Pharmacognosy Magazine
ISSN: 0973-1296

PHCOG MAG.
An official Publication of Phcog.Net

PHCOG MAG.: General Article

An Ayurvedic strategy for treatment of dementia of Alzheimer's disease

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Abstract

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive dementia leading to a gradual deterioration of intellectual abilities, neuropsychological deficits and personality changes. Dementia of Alzheimer's type is the commonest form of dementia, the other two forms being vascular dementia and mixed dementia. At present, the therapy of Alzheimer's disease is aimed at improving both, cognitive and behavioural symptoms and thereby, quality of life for the patients, but it doesn't cure the disease. Moreover, the cost, side effects and lack of efficacy of conventional drugs has made therapy of Alzheimer's disease difficult to be accepted by large group of people. Hence integrated knowledge of the modern science in the field of neurobiology with that of ancient traditional medicine system is required to identify therapeutics for dementia of the AD. Ayurveda is among one of the oldest form of ancient medicine system and evidences for memory improving herbal drugs are well documented in Ayurveda. Moreover, many herbal plants are screened worldwide for memory improving activity in animal models of AD. Hence, attempt has been made in this review regarding the Ayurvedic concepts of AD and some herbal plants used for treating the dementia of AD with special reference to their mechanism of action as well as pharmacological screening part.

Keywords: Alzheimer's disease; Ayurveda; Treatment; Herbal drugs

Abbreviations: Alzheimer's disease – AD, Extract of Ginkgo biloba – EGb761, Acetylcholinestrase – AChE, Acetylcholine – ACh.

Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by irreversible, progressive loss of memory followed by complete loss of memory (dementia) (1). The cognitive decline is accompanied by impaired performance of daily activities, behavior, speech and visual-spatial perception (2). The disease, along with vascular and mixed dementia, is the commonest form of dementia affecting older people and accounts for 60–65% of dementia cases whereas vascular dementia and mixed dementia account for 15–20% of the cases each (3). The disease progresses further and the complications encountered are anomia (form of aphasia characterized by inability to name objects or difficulty in speech), agnosia (failure to recognize or identify objects) and apraxia (impaired motor activities) and complete loss of memory and learning abilities (4). Epidemiological studies of population reveal that dementia of AD is largely a hidden problem in the world. In India, prevalence rates for dementia increases

exponentially with advancing age. Persons above 40 years of age show 0.43% prevalence whereas those aged above 65 years show 2.44% prevalence. This prevalence rate rises to 54.8% in individuals above 95 years of age. The incidence of women suffering from AD is found to be higher than men (5).

Since the discovery of Alzheimer's disease by Alois Alzheimer, many pathological mechanisms have been proposed which led to the testing of various new treatments. AD is associated with shrinkage of brain tissue, with a localized loss of neurons, mainly in the hippocampus and basal forebrain (6). The brain tissue of patients with Alzheimer's disease exhibits three distinct and characteristic features:

- Neurofibrillatory tangles, NFT (fibrous proteins).
- Neuritic plaques (composed of degenerating axons and dendrites).
- Granulovascular changes.

Additional structural changes include cortical atrophy, ventricular dilation, and deposition of amyloid (glycoprotein) around the cortical blood vessels and reduced brain volume. Selective loss of cholinergic neurons occurs in the pathways to the frontal lobe and hippocampus areas that are important for memory and cognitive functions (7). In contrast to normal brain where APP (amyloid precursor protein) processes into integral proteins by the action of secretases α, due to its elevation in Alzheimer's disease is converted into amyloid β protein that produces aberrant Ca^{+2} channels responsible for accretion into NFT and senile plaques by the action of secretases β and γ (6, 8). A mutation in the APP gene, or expression of the unrelated presenilin genes also facilitates Aβ formation with resultant increase in plaque formation (6).

Many conventional medicine are available in the market for the treatment of one or the other defects and symptoms of the diseases, such as cholinesterase inhibitors like tacrine and donepezil, nootropic agents like piracetam, CNS stimulants and activators like pyritinol, non-steroidal anti-inflammatory drugs (selective COX-2 inhibitors) etc. But none of these drugs have been able to completely cure the disease. Moreover, the adverse effects associated with these drugs like anorexia, epigastric distress, nausea, vomiting, headache, fatigue, sleep disturbances have decreased their use (9). Since conventional system of medicine is yet to provide a radical cure, it is worthwhile to explore new directions for treating memory deterioration in patients with neuro-psychiatric disorders such as Alzheimer's disease (5). So, nowadays-special emphasis is given on the Ayurvedic medicine. Moreover, research effort on medicinal and nootropic herbal drugs has gained momentum in last 5 to 10 years, which has generated substantial data, giving a basis to Ayurvedic remedies for deficits in learning and memory (9).

