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A review study on medicinal plants used in the treatment of learning and memory impairments

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Comments

This is an interesting review article on the tropical available plants that can be used in the treatment of learning and memory impairments (such as Alzheimer). The article can fulfill the present scattering knowledge in medicinal plants. The topic is interesting and can be further referenced. The review data can be the source for used in further study in tropical ethnopharmacology study.
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ABSTRACT

Alzheimer's disease (AD) is a progressive brain disorder that gradually impairs the person's memory and ability to learn, reasoning, judgment, communication and daily activities. AD is characterized clinically by cognitive impairment and pathologically by the deposition of β amyloid plaques and neurofibrillary tangles, and the degeneration of the cholinergic basal forebrain. During the progression of AD patients may produce changes in personality and behavior, such as anxiety, paranoia, confusion, hallucinations and also to experience delusions and fantasies. The first neurotransmitter defect discovered in AD involved acetylcholine as cholinergic function is required for short-term memory. Oxidative stress may underlie the progressive neurodegeneration characteristic of AD. Brain structures supporting memory are uniquely sensitive to oxidative stress due to their elevated demand for oxygen. The neurodegenerative process in AD may involve β amyloid toxicity. Neurotoxicity of β amyloid appears to involve oxidative stress. Currently, there is no cure for this disease but in new treatments, reveals a new horizon on the biology of this disease. This paper reviews the effects of a number of commonly used types of herbal medicines for the treatment of AD. The objective of this article was to review evidences from controlled studies in order to determine whether herbs can be useful in the treatment of cognitive disorders in the elderly.

KEYWORDS

Alzheimer's disease, Medicinal plants, Oxidative stress, Cholinergic function

1. Introduction

Alzheimer's disease (AD) is a progressive, irreversible neurological disorder that occurs gradually and results in memory loss, unusual behavior, personality changes, and loss of the ability to thinking[1]. It is estimated to affect 15 million people worldwide. AD is the cause of dementia in the elderly. AD is a progressive neurological disorder with duration of around 8.5 years between onset of clinical symptoms and death[2].

AD starts with loss of short term memory, forgetting names and addresses, as this condition progresses, the change become more marked and even individuals forget the home way. Unfortunately, AD has not any cure but can be prevented from progressing. Seventy percent of causes for AD is genetic and 21% is environmental. Most cases of

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Alzheimer's, approximately 95%, are the late-onset form, which develops after age 60[3].

The causes for disease progress in American and European countries are feeding, and reduced physical and mental activity. Unfortunately, the number of people with AD is expected to triple in the next 50 years. The average cost per patient is estimated 150 thousand dollars that expected future increases to 450 thousand dollars[3].

Brain areas associated with cognitive functions, particularly the neocortex and hippocampus, are the regions that mostly affected by the pathology which is characteristic of AD[4].

The main cure for AD is pharmacological treatment. Better understanding of the disease process and designed clinical trial are step forward and have improved related treatments for cognitive and noncognitive symptoms. Pharmacological treatment strategies in AD include three categories of drug: 1) their mechanism is based on disease-modifying therapies such as vitamin E; 2) their mechanism is based on compensation of neurotransmitter such as a cholinesterase inhibitor; 3) psychotherapy factors that are prescribed for symptoms of conduct disorder[5].

At present, the most accepted AD treatment strategy is cholinesterase inhibitors that can inactivate the acetylcholinesterase (AChE) enzyme in order to increase acetylcholine levels in the brain. Acetylcholinesterase inhibitors include rivastigmine, tacrine, donepezil, and galantamine whereas methyl-D-aspartate receptor antagonist (memantine) has recently been prescribed. However, there is no cure for AD, except to relieve symptoms of the disease[6].

These results lead us to factor that increase levels of the acetylcholine in the brain.

In this study, medicinal plants that have shown the early promising signs of clinical efficacy in the treatment of AD have been investigated. One common feature of these plants is their ability to exert neuroprotective effects through inhibition of AChE or inhibition of oxidative stress.

Although recently several synthetic drugs have been introduced to treat learning and memory disorder, but their therapeutic effects is low and most of them have undesirable side effects. Today we can see the increasing tendency of people towards traditional medicine[7].

