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MEDICINAL PLANTS WITH ANXIOYTIC, ANTIDEPRESSANT, ANTICONNVULSANT AND NOOTROPIC EFFECT

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ABSTRACT

Anxiety concern is normal human emotions. When these emotions last for long time, they have effect on both physical and mental health. It is widely recognised as leading cause of disability around world. Generalized anxiety disorder, obsessive-compulsive disorder, post-traumatic stress disorder, panic attacks, phobias, and depression are also included in this category. Anxiety is treated with anti-anxiety medications. They work by lowering brain activation, which helps with anxiety, nervousness, mood stabilisation, and sleep. Anti-anxiety medication usage over time can lead to psychological and physiological dependency. Most medicinal plants were found to have antidepressant effects by controlling serotonin, noradrenaline, and dopamine synaptically, regulating hypothalamic-pituitary-adrenal axis function, strengthening anti-oxidant defences, and lowering inflammatory mediators, according to study. Modern drugs can be found in abundance here. In herbal medicine, various plants are used to cure epilepsy, and various plants have yet to be scientifically studied. Phytoconstituents have been used to cure variety of disorders in humans, including epilepsy. Herbal products are widely used for treatment of variety of diseases around world, particularly where allopathic medicine fails or has serious side effects. Physical dependency,

resistance, loss of cognitive ability, and effects on gastrointestinal, cardiovascular, and immune systems are all significant side effects of psycho neural medications.

INTRODUCTION

One of most common psychiatric disorders that people encounter on daily basis is anxiety disorder. It is totally natural state of fear and worry in humans. These feelings have effect on both physical and emotional wellbeing as they last for long time. One-eighth of world's population is affected. It is frightening syndrome characterised by nausea, nervousness, restlessness, thanatophobia, sweating, stomach upset, and dry mouth. Anxiety is referred to as phobia where it is correlated with intense perceptions of things or environments (e.g., snakes, open fields, flying, or fire), and social disorder where fear is combined with social interactions. Obsessive compulsive disorder affects people who have recurrent and fresh intrusive feelings, and who carry out repetitive and compulsive actions to escape these distressing thoughts. GABA, monoamines (Dopamine, noradrenaline, and serotonin), neuropeptides (galanin, neuropeptides Y, arginine vasopressin, tackykinin, and substance P), neurosteroids, and cytokines are all implicated in fear. Depression is multifactorial, persistent, and life-threatening condition that affects vast amount of individuals around world. Depression affects 29 percent of world's population, making it one of top ten leading causes of death. Depression will be second most common illness in developing countries by 2020, according to WHO. Not only patients, but also their friends and family, are affected by depression. Common signs of depression include social isolation, lack of energy, sexual dysfunction, sleep disturbances (which affect 75 percent of patients), nightmares, depressive mood, and anhedonia. Suicidal thinking and sadism are found in 15% to 25% of people with depression. Researchers are now looking for more precise medications that are both safe and affordable. Researchers in this area are interested in herbal plants because they have long been used to cure variety of illnesses, including mental conditions, because they have fewer side effects than pharmaceutical and chemical medicines. Aim of this paper is to summarise results of research on medicinal plants' antidepressant effects and mechanisms of action, as well as biological compounds in these plants that are responsible for antidepressant action.[1]

Anticonvulsants: Epilepsy is concept that refers to category of severe seizure conditions that all share one thing in common: abrupt onset and transient periods of deprivation or disruption of consciousness (seizures) state of consciousness, generally but not always with distinguishing attribute Convulsions are form of body movement that occurs when autonomic

nervous system is overworked. Hyperactivity is term used to describe person who Epilepsy can be divided into two categories.