Ayurveda the "science of life" due to safety aspects and the freedom from numerous side effects has gained tremendous momentum. This traditional system of India, which is also called as "Indian System of Medicine" is the oldest and most complete medical system in the world that dates back to 5000 B.C. (10) and has been practiced for a long period of time with a very strong conceptual base (11). Ayurveda has been derived from the *Vedas* (especially *Artharva Veda*) and *Samhitas*, which gives guidance on health care and describes the medical procedure including surgery and massages of vital energy points (10). Indian people have a tremendous passion for medicinal plants and use them for a wide range of health related applications from common cold to memory improvement and enhancement of general immunity. India has one of the richest plant medical cultures in the world that is of tremendous complementary relevance for assuring health, security to the teeming millions and provides safe herbal drugs to the entire world (12). According to Ayurveda, good health is based on equilibrium of Dosha (humor), Agni (digestive fire), Dhatu (seven body tissues like lymph, blood, muscle, adipose tissue, bone marrow, semen) and Mala (Faeces, urine) (13). In Ayurveda it is considered that body acts in unison of spirit and emotions and for the overall health and well being the equilibrium must be maintained. The use of herbal medicine in spite of being ancient is still widely used (10). Another important thing to be cited is that globalization of Ayurveda has gained momentum in recent years. Many active groups have been formed which are actively engaged in spreading the concept and practice of Ayurveda (11).

So far nervous disorders (Vata Vyadhi) are concerned, Ayurveda describes them as Apasmala (epilepsy), Unmada (pyschosis), Murcha (loss of consciousness, Fainting), Pramoha (impairment in functioning of mind), Vismriti (amnesia) etc (14, 15). In Ayurvedic literature, many herbal drugs have been cited to possess memory-enhancing properties, the evidence of which can be given from Abhang's review of 'Medhya Rasayana' (special class of drugs used for Mental faculties, learning, memory) (16) and from available texts of Ayurvedic physician Charaka (400 B.C.) and Sushruta (500 B.C.) in their respective Samhitas (17).

Essential thing to be cited is that the use of traditional medicines, such as plant extracts, in dementia therapy varies according to the different cultural traditions. In the context of current models of AD, memory-enhancing plants have not been extensively investigated for its pharmacological properties in orthodox Western medicine. The only exception is *Ginkgo biloba* whose therapeutic efficacy has been reported in placebo controlled clinical trials similar to currently prescribed drugs such as tacrine or donepezil. Many Old European reference books on medicinal herbs, have documented plants such as *Salvia officinalis* (sage) and *Melissa*

officinalis (balm) whose cholinergic activities have recently been identified responsible for its memory-improving properties (18).

With limited efficacy of conventional therapies and advances in understanding of pathogenesis of AD has made a timely approach to re-explore historical archives for new drug development. This article reviews herbal drugs used since ancient time for improving learning and memory and recently has gained enormous importance for the treatment of Alzheimer's disease and related memory disorders.

Ginkgo biloba

The standardized ginkgo extract EGb761 has been shown to have four actions: vasoregulatory, cognition enhancement, stress alleviating and at gene-regulation. The major therapeutic components of extract of *Ginkgo biloba* (EGb 761) are believed to be flavonoids, terpenoids, ginkgolides and bilobalide. *Ginkgo biloba* extract accelerates and prolongs activation of microglia and astrocytes at the site of brain injury and it is well known that astrocytes and microglia play a pivotal role in recovery process. It reestablishes homeostasis, synthesis and release of neurotransmitter. Extract of *Ginkgo biloba* (Egb761) has been used for treating cerebral insufficiency. In the double-blind, placebo-controlled trial it stabibilized and improved the cognitive function of patients suffering from dementia. The antioxidant property is regarded for its neuroprotective effect. This is also supported by *in vitro* studies, which showed that EGb761 reduced lipid peroxidation.

