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## REVIEW ARTICLE

### HERBS USED IN NEURODEGENERATIVE DISORDERS: AN OVERVIEW

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#### ABSTRACT

Herbalism is becoming more mainstream as up-to-date analysis and research show their value in the treatment and prevention of disease. Continual investigation of the mechanisms underlying neuroglial activation, regulation of neuroinflammation, modulatory role of herbal medicine in these processes would not only lead to the discovery of novel neuroprotective agents based on medicinal herbs, but also help to understand complex pathophysiology of neurodegenerative diseases

#### INTRODUCTION

The nervous system is the master controller of the body. It is a collection of cells, tissues, and organs & can be split into two separate divisions: the central nervous system and the peripheral nervous system. The central nervous system (CNS) acts as the command center of the body and consists of two major parts: the brain and the spinal cord. The peripheral nervous system (PNS) consists mainly of nerves that extend from the brain and spinal cord to areas in the rest of the body. Brain is the central controlling and coordinating organ of the nervous system while spinal cord is a long cord of nerve tissue. The four principal sections of the human brain are the brain stem, the diencephalon, the cerebrum, and the cerebellum. Association areas located in the lobes of the cerebrum process innumerable impulses that result in memory, emotions, judgment, personality, and intelligence: what truly makes each person an individual. Neurons are the cells making up the brain, spinal cord, and nerves. The electrical charges (nerves impulses) created by neurons in the brain combine to generate an electrical field. When the impulse or electrical current has reached the terminal branches or end of the axon, it stimulates the branches to release chemicals known as neurotransmitters, for eg. Acetylcholine, dopamine, serotonin, GABA (gamma-aminobutyric acid), etc.. Neurotransmitter is a chemical released by the axon of a neuron that travels across a synapse and binds to receptors on the dendrites of other neurons or body cells ([http://www.alz.org/downloads/Facts\\_Figures\\_2011.pdf](http://www.alz.org/downloads/Facts_Figures_2011.pdf); Wright, 2010; Holmes, 2008) Neurons (nerve cells) are electrically excitable cells in the nervous system that process and transmit information.

- **Excitatory neurons** excite their target neurons. Glutamate, acetylcholine, etc. are used as an excitatory neurotransmitter.
- **Inhibitory neurons** inhibit their target neurons. The primary inhibitory neurotransmitters are GABA and glycine.
- **Modulatory neurons** evoke more complex effects. They use dopamine, acetylcholine, etc. as neurotransmitters.

#### Neurodegeneration

Is progressive loss of structure or function of neurons, including death and atrophy of neurons in the brain. As nervous system is the master controller of the body, when it becomes disabled, injuries to brain & spinal cord occurs resulting in many neurological disorders.

#### Some of the neurodegenerative disorders can be listed as:

- Alcoholism
- Alexander's disease
- Alzheimer's disease
- Amyotrophic lateral sclerosis
- Bovine spongiform encephalopathy
- Cockayne syndrome
- Corticobasal degeneration
- Epilepsy
- Frontotemporal lobar degeneration
- Huntington's disease

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- Kennedy's disease
- Multiple System Atrophy
- Parkinson's disease
- Pick's disease
- Primary lateral sclerosis
- Subacute combined degeneration of spinal cord
- Spinal muscular atrophy

Whole herbs contain many ingredients, and it is likely that they work together to produce the desired medicinal effect. Drug treatments often become less effective over time and their prolonged usage has variety of side effects. Thus, as the herbs are capable of eliciting complex physiological responses and most of them are safe natural composition, they can be preferred over synthetic drugs (Suk, 2005; Adams, 2007; Mc Clatchey, 2009).

