HERBAL APPROACH FOR THE PREVENTION AND TREATMENT OF ALZHEIMER’S DISEASE

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ABSTRACT

Alzheimer’s disease (AD) is the most common form of dementia which occurs among older people above the age of 60 years. The prevalence rate being 0.4 – 1.0% for the age group of 60 – 65 years while 20 – 40% for 85 – 90 years and 55% for above 90 years. Alzheimer’s disease is characterized by massive loss of neurons and disrupted signaling between cells in the brain. The cholinergic deficit in this disease is responsible for much of the short term memory and it leads to progressive loss of memory, deterioration of virtually all intellectual functions, increased apathy, decreased speech function, disorientation and gait irregularities. The currently available drugs for the treatment of Alzheimer’s disease are symptomatic only and produce adverse reactions in the patients thereby having a limited scope for the treatment of the patients. Thus, there is a need to develop a targeted effective therapeutics for the treatment of Alzheimer’s disease which alter the course or progression of the underlying disease. The herbal remedies have become more and more popular in the recent years and have provided very promising benefits to the patients of this disease. The current paper reviews the clinical effects of a few commonly used herbs for the treatment of Alzheimer’s disease.

KEY WORDS

Alzheimer’s disease, Herbal treatment, Acetyl cholinesterase inhibitors

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INTRODUCTION

Dementia is a syndrome with many causes which implies deterioration in cognitive abilities which lead to the impairment of previously successful performance of activities of daily living. The most common causes of dementia are Alzheimer’s disease, vascular dementia, alcoholism, Parkinson’s disease and drug intoxication\(^1\). The current paper focuses on the herbal approach to prevention and treatment of Alzheimer’s disease (AD) which is responsible for about more than 50% of all cases of dementia and most common form in the elderly. According to Zaven Khachaturian “AD is a scientific puzzle, a medical whodunit, a psychological tragedy, a financial disaster and an ethical, legal and political dilemma”\(^2\).

AD is characterized by a progressive process that kills brain cells and destroys synaptic connections known as nerve cells in the brain. The disease is traditionally characterized by the presence of neuritic and senile plaques and neurofibrillary tangles and loss of nerve cells which rely on acetylcholine as a neurotransmitter\(^3\). AD leads to progressive loss of memory, deterioration of virtually all intellectual functions, increased apathy, decreased speech function, disorientation and gait irregularities. The generally acknowledged risk factors for AD include age, family history, ApoE genetics, sex (risk higher in females) and Down’s syndrome\(^4\). Currently, Acetyl cholinesterase (AChE) inhibitors are used for the treatment for AD. In AD, degeneration of presynaptic cholinergic neurons occurs leading to a reduction in the availability of acetylcholine, resulting in an under activation of postsynaptic neurons\(^5\). Commonly used drugs are Tacrine, Donepezil and Rivastigmine. They increase the acetylcholine by inhibiting the breakdown in the synaptic cleft. Benefits from these drugs are limited; they are extremely expensive and can have pronounced side effects (e.g. Tacrine is hepatotoxic). Therefore, a cost effective drug therapy with minimal side effects is required and it is the need of the hour to switch over to natural products for safe and effective medication. Promising leads in the natural products area include Rivastigmine (an analogue of Physostigmine)\(^6\), Galanthamine (from narcisous bulb and the snowdrop) and Huperzine A (from the Chinese herb Huperza serrata)\(^7\).

HERBAL TREATMENTS

BACOPA MONNIERA

Various studies have shown that patients suffering from age-related cognitive decline gain significant benefit from Bacopa monniera both in terms of memory and life quality. In a study conducted in animal model, it has shown to decrease whole brain AChE activity which reflects that Bacopa might prove to be a useful memory restorative agent in the treatment of AD and dementia\(^8\). Loss of cholinergic neuronal activity in the hippocampus is the primary feature of AD. Based on animal study results, bacosides appear to have antioxidant activity in the hippocampus, frontal cortex and striatum\(^9\). Mentat, an herbal formulation mainly containing Bacopa monniera, which has been categorized in Ayurveda as Medharasayanas has shown to improve memory and cognitive deficits associated with chronic illness and aging\(^10\). The results of a clinical trial have shown that Bacopa monniera standardized extract (300 mg twice a day orally) for 6 months results in improvement of some cognitive functions in geriatric patients suffering from AD\(^11\).

