A Review on Medicinal Herbs used in Treatment of Anxiety

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Abstract

One of the most common mental health issues in the world is anxiety disorders, which has led to a need for practical and affordable therapies. This review looks at the history, pharmacological characteristics, and therapeutic effectiveness of medicinal herbs in the treatment of anxiety. Many herbs, such as chamomile, lavender, passionflower, and ashwagandha, have been examined for their ability to reduce anxiety. These effects are frequently attributed to changes in neurotransmitter systems, such as serotonin and gamma-aminobutyric acid (GABA). These herbs may significantly reduce anxiety symptoms, according to clinical trials and observational studies, and frequently with less adverse effects than traditional medications. To provide standardized recommendations for their use, additional study is necessary because to variations in preparation techniques, doses, and patient reactions. This study highlights the potential of medicinal herbs as supplemental therapy for the treatment of anxiety and advocates for further thorough clinical trials to confirm their safety and effectiveness.

Keywords : *Anxiety disorders, medicinal herbs, anxiolytic effects, Chamomile, Lavender, Passionflower, Ashwagandha, herbal medicine.*

INTRODUCTION

The process of creating anxiolytic and antidepressant medications derived from plants includes phytochemical, pharmacological, and ethnopharmacological research (a thorough examination of traditional medicinal uses). A crucial first step in any pharmacological investigation is choosing an appropriate plant. Traditional use, chemical composition, toxicity, randomized selection, or a mix of multiple criteria are pertinent indicators for accomplishing this phase.(1) The most successful approach is, by far, to select medicinal plants with the goal of finding new pharmacological compounds based on their widespread use. The most obvious source of botanical material for the study of medicinally effective medications is the plants that have been used widely for many years. Quantitative and qualitative analyses using various techniques, such as thin-layer chromatography, column chromatography, high-performance liquid chromatography, nuclear magnetic resonance, and other phytochemical techniques, typically follow the collection of plant material, identification, and specimen deposition in the herbarium (2) .

Biological research of botanicals are a necessary step after the ethnopharmacological survey and phytochemical studies. The discovery of novel medications has benefited from the use of animal models of depression and anxiety. Consistent preclinical and clinical results of new anxiolytic and antidepressant medications may result from a well-validated test. Some of the conventional preclinical techniques have seen advancements and adjustments recently. The purpose of this review was to provide an overview of the history of anxiety and depression, pharmaceutical interventions, medicinal plants with anti-anxiety and antidepressant qualities, and preclinical approaches for the study of phytoconstituents or extracts that may have anxiolytic or antidepressant activities (3).

One of the most common and highly associated mental illnesses is anxiety disorders. Many herbal medications have been used to treat anxiety disorders in adults throughout the last ten years. In addition to doctors, the majority of people are seeing herbalists, naturopaths, and other healers due to the growing popularity of herbal remedies. According to a study, 44% of psychiatric patients with anxiety problems had taken herbal medicine in the preceding 12 months, primarily for psychiatric causes .However, there is little information available about the advantages and risks of using herbal medicines. In general, these drugs have been regarded as safe and effective, and there have been few reports of significant side effects, disorders are considered to be a major cause of disability worldwide, and comprise generalized

anxiety disorder and other commonly associated conditions, such as phobias, postmenopausal stress, post-traumatic syndrome, somatization and cognitive dysfunction, among others. Patients diagnosed with generalized anxiety disorder exhibit functional impairment as well as a tendency to develop comorbid psychiatric disorders (4).

1 Effective treatments for this condition are usually focused one liminating anxiety symptoms and restoring normal function. It is believed that traditional anxiolytic medication therapy is safe, efficient, and has a broad range of effects.

