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Review on Herbal Drugs in Treatment of Anxiety Disorder

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Abstract: *Anxiety is the most common mental health disorders and is a major cause of disability around the world. Traditional herbal medicines are receiving significant attention in global health debates. Compare to pharmaceutical medicine herbs are safer, digestible, effective, economical and having less undesirable facet effects. Herbs are the foremost effective different to the pharmaceutical medicine in numerous health conditions. The herbs promote and improve the general health once. Combined with a raw vegetarian diet and regular exercise. The leaves, roots, stems of various plants are the supply of vitamin C, Minerals, Amino Acids which will be useful just in case of system disorders. These comprising generalized anxiety disorder (GAD), anxiety disorder, post-traumatic stress disorder (PTSD) and psychoneurotic compulsive disorder (OCD) are the foremost frequent behavioral disorders within the us, touching seventeen.2% of the population. In this review an attempt is made to describe various types of anxiety and medicinal plants having anti-anxiety activity.*

Keywords: Traditional Herbal Medicines; Generalized Anxiety Disorder; Sleep Disorders; Sedative; Anxiolytic, CNS, Central Nervous System, etc.

I. INTRODUCTION

Anxiety and insomnia are among the most common mental health disorders and are a major cause of disability around the world [1–4]. GAD (generalized anxiety disorder) [5] has received increasing attention in recent years as a prevalent disorder associated with significant impairment [6]. Patients with GAD complain that they worry excessively, are excessively aroused, have heightened muscle tension, and a have variety of autonomic symptoms [7].

The impact of the anxiety is not limited to consistent stress, which is associated with higher risk of cardiovascular and cerebrovascular diseases, but also has debilitating physical manifestations such as headaches, uncontrolled trembling, and sweating [8]. Insomnia symptoms are generally considered to encompass difficulty in initiating sleep, disrupted sleep, and early morning awakenings [9]. Gamma-aminobutyric acid (GABA), the main inhibitor neurotransmitter in the central nervous system (CNS), plays an important role in anxiety [10]. Anxiety and related neurological disorders often result from low GABA levels in CNS [11].

The anabolism and catabolism of GABA are regulated by two enzymes: glutamic acid decarboxylase (GluAD) and GABA transaminase (GABA-T), respectively. The most common strategies to increase GABA level in the brain are based on the affinity to the benzodiazepine (BZD) site of the GABAA receptors, the stimulation of GluAD, and the inhibition of GABA-T. Important pharmacotherapy agents used in GAD are the selective serotonin reuptake inhibitors (SSRIs) and the serotonin and noradrenaline reuptake inhibitors (SNRIs) [12,13]. In most cases, the medications used in these limited treatment options for anxiety and insomnia (e.g., anxiolytics, sedative-hypnotics, antidepressants, and sleep aids drugs) are often associated with serious and unpleasant side effects such as dependence, nausea, tremors, cognitive impairment, increased risk of motor vehicle accidents, falls, weight gain, and fractures [14,15].

To overcome this issue, the use of natural products such as herbal medicines is becoming an appealing approach, especially for those individuals with mild to moderate symptoms of anxiety and sleep-disorders [16]. As defined by the World Health Organization, traditional herbal medicines are naturally occurring, plant-derived substances with minimal or no industrial processing that have been used to treat illness within local or regional healing practices [17]. Over the

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past few years, the use of natural or herbal remedies as a form of self-treatment of various stress-related afflictions has become increasingly popular in Western societies [18,19]. Nowadays, herbal medicine represents one of the most frequently used complementary or alternative treatments of insomnia [20]. However, the efficacy of traditional medicinal herbs in complementary and alternative medicine of the mental health disorders has not been exhaustively explored yet, especially concerning the mechanism of actions of phytocomponents. Ethnopharmacology can be defined as a multi-disciplinary area of research concerned with the observation, description, and experimental investigation of indigenous drugs and their biological activities [21,22] that also seeks to further develop the use of this local knowledge [23]. These types of research have great importance not only because of their contribution to healthcare but also for the preservation of biodiversity, for the raising of environmental consciousness, and because of different sociological and economic aspects [24].

These studies have focused on plants' practical uses through traditional knowledge, with particular attention paid to medicinal plants. Despite this, the use of plants as remedies for anxiety and insomnia.

Occurrence [25]

Anxiety problems are the most usual type of psychiatric disorders. The one-year occurrence rate of anxiety disorder was 13.3% in person aged 18 to 54 years and 10.6% in those persons which are over age 55 years. Lifetime occurrence is 28.8%.

