

Edible plants: promising source for prevention and management of Parkinson's and Alzheimer's disease

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Commentary

India can be regarded as an agricultural country where 46% of its land is utilized for farming [1]. Since ancient times, plants have been utilized for their edible properties and for medicinal and therapeutic purposes. The ancient medicinal science Ayurveda strongly recommends the use of natural ingredients in the form of food to remain healthy and also to cure various ailments. No medicine is considered better than food, and what a person eats is not a medicine but a *Mahabhaishya* (equivalent to life). The food has a direct impact on the mind and body of a person, and purity of the mind depends on *Sattvik* (light and healthy) diet [2]. Even today majority of the Indian population is vegetarian in diet, eating only vegetables, fruits, cereals, grains, dairy products, etc. In an estimate, approximately 800 varieties of wild plant species are consumed in India for various uses, including the preparation of food cuisines [3]. However, many of the plant species in India are not of Indian origin and have been introduced and cultivated from other parts of the world through foreign settlers. *Acorus calamus* L., is used as a flavoring agent in Indian cuisines in the name of calamus or sweet flag. This plant is native to Kazakhstan and was introduced in India [4]. It is also widely used in mental ailments such as memory disorders, learning performance, and epilepsy, in the Indian system of medicine [5]. Fenugreek (*Trigonella foenum-graecum*) is native to Afghanistan, Iran, Iraq and Pakistan of today and is widely used as a spice and condiment in the preparation of Indian vegetables. It is also medicinally acclaimed for its health-promoting effects in traditional Chinese medicine and Indian Ayurveda [6]. Many more examples of this type can be traced out easily. There are many more examples of such plants brought to India centuries ago, like strawberry, tea, pistachio, potato, tomato, etc., and today they form an intricate part of Indian cuisines and the medicinal system. In a recent research, it was found that the plants commonly used as vegetables in India are also used medicinally for various diseases. Approximately 156 plants used as vegetables are also used medicinally. Seventy-one species from them were not of Indian origin but widely acclaimed for edible and medicinal purposes. These edible plants are also used for the treatment of neurological disorders, including Alzheimer disease, Parkinson's disease, headache, migraine, depression, insomnia, etc. (Table 1).

Some of those plants have been used for medicinal purposes in other traditional medicinal systems of the world [7]. *Amaranthus* is widely used as a green leafy vegetable and is used in Nepal and China as traditional medicine [8]. *Ipomoea aquatic* Forrsk., leaves are used to prepare vegetables in India and for mental illness in Tanzania and intestinal problems in Somalia [9]. The plants like *Ginkgo biloba*, *Curcuma longa*, *Salvia officinalis* and many others are used against neurological problems and are used for edible purposes in many types of preparations. The seeds of *Ginkgo biloba* are first steamed to open the hard outer shell; kernels are removed and boiled in water and sugar to make a sweet soup. They are also roasted and eaten dry. However, precautions must be taken not to consume excessively, as they contain certain toxic substances which are eliminated after boiling [10]. The rhizomes of *Curcuma longa* are first steamed and then dried. These may even be boiled first and then dried. The

Table 1. Indian vegetables used in neurological disorders.