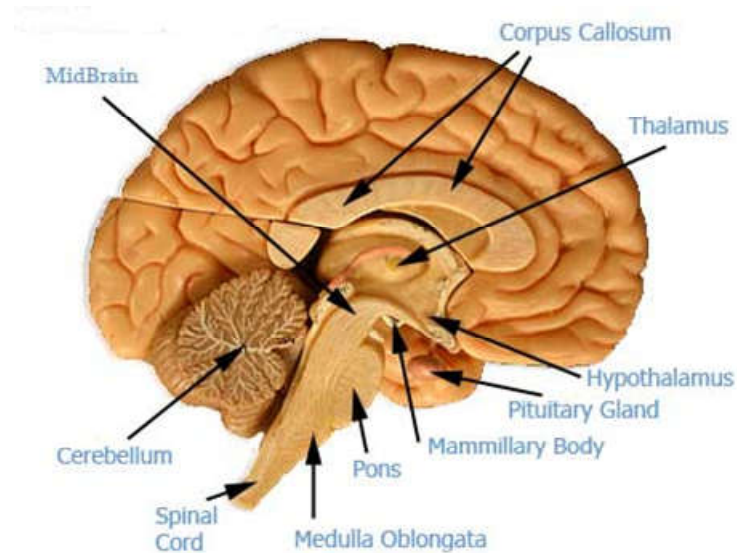


Fig. 1. Sagittal view of human brain

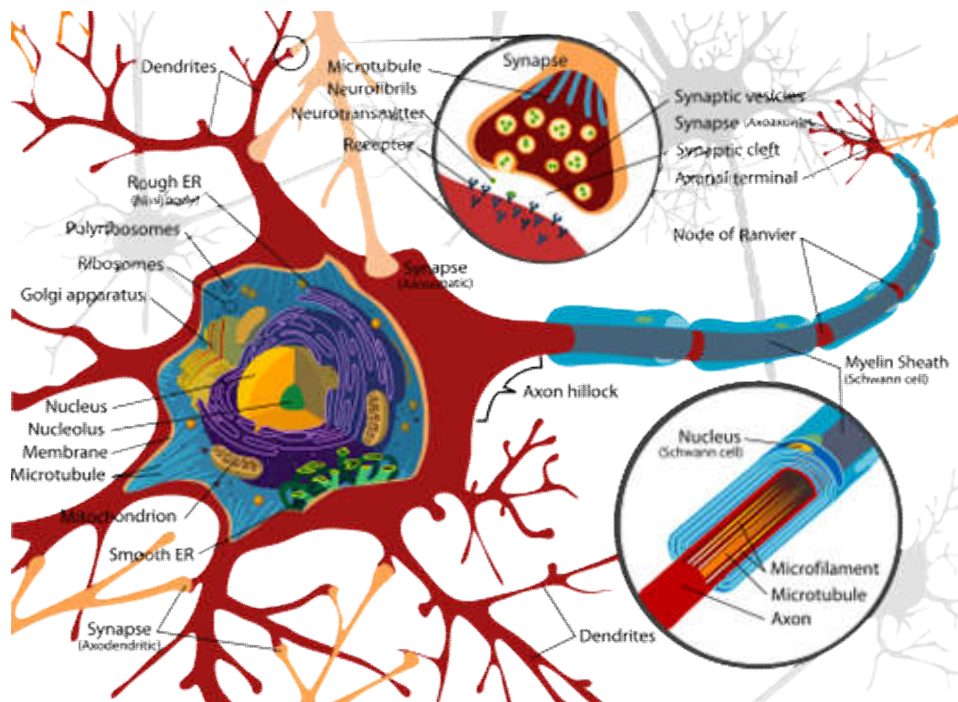


Fig. 2. Diagram of a typical myelinated vertebrate neuron

### Treatment Using Herbs

Herbal medicine, also called botanical medicine or phytomedicine, refers to the use of any plant's seeds, berries, roots, leaves, bark, or flowers for medicinal purposes. They contain complicated mixtures of organic chemicals, which may include fatty acids, sterols, alkaloids, flavonoids, glycosides, saponins, tannins, terpenes and so forth. Herbs are available in different forms: teas, syrups, oils, liquid extracts, tinctures, and dry extracts (pills, capsules or lozenges).

The herbs used can be listed as

For Alzheimer's

Vital herbs: (Luo, 2006; Bent, 2004; Anekonda *et al.*, 2005)

- Ginkgo
- Gotu Kola
- Bacopa
- Ashwagandha

- Nicotine
- Black Pepper
- Garlic
- Turmeric
- American Ginseng
- Asian Ginseng
- Drumstick tree
- Ginger
- Indian Noni

**Ayurvedic herbs: (Zhang, 2014; Das *et al.*, 2002; Dhuley, 2001)**

- Winter cherry OR Ashwagandha (*Withania somnifera*)
- Brahmi (*Herpestis monniera*)

**Herbal remedies**

- **Balataila**
- **Bu Nao Wan (Supplement Brain Pills)**

**Herbal formula**

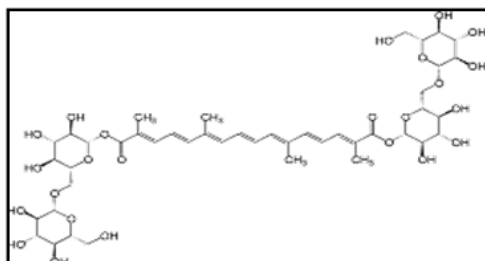
- NeuroPlus (New life # 160) (Nao Wei Kang Wan)

**Saffron** (Saeidnia, 2012; Evans, 1997; Harper, 2006)

**Botanical Name:** *Crocus sativus*

**Common Name:** Saffron, American saffron

**Family:** Iridaceae



**Fig. 12. Saffron**

**Crocin**

Saffron is derived from the dried stigma of the flower of the saffron crocus (*Crocus sativus*). Native to the Mediterranean region, cultivated in Spain, France, Italy, and the Middle East. Available in tincture form, but is quite expensive.

Saffron may help to treat several health conditions, including depression. It adds colour and flavour to food. The bitter glucoside picrocrocin is responsible for saffron's flavour. The two active ingredients are crocin and safranal. Crocin is a natural carotenoid and is responsible for the color of saffron. Safranal is responsible for the aroma of saffron. Steep 6-10 stigmas in 1/2 cup water. Take 1/2 to 1 cup a day, unsweetened, a mouthful at a time (McClatchey, 2009)

**Use in Alzheimer's**

Saffron scavenges free radicals and attenuates memory impairment. It contains many carotenoids which scavenge free radicals and protect cells from oxidative stress. Crocin act as potent antioxidant Due to this antioxidant activity, it is used in therapy of Alzheimer's. Oral administration of *C. Sativus* extract (CSE) has improved ethanol-induced impairment of memory and learning behaviour.

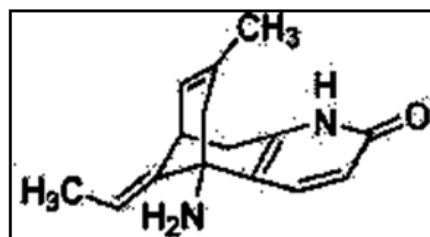
**Huperzine** (Desilets *et al.*, 2009; <http://www.clinicalpharmacology-ip.com/Forms/Monograph/monograph.aspx?cpnum=2360&sec=moncomm>; Zhang *et al.*, 2001)

**Botanical Name:** *Huperzia serrata*

**Common Name:** Toothed clubmoss

**Family:** Lycopodiaceae

**Huperzine A**



**Fig. 13. Huperzia serrata**

Huperzine A is a compound extracted from the Chinese plant *Huperzia serrata*. The active constituent is believed to be Huperzine A (L-Huperzine). It has a long history of use, but primarily in China. Huperzine A is a sesquiterpene alkaloid purified from the Chinese medicinal herb '*Huperzia serrata*'. It exhibits a broad range of neuroprotective actions.

**Use in Alzheimer's**

Huperzine A is an acetylcholinesterase inhibitor. Huperzine A works by inhibiting acetylcholinesterase, a chemical that promotes the breakdown of acetylcholine.

This inhibition of acetylcholinesterase increases the amount of acetylcholine available for the transfer and storage of information throughout the brain. It helps in the slow progression of AD. This compound is effective in improving memory and cognitive abilities in humans.

#### Ayurvedic herbs(19 20 21)

The following Ayurvedic herbs are traditionally used to treat brain disorders in elderly people:

- **Winter cherry OR Ashwagandha (Withania somniferum)**— demonstrates antioxidant and anti-inflammatory properties in the laboratory; enhances the tolerance of stress in animals.
- **Brahmi (Herpestis monniera)**—improves motor skills as well as the ability to learn and retain information.(7)

#### Herbal remedies

- **Balataila (Bala Taila, Bala Thailam)** –This is an Ayurvedic herbal oil used for nervous diseases. It is very efficacious in curing those diseases when they are due to inflammation of the nerves.
- **Bu Nao Wan (Supplement Brain Pills)** –This Chinese herbal remedy calms the spirit, supplements blood, heart and kidney. It is recommended for poor concentration/memory.

