Anxiety-A Treatment by Herbal Approach: A Review

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Abstract

Anxiety is a state of excessive fear and apprehension regarding the occurrence of even normal things in life. It is characterized by motor tension, sympathetic hyperactivity, and apprehension and vigilance syndromes. Anxiety may interfere with intelligence, psychomotor function and memory. Anxiety disorder may develop from a complex set of risk factors including genetic predisposition, brain chemistry, stress and sudden life changes. The principle brain region implicated in the processing of fearful material is the amygdale (fear centre), which coordinates the automatic threat response; integrating information from sensory pathways via cortical and sub-cortical inputs. The pathophysiology of anxiety disorders is not well fully understood. Animal studies have demonstrated the existence of a "fear network" involving the amygdala and its interactions with the hippocampus and the medial prefrontal cortex, thought to be important in generating conditioned fear responses.

Keywords: Anxiety, Models, Essential oils, Plants.

Introduction

The word anxiety is derived from the Latin, *angere,* which means to choke and strangle. The anxiety response is often not attributable to a real threat. Nevertheless it can still paralyze the individual into inaction or withdrawal. Anxiety is a state of fear or a subjective feeling of apprehension, dread or foreboding. This psychological state is often accompanied by signs of autonomic activation or other physical symptoms.

Anxiety is a cardinal symptom of many psychiatric disorders and an almost inevitable component of many medical and surgical conditions. Indeed, it is a universal human emotion, closely allied with appropriate fear and presumably serving psychobiologically adaptive purposes.

Symptoms of anxiety commonly are associated with depression and especially with dysthymic disorder (chronic depression of moderate severity), panic disorder, agoraphobia and other specific phobias, obsessive-compulsive disorder, eating disorders, and many personality disorders.[1,2] Sometimes, despite a thoughtful evaluation of a patient, no treatable primary illness is found, or if one is found and treated, it may be desirable to deal directly with the anxiety at the same time. In such situations antianxiety medications are frequently and appropriately used.[3]

Anxiety disorders as recognized clinically include

• Generalized anxiety disorder (an ongoing state of excessive anxiety lacking any clear reason or focus)

• Panic disorder (sudden attacks of overwhelming fear occur in association with marked somatic symptoms, such as sweating, tachycardia, chest pains, trembling and choking). Such attacks can be induced even in normal individuals by infusion of sodium lactate, and the condition appears to have a genetic component)

• Phobias (strong fears of specific objects or situations, e.g. snakes, open spaces, flying, social interactions)

• Post-traumatic stress disorder (anxiety triggered by recall of past stressful experiences)

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• Obsessive compulsive disorder (compulsive ritualistic behaviour driven by irrational anxiety, e.g. fear of contamination). It should be stressed that the treatment of such disorders generally involves psychological approaches as well as drug treatment. Furthermore, other types of drug, particularly antidepressants and sometimes antipsychotic drugs, are often used to treat anxiety disorders.

Herbal medication for anxiety

The major limitation to developing new antidepressant and antianxiety drugs is a fundamental lack of a coherent pathophysiology and etiology for major depression, bipolar disorder, and common anxiety disorders. Current medications (SSRIs and tricyclic antidepressants) focus on blockade of norepinephrine and serotonin uptake, thereby prolonging their synaptic effects. The relative success of these agents creates a conceptual impasse that limits identification of novel therapeutic targets for these disorders.[4,5] A number of medicinal plants and medicines derived from these have been found to show anxiolytic properties by virtue of their medicinal constituents.

***Albizia lebbeck* Benth**

Family: Minosaceae
It is native to Asia and is used in traditional Chinese medicine to treat anxiety. Butanolic fraction of dried leaves extract (25mg/kg) presented anxiolytic effect in mice when tested in Elevated Plus Maze. Antianxiety activity of the plant might be due to effect on GABA or saponins present in the extract.[6]

***Albizia julibrissin* Durazz.**

Family: Fabaceae
The plant is used in traditional Chinese medicine to treat depression and anxiety. Single or repeated treatment (for 7 days) of male rats with aqueous extract (100 or 200 mg/kg, p.o.) significantly showed antianxiety effect in elevated plus maze (EPM). The mechanism of action is supposed to be as the involvement of serotonergic nervous system.[7]

