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A TRADITIONAL APPROACH TO HERBAL NOOTROPIC AGENTS: AN OVERVIEW

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ABSTRACT

Nootropic drugs used as a memory enhancer can improve thinking, memory, and alertness in people with Alzheimer's disease and other disease that affect the mind. Memory is perhaps the most vital of all aspects that differentiates human beings from other animals. However, memory can become faulty due to several reasons, and in that case the person is not able to make full use of his or her potentials. Since ages, drugs and natural remedies have been prescribed to enhance memories in people. 4 million people are thought to be suffering from age related memory and increased risk of developing Alzheimer's disease. Although several nootropic drugs are available to treat memory problems. In recent years research on medicinal plants have been studied for nootropic activity. *Bacopa monnieri* (Brahmi), *Evolvulus alsinoides* (Shankhpushpi), *Withania somnifera* (Ashwagandha), *Acorus calamus* (Bach) etc., are used as a memory enhancer drugs. The abstract refers to several plants with their activity. The main aim of this article is to give up the data reviews on plants with nootropic properties.

INTRODUCTION: Nootropics also referred to as smart drugs, memory enhancers, and cognitive enhancers, are drugs, supplements, nutraceuticals, and functional foods that are purported to improve mental functions such as cognition, memory, intelligence, motivation, attention, and concentration.

Nootropics are thought to work by altering the availability of the brain's supply of neurochemicals (neurotransmitters, enzymes, and hormones), by improving the brain's oxygen supply, or by stimulating nerve growth.

Memory is the ability of an individual to record sensory stimuli, events, information, etc., retain them over short or long periods of time and recall the same at a later date when needed. Poor Memory, lower retention and slow recall and are common problems in today's stressful and competitive world. Age, stress, emotions are conditions that may led to memory loss, amnesia, anxiety, high blood pressure, dementia, to more ominous threat like schizophrenia and Alzheimer's diseases.

MEDICINAL PLANTS WITH NOOTROPICS ACTIVITY AND THEIR BENEFICIAL PROPERTIES:

Plant Name	Ayurvedic /Common Name	Nootropic and other beneficial effect In traditional medicine	Reference(s)
Bacopa monnieri	Brahmi	Improve Memory	01
Acorus calamus	Bach	Improve Memory Functions	02
Withania somnifera	Ashwagandha	Improve Memory Functions	03
Evolvulus alsinoides	Shankhpushpi	Improve Memory Functions	04
Embelica officinalis	Amla	Improve Memory	05
Centella asiatica	Mandookaparni	Improve Memory Functions	06
Prunus amygdalus	Badam	Nerve Tonics	07

Zingiber officinale	Sonth	Improve Memory Functions	08
Celastrus Paniculatus	Malkangni	Improve Memory Functions	09
Foeniculum Vulgare	Bari Saunf	Memory-strengthening effect	10
Panax ginseng	Ginseng, five fingers	Improvement in certain psychomotor functions, Mental health. Enhancing physical performance, Improved fasting blood glucose levels, Elevated mood.	11
Vitis vinifera	Grape seed	Nootropic, Adaptogenic	12
Albizzia lebbeck	Indian Siris	Nootropic, Anxiolytic	13
Clitoria ternatea	Butterfly Pea	Memory enhancer, Nootropic, Antistress, anxiolytic	14
Amazonian herbal	Marapuama	Nootropic	15
Tabernaemontana divaricata	Crape jasmine	Preventing forgetfulness and Improving the memory	16
Leontopodium alpinum	Edelweiss	Memory Enhancer	17
Hypericum perforatum	St. Johnswort	Nootropic, Antiamnestic effects	18
Thespesia populnea	Indian Tulip Tree	Alzheimer's disease	19
Rubia cordifolia Linn.	Indian Madder	Antihyperglycemic, Antistress and Nootropic activity	20
Commiphora whighitii	Guggul	Learning and Memory	21
Glycyrrhiza glabra	Mulethi	Learning and Memory	22
Pueraria tuberosa (Roxb).	Indian Kudzu	Nootropic activity	23
Murraya koenigii	Curry leaf	Antiamnesic	24
Anemarrhena asphodeloides	Zhi Mu	Learning and Memory	25
Cornus officinalis	Dogwood fruit	Anti-amnesic	26
Albizzia julibrissin	Mimosa, Persian Silk Tree	Antidepressant	27
Marsilea minuta Linn	Nardoo, Pepperwort	Antidepressant, In treatment of insomnia	28
Artemisia absinthium L.	Absinth, Green ginger	Improve memory & for the restoration of declining mental function.	29
Leuzea carthamoides	Maral root	Nociception , Anxiety	30
Ptychopetalum olacoides	Muira puama	Improve memory	31
Passiflora actinia	Passion flower	Anxiolytic	32
Eclipta alba	Bhringraj	sedative, muscle-relaxant, anxiolytic, nootropic and anti-stress	33
Eclipta prostrata	False daisy	Prevent dementia & to Enhance memory	34
Ficus religiosa	Peepal Tree	Anti-amnesic	35
Polygala tenuifolia	Chinese Senaga	cognition-enhancing activity	36

