test both revealed that embelin greatly increased the recognition index and memory retention. In addition, embelin considerably improved the recognition index when challenged with chronic scopolamine therapy and significantly improved memory in the absence of scopolamine at particular doses (0.3 mg/kg, 0.6 mg/kg, and 1.2 mg/kg). Furthermore, rats treated with embelin (0.6 mg/kg) demonstrated an increase in inflection ratio in nootropic activity in the elevated plus maze test (Bhuvanendran et al., 2018).

Withania somnifera

Withania somnifera one of the most well-known herbs used as a brain rejuvenator for Alzheimer's disease, also is known as Ashwagandha, Indian ginseng, or winter cherry. In Ayurveda it is prescribed as a nerve tonic, energy booster, and general health and longevity improvement.

Ashwagandha contains a number of highly intriguing bioactive substances, including ergostane-type steroidal lactones, withanolides A–Y, dehydrowithanolide–R, withasomniferin–A, withasomidienone, withasomniferols A–C, withaferin–A, withanone, and others. In addition, alkaloids, β-sitosterol, and phytosterols such as sitoindosides VII–X are present (Gregory et al., 2021).

It has been demonstrated that ashwagandha contains antioxidant and free radical scavenging properties as well as the ability to maintain a healthy immune system.

Glycowithanolides in *Withania somnifera* (Ashawgandha) have a significant antioxidant potential, enhancing the activities of catalase, glutathione peroxidase, and superoxide dismutase. The level of cholinesterase inhibition was assessed using a colorimetric method based on Ellman's reaction.

The research shows that *W. somnifera* extract strongly suppressed AChE in a concentration-dependent manner (Sharma D. et al, 2021).

The APP/PS1 mouse model of Alzheimer's was treated orally with a semi-purified ashwagandha extract to correct behavioral impairments and prevent the buildup of Aβ peptides. Researchers found that therapy with ashwagandha reduced the toxicity of Aβ while also promoting longevity in a Drosophila melanogaster Alzheimer's model (Gregory et al., 2021).

Emblica officinalis

Emblica officinalis, Amla, also known as *Phyllanthus emblica* or Indian gooseberry belongs to genus Phyllanthus (*Euphorbiaceae*). For the treatment of numerous antiaginig, rejuvenative, infectious and non-infectious disorders, all parts of *E. Officinalis*, most notably the fruits, have been used alone or in conjunction with other conventional medications as part of Ayurvedic Rasayana.

Compared to other citrus fruits, it has a higher concentration of minerals and vitamin C. Moreover, amla contains chemical components with therapeutic value as polyphenols, tannins, and epigallocatechin-3-gallate like emblicanin (A, B), penigluconin and peduculagin. The potential benefits of *E. officinalis*, such as its anti-oxidative, anti-inflammatory, anti-diabetic, anti-hyperlipidemic, anti-cancer and antiproliferative, anti-mutagenic, cardioprotective, hepatoprotective, etc., are revealed by a large body of evidence (Husain et al., 2019).

The therapeutic potential of *Emblica officinalis* extract was initially investigated in animal models of dementia brought on by scopolamine and diazepam. It was shown that administration of *E. officinalis* extract in large doses significantly reversed dementia and improved memory and cognitive abilities.

Additional molecular research verified that these extracts prevent the development of β amyloid plaques by suppressing the expression of secretase enzymes, which are necessary for the processing and cleavage of amyloid precursor proteins (Shah et al., 2020).

A study demonstrated the potential of *E. officinalis* as a neuroprotective and antioxidant agent against aluminum chloride-induced Alzheimer's. Aluminum chloride was administered intraperitoneally for 28 days at a dose of 4.2 mg/kg to induce Alzheimer's disease. In prophylactic

experiments, aluminum chloride was given along with the unfortified amla powder (300 mg/kg) and plain amla powder (500 mg/kg). In the therapeutic trial, rats with Alzheimer's disease were given 500 mg/kg of the fortified amla powder. Morris water maize was used to gauge the nootropic action, which indicated memory impairment. The parameters of oxidative stress, such as malondialdehyde (MDA), superoxide dismutase (SOD), and catalase, were assessed at the end of the treatment. When compared to the controlled Alzheimer's-induced group, the present investigation revealed a statistically significant improvement in nootropic activity in terms of a decrease in latency period in the therapy groups. The administration of plain and fortified amla fruit powder reduced MDA levels while raising SOD and catalase levels (Vishala et al., 2019).

