Asian Journal of Pharmaceutical and Clinical Research

ROLE OF TRADITIONAL MEDICINE IN NEUROPSYCHOPHARMACOLOGY

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Memory is the ability of an individual to record the information and recall it whenever needed. Dementia is a mental disorder characterized by loss of intellectual ability (judgment or abstract thinking) which invariably involves impairment of memory. The most common cause of dementia is Alzheimers disease (AD), which is a progressive neurodegenerative disorder associated with loss of neurons in distinct brain areas and cord. Stressful conditions are often associated with loss of memory and cognitive functions which may lead to threats of schizophrenia and AD. Traditionally herbal drugs have been used to enhance cognitive functions and to alleviate other functions associate with the AD. A number of medicinal plants per se and medicines derived from these plants have shown memory enhancing properties by virtue of their medicinal constituents. One of the mechanisms suggested to dementia is decreased cholinergic activity in brain. Therefore cholinergic drugs (of plant origin) like: muscarinic agonists (e.g. arecoline, pilocarpine etc.), nicotinic agonists (e.g. nicotine) and cholinesterase inhibitors (e.g. huperzine) can be employed for improving memory. Some other classes of drugs used in dementia are: stimulants or nootropics (e.g. piracetam, amphetamine), putative cerebral vasodilators (e.g. ergot alkaloids, papavarine), calcium channel blocker (e.g. nimodipine). Since allopathic system of medicine provides radical cure so more concentration is provided on natural products to cure dementia, and some excellent results with certain plants justified their use as memory enhancer. Traditional System of medicine already mentioned some plants while recent screening is also going on different plants. Examples of some plants showing promising activity in neuropsychopharmacology are: *Allium sativum, Bacopa monnierae, Centella asiatica, Celastrus paniculatus, Nicotiana tabaccum, Withania somnifera, Ricinus communis, Salvia officinalis, Ginkgo biloba, Huperiza serrata, Angelica sinensis, Korean ginseng, Uncaria tomentosa, Hypericum perforatum, Physostigma venosum, Acorus calmus, Curcuma longa, Terminalia chebula, Crocus sativus, Enhydra fluctuans, Vitex negandu, Valeriana wallichii, Glycyrrhiza glabra* etc.

Rapid industrialization has resulted into various neurons disorder in human which has forced us to look back for cure at our old age system of medicine that is Ayurveda.

Keywords :

INTRODUCTION

Learning is defined as acquisition of information and skills. Subsequent retention of this information is called as memory. In Ayurveda there are three aspects of mental ability

1. Dhi (Process of acquisition/Learning)
2. Dhuti (Process of retention)
3. Smriti (Process of recall)

Any disturbance in these aspects resulted in the loss of mental ability. Dementia and other cognitive disorders like Alzheimers disease (AD) pose a challenge to physicians. Dementia is a serious and common problem that affects more than 4 million Americans and costs society more than $50 billion annually. 10% of persons over age 70 years and 20 to 40% of individuals over age 85 years have clinically identifiable memory loss. Dementia is a syndrome with many causes. A simple definition of dementia is a deterioration in cognitive abilities that impairs the previously successful performance of activities of daily living. Memory is the most common and most important cognitive ability that is lost. Other mental faculties may also be affected such as attention, judgment, comprehension, orientation, learning, calculation, problem solving, mood, and behavior. Agitation or withdrawal, hallucinations, delusions, insomnia, and loss of inhibitions are also common. Individuals with mental retardation and psychosis may become demented if a decline in intellectual function occurs. Many common forms of dementia are progressive, but some dementing illnesses are static and unchanging. Dementia is a chronic condition, whereas delirium is and acute confusional state associated with a change in level of consciousness (ranging from lethargy to agitation).

Memory is a complex function of the brain that has fascinated philosophers and scientists for centuries. Memory is currently viewed as a mental process that uses several storage buffers of differing capacity and duration.

