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Herbal Memory Enhancer: A review

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ABSTRACT

Now a day's use of herbal products has been increasing greatly in developing countries. There are various natural products which are used as therapeutic in the treatment for diverse purposes such as loss of memory. Memory is necessary aspect for the human beings. It stores the information temporary or permanently which helps in learning and modify it according to our own need. Loss of memory occurs due to aging or alzheimer's disease. So, there are number of herbal drugs which have cognitive enhancing property due to its chemical constituents. The drugs which are used to enhance memory are called as nootropic drugs. This review article shows memory enhancing property of commonly used plants. The plants which are used for treatment of loss of memory are known as nootropic plants and their constituents are known as smart drugs. These drugs enhance the memory, increase blood circulation and increase acetylcholine level in brain.

Keywords: Nootropic, Memory, Cognitive, Herbal, Enhance.

INTRODUCTION

In brain, memory stores the information temporary or permanently which helps in learning and modify it according to our own need. It is of three types- First: sensory memory- it acts when signals reaches to any of the five senses i.e. sight, hearing, smell, taste and touch. It is for only few seconds. Second: short term memory or working memory- in this memory information remains for only short period of time of 5 minutes. Third: long term memory or permanent memory- in this memory information is stored for long period of time [1]. But now a day's loss of memory occurs due to several factors. There are two major factors i.e. Aging

(changes in structure of brain due to increase in age) and Alzheimer's disease [2]. Loss of memory can be treated with the help of drugs which enhance the memory. Those drugs are called as Nootropic drugs or memory enhancer or cognitive enhancer. The term Nootropic was given by Dr. Giurgea in 1972. He derived it from Greek words noos means mind and tropein means to turn toward. These are heterogeneous compounds of different chemical composition and biological function that are used to enhance learning and memory or overcome from cognitive dysfunction [3]. Piracetam and oxiracetam are nootropic drugs. They are five-membered heterocyclic lactams belonging to the pyrrolidinone class [4]. Nootropic agents help to produce psychological activation. They also have stabilizing effect, enhance centrally acting homoeostatic functions and have less risk of tolerance and physiological dependence when they are compared with psychostimulant [5]. They also have beneficial effects on hypoxia-induced cognitive and memory disorders [6]. Nootropic drugs enhance memory by inhibiting acetylcholinesterase activity and increasing Acetylcholine level in brain. It also decreases oxidative stress in brain [7]. A large number of synthetic drugs have been developed for enhancing memory but due to its side effects people are moving towards herbal treatment. Some herbal nootropic agents are shown in table. 1.

Table 1: Some herbal nootropic plants

S.No.	Plant Name	Family	Part Used
1	*Prunus amygdalus* (Almond)	Rosaceae	Fruit
2	*Zingiber officinale* (Ginger)	*Zingiberaceae*	Rhizome
3	*Ginkgo biloba* (Maidenhair tree)	*Ginkgoaceae*	Leaves
4	*Albizia lebbeck* (rattle pod)	Fabaceae	Dried leaves
5	*Hemidesmus indicus* (Indian sarsaparilla)	Asclepiadaceae	Root
6	*Ocimum sanctum* (Tulsi)	Lamiaceae	Whole plant
7	*Myristica fragrans* (Nutmeg)	*Myristicaceae*	Fruit
8	*Tinospora cordifolia* (Giloy)	*Menispermaceae*	Stem
9	*Thespesia populnea* (Indian Tulip Tree)	Malvaceae	Bark
10	*Emblica offcinalis* (Amla)	*Euphorbiaceae*	Fruit
11	*Argyreia speciosa* (Woolly Morning Glory)	Convolvulaceae	Root
12	*Asparagus racemosus* (Shatavari)	*Liliaceae*	Leaves and tuber
13	*Convolvulus pluricaulis* (Shankhpushpi)	Convolvulaceae	Whole plant
14	*Clerodendron phlomidis* (Arni)	Verbenaceae	Bark
15	*Desmodium gangeticum* (Sarivan)	Leguminosae	Leaves and root
16	*Cissampelos pariera* (Abuta)	*Menispermaceae*	Root
17	*Nardostacys jatamansi*	Valerianaceae	Rhizomes