***Azadirachta indica* A. Juss.**

Family: Meliaceae
This tree is found everywhere in India. Aqueous extract of neem leaves (10-200 mg/kg, p.o.) produced anxiolytic effect in elevated plus maze and open field test in rats. The extract (500 mg/kg/day for 15 days) reduced cerebral hypoperfusion-induced behavioural disturbances of anxiety in rats, assessed in open field test. The extract has been found to contain margosine, margosic acid and margosopicrin as active moieties.[8]

***Bacopa monnieri* (Linn.) Penn.**

Family: Scrophulariaceae
It is found in wet, damp and marshy places throughout India and subtropical region up to a height of 1000m. In ayurveda it is used as a nervine tonic and memory enhancer. It has been reported to possess anxiolytic activity in humans.[9]

***Citrus sinensis* (Linn.) Osbeck**

Family: Rutaceae
Commonly known as orange, sweet orange or round orange is assumed to have originated in southern china, north eastern India and perhaps south eastern asia (formely Indochina). The essential oils from peel (1.0 g/kg, p.o.) showed anxiolytic activity in mice tested in elevated plus maze.[10]

***Coriandrum sativum* Linn.**

Family: Apiaceae
Coriander is native to South western Asia and west to north Africa. It has been recommended for relief of anxiety and insomnia in Iranian folk medicine. Aqueous extract at 100 mg/kg, p.o. showed an anxiolytic effect in the elevated plus maze in male albino mice.[11]

***Euphorbia hirta* Linn.**

Family: It is found in India and most tropical countries. Lyophilised aqueous extract (12.5 and 25 mg/kg, p.o.) produced antianxiety effect in mice employing staircase test and light/dark choice situation test. Euphorbone is the active constituent.[12]

***Ginkgo biloba* Linn.**

Family: Ginkgoaceae
Ginkgo trees are native to East Asia and are grown ornamentally in Europe and North America. The extract (0.063-1 g/kg, p.o.) administered daily for 7 days in male mice produced anxiolysis in elevated plus maze (EPM).[13]

***Hypericum perforatum* Linn.**

Family: Hyperiaceae
It is a perennial plant, commonly known as St. John's Wort. The plant is distributed in Europe, Asia, North Africa and North America. Ethanolic extract (50%) administered at the rate of 100 and 200 mg/kg, p.o. was found to exert anxiolysis in rats employing various experimental paradigms of anxiety viz. open field

exploratory behavior, elevated plus maze, elevated zero maze, novelty induced suppressed feeding latency and social interaction tests. Hypericin has been the active component.14

Panax ginseng C.A.Mey.

Family: Araliaceae
Both Chinese ginseng (P.ginseng C.A. Mey.) and North American ginseng (P. quinquefolius Linn.) are associated with the treatment of mood and anxiety disorders. Ginseng powder and crude saponin ginseng fraction significantly increased the frequency and duration of open arm enteries in male ICR albino mice. Pure ginsenoside; ginsenoside Rb 1 (2.5 mg/kg, i.p.) increased both the frequency and duration of open arm entries.[15]

***Piper methysticum* G. Forst.**

Family: Piperaceae
Commonly known as kava-kava, is used as traditional psychoactive beverage in south pacific. It is well known for tranquilizing and anxiolytic effects. Dihydrokavain, a major kavalactone is necessary and sufficient to mediate anxiolytic effect of P. methysticum G. Forst. The anxiolytic effect may involve agonism at GABA (A)-benzodiazepine receptor complex.[16]

Different extracts of *Salvia officinalis* Linn., *Sesbania grandiflora* Pers., *Tragia involucrate* Linn., *Valeriana edulis* ssp. Procera Mey., *Withania somnifera* (Linn.) Dunal, *Zinziber officinale* Rosc. have also been studied for their sedative and anxiolytic activity. Almost 56 species of plants have been shown anxiolytic activity in laboratory animals, only 4 plants viz. *Bacopa monnieri* (Linn.) Penn., *Ginkgo biloba* Linn. *Piper methysticum* G. Forst. and Salvia officinalis Linn. have been reported to be effective clinically and active constituents from most of these plants need to be isolated to establish them as potential antianxiety plants.