1. **Tonic clonic seizures/Grandmal/Major epilepsy:** This is marked by complete lack of consciousness, accompanied by generalised tonic convulsive movements, and then clonic convulsive movements. Duration of headache, drowsiness, confusion, and exhaustion follows. Tongue chewing, frothing at mouth, and incontinence may accompany assault.
2. **Petit-mal/Absence epilepsy:** This form of seizure is characterised by rapid lack of continued conscious function without convulsions or loss of postural balance. For one second to one minute, patient seems to go silent, which may be related to bilateral clonic motor function, such as eyelid blinking.[2]

Nootropic medications that are used as memory enhancers can assist with memory, as well as Alzheimer's disease and other mental disorders. Memory is perhaps most significant attribute that separates humans from other species. However, memory problems may occur for variety of causes, and in that situation, individual is unable to fully use his or her abilities. Alzheimer's disease has three distinct characteristics in terms of brain histopathology: appearance of amyloid plaques, presence of neurofibrillary tangles, and destruction of neuronal cells. Since lack of neurons causes defects of neurotransmission, even neurons that are not dead in Alzheimer's disease may have compromised neurotransmission. As result, neurons that are malfunctioning pose appealing goal for symptomatic treatment of Alzheimer's disease, as correcting their defective neurotransmission may lead to therapeutic changes.[3]

Anxiolytic medication

Anxiety conditions are treated with these drugs, which are also used as mild tranquillizers. Barbiturates were widely used as anti-anxiety medications prior to advent of benzodiazepines. Anxiety was often treated with Phenobarbital and other long-acting barbiturates. Barbiturates were replaced by benzodiazepines for treatment of anxiety in 1960s. Since they have greater margin of protection in event of overdose, benzodiazepines are used more often than barbiturates. Benzodiazepines, on other hand, are linked to violence, dependency, and withdrawal symptoms. Another drug used to combat anxiety is buspirone, nonbenzodiazepine. Buspirone, unlike benzodiazepines, is not linked to addiction or withdrawal effects. Antidepressants are also helpful in management of anxiety conditions such as panic disorder, generalised anxiety disorder, post-traumatic stress disorder, and

obsessive-compulsive disorder. There are only handful synthetic anti-anxiety drugs on market. Anxiety patients face number of problems by taking commercially accepted anti-anxiety treatments. As result of their widespread use and medicinal effectiveness with little side effects, demand for herbal drugs is increasing.[4]

Table 01: Summary of several anxiolytic herbs.

Sr.	Botanical Source	Common Name	Other Biological Activities
1.	*Abies pindrow* Family: Pinaceae	Pindrow fir	Bronchoprotection and ulcer protection
2.	*Achiellea millefolium* Family: Asteraceae	Yarrow	Anti-inflammatory, anti-microbial and anti-spasmodic
3.	*Aegle marmelos* Family: Rutaceae	Bael	Anti-diabetic, anti-inflammatory, anti-pyretic, analgesic and anti - Hyperlipidaemic
4.	*Albizia julibrissin* Family: fabaceae	Pink silk tree	Anti-microbial and anti-depressant
5.	*Albizzia lebbeck* Family: Mimosaceae	Lebbeck	Anti-tumour, anti-diabetic and anti-inflammatory
6.	*Aloysia polystachya* Family: Verbenaceae	Burrito	Anti-spasmodic, anti-depressant and anti-emetic
7.	*Angelica sinensis* Family: Apiaceae	Female ginseng	Anti-alzheimer and anti-osteoporosis
8.	*Aniba riparia* Family: Lauraceae	Nees	Anti-depressant, anti-inflammatory and analgesic
9.	*Annona cherimola* Family: Annonaceae	Custard apple	Anti-diabetic, anti-microbial and anti-tumour
10.	*Apocynum venetum* Family: Apocynaceae	Luobuma	Anti-depressant, anti-hypertensive and hepatoprotective
11.	*Azadirachta indica* Family: Meliaceae	Neem	Anti-ulcer, anti-bacterial, hepatoprotective, hypoglycaemic
12.	*Bacopa Monniera* Family: Plantaginaceae	Brahmi	Anti-stress, anti-inflammatory, anti-amnesic, anti-microbial
13.	*Calotropis gigantea* Family: Asclepiadaceae	Crown flower	Antibiotic, anti-asthmatic and wound healing
14.	*Casimiroa edulis* Family: Rutaceae	White sapote	Anti-depressant, sedative, anti-convulsant and hypotensive
15.	Cassia siamea	Siamese senna,	Analgesic, anti-inflammatory and anti-diabetic

