

PLANTS WITH NOOTROPIC ACTIVITY: A REVIEW**Sangeeta Paul*, Balawant Rajawat, Rishu Tiwari**

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Author****Sangeeta Paul**Department of Pharmacy,
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Dementia is a set of symptoms arising in brain and is associated with the impairment of learning capacity, memory, thinking, orientation, language and judgment. According to a recent report by Alzheimer's and related disorders society of India, over 3.7 million people are affected by dementia and it is expected to double by 2030. Various nootropic drugs like physostigmine, rivastigmine, donepezil, galantamine and tacrine are available in the market for treating dementia but they are associated with side effects like excitement, convulsions, tremors and are required to be used cautiously in peptic ulcer, asthmatic and hypotensive patients. India has a diverse variety

of medicinally important plants which have been claimed with beneficial therapeutic effects along with better tolerability in terms of side effects. Many medicinal plants have been claimed to possess learning and memory enhancing activity by different mechanisms like inhibition of AChE, antioxidant effect, induction of neurotrophic factors and cell death mechanisms. Although pre-clinical studies identified promising candidates for dementia, clinical evidences are still need to be studied. This review serve as useful source of information for ready reference for plants with established nootropic activity.

KEYWORDS: nootropic drugs like physostigmine, rivastigmine, donepezil, galantamine and tacrine.

INTRODUCTION

Ayurveda is an ancient system of medicines and developed therapeutic measures for variety of disease and ailments. Agents have been developed to delay ageing and rejuvenating whole functional dynamics of the body system. This kind of rejuvenation therapy is known as the 'Rasayana chikitsa' (rejuvenation therapy). Ayurveda claims that several plants, called as the "Medhya" plants (intellect promoting) herbs are beneficial in cognitive disorders. Now drugs

and natural remedies have been prescribed to enhance memories and prevent from memory deficits in the brain for curing dementia. Memory enhancer herbs enhance the memory and increase the blood circulation in the brain. Nootropics have been employed in cases of degenerative brain disorders such as Alzheimer's or Parkinson's disease, with some success. The effort to find the substances that might enhance brain function is a very difficult one. In the light of above we tried to compile medicinal plant with nootropic activity from literature.

Mentat

BR-16A (Mentat, The Himalaya Drug Co.) consists of Brahmi (*Hydrocotyl asiatica*), Shatavari (*Asparagus racemosus*), Jatamansi (*Nardostachys jatamansi*), Bidarikand (*Ipomoea digitata*), Bachh (*Acorus calamus*), Ashwagandha (*Withania somnifera*), Giloe (*Tinospora cordifolia*), Amla (*Emblica officinalis*), Shankhapushpi (*Evolvulus alsinoides*), Triphala, Kuth (*Saussurea lappa*). Reduction in percentage of time spent in open arms and the per cent preference of open arms for the first arm entry in mice in elevated maze was observed with mentat. Reversal effect of Mentat was enhanced by aniracetam (50 mg/kg) suggesting its nootropic action.[1, Verma et al, 1991]

Phyllanthus amarus

Phyllanthus amarus (*bhumi amla*) is a small herb of euphorbiaceae family widely used in ayurvedic system of medicines for various ailments. Aqueous extract produce dose dependent improvement in memory scores at 50, 100 and 200 mg/kg of young and older mice as measured in elevated plus maze and passive avoidance and reversed amnesia induced by scopolamine at a dose of 0.4 mg/kg and diazepam at a dose of 1 mg/kg and further brain acetylcholinesterase activity was also reduced. [2, Joshi et al, 2007].

Bacopa monnieri

Bacopa monnieri has been referred in Ayurveda since centuries as a "Medhya Rasayan". In a study in Alzheimer's disease patient, consisting of open label non-randomized trial on cognitive function *Bacopa monnieri* standardized extract is administered at 300 mg twice a day daily for 6 months. Baseline scores on Mini Mental State Examination Scale (MMSES) were recorded and patients showed statistically significant improvements in various components of MMSES including orientation, attention and in language component in context of writing, reading & comprehension at the end of study. [3, Goswami et al, 2011]

In another study, the effect of *Bacopa* on scopolamine-induced amnesia is assessed by employing Morris water maze scale to test the amnesic effect of scopolamine and its reversal

by *B. monniera*. *Bacopa monniera* extract attenuates both scopolamine induced anterograde and retrograde amnesia. So *B. monniera*'s effects on cholinergic system may be helpful for developing alternative therapeutic approaches for the treatment of learning and memory disorders.[4,Saraf et al, 2011]

In a study,bacopa monniera standardized extract at a dose of 20 mg/kg, 40 mg/kg, and 80 mg/kg shows improvement in spatial learning performance and enhanced memory retention in spatial learning (T-maze) and passive avoidance tests in rats showing improvement in learning and memory. [5, Vollala et al, 2010]

In a study, effect of bacopa on memory deficit produced by administration of topiramate for treatment of epilepsy in mice is studied . Bacopa significantly reversed Topiramate induced impairment by decreasing escape latency Time , increasing time spent in target quadrant in morris water maze test and decreases AChE levels [6,Kotadia et al, 2011].