2 Butside effects often reduce quality of life, discouraging patients to follow medication protocols. Moreover, many of the medicines used for anxiety include antidepressants, and the use of such agents can cause troubling side effects, i.e, cholinergic symptoms ,weight gain, sleep disturbances, sexual dysfunction, medication dependence, or The symptoms of anxiety disorders include feelings of anxiety and fear. Generalized anxiety disorder, panic disorder, phobias, social anxiety disorder, OCD, and PTSD are among the several forms of anxiety disorders. The symptoms are usually chronic and might be mild, moderate, or severe. Tricyclic antidepressants, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, norepinephrine and dopamine reuptake inhibitors, and serotonin antagonist and reuptake inhibitors are among the medications used in pharmacological therapy for depressive disorders. Pregabalin, tricyclic antidepressants, buspirone, benzodiazepines, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, and selective serotonin and norepinephrine reuptake inhibitors are among the medications used in the pharmacological treatment of anxiety disorders. However, patients often do not adhere to these synthetic antidepressants or anxiolytic therapies due to adverse events or signatory delay in effectiveness gastrointestinal problems (5).

Epidemiology

A number of epidemiological studies have shown that anxiety disorders are highly prevalent and important causes of functional impairment.Several previous studies conducted in the USA,UK,and Germany have highlighted these problems. The Epidemiological Catchment Area (ECA) survey8is the largest and most famous psychiatric epidemiological study carried out in a general population of five American states (Connecticut, Maryland, Missouri, North Carolina, and California We'll focus on talking about the ECA findings on anxiety and neurotic illnesses from now on. Only a few of the research areas addressed the other anxiety disorders. The prevalence of PTSD was 1% in Saint Louis (0.5% in men,1.3% in women;3.5% in crime victims,20% in
Vietnam veterans). GAD has a 12-month prevalence of 2.3% in Durham, NC (0.8% in men and 2.6% in women) and is not associated with another psychiatric condition in two cases out of three. Similar to the majority of prior studies, the ECA study emphasizes the high comorbidity of neurotic and anxiety disorders, whether they are associated with other anxiety disorders (6).

Prevalence

1. **Types of Anxiety Disorders:**
   - Common types include Generalized Anxiety Disorder (GAD), Panic Disorder, Social Anxiety Disorder, and Specific Phobias.
   - Each type has its own prevalence rate, with Specific Phobias and Social Anxiety Disorder typically being the most common.
2. **Age of Onset:**
   - Anxiety disorders often begin in childhood or adolescence.
   - The median age of onset can vary; for instance, Social Anxiety Disorder often starts in early adolescence, while Generalized Anxiety Disorder may start in adulthood.
3. **Gender Differences:**
   - Women are generally at a higher risk for most anxiety disorders compared to men.
   - Gender differences in prevalence rates are often attributed to both biological factors and social influences.
4. **Comorbidity:**
   - Anxiety disorders frequently co-occur with other mental health conditions, such as depression and substance use disorders.
   - The presence of comorbid conditions can complicate treatment and impact overall functioning.
5. **Risk Factors:**
   - Genetic predisposition, early life stressors, and environmental factors can contribute to the development of anxiety disorders.
   - Traumatic events, chronic stress, and certain personality traits are also significant risk factors.
6. **Impact and Burden:**
   - Anxiety disorders can significantly impact quality of life, including work, social relationships, and overall well-being.
   - The economic burden includes direct costs like medical expenses and indirect costs such as lost productivity.

7. **Treatment and Access:**
    - Effective treatments include psychotherapy (such as Cognitive Behavioral Therapy), pharmacotherapy, and lifestyle changes.
    - Despite available treatments, many individuals with anxiety disorders do not receive adequate care due to barriers like stigma, lack of access to mental health services, and personal reluctance (7).

Etiology

1. **Biological Factors:**

- **Genetics:** Anxiety disorders often run in families, suggesting a genetic component. Twin and family studies indicate that genetics can contribute significantly to the risk of developing anxiety disorders.
- Specific genes related to neurotransmitter systems (e.g.,serotonin, norepinephrine) have been implicated, although no single gene is responsible for anxiety.
- **Neurobiological Factors:**
- **Neurotransmitters:** Imbalances in neurotransmitters such as serotonin, norepinephrine, and gamma-aminobutyric acid (GABA) are associated with anxiety.
- **Brain Structures:** Abnormalities in brain regions like the amygdala, which is involved in fear processing, and the prefrontal cortex, which is involved in regulation of emotional responses, can contribute to anxiety.
- **Neuroendocrine System:** Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, which controls the body's response to stress, is often observed in individuals with anxiety disorders (8).

