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Review

Herbs Used for Brain Disorders

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Abstract

Human brain disorders vary a wide rage which includes Alzheimer's disease, Parkinson's disease, depression, epilepsy, schizophrenia, anxiety, Huntington's disease etc. Psychotherapeutics does not meet properly for therapeutic possibilities for majority of patients with mental health problems but herbal remedies are ultimate therapeutic hope for such patients. Many synthetic drugs because of many unwanted but unavoidable side effects have poor patient compliance. Therefore herbal treatment is being preferred over conventional treatments. Much attention and so scope is drawn towards herbal remedy of many brain disorders. This session covers a broad spectrum of natural drugs used in specific brain disorders. This topic also discusses the source of active constituent and specific part of the plant being used.

Keywords: Reverse pharmacology, Bioavailability, Alzheimer's disease, Parkinson's disease, Depression, Epilepsy, Schizophrenia, and Anxiety.

1. Introduction

Nature is the best combinatorial chemist and possibly has answers to all diseases of mankind. Failure of some synthetic drugs and its side effects have prompted many researches to go back to ancient healing methods which use herbal medicines to give relief. Many of the thousands of plant species growing through out the world have a direct pharmacological action on the body[1-7].Herbal treatment is a natural form of healing or alternative therapy where herbs and plants are used in the form of extracts, pills, syrup or powder to cure ailments or diseases of human beings and in some cases animals too. Today herbal remedies are back into prominence. The efficacy of many conventional medicines which once had near universal effectiveness against serious infections is on the wane.

In Ayurveda-drug discovery uses "Reverse pharmacology", in which drug candidates are first identified, based on large scale use in the population and validated in clinical trials. Till now, natural product compounds discovered from medicinal plants (and their analogues also) have provided numerous clinically useful drugs. Four billion people or about 80% of the world's population uses herbal medicine as part of health care. In India itself, there are more than 1100 medicinal plants grown all over the wild forests. Of these, some 60 genuses are used immensely in medicinal preparations[8, 9, 10]. The hydro soluble fiber *plantago ovata* husk improves levodopa with carbidopa bioavailability after administration in Parkinson's disease.

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Curcuma oil modulates the nitric oxide system response to cerebral ischemia/reperfusion injury. Nimbolide a limonoid from *azadirachta indica* inhibits proliferation and induces apoptosis of human choriocharcinoma cells in Parkinson's disease.

Effects of a standardized *Bacopamonniera* extract on cognitive performance, anxiety & depression in the elderly. Curcumin has anti convulsant activity on increasing current electric shock seizures in mice[11, 12]. Common brain disorders include Alzheimer's disease, Parkinson's disease, depression, epilepsy, schizophrenia, anxiety and Huntington's disease[13-16].

Alzheimer's disease:

Alzheimer's disease originally defined as prsenile dementia, means an acquired organic mental disorder with loss of intellectual abilities of sufficient seviarity to interfere with social or occupational functioning. It is associated with brain shrinkage and localized loss of neurons, mainly in the hippocampus and basal fore brain. Two microscopic features are characteristic of the disease namely extra cellular amyloid plaques consisting of amorphous extracelluar deposits of β-amyloid protein and intranuronal neurofibrillary tangles, comprising filaments of phosphorilated form of a microtubule associated protein. This disease is also considered as a short term memory loss.

Parkinson's disease:

It is a progressive disorder of movement associated with continuous shivering that occurs mainly in the elderly. It is commonly associated with dementia. The symptoms include tremor at rest usually starting in the hands, muscle rigidity detectable as an increased resistance in passive limb movement, hypokinesis suppression of voluntary muscles. In this condition the neurotransmitter levels are decreased in brain, such as dopamine,5-HT, acetylcholine ,nor epinephrine. These neurotransmitters are decreased mainly in the substantianigra and carpus striatum of brain.