CLASSIFICATION OF MEMORY

Type	Time Interval	Probable Cerebral Location
(1) Sensory		
a) Iconic (Visual)	<1s	Visual cortex
b) Echoic (auditory)	1-2s	Auditory cortex

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(2) Immediate(Primary/working)	30s	Perisylvian cortex, frontal lobe
(3) Recent(Secondary/reference)	Minutes-weeks/months	Hippocampus, recall trip last week
		Mamiliothalamic tract, dorsomedial thalamus.
a) Declarative (explicit)		Limbic system, association cortex
i) Episodic ii) Sementic		
b) Procedural (implicit)		Amygdala, cerebellum, association cortex, frontal lobe and others.
(4) Remote (reference)	Months to years	Association cortex and others

The most common cause of dementia is Alzheimers disease, which is a progressive neurodegenerative disorder associated with loss of neurons in distinct brain areas or spinal cord. Degenerative disease may be sporadic or familial with considerable clinical variability. AD is the most common cause of dementia in elderly. Most of the causes are sporadic with about 10% familial. Epidemiological studies of Indian population reveal that dementia is largely hidden problem in our country. Prevalence rates for dementia increases exponentially with advancing age. Persons above 10 years: 0.43%, above 65 years: 2.44% & above 95 years: 54.8%. AD is the most common cause of dementia in western countries and was first described in 1907 in 55 year old women by Professor Alois Alzheimer in Germany .

Although the cause of AD, is unknown but some factors identified are as follows :

1. Genetic factors; familial AD due to amyloid deposition at different sites of brain because of changes in chromosome 2 (known to encode amyloid precursor protein APP.) and also mutations in genes Pricenilin 1 & 2 located on chromosome 14, 1.
2. Deposition of a form of amyloid; mainly ï•¢-amyloid
3. Hyperphosphorylation of the protein tau; interfere with maintenance of natural microtubule.
4. Expression of specific alleles of Apoprotein E (ApoE); in both sporadic & familial.

The brain in AD is usually atrophic, most evident in frontal, temporal or parietal lobes with involving all cortical areas to some degree. Microscopic changes involving reurafibrallary tangles, hyperphosphorylation of tau protein senile plaques & amyloid angiopathy etc. [1-11]

TREATMENT

The management of Alzheimerâ•™s disease is difficult and frustrating, because there is no specific treatment and the primary focus is on long-tern amelioration of associated behavioral and neurological problems. Building rapport with the patient, family members, and other caregivers is essential to successful management.

Tacrine [1] (tetrahydroaminoacridine) and **Donepezil** [1] (Aricept) are the only drugs presently approved by the U.S. Food and Drug Administration (FDA) for treatment of AD. Their pharmacological action is presumed to be inhibition of cholinesterase, with a resulting increase in cerebral levels of acetylcholine. Double blind placebo controlled crossover studies with cholinesterase inhibitors have shown them to be associated with improved caregiver ratings of patients functioning and with an apparent decreased rate of decline in cognitive test scores over periods of up to 2 years. Such studies are difficult to perform because of the subjective nature of many of the observations and the lack of a uniform rate of decline among patients. Nevertheless, a small but important minority of AD patients (approximately 10 to 20% appear to show a modest response to these agents and tolerate their side effects (which include dose related nausea, vomiting, diarrhea, bradycardia, and dizziness). Contraindications for cholinesterase inhibitor treatment include liver disease alcoholism, peptic ulcer disease. In a recent prospective observational study, the use of estrogen replacement therapy appeared to protect by about 50% - against development of AD in women.

Since Allopathic system of medicine is yet to provide a radical cure, it is worthwhile to look for new directions, which would minimize the memory loss of patients with neuro-psychiatric disorders. The utility of traditional medicines needs to be explored for treating patient with dementia. MENTAT, an Ayurvedic herbal formulation consisting of 26 plant species is reported to reverse scopolamine induced memory impairment in animal models. TRASINA [1] (5 plant species extract) also found to do the same with the surgical lesions of the cholinergic basal forebrain.

In patients with moderately advanced AD a prospective trail of the antioxidants Selegiline, ï•¡-Tocopherol (vitamin E) or both demonstrated no significant benefit on primary outcomes of progression. A randomized double blind placebo-controlled trial of an extract of *Ginkgo biloba* found modest improvement in cognitive function in subjects with AD and vascular dementia. As noted above, several retrospective studies have also suggested a protective effect on dementia of non-steroidal anti-inflammatory

agents; controlled prospective studies are in progress. In an APP mutation mouse model of AD, weekly immunization with AB peptide both prevented the occurrence and reversed the accumulation of amyloid plaques in the brains. [1,12-16]

apparent ant-anxiety activity, ant-fatigue and memory enhancing effects attributed to its Bacosides A & B. Brahmi increases protein kinase activity and decreases stress induced biochemical markers (Heat shock proteins and lipid oxides) in all the brain regions particularly the