2. **Psychological Factors:**

- **Cognitive Factors:**
- **Cognitive Biases:** Individuals with anxiety disorders may have cognitive biases, such as catastrophic thinking or overestimating the likelihood of negative outcomes.
- **Self-Efficacy:** Low self-efficacy and a tendency to perceive oneself as unable to cope with stress can contribute to anxiety.
- **Personality Traits:** Certain personality traits, such as neuroticism, are associated with a higher risk of developing anxiety disorders.
- Traits like perfectionism and high sensitivity to stress can also be risk factors.

3. **Environmental Factors:**

- **Early Life Experiences:**
- **Trauma and Abuse:** Exposure to traumatic events or abuse during childhood can increase the risk of developing anxiety disorders later in life.
- **Parenting Style:** Overprotective or excessively controlling parenting can contribute to the development of anxiety in children.
- **Stressful Life Events:** Major life changes or stressful events, such as job loss, divorce, or financial difficulties, can trigger or exacerbate anxiety disorders.
- **Socioeconomic Factors:** Low socioeconomic status and associated stressors, such as financial instability and limited access to resources, are linked to higher rates of anxiety (9).

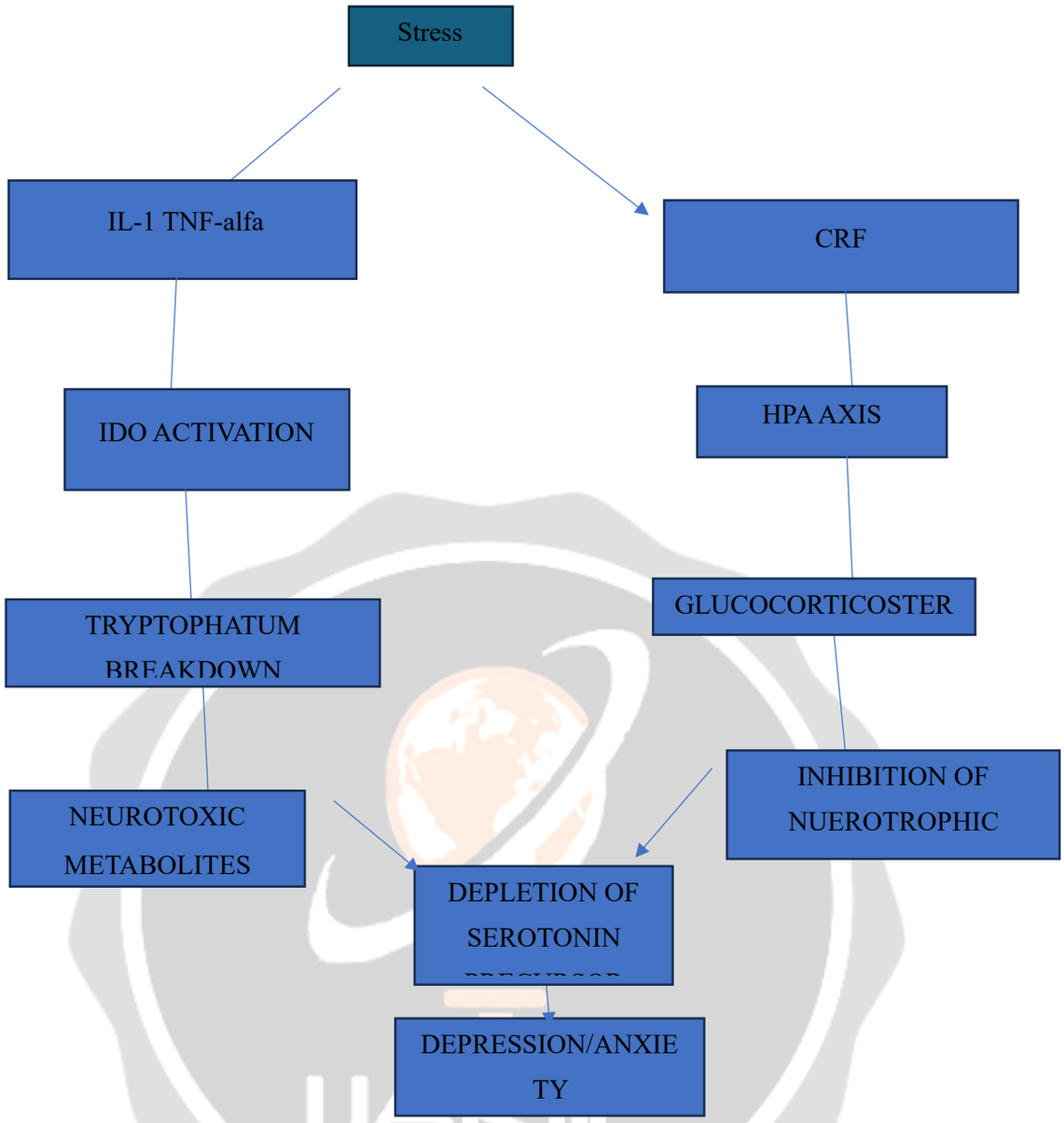
4. **Developmental Factors:**

- **Attachment Theory:** Insecure attachment styles, formed in early childhood, can influence the development of anxiety. For example, children with anxious or ambivalent attachment patterns may be at higher risk.
- **Developmental Milestones:** Certain developmental milestones, such as the transition to adolescence or adulthood, can be associated with an increased risk of anxiety due to changes in social and environmental demands (10).

5. **Biopsychosocial Model:**

- **Interaction of Factors:** The biopsychosocial model suggests that anxiety disorders result from the interaction of biological, psychological, and social factors. This integrated approach recognizes that no single factor is responsible, but rather a combination of influences contributes to the onset and maintenance of anxiety (11).