Depression:

Depression is the most common affective disorder which is accompanied by hallucination and delusions. It is a common affective disorder of mood rather than disturbances of thought or cognition. In this disease condition the neurotransmitters levels in brain is increased such as dopamine, acetylcholine, nor epinephrine etc.

The symptoms of this disease are of two types- emotional symptoms: Feelings of guilt, loss of motivation, ugliness etc and biological symptoms: Retardation of thought, loss of libido, sleep disturbance and loss of appetite.

There are 2 types of depressive syndrome namely

1) Unipolar depression: In this mood swings are always in the same direction.
2) Bipolar depression: In which depression alternates with mania.

Epilepsy:

The characteristic event in epilepsy is seizure. This is associated with high frequency discharge of impulses by group of neurons in the brain. It is divided into 1) Partial epilepsy: In which the discharge begins locally. In which localized areas of brain are damaged; the symptoms depend on the brain region or regions involved and 2) Generalized epilepsy: In which total brain is damaged, including reticular system.

Schizophrenia:

It is one of the most important forms of psychiatric (mental) illness. In this diseased condition patient don't know what is happening at present and he does not cooperate with the physician for treatment.

The symptoms of this disease are 2 types:

1) Positive symptoms: delusions (often paranoid in nature), Hallucination, thought disorders, abnormal behaviour.
2) Negative symptoms: withdrawal from social contact, flattening of emotional responses.

In this condition the level of neurotransmitter such as dopamine, 5HT, acetylcholine, nor epinephrine level is increased in the brain.

Huntington's disease [HD]

Huntington's disease is called as Huntington disease, Huntington's chorea, chorea major, or simply HD and is the most common genetic cause of chorea. This incurable, neurodegenerative disorder was named after the American physician George Huntington who accurately described it in 1872. Prevalence, per country, is up to 7 people in 100,000 (in populations of Western European inheritence), and can be much higher in localized regions. Onset of physical symptoms can begin at any age, although the mean age of onset is 35 to 44 years of age. Less commonly, onset is before the age of twenty, and the condition is classified as juvenile HD (also known as akinetic-rigid HD or Westphal variant HD) - which progresses faster with slightly different symptoms. In 1993 genetic testing was made possible with the discovery of a single causal gene, the first non-sexlinked dominant disease gene to be found,as such counselling for HD had to be developed and became a model for other dominant disorders. The test can be performed before the onset of symptoms, at any age - even pre-birth, which has raised various ethical issues and their debate is heated.

The mechanism of the disease is not fully understood, but a number of factors have been identified. A mutation in the Huntingtin gene, causes the production of the mutant protein huntingtin, which in turn produces cell and macroscopical changes in the brain.There is no cure for HD, although there are treatments to relieve some of its symptoms. The most characteristic initial physical symptoms are jerky, random, and uncontrollable movements called chorea. Rigidity and dystonia become evident as the disorder progresses, and gradually become the dominant physical symptoms.

Anxiety:

Anxiety is a psychological and physiological state characterized by cognitive, somatic, emotional, and behavioral components. These components combine to create an unpleasant feeling that is typically associated with uneasiness, fear, or worry. Anxiety is a generalized mood state that occurs without an identifiable triggering stimulus. As such, it is distinguished from fear, which occurs in the presence of an external threat. Additionally, fear is related to the specific behaviors of escape and avoidance, whereas anxiety is the result of threats that are perceived to be uncontrollable or unavoidable.

Different types of herbs for anxiety

Lavender is a herb with properties that is excellent for treating panic and anxiety. It affects the central nervous system in much the same way as some drugs without the negative side effects. Passion flower can help in high blood pressure and when used as herbs for anxiety it can be put in tea or food. It is also an ingredient in many herbal remedies. Ginseng has long been used for anxiety and is a natural immune booster. The Chinese have known this for a long time. Cannabis sativa is usually smoked but can be eaten and is a great anxiety reliever. Many are aware of this and people worldwide are abusing this remedy. Valerian is used throughout the world as a natural sedative and helps with insomnia and panic attacks. It is also a mild painkiller and is considered very safe for short term use. Kava Kava is a root used for anxiety and is also well known in the treatment of sleep disorders such as insomnia. Lemon balm is good for headaches and also for relieving stress and anxiety. It is a natural sedative and is good for easing tension.Chamomille is put into tea and has been a highly touted herb for anxiety[17-21].