***Bacopa monnieri*:** *Bacopa monniera* Linn. (Brahmi) has been used since times immemorial as nerve tonic for Improvement of memory. The chemical constituent responsible for the effect of brahmion learning schedules was identified as a mixture of two saponins designated as bacosides A and B. They also enhanced protein kinase activity and produced an Increase in protein in hippocampus. Bacosides were also found to be safe in regulatory pharmacological and toxicological studies [1].

***Acorus calamus*:** The neuropsycho-pharmacological effect of a polyherbal formulation Bramhi Ghrita (BG) on learning and memory processes in rats by elevated plus maze, and in mice by Morris water maze model. BG contains *Acorus calamu*. Its effect (30, 50 and 100 mg/kg, p.o.) was tested on learning and memory processes. BG may act as a memory enhancer formulation and may also be useful as a supportive adjuvant in the treatment of impaired memory functions [2].

***Withania somnifera*:** *Withania somnifera*, popularly known as Ashwagandha is widely considered as the Indian ginseng. In Ayurveda, it is classified as a rasayana (rejuvenation) and expected to promote physical and mental health, rejuvenate the body in debilitated conditions and increase longevity. The use of *W. somnifera* in various central nervous system (CNS) disorder, neurodegenerative diseases such as Parkinson's and Alzheimer's disorders, tardive dyskinesia, cerebral ischemia, and even in the management of drug addiction [3].

***Evolvulus alsinoides*:** *Evolvulus alsinoides* (EA), considered as Shankhpushpi on learning and memory in rodents. Nootropic activity using Cook and Weidley's pole climbing apparatus, passive avoidance paradigms and active avoidance tests were used to test learning and memory. The ethanol extract of EA and its ethyl acetate and aqueous fractions were evaluated for their memory enhancing properties [4].

***Embelica officinalis*:** The effects of Anwala churna (*Emblica officinalis* Gaertn.), an Ayurvedic preparation on memory increases the total serum cholesterol levels and brain cholinesterase activity in mice. Elevated plus maze and passive avoidance apparatus served as the exteroceptive behavioral models for testing memory. Anwala churna (50, 100 and 200 mg/kg, p.o.) produced a dose-dependent improvement in memory scores of young and aged mice. Anwala churna may prove to be a useful remedy for the management of Alzheimer's disease on account of its multifarious beneficial effects such as, memory improving property, cholesterol lowering property and anticholinesterase activity [5].

***Centella asiatica*:** *Centella asiatica* (L.) is a perennial, creeper, faintly aromatic and a valuable medicinal. *Centella asiatica* is one of the chief herbs for treating skin problems, to heal wounds, for revitalizing the nerves and brain cells, hence primarily known as a "Brain food" in India. *Centella asiatica* is one of the important medicinal plants in the International market of medicinal Plant Trade [6].

***Prunus amygdalus*:** *Prunus amygdalus* (PA) nuts used as cognitive functions, total cholesterol levels and cholinesterase (ChE) activity, learning and memory parameters were evaluated using elevated plus maze (EPM), passive avoidance and motor activity paradigms. PA reduced the brain ChE activity in rat. PA proves to be a useful memory-restorative agent. It would be worthwhile to explore the potential of this plant in the management of Alzheimer's disease [7].