1. ***Prunus amygdalus*** - Kulkarni et al. showed memory enhancing activity of nuts of *Prunus amygdalus* (PA) belonging to family Rosaceae. They formed paste of nuts with the help of distilled water and administered orally to rats in three doses of 150, 300 and 600 mg/kg/day. They perform elevated plus maze, passive avoidance paradigm, locomotor activity, estimate different biochemical parameters and estimate acetylcholine level in brain. They administered scopolamine in rat which causes amnesia. In elevated plus maze scopolamine increases the transfer latency when compared with the *Prunus amygdalus* administered rat. *Prunus amygdalus* at the above doses shows decrease in transfer latency indicates the improvement in memory. In passive avoidance paradigm step down latency is recorded which is measured when rats put its all paws on the grid floor. The cut off time for step down latency is 180 sec. By the administration of *Prunus amygdalus* to rats shows increase in step down latency when compared with scopolamine induced rats which indicate improvement in memory. Locomotor activity was performed on the actophotometer. In this activity scopolamine did not produce any effect on locomotor activity when control and standard groups were compared with them. Similarly *Prunus amygdalus* administered rats also did not show any effect on locomotor activity. In biochemical estimation blood was taken from fasted rat eye and estimate different parameters by using colorimetric method from the different provided kits. In *Prunus amygdalus* administered rats serum cholesterol and triglyceride level gets reduced and slight increment in glucose level of rats. In estimation of acetylcholine level rat was euthanized by cervical dislocation and brain was removed. The brain was washed with ice cold phosphate buffer and then homogenized in glass Teflon homogenizer. Than enzyme activity was measured with the help of Augustinsson's method of analysis. *Prunus amygdalus* administered rat decreases acetylcholinesterase activity in rats which shows enhancement in memory. They also found that omega 3 fatty acid is main constituent of *Prunus amygdalus* oil which is evaluated from Gas Chromatography Mass Spectroscopy analysis and responsible for memory enhancing activity. They conclude that administration of *Prunus amygdalus* for 7-14 days continuously decreases serum cholesterol and increases Acetylcholine level in brain of rats and thus enhances memory [8].
2. ***Zingiber officinale*** - Joshi et al. showed memory enhancing activity of ethanolic extract of dried rhizomes of *Zingiber officinale* belonging to family

Zingiberaceae. They selected 50 mg/kg and 100 mg/kg dose of extract for swiss mice of weight 18 and 25 g. They perform elevated plus maze, passive avoidance paradigm and estimate acetylcholine level in brain. In elevated plus mazced scopolamine and diazepam induced mice shows increase in transfer latency which indicates destruction of memory whereas ginger extract induced mice shows decrease in transfer latency which indicates enhancement in memory. Similarly in passive avoidance paradigm ginger extract mice shows increase in step down latency as compared to scopolamine and diazepam induced mice which show improvement in memory. They performed brain acetylcholinesterase activity by Ellman method by the determination of yellow colour which was formed by the the reaction of thiocholine with dithiobisnitrobenzoate ions. The optical density of yellow colour is measured 412nm. The protein content was measured by the Folin's method. Formula to calculate acetylcholinesterase activity:

R = δ O.D. X Volume of Assay (3 ml)/E X mg of protein

Where R= rate of enzyme activity in 'n' mole of acetylcholine iodide hydrolyzed / minute / mg protein

δ O.D.= Change in absorbance/minute

E = Extinction coefficient = 13600 / M / cm

They showed that phenytoin increases acetylcholinesterase level whereas piracetam and ginger extract decreases acetylcholinesterase level and thus enhances memory. They conclude that *Zingiber officinale* has inhibitory action on acetylcholinesterase level, anti-inflammatory, antioxidant and neuroprotective activity which helps to enhance memory [9].

