

A REVIEW ON ANXIETY WITH ITS HERBAL TREATMENT USING EPM MODEL

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ABSTRACT:

Traditional Medicines derived from medicinal plants are used by about 60% of the world's population. This review focuses on Herbal drugs used in the treatment of Anxiety disorder. Anxiety disorders including generalized anxiety disorder (GAD), panic disorder, posttraumatic stress disorder (PTSD) and obsessive compulsive disorder (OCD) are the most prevalent behavioral disorders in the United States, affecting 17.2% of the population. The use of herbal supplements to treat anxiety has been increasing and the mechanisms of action of several are being elucidated. Compare to pharmaceutical drugs herbs are safer, digestible, effective, economical and having less undesirable side effects. Herbs are the most effective alternative to the pharmaceutical drugs in various health conditions. The herbs promote and improve the overall health when combined with a raw vegan diet and regular exercise. The leaves, roots, stems of different plants are sources of vitamin c, minerals, amino acid that can be helpful in case of CNS disorders. A list of medicinal plants with proven antianxiety effects used in treatment of Anxiety is compiled. These include *Gastrodia elata*, *Apocynum venetum*, *Abies pindrow* Royle, *Citrus paradise*, *Ginkgo biloba*, *Centella asiatica*, *Passiflora incarnate* and *Melissa parviflora*.

KEYWORDS: Herbal Drugs, Anxiety, Antianxiety, EPM –Elevated Plus Maze, Stress management, Psychotherapy

1. INTRODUCTION:

Psychiatric manifestations of the modern society and lifestyles include stress and anxiety. Stress and worry, in modest doses, can be beneficial; they can inspire and assist one in being more productive. However, excessive stress or a strong reaction to stress might be hazardous. It can lay the stage for both general ill health and specific medical or psychological disorders such as infection, heart disease, or depression. Stress that is constant and severe can lead to anxiety and undesirable behaviours¹.

Anxiety is a Central Nervous System disorder. It is a common emotional phenomenon in humans². It is an emotional state, unpleasant in nature and is associated with uneasiness, discomfort and concern or fear about some defined or undefined future threat³. Anxiety is considered to be a normal reaction to stress and is characterized by heart palpitations, fatigue, nausea and shortness of breath. Anxiety is the most common mental illness affecting one eighth of the total population and has become a very important area of research in psychopharmacology in the current decade⁴.

Anxiety disorders are psychiatric disorders that afflict almost 25% of all adults at some point in their lives. Anxiety disorders are prevalent in 30.5% of women and 19.2% of males, respectively⁵. Anxiety problems are quite common among teenagers and young adults. Anxiety disorders were found to be prevalent in 15.4% of children aged 7 to 11. According to a survey, only about 14% of persons with such psychiatric problems receive treatment⁶. Anxiety can exacerbate a variety of physical and mental illnesses, as well as make it more

difficult to recover from other issues. Anxiety is often divided into two types: 'state' and 'trait' anxiety. Anxiety that a subject feels at a specific time and is heightened by the presence of an anxiogenic stimuli is referred to as "state anxiety." alternatively⁷.

2. SYMPTOMS:

Some anxiety symptoms include⁸:

- Feeling anxious, fretful or tense
- Have an expanded in heart rate
- Breathing quickly
- Hyperventilation
- Sweating
- Fluttering
- Tiredness
- Trouble focusing or contemplating something besides the present stress
- Insomnia
- Experiencing gastrointestinal (GI) issues
- Difficulty in control the stress.

3. TYPES OF ANXIETY DISORDER:

The diagnostic and statistical manual of mental disorders (DSM-IV, 1994) classifies anxiety disorders in following categories.

3.1 Generalised Anxiety Disorder

The vital feature of GAD is tension and excessive worry, about a number of events or without panic and phobic symptoms⁹. Fatigue, restlessness, sleep disturbances, difficulty in concentrating and muscle tightness are some of the other symptoms. The diagnosis of GAD is verified when an individual has excessive anxiety about a variety of events for more than six months.

3.2 Panic Disorder

This type of anxiety disorder starts with a series of panic attacks, which include extreme fear akin to that experienced while facing a life-threatening situation¹⁰. Sweat, palpitation, shaking, chest pain and a feeling of suffocation, chills, or hot flashes are all possible symptoms. A condition is diagnosed when a person has repeated anticipated panic attacks and at least four of the following symptoms started abruptly and peaked within 10 minutes.

3.3 Phobia

3.3.1 Social Phobia

The fear of being assessed, adversely evaluated, or rejected in a social or performance context is a defining aspect of social anxiety disorder, also known as social phobia. People with social anxiety disorder may worry about being judged as foolish, awkward, or uninteresting if they act or appear anxious (e.g., blushing, stumbling over words). As a result, they frequently avoid social or performance situations, and when they are unable to avoid them, they experience severe anxiety and distress¹¹.