Aromatherapy

Aromatherapy is one of the alternative medical methods used in many countries. The controlled use of essential oils for treatment is defined as aromatherapy.[17] Aromatherapy is a natural treatment method utilizing the chemical structure and effects of essential oils. It has various applications such as massage, inhalation, compress, and baths. It is usually used for relieving, relaxing, and resting the body. One of the methods used in aromatherapy is release of odor to a particular environment. The sense of smell plays an important role in the physiological function of the individual. The odor molecules of essential oils are transmitted to the brain by olfactory sensory neurons in the nasal cavity; thus, they stimulate smell–memory work and influence memory, thoughts, and emotions. Even a small amount of small molecules taken by respiration causes an indirect physical effect by activating smell memory or by infiltrating the blood.[18] The impacts of odor have been investigated in many studies. According to a study by the Japanese firm Takasago, it was observed that when the workplace was scented with lemon oil, computer–operator error decreased by 54%. Aromas are used in increasing productivity, psychology, and education; treating emotional problems; giving support to children with learning difficulties; and learning foreign language education.[19,20]
In a study evaluating the working performance of young males carried out by Sakamoto, Minoura, Usui, Ishizuka, and Kanba (2005)[21], it was determined that the group exposed to lavender aromatherapy had a higher concentration rate than that in the control group. Sugawara et al. (1999)[22] reported that different aromas should be used for different occupations. Almeida, Motta, Faturi, Catallani, and Leite (2004)[23] found that inhalation of rose odor produced effects similar with anxiolytic drugs in rats. In another study, the effects of lemon aromatherapy were evaluated in rats, and corticosteroid levels were lower in those taking lemon inhalation than those in the controls.[24] In addition, aromatherapy is heavily used for behavioral purposes. Aromas are used for a wide variety of conditions, such as stress, depression, Alzheimer's disease, and epilepsy; in hyperactive children to increase evocation and concentration; and in workplaces to enhance productivity and to reduce mistakes.[19,23]

Apart from the traditional use of aroma as an aesthetic and therapeutic agent, it has attracted much interest in recent years for its potential effect in changing behavioral features and on learning. Some studies show that aroma has an important impact on attention level, cognitive performance, creativity, mathematical success, writing skills, motor skills, and increased perception and memory.[19]

It has also been pointed out that aroma has a significant positive influence on emotional state, which has a very important role in directing one's attitude and in increasing activity, speed, and permanence of learning. A study of the role of aroma in the learning process found that it improved memory and cognitive functions.[19,25, 26]
Aromas may also affect the learning process because of their effect on emotions. The use of aroma in education is innovative and as yet limited. The role of senses in

the education process has been a matter of interest in recent years. It is emphasized that low levels of stress are of great importance for active learning. Aromas released into the classroom as scented stimuli decrease stress and anxiety, which are obvious obstacles to learning, and may

contribute to the development of a positive effect in the classroom, thus helping the students to cope with anxiety.[19] Aromas with fragrant stimuli may provide a useful role in preparing a comfortable learning atmosphere away from stress: Positive psychological–emotional effects of aromas may help students to listen more actively and observe what is going on in the classroom more closely.[19,27] The roles of aroma in the learning process include creating a positive atmosphere by activating emotions, providing contextual clues, and supporting memory by neurochemical and neurobiological effects.[28] Under the influence of aromas, the students have higher levels of attention and concentration, a better psychological condition, increased permanence of learning subjects, improved memory support, and a reduced level of stress.[19] Examinations in the learning process are tools of measurement and appraisal, increasing the stress levels of the students. This study was planned to determine the positive effects of aromas on the education atmosphere and the memory, attention span, and concentration of the students.