3. ***Ginkgo biloba*** - The leaves of *Ginkgo biloba* belonging to family *Ginkgoaceae* is used as memory enhancer. Ginkgolides is the main constituent to enhance the memory. Ginkgo extract EGb 761 has memory enhancing and neuroprotective property [10]. It has two main constituents which is responsible for enhancement of memory i.e. 24% flavanoids and 6% terpenoids. It shows nootropic effect in hippocampal formation [11]. Ginkgo leaves extract is common treatment for cerebral insufficiency which includes concentration and memory, confusion, absence of energy, fatigue and decrease of physical performance, depression and anxiety and mainly associated with aging in many countries such as USA, Europe, France and Germany. It is also used for neuropsychiatric problems. It showed its anti-stress effect by inhibiting the Monoamine oxidase and decreases the formation of glucocorticoid [12].

4. ***Albizia lebbeck*** - Chintawar et.al. showed memory enhancing activity of n-butanolic fraction of dried leaves of *Albizia lebbeck* belonging to family Fabaceae. It contains saponin which helps to enhance learning and memory. In their study fasted albino mice (20-22 g) received 10, 25 or 50 mg/kg of n-butanolic fraction. They performed number of test to check the nootropics activity- passive avoidance test, elevated plus maze, clonidine induced hypothermia, lithium induced head twitch, haloperidol-induced catalepsy, estimation of serotonin, dopamine and gamma amino butyric acid concentration in the mouse brain. In passive avoidance test step down latency was measured by inflexion ratio. Lower doses of n-butanolic fraction shows increased inflexion ratio whereas higher doses of n-butanolic fraction shows decreased inflexion ratio. This indicates that lower doses inhibit the effects of scopolamine whereas higher dose increases the effects of scopolamine. In elevated plus maze transfer latency is also measured by inflexion ratio. So, n-butanolic fraction shows increased inflexion ratio at all the three doses which indicate that all doses inhibit the effect of scopolamine. In clonidine induced hypothermia all the three doses of n-butanolic fraction show decrease in the rectal temperature. There was no effect of n-butanolic fraction on rats in lithium induced head twitch. In haloperidol-induced catalepsy lower doses of n-butanolic fraction shows no effect whereas higher dose increases and continue catalepsy. At lower dose of n-butanolic fraction serotonin level increases by 33% and 44% whereas at higher dose serotonin level decreases by 33%. n-butanolic fraction decreases gamma amino butyric acid level by 30% and 49% at lower doses whereas higher dose increase gamma amino butyric acid level by 14%. Thus lower dose of n-butanolic fraction shows improvement in memory and higher dose of n-butanolic fraction shows adverse effect on memory [13].
5. ***Hemidesmus indicus*** - Roots of *Hemidesmus indicus* belonging to family Asclepiadaceae is also used to enhance memory and learning. Shete et.al. compared the nootropic effects of two fraction of *Hemidesmus indicus* - chloroform fraction of *Hemidesmus indicus* and n-butanol fraction of *Hemidesmus indicus* which is obtained from the ethanolic extract. Analysis of fraction was done by *high-performance thin layer chromatography* method and n-butanol fraction of *Hemidesmus indicus* indicated the presences of various components such as alkaloids, saponin, triterpenoids and carbohydrates. Both the fraction had no or less toxicity according to the OECD guidelines is determined by the acute toxicity study. The Nootropic activity is determined by object

recognition test in which n-butanol fraction of *Hemidesmus indicus* showed greater discrimination index whereas chloroform fraction of *Hemidesmus indicus* did not. They use swiss mice of 18-25g in their study and administered 3, 10, 30 mg/kg p.o. doses of extract to them. They perform step down type of passive avoidance response, Radial arm maze method. In step down type of passive avoidance response n-butanol fraction of *Hemidesmus indicus* showed increase in the step down latency and decreased in latency in search of food in the Radial arm maze which shows the presence of nootropic activity only in the n-butanol fraction of *Hemidesmus indicus* and thus confirms the presence of nootropics activity in *Hemidesmus indicus* They also concluded that *Hemidesmus indicus* has anti-inflammatory and antioxidant activity which helps to enhance memory [14].