Brahmi Rasayana comprises coarse powders of dried leaves of *B. monnieri* ,flower buds of *Eugenia caryophyllus*, seeds of *Elettaria cardamomum* , inner bark of shoots of *Cinnamomum zeylanicum*, and fruits of *Piper longum* and *Piper niger*. Brahmi Rasayana significantly improved learning and memory in young mice and reversed the amnesia induced by both scopolamine (0.4 mg kg i.p.) and natural ageing. [7,Joshi et al,2006]

Bacomind an enriched phytochemical preparation from *Bacopa monnieri* at 225 mg/kg as single oral dose for duration of four months showed significant changes in baseline value of working memory and short time verbal memory in 70.83 percent of children population,significant improvement is seen in logical memory related to personal life suggesting cognitive enhancing activity in children. [8,Usha et al,2008]

Withania somnifera

Ashwagandha (*Withania somnifera*: solanaceae) also known as Indian Ginseng is one of the widely used herbs in the Indian traditional system of medicines. Ashwagandha is also used as an “adaptogen” to help the body cope with daily stress and as a general tonic. Biologically active constituents of Ashwagandha leaves contains alkaloids, saponins , steroidal lactones [10, Konar et al,2011] that possess immune modulatory, anti-stress, anti-oxidant, analgesic, adaptogenic and immunostimulant properties. Several authors have described role of Ashwagandha in neuroregeneration as it contains withanones ,withanolides.

In a study after isolation from methanolic extract of Ashwagandha, withanoside IV is obtained which upon enzymatic action gives sominone. It is shown to improve memory deficit in mice induced by amyloid beta by phosphorylation of RET (a receptor for the glial cell line-derived neurotrophic factor) [9, Tohda et al, 2009]

Alcoholic extract of Ashwagandha, attenuated decreased level of BDNF and GFAP caused by administration of scopolamine. And it also caused scopolamine induced cytotoxicity in IMR32 neuronal and glioma C6 cells. It also causes reversal of down regulation of different neuronal cell markers NF-H (Neurofilament NF-H), MAP2 (Microtubule-associated protein), PSD-95 (Postsynaptic marker protein) and GAP-43 (Growth-associated protein) and glial cell marker GFAP and with upregulation of DNA damage- γ H2AX and oxidative stress- ROS markers on scopolamine treatment. [10, Konar et al, 2011]

Mamsyadi kwatha

Mamsyadi Kwatha is an ayurvedic formulation containing Jatamansi, Ashwagandha and arasika yavani. In a study it causes decrease in trial per minute in rotarod performance model in albino mice significantly ($p < 0.05$) showing its learning enhancing activity. [11, Shreevathsa et al, 2011]

Rosa damascene

Rosa damascene also known as damask rose is a rose hybrid whose flowers are renowned for their fine fragrance, and are commercially harvested for making rose water and rose oil in perfumery. Chloroform extract of the buds of *Rosa damascena* significantly induced the neurite outgrowth activity and inhibited the $A\beta(25-35)$ -induced atrophy and cell death in rats. The length of dendrite in the cells treated with compound isolated from extract are comparable to those of nerve growth factor (NGF) treated cells. [12, Awale et al, 2011]

Scrophularia buergeriana

Scrophularia buergeriana of family scrophulariaceae is a herbaceous flowering plant used in traditional chinese medicines commonly known as figwort. The cognitive-enhancing activities of E-harpagoside and 8-O-E-p-methoxycinnamoylharpagide isolated from *Scrophularia buergeriana* were evaluated in scopolamine-induced amnesic mice by Morris water maze and by passive avoidance tests. E-harpagoside and 8-O-E-p-methoxycinnamoylharpagide [MCA-Hg] isolated from roots of *Scrophularia buergeriana* administered to sprague dawley rat at 2 and 1mg/kg significantly improved the impairment of

reference memory induced by scopolamine in the morris water maze model. Mean escape latency, path length and swimming movement were also improved by both isolates. E-harpagoside and MCA-Hg (2 mg/kg, p.o.) significantly attenuated amnesia induced by scopolamine in passive avoidance test to 70% of the level found in normal control mice and also significantly decreases TBARS level which was accompanied by an increase in the activities or contents of glutathione reductase, SOD and reduced GSH. [13,Jeong et al,2008]

Ipomoea aquatica

Ipomoea aquatica of family convulvaceae is a semiaquatic plant used as a vegetable for its tender leaves and shoots. It is also known as water spinach, water morning glory or water convolvulus. A study is designed to evaluate the acetylcholine enhancing activity of methanolic leaf extract of *Ipomoea aquatica*. It is found that treatment with 200 and 400 mg/kg of extract, for 30 days in neonatal and young adult rats, significantly increases acetylcholine level in their hippocampus as compared to age matched control showing basis for improved learning and memory. [14,Sivaraman et al,2010]

