A REVIEW ON MEDICINAL PLANT EXHIBITING ANXIOLYTIC ACTIVITY

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ABSTRACT

Herbs are always exemplary sources of drugs; many of the currently available drugs were derived directly or indirectly from plants. In the ancient period, research has been focused on scientific, pharmacological evaluation of traditional drugs from plant source for the treatment of various types of diseases. This article reviews anxiolytic plants for anxiety disorders; Anxiety is an overwhelming sense of uneasiness or discomfort. We have highlighted some of important plants reported anxiolytic activity, habitat, uses, models and doses for anxiolytic activity & results. It was concluded that further research remains to be done to improve quality, ultimately use of herbal medicines.
INTRODUCTION:
Anxiety is generally defined as an overwhelming sense of uneasiness or discomfort. It may be related to a precipitating condition or situation (i.e. an upcoming examination) though at times the cause may not be readily discernible [1]. In the developing countries 10–44% suffers from depression and anxiety disorders (D&A), less than 35% receive medical care and according to an estimate 50.8 million people suffer from major depression [2]. Anxiety disorders are common mental diseases of the central nervous system and present proliferating health problem worldwide. Anxiety disorders present in a number of forms, although probably all share a number of common neurological circuits. While certain psychological treatments are of proven efficacy [3]. Pharmacotherapy remains the most widespread & efficacious treatment, especially in severe cases [4]. The efficacy of drugs for these conditions is very limited so the need for newer, better-tolerated and more efficacious treatments is remaining high [5].

Since long the benzodiazepines remain to be the most frequently prescribed synthetic drugs of choice for acute anxiety & other allied disorders including depression, epilepsy & insomnia [6]. Benzodiazepine facilitates GABAnergic neurotransmission; have a number of therapeutic actions, including anxiolytic, sedative hypnotic, anticonvulsant & muscle relaxant effects & stimulation of food intake. Long term use of these drugs have very serious side effects ranging from respiratory, digestive & immune system dysfunctions to deterioration of cognitive function, physical dependence & tolerance [6,7]. In the search for new therapeutic products for the treatment of neurological disorders, research into medicinal plant worldwide has been intensified and thus, revealed the pharmacological effectiveness of different plant species in a variety of animal models. An increasing number of herbal products have been introduced into psychiatric practice, as alternative or complementary medicines [8].

1. Albizia julibrissin (Leguminoceae)
Widely used traditionally for the treatment of insomnia, calming mind and for traumatic injuries. Anxiolytic like effect of aqueous extract of Albizia julibrissin stem bark (at 100/200 mg/kg) using model, elevated plus maze in rats, buspirone (1mg/kg) as a reference standard have been studied. Result suggested that it might prove to be an effective anxiolytic agent [9].

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2. *Angelica sinesis* Diels (Apiaceae)

It is a most important herb in traditional Chinese medicine. It possesses hemogenic, analgesic, sedative activity, also useful in menstrual disturbances & anemia. The volatile oil ligustilide is the major pharmacological component of this herb. The effect of angelica essential oil at 21 and 42 mg/kg in social interaction test and hole board test for anxiolytic activity in mice with diazepam as a reference standard was done. Results indicated that the potential usefulness of angelica essential oil against various types of anxiety-related disorders [10, 11].

3. *Annona cherimolia* Miller (Annonaceae)

It is a small tree native to Ecuador and Peru, wide spread in subtropical areas of America, Africa and Asia and in the south of Europe. The plant is also in folk medicine as a parasiticide and an insecticide. A hexane extract of leaves of *Annona cherimolia* produced anxiolytic like actions on mice at doses of 6.25, 12.5, 25.0, and 50.0 mg/kg using animal models, mouse avoidance exploratory behavior and the burying behavior test, diazepam used as a reference standard have been studied. Result showed that anxiolytic like actions [12].

4. *Apocynum venetum* Linn (Apocynaceae)

It is a wild shrub widely distributed throughout mid and north western China. In Japanese widely used traditionally for treatment of the hypertension, nephritis, neurasthenia, antiaging, nutritional supplements, diuretic, antihypertensive, antihyperlipidaemic, antioxidant, antidepressant. The putative anxiolytic like activity of an ethanolic extract of *Apocynum venetum* (leaves) at doses of 30 and 125 mg/kg P.O using elevated plus maze in mice, diazepam as a reference standard was studied. Results indicated that it possesses anxiolytic activity equal to that of benzodiazepine [13].