3.3.2 Specific Phobia

This type of phobia contains excessive fear for specific object or situation (e.g. Insects, height, public transportation etc.).

3.3.3 Obsessive Compulsive Disorder

There are persistent and repeated thoughts, as well as ritualistic activities and behaviour, with this form of disease. A compulsion is a behaviour or mental act that is performed repeatedly, purposefully, and intentionally in response to an obsession (e.g. frequent hand washing, checking, ordering, counting, repeating words, silently preying etc.).

3.4.4 Post Traumatic Stress Disorder

This disorder is caused by witnessing or experiencing traumatic or terrifying life events. (For example, a violent crime or a terrible accident). Insomnia, hypersensitivity to external stimuli, and a loss of recollection of the time leading up to the traumatic experience are all symptoms of this illness. PTSD is diagnosed when a patient continues to relive the traumatic incident by dreaming about it, having hallucinations, or experiencing flashbacks. These symptoms can last for

more than a month, but they can also occur after a significant period of time has passed after the traumatic occurrence¹².

4. CAUSES:

Genetics: Anxiety disorders can be passed down via families.

Brain chemistry: Some research suggests anxiety disorders may be linked to faulty circuits in the brain that control fear and emotions.

Environmental stress: This refers to stressful events you have seen or lived through. Life events often linked to anxiety disorders include childhood abuse and neglect, a death of a loved one, or being attacked or seeing violence.

Drug withdrawal or misuse: Certain drugs may be used to hide or decrease certain anxiety symptoms. Anxiety disorder often goes hand in hand with alcohol and substance use.

Medical conditions: Some heart, lung, and thyroid conditions can cause symptoms similar to anxiety disorders or make anxiety symptoms worse. It's important to get a full physical exam to rule out other medical conditions when talking to your doctor about anxiety¹³.

5. 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 function¹⁴.

6. TREATMENT OF ANXIETY:

Anxiety can be treated with the psychological counseling, 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



Fig 1: Various treatments of anxiety disorder

6.1 Self Treatment

Some cases, a person can treat an anxiety disorder at home without clinical supervision. However, this may not be effective for severe or long-term anxiety disorders.

There are several exercises and actions to help a person cope with milder, more focused or shorter-term anxiety disorders, including:

- Stress management: Learning to manage stress can help limit potential triggers.
- Relaxation techniques: Simple activities can help soothe the mental and physical signs of anxiety. These techniques include meditation, deep breathing exercises, long baths, resting in the dark and yoga.
- Exercises to replace negative thoughts with positive ones: Make a list of the negative thoughts that might be cycling as a result of anxiety, and write down another list next to it containing positive, believable thoughts to replace them.
- Support network: Talk with familiar people who are supportive, such as a family member or friend. Support group services may also be available in the local area and online.
- Exercise: Physical exertion can improve self-image and release chemicals in the brain that trigger positive feelings.

6.2 Psychotherapy

6.2.1 Counseling

A standard way of treating anxiety is psychological counseling. This can include cognitive-behavioral therapy (CBT), psychotherapy or a combination of therapies.

6.2.2 CBT

This type of psychotherapy aims to recognize and change harmful thought patterns that form the foundation of anxious and troublesome feelings. In the process, practitioners of CBT hope to limit distorted thinking and change the way people react to objects or situations that trigger anxiety.

For example, a psychotherapist providing CBT for panic disorder will try to reinforce the fact that panic attacks are not really heart attacks. Exposure to fears and triggers can be a part of CBT. This encourages people to confront their fears and helps reduce sensitivity to their usual triggers of anxiety.

6.3 Allopathy: Medications

A person can support anxiety management with several types of medication.

Medicines that might control some of the physical and mental symptoms include antidepressants, benzodiazepines, tricyclics, and beta-blockers.

6.3.1 Benzodiazepines

A doctor may prescribe these for certain people with anxiety, but they can be highly addictive. These drugs tend to have few side effects except for drowsiness and possible dependence. Diazepam, or Valium, is an example of a commonly prescribed benzodiazepine.

6.3.2 Antidepressants

These commonly help with anxiety, even though they also target depression. People often use serotonin reuptake inhibitors (SSRI), which have fewer side effects than older antidepressants but are likely to cause jitters, nausea, and sexual dysfunction when treatment begins.

Other antidepressants include fluoxetine, or Prozac, and citalopram, or Celexa.

6.3.3 Tricyclics

This is a class of drugs older than SSRIs that provide benefits for most anxiety disorders other than OCD. These drugs might cause side effects, including dizziness, drowsiness, dry mouth, and weight gain. Imipramine and clomipramine are two examples of tricyclics¹⁵.

Additional drugs a person might use to treat anxiety include:

- monoamine oxidase inhibitors (MAOIs)
- beta-blockers
- buspirone

7. HERBAL DRUGS VERSUS SYNTHETIC DRUGS:

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.