SOME PLANTS USED AS MEMORY ENHANCERS

Plants	Useful parts	Active constituents
Allium sativum	Bulb	Sallylcysteine
Bocopa monniera	Whole plant	Bacosides A & B
Celastrus peniculatus	Seeds	Celapagine & Celapanigine
Nicotiana tobaccum	Leaves	Nicotine
Withania somnifera	Roots	Withanolides
Ricinus communis	Beans	Ricinine
Salvia officinalis	Leaves	Monoferpenoid
Ginkgo biloba	Leaves	Ginkgolides
Huperzia serrata	Moss	Huperzine
Angelica sinensis	Root	--
Korean ginseng	Root	--
Uncaria tomentosa	Bulbs	Total alkaloids
Hypericum perforatum	Roots	
Physostigma vennosam	Beans	Physostigmine
Acorus calmus	Rhizomes	asarone& methyl isoeugenol
Curcuma longa	--	Curcumin
Terminalia chebula	Rhizome	Chebulic acid
Crocus sativus		Crocin, Crocetin
Centella asiatica		Madicasoside, Asiaticoside & Brahmoside

Methanolic extract of ripe fruit of *Teminalia chebula* containing phenolic compounds, chebulic acid and gallic acid are reported to bind to NMDA and GABA receptors and believed to promote intellect and memory.[17]

Nicotine obtained from *Nicotiana tobacum* is known to enhance memory in animal models and human volunteers.[17]

Physostagmine obtained from *Physostigma venenosa* is a cholinesterase inhibitor can also be used as memory enhancer.[17]

Panax ginseng (Korean ginseng) among its numerous beneficial effects was found to improve memory.[17]

Salvia offiicinalis (Sage) is the member of family Labiateae, had a reputation of memory enhancement as well as popular Ayurvedic medicine for emotional disturbances and promoting calmness and clarity.[17]

Rosmarinus officinalis (Rosemary) was observed by ancient Greeks to possess memory enhancing property.[18]

Protropine an alkaloid from *Corydalis ternata* shows both anti-cholinesterase and anti-amnesic properties.[18]

Bacopa monniera (Brahmi) is an Ayurvedic plant with hippocampus region which is concerned with the learning and memory.[20-22]

Seed oil of *Celastrus paniculatis* (Malkangni) reversed scopolamine-induced deficits in navigational memory task in young adult rats.[24]

Galanthamine derived from bulbs of *Galanthus nivalis* (Snow drop) is a non-competitive nicotinic-channel activator which may be of added value of AD.[25]

Extracts of *Ginkgo biloba* (Maiden hair tree) leaves contain Ginkgolides which interacts with the cholinergic system and have neuroprotective or regenerative activities. Moreover, the anti-inflammatory role of Ginkgo helps in ameliorating the disease process in AD. Standardized Ginkgo extract EGb 761has been shown to have four actions: vasoregulatory, cognition enhancing, stress alleviating and gene regulatory.[27]

Plant cholinesterase inhibitor, Huperzine, derived from Chinese moss *Huperzia serrata,* which was traditionally used to treat inflammation and fever, is also helpful in AD therapy in China.[28]

Ricinine a neutral alkaloid obtained from extract of pericarp of castor bean i.e. *Ricinus cmmmunis* has shown

memory enhancing property.[27]

Systemic administration of *Withania somnifera* (Ashwagandha) led to differential inhibition of acetyl cholinesterase and enhanced M_1 muscarinic receptor binding in rat brain.[33]

A semi-aquatic medicinal herb *Acorus calamus* is traditionally employed in nervous disorders. It has got prominent action on central nervous system where it improve grasping power, memory, intellect, speech and correct aberrations of emotions, mood and personality of an individual.[35]

Convolvulus pluricaulis (Shankhapushpi) is an indigenous plant commonly mentioned in Ayurveda, as Rasayana is mainly advocated for use in rejuvenation therapy. Most of its constituents like Shankhapushpine, Evolvine,and Betaine are considered as best brain tonic materials. They strengthen brain, brighten the memory and intellect and are indicated in the treatment of memory loss and associated mental disorders like insanity and epilepsy.[18, 36]

Aqueous extract of plant of *Curcuma longa* (Turmeric) demonstrated activity in mice following oral administration, which was associated with the inhibition of brain monoamine oxidase A. Curcumin, the major constituent from this plant was shown to be neuroprotective against ethanol induced brain injury.[37]

Several other herbal drugs which are claimed to possess memory enhancing activity in different traditional systems of medicines are: *Polygala tenuifolia, Biota orientalis, Codonopsis pilosula, Crocus sativus,*[38] *Evodia rutaecarpa, Tinospora cordifolia, Gastrodia elata, Coptis chinensis, Clitoria ternatea, Centella asiatica*[40] and so on.

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