#### Herbal formula

##### NeuroPlus (New life # 160) (Nao Wei Kang Wan)

The herbal formula of choice is *Neuro Plus*, formulated by Dr. H. Zhang. It functions to tonify the kidney and its essence, regulate blood circulation and open up the sensory orifices. Clinical applications of Neuro Plus include patients with different types of neurodegenerative disorders who exhibit a decrease in both mental and physical functions. The recommended dosage is 6 grams per day, or 4 capsules three times daily.

The patients will generally begin to show improvements after two to four weeks of therapy. For chronic type of disorders such as Alzheimer disease, the patient should take the herbs continuously for three months prior to making a clinical evaluation. Neuro Plus is a patented herbal formula in Tianjing, China and is currently distributed by **Evergreen** in the United States. The list of ingredients & their applications are as follows:

- **Morinda, eucommia, lycium fruit, polygonum, alpinia fruit, cuscuta, cornus, cordyceps** (nourishes the kidney).
- **Ginseng, dioscorea, astragalus, american ginseng, white atractylodes, poria** (calm the spirit and increase mental function).
- **Pseudoginseng, crataegus, leech, salvia root, carthamus, anteatr scales, gastrodia, tokoro, fresh rehmannia, scolopendra** (open the channels, increase blood circulation and remove blood stasis).
- **Polygala, acorus, angelica** (open up the sensory orifices and calm the spirit).
- **Testudinis and cornus cervi fragments** (tonify the kidney and generate blood flow).

- **Ginkgo leaf** (improves memory function in patients with Alzheimer's).

#### Other herbs

- **Cumin** (*Cuminum cyminum*)
- **Cardamom** (*Elettaria cardamomum*)
- **Houpa Magnolia** (*Magnolia officinalis*)
- **Berries – Blueberry** (*Vaccinium corymbosum*)
- **Strawberry** (*Fragaria x ananassa*)

For Parkinson's: (Zheng, 2009; Yang, 2005; Ernst, 2006)

#### Vital herbs

- Ginkgo
- Gotu Kola
- Bacopa
- Ashwagandha
- Nicotine
- Black Pepper
- Garlic
- Turmeric
- American Ginseng
- Asian Ginseng
- Drumstick tree
- Ginger
- Indian Noni
- Milk Thistle
- Passion flower
- Valerian root
- Velvet Bean
- Grape Seed
- Evening Primrose
- St. John's Wort

#### Herbal remedies

- **Scull cap**
- **Combination of rhubarb,peony(paeonia),licorice & magnolia bark**

Vital herbs (Akhtar *et al.*, 1990; Amin *et al.*, 1996; Awang, 1997)

#### Velvet Bean

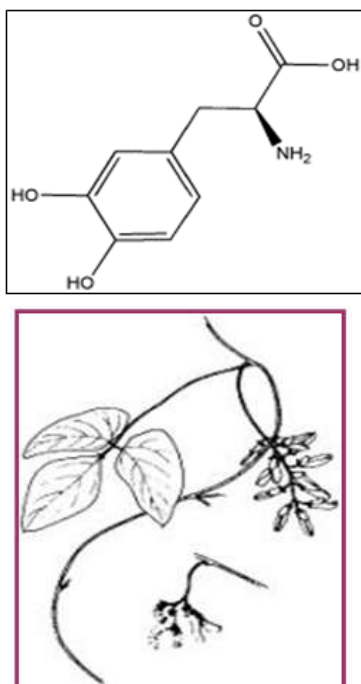
**Botanical Name:** *Mucuna pruriens*

**Common Name:** Kapikachu

**Family:** Fabaceae

#### Levopoda

Velvet bean is an annual climbing vine which grows 3-18 m in height. It is indigenous to tropical regions, especially Africa, India and the West Indies. Its flowers are white to dark purple and hang in long clusters. The plant produces clusters of pods which contain seeds known as mucuna beans. The seeds of velvet bean are high in protein, carbohydrates, lipids, fiber and minerals. The main plant chemicals include: alkaloids, dopamine, l-dopa, serotonin, etc. Concentrations of serotonin have been found in the pod, leaf and fruit. Traditional preparation involves 1/2 to 1 cup of a seed decoction twice daily.



**Fig. 14. Velvet Bean**

Alternatively 1-2 g twice daily of seed powder (tablets or capsules) can be substituted. For standardized extract products: labeled dosages are provided.

#### **Use in Parkinson's**

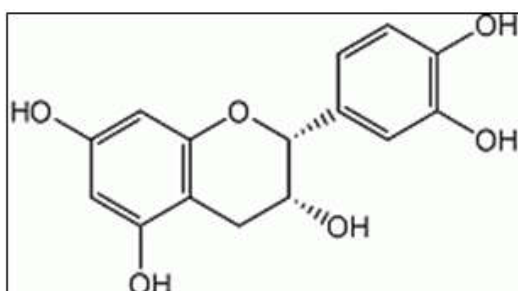
The major active compound present in *Mucuna pruriens* is natural levodopa. Thus, it is mainly used for Parkinson's disease. The seeds of all *mucuna* species contain a high concentration of L-dopa; velvet bean seeds contain 7-10% L-dopa. Levodopa is the major drug used in the treatment of Parkinson's disease. Several preparations containing *Mucuna pruriens* were described for treatment of patients with *Kampavata*. It was found to slow the progression of Parkinson's symptoms (such as tremors, rigidity, slurring, drooling, and balance). According to a study published in the *Journal of Neurology Science*, the *Mucuna Pruriens* preparation exhibit a better response on patients compared to those who took *Levodopa/carbidopa*. To top it all, the side effects of *Mucuna* are minimal.

**Grape Seed (Lininger *et al.*, 1998; Simonetti *et al.*, 2002; Von Bruchhausen, 1998)**

**Botanical Name:** *Vitis vinifera*

**Common Name:** Grape seed

**Family:** Vitaceae



**Fig. 15. Grape seed Proanthocyanidin**

Grapes are native to Asia near the Caspian Sea, but were brought to North America and Europe around the 1600's. This plant's climbing vine has large, jagged leaves, and its stem bark tends to peel. The grapes may be green, red, or purple. Vitamin E, flavonoids, linoleic acid, and compounds called procyanidins (also known as condensed tannins, pycnogenols, and oligomeric proanthocyanidins or OPCs) are highly concentrated in grape seeds. Grape seed is available in capsules, tablets, and fluid extracts. Grape seed extracts and supplements are not currently recommended for children. To prevent circulatory disorders, 50 mg standardized extract (standardized to 95% OPC content) is taken per day. For specific illnesses, 150 to 300 mg per day may be recommended.