- Occurrence rate of generalized disorder for one year is 28%. It is more frequent in women (2%) than men (1%).
- Panic disorder with or without fear has life time occurrence rate of 2 to 4%. It is about double as common among women as men.
- The occurrence rate of PSTD is 3.6% in 1 year. It is more frequent in women than men (8.2).
- The occurrence rate for obsessive compulsive disorder is 2.4% in 1 year in person aged 1 to 54 years and 1.5% in those people which are over age 55 years. Life time occurrence is 2.3%

Manifestation [26,27]

Anxiety is associated with physical effects such as fatigue, heart palpitation, trouble and chest pain, shortness of breath, muscle tension, trembling, stomach aches, or headache, blood pressure, nervousness, sweating etc. External signs of anxiety may incorporate pale skin, trembling, sweating and papillary dilation. Anxiety does not only compose of physical symptoms. These are many emotional symptoms. There are many emotional symptoms
concerned as well. Some of them include "Feeling of fear or dread, feeling tense, supposing the worst, restlessness, irritability and feeling like your mind's gone blank.

II. TYPES OF ANXIETY DISORDER

Generalised Anxiety Disorder The vital feature of GAD is tension and excessive worry, about a number of events or without panic and phobic symptoms. Other symptoms may involve fatigue, restlessness, sleep disturbance, difficult concentrating, muscle tension. When an individual experience excessive worrying about number of events for more than six-month, GAD diagnosis is confirmed.[28]

1. **Generalised Anxiety Disorder**
   The vital feature of GAD is tension and excessive worry, about a number of events or without panic and phobic symptoms. Other symptoms may involve fatigue, restlessness, sleep disturbance, difficult concentrating, muscle tension. When an individual experience excessive worrying about number of events for more than six-month, GAD diagnosis is confirmed. [29]
2. **Panic Disorder**
   This kind of disorder begins as a series of spontaneous panic attacks, including an intense hysterical fear, similar to that caused by life threatening danger. [8] Symptoms may incorporate sweat, palpitation, trembling, chest pain and feeling of choking, chills or hot flashes. When a person experiences recurrent expected panic attacks and at least four of the following symptoms developed abruptly and reached a peak within 10 minutes, disorder is diagnosed. [30]
3. **Phobia [31]**

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- **Social Phobia**
  The defining feature of social anxiety disorder, also called social phobia, is intense anxiety or fear of being judged, negatively evaluated, or rejected in a social or performance situation. People with social anxiety disorder may worry about acting or appearing visibly anxious (e.g., blushing, stumbling over words), or being viewed as stupid, awkward, or boring. As a result, they often avoid social or performance situations and when a situation cannot be avoided, they experience significant anxiety and distress.
- **Specific Phobia**
  This type of phobia contains excessive fear for specific object or situation (e.g., Insects, height, public transportation etc.).
- **Obsessive Compulsive Disorder**
  In this type of disorder there is persistent and repeated thought and repetitive ritualistic activities and behaviour. A compulsion is a repetitive, purposeful, intentional behaviour or mental act usually performed in response to an obsession (e.g., frequent hand washing, checking, ordering, counting, repeating words, silently preying etc.).
- **Post-Traumatic Stress Disorder**
  This disorder is caused by witnessing or experiencing traumatic or terrifying life events. (e.g.violent crime, serious accident). Symptoms of this disorder may include insomnia, hypersensitivity to external stimuli and loss of memory of time surrounding the traumatic experience. A detailed diagnosis of PSTD also states that when a patient continuously reexperience the traumatic event by dreaming about it, experiencing hallucination or flashbacks. These types of symptoms may be present for more than one month but may happen after a long time of that traumatic event.

III. Mechanism of Action of Herbal Medication

The mechanism of action of herbal drugs mainly involves modulation of neuronal communication via specific plant metabolites binding to neurotransmitter/neuromodulator receptors and via alteration of neurotransmitter synthesis and general function. [32]

Treatment of Anxiety [33]

Anxiety can be treated with the psychological counselling, medically or independently. The treatment depends on the cause of the anxiety and the patient's preferences. Often treatments will consist of a combination of psychotherapy, behavioural therapy and medications. Sometimes alcoholism, depression, or other coexisting conditions have such a strong effect on the individual that treating the anxiety disorder must wait until the coexisting conditions are brought under control. [33]

Figure: Various Treatments of Anxiety Disorder

Herbal Drugs versus Synthetic Drugs [34]

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Compared to pharmaceutical drugs, herbs are safer and more digestible, effective and economical and having less undesirable side effects. Herbs are the most effective alternatives to pharmaceutical drugs in various health conditions. Herbs promote an improvement in overall health when combined with a raw-vegan diet and regular exercise. It has led scientists to investigate plants which are commonly employed in traditional and alternative systems of medicine for sleep disorders and related diseases.