5. *Azadirachta indica* (Malaceae)

It is an evergreen tree in the Indian subcontinent. Leaves and seeds have been used in Ayurvedic medicines. The effect of leaf extract on rat for anxiolytic activity showed at 1ml/kg in open field test and elevated plus maze test apparatus was studied. It concluded that neem extract could attenuate anxiogenic [14].
6. *Casimiroa edulis* (Rutaceae)

Aqueous extract of the dried leaves of plant are claimed to possess anticonvulsant properties. Anxiolytic like action of an aqueous extract of the dried leaves at doses (25.0mg/kg, 35.0mg/kg) & diazepam (1.30 mg/kg) as a reference standard were studied in male Wistar rats in elevated plus maze test was studied. Conclusion, the leaves showed anxiolytic like action [15, 16].

7. *Casimiroa pringlei* (Rutaceae)

It is a small tree, widely distributed along the states of central Mexico. The anxiolytic effect of essential oil from *Casimiroa pringlei* on an animal models, elevated plus maze, open field test, hole board test & bromazepam used as reference standard & caffeine was used as a reference point for anxiogenic on male Wistar rats have studied. The findings showed that the essential oil having anxiolytic activity at 795mg/kg doses [17].

8. *Cinnamomum cassia* (Lauraceae)

It has been traditionally used to treat dyspepsia gastritis, blood circulation disturbances and it has been reported to have significant antiallergic, antiulcerogenic, antipyretic, and analgesic activity. An elevated plus maze test, locomotor activity and horizontal wire test models were used to determine the anxiolytic like effect of 50% Et OH extract of *Cinnamomum cassia* in mice at 750mg/kg P.O & compared with the reference standards was done. Result, It has might be an effective anxiolytic agent [18].

9. *Cissus Sicyoides* L.(Vitaceae)

It widely distributed throughout tropics, mainly in Brazil and Caribbean. It is used in medicine as a diuretic, anti-inflammatory, anti diabetic, antibacterial activity, anticonvulsant property and cytotoxic activities. Anxiolytic effect of hydroalcoholic extract obtained from the aerial parts of *Cissus Sicyoides* on male and female mice using several behavioral assays, mice were treated via intraperitoneal (IP) with doses of 300, 600 and 1000 mg/kg, showed significant action in elevated plus maze, hole board test, marble – burying test compared to diazepam 2.5mg/kg, IP as a reference standard was studied. Result indicated that an anxiolytic like action, probably due to the action of flavonoids, Linalool, and α tocopherol present in the plant leaves [19].
10. *Commelina benghalensis* Linn (Commelinaceae)

It is a perennial herb native to tropical Asia and Africa, used in the Indian subcontinent as a folk medicine for the treatment of leprosy, headache, fever, constipation, jaundice, snake bite, mouth thrush, inflammation of the conjunctiva, psychosis, epilepsy, nose blockage in children, insanity, exophthalmia, diuretic, febrifuge and anti-inflammatory. The plant is also reported to have antitumor, anticancer and antioxidant activity. Anxiolytic properties of the four different fractions (chloroform, pet ether, *n*-butanol and hydromethanol) soluble fractions, of the aerial parts of *Commelina benghalensis* using rodent behavioral models, such as hole cross, open field and elevated plus-maze (EPM) test, at the doses of 200 mg/kg, *p.o.* and 400 mg/kg, *p.o.*, maximum effect was shown by chloroform and pet ether fractions compared to reference standard diazepam. Findings, *C. benghalensis* in general, and chloroform and pet ether (soluble fraction has significant anxiolytic effects [20].

11. *Coriandrum sativum* L (Umbelliferae)

Is in Iranian traditional medicine, has been indicated for a medical problems such as dyspeptic complaints, loss of appetite, convulsion, insomnia and anxiety. The anxiolytic effect of aqueous extract (100 mg/kg, *i.p.*) was examined in male Albino mice using elevated plus-maze model. The effects of the extract on spontaneous activity and neuromuscular coordination were assessed using Animex Activity Meter and rotarod, respectively compared to diazepam as reference standard group. Result suggested that, *C. sativum* (seeds) has anxiolytic activity [21].

12. *Cymbopogon citratus* (DC) stapf (Poaceae)

*C. citratus* herb known worldwide as lemongrass is widely used in tropical countries as a source of ethno medicines. Tea obtained from leaves of *Cymbopogon citratus* start is used for its anxiolytic, hypnotic and anticonvulsant properties in Brazilian folk medicine. Essential oil at 0.5/1.0g/kg was evaluated for anxiolytic activity by elevated plus maze and light and dark box, compared with reference standard diazepam. Results are in accordance with the ethnopharmacological use of *Cymbopogon citratus*, as anxiolytic activity [22].