2. Details of Plants having CNS activity

1. *Hypericum perforatum*(St.John's wort):

It consist dried aerial parts and flowers of *Hypericum perforatum* Family Hypericaceae (Clusiaceae).Chemical constituents include anthraquinones mainly hypercin and pseudohypercin. The current use of St.John's wort for the treatment of mild to moderate depression. The antidepressant activity of "hypercin" is attributed to inhibition of neuronal uptake of seratonin,nor epinephrine and dopamine like many other antidepressants and also inhibits GABA & glutamate uptake in brain[22,23].

2. *Piper methysticum*(kava-kava):

It consists of dried root of *Piper methysticum* Family Piperaceae. It contains piperdine, kava pyrones. It is used as sedative, anxiolytic and hallucinogen. The active constituents kava pyrones have a variety of actions like inhibition of voltage dependent sodium channels, increasing neither GABA-A receptor density blocking nor epinephrine reuptake and suppressing the release of glutamate[18].

3. Valeriana walchii:

It consists of the dried rhizomes, stolons and roots of *Valeriana walchii*. Family Valerianaceae. It contains sesquiterpenes like balerenal; also contain esters like bornyl formate, euginyl isovalerate, and alcohols, eugenol. It comprises of acids, esters, ketones like faurinone. The mechanism of action of valerian tends to sedate by stimulating activity of the nerve transmitter GABA that dampens the brain arousal system[9].

4. *Ginkgo*(Maiden hair-tree):

Leaves are obtained from the dioeceous tree *Ginkgobiloba* family Ginkgoaceae. It is only living plant in this family containing flavonoid glycoside. It contains diterpine lactones

like ginkgolides A, B, C, J, and M. It is used in symptoms of short term memory in Alzheimer's disease and also in anxiety[9].

5. *Centella asiatica*(Jal brahmi,mandukparani):

It consists of fresh or dried leaves and stems of *Centella asiatica* family Umbelliferae. It contains saponins Asiaticosides also contain Asiatic acid, madacassic acid, betulic acid. Used as anxiolytic agent, used in epilepsy and also considered as antidepressant. It decreases the levels of malondialdehyde (MDA) with simultaneous increase in the levels of glutathione in the brain[22].

6. Withania somnifera (Ashwagandha):

It consists dried roots and stem bases of *Withania somnifera* family Solanaceae. The main constituent is steroidal lactone, withaferin and withanolides. These withaferin A, B, C, also contain active principles of sitoindosides VII, VIII. It has sedative and hypnotic properties. The active principles sitoindosides have shown anti stress activity. Used as antidepressant. Both Ashwagandha and lorazepam group demonstrated reduced brain levels of a marker of clinical anxiety. It also exhibits anti depressant effect comparable to that induced by imipramine in the forced swim induced behavioral despair and "learned helplessness" tests[24].

3. Discussion

Herbal remedy for human brain disorders is much preferred over synthetic drugs because of various side effects of synthetic drugs ranging from sleep disorders to withdrawal syndromes. Herbal treatment not only improves patient compliance but also there are possibilities of enhancing the bioavailability of many drugs. Active constituents extracted from specific parts of various plant origins have proved to be beneficial. Although some formulations have drawn attention, in depth clinical trials should be conducted which will be a major tool to prove the benefits for a patient. That is what matters!