6. ***Ocimum sanctum*** - *Ocimum sanctum* belonging to family Lamiaceae used for various beneficial effects such as antistress, anti-ulcer, anti-cancer, anticonvulsant etc. Joshi et al. showed the nootropic effect of aqueous extract of whole dried *Ocimum sanctum* plant. They selected Swiss mice for their experiment and administered 50, 100, 200 mg/kg p.o. to them. They perform elevated plus maze, passive avoidance shock, locomotor activity on them to show the memory enhancing property. They induce amnesia by scopolamine, diazepam. In locomotor activity *Ocimum sanctum* extract shows no effect in their locomotor functions when compared with control group. In elevated plus maze *Ocimum sanctum* extract decreases the transfer latency in both young and aged mice when compared with control group. High dose of *Ocimum sanctum* shows enhancement in memory in aged mice as compared to young mice. In passive avoidance shock *Ocimum sanctum* extract increases step down latency in young mice when compared with control group and reverse the effect of scopolamine and diazepam. Thus *Ocimum sanctum* extract shows the enhancement in memory by enhancing cholinergic transmission [15].

7. ***Myristica fragrans*** - Parle M et al. showed nootropic effect in n-hexane extract of seeds of *Myristica fragrans* belonging to family *Myristicaceae*. They had given 5, 10, and 20 mg/kg p.o for three days to swiss young and aged mice. They perform activity on elevated plus maze, passive avoidance shock by inducing amnesia through scopolamine, diazepam. In elevated plus maze low doses of *Myristica fragrans* extract decreases the transfer latency in both young and aged mice when compared with control group. In passive avoidance shock *Myristica fragrans* extract increases step down latency in young mice when compared with control group and reverse the effect of scopolamine and diazepam. Thus this extract enhances the memory in both

young and aged mice. They concluded that plant extract has anti-inflammatory and antioxidant property [16].

8. ***Tinospora cordifolia*** - Agarwal et al. showed the memory enhancing property of *Tinospora cordifolia* belonging to family *Menispermaceae* on eleven groups of male albino rat of wistar strain of 70-90 days of age. They made two extracts - aqueous extract and alcoholic extract of this plant and give 100 mg/kg of aqueous extract and 200 mg/kg of alcoholic extract. They perform Assessment of learning and memory on Hebb William Maze, passive avoidance apparatus. Cyclosporine is used to induce memory deficits. In Hebb William Maze both alcoholic and aqueous extracts show decline in learning scores and retention memory which indicates the enhancement or improvement of learning and memory. In passive avoidance apparatus both alcoholic and aqueous extracts show increase in step down latency when compared with cyclosporine treated animals. They also perform brain histopathological study by taking brain from euthanized rat and put into 10% formaline than it was stained with cresyl violet and observed hippocampus region under microscope. There were no structural changes observed in the brain of rats when effect of *Tinospora cordifoli* was seen. Cyclosporine shows neurodegenerative features in rats whereas combined effect of both shows improvement in memory and learning. Thus *Tinospora cordifoli* enhances memory by increasing the synthesis of Acetylcholine through supplying of choline which is main constituent of this plant [17].
9. ***Thespesia populnea*** - Vasudevan et al. showed the memory enhancing property of ethanolic extract of *Thespesia populnea* bark belonging to family Malvaceae on male Wistar rats. Animals received 100, 200, 400 mg/kg p.o. for 7 days. Amnesia is induced in rats by scopolamine or diazepam. In elevated plus maze high dose of extract shows decrease in transfer latency which indicates improvement in memory in both young and aged rats. In Hebb William Maze high dose of extract shows decrease in time taken to reach the reward chamber in both young and aged rats when compared with control group and thus improves memory. As this plant extract causes decline in the cholesterol level in rats, so it is used as anti-Alzheimer agent. It has antioxidant property, so it reduces oxidative stress and reduces brain damage. It also increases Acetylcholine synthesis by decreasing cholinesterase activity in brain and hence improves memory [18].
10. ***Emblica offcinalis*** - Vasudevan et al. showed the memory enhancing property of *Emblica offcinalis* belonging to family *Euphorbiaceae*. They selected male Wistar rats for their experiment and administered 50, 100, 200 mg/kg p.o. for

15 days to them. They induce amnesia by scopolamine hydrobromide, diazepam injection. They showed the effect of Anwala churna on rats. They divided the rats into three groups and give low, medium and high dose of Anwala churna. On 15th day rats were trained for elevated plus maze and hebb william maze. Amnesia was induced after 90min. of last dose of administration of test drug. Then memory of animal was measured after 24hrs of administration of drugs inducing amnesia. In elevated plus maze shows decrease in transfer latency and in Hebb William Maze also show decrease in the reward chamber in both young and aged rats and reverse the effect of amnesia producing drugs. Amla increases cholinergic transmission and produce less oxidative stress as it contains ascorbic acid and tannins which have anti-oxidant property and thus help in enhancing the memory [19].