#### **Use in Parkinson's**

The active compound in grape seed i.e. proanthocyanidin, are believed to have antioxidant properties. A recent study found that supplementation with grape seed extract substantially increased levels of antioxidants in the blood. Antioxidants are substances that scavenge free radicals (damaging compounds in the body that alter cell membranes, tamper with DNA and even cause cell death).

Free radicals occur naturally in the body, but environmental toxins can also increase the number. Free radicals are believed to contribute to the aging process as well as the development of a number of health problems. Antioxidants found in grape seeds can neutralize free radicals and may reduce or even help prevent some of the damage they cause. Today, professional herbalists use standardized extracts of grape seed to treat a range of health problems related to free radical damage. Studies in laboratories, animals, and people lend some support to these uses.

**Evening Primrose (Von Bruchhausen, 1998; Briggs, 1986; Bruneton, 1995)**

**Botanical Name:** *Oenothera biennis*

**Common Name:** Sun Drop

**Family:** Onagraceae

#### **Gamma-linolenic acid (GLA)**

A circle of leaves grows close to the ground around evening primrose stems after the first year it is planted. Flowers bloom during the second year. Stems are branched, with alternate leaves.

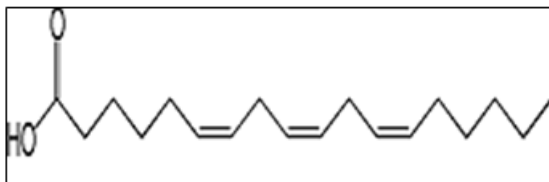


Fig.16. Evening Primrose

Oil is extracted from the seeds and prepared as medicine using a chemical called hexane. The seeds contain up to 25% essential fatty acids including linoleic acid (LA) and gamma-linolenic acid (GLA). Both LA and GLA belong to the omega-6 family of fatty acids. Evening Primrose Oil (EPO) is available as oil or in capsules (the preferred form). EPO products should be kept in the refrigerator. EPO is usually standardized to contain 8% gamma-linolenic acid. It is recommended both for children and adults.

#### Use in Parkinson's

Evening Primrose Oil (EPO) is high in the essential fatty acid, gamma-linolenic acid or GLA and has been used as a clinical treatment for Parkinson's and other tremor-causing disorders. It improved Parkinson's-induced tremors in 55 percent of those who took the equivalent of two teaspoons a day for several months. The oil contains traces of the amino acid tryptophan, which boosts the effectiveness of L-dopa. (Ground evening primrose seeds contain even more). Doses should be 2 tablespoons Evening Primrose Oil per day or 1500 to 2400 milligrams in capsules per day.

**St. John's Wort** (Agostinis *et al.*, 2002; Akhlaghi, 2002; Singhi, 1980)

**Botanical Name:** *Hypericum perforatum*

**Common Name:** Klamath weed, Tipton's weed

**Family:** Clusiaceae

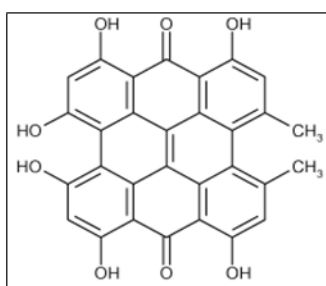


Fig. 17: St. John's Wort

#### Hypericum

*Hypericum perforatum* is a yellow-flowering, perennial herb, indigenous to Europe. The plant gets its name because it is often in full bloom around June 24, the day traditionally celebrated as the birthday of John the Baptist. Both the flowers and leaves are used for medicinal purposes. The active components are hypericin, pseudohypericin and hyperforin found in both the leaves and flowers. Essential oils and flavonoids may also be involved. St. John's wort can be obtained in many forms: capsules, tablets, tinctures, teas, and oil-based skin lotions. Chopped or powdered forms of the dried herb are also available. St. John's wort products should be standardized to contain 0.3% hypericin. Dosage should be directed by a qualified practitioner in children. In adults, dry herb (in capsules or tablets), liquid extract, tea and oil or cream form the usual dosage. Internal dosages generally require at least eight weeks to get the full therapeutic effect.

#### Use in Parkinson's

Since dopamine is a chemical in the brain that produces positive feelings, some natural treatments that are used for Depression can also help people who suffer from Parkinson's Disease. St. John's Wort contains Hypericin. Hypericin has been proven to successfully treat depression. To help relieve the symptoms of Parkinson's Disease, St. John's Wort can be drunk as a tea, used as a tincture, or taken in capsule form. The enzyme monoamine oxidase (MAO) depresses dopamine, so the medications that inhibit MAO (MAO inhibitors) would boost dopamine and decrease Parkinson's risk, just as nicotine does. MAO inhibitors are a major class of antidepressant medications and St.-John's-wort is one reported herbal MAO inhibitor. <http://en.wikipedia.org/wiki/File:Hyperforin.png>

#### Herbal remedies

- **Scull cap**—Strengthens the brain. Standard infusion or 3-9 g; tincture, 10-30 drops (Very often, instead of skullcap germander is given as skullcap. Ask for the genuine herb.).
- **Combination of rhubarb, peony (paeonia), liquorice & magnolia bark**— A combination of herbs that include rhubarb, peony (paeonia), liquorice and magnolia bark are said to stop tremors and relax stiff muscles. Consult a herbalist for proper dosage.

#### Other herbs

- **Coffee & Tea**—One unit of coffee & Tea (3 cups / day for 10 yrs) —lead to a 22% and 28% risk reduction of PD.

- **Cumin** (*Cuminum cyminum*)
- **Cardamom** (*Elettaria cardamomum*)
- **Berries – Blueberry** (*Vaccinium corymbosum*)
- **Strawberry** (*Fragaria x ananassa*)
- **Dandelion root** (*Taraxacum officinale*)
- **Cayenne or Red pepper** (*Capsicum annum*)
- **Goldenseal** (*Hydrastis Canadensis*)
- **Mullein** (*Verbascum thapsus*)
- **Siberian ginseng or eleuthero** (*Eleutherococcus senticosus*)
- **Liquorice** (*Glycyrrhiza glabra*)

**For Epilepsy** (Singhi, 1980; Pandey Neeti, ?; Chauhan, ?)

#### Vital herbs

- Bacopa
- Ashwagandha
- Nicotine
- Black Pepper
- Turmeric
- American Ginseng
- Asian Ginseng
- Drumstick tree
- Milk Thistle
- Passion flower
- Valerian root

#### Ayurvedic remedy

- Pellitory Combination Herbal Powder
- Jatamansi-Aloe Home Remedy
- Susruta's Epilepsy Remedy

#### Ayurvedic remedy

- **Pellitory Combination Herbal Powder**–This is a useful remedy for Epilepsy.
- **Jatamansi-Aloe Home Remedy**–This Ayurvedic home remedy is used in epilepsy, hysteria and convulsions.
- **Susruta's Epilepsy Remedy**– This is a classical Ayurveda remedy for epilepsy.