The results of another *in vitro* investigation to evaluate the butyrylcholinesterase and acetylcholinesterase inhibitory activities of the dry fruit extract of *E. officinalis* showed that the crude methanolic extract inhibited AChE at an IC_{50} of 53.88 g/mL and BuChE at an IC_{50} of 65.12 g/mL (Husain et al., 2019).

Nardostachys jatamansi

Nardostachys jatamansi, also known as Jatamansi, Tapaswani, in Ayurveda is described as a powerful form of medicine that has a solid track record of helping people with neurodegenerative diseases regain their memory function. It is described to treat epilepsy, hysteria, syncope, convulsions, and mental weakness.

Plant's rhizomes and roots contain a variety of bioactive compounds, including sesquiterpenes, coumarins, and valeranon, as well as the terpenoids spirojatamol, nardostachysin, jatamols A and B, and calarenol (Kumar et al., 2021).

Nardostachys jatamansi extracts significantly reduced all of the symptoms of chronic fatigue syndrome in rats, according to studies on the plant's function in the central nervous system.

Nardostachys jatamansi extracts decreased chronic fatigue syndrome-induced elevations in lipid peroxidation, nitrite, and superoxide dismutase levels as well as low catalase levels. The studies show that *Nardostachys jatamansi* has strong antioxidant properties. Similar to this, giving an alcoholic extract of this plant to young and old mice significantly improved their learning and memory while also reversing the amnesia caused by scopolamine and diazepam. Additionally, it reversed mice's naturally occurring aging-induced amnesia, indicating that the substances in this plant may be helpful in regaining memory in older people as well as in those suffering from age-related dementia (Rao et al., 2012).

Table 1. Plants from Ayurveda and in vitro/in vivo evaluation

Name of the plant	Traditional name	Traditional usage	*In vitro, in vivo* evaluation
Bacopa monnieri	Brahmi	Mental stress, memory loss, epilepsy, sleeplessness, and asthma	Antioxidant and free radical scavenging effect
Baliospermum montanum	Danti	Promote life expectancy, slow down the aging process, and prevent fatigue and drowsiness	Contribute to increase acetylcholine in cholinergic neurons
Benincasa hispida	Kushmanda	Brain tonic, memory-enhancing, refrigerant, restorative, rejuvenator, and vitalizer	Boosted antioxidant levels in several brain regions
Boerhavia diffusa	Punarnava	Antiaging, reestablishing youth, strengthening life and brain power, and disease prevention	Strong anti-inflammatory, stronger antioxidant abilities

Convolvulus pluricaulis	Shankhapushpi	Nerve tonics for treating aging and neural illnesses	Anti-AChE activity, neuroprotective properties
Centella asiatica	Gotu kola	Revitalizing herb for nerve and brain cells,able to increase intellect, lifespan, and memory	Suppress β -amyloid, lower levels of free radicals, decreases hippocampus Aβ levels and apoptosi
Celastrus paniculats	Jyotishmati	Improve memory and focus	Scavenge DPPH free radicals and moderate anticholinesterase activity
Curcuma longa	Turmeric	Painkilling and anti-inflammatory substance to treat pain and inflammation	Antioxidant and anti-inflammatory capabilities
Cuscuta reflexa	Amarbail Akashbail	Treat brain problems	Stronger antioxidant activity
Commiphora mukul	Guggul[*1]	Arthritis, inflammation	inhibite β amyloid-forming amyloidogenic pathway
Cynodon dactylon	Doob Doorba	Madness and epilepsy.	Decreas AChE enzyme levels and increas antioxidant levels
Desmodium triquetrum	Baloliya	Widely used for treatment of chronic cough and tuberculosis	Boosted the amount of acetylcholine, neuroprotection
Desmodium gangeticum	Shalparni	Treat neurological disorders	Nootropic action and improving AChE activity
Embelia ribes	Vidanga	Treat mental disorders and as a brain tonic	Activity against all three enzymes AChE, BChE, and BACE-1 enzymes
Withania somnifera	Ashwagandha	Nerve tonic, energy booster, and general health and longevity improvement	Antioxidant and free radical scavenging properties, strongly suppressed AChE
Emblica officinalis	Amla	Antiaging, rejuvenative, infectious and non-infectious disorders	Anti-oxidative, anti-inflammatory, suppress AChE
Nardostachys jatamansi	Jatamansi Tapaswani	Treat epilepsy, hysteria, syncope, convulsions, and mental weakness.	Antioxidant property