Table - 1. ***Herbal drugs used for the treatment of Dementia of Alzheimer's disease***

Sr.no	**Herbal drug**
1.	*Albizzia lebbeck* (Siris)
2.	*Allium sativum* (Lehsun)
3.	*Angelica sinensis*
4.	*Bacopa monneiri* (Brahmi)
5.	*Celastrus paniculatus* (Malkangni)
6.	*Centella asiatica* (Gotu kola)
7.	*Clitoria ternate* (Aparajit)
8.	*Convolvulus pluricaulis* (Shankhpushpi)
9.	*Cordydalis ternate*
10.	*Eugenia caryophyllus* (Laung)
11.	*Evodia rutaecarpa*
12.	*Galanthus nivalis* (Snow drop)
13.	*Ginkgo biloba* (Maiden hair tree)
14.	*Huperzia serrate*
15.	*Hypericum perforatum* (St. John's wort)
16.	*Lawsonia inermis*
17.	*Melissa officinalis* (Lemon balm)
18.	*Narcissus pseudonarcissus* (Daffodil)
19.	*Nardostachys jatamansi* (Jatamansi)
20.	*Nicotiana tobaccum* (Tobacco)
21.	*Paenia lactiflora*
22.	*Paenia suffruticosa* (Paeony)
23.	*Panax ginseng*
24.	*Pegasus lateranarium*
25.	*Pegasus lateranarium*
26.	*Rhodiola rosea*
27.	*Rhodiola sachalinensis*
28.	*Ricinus communis* (Castor)
29.	*Rosmarim officinalis* (Rosemary)
30.	*Salvia officinalis* (Sage)
31.	*Uncaria tomentosa*
32.	*Withania somnifera* (Ashwagandha).

It has some inhibitory effect on monoamineoxidase (MAO) and is said to be involved in neuroprotective effect. nitric oxide (NO) is neuronal messenger whose overproduction initiates neurotoxic effects. The generation of NO to neuronal death includes formation of peroxynitrite, release of intracellular Ca^{+2} and activation of PKC (protein kinase C) and phospholipases. EGb761 scavenges free radicals, reduces Ca^{+2} stimulated events and modulates the signal transduction events through phospholipase A and C and PKC (19).

In placebo controlled, double- blind trial the standardized gingko extract EGb 761 (120 mg per day for a year) produced significant improvements in cognitive function. However, higher dose of extract of ginkgo (240 mg per day) produced better memory improvement than dose 120 mg / day. Short term (6 weeks) utilization of *Ginkgo biloba* extract EGb 761 may prove efficacious in enhancing certain neurocognitive functions. In a double-blind study, 90 patients were treated with a divided dose of 150 mg / day of Li 1370 (kaveri, gingko extract) for a period of 12 weeks, and there was significant improvement in attention and memory. The cognitive enhancing effects of *Ginkgo biloba*extract are more pronounced in individuals aged 50-59 years. Administration of *Ginkgo biloba* extract in healthy individuals for 30 days has shown a significant improvement in unwanted symptoms such as memory loss, difficulties in concentration, fatigue, anxiety and depressed mood. Long- term use has been associated with increased bleeding time and spontaneous hemorrhage. Ginkgo should be used cautiously in patients receiving non steroidal anti inflammatory drugs (NSAIDS) or anticoagulants (5).

It is an ayurvedic plant with apparent anti-anxiety, anti-fatigue and memory enhancing effect attributed to its bacoside A and B (5). This plant has been investigated at Central Drug Research Institute (CDRI), Lucknow, India and is a component of Mentat (Polyherbal preparation). It facilitated acquisition, consolidation and retention of memory in active conditioned avoidance response, Sidman's continuous avoidance response and Foot- shock motivated brightness discrimination in rat. *B. monneiri* increases protein kinase activity and cause new protein synthesis in brain cells, thereby improving learning and memory (20-25). *B. monneiri* favorably decreases stress induced biochemical markers (heat shock protein and lipid peroxides) in all the brain regions particularly in the hippocampus region, which is concerned with learning and memory. *B. monneiri* is also potent anti-oxidant (5). *B. monneiri* improved cognitive deficit induced by phenytoin (25 mg/orally for 14 days). An extract of this plant (memory plus) in the dose of 40 mg/kg orally for 7 days significantly reversed phenytoin induced cognitive impairment without affecting its anticonvulsant efficacy (20-25).