#### Some Common Herbs

#### For Alzheimer, Parkinson & Epilepsy

**Bacopa** (Bammidi *et al.*, 2001; Mukherjee, 1966; Chopra, ?)

**Botanical Name:** *Bacopa monnieri*

**Common Names:** Waterhyssop, Neeri Brahmi (Sanskrit)

**Family:** Scrophulariaceae

Bacopa monnieri leaf extract is called brahmi in Ayurvedic medicine and is widely used in India, especially for enhancing memory and analgesia (pain relief). Bacopa commonly grows in marshy areas throughout India. It is an adaptogenic herb. Most research on bacopa has concentrated on its effects on learning. 350 milligrams has been taken three times daily for three months in children aged 6-8.



**Fig. 18. Bacopa**

In adults, according to tradition, 50-150 milligrams two or three times a day has been used.

#### *Use in Alzheimer's*

Its active ingredients (bacosides A and B) have been shown to enhance nerve transmission and are potent antioxidants, which protect brain cells from free radicals and other toxic substances. Human studies indicate that Bacopa Monnieri can preserve memory function and is used in treatment of various conditions involving memory loss. It is shown to be the herbal equivalent of anticholinesterase: a drug approved by the FDA for treatment of Alzheimer's. It increases number of dendrites leading to regeneration of brain cells.

#### *Use in Parkinson's*

Bacopa is an Ayurvedic herb that is often used to treat people with Parkinson's. Studies have pointed to its effectiveness as an antioxidant for the brain and suggest that it improves circulation to the brain, as well as improving mood, cognitive function, and general neurological function. Dosage guidelines vary among practitioners, but 100 - 200 mg twice daily is often recommended.

#### *Use in Epilepsy*

Bacopa has strong antioxidant properties, protects mental function in those with epilepsy. An extract of bacopa, an Ayurvedic herb, reduced the frequency of epileptic seizures in a small group of people. It was found to exert anti-epilepsy role over long periods. The dose near LD50 showed effect against seizures. Research in India found hirsaponin to exert some anticonvulsant effect. So it could better be used as an adjuvant in treatment of Epilepsy. B. monnieri extracts have corrective effect on phenytoin induced cognitive deficit.

**Ashwagandha** (Abdel-Magied, 2001; Archana, 1999; Begum *et al.*, 1987)

**Botanical Name:** *Withania Somniferum*

**Common Name:** Winter Cherry

**Family:** Solanaceae

#### *Withaferin*

Ashwagandha, also called as Indian Ginseng, is native to the Mediterranean region, the Middle East, Africa and all parts of Asia, growing in stony and semi-arid regions: cultivated widely.

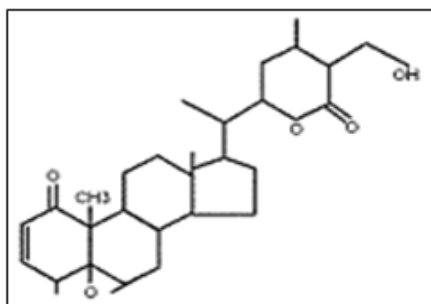


Fig. 19. Ashwagandha

It flowers all year round. This grows in temperate climate and survives for upto 4 to 5 years. The leaves are bowl shaped, small and without thorns. Crushing the fresh leaves and raw roots gives urine like smell hence named Ashwagandha. Withanolides and alkaloids are the active ingredients of the plant. It is considered to be an adaptogen. The herb can be considered as 'daily health supplement'. There are no dietary restrictions with ashwagandha. A daily dose is approximately 250 – 500 milligrams of standardized extract Ashwagandha; 4 – 5% withanolides. 1-2 capsules two times a day after meal or as directed by a health professional. Morpheme A is the highest quality and most effective form of Ashwagandha Extract available in Vegetable capsules.

#### *Use in Alzheimer's*

Ashwagandha can restore the neurotransmitters and hence can be useful in various mental disorders. It contains flavonoids having antioxidant effects. The root of the plant appears in remedies for diminished brain function. It delays the process of aging, act as memory boosters and shows increase in number of dendrites. Consumption of Ashwagandha removes weakness and makes the body strong. Memocare is a product containing ashwagandha to enhance memory, memory alertness and stress.

#### *Use in Parkinson's*

Clinical trials and animal research support the use of ashwagandha for treating Parkinson's disease and as a potentially useful adjunct. Numerous studies on both animals and humans have attested to the mind calming properties of ashwagandha. Specific alkaloids found in ashwagandha root have noted calming, anti-convulsant properties. In a recent study using a standardized model of human Parkinson's disease, ashwagandha extract reversed all parameters of Parkinson's-type neurodegeneration significantly and in a dose-dependent manner.

#### *Use in Epilepsy*

Free-radical damage plays a role in normal ageing and neurological conditions as epilepsy. Ashwagandha has traditionally been used to treat various diseases associated with nerve tissue damage related to the destructive molecules known as free radicals. Ashwagandha also shows significant protection against seizures in experimental models of epilepsy, indicating its potential utility for treatment of petitmal epilepsy.

**Nicotine (Carlson, 2001; Slotkin *et al.*, 2002; Zanardi *et al.*, 2002)**

**Botanical Name: Nicotiana Tobacum**

**Common Name: Tobacco**

**Family: Solanaceae**

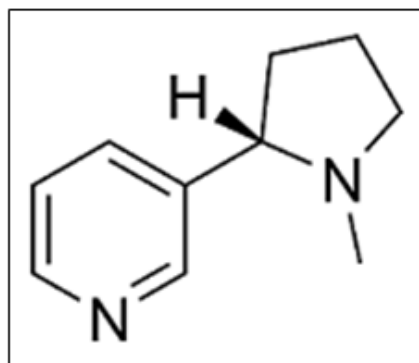


Fig. 20. Nicotine

#### *Nicotine*

Of the many species of tobacco, Nicotiana Tobacum is grown throughout the world and is the main crop used in manufacturing cigarettes. Dried leaves of the plant are used for composition of various products. It shows therapeutic activity in alleviating neurological conditions.