Pathophysiology



Pharmacological treatment of anxiety and depression

Although many pharmacological types are available to treat anxiety and depression, complete remission of illness symptoms has not been achieved. These medications' poor tolerability profile and typical adverse effects limit their clinical use. Certain first-line anxiolytic and antidepressant medications improve monoaminergic function by blocking the enzymes that break down dopamine, serotonin, and adrenaline, as well as by preventing monoamines from being reabsorbed to raise their concentration in the synaptic cleft. A number of additional pharmacological mechanisms with anti-anxiety and antidepressant effects (12).First-line anxiolytic and/or antidepressant drugs are widely sought after by patients with or without prescription. Benzodiazepines that are the most commonly used anxiolytic drugs potentiate the inhibitory GABAergic transmission. It's interesting to note that several anxiolytic medications also have depressive properties, suggesting that the etiology of both mental illnesses may overlap. Anxiolytic and antidepressant properties are predicted by the way serotonin agonists, such as buspirone and gepirone, interact with presynaptic and postsynaptic 5-hydroxytryptamine1A (5-HT1A) receptors. Meanwhile, some of the drugs that are currently on the counter seem to be characterized with cases of side effects, for example benzodiazepines which induce sedation, ataxia, and amnesia among others. Many patients' therapeutic demands remain unmet even with advancements in the treatment of anxiety and depression.The efficacy, duration of effects and side effects of available drugs have constituted serious concern and the need for newer drugs. The diversity in neural targets makes phytomedicine a promising candidate for the treatment of these diseases (13).