Bacopa monneiri

Table 2. ***Plants improving memory in Alzheimer's disease according to different geographical source*** **(5).**

Geographical source	Plant species	Useful parts	Active constituent
1) India	*1) Allium sativum*	Bulbs	S-allyl Cysteine
	2) Bacopa monnieri	Whole plant	Bacoside A and B
	3) Celastrus paniculatus	Seeds	--
	4) Nicotiana tobacum	Leaves	Nicotine
	5) Withania somnifera	Roots	Withanolides
	6) Ricinus communis	Beans	Ricinine
	7) Salvia officinalis	Leaves	Monoterpenoids
2) China	*1) Ginkgo biloba*	Leaves	Ginkgolides
	2) Huperzia serrata	Moss	Huperzine
	3) Paeonia suffruticosa	Root	Paeonifolin
	4) Evodia rutaecarpae	Root	Dehydro-evodiamine
	5) Angelica sinensis	Root	--
	6) Pegasus laternarius	Tuber	Taurine
	7) Rhodiola Sachalinensis	Rhizome	--
3) U.K.	*1) Galanthus Nivalis*	Bulbs	Galanthamine
	2) Narcissus Pseudonarcissus	Bulbs	Galanthene
	3) Melissa officinalis	Leaves	--
	4) Rosmarinus officinalis	Flowers	--
4) Korea	*1) Corydalis ternate*	Bulbs	Protropine
	2) Korean ginseng	Root	--
5) Japan	*1) Uncaria tomentosa*	Bulbs	Total alkaloid
6) Egypt	*1) Hypericum perforatum*	Root	--
7) West Africa	*1) Physostigma venenosa*	Beans	Physostigmine

Convolvulus pluricaulis

A twining perennial herb, *C. pluricaulis* occurs in the plains of Northern Indian and Bihar. The whole plant is one of the most important medhya rasayana drugs in Ayurveda. Its use improves the balance and vitiation in kapha-vata-pitta doshas. Chemical studies of whole plant have shown the presence of glycosides, coumarins, flavonoids and alkaloids. Shankhapushpine (the alkaloid) has been identified as active principle. *C. pluricaulis* is used traditionally to treat nervous debility as a brain

tonic (26). The plant is reported to be a prominent memory-improving drug. It is used as a psychostimulant and tranquilizer. It is reported to reduce mental tension (27). The drug decreases acetylcholine content of whole brain homogenate but markedly increases in the cortex. 5-HT and catecholamines was raised in cortex. These changes were pronounced in rats subjected to swimming stress (28).

Withania somnifera

The plant has been used in herbal formulations of the Ayurvedic to attenuate a cerebral function deficit in the geriatric population, and to augment the faculty of learning and memory to provide a non-specific host defense. These beneficial effects help the organism to ward off stress and act as an adaptogen (29). The effect of this drug was observed in animal model of AD (ibotenic acid induced lesioning of nucleus basalis magnocellularis) in rats. The drug (50 mg/kg) reversed the cognitive deficit caused by lesions. The mechanism underlying is that *W. Somnifera* induces depletion of acetylcholine (ACh) and catecholamines and increases serotonin and histamine concentration in whole brain. It elicits effect on acetylcholine esterase (AChE) activity in basal forebrain nuclei, with enhancement in M_1 muscarinic cholinergic receptor binding in septum and frontal cortex. The drug also induces an increase in cortical muscarinic ACh receptor capacity. This finding partly explains nootropic action of *W. Somnifera* (30-32).

Centella asiatica

Aqueous extract of *C. asiatica* improved learning and memory in shuttle box, step-down paradigm, and elevated plus maze in rats. It decreases brain levels of malondialdehyde and in turn increases glutathione and catalase level. Thus it exerts antioxidant mechanism in enhancing cognition (33). Double- blind studies revealed favorable effects in mentally retarded children free from epilepsy. This effect was observed after the administration of drug for only 12 weeks. Another double-blind study of 30 mentally retarded children of age from 9 to 13 years with IQ range 55-90 was carried and revealed better intelligence scores and psychological and biochemical parameters after treatment with drug for 9 months (34-36).