IV. PLANTS PROVED TO RETAIN ANXIOLYTIC ACTIVITY

Abies Pindrow Royle (Family-Pinaceae)

The aerial parts of Abies pindrow have been used by elevated plus maze model (EPM). Properly identified A. pindrow aerial parts were successively and exhaustively extracted using solvents in increasing order of polarity viz., n-hexane, chloroform, methanol and water. All crude extracts were subjected to antianxiety activity at the doses of 100, 200 or 400 mg/kg, p.o. in mice. Efficacy of A. pindrow was statistically compared with the standard anxiolytic drug, diazepam (2 mg/kg, i.p.). Amongst various extracts, chloroform and methanol extract exhibited significant antianxiety activity with respect to control and statistically equivalent to the standard drug at the dose of 200 and 400 mg/kg, respectively. [35]

Acatia Spicata (Family-Ranunculaceae)

The preliminary anti-anxiety screening studies were done with Acatia spicata, with a view to ascertain the verity of its traditional use as an anxiolytic. The roots of the plant were extracted using solvents in order of increasing polarity viz., petroleum ether (60-80 C), chloroform, methanol and distilled water. All the crude extracts were evaluated for anti-anxiety activity in mice using elevated plus maze apparatus. Among all these extracts, only methanol extract exhibited significant anti-anxiety activity at a dose of 100 mg/kg in mice with respect to control as well as standard (diazepam, 2 mg/kg). [36]

Albizzia lebbeck (Siras):(Family-Mimosaceae) Albizzia lebbeck (Linn.) Benth. is a medium to large sized tree distributed throughout India. The effect of saponin containing, n- butanolic fraction (BF), extracted from dried leaves of Albizzia lebbeck, was studied on cognitive behavior and anxiety in albino mice. The anxiolytic activity of BF (0, 10,25 and 50 mg/kg) was assessed by studying its effect on the duration of occupancy in the closed arm. Animals treated with BF (25 mg/kg) spent more time in the open arm in a dose-dependent manner. [37]

Brassica oleracea (Family-Brassicaceae)

This is an edible green vegetable plant belongs to Brassicaceae family in which flower head is eaten as a vegetable. Like other species of the Brassica family, broccoli is very rich source of health promoting phytochemicals. It is rich in phenolic compounds, particularly flavonoids. It also contains ascorbic acid, vitamins C and E, amino acid, the flavonols quercetin and kaempferol, the carotenoids b-carotene, lutein and the glucosinolate. From the research study, it is concluded that hydro-alcoholic extract of Brassica oleracea after acute dosing possess significant anxiolytic activity at dose of 200 mg/kg. The petroleum ether extract was devoid of anti-anxiety effect. Further studies are being conducted to ascertain the bioactive constituent responsible for the activity. [38]

Cecropia Glazioui: (Family-Cecropiaceae)

This plant has been used in most Latin American countries as an antihypertensive, cardiotonic and anti-asthmatic folk medicine. Its anxiolytic activity was studied by F.F. Rocha. Swiss mice were treated with AE (0.25–1 g/kg po) acutely (1 h) or repeatedly (24, 7 and 1.5 h before the test). After repeated administration of aqueous extract, the frequency of entries in the open arms of EPM was increased threefold. The AE of C. glazioui promotes an anxiolytic-like effect in mice. The active principles responsible for this action are present in the less polar fraction of the extract, the main constituents of which are flavonoids and terpenes, among other compounds. [39]

Citrus Paradisi (Grapefruit): (Family=Rutaceae)

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Citrus paradisi has been used traditionally to reduce stress and anxiety. The present study was designed to evaluate the anti-anxiety activity of various extracts viz petroleum ether, chloroform, methanol and water, of the leaves of Citrus paradisi var. star ruby using elevated plus maze (EPM) model in Swiss albino mice. Albino mice were treated orally with different doses of the extracts (i.e.100, 200 and 400 mg/kg) and behavior was observed on the EPM. Diazepam (2mg/kg, P.O) was used as a positive control. Results show that methanol extract at the dose of 100mg/kg of the leaves of Citrus paradisi var. star ruby markedly increased the average time spent in the open arms of the EPM. This effect was comparable to the effect produced by diazepam. [40]