S. No	Scientific name	Common name	Edible part	Used in	Medicinal part
1	<i>Bacopa monnieri</i>	Brahmi	Leaf	Memory disorder	Leaf
2	<i>Benincasa hispida</i> (Thunb.) Cogn	Ash gourd, winter melon	Leaf, fruit	Insanity, schizophrenia and other psychological and mental disorders	Fruit
3	<i>Celastrus paniculatus</i> Willd.	Jyotimati	Leaf, root bark, seed oil	Depression	Leaf
4	<i>Cleome gyandra</i> L.	African spider powder, Tilaparnika	Leaf	Epilepsy	Leaf, seed
5	<i>Centella asiatica</i>	Gotu katu	Leaf	Anxiolytic agent	Leaf
6	<i>Colocasia esculenta</i> (L.) Schott	Taro, arbi	Tuber, leaf	Neurological disorders	Leaf, tuber
7	<i>Cucurbita maxima</i> Duchesne	Kumhada, Winter squash	Fruits, seed	Migraine, nervous debility	Fruit, tender shoot, flower
8	<i>Cucurbita pepo</i> L.	Pumpkin	Tender fruit	Headache, fatigue, neuralgia	Tender fruit
9	<i>Diplazium esculentum</i> (Retz.) Sw.	Fiddlehead greens	Tender fruit	Headache,	Tender fruit
10	<i>Eruca vesicaria</i> (L.) Cav.	Rocket	Leaf	Neurodegenerative disease	Leaf
11	<i>Ipomoea aquatica</i> Forssk.	Water spinach	Leaf, tender shoot	Mental illness, central nervous system depression	Leaf, tender shoot
12	<i>Lagenaria siceraria</i> (Molina) Standl.	Bottle gourd, Lauki, Tumbi, Katutumbi	Leaf, fruit, seed	Headache, migraine	Fruit, seed
13	<i>Lavandula angustifolia</i> Mill.	Lavender	Leaf, oil	Insanity	Bud, shoot, leaf
14	<i>Luffa acutangula</i> (L.) Roxb.	Kosataki, Torai, Ridge gourd	Root, leaf, seed, fruit	Headache	Fruit
15	<i>Marsilea minuta</i> L.	Sunisanaka, Water clover	Leaf	Insomnia, mental disorders	Leaf
16	<i>Merremia emarginata</i> (Burm.f.) Hallier f.	Akhukarni, Musakarni	Plant	Headache	Leaf
17	<i>Mucuna pruriens</i> (L.) DC.	Drumstick, Moringa	Seed	Parkinson's disease, nervous disorder	Seed
18	<i>Murraya koenigii</i>	Curry patta	Leaf	Amnesia, memory disorder	Leaf
19	<i>Nelumbo nucifera</i> Gaertn.	Sac red water lotus	Buds, flower, anthers, stamens, fruits, leaf, stalks, rhizomes, roots	Depression, insomnia	Rhizome
20	<i>Oxalis corniculata</i> L.	Creeping wood sorrel	Whole plant, leaf	Insomnia	Shoot
21	<i>Pastinaca sativa</i> L.	Parsnip	Leaf	Headache	Leaf
22	<i>Perilla frutescens</i> (L.) Britton		Leaf, seed	Depression related disease, anxiety	Tender shoot
23	<i>Sida cordifolia</i> L.	Bala, country mellow	Root, seed, leaf	Headache, nervous diseases	Leaf, young fruit
24	<i>Trichosanthes cucumerina</i> L.	Kuloka, Snake gourd	Aerial parts root, fruit	Headache	Fruit, root

dried rhizomes are powdered and then used in food preparations. This powder form is widely used for its characteristic color in food. It can be used to prepare tea or as a spice in curries, smoked foods, pickles, and some cakes. Not only in India, but also in many other countries, it is used for culinary purposes. In Anatolia (Turkey) it is used in a dessert called zerde (saffron rice dessert, served at weddings) for its color. The essential oil of *Salvia officinalis* is used in food preservation. It is also used as a spice, providing a specific aroma and promoting the digestion of food, so widely used in the preparation

of meat and poultry dishes. It is also used as a flavoring agent in the perfume and cosmetic industries. The plants are grazed by bees that produce honey with a characteristic aroma and high medical value [11]. Flowers of some plants, such as alliums (leeks, chives, garlic), thyme (*Thymus vulgaris*), summer savory (*Satureja hortensis*), marjoram (*Origanum majorana*), mint (*Mentha* spp.) and common sage (*Salvia officinalis*), are used to improve the flavor of dishes as well as to treat various neurological problems, including headache [12]. *Glycyrrhiza glabra* is used for the production of liquorice honey,

in various baked goods, alcoholic beverages, nonalcoholic beverages, chewing gum, candy, and as seasonings to add fragrance to food [13]. However, the exact curative mechanism for all the vegetable plants is very little known, and there is a need to trace and elucidate the exact mechanism behind their preventive and curative effects. The plant species used are either in raw form in salads, pickles, etc., or in cooked form as vegetables, fritters, or jams. Some of the species are used as spices and condiments added to various dishes to increase the flavor and aroma of the dish [7].