Coriandrum sativum

Coriandrum sativum of the family *umbelliferae* is a widely cultivated spice all over the world. Administration of aqueous extract of fruit of *C. sativum* extract (100, 200 and 300 mg/kg) significantly decreased the stress-induced urinary levels of vanillyl mandilic acid and increased the ascorbic acid excretion levels in rats. The amnesic deficits caused by scopolamine (1mg/kg, i.p.) as assessed in conditioned avoidance response was reversed and it also inhibits lipid peroxidation in rat liver and brain to a greater extent than the standard antioxidant, ascorbic acid.[15,Koppula et al, 2012]

Anethum graveolens

Administration of aqueous extract of *A. graveolens* fruit at a dose of 100,200 and 300 mg/kg dose 1 h prior to induction of stress, inhibited stress-induced increase in vanillyl mandelic acid and cause an increase in ascorbic acid. It also causes changes in cognition when determined by the acquisition, retention and recovery dose-dependently using Cook's pole climbing apparatus in normal and scopolamine-induced amnesic rats and caused significant lipid peroxidation inhibition in both rat liver and brain compared to ascorbic acid showing its anti oxidant,anti stress and memory enhancing activity.[16, Koppula et al,2011]

Pterocarpus marsupium

Administration of methanolic extract of wood of *P. marsupium* at 25 and 50 mg/kg causes significant increase in inflexion ratio and reduction in transfer latency in scopolamine amnesic mice in elevated maze and improved the impairment of spatial memory induced by scopolamine in morris water maze showing promising learning enhancing activity.[17, Chauhan et al,2012]

Michelia champaca

Hexane extracts of leaves of *Michelia champaca* at 200 mg/kg shows better learning behaviour in scopolamine amnesic wistar mice in rectangular maze and Y maze test. Results are close as that for the standard drug Brahmi. [18, Ahmad et al,2011]

Embilica officinalis

Embilica officinalis is used in ancient indian traditional phytomedicine to treat various human diseases including neurodegenerative diseases. Hydroalcoholic extract of fruits of *Embilica officinalis* at graded doses of 150, 300, 450 and 600 mg/ kg reversed the amnesia induced by scopolamine significantly as assessed in elevated maze and passive avoidance test and significantly ($p < 0.001$) reversed the rise in malonaldehyde, glutathione and brain acetyl cholinesterase level caused by scopolamine. [19, Golechha et al,2012]. In a study *E.officinalis* churan reversed the amnesia induced by scopolamine (0.4 mg/kg, i.p.) and diazepam (1 mg/kg, i.p.) and also decreases brain cholinesterase activity and total cholesterol . [20, Vasudevan et al,2007]

Cornus officinalis

Oral treatment of mice with methanolic extract of *Cornus officinalis* fruits extract (100 mg/kg) and loganin (1 and 2 mg/kg) significantly mitigated scopolamine-induced memory deficits in passive avoidance test and Morris water maze test, moreover loganin (2 mg/kg) significantly inhibited acetylcholinesterase activity by 45% in mouse hippocampus indicating anti-amnesic activity.[21, Lee et al,2009]

Celastrus paniculata

Jyothismathi oil made from seeds of *C paniculata*, at a dose of 400mg/kg cause enhancement in radial arm maze acquisition with chronic administration in adult male wistar rats and a decrease in acetylcholinesterase activity in hypothalamus, frontal cortex and hippocampus leading to increased cholinergic activity in the rat brain. [22, Lekha et al,2010]

Alternanthera sessilis

Aqueous and 95% ethanolic extracts of aerial parts of *A. sessilis* at doses of 125 mg/kg, 250 mg/kg and 500 mg/kg for a period of 9 days significantly decrease transfer latency, increases number of entries in to an enclosed arm of scopolamine amnesic mice in elevated plus maze and are highly comparable to standard drug piracetam. [23, Kumar et al, 2011]

Dioscorea composita

Chloroform soluble extract of rhizomes of *D. composita* [200mg/kg] showed significant spatial learning and memory improvement on mice in morris water maze and passive avoidance in scopolamine amnesic test, further extract exert neuroprotective effects on glutamate and hydrogen peroxide- induced neurotoxicity in primary cultured cortical neurons. [24, Yang et al, 2009]

Calotropis procera

Extract of latex of *C. procera* at a dose of 100 and 200mg/kg decreased transfer latencies in elevated plus maze model and also reversed amnesia induced by scopolamine, diazepam and natural ageing and significantly reduced acetylcholinesterase activity at a dose of 100mg/kg indicating its use as a memory restoring agent. [25, Joshi et al, 2011]

Rosa alba

Aqueous extract of calyces of *R. alba* at 100 and 200mg/kg reversed the amnesia induced by diazepam and improve learning and memory of mice as indicated by decreased transfer latency and increased step down latency in elevated plus maze and passive avoidance respectively showing its usefulness as memory restorative agent in treatment of cognitive disorders. [26, Naikwade et al].

