A Review on Medicinal Plants for Alzheimer's Disease

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Abstract

Neurodegenerative diseases are commonly induced by irreversible destruction of central nervous system and neuronal networks which result in permanent functional impairment. There are several reported neurodegenerative disease, among them Alzheimer’s disease is very common. There is no cure available for Alzheimer’s disease, but symptomatic treatment may improve the memory and other related problems. Natural products such as herbs and medicinal plants have been used in the treatment of many memory disorders such as dementia, amnesia, as well as Alzheimer’s disease since a long time. Medicinal plants have been utilized for treatment of various diseases and it shows potential roles in the management and cure of memory disorders. Most of herbs and plants have been chemically evaluated and their efficacy has also been proven in clinical trials. However, the underlying mechanisms of actions are still on the way. In this review role of different medicinal plants against Alzheimer’s disease has been discussed.

Introduction

Neurodegenerative diseases are heterogeneous group of genetic disorders characterized by loss of neuronal structure, function and generally accompanied by neuronal loss. These diseases may result directly from degeneration of particular neuronal populations or indirectly from alterations in glial support cells. The particular topological pattern of brain involvement determines the specific clinical manifestations of each disease. Several of these diseases are characterized by an accumulation of abnormal or aggregated proteins or other biological materials either extracellular or within neurons. These accumulations take various forms and result in the neuritic plaques or neurofibrillary tangles in Alzheimer’s disease, Lewy bodies in Parkinson’s disease, glycogen and polyglucosan bodies in Lafora disease, or glycolipids and complex carbohydrates in the lysosomal storage diseases of the neurodegenerative diseases. Alzheimer’s disease is considered to be responsible for 60% of all dementia in people aged 65 or older [1]. Alzheimer’s disease (AD) is an age related progressive neurodegenerative disorder caused due to aggregation of mis-folded proteins which accumulate fibrillary amyloid deposits in selective regions of central nervous system. Alzheimer’s disease results in memory loss, unusual behaviour, personality changes, and loss of the ability to thinking. It 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. Seventy percent of causes for Alzheimer’s disease are genetic and twenty one percent is environmental. Most cases of Alzheimer’s disease, approximately 95%, are the late-onset form, which develops after age of 60 [2]. At present, the most accepted...
Alzheimer’s disease treatment strategy is cholinesterase inhibitors that can inactivate the acetyl cholinesterase (AChE) enzyme in order to increase acetylcholine levels in the brain. Acetyl cholinesterase inhibitors include rivastigmine, tacrine, donepezil, and galantamine whereas methyl-D-aspartate receptor antagonist (memantine) has recently been prescribed. However, there is no cure for Alzheimer’s disease, except to relieve symptoms of the disease [3]. The lifetime risk of Alzheimer’s disease for those 65 years of age is estimated to be 10.5%. Although some risk factors have been implicated, expert consensus at the National Institutes of Health’s State-of-the-Science Conference in 2010 indicates that firm conclusions cannot be drawn on modifiable risk factors for Alzheimer’s disease. It appears to be a multi-factorial disease that consists of socio-demographic, genetic, environmental, and lifestyle risk factors. Studies on risk factors remain challenging due to long latency periods from risk factor to disease onset [4]. The present review deals with the information on medicinal plants used to cure the Alzheimer’s disease.

Medicinal Plants against Alzheimer’s Disease

Medicinal plants synthesize and conserve a variety of biochemical products, many of which are extractable and used as raw material for various scientific investigations. Many secondary metabolites from plant are commercially important and are used as pharmaceutical compounds. Over the past few years, the medicinal plants have regained a wide recognition due to a growing faith in herbal medicine in view of its lesser side effects compared to allopathic medicine and the necessity of meeting the requirements of medicine for an increasing human population. However, a continuous supply of the source material often becomes difficult due to the factors like environmental changes, cultural practices, diverse geographical distribution, labour cost, and selection of the superior plant stock and over exploitation by pharmaceutical industry [5]. Alzheimer’s disease is the most common neurodegenerative diseases. Several studies have been reported that medicinal plants are used in the treatment of Alzheimer’s disease. There are several medicinal plants recognized for the treatment of Alzheimer’s disease which includes Ginkgo biloba, Centella asiatica, Withania somnifera, Bacopa monnieri, Melissa officinalis, Salvia officinalis, Tinospora cordifolia, Hypericum perforatum etc.