Neurodegenerative Diseases in Ayurveda

In Ayurveda, the description of degenerative disease has been mentioned, which mainly arises due to an imbalance of *vata* (humour of air and space) in the body and is commonly known as *VataVyadhi*. The imbalance of *vata* in the brain brings dryness in the tissues of the brain due to lack of proper nourishment, which can be due to physical or emotional factors or even both. The imbalance can also occur in any other part of the body [1]. The extent of these imbalances varies in each person and differs from one individual to another. Thus, emphasis is laid on the nourishment of the brain through preventive and responsive measures. Hence, the correction of the imbalance in body and mind can be achieved through a change of dietary habits, the use of herbo-mineral formulations, and lifestyle changes. The use of numerous plants has been mentioned in classical texts of Ayurveda, which provide therapeutic benefits for the treatment of neurodegenerative diseases. All these substances act on the principles of homologous (*samanya*) and antagonistic (*visesha*) action. The substances which possess *samanya* properties and actions help to increase relevant constitution or elemental properties in the body, and those having *visesha* action decrease those constituents or properties. In case of *doshas* (imbalance), the rational use of these naturally available substances helps to restore the balance in the mind and body, thereby curing the disease [14]. The plants rich in antioxidants help to limit neuronal dysfunction and help to maintain the integrity of cellular interaction in the brain, thereby maintaining neural stability and neural functions and thus play an important role as a therapeutic agent for neuroprotection. Even the practice of *asana* and yogic postures (physical and mental exercise), *panchkarma* therapies (bio-purification procedures), helps in the successful treatment of neurodegenerative disease [15]. In Ayurveda, the use of plants like *Bacopa moneri* (brahmi), *Withamnia somnifera* (ashwagandha), *Centella asiatica* (gotu kola), and *Mucuna pruriens* (velvet bean), is given for various neurological disorders.

Pathogenesis of Neurodegenerative Diseases

In scientific terminology of today, neurodegenerative disorders or diseases are characterized by progressive loss of neurons, thereby altering physicochemical properties of brain and in peripheral organs. The common neurodegenerative diseases Parkinson's and Alzheimer's were described more than 100 years ago and remain incurable due to an unclear understanding of its pathogenesis and exact mechanisms applicable for their cure. In an estimate, the patients with symptoms and signs of Parkinson's disease were estimated to be approximately 10 million globally, making up 0.3% of the total population of the world, and 1% were found to be more than 60 years in age [16]. Although in the past few years scientific research has led to elucidate the possible role played by various genes, trace mechanisms of neurodegeneration, along with some ways of neuronal protection [17,18]. The deposition of proteins in neurons is considered to be