#### *Use in Alzheimer's*

Nicotine slows the progression of AD and improve memory and behaviour. It is distributed quickly through the bloodstream and can cross the blood-brain barrier.



On average it takes about seven seconds for the substance to reach the brain when inhaled and immediately stimulates the release of acetylcholine. Nicotine appears to enhance concentration, memory and alertness due to the increase of acetylcholine. Evidence suggests that the risks of Alzheimer's disease might be twice as high for non-smokers than for smokers.

#### *Use in Parkinson's*

It is suggested that the risks of Parkinson's disease might be twice as high for non-smokers than for smokers. Dopamine is one of the key neurotransmitters actively involved in the brain. Nicotine acts on the nicotinic acetylcholine receptors. By binding to nicotinic acetylcholine receptors, it increases the levels of dopamine. It is thought that increased levels of dopamine in the reward circuits of the brain is what is responsible for the lower risk of Parkinson's disease.

#### *Use in Epilepsy*

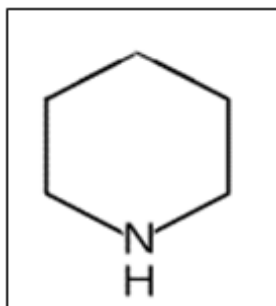
Recent studies have indicated that nicotine can be used to help adults suffering from Autosomal dominant nocturnal frontal lobe epilepsy. The same areas causing seizures in that epilepsy are also responsible for processing nicotine in the brain.

**Black Pepper (Ahn *et al.*, 2001; Allensworth *et al.*, 2012; Banks, 2009)**

**Botanical Name:** Piper Nigrum

**Common Name:** Black pepper, Gol Mirch

**Family:** Piperaceae



**Fig. 21. Black Pepper**

#### *Piperidine*

Black pepper is the ripened berries of *Piper nigrum*, commonly known as Gol Mirch in Hindi belongs to the

Piperaceae family. Black pepper is a tropical evergreen vine that is cultivated widely in India and South East Asia. Dried fruits of the plant are used for composition of various products. Piperidine is the main active chemical. The fruit when ripe is red. It is gathered before it is fully ripe and spread on mats in the sun, when it loses its red color and becomes black and shriveled. Black pepper is commonly used as a cooking spice and has traditional use in Ayurveda (India system of herbal medicine) for treatment of various disorders. It shows therapeutic activity in alleviating neurological conditions.

#### *Use in Alzheimer's*

With the goal of developing Alzheimer's disease therapeutics, new piperidine derivatives having dual action of acetylcholinesterase (AChE) and beta-amyloid peptide aggregation inhibition were designed and synthesized. The present invention relates to novel piperidine derivatives having effect of inhibiting acetylcholinesterase and aggregation of amyloid, Alzheimer's disease-induced protein, and treatment for Alzheimer's disease containing the same. Vitamin C extracted from peppers contain antioxidant properties.

#### *Use in Parkinson's*

The present invention relates to chemical compounds, to pharmaceutical and veterinary compositions, and to the use of such compositions for the treatment or prevention of neurodegenerative pathologies and syndromes such as Parkinson's disease. The disease is associated with an excess production of reactive free radicals. More particularly, the present invention relates to compositions containing antioxidant cyclic hydroxylamines derived from N-piperidine as pharmaceutical compositions for the prevention and treatment of pathologies.

#### *Use in Epilepsy*

Black pepper has been used for the treatment of epilepsy. Based on this traditional application, a new anti-epileptic drug called Antiepilepsine has recently synthesized by Chinese researchers. Antiepilepsine is a chemical relative of piperine, the main alkaloid phytochemical found in plants of the family Piperaceae. Black pepper has also been used as a nerve tonic.

**Turmeric (Aggarwal, 2007; Begum, 2008; Chainani, 2003)**

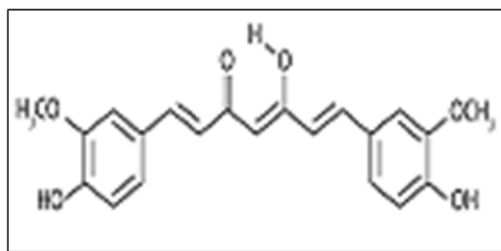
**Botanical Name:** *Curcuma longa*

**Common Name:** Indian saffron, haldi

**Family:** Zingiberaceae

#### *Curcumin*

The bright yellow color in curry powder is from the ground root of turmeric (a relative of ginger); its main active constituent, which is also bright yellow in color, is curcumin (also known as diferuloylmethane). Turmeric is a member of the ginger family and has been used for healing. The rhizome (root) of turmeric is used in traditional Asian medicine to treat various disorders. Laboratory and animal research has demonstrated antioxidant properties of turmeric and curcumin. Studies have indicated potential benefits of curcumin for Alzheimer's disease, Parkinson's disease and Epilepsy.



**Fig. 22: Turmeric**

Typically, turmeric may be used as a powder or mixed with oil and made into a paste. In Adults (over 18 years old) doses used range from 450 milligrams of curcumin capsules to 3 grams of turmeric root daily, divided into several doses, taken by mouth.

As a tea, 1 to 1.5 grams of dried root may be taken twice daily. Average dietary intake of turmeric in the Indian population may range between 2 to 2.5 grams, corresponding to 60 to 200 milligrams of curcumin daily. There is no proven or safe medicinal dose of turmeric in children.

#### **Use in Alzheimer's**

Turmeric is known to be a strong antioxidant, a substance thought to protect body cells from damage caused by a chemical process called oxidation. Antioxidants in turmeric protects the brain. Curcumin is used in preventing and treating Alzheimer's disease. Chemicals in turmeric have appeared to affect several of the pathways that are thought to cause accumulation of the proteins associated with Alzheimer's disease. Elderly Indian populations that consume considerable amounts of dietary turmeric are less likely than their Western counterparts to develop Alzheimer's. Studies in animal models of Alzheimer's disease (AD) indicate a direct effect of curcumin in decreasing the amyloid pathology of AD. Curcumin is a promising agent in the treatment and prevention of AD. The unconventional antioxidant curcumin was effective in lowering oxidative damage, cognitive deficits, and amyloid deposition. The neuroprotective effect of curcumin against neuronal damage to its antioxidant capacity in reducing oxidative stress and apoptotic cell death is attributed.