Table 1. Herbal drugs used in Schizophrenia [18, 19]

Sl.no	Plant name	Family	Common name	Mode of use	Chemical constituents
1	Catharanthus rosea	Apocynaceae	Red periwinkle	Dried Root	Indole and indoline alkaloids- ajmalicine, lochnerine, dimeric; indole base of monoterpene- vinblastine, vincristine.
2	Rauwolfia serpentine	Apocynaceae	Sarpaganda	Dried Root	Indole alkaloids- reserpine, ajmaline, serpentine
3	Canscora diffusa	Gentianaceae	Janjada	Fresh whole plant	Beta amyrin, xanthones
4	Datura metel	Solanaceae	Nalla ummetta	Dried whole plant	Tropane alkaloids- hyoscyamine, scopolamine, flavonoids

Table 2. Herbal drugs used in Alzheimer's disease [9, 19, 21, 25]

Sl.no	Plant name	Family	Common name	Mode of use	Chemical constituents
1	Melissa officinalis	Labiatae	Lemon balm	Fresh leaf	Lutiolin(flavonal glycoside)
2	Salvia officinalis	Labiatae	Sage leaf	Fresh leaf	A,β-thujone together with cineole
3	Centella asiatica	Apiaceae	Indian penni wort	fresh root	Aciaticosides(saponins)
4	Catharanthus roseus	Apocynaceae	Periwinkle	Dried root	Vincristine, vinblastine
5	Ginkgo biloba	Ginkgonaceae	Maiden hair tree	Dried leaf	Ginkgolides (A,B,C,J,M)

Table 3. Herbal drugs used in Parkinson's disease [18, 25]

Sl.no	Plant name	Family	Common name	Mode of use	Chemical constituents
1	Blepharis maderaspatensis	Acanthaceae	Nethirs poondu	Dry seed	Steroids- gomisin D
2	Smilax perfoliata	Smilacaceae	Ram damtena	Dry root	Steroidal sapogenins-diosgenin
3	Smilax zeylanica	Smilacaceae	Rough blind weed,hill lotus	Dry root	Alpha, beta hydroxy acids
4	Plantago ovata	Plantaginaceae	Flax seed	Husk fibre	Mucilage, cyano genetic glycocydes- Linamarin, lotaustralin
5	Azadirachta indica	Maliaceae	Neem,margosa	Fresh leaf	Meliacin- nimbolide, quercetin, kaempferol
6	Emblica officinalis	Euphorbiaceae	Amla,Indian goose berry	Fruit	Tannins, Phyllembelin, Pectins, Vitamin C

Table 4. Herbal drugs used in Depression (affective disorder) [12, 22, 23]

Sl.no.	Plant name	Family	Common name	Plant part used	Chemical constituents
1	Dendrophthoe falcata	Loranthaceae	Honey suckle-mistletoc	Fresh/ dried whole plant	Tanins, flavons, oleanolic acid, beta sitosterol, stigmasterol
2	Breynia retusa	Euphorbiaceae	Kanumu chettu	Dried bark	Triacontane, peonidin, lanosterol
3	Celtis philippensis	Ulmaceae	White Indian nettle	Fresh/ dried whole plant	Betulin, di- methyl elagic acid, gallic acid, leucocyanide glycoside
4	Asparagus recemosus	Liliaceae	Water roof,wild carrot, satavari	Fresh tuber	Asperagin, shatavarin
5	Hipericum perforatum	Hypericaceae	St.John's wort	Dried arial parts	Hypercin, pseudo hypercin

Table 5. Herbal drugs used as Sedatives & Hypnotics [1, 24, 25]

Sl.no	Plant name	Family	Common name	Mode of use	Chemical constituents
1	Sonchus oleraceus	Compositae	Sow thistle, milk thistle	Dried Stem	Glyphosphate
2	Xanthium indicum	Compositae	Cocklebur	Dried whole plant	Alkaloids, polyplenolic compounds, saponins,
3	Aganosma dichotoma	Apocynaceae	Nallateega	Dried whole plant	Kampferol, phenolic acid
4	Nicotiana tubacum	Solanaceae	Tobacco	Dried leaf	Alkaloids-nicotine, nornicotine, anablastine

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