Although the mechanism of anti-dementia effect of most herbal extracts and their compounds is not yet fully understood, one or more of medicinal plants and their constituents that are discussed in this study act through inhibition of AChE and activation of the synthesis of acetylcholine. While cholinesterase inhibitors which have been recently introduced such as tacrine and donepezil reduced the number of AD patients and relieve their symptoms, most of Alzheimer's patients have not still benefited considerably from major financial investments in research and development programs[8].

Recent studies have shown promising results of the effectiveness of herbal medicines for the treatment of various diseases include memory problems[9-13], stroke [14-19], gastrointestinal problems[20], and many others disease. Although these effects can related to their specific compounds, but most of them have been related to their antioxidant properties.

2. Pathogenesis of AD

Impairment of learning and memory, the most characteristic manifestation of dementia can be chemically induced in experimental animals by scopolamine. Scopolamine is a known cholinergic antagonist that involved in the transmission of acetylcholine in the central nervous system[21]. Cholinergic transmission is mainly terminated by acetylcholine hydrolysis by the enzyme AChE, which is responsible for degradation of acetylcholine to acetate and choline in the synaptic cleft[22].

Scopolamine-induced amnesia in animal models is widely used to screen for compounds with potential therapeutic value in treatment of dementia[23].

Decrease of acetylcholinetransferase enzyme activity and loss of cholinergic neurons were observed in the basal part of the frontal brain of AD patient that associated with cognitive impairment[24].

Lesion patterns of the nucleus basalis of Meynert (NBM) is used to study the role of cortical cholinergic system in awareness and understanding, also to indicate cognitive deficits that caused in AD[25]. Destruction of NBM in animal models showed reduction in cholinergic markers include levels of acetylcholine, acetylcholine release and turnover, uptake of acetylcholine, AChE activity and number of cholinergic muscarinic receptors in the frontal cortex[26]. Because the cholinergic ramifications are sent from Maynert nuclei into the cortex and septal area, electrical destruction of NBM causes death of the cholinergic cells in this nucleus and reduces the amount of acetylcholine in the cortex[27].

Hippocampus plays a critical role in learning and memory, which is a complex biological process including the acquisition, consolidation and retrieval of information[28]. Neurogenesis in the hippocampus, defined as the generation of new nerve cells, is involved in memory formation. Increased neurogenesis is improved spatial memory while impaired neurogenesis indicates poor cognitive function[29]. Important neuropathological features of AD include deposition of amyloid plaques in brain tissue and meningeal blood vessels as well as presence of neurofibrillary tangles in the hippocampus and the cerebral cortex of the brain[30]. Recent studies have demonstrated that AD is associated with inflammatory processes. Reactive oxidative species can damage cellular components and function as a second messenger in the inflammation. Utilization of antioxidants may be useful in prevention and treatment of AD[31].

One factor that plays an important role in the pathogenesis of AD is oxidative stress that is an imbalance between free radicals and antioxidant systems. Oxygen free radicals

can attack proteins, nucleic acids and lipid membranes, therefore disrupt cellular function and integrity. Brain tissue contains large amounts of polyunsaturated fatty acids which are particularly vulnerable to free radical attack. Lipid peroxidation is thought to be destructive form of oxidative degradation that damage cell membrane and produces a number of secondary products, both of the loop and splitting forms of oxygenated fatty acids have neurotoxic effects[32]. Increase in the levels of malondialdehyde (MDA), one of the reactive oxidative species, has been recognized as an important lipid peroxidation indicator[33].

Extensive researches on different plants are underway worldwide. Plant extracts have rather more therapeutic benefits and fewer side effects and are more economical. Plant extracts may provide a source of new compounds including many drugs that are derived from plant sources.

3. Medicinal plants used for the treatment of AD

3.1. Hypericum perforatum

Hypericum is herbaceous perennial plant with a height of 30-80 cm. It has glabrous and somewhat creepy stem. This plant's leaves are spoon-shaped and sessile, with numerous cavities of essential oil and its species name (perforatum) is derived from this feature. Flowering branches and leaves of this plant contain compounds such as essential oils, tannins, hayperciyn, hayperpyron, choline and flavonoids. Clinical effects of *Hypericum* include amelioration of neurological diseases, antidepressant, anti-anxiety, anti-inflammatory, wound healing and analgesic effects[34].