***Zingiber officinale*:** The potential of an ayurvedic rasayana (rejuvenator) drug *Zingiber officinale* Roscoe used as a memory enhancer. Elevated plus maze and passive avoidance paradigm were employed to evaluate learning and memory parameters. Z. officinale significantly increased whole brain acetyl cholinesterase inhibition activity. *Z. officinale* prove to be a useful memory restorative agent in the treatment of dementia seen in the elderly [8].

***Celastrus paniculatus*:** *Celastrus paniculatus* Willd. (Celastraceae) is used for learning and memory. In elevated plus maze model, *Celastrus paniculatus* extract has showed statistically significant improvement in memory process. The estimation of acetylcholinesterase enzyme in rat brain supports the plus maze and passive avoidance test by reducing acetylcholinesterase activity which helps in memory performance [9].

***Foeniculum vulgare*:** *Foeniculum vulgare* Linn. Extract used as a nootropic and anticholinesterase agent in mice. *F. vulgare* extract increased step-down latency and acetylcholinesterase inhibition in mice significantly. *F. vulgare* is employed in treatment of cognitive disorders such as dementia and Alzheimer's disease [10].

***Panax ginseng*:** crude ginseng extracts enhance performance on shock motivated tasks whether such performance enhancements are due to memory-enhancing (nootropic) properties of ginseng. It shows nootropic and anxiolytic effects of the ginseng saponin Rb_1, Rb_1 can improve memory for a visual discrimination task and that the nootropic effect may be related to changes in anxiety [11].

***Vitis vinifera*:** The aerial parts of *Vitis vinifera* (common grape or European grape) have been widely used in Ayurveda to treat a variety of common and stress related disorders. In the present investigation, the seed extract of *V. vinifera* was evaluated for antistress activity in normal and stress induced rats. Furthermore, the extract was studied for nootropic activity in rats and *in-vitro* antioxidant potential to

correlate its antistress activity. The Nootropic activity of *V. vinifera* was evaluated by using the conditioned avoidance response (*CAR*) in rats as described by Cook and Weidley [12].

***Albizzia lebbeck*:** The effect of saponin containing *n*-butanolic fraction (BF) extracted from dried leaves of *Albizzia lebbeck* on learning and memory was studied in albino mice using passive shock avoidance paradigm and the elevated plus maze. The involvement of BF of *A. lebbeck* as monoamine neurotransmitters in the nootropic action has been shown [13].

***Clitoria ternatea* L.:** *Clitoria ternatea* L. (CT) commonly known as 'Butterfly pea', a traditional Ayurvedic medicine, has been used for centuries as a memory enhancer, nootropic, antistress, anxiolytic, antidepressant, anticonvulsant, tranquilizing and sedative agent.Its extracts possess a wide range of pharmacological activities including antimicrobial, antipyretic, anti-inflammatory, analgesic, diuretic, local anesthetic, antidiabetic, insecticidal, blood platelet aggregation-inhibiting and for use as a vascular smooth muscle relaxing properties. [14]

Amazonian herbal: Promnesic, anti-amnesic and AChEI properties were identified in a standardized ethanol extract from *Ptychopetalum olacoides* (POEE), a medicinal plant favored by the elderly in Amazon communities. The purpose of this study was to provide conclusive anticholinesterase activity compatible with the observed promnesic and anti-amnesic effects of POEE in mice, reaffirming the potential of this extract for treating neurodegenerative conditions where a hypo-functioning cholinergic neurotransmission is prominent [15].

***Tabernaemontana divaricata*:** *Tabernaemontana divaricata* (TD), a Thai medicinal herb, has been widely used as an analgesic, sedative, or a cough syrup. Moreover, it has been used in traditional rejuvenation remedies as for preventing forgetfulness and improving the memory [16].

***Leontopodium alpinum*:** *Leontopodium alpinum* ('Edelweiss') enhance cholinergic neurotransmission. The potency to increase synaptic availability of acetylcholine (ACh) in rat brain Isocomene investigated with behavioural tasks in mice. It restored object recognition in scopolamine-impaired mice and showed nootropic effects in the T-maze alternation task in normal and scopolamine-treated mice. Additionally, this sesquiterpene reduced locomotor activity of untreated mice in the open field task, while the activity induced by scopolamine was abolished [17].