CORYDALIS TERNATA

Protopine, an alkaloid from Corydalis ternata shows both anti-cholinesterase and anti-amnesic properties\(^12\,13\). In a screening study, the methanolic extract prepared from tubers of Corydalis ternata was found to have a potent inhibitory activity by the Ellman method which
CROcus SATIVUS

Studies suggest that *Crocus sativus* stigmas extract may have antioxidant and anti-amyloidogenic activity, thus reinforcing ethnopharmacological observations that saffron has a positive effect on cognitive function. The main carotenoid constituent, trans-crocin-4, the digentibiosyl ester of crocetin inhibited Aβ fibrillogenesis formed by the oxidation of amyloid β-peptide in AD. Crocin demonstrated cognitive enhancing activity in mice.

FUMARIA

Various species of Fumaria like *F. asepala, F. capreolata, F. cilicica, F. densiflora* etc. show AChE inhibitory activity by the Ellman method. *F. vaillantii* extract having 94.23% inhibition was applied to the bioactivity directed fractionation in order to isolate the constituents responsible for the activity.

GALANTHUS CAUCASICUS

*Galanthus caucasicus* has been found to be a competitive and selective AChE inhibitor. It is hypothesized that this action might relieve some of the symptoms of AD.

GINKGO BILoba

An extract of *Ginkgo biloba* has been found in several studies to improve the symptoms and slow the progression of AD. It is most effective in early stages of AD and has been shown to have normalized the acetylcholine receptors in the hippocampus area of the brain in aged animals. A study compared the effectiveness of the most common Alzheimer’s drugs, such as Donepezil and Rivastigmine, to that of a Ginkgo extract called EGb761 and was found to be as effective as any of these commonly prescribed drugs in treating the symptoms of AD. A different study found that EGb761 prevents β-amyloid toxicity to brain cells, a key part of the development of the disease.

PANAX GINSENG

Ginseng has been suggested to be beneficial in relation to symptomatic treatment and neuroprotection in age related cognitive disorders. The studies conducted to evaluate the efficacy of *Panax ginseng* in the treatment of AD have demonstrated significant effect in favour of ginseng on the Mini-Mental Status Examination and on Alzheimer’s disease Assessment Scale (ADAS). Researchers have found that even a single oral feeding of ginsenosides Re, Rg1 and Rg3 to APP transgenic mice could reduce the level of Aβ in mice brains. Another study shows that metabolites of ginsenoside are able to antagonize memory impairment, axonal atrophy and synaptic loss in Aβ injected mice. A recent trial examined the effect of 4.5g *Panax ginseng* powder daily for 12 weeks on 58 patients with probable AD, with 39 patients serving as control. The ginseng group gradually improved over the 12 weeks of treatment whereas the placebo group gradually declined.
**HUPERZIA SERRATA**

Huperzine-A is a natural cholinesterase inhibitor from *Huperzia serrata* and has been shown to possess antioxidant and neuroprotective properties thereby suggesting its potential in the treatment of AD\(^{29}\). Three Chinese Double Blind Clinical Trials on Huperzine A on more than 450 patients suggest that it may significantly improve the symptoms of AD\(^{30}\).

**MELISSA OFFICINALIS**

*Melissa officinalis* has been shown to improve the cognitive function and to reduce the agitation in patients with mild to moderate AD. A parallel, randomized, placebo-controlled study assessed the efficacy and safety of *Melissa officinalis* in 42 patients with mild to moderate AD and the results indicated that patients receiving its extract experienced a significant improvement in cognition after 16 weeks of treatment\(^{31}\).