13. *Drymaria cordata* L (caryophyllaceae)

Wild, locally known as Laijadori is traditionally used as antidote, appetizer, depurative, emollient, febrifuge, laxative and stimulant, the pounded leaf is applied to snake bites. It
exhibited antitussive activity, antibacterial, anti-inflammatory. *Drymaria cordata* hydroethanolic extract at 25, 50 and 100 mg/kg (PO) for study, anxiolytic effect on male Albino Swiss mice by using hole board, open field, elevated plus maze, light and dark exploration model were used, diazepam 1mg/kg used as a reference standard was done. *Drymaria cordata* exhibited anxiolytic activity might be due to the presence of phytochemicals, triterpenes, diterpenes, steroids and tannins [23].

14. *Echium amoenum* (Boraginaceae)

It is a very important medicinal plant in Iranian traditional medicine which is used as a diaphoretic, tranquillizer, tonic, cough remedy, sore throat and pneumonia. An aqueous extracts from petals of *E. amoenum* was used in 125mg/kg concentrations as compared with diazepam 1mg/kg intraperitoneal, during 2 different treatment courses, 15 and 30 days on rats using the elevated plus maze model. Result revealed that in 30 days treatment course. *Echium amoenum* showed a significant time dependent increase in time spent in open arms has been studied. These results are suggestive that it has an anxiolytic effect in elevated plus maze test [24, 25].

15. *Euphorbia hirta* L (Euphorbiaceae)

An herbaceous wild plant native to Australia, is now very common in all tropical countries and has been widely used in traditional medicine, in Asia. *E. hirta* traditionally has been used for diseases of the digestive system, respiratory system, urinary apparatus and genital apparatus. Anxiolytic activity of lyophilized aqueous extract of plant at doses 100mg of dried plant/kg on mice and reference standard, benzodiazepine using staircase test and light and dark models was studied. Findings suggested that the traditional use of *E. hirta* as anxiolytic properties [26].

16. *Eurycoma longifolia* Jack (Simaroubaceae)

Locally identified as “Tongkat Alait”, is primary and secondary, evergreen and mixed deciduous forest in Burma, Indochina, Thailand, Malaysia, Sumatra, Bornea, and the Philippines. It is use for the treatment of fevers, aches, sexual insufficiency and health supplements. Traditionally decoction of the roots in the water as a health tonic and antistress remedy may have been attributed to various quassinoids, squalene derivatives, biphenyl neolignans, triucallane type triterpenes, canthine-6-one and β carboline alkaloids. Anxiolytic effect of *Eurycoma longifolia* in mice was examined at doses 0.3gm/kg and models, open field, elevated plus maze test were used. Results were found to be consistent with anxiolytic effect produced by diazepam [27].
17. *Hippophae rhamnoides* (Hippophae)

Sea buckthorn (*H. rhamnoides*) well known in Asia, Europe and North America since last decade. It is used in psychotic disorders. Sea buckthorn berry enriches nutritional components. Anxiolytic profile of aqueous fruit extract of a plant Sea buckthorn, 20 and 40 mg/kg P.O, diazepam as a reference standard at doses 3mg/kg I.P in animal models, elevated plus maze, light and dark, open field test on rats have been studied. Result, it is an effective anxiolytic agent [28].

18. *Marsilea minuta* Linn (Marsileaceae)

Widely found in wet and flooded low lands. The plant as a whole is used as sweet, astringent, cooling, digestive, diuretic, hypnotic, and expectorant, treatment for psychopathy, diarrhoea, cough, bronchitis, skin diseases and fever were also been reported in Ayurveda. The use as sedative has been referred in many text of Ayurveda for the treatment of insomnia and other mental disorders. The effect of ethanolic extract of *M. minuta* (200 and 400 mg/kg) was investigated for its putative anxiolytic activity on anxiety models; open field test, social interaction test, novelty induced suppressed feeding latency and two compartmental exploration in rodents, & diazepam (1 mg/kg, i.p.) was administrated acutely as reference drug studied. It concluded that it possess anxiolytic activity [29].