8. PLANTS PROVED TO RETAIN ANXIOLYTICACTIVITY:

Gastrodiaelata: (Family-Orchidaceae)

The anxiolytic-like effects of the aqueous extract of the rhizome of *Gastrodiaelata* along with its phenolic constituents, 4hydroxybenzyl alcohol (HA) and 4hydroxybenzaldehyde (HD), using an elevated plus maze (EPM) in mice were characterized. A single treatment of the aqueous *G. elata* extract significantly increased the percentage of time spent and arm entries into the open arms of the EPM versus the saline controls. Among the phenolic constituents of *G. elata*, HA and HD significantly increased the percentage of time spent and arm entries into the open arms of the EPM versus saline controls ($p < 0.05$)¹⁶.

ApocynumvenetumL. : (Family-Apocynaceae)

O. Grundmann et al. evaluated the anxiolytic activity of an aqueous extract of *Apocynumvenetum* L. (Apocynaceae) and bioguided its fractionation using the elevated plus maze (EPM) in mice as a model of anxiety. A single treatment of AV extract markedly increased the percentage time spent on the open arms of the EPM in two distinct concentration ranges of 22.5–30 and 100–125 mg/kg p.o., respectively, indicating a putative anxiolytic-like activity¹⁷.

Abies pindrowRoyle: (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, respectively¹⁸.

Citrus paradisi (Grapefruit): (Family-Rutaceae)

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 diazepam¹⁹.

Ginkgo biloba :(Family-Ginkgoaceae)

Extract of *Ginkgo biloba* (EGb 761) significantly reduced the detrimental effect of learned helplessness in a subsequent conditioned avoidance task. In the elevated plus maze, senescent mice treated with EGb 761 spent more time in open arms than those treated with vehicle control (Ward et al., 2002). Woelke et al. (2007) compared a standardized extract of *Ginkgo biloba* L. (EGb 761) in doses of 480mg and 240mg with placebo for four weeks, involving patients with GAD and adjustment disorder with anxious mood (DSM-III-R). The two doses of EGb 761 showed a greater reduction in HAMA scores compared to placebo, as well as a statistically significant reduction in somatic symptoms compared to baseline (which was not observed in the placebo group)²⁰.

Centella asiatica (Mandookaparni or Gotu Kola): (Family-Apiaceae)

Centella asiatica is reputed for its beneficial effects in various neurological disorders. Gotu Kola has been used for centuries in Ayurvedic and traditional Chinese medicine to alleviate symptoms of depression and anxiety. Recent studies in the rat have shown that long-term pretreatment with Gotu Kola decreases locomotor activity, enhance elevated-plus maze performance and attenuate acoustic startle response (Chen et al., 2006; Wijeweera et al., 2006). In a double-blind, placebo-controlled study, the anxiolytic activity of *Centella asiatica* in healthy subjects was undertaken and compared to placebo, Gotu Kola significantly reduced peak acoustic startle response amplitude 30 and 60 minutes after treatment (Bradwejn et al., 2000). In another clinical study, 70% hydro-ethanolic extract of *Centella asiatica* was given to 33 participants for two months and Hamilton's Brief Psychiatric Rating Scale (BPRS) was used to screen the subjects. The results show that, Mandookaparni significantly attenuated anxiety related disorders (Jana et al., 2010). These preliminary findings suggest that *Centella asiatica* has anxiolytic activity in humans and it remains to be seen whether this herb has therapeutic efficacy in the treatment of anxiety syndromes in large population²¹.

Passiflora incarnata L. (Passion flower) : (Family-Passifloraceae)

It is a benzodiazepine receptor partial agonist and causes GABA-system mediated anxiolysis. Animal behavioural models have shown non-sedative anxiolytic effect. In an in vivo study employing a methanol extract of passion flower (125 mg/kg, orally) measured anxiolytic activity in mice, using the elevated plus-maze model, an increase in number of entries in open arm was demonstrated. A 4 week RCT using passion flower extract on patients with GAD (n=36) showed that passion flower was as effective as oxazepam (30 mg/day) in reducing anxiety and it had less number of side effects. In an acute study RCT (n=60) using 500 mg of passion flower vs placebo for presurgical anxiety, it was demonstrated that anxiety scores were significantly lower in the passionflower group than in the control group on a numerical rating scale²².

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 maze²³.

CONCLUSION:

Anxiety disorders are psychiatric disorders affecting nearly 25% of the adult population at some point in their life. Herbs have been proved as a great alternative to the pharmaceutical drugs for the treatment of various health conditions. The leaves, roots, stems of different plants are sources of vitamin c, minerals, amino acid that can be helpful in case of CNS disorders. Synthetic drugs and medications possess enormous side effects, so these herbs with a wide therapeutic applicability promise to alleviate anxiety with very few adverse effects. This review of study, we concludes that anxiolytic activities of different extracts of different plants in mice/rat, at the different doses have shown significant results as a anxiolytic activity using EPM

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CONFLICTS OF INTEREST:

There are no conflicts of interest among the authors.

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