**POLYGONUM MULTIFLORUM**

The dried roots of *Polygonum multiflorum* has been used as a tonic and an antiaging agent in many remedies in traditional Chinese medicine\(^{32}\). THSG is one of the active components extracted from *Polygonum multiflorum* and has been shown to exhibit strong anti-oxidant activity in vitro\(^{33}\). Researchers have shown that THSG can diminish peroxidation levels in the brain in a mouse model of AD\(^{34}\).

**WITHANIA SOMNIFERA**

*Withania somnifera* has been shown to slow, stop, reverse and remove neuritic atrophy and synaptic loss, the main cause for neurodegenerative disorders including AD and dementia as confirmed by several clinical studies\(^{35}\). Another study has shown that chronic oral administration of withanoside IV attenuated the axonal, dendritic and synaptic losses and memory deficits induced by amyloid peptide Aβ in mice\(^{36}\). Oral administration of Ashwagandha to mice reversed the damage to hippocampus and cortex by decreasing neurite atrophy, restoring synapsis and improving memory\(^{37}\). The in-vitro cultured plantlets of *Withania somnifera* have been rooted and acclimatized for field conditions and the methanolic extract prepared from these roots were studied for neurodegenerative disorders\(^{38}\). Administration of the standardized root extracts improved cognitive dysfunction in vivo\(^{39}\). A hydroalcoholic extract of the roots standardized for withanolides and withanoles showed neuroprotective effect in vivo\(^{40}\).

**CATHARANTHUS ROSEUS**

It is used as a treatment for memory loss and mental impairments. Studies have demonstrated that Vinpocetine (an alkaloid present in *Catharanthus roseus*) possess neuroprotective effects\(^{41}\). Several double-blind studies have evaluated Vinpocetine for the treatment of AD and related conditions\(^{42}\). The clinical trials of Vinpocetine on 728 patients with AD have produced significant result in the improvement of Alzheimer’s disease. Further, a 16-week double-blind placebo-controlled trial of Vinpocetine on 203 patients with mild to moderate dementia produced significant benefit in the treated group\(^{42}\).
**ROSMARINUS OFFICINALIS**

It has been found in studies that the essential oil of *Rosmarinus officinalis* has produced a significant decrement in performance of working memory, and impaired reaction times for both memory and attention based tasks. The findings of the study indicate that the olfactory properties of this essential oil can produce objective effects on cognitive performance, as well as subjective effects on mood\(^4\).

**CENTELLA ASIATICA**

The studies have revealed that *Centella asiatica* has ability to prevent cognitive deficits that occur following treatment with Streptozotocin and to protect cholinergic neurons from the toxic effects of aluminium indicating its role in reducing the Alzheimer’s disease neuropathy\(^4\). A study conducted on transgenic animal model to evaluate the efficacy of the extracts of *Centella asiatica* in the management of AD has shown that it possess the potential to modulate the components of the oxidative stress response that has been implicated in the neurodegenerative changes occurring in Alzheimer’s disease\(^4\).

**GLYCyrRHiza GLaBRA**

Recent studies have indicated that the dose of 150 mg/kg of the aqueous extract of Liquorice significantly improved learning and memory of mice\(^4\). The studies conducted on animal model have revealed that 9 mg/kg/day of natural product 2, 2′, 4′- Trihydroxychalcone (TDC) from *Glycyrrhiza glabra* has been found to decrease β Amyloid production and β Amyloid plaque formation. The findings thus demonstrated that the natural product TDC as a new beta-site amyloid precursor protein (APP)-cleaving enzyme1 inhibitor could ameliorate memory impairment in mice, and is expected to be used as a lead compound for further anti-AD reagent development\(^4\).

**FUTURE PROSPECTIVE**

The currently available drugs approved by Food and Drug Administration (FDA), USA are not satisfactory for the treatment and complete cure of AD and they produce various side effects. This demand for a better , economical and abundantly available therapeutics with least side effects. Thus, numerous investigations on medicinal herbs including the studies on animal models followed by clinical trials are required in order to develop effective therapeutic protocols for the management of AD.

**REFERENCES**