#### **Use in Parkinson's**

Curcumin, the wonder compound in turmeric, has found a therapeutic use for treatment of Parkinson's Disease. Our Preliminary studies have indicated that curcumin from turmeric may be used as a dopamine agonist in the early stages of treatment of parkinson's disease. Curcumin may prolong the action of dopamine in the brain and also prevent free radical

generation, and inhibition of its major catabolic enzyme monoamine oxidase B. . Researchers conducting experiments on mice have shown that curcumin increased the content of glutathione (GSH), an anti-oxidant in certain nerve cells of the brain that control body movement.

#### **Use in Epilepsy**

Recent studies suggest that curcumin, a potent antioxidant, may provide protection for oxidative stress. The effects of curcumin treatment in mice with KA-induced seizures were investigated. However, marked cell death was not observed in mice treated with curcumin. In addition, curcumin treatment reduced the KA-induced immunoreactivity. Similarly, immunoreactivity analyses indicated that KA causes upregulation of hippocampal GFAP, eNOS, and HO-1 levels, all of which were reduced in animals those received the curcumin treatment. Our findings indicate that curcumin is a potent inhibitor of reactive astrocyte expression and thus, prevents hippocampal cell death. These results also support its potential for use in the treatment of neurodegenerative diseases.

#### **Ginseng (Braak, 2003; Schapira, 2009; Selkoe *et al.*, 2003)**

**Botanical Name:** *Panax ginseng*, *Panax quinquefolium*

**Common Name:** Asian Ginseng, American Ginseng

**Family:** Araliaceae



**Fig. 23: American**

## Ginseng

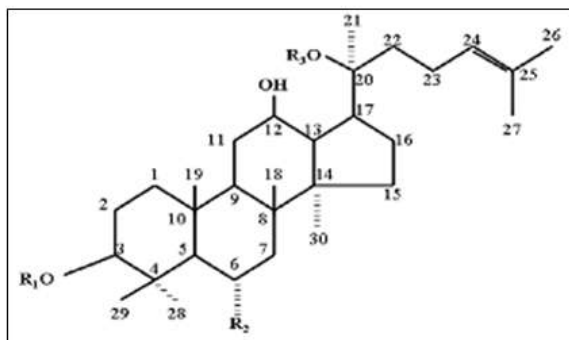


Fig.24. Asian Ginseng

### Basic chemical structure of ginsenosides

The term ginseng means "man-root, and the ancient Chinese believed it could benefit all aspects of human body; today, it is mostly used as an energy booster. This plant has leaves that grow in a circle around a straight stem. Yellowish-green umbrella-shaped flowers grow in the center and produce red berries. Wrinkles around the neck of the root tell how old the plant is. Ginseng products are made from the ginseng root and root hairs. Ginseng, the root of *Panax* species, is a well-known herbal medicine and is now a popular and worldwide used natural medicine. The active ingredients of ginseng are ginsenosides (called ginseng saponins) which are unique to *Panax* species. Ginseng has been used primarily as a tonic and adaptogen. Recent research has suggested that some of ginseng's active ingredients exert beneficial effects on aging, CNS disorders, and neurodegenerative diseases. White ginseng (dried, peeled) or red ginseng (unpeeled root, steamed before drying) is available in water, water-and-alcohol, or alcohol liquid extracts, and in powders or capsules. This herb is not recommended for use in children because of its stimulant properties. In adults, it is consumed in the form of fresh root, dried root, tincture, liquid extract or Standardized extract (4% total ginsenosides).

### Use in Alzheimer's

American ginseng or Asian ginseng may slow the progression of Alzheimer's and improve memory and behaviour. Early research shows that ginseng may improve performance on things such as mental arithmetic, concentration, memory and other measures. For eg., significant improvement in learning and memory has been observed in aged and brain-damaged rats after local administration of ginseng powder. Ginseng or ginseng extract had significant effects on neurological symptoms in aged humans. This positive effect of ginseng on cognition performance is owing to its direct action on the hippocampal neurons. Moreover, Shen and Zhang suggested that the influence of ginsenoside Rg1 on the proliferating ability of neuronal progenitors may serve as an important mechanism underlying its anti-aging effects on learning and memory.

### Use in Parkinson's

Agents such as 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) can cause parkinsonian features in man and experimental animals.

Prolonged oral administration of ginseng extract G115 significantly prevented neurotoxic effects of MPTP in rodents.

1-methyl-4-phenylpyridinium (MPP<sup>+</sup>), an active metabolite of MPTP is selectively toxic to dopaminergic neurons. The degenerative changes by MPP<sup>+</sup>, is effectively reduced by ginsenoside Rb1. Neuroprotective mechanism of ginseng for dopaminergic neurons is elucidated by the inhibitory role of ginseng on MPP<sup>+</sup> uptake in dopaminergic neurons, the suppression of oxidative stress induced by autooxidation of dopamine, etc.

### Use in Epilepsy

The effect of ginseng in the treatment of epilepsy is not immediate, but continuous and prolonged use brings a complete cure. The cure was due to the rejuvenation of the brain cells. There is also proper formation of acetylcholine and cholinesterase. Acetylcholine stimulates the nerve cell to generate small electric charge which is transmitted to the next cell carrying messages back and forth from the brain. Cholinesterase enables the nerve cell to recuperate and recharge itself. Thus promotes the normal formation and transmission of impulses. There are also many instances were seizures stopped completely when only ginseng was given. No conventional drugs were used in the treatment of their epilepsy.

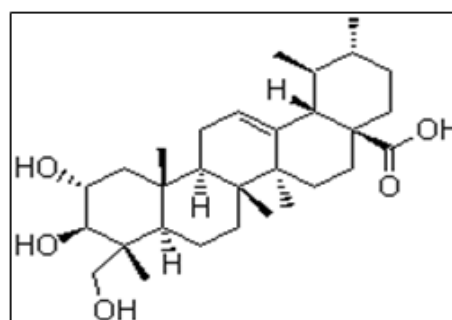
### For Alzheimer and Parkinson

Gotu Kola (Cervenka *et al.*, 2008; Dhanasekaran, 2009; Xu *et al.*, 2008)

**Botanical Name:** *Centella asiatica*

**Common Names:** Centella, Asiatic Pennywort, Brahmi (Sanskrit)

**Family:** Apiaceae





**Fig. 26: Gotu Kola**

#### *Asiatic acid*

Gotu kola is a perennial plant native to India, Japan, China, Indonesia, South Africa, Sri Lanka, and the South Pacific. It is a tasteless, odorless plant that thrives in and around water. It has small fan-shaped green leaves with white or light purple-to-pink flowers and it bears small oval fruit. The leaves and stems of the plant are used for medicinal purposes. Gotu kola is available in teas, as dried herbs, tinctures, capsules, tablets, and ointments. It is not recommended for those under 18 years old. Adult dosage of gotu kola may vary depending on the condition being treated and also on the form. Gotu kola's key ingredient is asiatic acid, a pentacyclic triterpene which enhances induction of antioxidant levels at an initial stage of healing.