Bacopa Monnieri

Bacopa monnieri (Brahmi) is a bitter-tasting creeper plant found in damp and marshy areas and is commonly used in Ayurvedic medicine as a nervine tonic, diuretic, and cardiotonic and as a therapeutic agent against insomnia, asthma, epilepsy, and rheumatism. The principal constituents of Bacopa monnieri are saponins and triterpenoid bacasoapo nins that include bacopasides III to V, bacosides A and B, and bacosaponins A,B,C. other saponin glycosides include the jujubogenin bisdesmosides bacopasapones D, E, and F. Other constituents include alkaloids, plant sterols, betulic acid, polyphenols, and sulphydryl compounds that confer antioxidant activity [6]. Traditionally, B. monnieri was used to improve memory and cognitive function. B.monnieri extracts have been investigated extensively for their neuropharmacological effects and their nootropic actions [7]. In the hippocampus, B. monnieri enhances protein kinase activity that may contribute to its nootropic action [8]. B. monnieri also inhibited cholinergic degeneration and displayed a cognition-enhancing effect in a rat model of AD [9]. It has been reported that a standardized extract of B. monnieri reversed the cognitive deficits induced by intracerebroventricularly administered colchicines and ibotenic acid into the nucleus basalis magnocellularis [10]. In the same study, B. monnieri also reversed the (a) depletion of acetylcholine, (b) reduction in choline acetyltransferase activity, and (c) decrease in muscarinic cholinergic receptor binding in the frontal cortex and hippocampus [10]. B. monnieri extracts protected neurons from beta-amyloid-induced cell death by suppressing cellular acetylcholinesterase activity. In addition, B. monnieri extract-treated neurons expressed a lower level of reactive oxygen species, suggesting that B. monnieri restrained intracellular oxidative stress [11]. An enriched phytochemical composition of B. monnieri was evaluated for short-term safety and tolerance in healthy adult volunteers.

Centella Asiatica

Centella asiatica belongs to the Apiaceae family and commonly known as gotu kola. Asiaticoside derivatives, including asiatic acid and asiaticoside, were shown to reduce hydrogen peroxide-induced cell death, decrease free radical concentrations, and inhibit beta-amyloid cell death in vitro, suggesting a possible role for gotu kola in the treatment and prevention of Alzheimer’s disease and beta-amyloid toxicity [12]. Centella asiatica extracts reversed the beta-amyloid pathology in the brains of mice and modulated the components of the oxidative process.
stress response [13]. It is one of the important rejuvenating herbs for nerve and brain cells and is believed to be capable of increasing intelligence, longevity, and memory [7].

**Commiphora whighitti**

It belongs to the Burseraceae family. It shows potential role in memory improvement in scopolamine induced memory deficits [14]. Memory enhancing and anti-dementia activity of *Commiphora whighitti* has been reported due to its reduction in acetylcholinesterase contents in the hippocampus [15].

**Curcuma longa**

It belongs to the Zingiberaceae family. It possesses anti-inflammatory activity which is also associated with reduced risk of Alzheimer’s disease [16]. Curcumin reduces the deposition of plaque in the brain. It decreases oxidative stress and amyloid pathology [17]. In a study, low doses of *Curcumin* reduced Aβ level up to 40% in mice with Alzheimer’s disease as compared to control drug. At lower dose curcumin caused 43% decrease in the plaque burden that these Aβ have on the brain of mice with Alzheimer’s disease [17].

**Ginkgo biloba**

*Ginkgo biloba* is the oldest tree on the earth, and it is native to China. *G. biloba* extract treat insufficiency of blood circulation problems, loss of consciousness, headaches, and depression in the elderly [18]. 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 [18]. 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 [19]. 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 Alzheimer’s disease without altering the histopathological consequences of overexpression of β amyloid precursor protein [20]. *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 [21].

**Glycyrrhiza glabra**

It belongs to the Fabaceae family. It contains several bioactive compounds linalool oxide, terpinen, tetramethyl pyrazine, geraniol, benzoic acid, propionic acid, ethyl linolenate, butanediol, feuferaldehyde, methyl ethyl ketone, furfuryl formate, trimethylpyrazine, glycyrrhizin, tannin, and glycyrrhizic acid [22]. [23] Reported that in mice Glycyrrhiza glabra enhances memory. Three dose levels (75, 150, 300 mg/kg) of plant extracts were administered to mice in seven successive days and dose at 150 mg/kg was found effective in memory enhancement.