Pueraria tuberosa

Alcoholic (50, 75, 100mg/kg) and aqueous extract (100, 200 and 400 mg/kg) of tubers of *P. tuberosa* exert significant increase in inflexion ratio as recorded in elevated plus maze, scopolamine and diazepam induced amnesia. A significant reversal effect was observed on rectal temperature in cloinidine induced hypothermia and reduction of head twitches in lithium induced head twitches model. However no significant reduction in catalepsy scores in haloperidol induced catalepsy model is seen showing that extract shows significant nootropic effect in mice and rats by interacting with cholinergic, GABAnergic, adrenergic and serotonergic systems. [27, Rao et al, 2008]

Mimusops elengi

Alcoholic extract of flowers of *M. elengi* at 200mg/kg shows significant increase in step down latency and decrease in transfer latency of passive avoidance and elevated plus maze test in scopolamine amnesic albino rats when compared to standard drug mentat, as well as cause decrease in acetyl cholinesterase activity showing significant cognitive enhancing activity due to the presence of triterpenoids [28,Hadaginhil et al,2010]. Similar studies is done by Joshi et al to study effect of alcoholic extract of stem bark of *mimusops elengi* at 100 and 200mg/kg in swiss albino mice and shows positive results.[29,Joshi et al,2011]

Salvia lavandulaefolia

A placebo-controlled, double-blind, balanced, crossover design study is developed by Tildesley et al in order to comprehensively assess mood and cognition modulation by *S. lavandulaefolia*. *S. lavandulaefolia* administration causes an improvement on the Speed of Memory T factor. There was also an improvement on the Secondary Memory T factor for the 25-AI dose. Mood was consistently enhanced, with increases in self-rated d alertnessT, dcalmnessT and dcontentednessT following the 50-AI dose and elevated dcalmnessT following 25 AI. These results represent further evidence that *Salvia* is capable of acute modulation of mood and cognition in healthy young adults. [30,Tildesley,2005]

Ziziphus mauritiana

N-Butanolic fraction of methanolic extract of leaves of *Z. mauritiana* causes decrease in the transfer latency and increase in step down latency on the elevated plus maze and passive avoidance paradigm after 24 hrs and an increase in recognition index in object recognition test. Piracetam is used as reference standard. [31,Dureshahwar et al,2012]

Hemedesmus indicus

The chloroform and n-butanol fractions of ethanolic extract of *H. indicus root* (3, 10 and 30 mg/kg, p.o.) is assessed for learning and memory in mice using object recognition, passive avoidance and radial arm maze test. At all doses butanolic fractions shows significant learning and memory enhancing activity [32,Shete et al,2010]

Carum carvi

Carum carvi at doses of 100, 200 and 300 mg/kg body weight one hour prior to induction of stress inhibited the stress induced urinary biochemical changes in a dose dependent manner. But there is no change in excretion of VMA and ascorbic acid through urine in normal

animals at all doses. Measurement of acquisition and retention which is a determinant of cognition in rats appears to be dose dependent. Extract produced significant inhibition of lipid peroxide formation in comparison with ascorbic acid in a dose dependent manner in both liver and brain. Nootropic activity of the extract was studied by conditioned avoidance response using Cook's pole climbing apparatus. The present study provides scientific support for the nootropic, antioxidant and antistress activities of *C. carvi* extract and substantiates its traditional use as a culinary spice in foods as beneficial and scientific in combating stress induced disorders.

B. papyrifera

B. papyrifera (50, 100 and 150 mg/kg) or piracetam (150 mg/kg) showed a decrease in number of days required to learn ($P < 0.05$) and time taken to find food by the learned mice in radial arm maze ($P < 0.01$) and causes a dose dependent improvement in spatial learning in morris water maze . [33, Farshchi et al, 2010]

Vitis vinifera

Methanolic extract and methanolic fraction of resins of *V. vinifera* at 30 and 100 mg/kg significantly ($P < 0.05$) reversed scopolamine-induced amnesia in mice. Both exhibited significant ($P < 0.05$) nootropic activity in passive shock avoidance, elevated plus maze and object recognition models of memory. And decreased lithium induced head twitches, decreased percentage mortality induced by sodium nitrite and modified catalepsy induced by haloperidol. However, hypothermia induced by clonidine was not modified showing its action through 5-HT, DA and ACh. [34, Kakad et al, 2008]

Ginkgo biloba

After the administration of the standardized extract of *Ginkgo biloba* leaves for 3 months at 50, 100 and 150 mg/kg significant differences in the content of monoamines and metabolites between the treatment groups is observed compared to the control after assessment in water maze and hole board test. The increased level of 5-hydroxytryptamine in the hippocampus and 5-HIAA (5-HT metabolite) in the prefrontal cortex correlated positively with the retention of spatial memory, suggesting that long-term administration of *Ginkgo biloba* extract improves spatial memory and motivation with significant changes in the content and metabolism of monoamines in several brain regions. [35, Klin et al, 2009]