Panax ginseng

Ginseng is reported to possess following properties1. Enhances memory2. Protect neurons against ischemic damage3. Possess immunomodulating actions (37). Korean ginseng among its numerous beneficial effects was found to improve memory. It has also been reported to enhance cholinergic activity in animal models and to have neuroprotective effects *in vitro*. Korean red ginseng contains saponins with low ratio of protopanaxodion (PD) and protopanaxatriol (PT). Saponin improves scopolamine-induced learning disability and spatial working memory in mice but saponin with a high PD/PT ratio did not improve memory. Red ginseng ameliorates learning and memory deficits partly through effects on hippocampal formation. American ginseng extract reduced scopolamine induced memory deficits in rats (5).

Narcissus pseudonarcissus

Galanthamine is the constituent present in *N. pseudonarcissus* that is used in treatment of AD. Galanthamine is a long lasting AChE inhibitor. It is relatively selective for AChE over butyrylcholinesterase. The inhibition of AChE slows the degradation of acetylcholine and thus increases the endogenous acetylcholine level. Galanthamine increase the frequency of opening of nicotinic receptor channel, suggesting its role in modulating the activity of nicotinic currents. Galanthamine binds to an allosteric site on the α-subunit of nicotinic ACh receptor. In one study, 65% inhibition of AChE was observed within 2 min of bolus injection of 10 mg Galanthamine, enzyme activity returning to baseline within 24 hours (4).

Huperzia serrata

Plant cholinesterase inhibitor, huperzine derived from Chinese moss *H. serrata*, is helpful in treating dementia of Alzheimer disease. It is a relatively selective inhibitor of cortical and hippocampal cholinesterase. Huperzine ameliorated the impaired memory of aged rats in Morris water maze performance (5). Huperzine has shown promising results for treating Alzheimer's dementia in an 8-week, prospective, double-blind study of 100 patients (38).

Paeonia suffruticosa

Several traditional Chinese medicinal herbs have been investigated for their effects on dementia e.g. paeony (*P. suffruticosa*) is a component of traditional Chinese herbal prescription used for treating dementia. A major component of this plant, paeoniflorin, improves radial maze performance in rats impaired by scopolamine. Other components of paeony root are albiflorin, oxypaeoniflorin and benzyl paeoniflorin. Hacsimijiogem (Japanese herbal medicine) also contains paeony root and part of seven other plants (roots of *Rehmannia glutinosa* var. purpurea and *Aconitum carmichaeli*, fruit of *Cornus officinalis*, rhizomes of *Dioscorea bataten*, *Alisma orientalis*, sclerotium of *Tosia cocos*, bark of *Cinnamomum cassia*). It improves radial maze performance in scopolamine induced memory impaired rats and it also increases brain cholinergic activity. Shimotsuto (Chinese herbal medicine) consists of four herbs Japanese angelica (*Angelica sinensis*) root, cnidium rhizome (*Cnidium officinalis*) paeony root (*Paeonia lactiflora*) and rehmannia root (*Rehmannia glutinosa*). It improves spatial working memory in rats (5).

Physostigma venenosa

Physostigmine obtained from *P. venenosa*, is a cholinesterase inhibitor. It has short half-life *in vivo*, so it cannot be used for memory enhancement (5) but the prescription medication, Rivastigmine, is a physostigmine analogue. A study of 475 patients taking

30 to 36 mg/day of physostigmine enhanced cognitive scores on both Alzheimer's Disease Assessment Scale (ADAS) and Clinical Global Impression of Change (CGIC) with only a few incidents of nausea and diarrhea reported (38).

Salvia officinalis

S. officinalis is a member of labiatae family also has a reputation for memory enhancement. *S. officinalis* has been popular in Ayurvedic medicine to clear emotional disturbance and for promoting calmness and clarity. Amongst a range of different plant extracts tested, *S. officinalis* exerted significant dose-dependent inhibitory effects on acetylcholinesterase. *S. officinalis* was shown to be toxic in high doses on account of its thujone content. However, thujone is not present in significant amount of *Salvia lavenderiaefolia* (Spanish sage), which has equally potent anticholinesterase activity. The active constituents are likely to be monoterpenoids other than thujone, which inhibit acetylcholinesterase (5).