Plant species with anti-anxiety and/or antidepressant properties

Regulatory bodies provide definitions for herbal medicinal products. They are those obtained with exclusive use of botanicals with recognized efficacy, acceptable level of safety, scientific data, preclinical (pharmacological and toxicological studies) and clinical publications. Regulatory agencies have authorized the use of certain herbal remedies to treat mental illnesses. In Brazil, the National Agency of Sanitary Surveillance (ANVISA) included products that are derived from Passiflora incarnata, Piper methysticum, Valeriana officinalis, Cimicifuga racemosa for the treatment

of anxiety disorders and/or depression. Like ANVISA, European Medicines Agency (EMA) included Hypericum perforatum L. (St. John's Wort, SJW), Melissa officinalis L. (Melissa leaf), V. officinalis L. (Valerian Root) among others in the list of Herbal medicines for the treatment of mental stress and mood disorder (14).

The herbal medicines derived from P. in carasnata are prescribed in many parts of the world to treat some CNS disorders. This plant is used for the treatment of insomnia and anxiety disorders in Brazil, Europe and USA (15). Clinical applications of this species worldwide have led to its inclusion in British Herbal Pharmacopoeia (1983), Homoeopathic Pharmacopoeia of India (1974), United States Homoeopathic Pharmacopoeia (1981), Pharmacopoeia Helvetica (1987), and in the pharmacopoeia of Egypt, France, Germany and Switzerland. Phytochemical studies of P Flavonoids (orientin, isoorientin, vitexin, isovitexin, and chrysin), cyanogenic glycosides, and indole alkaloids were detected in incarnata. Chrysin was shown to have an anxiolytic-like effect in rats by Zanoli e. and Brown et al. This action may be caused by a benzodiazepine receptor ligand. However, the anxiolytic effects of P. incarnata do not seem to be associated solely chrysin or another compound, but it seems associated with phytocomplex (different phytoconstituents) acting in a synergistic manner (16).

Sr. No	Plant species	Common name	Active compounds	Uses
1	Lavandula angustifolia	Lavender	Linalool, linalyl acetate	Aromatherapy, teas, essential
				oils
2	Rhodiola rosea	Rhodiola	Rosavins, salidroside	Adaptogen, stress relief
3	Valeriana officinalis	Valerian root	Valerenic acid	Sleep aid, anxiety relief
4	Passiflora incarnata	Passionflower	Harman, flavonoids	Anxiety relief, calming effects
5	Hypericum perforatum	St. John's Wort	Hypericin, hyperforin	Antidepressant
6	Withania somnifera	Ashwagandha	Withanolides	Stress reduction, mood enhancer
7	Matricaria chamomilla	Chamomile	Apigenin	Calming effects, sleep aid
8	Melissa officinalis	Lemon balm	Rosmarinic acid	Anxiety relief, sleep aid
9	Glycyrrhiza glabra	Licorice root	Glycyrrhizin	Stress relief, mood support
10	Panax ginseng	Ginseng	Ginsenosides	Energy boost, stress relief
11	Avena sativa	Oats	Avenanthramides	Mild sedative, mood enhancement
12	Nardostachys jatamansi	Spikenard	Jatamansone	Anxiolytic, calming effects
13	Scutellaria baicalensis	Baikal skullcap	Baicalin, baicalein	Anxiety relief, calming effects
14	Corydalis yanhusuo	Corydalis	Tetrahydropalmatine	Pain relief, anxiolytic

15	Zingiber officinale	Ginger	Gingerol	Digestive aid, anti-anxiety effects
16	Zataria multiflora	Avishan-eshirazi	Thymol, carvacrol	Mood enhancement
17	Piper methysticum	Kava	Kavalactones	Anxiolytic, relaxation
18	Camellia sinensis	Green tea	L-theanine	Calming effects, focus
19	Curcuma longa	Turmeric	Curcumin	Mood enhancement, a
20	Eschscholzia californica	California poppy	Protopine, allocryptopine	Anxiolytic, sleep aid

Withania somnifera

Figure 1: Withania somnifera (ashwagandha)

Biological Source

W. somnifera is grown in much of India's arid regions. It can also be found in Yemen, China, Sri Lanka, and Nepal. It favors sun to partially shaded, dry, stony soil. It can be multiplied by greenwood cuttings in the later spring or by seeds in the early spring.