***Hypericum perforatum*:** St. John's wort extract is commonly used as a wound healing, anti-inflammatory, anxiolytic, diuretic, antibiotic, antiviral and cancer chemoprotective agent. It also has nootropic and/or antiamnestic effects that single administration of St. John's wort extract (500 mg/kg) caused PPI disruption in rats. The effect of antiamnestic doses of the extract on PPI has not been investigated despite the coexistence of impaired memory and PPI deficit in some neurological disorders [18].

***Thespesia populnea*:** *Thespesia populnea* (Malvaceae) is a large tree found in the tropical regions and coastal forests of India. Various parts of *T. populnea* are found to possess useful medicinal properties, such as antifertility, antibacterial, and anti-inflammatory. The learning and memory parameters were assessed using elevated plus maze and passive avoidance appara. It showed significant improvement in memory of young and aged mice. *T. populnea* bark possessed a powerful memory enhancing activity in mice. Since diminished cholinergic transmission and increased cholesterol levels appear to be responsible for development of amyloid plaques and dementia in Alzheimer patients [19].

***Rubia cordifolia*:** Effect of alcoholic extract of roots of *Rubia cordifolia* investigated on cold restraint induced stress and on scopolamine-induced memory impairment. Alcoholic extract enhanced brain gamma-amino-n-butyric acid (GABA) levels and decreased brain dopamine and plasma corticosterone levels. Acidity and ulcers caused due to cold restraint stress were inhibited by alcoholic extract. Animals treated with alcoholic extract spent more time in open arm in elevated plus maze model. It also antagonized scopolamine induced learning and memory impairment [20].

***Commiphora whighitii*:** Gugulipid, an ethyl acetate extract of the resin of plant *Commiphora whighitii* is an established hypolipidemic agent in clinical practice.

Gugulipid was investigated for its effect on learning and memory, parameters of oxidative stress (GSH and MDA) and acetylcholinesterase (AChE) activity in the STZ (ic)-treated mice. The study demonstrated that gugulipid has significant protective affect against streptozotocin-induced memory deficits model of dementia that can be attributed to anti-oxidant and anti-AChE activity of gugulipid [21].

***Glycyrrhiza glabra*:** Glabridin was isolated from the roots of *Glycyrrhiza glabra* and its effects on cognitive functions and cholinesterase activity were investigated in mice. Glabridin appears to be a promising candidate for memory improvement and it will be worthwhile to explore the potential of glabridin in the management of Alzheimer patients [22].

***Pueraria tuberose*:** Nootropic effect of alcoholic and aqueous extracts of *P. tuberosa* was evaluated by using Elevated Plus Maze (EPM. A significant reversal effect was observed on rectal temperature in CIH model, reduction of head twitches in LIH models. However no significant reduction in catalepsy scores in HIC models were observed with test extracts and standard piracetam. The results indicate that nootropic activity observed tuber extracts of P. tuberosa could be through improved learning and memory either by augmenting the noradrenaline (NA) transmission or by interfering with 5-hydroxytryptamine (5-HT) release ALE and AQE extracts of tubers of *P. tuberosa* (Roxb) and these active principles may be responsible for nootropic activity [23].

***Murraya koenigii*:** *Murraya koenigii* leaves commonly known as curry patta are added routinely to Indian gravy and vegetarian dishes as a favorite condiment. The MKL diets produced a significant dose-dependent improvement in the memory scores of young and aged mice and significantly reduced the amnesia induced by scopolamine (0.4 mg/kg, i.p.) and diazepam (1 mg/kg, i.p.).

The underlying mechanism of action for the observed nootropic effect may be attributed to pro-cholinergic activity and a cholesterol lowering property. Therefore, it would be worthwhile to investigate specifically the therapeutic potential of MKL in the management of Alzheimer patients [24].

***Anemarrhena asphodeloides*:** *Anemarrhena asphodeloides* Bunge. (AA, family Liliaceae), which primarily contains xantones, such as mangiferin, and steroidal saponins, such as timosaponin the memory-enhancing effects of these saponins were investigated in scopolamine-treated mice The memory-enhancing effect of timosaponin AIII (TA3) was greater [25].

***Cornus officinalis*:** The anti-amnesic activity of the methanolic extract of *Cornus officinalis* fruits (COT) and a major constituent, loganin using scopolamine-induced (1 mg/kg body weight, s.c.) amnesic mice with both passive avoidance and the Morris water maze tests. Oral treatment of mice with COT (100 mg/kg body weight) and loganin (1 and 2 mg/kg body weight) significantly mitigated scopolamine-induced memory deficits in passive avoidance test.