Antidepressant medicinal plants

For thousands of years, herbal plants have been used to cure depression. Poppy (opium), Atropa belladonna (deadly nightshade), Indian hemp (hashish), henbane (hyoscyamine), thorn apple (scopolamine), and St. John's wort (hypericum oil) are few of them. Sumerians of third millennium BC cultivated and used opium poppy extensively. Opium was also found in

Minoan civilization during Bronze Age in 3rd and 2nd millennia BC, as congealed latex from unripe poppy capsules. Egypt and Asia used and bred Atropa belladonna (deadly nightshade) and hashish (Indian hemp) as early as third millennium BC. Iconic Ebers Papyrus contains hyoscyamine and scopolamine.[5]

1. *Danggui-Shaoyao-San*

Plants enhance memory and learning disability through preventing nerve cell death and oxidative stress, decreasing and preventing amyloid beta plaque formation, rising synaptic plasticity, and reinforcing long-term potentiating. This plant-based mixture has also been found to have analgesic properties. In research, it was discovered to have beneficial effects on chronic stress. Additionally, this remedy was effective in treating weight loss, anorexia, forensic and locomotive operations, and insomnia, both of which are depression-related symptoms. Chronic stress affects those neurotransmitters that regulate sleep-wake cycle, such as dopamine, serotonin, and norepinephrine, resulting in sleep disorders. Danggui-Shaoyao-San was shown to induce spike in monoamine neurotransmitters in brains of elderly mice in study. Analysis of Danggui-Shaoyao-antidepressant San's function found that it restored noradrenaline and dopamine levels that had been depleted by persistent stress, as well as decrease in malondialdehyde and rise in superoxide dismutase. Key compounds found in herb, such as albiflorin, paeonflorin, fluoric acid, ligustrazine, and ligustilide, can be linked to antidepressant effects of Danggui- Shaoyao-San. Fluoric acid is phenol compound that aids in treatment and prevention of wide range of diseases and disorders. Chinese FDA has licenced its sodium salt for treatment of cerebrovascular and cardiovascular disorders. Fruolic acid functions as antidepressant by affecting serotonergic system. Another major compound of Danggui-Shaoyao-San, paeonflorin, triggered release of serotonin and norepinephrine from synaptosomes, resulting in anti-stress effects.[6]

2. *Chrystactinia mexicana*

Apigenin, caffeic acid, fruolic acid, and coumaric acid are major compounds present in aqueous C. mexicana extract. Caffeic acid, coumaric acid, and fruolic acid are phenylpropanoids that have been shown to have antidepressant properties in C. mexicana. Frucolic acid and caffeic acid have been found to have antidepressant properties. Fruolic acid tends to be beneficial in treatment of neurodegenerative disorders due to its antioxidant and anti-inflammatory properties. Fruolic acid prevents nerve cells from NMDA excitotoxic effects by acting as NMDA receptor antagonist. In addition, in vivo and in vitro, fruolic acid

affects nerve cell cycle and induces increase in neural stem cell differentiation. Apigenin is flavonoid agent of sedative, anti-anxiety, and antidepressant effects present in most plants. C. mexicana has been shown to have antidepressant properties in vivo. Apigenin binds to benzodiazepine binding site in GABAA receptors and has pharmacological effects.[7]

3. *Lavandula officinalis*

The Lavandula genus, which belongs to Lamiaceae family, comprises 39 distinct species with global distribution.

Gastrotonic, diuretic, perspiratory, anticonvulsant, carminative, antiheadache, nerve tonic, sedative, insomnia-treating, antianxiety, and anti-disease Alzheimer's are some of properties of lavender. Pregnant women's plasma levels of serotonin 7 metabolites increased after inhaling L. officinalis extract. DailyVbathing with L. angustifolia essential oil increased mood and substantially decreased depressive symptoms in single-blind, controlled, random clinical trial. Linalool, major compound in L. angustifolia essential oil and extract, has antidepressant effects. Linalool's antidepressant effects were blocked by pretreatment with WAY100635 and yohimbine, but other compounds had little effect on linalool's antidepressant function. Linalool's antidepressant properties are mediated by serotonergic and noradrenergic receptors.[8]