*1is produced by a number of different plant species including Commiphora mukul, C. molmol, C. abyssinica, C. Burseraceae, and C. Whighitii

Saraswatarishta (Baidyanath)

Ayurvedic liquid formulation Saraswatarishta, contains juice of C. asiatica, A. racemosus, P. tuberose, T. chebula, F. vulgare, Z. officinale, V. zizanioidis, W. fruticosa, V. negundo, O. turpethum, and honey.

Self-generated alcohol makes up 5–10% of Saraswatarishta. The product's water content and self-produced alcohol act as a means for the body to absorb the active herbal ingredients that are both water- and alcohol-soluble. The formulation (20 mL twice day for a year) demonstrated strong antiepileptic effect in a clinical investigation with 25 patients. *In vivo*, the drug's anticholinesterase action demonstrated nootropic effects on a number of experimental animals (Patel et al., 2014).

Ashtanga Ghrita

In ancient Ayurvedic texts, Ashtanga Ghrita, a cow Ghrita-based polyherbal composition, has been well defined to improve speech, intelligence, and memory. Clarified cow butter, milk, and eight strong neuroprotective herbs are all included in the formula like *Acorus calamus, Psoralea corylifolia, Centella asiatica, Convolvulus pluricaulis, Asparagus racemosus, Asparagus racemosus, Tinospora cordifolia, Bacopa monnieri.*

In one study rats were divided into five groups (n=6) to test whether scopolamine-induced dementia and brain oxidative stress could be prevented by Ashtanga Ghrita. Groups one and two were treated with scopolamine-induced dementia (1 mg/kg b.w., i.p.), while groups three to five received different doses of Ashtanga Ghrita (1.25, 2.5, and 5 g/kg b.w., orally). Behavior (Y-maze test) and brain biochemical alterations were assessed in all groups following the treatment schedule. This study shows that Ashtanga Ghrita promotes brain antioxidant activity, which protects the brain from scopolamine-induced dementia and may make Ashtanga Ghrita a potential medication for the treatment of neurodegenerative disorders (Sharma et al., 2021).

Triphala

Emblica officinalis (Amalaki), *Terminalia bellerica* (Bibhitaki), and *Terminalia chebula* (Haritaki) fruits make up the well-known and very effective polyherbal Ayurvedic medicine known as triphala ("three fruits"). Triphala is used to address digestive and rejuvenative issues (Peterson et al., 2017).

Triphala may have antioxidant, anti-inflammatory, immunomodulatory, antibacterial, antimutagenic, hypoglycemic, and antineoplastic properties, according to research investigations. Triphala may prevent degenerative and metabolic illnesses by modulating cytochrome P450, perhaps by preventing the generation of lipid peroxide and scavenging free radicals, according to *in vitro* research.

All three fruits contain several bioactive substances with various characteristics.

Spirochetes, oral bacteria, herpes viruses, and fungi are just a few of the pathogens that have been found in the oral cavities and brains of Alzheimer's patients that could cause an innate immune response. Triphala therapy is therefore one of the methods to lessen Alzheimer's related chronic innate immune system activation (Gregory et al., 2021).

Saraswata Churna

It has been asserted that the traditional Ayurvedic formula Saraswata Churna possesses nootropic and cognitive-enhancing properties. Some of the plants include: Ashwagandha (*Withania somnifera* Dunal.), Kustha (Saussurea Lappa), Shankhpushpi (*Convolvulus pluricaulis* Choisy Lin.), Vacha (Acorus calamus Linn.), Bramhi (*Bacopa monnieri* Linn.), Amalaki (*Embellica officinalis*), Termeric (*Curcuma longa*), etc (Radheyshyam et al., 2021).