In the Morris water maze test, oral treatment of loganin significantly ameliorated scopolamine-induced memory deficits showing the formation of long-term and/or short-term spatial memory. Moreover, loganin (2 mg/kg body weight) significantly inhibited acetylcholinesterase activity by as much as 45% of control in the mouse hippocampus. These results indicate that loganin may exert antiamnesic activity in *in-vivo* through acetylcholine- esterase inhibition [26].

***Albizia julibrissin*:** The antidepressant-like effects of the methylene chloride fraction of *Albizzia julibrissin* (MCAJ) using a tail suspension test in mice was done. MCAJ was orally administered at 50, 100, or 200 mg/kg to mice, 1 h before the tail suspension test [27].

***Marsilea minuta* Linn:** *Marsilea minuta* Linn. (Marsileaceae) has been referred in Indian traditional medicine system (Ayurveda) for the treatment of insomnia and other mental disorders. Marsiline isolated from *Marsilea minuta* also has sedative and anticonvulsant property. Antidepressant activity was studied using forced swimming test (FST), tail suspension test (TST), learned helplessness test (LHT) and 5-hydroxytryptophan (5-HTP) induced head twitches response in rodents [28].

***Artemisia absinthium* L.:** *Artemisia absinthium* L. has long been used as traditional herbal medicine for the treatment of gastric pain, cardiac stimulation, to improve memory and for the restoration of declining mental function. The brain oxidative stress and

damage, and behavioral deficits were significantly attenuated by pre-treatment with the methanol extract of *Artemisia absinthium* (100 mg/kg and 200 mg/kg, p.o.) [29].

***Leuzea carthamoides*:** The effects of *N*-feruloylserotonins, substances isolated from the seeds of *Leuzea carthamoides* (WILLD.), used as nociception and in anxiety. Nociceptive responses were measured using the plantar and tail-flick tests which were administered before and after swimming stress (3 min, water temperature 32°C). Anxiety was evaluated using an elevated plus maze. *N*-feruloylserotonins have selective stress-reducing effects in stress-sensitive animals [30].

***Ptychopetalum olacoides*:** Homemade remedies with *Ptychopetalum olacoides* (PO) roots are used by Amazonian peoples for treating various age-related conditions. *Ptychopetalum olacoides* ethanol extract significantly improved step-down inhibitory avoidance long-term memory in adult and reversed memory deficits in aging mice. Although the acetylcholinesterase inhibitory properties described for this extract may be of relevance for improving memory processes [31].

***Passiflora actinia*:** The leaves of *Passiflora actinia* resulted in anxiolytic-like effects in the elevated plus-maze. At higher doses, a sedative effect is produced and there is also an involvement of $GABA_A$ system in this effect [32].

***Eclipta alba*:** *Eclipta alba* used for sedative, muscle-relaxant, anxiolytic, nootropic and anti-stress activities. The results point towards the potential neuropharmacological activity of the plant *Eclipta alba* as a nootropic and also having the property of attenuating stress induced alterations [33].

***Eclipta prostrate*:** Eclipta prostrata has been used as a traditional medicinal plant to prevent dementia and to enhance memory in Asia. It's potential as a nootropic and as an antioxidant has been reported in mice [34].

***Ficus religiosa*:** *Ficus religiosa* Linn. (Moraceae) is a variety of fig tree. Its figs are known to contain a high serotonergic content, and modulation of serotonergic neurotransmission plays a crucial role in the pathogenesis of amnesia and also used in improvement of memory [35].

***Polygala tenuifolia*:** The cognition-enhancing activity and underlying mechanisms of a triterpenoid saponin (polygalasaponin XXXII, PGS32) is isolated from the roots of *Polygala tenuifolia* Willd. The Morris water maze was used to evaluate the spatial learning and memory. It improves hippocampus-dependent learning and memory, possibly through improvement of synaptic transmission [36].

CONCLUSION: The collection of herbal plants showing the nootropic activity were tabulated from the various journals and were reported above as we can conclude that herbal plants are very rich source of substance which are responsible of increasing nootropic activity.

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