Phytoestrogens

Phytoestrogens have been reported to improve verbal and non-verbal episodic memory. Hippocampal memory circuit comprising of hippocampus, parahippocampul gyrus and temporal lobes mediates the improvement. Cerebral blood flow has been said to be improved in postmenopausal women. Dietary phytoestrogens influences mental abilities, which is said to be controlled by the frontal lobes. Significant improvement was found in peoples consuming high soya diet on test of mental flexibility. It has also been seen that females respond to phytoestrogens in the improvement of memory more than males. However, further studies are required in this concern (39).

Curcuma longa

Curcuma longa is a member of the gingiberacea and has long been used for healing. Among other findings, researchers discovered that *C. longa* (especially the curcumin component) has rich stores of antioxidants and is evidenced by the test-tube studies done in the 1990s. In the body these important disease-fighting substances mop up unstable oxygen molecules called free radicals that can otherwise damage cells. The interest in the plant's potential for preventing neurologic diseases, such as multiple sclerosis (MS) and Alzheimer's disease, was spurred by the realization that elderly Indian populations that consume considerable amounts of turmeric in their diet are far less likely to develop such ailments. Scientists conjecture that *C. longa* benefits such neurologic illnesses by minimizing inflammation, a theory supported by recent findings that people (Westerners in this case) taking anti-inflammatory drugs regularly for arthritis are less likely to develop Alzheimer's disease. Further research in this area is clearly needed before any specific recommendations can be made (40).

Grape seed extract

The grape seed extract (GSE) was evaluated for nootropic activity using conditioned avoidance response in rats. The antioxidant activity of grape seed extract by *in vitro* method was carried out in albino rats. Satyanarayana *et al.*, 2002 evaluated memory-enhancing activity of GSE in scopolamine-induced amnesic model, in which albino rats were trained for conditioned avoidance response (CAR). The results showed higher percentage of avoidance in the grapes seed extract treated groups compared to the vehicle treated control group. The amnesia produced by scopolamine was less in GSE treated groups compared to control. The antioxidant activity of GSE was determined by scavenging the hydroxyl radical activity. It was found to be eight times more potent than ascorbic acid. The nootropic activity of GSE partly appears to be due to its antioxidant (anti stress) and cholinergic action (41).

Clitoria ternata

The effect of alcoholic extract of roots of *C. ternata* on radial maze task performance and associated changes in ACh and AChE activity in the brain after electroshock or scopolamine induced amnesia was investigated by Vyawahare *et al.*, 2002, in which the preselected trained rats were dosed once in a day with either alcoholic extract of roots of *C. ternata* or standard shankhapushpi syrup for ten days. On the 10^{th} day, 60 min after the last dose, animals of respective groups were subjected to electroshock or scopolamine treatment followed by radial maze task performance. Thereafter brain ACh and AChE estimation was carried out. The alcoholic extract of roots of *C. ternata* produced memory retention in 58.33% and 66.66% of rats subjected to electroshock and scopolamine treatment respectively. The action was associated with significant increase in ACh content of whole brain and decrease in AChE activity in different regions of the brain compared with respective controls qualitatively. Similar results were obtained in case of standard Shankhapushpi syrup, which is more effective in this respect. Alcoholic extract of root of *C. ternata* prevented the memory loss induced by electroshock or scopolamine treatment by increasing ACh content in brain. The action is mediated by decreasing AChE activity, thereby preventing destruction of ACh in the brain (42).

Celastrus paniculatus

C. paniculatus belonging to the genus of woody, climbing shrubs is distributed almost all over the India. In folk medicine the seeds are boiled and taken for blood purification. The seeds constitute the drug; they are bitter, and have an unpleasant odour and are traditionally used for sharpening the memory. Recent preclinical studies of the seed extract on male rats showed an improvement in learning and memory in both the shuttle-box and step-through paradigms. The study also demonstrates that the cognitive-enhancing properties of extract of *C. paniculatus* seed could be attributed to its antioxidant effect. Yet another study

investigated the effects of the seed oil of *C. paniculatus* on the 6-day performance of young adult rats in a navigational memory task- in the Morris water maze. These studies confirm the memory boosting properties of *C. paniculatus* (43).