In one study, Wistar adult male rats with epilepsy that were 4 months old showed cognitive changes after consuming Saraswata Churna. Memory loss is one of the most typical epilepsy symptoms. The impact of Saraswata Churna on rat learning and memory was evaluated using the elevated plus maze and Morris water maze tests. To cause epilepsy, pilocarpine (270 mg/kg BW, i.p.) was administered. The impact of Saraswata Churna on pilocarpine-induced epilepsy was assessed. By reducing latency in the raised plus maze, lowering escape latency during training, and increasing time spent in the target zone after recovery in the Morris water maze tests, Saraswata Churna (300 mg/kg b.w. orally) enhanced the rats' cognitive ability. Comparable to phenytoin (30 mg/kg b.w. i.p.), Saraswata Churna (300 mg/kg b.w. oral) has a memory-improving effect. The anti-inflammatory, antioxidant, and anticonvulsive effects of Saraswata Churna's phytoconstituents may account for its ability to improve memory in rats (Bakthavatchalam et al., 2022).

According to another study, Saraswata Churna is just as effective as Citalopram in the treatment of Geriatric Depression. For each drug to have the exact effect that is claimed, the authentic preparations of Ayurvedic medicines are crucial, and a specific procedure should be used as described in the classics. Hamilton Depression Rating Scale and the Geriatric Depression Scale (GDS-30) have been used to select and assess the patients (HDRS). Based on the results, it can be said that Saraswata Churna is an efficient treatment for geriatric depression management that has no negative side effects and instead encourages a better degree of symptom relief. As a result, the current study has demonstrated the potential for broad applicability in the treatment of geriatric depression (Radheyshyam et al., 2021).

Conclusion

This review assesses several medicinal plants and polyherbal formulations sourced from Ayurveda, which demonstrate promising outcomes in the treatment of Alzheimer's disease and other neurodegenerative disorders. In recent years, Ayurvedic medicine has gained popularity as an alternative food and treatment option. Initially, Ayurvedic herbal supplements were developed based solely on anecdotal or epidemiological data, without an understanding of their mechanism of action. However, current literature shows that the pharmacological effects of plants often align with their traditional medicinal use. The ethnopharmacological approach of selecting plants for research in treating specific conditions has proven somewhat successful in identifying plants and substances with potential therapeutic applications in neurodegeneration and cognitive diseases. To further facilitate the discovery of new functional leads for Alzheimer's and other age-related neurodegenerative diseases, it is recommended that the Ayurvedic knowledge base be integrated with combinatorial sciences and high-throughput screening techniques. This integration can aid in the development and use of Ayurvedic products and formulations in drug discovery initiatives.

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Резиме

Растенија од Ајурведската медицина кои се користат во лекување на Алцхајмерова болест и други невродегенеративни нарушувања

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Клучни зборови: етномедицина, Алцхајмерова болест, Ајурведа, деменција

Низ еволуцијата, многу болести ги погодија луѓето и многу лекови беа добиени од природата.

Традиционалната медицина препорачува бројни растенија и нивни состојки за подобрување на когнитивната функција, како и за олеснување на симптомите на депресија, губење на меморијата и други симптоми на Алцхајмерова болест.

Вообичаен проблем во етнофармаколошките студии е идентификација на болестите од старите записи, како резултат на тоа што локалната култура различно ја опишува состојбата или затоа што болеста во тоа време била непозната. Ова особено е точно за Алцхајмеровата болест, која како болест е идентификувана доцна, па затоа треба да се идентификуваат релевантни информации при пребарување низ литературата во поглед на растенијата што се користат за симптомите на заборавање и деменцијата.

Во овој преглед се обработени подгрупа на билки што се користат традиционално во Ајурведата, кои воедно ја поддржуваат традиционалната употреба во третманот на невродегенеративни нарушувања како и нарушувања поврзани со меморијата во третманот на Алцхајмерова болест.