Hypericum extract containing flavonoids such as quercetin and quercitrin which shows free radical scavenging activity, antioxidant activity of quercetinis also were shown by the inhibition of lipid peroxidation[35].

In a study learning and memory impairment, associated with change in brain oxidative stress status caused in rat by acute injection of scopolamine (1.4 mg/kg). Scopolamine injection increased MDA levels and glutathione peroxidase activity of the brain and also reduced brain glutathione levels. These are responsible for increase in brain oxidative stress. Increase in the glutathione level of brain can directly decrease reactive oxidative species level. Pretreatment with *Hypericum* (4, 8 and 12 mg), 30 min before injection of scopolamine, showed antioxidant activity through their effects on brain MDA and glutathione level and also on glutathione peroxidaze activity[33].

Repeated administration of *Hypericum* and its active ingredient, hyperforin improved passive avoidance memory in mice via shuttle box[36]. *Hypericum* extract as an antioxidant agent can be a new type of antidepressant with memory-enhancing properties[33].

3.2. Lepidium meyenii

Maca (*Lepidium meyenii*) grows at altitudes of 3 500 to 4 500 meters in the Andes of Peru. Maca is one of the few plants that have succeeded to survive in the difficult condition of high Andes altitude, burning sun, hot days, cold nights and dry winds[37].

In a study effect of different doses of aqueous and hydroalcoholic extract of maca on learning and memory deficits induced by scopolamine (1 mg/kg) in mice has been investigated for 35 d. Maca improved spatial learning and memory impairments and ameliorate passive avoidance learning and memory deficits. The results indicated that scopolamine increase AChE activity in the mice brain up to 1.5-fold. Maca extract reduced brain AChE activity by 45% compared to the group that received only scopolamine[38].

Black maca increased step-down latency in avoidance test when compared to ovariectomized control mice also Black maca decreased brain MDA and AChE levels in ovariectomized mice. Black maca improved experimental memory impairment induced by ovariectomy, by its antioxidant and AChE inhibitory activities[39].

Mice treated with ethanol took more time to find the hidden platform than control during escape acquisition trials in Morris water maze test; by the way, black maca reversed the effect of ethanol. Black maca ameliorated the deleterious effect of ethanol during the probe trial[40].

3.3. Prunella vulgaris (P. vulgaris)

P. vulgaris is widely distributed in Korea, Japan, China and Europe. It is a traditional Chinese and Korean medicine that has been used to treat inflammation, eye pain, headache and dizziness[41].

Previous studies have demonstrated that *P. vulgaris* contains several active compounds such as oleic acid, ursolic acid, butyric acid, flavonoids and rosmarinic acid[42]. In addition, this plant has anti-allergy, anti-inflammatory, antioxidant, antimicrobial and antiviral activity[43].

P. vulgaris extract (25 and 50 mg) reduced latency in rats that received scopolamine in the shuttle box test. In addition, the extract of *P. vulgaris* ameliorated scopolamine induced impairments in the Y-maze test. This plant's beneficial effects are the result of imitation of acetylcholine effect. *P. vulgaris* does not inhibit AChE activity *in vivo* or *ex vivo* conditions and memory-enhancing effects of *P. vulgaris* do not work through inhibition of AChE, this achieved by an indirect effect on cholinergic signaling. *P. vulgaris* express its beneficial effects on memory and learning via increase of cholinergic neurotransmitters and methyl-D-aspartate receptor signaling[41]. Flavonoids from

P. vulgaris exhibit significant antioxidant activities[44].

3.4. Cyperus rotundus (C. rotundus)

Sedge or *C. rotundus* belongs to the family Cyperaceae. The rhizome of *Cyperus* is rich in essential oils that contain pinene, a little cineole, terpenes, and a new alcohol called isociprol. Several chemical components have been isolated from ethanol extract of *C. rotundus* rhizome and some of these chemicals possess anti-AChE activity[45].

Studies have shown that the severity of dementia in AD depends on the reduction of neurons in the Meynert nucleus that accompanied by the significant decrease in the amount of acetylcholine transferase enzymes in the cortex and amygdala and causes impaired learning[46].