Prunus amygdalus

In a study by Haider et al rats were given almond paste orally for 28 days and memory function in rats was assessed by elevated plus maze and radial arm maze. Brain tryptophan, 5-HT and 5-HIAA were estimated at the end of the treatment by HPLC-EC method. A significant improvement in learning and memory was observed of almond treated rats compared to controls. Rats treated with almonds exhibited a significant decrease in food intake and plasma cholesterol levels while the change in growth rate (in terms of percentage) remained comparable between the two groups. Analysis of brain tryptophan monoamines exhibited enhanced tryptophan levels and serotonergic turnover in rat brain following oral intake of almonds. [36,Haider et al, 2012]. *Prunus amygdalus* paste also significantly reverse scopolamine induced amnesia as shown by decrease in transfer latency in elevated maze and step down latency in passive avoidance task and also reduces brain acetyl cholinesterase and reduction in cholesterol and triglycerides and increase in glucose level and hence act as a useful memory restoring agent.[37,Kulkarni SK,2012]

Litchi chinensis

Alcoholic and aqueous extracts of fruit of *L.chinensis* at 100,200 and 400 mg/kg increased Step-down latency, decreased time spent in shock zone & number of errors in Passive avoidance maze. They also cause a significant increase in inflexion ratio in elevated maze in diazepam induced amnesia. In sodium nitrite induced hypoxia both extract shows a significant increase in time for cessation of respiration time in mice.[38,Irene et al, 2012]

Saffron (Crocus sativus)

Chronic systemic administration of hydro alcoholic extract of *C. sativus* when tested in ovariectomized mice at 30mg/kg by both active and passive avoidance tests prevents and treat the learning impairment and memory deficit induced by D-galactose and sodium nitrite in male mice.[39,Dashti et al,2012]

Clitorea ternatia

The extract of *C. ternatia* decreased time required to occupy the central platform (transfer latency) in the elevated plus maze and increased discrimination index in the object recognition test suggesting its nootropic activity.[40,Jain et al,2003]

Hibiscus rosasinensis

Administration of ethyl acetate soluble fraction of the methanol extract of *H. rosasinensis* attenuated amnesia in ageing and scopolamine induced amnesic mice as indicated by

decrease in discrimination index in object recognition test and significant increase in step down latency in passive avoidance test, moreover extract significantly reduced lipid peroxidation and increase level of superoxide dismutase and glutathione showing its memory enhancing activity. [41,Nade et al,2012]. Aqueous extract of calyces of *H. Sabdariffa* also shows nootropic activity at 100 and 200 mg/kg as it decreases the transfer latencies and increased step down latencies significantly in the aged mice and scopolamine induced amnesic mice as compared with piracetam (200 mg/kg, i.p.) and also decreases acetyl cholinesterase activity.[42,Joshi et al,2006]

Lawsonia inermis

Acetone soluble fraction of petroleum ether extract of *Lawsonia inermis* on memory is assessed using elevated maze and passive shock avoidance paradigm at 100mg/kg. In passive shock avoidance paradigm extract significantly reduced latency time and number of mistakes thus antagonizing effect of scopolamine in a dose dependent manner. It also decrease transfer latency time in elevated maze significantly as compared to scopolamine group. Fractions also modified 5HT and NA mediated behaviour. [43, Iyer et al,1998]

Zingiber officinale

Zingiber officinale at 100mg/kg extract significantly improved learning and memory in young mice and also reversed the amnesia induced by diazepam (1 mg/kg, i.p.), and scopolamine (0.4 mg/kg, i.p.). Extract also reversed ageing induced amnesia due to natural ageing of mice and increased whole brain acetyl cholinesterase inhibition activity.[44,Joshi et al,2006]

Daucus carota

Ethanol extract of seeds of *D. carota* commonly known as carrot was administered orally in three doses (100, 200 and 400 mg/kg) for seven successive days to different groups of young and aged rats. Elevated plus-maze, Hebb-Williams maze and hexagonal swimming pool served as the exteroceptive behavioral models for testing memory. At a dose of 200 and 400 mg/kg extract showed significant improvement in memory of young and aged rats and reversed amnesia induced by scopolamine and diazepam. [45, Mani et al,2010]

***Celastrus paniculata*[Malkangini]**

An aqueous seed extract showed antioxidant effect in rat brain, which may be contributed to cognitive enhancing activity observed in vivo (46,Kumar and Gupta 2002a). Oil of seed

reversed scopolamine-induced task deficit (47, Gattu et al,1997). 48,Nalini et al. (1986) reported that treatment of mentally retarded children with the oil produced an improvement in their IQ score.

Centella asiatica

Aqueous extract of the whole plant enhanced cognitive function in rats, which was associated with the in vivo anti-oxidant activity of the extract (49,Kumar and Gupta 2002b). An aqueous leaf extract modulated dopaminergic, serotonic and adrenergic systems in vivo and improved learning and memory (50,Nalini et al . 1992).