Anticonvulsant Herbs and Practices

Anticonvulsant medications work by preventing convulsions from occurring by inhibiting discharge and causing hypnosis. Despite availability of many anticonvulsant medications to relieve convulsions, epilepsy therapy remains inadequate due to side effects and medication interactions. Intractable convulsions necessitate development of new, more powerful anticonvulsant medications. Nature, on other hand, is rich source of biological and chemical diversity, and variety of plants have been used in TM treatments, with others even being used to treat epilepsy. Herbal drugs are commonly used around world because of their large applicability and medicinal effectiveness with little side effects. Anticonvulsant function has been studied in number of medicinal plants.[9]

1. **Artocarpus heterophyllus:** Alcoholic extract of Artocarpus heterophyllus Lam stems had anticonvulsant function. plant has been used as antiepileptic agent in treatment of CNS-related diseases in TM. Prenylflavonoids found in A. heterophyllus Lam include artocarpine, artocarpesine, artocarpetin, artocarpetin A, cycloheterophyllin, and artonins and B. In alcoholic extract of A. heterophyllus stems, phytochemical analyses showed

existence of carbohydra tes, flavonoids, tannins, saponins, and triterpenoids. PTZ, STR, and MES mediated convulsion models were used to test anticonvulsant behaviour. PTZ and STR induced clonic convulsions were considerably delayed by alcoholic extract of Artocarpus heterophyllus stems, as was length of extensor process.[10]

2. **Carissa carandas:** Effect of ethanolic extract of roots of Carissa carandas on MES and chemo-induced seizures. Anticonvulsant action of ethanolic extract of roots of C. carandas was tested on MES and PTZ, picrotoxin-, bicuculline-, and N methyl dl aspartic acid-induced seizures. Number of animals shielded from tonic convulsions and duration of tonic convulsions were reported. ethanolic extract of C. carandas roots shortened length of MES-induced seizures substantially. Same doses have shielded animals from PT Z-induced tonic seizures and greatly delayed occurrence of picrotoxin- and N-methyl-dl-aspartic acid-induced tonic seizures. Bicuculline-induced seizures were not affected by extract. Since it shortened length of MES seizures and prolonged latency of seizures induced by PTZ and picrotoxin, ethanolic root extract of C. carandas may have anticonvulsant effects by nonspecific mechanisms.[11]

3. **Nauclea latifolia:** Anticonvulsant, anxiolytic, and sedative activities are found in root bark of Nauclea latifolia Smith (Rubiaceae). N. latifolia root bark significantly increased total sleep time induced by diazepam. It also protected mice from seizures caused by MES, PTZ, and STR. N. latifolia decoction, used in TM in Cameroon to treat fever, malaria, insomnia, anxiety, and epilepsy, as well as sedative.[12]

4. **Butea monosperma:** anticonvulsant activity of petroleum ether extract of Butea Monosperma was investigated, and active constituent was discovered to be triterpene in n hexane ethyl acetate (1:1) fraction. Mixture of lithium sulphate and pilocarpine nitrate was ineffective against STR and picrotoxin-induced convulsions, but triterpene greatly prevented seizure induced by MES, PTZ, and electrical kindling.[13]

Nootropic medicinal plants

Any of common Ayurvedic medicinal plants have been found to have nootropic effects. Plants with nootropic properties are known as Medhya- Rasayana. Below is list of some of plants that have been shown to have nootropic effect.[14]

Table 2: The following is list of few medicinal plants that have nootropic properties.[15]

Plant name	Common name	Family
Bacopa monnieri	Brahmi	Plantaginaceae
Centella asiatica	Mandookaparni	Apiaceae
Convolvulus pluricaulis	Sankhpushpi	Convolvulaceae
Emblica officinalis	Amla	Phyllanthaceae
Prunus amygdalus	Badam	Rosaceae
Vitis vinifera	Grape seed	Vitaceae
Albizia lebbeck	Indian siris	Leguminosae
Clitoria ternatea	Butterfly pea	Leguminosae
Thespesia populnea	Indian tulip tree	Malvaceae
Rubia cordifolia Linn.	Indian madder	Rubiaceae
Pueraria tuberosa	Indian kudzu	Leguminosae
Eclipta alba	Bhringraj	Asteraceae
Nardostachys jatamansi	Spikenard	Caprifoliaceae
Tabernaemontana divaricata	Crape Jasmine	Apocynaceae
Glycyrrhiza glabra	Mulhathi	Fabaceae