the molecular basis of neurodegenerative diseases. The proteins commonly involved in pathogenesis are prion protein, tau, amyloid, neuroserpin, ferritin, fused –in sarcoma protein, cerebral amyloidosis, etc. [19]. The common features in the mechanism of neurodegeneration are mitochondrial dysfunction and oxidative stress. Mitochondria are an organelle commonly called the power house of the cell, involved in energy production. It is considered to be a major reactive oxygen species producer and is also a vulnerable target of oxidative stress [20–22]. Oxidative stress is the result of an imbalance in the pro-oxidant /antioxidant homeostasis, which leads to the generation of toxic reactive oxygen species (ROS) and is thus tightly regulated in the body. These ROS are generated by the interaction of oxygen with redox-active metal ions and play a normal metabolic role in cell signaling. The extensive oxidative damage to proteins, lipids and DNA can lead to cell death by numerous mechanisms. Lipid peroxidation is regarded as one of the features of oxidative stress and is a hallmark of Parkinson's disease, Alzheimer's disease and other neurological conditions. It is thus also involved in cell death mechanisms resulting in the pathogenesis of neurodegenerative disorders [20,21,23]. In many studies, the role of mitochondria and lipid peroxidation in the mechanism of neuronal loss and analysis of therapeutic mechanisms for its prevention have been studied [20]. The drugs targeting mitochondria can be those compensating for energy deficit involved in neurodegeneration or neuroprotectors helping to increase the resistance of mitochondria to open the MPT (mitochondrial permeability transition) pores. However, it is suggestive that these drugs developed should be combined with those targets providing cognitive stimulating, neuroprotective effects and possess the ability to affect specific diseases forming mechanism. Although the examples of such approaches are greatly influenced and affected by the level of preclinical and clinical trials [21]. There had also been development of therapeutic strategies which are meant to slow down or halt the progression of these diseases to a great extent [24].

Preventive and Management Action by Using Plants

The management of neurodegenerative diseases has become a worldwide challenge and as such, no specific therapy or complete cure has been found. Therefore, the strategies which help in prevention of these degenerative disorders are of utmost importance. The intake of plants in various culinary forms daily can help to prevent the progression of neurodegenerative disorders to some extent. The various scientific studies also highlight the probable specific mechanism responsible for the prevention and treatment of neurological disorders. In **Table 2**, the use of a few plant species for various neurological problems has been given along with their native range of origin. These species have been widely studied for their pharmacological actions responsible for their curative and preventive actions. *Glycyrrhiza glabra* is widely used in the preparation of various delicacies in India. Since ancient times, it has also been used medicinally. In research it has been found that it presents excellent neuroprotective activity. The active component glycyrrhetic acid inhibited apoptosis by decreasing the level of mitochondrial Bax/Bcl-2 protein and activating PI3K/Akt pathways [25]. In a study, it was found that liquiritin upregulated the expression of functional glucose 6-phosphate dehydrogenase and antioxidants [26]. Dehydroglysperin–C reduced glutamate-mediated cytotoxicity and ROS generation in HT 22 cells [27]. The compound isoliquiritin exhibited antidepressant effects by increasing the level of serotonin

Table 2. Plant species used in neurological conditions.