Euphoria longans

Aqueous extract of *Euphoria longans* fruit increase step through latency in passive avoidance test [$p < 0.005$] compared to vehicle treated controls ,further immunohistochemical studies reveals that the number of cells immunopositive for brain-derived neurotrophic factor, phosphorylated cAMP response element binding protein and phosphorylated extracellular signal-regulated kinase pERK 1/2 was significantly increased in the hippocampal dentate gyrus and CA1 regions after treatment for 14 days ($P < 0.05$). Doublecortin DCX and 5-bromo-2-deoxyuridine BrdU immunostaining also revealed that extract significantly enhanced survival of immature neurons, but there is no effect on proliferation of neuronal cells in the subgranular zone of dentate gyrus region. [51, park et al,2010].

Discussion and conclusion

Ayurveda emphasizes use of herbs, nutraceuticals or lifestyle changes for controlling age related neurodegenerative disorders. In traditional practice of medicines, various plants have been used for neuroprotection. This review provides some evidence of the benefit of a wide range of herbs for the same. Plants with memory enhancing activity are compiled from various journals to serve as a reference for further research. In majority of the studies, the underlying mechanism was found to be anti acetylcholinesterase activity and free radical scavenging activity with the facilitation of the cholinergic transmission. Most widely used model for screening nootropic activity is elevated maze and passive avoidance paradigm along with other frequently used model like object recognition test, morris water maze test and some studies have also involved radial arm maze and y-maze test. Most of the studies used scopolamine to induce amnesia, other amnestic agents like diazepam,sodium nitrite are also used as well.

Also, many plants reversed age related disorders with unknown mechanisms. However further studies regarding the role of phytoconstituents and compounds responsible for exact mechanism are necessary in order to develop agent for the treatment of various learning and memory related disorders. Further large scale, multicenter studies are necessary to determine the effectiveness of these substances in the cognitive deterioration. Until then, this review provides some evidence of the benefit of a wide range of herbs. The review focuses on several natural memory enhancing herbal plants which are today popular all over the world. The present review is aimed at compiling an up to date and comprehensive review on herbal plants showing nootropic activity and also helps the scientific community to lessen the extensive search which is an integral part of literature survey.

REFERENCES

1. Verma A and Kulkarni S.K. Effect of a Herbal Psychotropic Preparation, BR-16A (Mentat), on Performance of Mice on Elevated Plus-Maze. *Indian Journal of Experimental Biology.*, 1991; 29: 1120.
2. Joshi H and Parle M. Evaluation of the anti-amnesic effects of *Phyllanthus amarus* in mice. *Colombia Médica.*, 2007; 38(2): 132-139.
3. Goswami S, Saoji A, Kumar N, Thawani V, Tiwari M and Thawani M. Effect of *Bacopa monnieri* on Cognitive functions in Alzheimer's disease patients. *International Journal of Collaborative Research on Internal Medicine & Public Health.*, 2011; 3(4): 285-293.
4. Saraf MK, Prabhakar S, Khanduja KL and Anand A. *Bacopa monniera* Attenuates Scopolamine-Induced impairment of Spatial Memory in Mice. *Evidence-Based Complementary and Alternative Medicine.*, 2011; 2011: 1-10.
5. Vollala VR, Upadhyaya S and Nayak S. Effect of *Bacopa monniera* Linn. (brahmi) extract on learning and memory in rats: A behavioral study. *Journal of Veterinary Behavior.*, 2010; 5: 69-74.
6. Kotadia D, Vaibhav S and Krishna KL. Effect of *Bacopa* on memory deficit produced by chronic administration of topiramate in rats. *International Journal of Pharmacy.*, 2011; 1(2): 118-124.
7. Joshi H and Parle M. Brahmi rasayana Improves Learning and Memory in Mice. *Evidence Based Complementary and Alternative Medicines.*, 2006; 3(1): 79-85.
8. Usha PD, Wasim P, Joshua JA, Geetharani P, Murali B, Mayachari AS, Venkateshwarlu K, Saxena VS, Deepak M and Amit A. Bacominde: A Cognitive Enhancer in Children Requiring Individual Education Programme. *Journal of Pharmacology and*

