

Nootropic Plants: A Review: Part I

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Abstract

The post Covid era has seen new challenges towards addressing diseases. Newer management techniques to tackle age old and new medical challenges are emerging. The whole world was looking at alternative medical practices to tackle Covid and other newer variants of Covid, since the molecular medicines could not handle the situation. Herbal medicines are slowly emerging and it is expected that the use of these medicines will be more in practice, particularly due to two major reasons: The one being the occurrence of MDR microorganisms and the other being, the side effects of molecular medicines. Similarly, as time is passing more and more cases on neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease etc. are on the rise due to various factors like, stress, pollution and other socioeconomic factors. There is an urgent need to enlist the herbal alternative to cure these diseases. The present review is a step in this direction. We have tried to cover as many plants as possible in this review which have some or the other contributing medicinal role in addressing neurological diseases. The present article, which contains the details of 6 plants, is Part I in the series of articles.

Key words:

Nootropic, MDR, Alzheimer's disease, Parkinson's Disease, Huntington's Disease, Herbal

Introduction

Identification and characterization of new medicinal plants to cure neurodegenerative diseases and brain injuries resulting from stroke is the major and increasing scientific interest in recent years. Malik and Tlustos, 2023 have discussed the a few important nootropic plants based on earlier relevant and experimental data. The present review was undertaken to list of nootropic plants as many as possible using existing data. Although it cannot be called complete but we have tried to do our best incorporate even small details that are available in published research articles.

Globally, in 2019, there were nearly 10 million deaths and 349 million DALYs (Disability- Adjusted Life Years) due to neurological disorders. Although there was a decrease in neonatal encephalopathy, communicable, maternal, neonatal and nutritional categories have reduced there was a sharp increase in Alzheimer's disease and other dementias and Parkinson's diseases. (Deng et al, 2022). Neurological illnesses accounted for the greatest percentage (6.2%) of Total DALY index among all diseases, according to the World Health Organization (WHO). Alzheimer's disease (AD) is the second most common neurological illness in the world, after Cerebro-vascular disease (12%), with epilepsy and migraine accounting for 8% apiece. The cognitive function of people with AD deteriorates over time. It is an irreversible, dynamically changing condition that will afflict approximately 65.7 million people worldwide by 2030.

With an Indian perspective Gouri-Devi, 2014 have reported the prevalence of neurological disorders in different parts of India ranged from 967-4070 with a mean of 2394 per 100000 populations, thus indicating that approximately over 30 million people suffering from various types of neurological disorders. In rural areas 6-8 million people with high case of fatality of stroke (27-42%). Ratheesh et al, 2017 have discussed that the overall use of herbal medicine provides promising alternatives to current therapies for neurodegenerative disorders. However, the potential of herbal medicine/natural compounds is immensely hindered by its poor pharmacokinetic properties. Malapur et al, 2021 have estimated the annual cost of care per patient with mild to moderate and severe Major Neuro-cognitive Disorders was INR 76288 and INR 167808, respectively. The cost increased with severity of the diseases. Soheil et al, 2021 have discussed the need of discovering new therapeutic agents with high effectiveness and lesser side effects and herbal medicines are the best alternatives sources for the same. Numerous synthetic medicines such as tacrine, donepezil, galantamine, rivastigmine, memantine, glutathione, ascorbic acid, ubiquinone, ibuprofen, and ladostigil, Piracetam etc. are routinely used for reduction of the symptoms and prevention of disease progression. Nowadays, herbal medicines have attracted popular attention for numerous beneficial effects with little side effects. Soto-Lara et al, 2023 have reported in their study that the prevalence of Complementary and Alternative medicine use in neurological diseases is highly variable (16% -100%), the most used type of CAM was biological therapies and the associated factors were female sex, age between 40 and 50 years old and high socioeconomic level.

There are more than 120 traditional medicines that are being used for the therapy of Central Nervous System (CNS) disorders in Asian countries. In the Indian system of medicine the following medicinal plants have shown promising activity in neuro-psychopharmacology: *Centella asiatica*, *Glycyrrhiza glabra* Linn., *Tinospora cordifolia* (Wild) Miers), *Convolvulus pleuricaulis* Chois, *Allium sativum*, *Bacopa monnieri*, *Centella asiatica*, *Celastrus paniculatus*, *Nicotiana tabaccum*, *Withania somnifera*, *Ricinus communis*, *Salvia officinalis*, *Ginkgo biloba*, *Huperiza serrata*, *Angelica sinensis*, *Uncaria tomentosa*, *Hypericum perforatum*, *Physostigma venosum*, *Acorus calmus*, *Curcuma longa*, *Terminalia chebula*, *Crocus sativus*, *Enhydra fluctuans*, *Valeriana wallichii*, *Glycyrrhiza glabra* etc. to name a few. In Chinese medicine, numerous plants have been used to treat stroke, and some of the them are: *Ledebouriella divaricata*, *Scutellaria baicalensis*, *Angelica pubescens*, *Morus alba*, *Salvia miltiorrhiza*, *Uncaria rhynchophylla*, and *Ligusticum chuanxiong*.