Formulations: (9)

Table 3. ***Plant ingredients of polyherbal formulations marketed in India for treating dementia of Alzheimer's disease:***

Sr.no	Plant ingredient
1.	*Acorus calamus* (Vacha)
2.	*Amomum subulatum* (Badi elaichi)
3.	*Asparagus racemosus* (Shatavar)
4.	*Bacopa monneiri* (Brahmi)
5.	*Butea frondosa* (Dhak, Palash)
6.	*Canscora decussata* (sankha holi)
7.	*Cinnamomum Zeylanicum* (Dalchini)
8.	*Convulvulus pluricaulis* (Shankhpushpi)
9.	*Delphinium denudatum* (Jadwar shireen)
10.	*Elettaria cardamomum* (Choti elaichi)
11.	*Emblica officinalis* (Amla)
12.	*Embelica ribes* (Vayu vidang)
13.	*Eugenia caryophyllus* (Laung)
14.	*Foeniculum vulgare* (Bari saunf)
15.	*Ipomea paniculata* (Vidari kand)
16.	*Nardostachys jatamansi* (Jatamansi)
17.	*Operculum tarpethum* (Nishoth)
18.	*Paenia emodi* (Uood saleeb)
19.	*Pandanus odoratissimus* (Keora)
20.	*Pimpinella anisum* (Saunf)
21.	*Piper aurantiacum* (Renuka)
22.	*Piper longum* (Peepal)
23.	*Prunus amygdalis* (Badam)
24.	*Rosa damascena* (Gulab)
25.	*Sassurea lappa* (Kuth)
26.	*Terminalia belerica* (Bahera)
27.	*Terminalia chebula* (Hareetaki)
28.	*Tinospora cardfolia* (Giloe)
29.	*Valerian wallichi* (Tagar)
30.	*Vetiverica zizinoides* (Khas)
31.	*Withania somnifera* (Ashwagandha)
32.	*Zinziber officinalis* (Adrakh)

Some marketed herbal formulations for treatment of dementia of AD

Mentat Tablets (From Himalaya, India) (44)

Mentat improves mental function by modulation of cholinergic and GABAergic neurotransmission. Mentat helps reduce the level of tribulin, an endogenous monoamine oxidase inhibitor that is elevated in Alzheimer's disease. It ameliorates attention fluctuation and behavioural disorders.

COMBO BLEND (From Viable Herbal Solution, USA) (45)

The herbs in this blend are well known for their ability to increase memory and stimulate mental performance. It is blend of 50% Ginkgo Biloba (24% Flavone Glycosides) and 50% Gotu Kola. Ginkgo Biloba and Gotu Kola are also renowned for their adaptogenic properties. They have been used in traditional medicine to increase mental acuity, improve concentration, improve overall brain function, and in the reduction of stress. This blend has also shown promise in reducing age related memory loss, senility, and dementia. Ginkgo Biloba has been shown to promote circulation to the brain. It is also an antioxidant, which helps protect the brain from dangerous free radicals. Gotu Kola has been used for centuries in India to increase energy, endurance, and mental stamina.

SYRUP SHANKHPUSHPI (From Baidyanath, India) (20)

This drug exhibits Nootropic activity in various animal models. It causes a reduction in the brain AchE activity. But no significant changes are seen on L-glutamate, L-aspartate, and GABA content. The maximum tolerated dose is >40 ml/kg orally, indicating it to be quite safe.

Conclusion

The clinical efficacy of many conventional drugs used in the treatment of the AD is unsatisfactory. Moreover, conventional medicine is primarily oriented towards treatment of disease and the drugs are developed on the concept of elimination of specific cause of disease, whereas in ayurveda medicine the emphasis is given towards prevention, health maintenance and treatment with complete cure and its principle lies in the fact that a disease is product of an imbalance in the body and mental elements. Thus ayurvedic practitioners and researchers in medical sciences can help to improve the AD therapeutics by increasing their involvement. This review highlights some traditionally used medicinal plants, which can be explored for use in the therapy of Alzheimer's disease. Hence, detailed and scientifically designed research on these plants would help to identify safe and effective drugs for AD.

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Milestones and achievements – Phcog.net (2004 -2005)

Phcog.net was started on July 6, 2004

- Development of Website – www.phcog.net
- Initiation of Discussion forum – http://groups.yahoo.com/group/phcog/
- Starting of a forum – www.phcog.net/forum.php
- Started a New Online magazine – **Pharmacognosy** Magazine (PHCOG MAG).
  Editorial team was finalized for the term of three years (2004-2007).
- Release of four issues in 2005.
- Project Phcog Refbase started in the month of May 2005.