NBM located in the frontal base of brain and majority of its cells are cholinergic[47]. Because the cholinergic ramifications is sent from Meynert nucleus to the cortex and septal, electrical lesion of NBM causes cholinergic cells death in the nucleus and reduces the amount of acetylcholine in the cortex[27].

In a study, rats with damaged NBM received two doses of *C. rotundus* extracts (100 and 200 mg/kg). *C. rotundus* extracts with anti-AChE effect improved spatial learning and memory as well as passive avoidance learning[11].

3.5. Zizyphus jujube

The immature jujube fruit is green in color, but as ripe, it becomes red and begins to wrinkle. The jujube fruit has long and elongated nucleus and is fully ripe in autumn. It is edible, sweet tasting and has medicinal properties. Jujube has soothing and anti-grouch properties, and has been used in traditional Korean and chinese medicine as a drug that reduces anxiety and strengthens the stomach, spleen and gastrointestinal system[48].

Terpenoid, flavonoid and alkaloid compounds have been isolated from the jujube fruit, a phenyl glycosides compound has also been obtained from jujube fruit[49].

Studies have shown that this herb contains compounds that exerted inhibitory activity against histamine release and activity of AChE and cyclooxygenase I and II. Furthermore, this herb has cytotoxic effect and activate biological compatibility. Jujube seeds contain large amounts of mucilage, malic acid, citric acid, sugar, protein, organic minerals and vitamin C[49-51].

Eight different types of flavonoids have been extracted from the jujube fruit and medicinal properties of jujube are attributed to the antioxidant properties of these compounds. Among the 50 examined plants, jujube extract showed the highest effect on the activation of acetylcholine transferase (34.1%) in the *in vitro*, a known compound that causes this effect is the cis-9-octadecenamide (oleamide)[52].

The increase in acetylcholine level in the cholinergic terminals may contribute to improve Alzheimer's symptoms and motor deficit[13].

A treatment strategy for AD is compensation of normal concentration of acetylcholine in the synaptic cleft to improve neuronal transmission in the brain cholinergic terminals. Acetylcholine transferase activator increase acetylcholine level in order to improve mild to moderate cognitive function of AD[53].

Jujube extract has restorative effects on learning and memory, motor coordination and behavioral disorders that caused by the Meynert nucleus lesion at the base of the rat brain's frontal lobe. This effect may be due to jujube extract effect on the activation of acetylcholine transferase. It can reduce the high price for AD treatment, and can be appropriate complement for synthetic and chemical drugs associated with high adverse effects[9].

3.6. Lavandula officinalis

Lavandula officinalis, known as lavender, has been traditionally considered. This plant has wide distribution and its flowers and essential oil is used in cosmetics and perfumes industry. Lavender is a plant of the genus *Lavandula*, its leaves looks like thyme leave but longer and thinner and has white flower[54].

So far, 48 species have been identified from this genus that grow in various parts of southern Europe and the Mediterranean countries, especially in southern Italy, Yugoslavia, Greece, Southern France and Northern Africa. This species is not a wild flower in Iran but it has recently been cultivated in some area. Its flowers are purple and usually its flowers and flower-stalks are used. Lavender has a very pleasant smell and a bitter taste. It is used in the perfume and cosmetics industries for its pleasant smell. Lavender essential oil is extracted via steam distillation from the flowers and flower-stalks. Lavender essential oil is yellow or greenish yellow liquid with a pleasant aroma. Until now, few studies have been conducted on the phytochemical characteristics of this plant species[54].

Many compounds have been detected in lavender extract, the most important of them include: geraniol, linalool, linalyl acetate, cineol, borneol, aflapin, camphor, butyric acid, valerianic acid, ursolic acid, and luteolin flavonoids, this compound may increase plant effects on central nervous system area, causing calming and soothing effects through GABA receptor[55].

Treatment with lavender essential oil significantly decreased neurologic deficit, stroke volume, the level of MDA, carbonyl and reactive oxygen species in rats subjected to ischemia and reperfusion and showed strong neuroprotective effect[56].