11. ***Argyreia speciosa*** - Joshi et al. showed nootropics effect on aqueous extract of roots of *Argyreia speciosa* belonging to family Convolvulaceae. They selected young and old swiss mice and administered 100, 200 mg/kg p.o. for 6 days. They induce amnesia by Scopolamine hydrobromide. They perform elevated plus maze, passive avoidance shock and estimate brain acetylcholinesterase activity. In elevated plus maze *Argyreia speciosa* decreased the transfer latency in young and aged mice when it is compared with control group which indicates enhancement in memory. In passive avoidance shock *Argyreia speciosa* increase the step down latency which also indicates enhancement in memory. The estimation of brain acetylcholinesterase activity was done by Ellaman method by measuring the formation of yellow colour which is end point and estimates that *Argyreia speciosa* reduces the acetylcholinesterase activity in brain and improves memory. They concluded that aqueous extract of *Argyreia speciosa* showed its memory enhancing effect against diazepam and scopolamine [20].
12. ***Asparagus racemosus*** - Sharma et al. showed the memory enhancing property of ethanolic extract of roots of *Asparagus racemosus* belonging to family *Liliaceae* and ethanolic extract of whole plant of *Convolvulus pluricaulis* belonging to family Convolvulaceae at 200 mg/kg. Both plants extract were analyzed and found that *Asparagus racemosus* contains polyphenols, flavanoids, tannins, saponins, glycosides and *Convolvulus pluricaulis* contains alkaloids, tannins, small amount of sugar. They selected male laka strain young and aged mice for their study. They perform following test- Elevated plus maze, tissue preparation for microscopy, preparation of incubation media and histochemical detection of acetylcholinesterase. They found both drugs showed their effect dose

dependently and have high percentage of retention when compared with standard drug. In tissue preparation for microscopy brain was taken out and cleaned with cold distilled water and then put into 10% calcium formal at 4^0C for 16 hrs. On other day brain was put into sucrose solution and then again cleans with distilled water and cut sections of thickness of 20 µm. They prepared incubation media of yellow green colour and section were putted into it and incubate it for 45 min. Than section was washed with distilled water and put it on slide which was coated with albumin. The slide was dried and purified with xylene and observed under microscope. *Asparagus racemosus* treated group showed increased staining of acetylcholinesterase on CA1 region when compared with control group. Same way *Convolvulus pluricaulis* treated group showed increased staining of acetylcholinesterase on CA3 region when compared with control group. They showed effect of extract of *Asparagus racemosus* against kannic acid which produces neurotoxicity and neurodegeneration in rats. They also showed effect of extract of *Convolvulus pluricaulis* by decreasing norepinephrine level in rats thus help in memory enhancement [21].

13. ***Clerodendron phlomidis*** - Joshi et al. showed memory enhancing activity of aqueous extract of bark of *Clerodendron phlomidis Linn.* belonging to family Verbenaceae in both young and aged swiss mice on elevated plus maze and passive avoidance paradigm. They also estimate the brain acetylcholinesterase activity. The animals received 100, 200 mg/kg p.o. They use Scopolamine and diazepam to induce amnesia in rats. In case of elevated plus maze the aqueous extract of plant decreases transfer latency in both young and aged mice when they were compared with control group and showed protective effect against amnesia. In case passive avoidance paradigm the plant extract increases step down latency on second day when they were compared with control group and this indicates enhancement in memory. In case of estimation of acetylcholinesterase by Ellman method and showed that the plant extract decreases the acetylcholinesterase activity and thus helps to enhances memory. They concluded that plant extract has antichlonesterase agent and thus helps to enhance memory [22].