1. *Bacopa monnieri*

B. monnieri Linn. has been used as nerve tonic for memory enhancement since dawn of time. Mixture of two saponins known as bacosides and bacosides B was established as chemical constituent responsible for brahmi's effect on learning schedules. They also increase protein kinase activity and protein levels in hippocampus. In regulatory pharmacological testing, it was found to be effective.[16]

2. *Emblica officinalis*

Amla (Emblica officinalis) is Ayurvedic herb that is abundant in vitamin C and low molecular weight hydrolysable tannins, making it good antioxidant. Tannins in amla, such as emblicanin-A, emblicanin-B, punigluconin, and pedunculagin, have been shown to shield rat peripheral blood erythrocytes from free oxygen radicals. On effects of E. officinalis on oxidative stress and renal impairment during ageing period. Following administration of E. officinalis extract, elevated levels of serum creatinine and urea nitrogen in aged rats were reduced. In addition, tail arterial blood pressure was reduced substantially. Extract significantly decreased amount of thiobarbituric acid in serum, renal homogenate, and mitochondria in aged rats, meaning that E. officinalis may help with oxidative stress caused by ageing. Expressions of inducible nitric oxide synthase and cyclooxygenase in aorta of aged rats were also suppressed substantially.[17]

3. *Pueraria tuberose*

Tuberosa Pueraria (Indian kudzu) Using Elevated Plus Maze, nootropic activity of alcoholic and aqueous extracts of P. tuberosa was assessed (EPM). In CIH model, there was major reverse effect on rectal temperature, and in LIH model, there was decrease in head twitches. With research extracts and normal piracetam, however, there was no substantial reduction in catalepsy scores in HIC models. Findings suggest that nootropic action of P. tuberosa tuber extracts can enhance learning and memory by either augmenting noradrenaline transmission or interfering with 5-hydroxytryptamine (5-HT) release.[18]

4. *Albizzia lebbeck*

Using passive shock avoidance model and elevated plus maze, effect of saponin-containing nbutanolic fraction derived from dried leaves of Albizzia lebbeck on learning and memory in albino mice was investigated. Leprosy is treated with seed oil, and scrofulous swellings are treated with powdered seed. It is also said to have astringent, pectoral, rejuvenating, and tonic effects. Anticonvulsant activity was detected in ethanolic extracts of A. lebback leaves. Saponins from leaves of A. lebbeck have been found to have nootropic and anxiolytic properties.[19]

CONCLUSION

Several plants have been mentioned that have been previously tested for their anti-anxiety function using animal models by different researchers, but only few controlled clinical trials have been performed. Clinical trials have host of logistical issues, such as insufficient number of participants and absence of placebo. When opposed to benzodiazepines, buspirone, and anti-depressants, only few plants, such as brahmi, gingko, and kava-kava, displayed positive effects of widespread clinical relevance. We gather data on anxiolytic possible herbs, including their biological source, common name, and other biological events, which could be useful to researchers working on new anti-anxiety herbal formulations. Toxicity of medicinal plants and margin of protection between therapeutic and toxic effects were not explored in most research on antidepressant effects. In rats, oral use of C. mexicana up to 5,000 mg/kg concentration resulted in no mortality. Successful concentration for treating depression was seven times higher than LD50, indicating that this dosage is healthy. Detection of certain fraction or active constituent may also provide more detailed outcomes, according to accounts of potential mechanisms of intervention. Since these herbal treatments have less adverse effects and interactions, they can make anticonvulsant care more fair and patient-

friendly. In addition, some herbal remedies were discovered in study. Analysis also discovered that some herbal medicines listed in various TM around world have not been completely exploited, and that these claims may be better focus for creation of more allopathic anticonvulsant alternatives. Medicinal plants are commonly used as raw materials for processing active ingredients and synthesising various drugs. Plant-based foods are used in laxatives, blood thinners, antibiotics, and antimalaria drugs, among other things. This study focuses on significance of certain nootropic plants that contain active compounds that can be used to treat neurological disorders.

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