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A REVIEW ON MEDICINAL PLANTS WITH NOOTROPIC ACTIVITIES

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ABSTRACT

Dementia is a brain disorder marked by cognitive dysfunctioning which causes loss of learning, thinking and memory. Nootropic drugs are those which are proclaimed to direct toward boosting the cognitive capabilities. Memory encodes, decodes, and stores information. Cognitive deficits or memory impairment that is present with neuropsychiatric conditions insists adoption of nootropics to improve cognitive abilities. Various drugs that possess nootropic activity are used for treatment of dementia but emerges side effects. To overcome these side effects plants with medicinal importance came into existence. India has wide variety of medicinal plants like *Centella asiatica*, *Clitoria ternatea*, *Ginkgo biloba*, *Curcuma longa* etc that has been claimed for nootropic activity with limited side effects. The current review article rehabilitates knowledge of medicinal plants with nootropic action and refurbishes knowledge on therapeutic and pharmacological actions along with major chemical constituents, safety, and conceivable mechanism of action of the chosen herbs from ayurvedic pharmacopoeia. Simultaneously, it comes up with further investigation and standardization on nootropic herbs.

KEYWORDS: Dementia; Medicinal plants; Nootropic activity, Ayurvedic pharmacopoeia.

INTRODUCTION

Dementia and cognitive deficit turn up to be a huge threat to the humankind in recent times and according to the WHO 2012 report, it was estimated that there are around 35.6 million populations getting adversely affected by dementia in the entire world.[1] Dementia is a gradual process of neurocognitive disorder and distinct by the evolution of numerous cognitive deficits such as aphasia, memory impairment, and also inability to initiate complex behaviors which is seriously sufficient to hamper the normal regular functioning. The present evaluation of 7.7 million different cases every year is a crucial benchmark worldwide, especially given the approximately low heights of heterogeneity among studies.[2] 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. The massive analyses in the territory of medicine and new drug exploration have reformed management of old age complications. Sadly, these advancements have failed to convey considerable cure to dementia associated problems. A few of the newer medications and nutritional therapy was investigated, but the cited notable results seem either too expensive or inconvenient to adapt. The abovementioned facts have aided to move toward conventional medication systems to renovate the chances of normal aging and improved condition of life for the aged persons. Rejuvenation (Rasayana) is the therapy which helps in procrastinating the complexities of aging and deficits correlated with it. It includes curative methods or preparation that on routinely practice will improve memory, immunity, strength, fitness, and thus increases life span. Rasayana preparations consist of individual herb in different medicinal forms and polyherbal mixture directed to target general health and targeted body tissues or aspects. Hence, they could be different types, Ayushkameeya Rasayana (the general health boosters and in long run improves the life span), Vayasthapana Rasayana (the one which delays the aging process), Medhya Rasayana (which shows nootropic actions) and Vyadhipratyaneeka Rasayana (its actions are disease specific).[3] Rasayana herbs that assist to

inhibit agerelated complexities and improve that cognitive faculty are the scope of this paper. Informations used are facts from investigations on animal models or on bioactive conventions with some of preclinical works on humans.

Neurobiological process of memory formation

Brain goes through physcial and chemical changes during learning procedures and memory formation that are addressed as synaptic plasticity. Induction of gene expression and engrossment of different signal transduction pathways includes in production of new synapses among nerve cells.[4] Memory can be categorized mainly into three parts, short-term memory (remains for seconds), long-term memory (remains for long time), intermediate long-term memory(remains for days to weeks). The formation of long term memory includes the binding of neurotransmitter to the N-methyl Daspartate and alpha-amino-3-hydroxy-5-methyl4-isoxazole propionic acid receptor which triggers the molecular events that causes activation of CREB and PKC pathways, leading to formation of new proteins that cement the synaptic connection among two communicating neurons leads to production of long-term memory.[5] Various evidences display the engrossment of NF-kB in the regulation of synaptic plasticity which also revealed the inhibition of NF-kB activity in neurons leads to enhanced cognitive functions.[6] At the initial stage of long-term potentiation (LTP) influx of calcium into NMDA receptor causes activation of calmodulindependent protein kinase and phosphorylation of pre-existing of AMPA glutamate receptor and infusion into the postsynaptic membrane of newly formed AMPA recpetors to glutamate. Receptors of AMPA responds instantly by opening of Na2+ and K+ ion channels that depolarizes cell membrane. Continuity of large number of electrical stimuli develops LTP. CREB mediated process of transcription leads to synapse-specific structural changes.