It is proved that the high activity of AChE enzyme and thus reduced amount of acetylcholine and synaptic transmission may contribute to the loss of spatial memory and cause AD. Inhibitory effects of different concentration of lavender extract on the AChE enzyme have been proved through

various tests on cell lines[57].

It has been reported that free radicals cause peroxidation of phospholipids, DNA damage and protein denaturation. The hippocampus is the key brain area for spatial learning and memory. Long term potentiation is one of the most important cellular mechanisms that underlie learning and memory. It has been shown that increased consumption of antioxidants improves spatial learning and long term potentiation induction in mice with AD[58].

In general, free radical production associated with several cellular processes such as cellular metabolism, mitochondrial respiration, cyclooxygenase and lipooxygenase activity, which may have been increased in brain. The amount of free radicals production in different part of the brain may be related to oxygen consumption on that area[59]. Since hippocampus that its oxygen consumption is higher, is more sensitive than other region. Protective effect of antioxidants may be due to their ability to give hydrogenation, or free radical scavenging strength[60].

Ethanol extract of lavender improves spatial learning and memory, motor coordination and passive avoidance learning, these neuroprotective effects may be due to its antioxidant properties[10].

3.7. Ginkgo biloba (G. biloba)

G. biloba, the oldest tree on the earth, is native to China and now cultivated in Europe and America. *G. biloba* extract treat insufficiency of blood circulation problems, especially in the brain that causes of memory loss, loss of consciousness, headaches, and depression in the elderly[61]. This extract is reported to contain about 24% flavonoids and 6% terpene lactones. There is reliable evidence that standardized ginkgo extract shows several molecular and cellular neuroprotective mechanisms, including the attenuation of apoptosis, the inhibition of membrane lipid peroxidation, anti-inflammatory effects and the direct inhibition of amyloid-b aggregation. There are extensive clinical investigations regarding its potential role in cognitive disorders[61].

Chronic treatment of *G. biloba* on learning and memory in mice showed that *G. biloba* improved acquisition, storage, and retrieval of a two-response sequence for food reward[62]. The antioxidant and free-radical scavenging properties of *G. biloba* extract are primarily attributed to the flavonoid fraction. *G. biloba* affects cognitive function in an animal model of AD without altering the histopathological consequences of overexpression of β amyloid precursor protein[63].

G. biloba extract significantly inhibit the AChE activity in the brain. The inhibition of AChE activity can be correlated with improvement observed in scopolamine-induced deficits in passive avoidance by *G. biloba* extract. The decrease in AChE activity indicates an increase in the basal level of acetylcholine[64].

3.8. Salvia officinalis (S. officinalis)

S. officinalis has a very old reputation for improving memory. It is singularly good for the head and brain[65]. The potential pharmacological effects of the herb, which may be relevant to AD include anti-inflammatory and antioxidant properties as well as weak AChE inhibitory effect. The leaves of *S. officinalis* L. (sage) are well known for their antioxidative properties[66]. Rosmarinic acid (the main active ingredient of *S. officinalis*) reduced a number of deleterious events induced by Aβ include reactive oxygen species formation, lipid peroxidation, DNA fragmentation, caspase-3 activation and tau protein hyperphosphorylation[67]. *S. officinalis* have a long history of use as memory enhancing agents coupled with cholinergic properties that may be relevant to amelioration of the cognitive deficits associated with AD[68]. Based on clinical evidence *S. officinalis* may help to prevent or alleviate symptoms of AD. In a randomized double-blind clinical study, patients with mild-to-moderate AD received *S. officinalis* extract. The result showed that *S. officinalis* had statistically significant effectiveness in the cognition after 16 weeks of treatment[69]. One small pilot trial showed that oral administration of *S. officinalis* essential oil to 11 patients showing mild-to moderate symptoms of AD significantly improved cognitive function.