In Indian traditional medicines Ayurveda, the four plants, namely, *Centella asiatica*, *Glycyrrhiza glabra* Linn., *Tinospora cordifolia* (Wild) Miers), *Convolvulus pleuricaulis* Chois are known as *Medhya rasayanas*, which are specific as nootropic medicines. (Basha et al, 2023). In Ayurveda plants are either used alone or as combination of some plants to have better results. In present study, the list of plants presented show nootropic effects as found in the literature and published data. We present the details of almost all the known important plants

which have some nootropic activity. The present article is Part I in the series of articles in which the nootropic role of 30 plants are discussed.

1. *Bacopa monnieri* (Bramhi)

Bramhi is a common household plant of India, which is given as raw juice or as cooked vegetable for memory retention particularly for children. *Bacopa monnieri* L. (Scrophulariaceae) is very widely recommended for the management of a range of mental conditions including anxiety, poor cognition and a lack of concentration, as a nerve tonic, for memory and intelligence improvement. There are many reports on the medicinal role of this plant particularly as a nootropic.

Krishnakumar et al, 2009 have demonstrated the therapeutic role of Bacopa extracts on epileptic rats. Saraf et al, 2011 also have shown the Bacopa attenuates the memory of scopolamine induced memory impairment in mice. Peth-Nui et al, 2012 have seen the effects of Bacopa consumption on attention, cognitive processing, and working memory in healthy volunteers. Kumar et al, 2016 have worked on the role of Bacopa extracts on the cognitive functions of medical students in a randomized placebo controlled trial.

The review of Kean et al, 2017 indicates that poly-herbal formulas containing Bacopa monnieri (L.) Wettst, may alleviate behavioural symptoms and improve cognitive outcomes in children and adolescents with developmental disorders. Nemtchek et al, 2017 have shown in their article that Bacopa inhibits the release of inflammatory cytokines from microglial cells and inhibits enzymes associated with inflammation in the brain. Sharma et al, 2018 have evaluated the role of Bacopa extracts against depressive like behaviour induced by ethanol withdrawal in rats. Fatima et al, 2022 have hypothesize that Bramhi could be effective in reversing Tau-mediated pathology in neurons. Varshney et al, 2020 have shown the effects of Bacopa on learning and memory in albino rats. Murugaiyan and Bhargavan, 2020 have reported that Bacopa alleviates aluminium chloride induced anxiety by regulating plasma corticosterone level in Wistar rats. Brimson et al, 2020 have reported the protective effect of Bacopa on glutamate toxicity in rats.

2. Jyotishmati (*Celastrus paniculata*)

Celastrus paniculatus Willd., known as Malkagani or Jyotishmanti in Ayurveda, has been used as medicine for various ailments. Seeds and seed oil of *Celastrus paniculatus* (Celastraceae) have been used in Ayurvedic medicine for “stimulating intellect and sharpening the memory.” A number of reviews have come up on the medicinal properties of this plant. Lekha et al, 2010 have the cognitive enhancement role of oil of *C. paniculatus*.

Alma and Haque, 2011 have reported the anti-Alzheimer activity of this plant. Valecha, 2014 also found anti-depressant role of oil of *C. paniculata* on chronic stress on mice. Raut et al, 2015 have studied the positive role of Jyotishmati oil (Seed oil of *C. paniculatus*) on spatial and fear memory induced by scopolamine in mice. Bhagya et al, 2016 have reported the neuro-protective role of *C. paniculatus* on cognitive impairment induced by chronic stress. Jakka, 2017 have studied the

nootropic effect of the methanolic extract of the whole plant on rats. Sharma et al, 2020 published a detailed review on the medicinal role of *C. peniculatus*. Bhagya and Jaideep, 2020 have also comprehensively reviewed the neuro-pharmacological and cognitive effects of this plant. Aleem et al, 2023 have reviewed the various reports on this plant which show that the extracts and active constituent of this plant possess potent nootropic activity.