Medicinal plants with nootropic activity

- ***Evolvulus alsinoides***

Shankhpushpi is another name of *Convolvulus pluricaulis* belongs to Convolvulaceae family. This herb is used as nootropic as it possesses memory potentiating, anxiolytic and tranquilizing properties. Shankhapushpi (Convolvulaceae) is a perennial herb. The major active components (Shankhapushpin, microphyllic acid, and 3, 4-dihydroxycinnamic acid) of this plant show neuroprotection action, protect the brain from oxidative damage, free radical damage or neurotoxicity, and act as cognitive enhancer.[7] Hippocampal area linked with the learning and memory functions exhibits dosedependent elevation in AChE activity in CA1 with AS and CA3 region with Shankhapushpi extracts treatment. This mechanism of the action of Shankhapushpi contributes to its antioxidant, neuroprotective, and cholinergic properties.[8]

- ***Centella asiatica***

Centella asiatica L. is a perennial plant commonly known as gotu kola belongs to Apiaceae family. This whole fresh plant is utilized as a cognitive enhancer for therapeutic purposes.[9] *Centella asiatica* is the herb that has the tendency to boost awareness interval, concentration, and revitalize peripheral nervous system and cerebrum.[10] *Centella asiatica* hinders memory impairment induced by scopolamine through the inhibition of AChE.[11]

- ***Clitoria ternatea***

Clitoria ternatea of Fabaceae family is commonly known as butterfly pea.[12] Dose of 100mg/kg of aqueous root extract when administer to young adult rat groups for 30 days period and to neonatal raised the content of Ach in hippocampus when compare to aged match control groups.[13] Increased content of Ach in hippocampus may also consider as a basis of neurochemical for their upgrade learning process and memory.[14]

- ***Bacopa monnieri***

Bacopa monnieri commonly called as brahmi is one of the members of the Scrophulariaceae family. This plant is known for its various therapeutics aspects such as memory enhancer, hepatoprotective, cognitive enhancer and tranquilizing effects. Presence of saponins, triterpenoids which is also called as bacosides are responsible for memory enhancement.[15]

- ***Emblica officinalis***

Emblica officinalis is a transient plant of family Phyllanthaceae also called as amla. Ayurvedic composition of *Emblica officinalis* acquire some evidences that shows their memory enhancing effects and has been demonstrated as effective cure in the Alzheimer's disease management. Therefore amla acts as potent memory enhancer that ascribe to its quality of reducing brain cholinesterase activity.[16]

- ***Ginkgo biloba***

Ginkgo biloba belongs to Ginkgoaceae family, also called as kew tree.[17] *Ginkgo biloba* serves as an antioxidant by removing free radicals, helps to increase oxygen supply and improves behavioral modification for memory enhancement. In vitro study has shown that extract of ginkgo has anti amyloid effect.[18] This extract also believed to increases transthyretin RNA levels which is a part of betaamyloid transport mechanism that inhibits further amyloid deposition in brain.[19]

- ***Sesamum indicum***

Sesamum indicum is also known as sesame belongs to Pedaliaceae family. Extensively distributed all around the world and is harvested for its palatable seeds that grow in shell. Some plentiful glycosides that are mostly found in *Sesamum indicum* are sesaminol glycosides which are lignin glycosides that show their presence in the seeds of seasame. The protective factor against

Abeta-induced learning and memory deficits in morris water maze test was dietary sesaminol.[20]

- ***Celastrus paniculatus***

Celastrus paniculatus, also known as jyotishmati belongs to Celastraceae family.[21] Aqueous seed extract of *Celastrus paniculatus* improves memory and cognitive function. This plant has shown antiarthritic and antioxidant effects in rat model.[22]

- ***Eclipta alba***

Eclipta alba (Bhringraj) contains a wide variety of phytoconstituents which includes glycosides, polyacetylenes, flavonoids, triterpenoids and alkaloids. *Eclipta alba* is widely used as it possess various medicinal properties like nootropic, muscle-relaxant, sedative, anti-stress and anxiolytic activities.[23] *Eclipta alba* has potential neuropharmacological activity as a nootropic also having the property of attenuating stress induced alterations.[24]

- ***Prunus amygladus***

Prunus amygladus commonly called as (Badam) used as cognitive enhancer. Various parameters like memory and learning, total cholesterol levels and cholinesterase activity were determined using elevated plus maze.[25] In rats *Prunus amygladus* reduced the brain cholinesterase activity. *Prunus amylgladus* demonstrated as a useful memory restoring agent. The potential of this plant would be explore further for the management of Alzheimer's disease.[26]

- ***Phyllanthus amarus***

Phyllanhus 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 200mg/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.[27]

- ***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 general tonics. Biologically active constituents of Ashwagandha leaves contains alkaloids, saponins , steroidal lactones.[28] 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.