Scientific name	Family	Common name	Alzheimer disease and other neurological conditions	Native range
<i>Acorus calamus</i> L.	Araceae	Sweet flag	Memory impairment, learning performance, behavior modification	Kazakhstan
<i>Angelica archangelica</i> L.	Umbelliferae	Dudhachoraa (Laghu Coraka)	Alzheimer disease	Greenland, Europe to West Siberia
<i>Bacopa monnieri</i> (L.) Wettst.	Plantaginaceae	Brahmi	Alzheimer disease	Tropics & Subtropics
<i>Celastrus paniculatus</i> Willd.	Celastraceae	Jyotismati	Alzheimer disease	Indian Subcontinent to Southern China and Indo-China
<i>Centella asiatica</i> (L.) Urb.	Apiaceae	Gotu kola, Manduka Parni	Alzheimer disease	Caucasus, Tropical & Subtropical Old World to Eastern Australia and West Pacific
<i>Clitoria ternatea</i> L.	Fabaceae	Aparajita	Alzheimer disease	Cape Verde, Tropical & Southern Africa, Arabian Peninsula
<i>Codonopsis pilosula</i> (Franch.) Nannf.	Campanulaceae	Poor man's ginseng	Alzheimer disease	Mongolia to Korea and China
<i>Collinsonia canadensis</i> L.	Lamiaceae	Stone root	Protect blood brain barrier	Southern Ontario to North Central & Eastern U.S.A
<i>Commiphora wightii</i> (Arn.) Bhandari	Burseraceae	Guggulu	Improve memory	Oman, Southern Pakistan to North west & Western India
<i>Convolvulus prostratus</i> Forssk. Syn. <i>Convolvulus pluricaulis</i> Choisy	Convolvulaceae	Shankhapusphi	Memory enhancer	Cape Verde to North West India
<i>Coptis chinensis</i> Franch.	Ranunculaceae	Chinese goldthread	Alzheimer disease	Central & East Central China
<i>Crocus sativus</i> L.	Iridaceae	Saffron	Alzheimer disease	Cultigen from Greece
<i>Curcuma longa</i> L.	Zingiberaceae	Turmeric	Alzheimer disease	Cultigen from Southwestern India
<i>Galanthus nivalis</i> L.	Amaryllidaceae	Snow drop	Anticholinesterase	Pyrenees to Ukraine
<i>Ginkgo biloba</i> L.	Ginkgoaceae	Fossil tree	Alzheimer's disease & cognitive impairment	China (Zhejiang)
<i>Glycyrrhiza glabra</i> L.	Fabaceae	licorice	Alzheimer disease	Central Mediterranean to Mongolia and Pakistan
<i>Huperzia serrata</i> (Thunb ex.Murray) Trevis	Lycopodiaceae	Toothed club moss	Alzheimer's disease & memory enhancer	Russian Far East to Northeast China and Japan, Hawaiian Islands, Mexico, Cuba to Hispaniola
<i>Hypericum veronense</i> Schrank syn. <i>Hypericum perforatum</i> L.	Hypericaceae	Klamath weed	Alzheimer's disease	Macaronesia, Central Europe, Mediterranean to SW. Sudan and W. Himalaya
<i>Lepidium meyenii</i> Walp	Brassicaceae	Maca	Improve memory	Southern Peru to Northwest Argentina
<i>Magnolia officinalis</i> Rehder & E.H.Wilson	Magnoliaceae	Talauma	Neurosis, anxiety,stroke, dementia	China
<i>Matricaria chamomilla</i> L. syn. <i>Matricaria recutita</i> L.	Asteraceae	Chamomile	Relieve anxiety, counteract insomnia, stimulate brain	Macaronesia, Northern Africa, Temperate Eurasia to Indo-China
<i>Melissa officinalis</i> L.	Lamiaceae	Lemon balm	Alzheimer's disease	Mediterranean to Central Asia

Scientific name	Family	Common name	Alzheimer disease and other neurological conditions	Native range
<i>Panax ginseng</i> C.A.Mey.	Araliaceae	Ginseng	Alzheimer's disease & brain disorders	Russian Far East to Korea
<i>Platycladus orientalis</i> (L.) Franco syn. <i>Biota orientalis</i> L.	Cupressaceae	Biota	Alzheimer's disease	Russian Far East to East Central China and Korea
<i>Piper latifolium</i> L.f. syn. <i>Piper methysticum</i> Frost.	Piperaceae	False kava	Alzheimer's disease	Santa Cruz Islands to the Pacific
<i>Polygala tenuifolia</i> Willd.	Polygalaceae	Japanese senga	Alzheimer's disease	Siberia to China and Korea
<i>Salvia rosmarinus</i> Spenn. Syn. <i>Rosmarinus officinalis</i>	Lamiaceae	Rosemary	Alzheimer's disease	Mediterranean region
<i>Salvia officinalis</i> subsp. <i>lavandulifolia</i> (Vahl) Gams syn. <i>Salvia lavandulaefolia</i> Vahl.	Lamiaceae	Sage	Alzheimer's disease	Central & East Spain
<i>Salvia officinalis</i> L.	Lamiaceae	Sage	Alzheimer's disease	Southwest Germany to Southern Europe
<i>Scutellaria baicalensis</i> Georgi	Lamiaceae	Wogon	Alzheimer's disease	Siberia to the Russian Far East and Vietnam
<i>Tetradium ruticarpum</i> (A.Juss.) T.G.Hartley	Rutaceae	Evodia fruit	Alzheimer's disease	Himalaya to Central & Southern China and Indo-China, Taiwan
<i>Tinospora cordifolia</i> (Willd.) Hook.f. & Thomson	Menispermaceae	Guduchi	Memory enhancer	Indian Subcontinent to Indo-China