19. *Momordica charantia* Linn. (Cucurbitaceae)

*M. charantia* widely distributed and cultivated in many parts of India. The fruit of the plant is widely used as vegetable. The fruits and leaves are useful in piles, leprosy, jaundice, diabetes, snake bite, vermifuge, antioxidant properties, antimalarial, anti-plasmodial properties. Anxiolytic activity of methanolic extract of dried leaves of *Momordica charantia* (100, 200 and 300mg/kg) was tested by elevated plus maze test. The results showed a significant anxiolytic effect comparable with diazepam (4mg/kg) [30].

20. *Saliva elegans* (Lamiaceae)

Is popularly known as “Mirto”, is a shrub that has been widely used in Mexican traditional medicine for the treatment of different central nervous system diseases, anxiety & insomnia. Plants having chemical constituents, essential oil, flavonoids, display nervous system depressor activities. Anxiolytic like effect of hydroalcoholic (60%) extract of *Saliva elegans* (leaves and flowers) at doses, 25-2000mg/kg and diazepam 1mg/kg used as a reference standard were evaluated in mice and models were used, elevated plus maze and light- dark test. Results showed that the potential anxiolytic activity [31].
21. Scutellaria baicalensis Georgi (Labiatae)

“Huangquin”, is the Chinese herbal drug, is the dry roots of Scutellaria baicalensis. The decoction has been shown to have a sedative effect. The interaction of aqueous extract of this plant interacts with the dopamine D₁, D₂, 5-HT₁₅ receptors, but not with the 5-HT₂ receptor and the GABA binding site of GABAA receptors. These effects are thought to be due to components of baicalin in plant. The putative anxiolytic activity of baicalin (80mg/kg, i.p.), diazepam (2.5mg/kg, i.p.) used as reference standard on Swiss Kunming strain mice by using the elevated plus maze test, light and dark test, hole board test and isolation –induced aggression test has been studied. Findings indicated that baicalin has an anxiolytic effect [32].

22. Sida tiagii bhandri (Sida pakistanica B) (Malvaceae)

Is a native species of Indian and Pakistan desert area, popularly known as “Kharinti”, in India; is used in the folk medicine as blood purifier, tonic muscle strengthenner. The anxiolytic effect of ethyl acetate extract of S.tiagii (100, 200, and 500mg/kg) were assessed by elevated plus maze on male Swiss mice compared with diazepam at 5mg/kg. Conclusion, S.tiagii possesses anxiolytic activity [33].

23. Spondias mombin (Anacardiaceae)

Is a fructiferous tree growing in the rain forest and coastal area of Africa. The fruits decoction is as a diuretic and febrifuge. The decoction of the bark and the leaves is used as emetic, anti-diarrhea, dysentry and for haemorrhoids, for gonorrhea and leucorrhoea. Use of tea of flowers and leaves as stomachache, gum employed as an expectorant and to expel tapeworm. Anxiolytic effect of Spondias mombin of the aqueous, methanol and ethanol extracts of the leaves were examined using aggressive behavior response on Albino Wistar rats and Swiss mice, diazepam acts as reference standard. It concluded that the active principle (ameliorate) of S. mombin is better extracted in ethanol and acts as anxiolytic agent [34].
24. Valeriana officinalis L. (Valerianaceae)

It is an herb that has long been used as tranquilizer & sleep inducer. The valepotriates exhibit an activity between sedation & tranquilization & are called aequilans, which have a specific dampening effect on the central nervous system. Putative anxiolytic effects of dichloromethane extracts of valerian (DEV) at doses, 0.1, 0.2 & 0.3gm/kg using elevated plus maze in adult male Wistar rats has been studied. Result suggested that DEV might prove to be effective anxiolytic agent [35].

25. Withania somnifera Dunal (Solanaceae)

Known as Ashwagandha in Ayurveda, active principles has been used as an antioxidant, adaptogen, anxiolytic, antidepressant, memory enhancer & antiulcerogenic agents. The effect of Withania somnifera root extract at doses 100, 200, 500mg/kg, oral & reference standard diazepam at 0.5, 1/2 mg/kg, i.p in social isolated induced behavior i.e. anxiety in rats. Rats were isolated for 6 week & the assessment of changed behavior were done on elevated plus maze test. Result suggested that Withania somnifera showed anxiolytic effect [36].

CONCLUSION

Many herbal medicinal products have potential Anxiolytic activity and encouraging safety profiles. However, only a limited amount of clinical research exists to support their efficacy. Further research is warranted to establish the value of these extracts in the treatment of Anxiety.

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