- ***Vitis vinifera***

Aerial parts of the plant *Vitis vinifera* have been used in Ayurveda system for the treatment of various stress related disorders.[25] The extract of the seed part of *Vitis vinifera* was evaluated for antistress activity in stress induced rats and normal rats.[26] The methanolic resin extract of *Vitis vinifera* at a dose of 30 mg/kg significantly exhibit nootropic activity in elevated plus maze and in passive shock avoidance.[29]

- ***Curcuma longa***

Curcuma longa belongs to Zingiberaceae family, also known as haldi. *Curcuma longa* possess various therapeutic aspects such as antidepressant, anti-cancer, hepatoprotective, antitumor and anti viral.[30] Extracts of *Curcuma longa* as aqueous reported antidepressant activity in reduction of brain monoamine oxidase type A.[31]

- ***Hibiscus sabdariffa***

Aqueous extract of calyces of *Hibiscus sabdariffa* at 100 and 200mg/kg showed nootropic activity in mice. As the latency transfer and increased step down latency are decreased in aged mice and in amnesic mice treated with scopolamine. Acetyl cholinesterase activity also decreased when compared with piracetam (200 mg/kg).[32]

- ***Terminalia chebula* (Hareetaki)**

According to Ayurveda, fruits of Hareetaki (Combretaceae) are useful in the treatment of asthma, fevers, cough, worms, urinary diseases, and piles; it also shows usefulness in dysentery and chronic diarrhea, vomiting, enlarged liver, and spleen.[33] The phytochemical constituents present are tannic acid, gallic acid, ethyl gallate, chebulagic acid, ascorbic acid.[34] mannitol, tannin, polyphenols, flavonoids, saponins, and alkaloids.[35] Hareetaki is a potential nootropic agent and acts as centrally acting reversible acetylcholinesterase inhibitor and the kind of variations of learning and memory produced by *Terminalia chebula* extract was same to that of donepezil, is one of the best medicines for the treatment of AD.[36] It has shown signs of anti-aging and body strengthening if taken regularly.[37] Hareetaki demonstrated maximal suppression in the TBARS (thiobarbituric acid reactive substance) formation, rehabilitates antioxidant enzyme SOD (superoxide dismutase) from the radiationinduced impairment. The methanol, water, and ethanolic extracts (dried fruit of Hareetaki) exhibit antioxidant activity and neuroprotective effect toward H2 O2 (Hydrogen peroxide)-induced toxicity.[38]

- ***Glycyrrhiza glabra* (Yashtimadhu)**

Yashtimadhu (Fabaceae) is harvested all over India. The major effective constituents are glycyrrhizine.[39] flavanones, and glycyrrhetenic acid.[40] Pseudoaldosteronism,[41] hyperkalemia,[42] and hypertension.[43,44] are the side effect for long-term usage of Yashtimadhu as it is cytotoxic in nature. The rhizomes

and roots extract of Yashtimadhu reported to possess free radical scavenging.[45] cognition,[46] as well as antioxidant efficiency against low-density lipoprotein oxidation.[47] The antihypoxic effects are enhanced by the aqueous extract mostly due to the plant's antioxidant properties.[48]

- ***Thespesia populnea***

Indian tulip tree is another name of *Thespesia populnea* a large tree mainly found in coastal forests of India and in tropical regions. Several parts of *Thespesia populnea* possess medicinal properties such as antibacterial, antiinflammatory and antifertility. By using passive avoidance and elevated plus maze various learning and memory parameters are assessed. Bark of *Thespesia populnea* showed powerful memory enhancing activity in mice.[49]

- ***Rubia cordifolia***

Rubia cordifolia is also known as Indian madder. Alcoholic root extract of *Rubia cordifolia* possess the enhancement in brain gamma-amino-nbutyric acid (GABA) levels and decrease in plasma corticosterone and brain dopamine levels. Scopolamine induced learning and memory impairment are also antagonized.[50]

- ***Tinospora cordifolia* (Guduchi)**

Guduchi (Menispermaceae) is harvested all over India. Guduchi extract (full plant) clinically acts as Medhya.[51] Antimalarial and antileprotic actions are possessed by the roots of the plant.[40] Glycosides, alkaloids, steroids, phenolics, sesquiterpenoid, and polysaccharides are the major chemical constituents of the plant.[52] Zinc and copper (trace elements) present in the plant preserves cells from harmful properties of oxygen radicals developed in the time of immune arousal and it also acts as antioxidants.[53] The plant also proved to possess the lead scavenging action.[54] Learning and memory improving therapeutic power is also present in the plant.[55] Amplified synthesis of acetylcholine and immune stimulation boosts the mechanism of cognitive action.[56]