3.9. Melissa officinalis (M. officinalis)

M. officinalis (lemon balm) is a cultivated perennial lemon scented herb. Records concerning its use date back over 2000 years with entries in the Historia Plantarum. In traditional medicine *M. officinalis* L. (Lamiaceae) has been used as a remedy for over 2000 years, and has been acclaimed for promoting long life and for restoring memory[65]. The leaves of this plant contain monoterpenes (*e.g.* citral) with weak anti-AChE activity, and phenol carboxylic acids-including rosmarinic acid, which shows antioxidative, anti-amyloidogenic and antiapoptotic effects. *M. officinalis* essential oil, given in canary wine, every morning will renew youth, strengthen the brain. Patients with mild to moderate AD receiving *M. officinalis* extract experienced significant benefits in cognition after 16 weeks of treatment[70]. *M. officinalis* has central nervous system acetylcholine receptor activity and modulates mood and cognitive performance following acute administration[71,72].

3.10. Ginseng

For thousands of years, ginseng root, especially the main root, has been used as an East Asian medicinal herb for treatment of various diseases[73]. Ginseng grows in Northeastern Asia. In traditional Chinese and Korean medicine, ginseng root is used for boosting energy. It is

believed to be a powerful adaptogenic aphrodisiac that can be applied for patients with low energy, weak immune system and sexual dysfunction. Use of ginseng extract may enhance cognitive and psychomotor functions and can benefit AD by improving brain cholinergic function, reducing the level of Aβ, and repairing neuronal networks damage[74-76]. Treatment with red ginseng significantly ameliorated place-navigation deficits in young and aged rats with hippocampal lesions in the place learning task[77]. Oral administration of ginseng powder prevented the ischemia-induced decrease in response latency, as determined by the passive avoidance test, and rescued a significant number of ischemic hippocampal CA1 pyramidal neurons in a dose-dependent manner[78]. One of the main bioactive components in ginseng is ginsenoside that play an important role in central nervous system[79,80]. It has been proved to be effective in the attenuation of learning deficits due to brain damage and aging in humans and animals[81].

3.11. Morinda citrifolia (M. citrifolia)

M. citrifolia, commonly known as noni, is widely used as food in tropical regions of the Indonesian to Hawaii Island. This species is a small tree with a straight trunk and cultivated in different parts of India[82].

As a popular herb, *M. citrifolia* juice is used as an alternative medicine for a variety of diseases such as arthritis, diabetes, high blood pressure, menstrual problems, heart disease, cancer, ulcers, depression, and atherosclerosis[83].

M. citrifolia fruit and extract have analgesic, anti-inflammatory and antioxidant properties[84]. Ethyl acetate extract of *M. citrifolia* prevented memory deficit and oxidative stress induced by amyloid beta peptide in mice[82]. Treatment with chloroform, ethyl acetate and butanol extracts of *M. citrifolia* in a dose-dependent manner reduced AChE enzyme activity in the brain of scopolamine-treated mice[84].

In addition, scopolamine-induced amnesia is associated with decreased cerebral blood flow and increased oxidative stress and AChE activity in rat brain, and treatment with the *M. citrifolia* extract improved scopolamine induced memory impairment in the shuttle box test[84].

3.12. Lycopodium serratum

Lycopodium is a genus of clubmosses, also known as ground pines or creeping cedar, in the family Lycopodiaceae, a family of fern-allies. The leaves contain a single, unbranched vascular strand and are microphylls by definition[85]. The genus *Lycopodium* (Lycopodiaceae), which produces a potential therapeutic agent, huperzine A, for the treatment of AD, has been extensively studied in recent years[85]. Huperzine A is an alkaloid extracted from *Lycopodium serratum* and has been used for centuries to treat fever, inflammation, blood disorders and schizophrenia[86]. It is a highly selective, reversible, and potent AChE inhibitor, and potency of AChE inhibition is similar or superior to that of physostigmine, galanthamine, donepezil and tacrine[87]. The huperzine A is a strong candidate for treatment of AD. Other potentially beneficial effects, as far as AD is concerned, include protection against Aβ-induced oxidative injury and neuronal apoptosis, regulation of nerve growth factor and reduction in glutamate-induced toxicity[88]. Huperzine A caused a significant increase in ACh levels in rat brain[88]. Huperzine A has several protective effects such as regulating amyloid precursor protein metabolism, protecting against Aβ mediated oxidative stress, apoptosis and mitochondrial dysfunction, as well as anti-inflammation[89].