and norepinephrine in the mouse hippocampus and cortex, thereby exhibiting antidepressant effects [28]. Liochalcone –B exhibited anti –Alzheimer activity by inhibiting aggregation of the amyloid beta protein by blocking salt bridge interaction at the C–terminus [29]. *Withania somnifera* (ashwagandha) is widely used in Ayurveda for its aphrodisiac, diuretics and adaptogenic properties. Its leaves, berries and roots are mainly used. It helps to normalize physiological functions, which are disturbed by chronic stress. It helps in the correction of imbalances in the neuroendocrine and immune systems. It is regarded as “*rasayana*”, an elixir that works, in a nonspecific, global fashion, to increase human health and longevity. The berries and roots are widely used for edible purposes. The fresh roots are boiled in milk to leach out undesirable constituents. The berries are sometimes used as a substitute to coagulate milk in cheese making [30,31]. In Parkinson's disease, a selective loss of dopaminergic neurons in substantia nigra par compacta (SNc) region of the brain occurs. The symptoms, such as stiffness, tremor, bradykinesia, and cramps, showed significant improvements after treatment with a polyherbal preparation containing ashwagandha [32], which is attributed mainly to its capacity to reduce oxidative stress. It was also found that the extract of ashwagandha helped to decrease lipid peroxidation, improve the reduced content of catecholamine, glutathione and many more, thereby indicating its possible role to counter oxidative stress [33].

The ongoing research are focused on scientifically validating the traditionally used plants for Alzheimer's and Parkinson's disease. The experiments have been conducted both *in vivo* and *in vitro*, along with clinical trials using the specific plant constituents as a

drug target for this disease. The other few plants considered for these studies are *Panax notoginseng*, *Dipascus asper* Wall, *Paeonia suffruticosa* Andrews, *Polygala tenuifolia* Willd., *Radix salvia* (Dashen), *Uncaria rhynophylla*, *Lycium barbarum*, *Cassia obtusifolia* and many more, including the fungus *Ganoderma lucidum*. This list can become endless as each day the researchers combine ancient traditional knowledge and bring results useful to mankind, not only in the form of medicine but also as a food component. Today, the plants described in Ayurveda for neurological disorders are in huge demand for various types of food production. Mostly, these plants like Ashwagandha, brahmi, etc., are widely investigated for their phytochemicals, pharmacological evidence, and are consumed as functional food in the form of powder, capsules, etc., and even in the preparation of cookies, biscuits, flavored drinks so that the body can be enriched with their health benefits. *Bacopa monnieri* (brahmi) is classified as a *Medhyarasayana*, in Ayurveda, a drug used to improve memory and intellect (medhya) and was used as a brain tonic to enhance memory development, learning, and concentration, and to provide relief to patients with anxiety or epileptic disorders. Besides its medicinal attributes, this plant is gaining popularity as one of the main ingredients in various products such as biscuits, flavored breakfast, cereals, drinks, *chavyanprash* (medicated jam) and many more [34,35]. The neurodegenerative diseases like Alzheimer's and Parkinson's can be prevented and cured to a great extent by changes in dietary habits. The daily intake of certain plants rich in antioxidants and other phytochemicals, which help in preventing oxidative stress and mitochondrial dysfunction, will certainly help in these diseases. However, it is a matter of curiosity globally how these phytochemicals in plants work on the pathogenesis of a particular

disease. The ongoing research in various fields like ethnobotany, molecular biology, pharmacology, protein chemistry and many others will probably one day give the precise answer to this question and help to understand our traditional ancient medicinal science, which widely uses natural ingredients to prevent and cure diseases, even like Alzheimer's and Parkinson's.

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