**Lepidium meyenii**

It belongs to Brassicaceae family. It is known for its improving learning abilities and memory function [24]. It exhibited memory enhancing activity in Alzheimer’s patients. It enhances memory by increasing the level of acetylcholine [25]. It improves experimental memory impairment induced by ovariectomy, due in part to its acetylcholinesterase inhibitory and antioxidant effects [26].

**Magnolia officinalis**

It belongs to the family Magnoliaceae. It improves the scopolamine induced memory deficits (Lee et al., 2009). It inhibits acetyl cholinesterase activity [27]. Magnolol and honokiol derived from *Magnolia officinalis*, have the ability to enhance the choline acetyltransferase effects and inhibit the acetylcholine cleavage and have also been shown to release acetylcholine from the hippocampus [28] Honokiol exhibits anti-inflammatory activity by reactive oxygen species synthesis inhibition [29]. As an anti-inflammatory and antioxidant agent, *Magnolia officinalis* plays an important role in the treatment of Alzheimer [30].

**Tinospora cordifolia**

*Tinospora cordifolia* (Menispermaceae) possesses memory enhancing property on learning and memory in normal and memory deficits animals. *Tinospora cordifolia* mechanism of cognitive enhancement by immunostimulation and increasing the synthesis of acetylcholine, this supplementation of choline enhances the cognitive function [31]. *Tinospora cordifolia* is known
as learning and memory enhancer) in Ayurveda. The pure aqueous extract of the root of *Tinospora cordifolia* was found to enhance verbal learning and logical memory [32].

**Withania somnifera**

*Withania somnifera* (Ashwagandha) is extensively used in Ayurveda as a nervine tonic (http://www.planetayurveda.com/ashwagandha_uses.htm), aphrodisiac, and ‘adaptogen’ and helps the body adapt to stress. *W. somnifera* is a member of the Solanaceae family, and the root is widely used. It is categorized as a rasayana and is believed to possess antioxidant activity, free radical scavenging activity, and an ability to support a healthy immune system [33]. Unlike other adaptogens, which tend to be stimulating, *W. somnifera* has a calming effect and thus may be particularly indicated in people with Alzheimer’s disease [34]. A recent double-blind, randomized, placebo controlled study of the effects of *W. somnifera* on stress found that it reduced symptoms of stress and inability to concentrate and reversed forgetfulness in a dose-dependent manner, and 500 mg/day was more effective [35]. No additional adverse effects were found. *W. somnifera* contains steroidal compounds of great interest to researchers, such as the ergostane-type steroidal lactones, including withanolides A to Y, dehydro withanolide R, withasomniferin A, withasomniferols A to C, withaferin A, and withanone. Other constituents include the phytosterols sitoindosides VII to X and beta-sitosterol as well as alkaloids (for example, ashwagandhine, cuscohygrine, tropine, pseudotropine, isopelletierine, and anaferine), a variety of amino acids (including tryptophan), and high amounts of iron [36]. A subset of these components (withanamides) has shown to scavenge free radicals generated during the initiation and progression of Alzheimer’s disease. Neuronal cell death triggered by amyloid plaques was also blocked by withanamides [37]. Molecular modeling studies showed that withanamides A and C uniquely bind to active motif of beta-amyloid (Aβ 25-35) and prevent fibril formation [38]. Aqueous extracts of *W. somnifera* have been found to increase cholinergic activity, including increases in the acetylcholine content and cholineacetyl transferase activity in rats and this might partly explain the cognition-enhancing and memory-improving effects [39]. In addition to the reconstruction of pre- and post-synapses in the neurons, methanol extracts of *W. somnifera* reversed amyloid peptide-induced memory deficit in mice [40]. These in vivo effects of *W. somnifera* were maintained even after the discontinuance of the drug.

**Conclusion**

Interests in the use of different herbal products increase day by day. As several studies show that the uses of synthetic drugs have side effects, so there is a need of alternative source of drugs which have low or negligible side effects. Medicinal plants contain wide range of bioactive compounds which is an alternative of synthetic drug for the treatment of Alzheimer’s disease. Medicinal plants can improve the quality of life of patients with AD and memory deficits. This review provides the information regarding the role of various medicinal plants against the Alzheimer’s disease.

**References**