3. Kushmanda (Benincasa hispida)

Kushmanda (*Benincasa hispida*) belonging to Cucurbitaceae is an extensive trailing or climbing herb cultivated throughout the plains of India as a vegetable. Chandre et al, 2011 have reported the clinical evaluation of Kushmanda ghrita (An Ayurvedic formulation) in the management of depressive illness. Ambikar et al, 2011 have evaluated the effect of *B. hispida* on the brain behaviour of laboratory animals. Nimbale et al, 2011 also evaluated the anxiolytic role of fruit extract of *B. hispida*. Islam et al, 2021 have reviewed the traditional uses, nutraceutical and phytopharmacological profile of *B. hispida*. Chaitali et al, 2022, have reviewed the phytochemical and pharmacological activities of *B. hispida*. Wankhade et al, 2023 have evaluated the ameliorative effect of *B. hispida* fruit on induced chronic foot shock in mice.

4. Acorus calamus

In Ayurveda *Acorus calamus* Linn is also known as VACHA and publically known as Bacha or sweet flag. It is also a main medhya drug, which has the property of improving the memory power and intellect. *Acorus calamus* (AC) has been used as traditional Indian and Chinese prescriptions for its beneficial effects on cognitive and memory enhancement, anti-aging and anticholinergic activity.

Manikandan and Devi, 2005 and Manikandan et al, 2005, attributed the noise induced stress was ameliorated due to the treatment with *Acorus* due to the presence of one phytochemical, namely, β -asarone in it. Houghton et al, 2006 have shown that Asarone present in *Acorus* inhibits Acetylcholine esterase enzyme in the brain. Shukla et al, 2006 reported the neuroprotective role of *Acorus* against ischemia induced by middle cerebral artery occlusion. Mukherjee et al, 2007 have reported the scientific validation of ayurvedic tradition from natural resources. It has been proved for its analgesic and anticonvulsant (Jayaraman et al, 2010). Sharma et al, 2022 have the anti-Parkinson's role of *Acorus*.

5. Jatamamsi (Nardostachys jatamamsi)

Jatamansi root is aromatic and its infusion has a number of activities like cardio protective, controlling epilepsy, hysteria etc. Ayurvedic practitioners include it in their formulations to address anxiety. Dhingra and Goyal, 2008 have reported the antidepressant like activity of *N. jatamansi*. Singh et al, 2009, have indicated *N. jatamansi* as a potential herb with CNS effects. Lyle et al, 2009 have reported the stress modulating antioxidant effect of *N. jatamansi*. Rahman et al, 2010 have reported the antidepressant role of methanolic extract of *N. jatamansi* on sleep deprived mice. Rahman et al, 2011 have suggested that inhibitory role of acetylcholinesterase enzyme of *N. jatamansi* helps in alleviating Alzheimer's in rat model. Karkada et al, 2012 shown that *Jatamansi* extract prevents chronic resistant, stress induced learning and memory deficits in animal model. Li et al, 2014 have reported that Nardosinone, a phytochemical from *N. jatamansi* improves the proliferation, migration and selective differentiation in mouse embryonic neural stem cells. Liu et al, 2015 have shown the neuroprotective roles traditional medicines against Alzheimer's in *Drosophila* model. Dhiman and Bhattacharya, 2020 have indicated the opportunities of harnessing the medicinal roles of *Jatamansi*. Sharma et al, 2023 have shown the protective role of *Jatamansi* on induced seizures in rats.

6. *Clitoria ternatea* L.

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. Rai 2010 has reported the neurogenic potential of *C. ternatea* aqueous extracts. Karuna et al, 2014 have studied the neuroprotective and nootropic activities of *C. ternate* leaf extracts on diabetes induced experimental animals. Sahnas and Akhila 2014 have done in vivo and in silico evaluation of *C. ternatea* as anti Alzheimer's agent.

Rameshwar et al, 2017 have evaluated the neuro-protective role of *C. ternatea* on induced Parkinson's on mice. Jiji and Muralidharan, 2022 studied the protective effect of *C. teranatea* on autism. Gajalakshmi and Harikrishnan 2023 have done in vivo experiment pharmacological experiment of *C. ternatea*.

CONCLUSION

The above lists of 6 plants are mostly used as neuroprotective and neuroregenerative plants in Ayurveda and Sidhha medicinal practices. This is the first list of nootropic plants and the series continues in subsequent issues.

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