- ***Nardostachys jatamansi* (Jatamansi)**

Jatamansi (Valerianaceae) is a rhizomatous plant. Rhizome finds therapeutic importance in improvement of cognition and in the treatment of psychiatric disorders.[57] The plant also possesses the capacity to treat cardiovascular disorders, insomnia, and neural diseases.[58] Major chemical components are nardostachysin I, terpenoids, coumarins, and sesquiterpenes. Enhancement of biogenic amine actions and cognition.[59] was found in the rhizome extract. Administration of alcoholic extracts to mice of all ages considerably enhanced cognition and inversed aging amnesia caused by scopolamine and diazepam.[60]

- ***Mucuna pruriens* (Kapikacchu)**

Kapikacchu (Fabaceae), in Ayurveda, different parts (roots, seeds, leaves, and hairs) of the plant are commonly known to be used as nervine, aphrodisiac, and rejuvenating tonic.[61] It is a great supplier of L-3, 4-dihydroxyphenyl alanine as a result, it is therapeutically important in the treatment of PD.[62] It was found to improve semen secretion and it functions as a curative in sexual dysfunction attributed to weakness or loss of sexual power.[63] Seeds of Kapikacchu show lipid-lowering capacity, hypoglycemic, antioxidant, and neuroprotective activity which could be due to the dopaminergic and antioxidant potentials.[64] The seeds consist of the active constituents such as mucunine, mucunadine, mucunadinine, prurienidine, nicotine, b-sitosterol, vernolic acid, gallic acid as well as alkaloids, alkyl amines, tryptamine, steroids, flavonoids, and metals such as iron, manganese, magnesium, copper, and zinc.[65] After the treatment of Kapikacchu, the nigrostriatal section of mouse brain who is suffering from Parkinson disorder displayed considerable increase in the heights of malondialdehyde (MDA), nitrite, and decrease rate of catalase as well as improved the behavioral deformities.[66]

- ***Benincasa hispida* (Kushmanda)**

Kushmanda (Cucurbitaceae) is also called as "winter melon". It is a wide-ranging crawling herb harvested all over India.[67] The plant gives large cylindrical fruits which are camouflaged with waxy coating.[53] Steroids, flavonoids, saponins, and alkaloids are the major phytochemical constituents of Kushmanda.[68] Antioxidant effective agent and ROS scavenger activity are shown by Kushmanda.[69] It has a tissue defensive effect on AD caused by colchicine by antioxidant activity.[70]

- ***Celastrus paniculatus* (Jyotishmati)**

Jyotishmati (Celastraceae) is also called "black oil plant". Seed oil of the plant majorly used for enhancing memory and cognitive function.[40] This seed oil consists of terpenoids (b-sitosterol, b-amyrin, paniculatadiol, celastrol, and pristimerin), esters, and sesquiterpenoids.[71] Jyotishmati seed oil improves the memory as well as cognitive function, and the plant is also reported to possess antiarthritic and antioxidant activity (decreased the level of lipid peroxidation) in rat model.[72] In navigational memory task performed on adult rats, the seed oil of Jyotishmati inversed scopolamine-induced deterioration.[73] Jyotishmati boosts learning and memorizing ability by selectively reversing the deterioration in spatial memory caused through acute central muscarinic receptor blockade, but it is not linked to an anticholinesterase-like action. It also shows free radical scavenging capacity, takes care of DNA cleavage as it has a defensive effect on DNA damage and cytotoxicity.[74,75]

CONCLUSION

Dementia is characterized as brain disorder that causes loss of learning, memory impairment, and disorientation. Different risks are marked such as oxidative damage, insufficient blood supply to brain. Treatments available for this disorder are cholinesterase inhibitors, N-methyl-D-aspartate antagonist. These nootropics can manage the disease to a certain extent and could be effectual but are associated with certain limits and side effects. Naturally occurring medicinal plants could be economically feasible treatment to a great extent. The medicinal plants that have been claimed for nootropic activity could be used for long term because of their memory enhancing effects. Ayurveda an integrated science arranges solutions for memory and cognitive disorders in a beneficial way. From the discussion, herbal nootropic drugs find beneficial usefulness in achieving adequate results in memory disorders. Thus, the effort has been made to consider rationally in the prospect of memory enhancement in a view to explore greener pastures. 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 neuroprotectant. 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. The present review is aimed at compiling an up to date and comprehensive review on herbal plants showing nootropic activity.

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