14. ***Desmodium gangeticum*** - Joshi et al. showed memory enhancing activity of aqueous extract of leaves and roots of *Desmodium gangeticum* belonging to family Leguminosae in scopolamine-induced mice. They selected adult albino mice and administered 100, 200 mg/kg/day p.o. to them. They perform locomotor activity on actophotometer. In this plant extract did not show any effect on locomotor activity when this group was compared with control group which

indicates enhancement of memory. On passive avoidance paradigm the treated group had increase step down latency on second day when it was compared with control group. This also indicates improvement in memory. They also found that in brain of mouse high dose of plant extract increase Acetylcholine level. In mid brain, cerebellum, medulla and cortex of mice plant extract decreases acetylcholinesterase activity whereas scopolamine increases acetylcholinesterase activity. Desmodium gangeticum also has anti-inflammatory and antioxidant property which helps to treat Alzheimer disease. Thus combined effect of all these helps to improve memory [23].

15. ***Cissampelos pariera*** - Kulkarni et al. Showed the memory enhancing activity of hydroalcoholic extract of roots of *Cissampelos pariera* belonging to family *Menispermaceae* in swiss mice of 18-20g or 22-25 g. The root extract was administered in mice at dose of 100, 200, 400-mg/kg p.o. They perform memory enhancement activity on elevated plus maze, passive avoidance paradigm and estimate brain acetylcholinesterase activity. In elevated plus maze 15 groups were prepared and each group contains 6 mice. Lower dose did not show any effect where as higher dose show decrease in transfer latency on 7^{th} and 8^{th} day that indicates improvement in learning and memory and reverse the effect of scopolamine. In passive avoidance paradigm also 15 groups were prepared and each group contains 6 mice. Lower dose did not show any effect where as higher dose show increase in step down latency on 7^{th} and 8^{th} day in young and aged mice that indicates improvement in learning and memory. They also showed effect of acetylcholinesterase level in brain. Low dose of plant extract did not show any effect on cholinesterase activity whereas higher doses show decrease in cholinesterase activity in brain of young and aged mice by using Ellman's kinetic colorimetric method. They concluded that *Cissampelos pariera* extract has anti-inflammatory, antioxidant property which helps to enhances memory. This extract also decreases acetylcholinesterase levels in brain of mice prevents from impaired memory. As it contains benzylisoquinoline alkaloid which inhibits acetylcholinesterase activity in brain and enhances memory [24].
16. ***Nardostacys jatamansi*** - Rahman et al. showed memory enhancing activity of methanolic extract of rhizomes of *Nardostacys jatamansi* DC *belonging to family* Valerianaceae in swiss albino male mice (20-25 gm). The plant extract was administered in mice at dose of 200, 400 mg/kg p.o. They showed memory enhancement on elevated plus maze, passive shock avoidance, y maze, morris water maze, object recognition test, sleep deprivation method. In elevated plus

maze doses of plant extract showed increase in inflexion ratio when it is compared with control group which indicates that extract prevent the memory loss. In passive shock avoidance treated groups showed increase in step down latency which indicates enhancement in memory. Y maze test was done to measure short term memory by measuring percentage alteration which is calculated by following formula-

% Alternation = {(No. of alternations) / (Total arm entries– 2)} x 100.

In this treated group showed rise in % Alternation which denotes that this extract protect from destruction of spatial working memory. In morris water maze treated group showed decline in escape latency which showed that this extract protect from loss of memory. In object recognition test exploration time was measured in which directing the nose towards object or touch the object with nose. Treated group showed decline in exploration time for new and old objects indicates enhancement in memory. They concluded that this plant extract protects from loss of memory and also protects from impairment which occurs because of loss of sleep. As it has antioxidant property, inhibit acetyl cholinesterase activity and increase activity of gamma amino butyric acid and thus helps to enhance memory [25].

CONCLUSION

From the above study it was concluded that herbal drugs play important role against loss of memory. Variety of herbal drugs and their extracts shows improvement in memory on rats. They have property to inhibit acetyl cholinesterase and reduce the risk of Alzheimer disease. Memory enhancement property is mainly shown in aqueous, alcoholic and hydro-alcoholic extract of plants. These extract of plants have ability to enhance memory and prevent from dementia. Thus herbal drugs shows memory enhancement with low side effects.

CONFLICT OF INTEREST

There is no Conflict of Interest for the present study.

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