- Toxicology*.2008; 3(4) :302-310. Tohda C and Eri Joyashiki. Somnifene enhances neurite outgrowth and spatial memory mediated by the neurotrophic factor receptor, RET. *Br J Pharmacol.*, 2009; 157(8): 1427–1440.
9. Konar A, Shah N, Singh R, Saxena N, Kaul SC, Wadhwa R and Thakur MK. Protective Role of Ashwagandha Leaf Extract and Its Component Withanone on scopolamine-Induced Changes in the Brain and Brain-Derived Cells. *PloS One.*, 2011; 6(11): 1-12.
 10. Shreevathsa, Ravishankar B, Rao RS, Krishnamurthy MS and Prashanth BK. Mamsyadikwatha as learning enhancer: An Experimental Study. *International Journal of Research in Ayurveda and Pharmacy.*, 2011; 2(5): 1451-1452.
 11. Awale S, Tohda C, Tezuka Y, Miyazaki M and Kadota S. Protective Effects of *Rosa damascena* and Its Active Constituent on $A\beta(25-35)$ -Induced Neuritic Atrophy. *Evidence-Based Complementary and Alternative Medicine.*, 2009; 2011: 1-8.
 12. Jeong EJ, Lee KY, Kim SH, Sung SH, Kim YC. Cognitive-enhancing and antioxidant activities of iridoid glycosides from *Scrophularia buergeriana* in scopolamine-treated mice. *European Journal of Pharmacology.*, 2008; 588: 78–84.
 13. Sivaraman D and Muralidaran P. Nootropic effect of *Ipomoea aquatica* forsk in rat hippocampus. *International Journal of PharmTech Research.*, 2010; 2(1): 475-479.
 14. Koppula S and Choi DK. Anti-Stress and Anti-Amnesic Effects of *Coriandrum sativum* Linn (Umbelliferae) Extract – an Experimental Study in Rats. *Tropical Journal of Pharmaceutical Research.*, 2012; 11(1): 36-42.
 15. Koppula S and Choi DK. *Anethum Graveolens* Linn (Umbelliferae) Extract Attenuates Stress-induced Urinary Biochemical Changes and Improves Cognition in Scopolamine induced Amnesic Rats. *Tropical Journal of Pharmaceutical Research.*, 2011; 10(1): 47-54.
 16. Chauhan B and Chaudhary AK. Memory enhancing activity of methanolic extract of *Pterocarpus marsupium* Roxb. *Phytopharmacology.*, 2012; 2(1): 72-80. 12
 17. Ahmad H, Saxena V, Mishra A, Gupta R and Saraf SA. Procognitive Effects of Hexane Extracts of *Michelia Champaca* Leaves in Normal and Memory Deficit Mice. *Pharmacognosy Communications.*, 2011; 1(2): 30-36.
 18. Golechha M, Bhatia J and Arya DS. Studies on effects of *Emblica officinalis* (Amla) on oxidative stress and cholinergic function in scopolamine induced amnesia in mice. *Journal of Environmental Biology.*, 2012; 33: 95-100.
 19. Vasudevan M, Parle M. Memory enhancing activity of Anwala churna (*Emblica officinalis* Gaertn.):an Ayurvedic preparation., 2007; 91(1): 46-54.

20. Lee KY, Sung SH, Kim SH, Jang YP, Oh TH and Kim YC. Cognitive-enhancing Activity of Logenin Isolated from *Cornus officinalis* in Scopolamine-induced Amnesic Mice. *Arch Pharm Res.*, 2009; 32(5): 677-683.
21. Lekha G, Kumar BP, Rao SN, Arockiasamy I and Mohan K. Cognitive enhancement and Neuroprotective effect of *Celastrus paniculatus* Willd. seed oil (Jyothismati oil) on male Wistar rats. *Journal of Pharmaceutical Science and Technology.*, 2010; 2(2): 130-138.
22. Kumar SM, Rani S, Kumar S and Astalakshmi N. Screening of Aqueous and Ethanolic Extracts of Aerial Parts of *Alternanthera sessilis* Linn. R.br.ex.dc for Nootropic Activity. *Journal of Pharmaceutical Sciences & Research.*, 2011; 3(6): 1294-1297.
23. Yang MH, Yoon KD, Chin YW, Park JH, Kim SH, Kim YC, Kim J. Neuroprotective effects of *Dioscorea opposita* on scopolamine-induced memory impairment in *in vivo* behavioral tests and *in vitro* assays. *Journal of Ethnopharmacology.*, 2009; 121: 130–134.
24. Joshi H , Gavimath CG,Hulekal P, Pattar P, Havannavar V. Investigations on the nootropic potential of Calotropis Procera in mice.*International journal of Pharmaceutical Research and development.*, 2011; 3(11): 8-14.
25. Naikwade NS, Mule SN, Adnaik RS, Magduni CS. Memory enhancing effect of Rose alba in mice. *International Journal of Green Pharmacy.*, 2009; 239-242.
26. Rao NV, Pujar B, Nimbal SK, Shantakumar SM, Satyanarayana S. Nootropic activity of tuber extract of *Pueraria tuberosa* (roxb) .*Indian Journal of Experimental Biology.*, 2008; 46: 591-598.
27. Hadaginhal RV, Tikare V P, Patil KS , Bhanushali MD, Desai NS and Karigar A. Evaluation of cognitive enhancing activity of *Mimusops elengi* linn on albino rats. *International Journal of Research in Ayurveda and Pharmacy.*, 2010; 1(2): 484-492.
28. Joshi H and Parle M. Evaluation of the Memory and Learning Improving Effects of *Mimusops elengi* in Mice. *International Journal of Drug Discovery & Herbal Research.*, 2011; 1(4): 185-192.
29. Tildesley NTJ, Kennedy DO, Perry EK, Ballard CG, Wesnes KA and Scholey AB. Positive modulation of mood and cognitive performance following administration of acute doses of *Salvia lavandulaefolia* essential oil to healthy young volunteers. *Physiology & Behavior.*, 2005; 83: 699–709.
30. Dureshahwar K, Mubashir M, Une HD, Hundekari GI and Dehghan MH. Nootropic activity of *n*-butanolic fraction of methanolic extract of leaves of *Ziziphus mauritiana* Lam. in mice. *Der Pharmacia Sinica.*, 2012; 3(2): 193-198.