#### *Use in Alzheimer's*

Gotu Kola popularly called as the "miracle elixirs of life" because an ancient Chinese herbalist lived for more than 200 years as a result of using this particular herb. It shows cognitive-enhancing property and traditionally used as memory enhancers. Study showed that the herb reduces an oxidant known as nitric oxide, which is triggered by the build-up in the brain of beta-amyloid plaques associated with Alzheimer's thus exhibiting antioxidant activity. It is an adaptogenic herb, which can be taken all the time in therapeutic doses without any side effects. Triterpenoids (active compounds in gotu kola) have been shown to boost mental function in mice.

#### *Use in Parkinson's*

Gotu Kola has a positive effect on poor blood circulation in the legs and the rest of the circulatory system. It improves the flow of blood while strengthening the veins and capillaries. The circulatory improvement occurs because gotu kola decreases vein hardening, improves the connective tissue around veins, and helps the blood to flow through veins. This helps in reducing tremors in Parkinson patients.

#### **Indian Noni (Noni, 2011)**

**Botanical Name:** *Morinda citrifolia*

**Common Name:** Indian mulberry

**Family:** Rubiaceae



**Fig. 30.**

#### **Indian Noni**

Noni grows in shady forests as well as on open rocky sandy shores. It reaches maturity in about 18 months and then yields between 4-8 kg of fruit every month throughout the year. It contains many seeds. The main micronutrient features of noni pulp powder include exceptional vitamin C content and substantial amounts of niacin (vitamin B3), iron and potassium. Vitamin A, calcium and sodium are present in moderate amounts. Noni fruit contains phytochemicals such as lignin, flavonoids, alkaloids, etc. Xeronine, a relatively small alkaloid, is physiologically active and important for the proper functioning of all cells in the body.

#### *Use in Alzheimer's*

Fruits of Noni are believed to be as an appetite and brain stimulant. Scopoletin, an important ingredient of Noni has also been found to exert strong anti-inflammatory activity. Impaired endogenous antioxidant system favors accumulation of free radicals which plays a central role in neurodegeneration. The role of free-radical-mediated oxidative injury is recognized in Alzheimer's. Indian Noni contains all the antioxidant vitamins, important trace minerals and is rich with phytochemicals. The synergistic actions of all those ingredients just make Indian Noni a very powerful antioxidant food supplement that may help in prevention and/as a therapeutic supplement for Alzheimer's.

#### *Use in Parkinson's*

*Morinda Citrifolia* stimulates the immune function. It has been helpful for Parkinson's disease sufferers and aids in relieving depression. *Morinda Citrifolia* fruit juice helps in inhibiting monoaminase oxidase (MOA) wherein the disorder is reduced or eliminated.

#### **For Parkinson and Epilepsy**

#### **Milk Thistle (Allain et al., 1999)**

**Botanical Name:** *Silybum marianum*

**Common Name:** St. Mary's Thistle

**Family:** Asteraceae

#### ***Silybum***

Milk thistle is native to the Mediterranean, but is now widespread throughout the world.

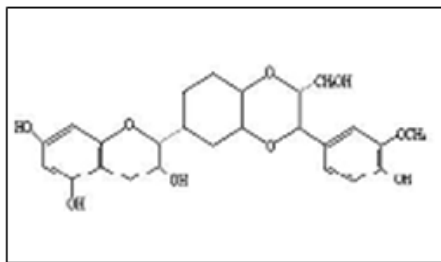


Fig. 31: Milk Thistle

This stout thistle usually grows in dry, sunny areas. The stem branches at the top, the leaves are wide with white blotches or veins. The flowers are red-purple. The small, hard-skinned fruit is brown, spotted, and shiny. It is easy to grow and it matures quickly, in less than a year. The active ingredient or liver-protecting compound is known as silymarin the substance, which consists of a group of compounds called flavonolignans. Silymarin reduces inflammation and has potent antioxidant effects. Most milk thistle products are standardized preparations extracted from the fruits (seeds) of the plant. Available forms are capsules of standardized dried herb, liquid extract, tincture, etc. The recommended adult dose is adjusted to account for the child's weight. For adults, recommended dose is generally 12 to 15 g dried herb per day.

#### Use in Parkinson's

Glutathione therapy is inexpensive, safe and can dramatically improve functioning for patients with Parkinson's Disease. It slows the disease by limiting free radicals. It allows the dopamine in brain to be more effective. But, it is digested very rapidly when given orally. Intramuscular injections are somewhat effective, but it's minimal. Milk Thistle causes retention of glutathione making it available and thus reducing risk of Parkinson's disease.



#### Use in Epilepsy

Some patients are turning to herbal remedies for the treatment of epilepsy. Milk thistle has strong antioxidant (destroys oxygen free radicals) and anti-inflammatory actions. Milk thistle inhibits the cytochrome P-450 system. This helps in reducing seizures. High GABA content in valerian itself. The amount of GABA present in valerian extract is sufficient to induce release of GABA in synaptosomes and may also inhibit GABA reuptake. Thus, it is used in the treatment of epilepsy.

#### Current Scenario

Recently some herbal formulations also claim to improve memory. Smriti Rasayans (memory rejuvenators), as they are called, include indigenous Indian herbs like Brahmi (Bacopa Monnieri), which is taken by millions of people in India to promote good memory and circulation. Recent extensive clinical and experimental trials in postgraduate medical and drug research institutes in Lucknow, Benares and Madras show that Brahmi "not only arrests further loss but also slows down the process of subsequent reduction in senile dementia". The herb has been shown to arrest memory loss due to normal ageing. Brahmi is a fascinating herb which has been said to improve brain and peripheral circulation, improve mood, promote positive personality and behaviour and to help reduce fits in epilepsy. Along with another herb called Mucuna pruriens, it has also been shown to help Parkinson's disease. This herb is an economical option for the treatment and prevention of memory loss and dementia and is very safe, without any side effects. Intensive studies are being carried out in medical institutes in the USA and India to evaluate this.

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