Essential oils

Essential oils are volatile, natural, complex compounds characterized by a strong odour and are formed by aromatic plants as secondary metabolites. They are usually obtained by steam or hydro-distillation first developed in the middle Ages by Arabs. Known for their antiseptic, i.e. bactericidal, virucidal and fungicidal, and medicinal properties and their fragrance, they are used in embalment, preservation of foods and as antimicrobial, analgesic, sedative, anti-inflammatory, spasmolytic and locally anesthesic remedies. Up to the present day, these characteristics have not changed much except that more is now known about some of their mechanisms of action, particularly at the antimicrobial level. In nature, essential oils play an important role in the protection of the plants as antibacterials, antivirals, antifungals, insecticides and also against herbivores by reducing their appetite for such plants. They also may attract some insects to favour the dispersion of pollens and seeds, or repel undesirable others. Essential oils are extracted from various aromatic plants generally localized in temperate to warm countries like Mediterranean and tropical countries where they represent an important part of the traditional pharmacopoeia. They are liquid, volatile, limpid and rarely coloured, lipid soluble and soluble in organic solvents with a generally lower density than that of water. They can be synthesized by all plant organs, i.e. buds, flowers, leaves, stems, twigs, seeds, fruits, roots, wood or bark, and are stored in secretory cells, cavities, canals, epidermic cells or glandular trichomes. There are several methods for extracting essential oils. These may include use of liquid carbon dioxide or microwaves, and mainly low or high pressure distillation employing boiling water or hot steam. Due to their bactericidal and fungicidal properties, pharmaceutical and food uses are more and more widespread as alternatives to synthetic chemical products to protect the ecological equilibrium. In those cases, extraction by steam distillation or by expression, for example for Citrus, is preferred. For perfume uses, extraction with lipophilic solvents and sometimes with supercritical carbon dioxide is favoured. Thus, the chemical profile of the essential oil products differs not only in the number of molecules but also in the stereochemical types of molecules extracted, according to the type of extraction, and the type of extraction is chosen according to the purpose of the use. The extraction product can vary in quality, quantity and in composition according to climate, soil composition, plant organ, age and vegetative cycle stage.[29] So, in order to obtain essential oils of constant composition, they have to be extracted under the same conditions from the same organ of the plant which has been growing on the same soil, under the same climate and has been picked in the same season. Most of the commercialized essential oils are chemotyped by gas chromatography and mass spectrometry analysis. Analytical monographs have been published[30] to ensure good quality of essential oils. Essential oils have been largely employed for their properties already observed in nature, i.e. for their antibacterial, antifungal and insecticidal activities. At present, approximately 3000 essential oils are known, 300 of which are commercially important especially for the pharmaceutical, agronomic, food, sanitary, cosmetic and perfume industries. Essential oils or some of their components are used in perfumes and make-up products, in sanitary products, in dentistry, in agriculture, as food preservers and additives, and as natural remedies. For example, d-limonene, geranyl acetate or d-carvone are employed in perfumes, creams, soaps, as flavour additives for food, as fragrances for household cleaning products and as industrial solvents. Moreover, essential oils are used in massages as mixtures with vegetal oil or in baths but most frequently in aromatherapy. Some essential oils appear to exhibit particular medicinal properties that have been claimed to cure one or another organ dysfunction or systemic disorder. [31, 32,33]

Owing to the new attraction for natural products like essential oils, despite their wide use and being familiar to us as fragrances, it is important to develop a better understanding of their mode of biological action for new applications in human health, agriculture and the environment. Some of them constitute effective alternatives or complements to synthetic compounds of the chemical industry, without showing the same secondary effects.[34]

Conclusion

Anxiety is a cardinal symptom of many psychiatric disorders and an almost inevitable component of many medical and surgical conditions. Indeed, it is a universal human emotion, closely allied with appropriate fear and presumably serving psychobiologically adaptive purposes.

It should be stressed that the treatment of such disorders generally involves psychological approaches as well as drug treatment. Furthermore, other types of drug, particularly antidepressants and sometimes antipsychotic drugs, are often used to treat anxiety disorders. The major limitation to developing new antidepressant and antianxiety drugs is a fundamental lack of a coherent pathophysiology and etiology for major depression, bipolar disorder, and common anxiety disorders.

A number of medicinal plants and medicines derived from these have been found to show anxiolytic properties by virtue of their medicinal constituents. But only some plants have been found to be anxiolytic clinically and active constituents from most of these plants need to be isolated to establish them as potential antianxiety plants.

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