Colocasia Esculenta (Arvi):(Family-Araceae)

This is. commonly known as elephant ear (English), possesses diverse pharmacological activities. The neuro pharmacological activities of hydro-alcoholic extract of leaves of Colocasia esculenta were evaluated. The anxiolytic activity of HECE (100, 200 and 400 mg/kg) per os (p.o.) was characterized by increased time spent and number of entries in open arms in the EPM paradigm as compared to control group ($p < 0.001$). The presence of flavonoids, beta-sitosterol and steroids might contribute to its anxiolytic activity. [41]

Drypetes Roxburghii (Family-Euphorbiaceae)

The ethanol and aqueous extract of the leaf of plant Drypetes roxburghii was evaluated for its anti-anxiety activity in Swiss Albino Mice at dose of 500 mg/kg body weight. Anti-anxiety activity was assessed by using elevated plus maze and light and dark model methods. Both extracts exhibit anxiolytic effect in experimental mice. However the ethanolic extract shown effective anxiolytic activity than that of the aqueous extract. Drypetes anti-anxiety activity was performed by elevated plus maze model and light-dark model. Diazepam was taken as standard reference drug. [42]

Habenaria intermedia (Family-Hamamelidaceae)

Pharmacological reports on H. intermedia reveal that the plant has not been screened for antianxiety activity. Thus, it was envisaged to subject H. intermedia for screening of antianxiety activity using elevated plus maze model. The crude extracts (n-hexane, chloroform, methanol and water extracts) of plant material were prepared successively in increasing order of polarity. The anxiolytic activity was assessed by comparing number of entries and average time spent by mice treated with test extracts (200 or 400 mg/kg, p.o.) in open arms of EPM with respect to control and standard drug, diazepam (2 mg/kg, p.o.). Significant antianxiety activity was observed in methanol extract with respect to control, whereas n-hexane, chloroform and water extracts did not exhibit antianxiety activity. [43]

Melissa Parviflora (Family-Lamiaceae)

Melissa parviflora Benth has been traditionally used as a tranquillizer, relaxants, nervine and sleeping aids throughout the world. Various extracts viz. petroleum ether, chloroform, methanol and aqueous were prepared by successive soxhlet extraction method. Anxiolytic activity of various extracts of the plant was evaluated using elevated plus-maze apparatus and light and dark test model of anxiety in Wistar rats of either sex. The bioactive extract was standardized on the basis of total phenolic and flavonoid content estimation using colorimetric method. Results showed that only methanol extract of M. parviflora exhibited significant anxiolytic activity (100 and 200 mg/kg, p.o.) using elevated plus maze. [44]

Moringa oleifera (Family-Moringaceae\)

Moringa oleifera lam is commonly known as drumstick. It is found and commonly cultivated in all places of India. It is a short, slender, deciduous perennial tree; widely distributed in India, Arabia and cultivated in tropical Africa, tropical America, Sri Lanka, India, Mexico and Malaysia. M. oliefera, increased the number of entries, time spent and rearing in open arms in the elevated plus maze paradigm. In light and dark paradigm, the test drug significantly increased the time spent in light arena, rears in both light and dark arena and transition between chambers. [21] 8.12 Panax ginseng:(Family-Araliaceae) The putative anxiolytic activity of the white and red varieties of ginseng, the root of Panax ginseng, was investigated in rats and mice by S.K. Bhattacharya et al. White and red varieties of ginseng (20 and 50 mg/kg) showed positive results when tested against several paradigms of experimental anxiety. Both were effective in the open-field and elevated plus-maze tests. [45]

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V. CONCLUSION

Herbs are verified as a good different to the pharmaceutical medicine for the treatment of various health conditions. once herbs area unit combined with a raw- vegetarian diet and a few different regular exercises then they'll promote associate improvement within the overall health which cannot be seen within the case of pharmaceutical medicine. The leaves, roots, stems of various plants area unit sources of water-soluble vitamin, minerals, aminoalkanoic acid that may be useful just in case of system disorders. In review of study, we tend to studied those anxiolytic activities of various extracts of various plants in mice/rat, at the various doses have shown vital results as a anxiolytic activity mistreatment EPM and different parameters severally. but use of specific healthful plants for management of specific subtypes of tension disorder is nonetheless to be supported**.**

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