31. Shete RV and Bodhankar SL. Hemedesmus indicus: Evaluation of its nootropic effect in mice. *International Journal of Pharma and Bio Sciences.*, 2010; 1(3): 1-10.
32. Farshchi A, Ghiasi G, Farshchi S, Khatabi PM. Effects of *Boswellia Papyrifera* Gum Extract on Learning and Memory in Mice and Rats. *Iranian Journal of Basic Medical Sciences.*, 2010; 13(2): 9-15.
33. Kakad VD, Mohan M, Kasture VS and Kasture SB. Effect of *Vitis vinifera* on memory and behaviour mediated by monoamines. *Journal of Natural Remedies.*, 2008; 8(2): 164 – 172.
34. Klin KB, Piechal A, Joniec I, Pyrzanowska J, Tyszkiewicz EW. Pharmacological and biochemical effects of *Ginkgo biloba* extract on learning, memory consolidation and motor activity in old rats. *Acta Neurobiologiae Experimentalis.*, 2009; 69: 217–231.
35. Haider S, Batool Z and Haleem DJ. Nootropic and hypophagic effects following long term intake of almonds (*Prunus amygdalus*) in rats. *Nutricion Hospitalaria.*, 2012; 27(6): 2109-2115.
36. Kulkarni SK, Kasrure SB and Mengi SA. Efficacy study of *Prunus amygdalus* (almond) nuts in scopolamine-induced amnesia in rats. *Indian Journal of Pharmacology.*, 2010; 42(3): 168-173.
37. Irene PR, Babu DJM1, Ventak Rao N and Sheikh RA. Nootropic activity of fruit extracts of Litchi Chinensis Sonn (Sapindaceae). *International Journal Of Pharmacy&Technology.*, 2012; 4(3): 4795-4804.
38. Dashti MH, Zeinali F, Anvaric M and Hosseini SM. Saffron (*Crocus Sativus* L.) extract prevents and improves D- galactose and sodium nitrite induced memory impairment in mice *EXCLI Journal.*, 2012; 11: 328-337.
39. Jain NN, Ohal CC, Shroff SK, Bhutada RH, Somani RS, Kasture VS and Kasture SB. *Clitoria ternatea* and the CNS. *Pharmacology Biochemistry and Behavior.*, 2003; 75(3): 529-536.
40. Nade VS, Kanhere SV, Kawale LA and Yadav AV. Cognitive enhancing and antioxidant activity of ethyl acetate soluble fraction of the methanol extract of *Hibiscus rosa sinensis* in scopolamine-induced amnesia. *Indian Journal Of Pharmacology.*, 2011; 43(1): 6-12.
41. Joshi H, Parle M. Nootropic Activity of Calyces of *Hibiscus sabdariffa* Linn. *Iranian Journal of Pharmacology and Therapeutics.*, 2006; 5(1): 15-20.
42. Iyer MR, Pal SC, Kasture VS and Kasture SB. Effect of *Lawsonia inermis* on memory and behaviour mediated via monoamine neurotransmitters. *Indian Journal of Pharmacology.*, 1998; 30: 181-185.

43. Joshi H and Parle M. Zingiber officinale :Evaluation of its nootropic effect in mice. *African Journal of Traditional, Complementary and Alternative Medicines.*, 2006; 3(1): 64-74.
44. Mani V, Parle M, Ramasamy K and Majeed ABA. Anti-Dementia Potential of Daucus carota Seed Extract in Rats. *Pharmacologyonline.*, 2010; 1: 552-565.
45. Kumar MHV and Gupta YK. Antioxidant property of Celastrus paniculatus Willd.: A possible mechanism in enhancing cognition. *Phytomedicine.*, 2002; 9(4): 302-311.
46. Gattu M, Boss KL, Terry AV and Buccafusco JJ . Reversal of scopolamine- induced deficits in navigational memory performance by the seed oil of Celastrus *paniculatus* *Pharmacology Biochemistry and Behaviour.*, 1997; 57(4): 793-799.
47. Nalini K, Aroor AR, Kumar KB and Rao A. Studies on biogenic amines and their metabolites in mentally retarded children on Celastrus oil therapy. *Alternative Medicine* 1 , 355-360 .
48. Kumar MHV, Gupta YK Effect of different extracts of Centella asiatica on cognition and markers of oxidative stress in rats. *Journal of Ethno- pharmacology.*, 2002; 79: 253-260.
49. Nalini K, Aroor AR, Karanth KS, Rao A (1992) Effect of Centella asiatica fresh leaf aqueous extract on learning and memory and biogenic amine turnover in albino rats. *Fitoterapia.*, 1992; 63: 232-23.
50. Park SJ, Park DH, Kim DH, Lee S, Yoon BH, Jung WY, Lee KT, Cheong JH, Ryu JH. The memory-enhancing effects of Euphoria longan fruit extract in mice., 2010; 128(1): 160-5