3.13. Polygala tenuifolia (P. tenuifolia)

P. tenuifolia is one of the 50 fundamental herbs used in traditional Chinese medicine. The root of *P. tenuifolia* used as an expectorant, a tonic, and a tranquillizer for treating and preventing dementia[90,91].

Tenuigenin (which is a compound extracted from the Chinese herb *P. tenuifolia*), exhibits the property of soothing the mind and is indicated for insomnia, mental confusion and disorientation in Chinese medicine. Studies have suggested that tenuigenin can inhibit the secretion of Aβ from cultured cells and thus ameliorate the reduction in cholinergic function on rat models induced by Aβ[92]. Treatment with *P. tenuifolia* in NBM lesioned rats both the impaired rats' behavioral expression and memory test results had improved[93].

P. tenuifolia showed the ameliorative effect on scopolamine-induced decrease of the retention of passive avoidance by enhancing the central cholinergic system[94]. The water extract of *P. tenuifolia* up-regulated the choline acetyltransferase activity *in vitro*[95]. Gycoside-rich fraction from P. tenuifolia has improvement effect on the retrieval process in spatial cognition using eight-arm radial maze assay systems[96].

3.14. Celastrus paniculatus (C. paniculatus)

C. paniculatus (Celastraceae) is an Indian medicinal plant which has been used in the traditional Ayurvedic system of medicine for years. *C. paniculatus* may be employed as a stimulant nervine tonic, rejuvenant, sedative, tranquilizer and diuretic[97].

Plant seed and seed oil are reported to be highly beneficial in stimulating intellect and sharpening the memory. A study suggested that the oral administration of the seed oil decreased levels of noradrenaline, dopamine and 5-hydroxytryptamine in rat brain and thus improved learning and memory processes, in addition, the oil was not neurotoxic[98].

Administration of the seed oil to rats also reversed a scopolamine-induced task deficit. An aqueous seed

extract showed an antioxidant effect in the central nervous system, which may also explain the reputed benefits on memory, since this extract enhanced cognition *in vivo*[98]. The aqueous extract of *C. paniculatus* at a dose of 200 mg/kg showed improvement in learning and memory tasks in both the shuttle-box and step through paradigms[99]. There is a marginal increase in activity of AChE in the hippocampus when the animal is treated with 200 mg/kg body weight of *Celastrus* seed oil[100].

4. Conclusions

No treatment is available to slow or stop AD. The U.S. Food and Drug Administration has approved five drugs that temporarily improve symptoms. The effectiveness of these drugs varies across the population. None of the treatments available today alters the underlying course of this terminal disease[2].

Herbs show promise in AD treatment because of their cognitive benefits and more importantly, their mechanisms of action with respect to the fundamental pathophysiology of the disease.

In summary, preliminary clinical evidence demonstrated that some herbal medicines can ameliorate learning and memory in patients with mild-to-moderate AD. Potential beneficial actions exerted by the active components of these herbs are not limited to the inhibition of AChE and include the modification of Aβ processing, protection against apoptosis and oxidative stress, and anti-inflammatory effects.

The use of medicinal plants in the treatment of AD should be compared with the pharmacological treatment currently in use. These studies should include fundamental identification in order to confirm the clinical trial.

Conflict of interest statement

We declare that we have no conflict of interest.

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Comments

Background

AD is a progressive, irreversible neurological disorder that occurs gradually and results in memory loss, unusual behavior, personality changes, and loss of the ability to thinking. This review article focuses on medicinal plants used in the treatment of learning and memory impairments. The topic is interesting and can be further referenced.

Research frontiers

This is an interesting review article on flora medical science and can be useful in further ethnopharmacology study.

Related reports

There are some relating reports as cited and quoted in this review article.

Innovations and breakthroughs

In this present work, authors made an attempt to show interesting summative review of the available information of the madicinal plants used in the treatment of learning and memory impairments.

Applications

This work can be further applied in pharmaceutical research and it can also be further referenced in tropical biomedicine.

Peer review

This is an interesting review article on the tropical available plants that can be used in the treatment of learning and memory impairments (such as Alzheimer). The article can fulfill the present scattering knowledge in medicinal plants. The topic is interesting and can be further referenced. The review data can be the source for used in further study in tropical ethnopharmacology study.

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