Family : Solanaceae

Uses

- It reduce stress and anxiety
- It reduce serum cortisol
- It also reduce sleeplessness and fatigue.

Panax ginseng

Figure 2: Panax ginseng (Korean ginseng)

Biological source

Its biological source is primarily the root, which is the part used for medicinal and therapeutic purposes. The plant is native to East Asia, particularly found in countries like China, Korea, and Siberia.

Family : Araliaceae

Uses

- **Energy Boost**: Often used to combat fatigue and enhance physical stamina.
- **Cognitive Function**: May improve memory, concentration, and mental clarity.
- **Immune Support**: Believed to help strengthen the immune system and reduce the risk of illness (17).

Experimental studies of Mexican plants with anxiolytic arises from both specific and generic stimuli that are thought to pose a future threat. This perception often results in an apprehensive mood accompanied by increased arousal .when anxiety becomes overwhelming, That could be categorized as an anxiety disorder. It is interesting to note that over 40% of the culture bound syndromes listed in Appendix I of DSMIV explicitly are overlapped with anxiety pathology, and research has focused on the links between these syndromes and anxiety disorders The elevated plus maze (EPM) is one of the basic behavioral tests used to detect anxiety in laboratory mice. Anxiety can also be modeled using both light-enhanced, and dark-enhanced startle paradigms Anxiety is considered to be a normal reaction to a stressor, characterized as a state of being that, co Contemporaneously, The use of herbal medicine is widespread amongst suffers of mood and anxiety disorders Anxiolytics include species like Melissa officinalis (lemon balm), Matricaria recutita (chamomile), and Humulus lupulus (hops) that are known to exist around the world; research into their mechanisms of action is just beginning . The species utilized in México scientifically examined for anxiety models are: Galphimia glauca, Tilia americana L. var. mexicana, Lippia alba, Ipomoea stans, Casimiroa edulis, Montanoa frutescens, Magnolia dealbata, Valeriana edulis sspntext conditioning, and by exploiting the unpredictability of aversive events, such as mild shock (18).

Pharmacological action of drugs Benzodiazepines:

- **Mechanism**: These drugs enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) at the GABA-A receptor. By increasing GABAergic activity, benzodiazepines produce a calming effect, reduce anxiety, and have sedative, muscle relaxant, and anticonvulsant properties.
- **Examples**: Diazepam, Lorazepam, Clonazepam.
- **Considerations**: They are typically used for short-term management due to risks of dependence and tolerance.

- **Selective Serotonin Reuptake Inhibitors (SSRIs)**:

  Mechanism: SSRIs increase the levels of serotonin in the brain by inhibiting its reuptake into neurons. This leads to enhanced serotonergic neurotransmission, which can improve mood and reduce anxiety.

  Examples: Sertraline, Escitalopram, Paroxetine.

  Considerations: SSRIs are often used for long-term management of anxiety disorders and are generally well-tolerated, though they may have delayed onset of effects.

- **Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)**:

Mechanism: SNRIs inhibit the reuptake of both serotonin and norepinephrine, leading to increased levels of these neurotransmitters in the brain. This can help alleviate anxiety and improve mood.

Examples: Venlafaxine, Duloxetine.

Considerations: Similar to SSRIs, SNRIs are used for long-term management and may have a delayed onset of therapeutic effects.

- **Buspirone**:

Mechanism: Buspirone is a non-benzodiazepine anxiolytic that primarily acts as a partial agonist at serotonin (5-HT1A) receptors. It also has some effects on dopamine receptors.

Examples: Buspirone (brand name BuSpar).

Considerations: It is less sedating than benzodiazepines and has a lower risk of dependence, but may take several weeks to be fully effective.

- **Beta-Blockers**:

- **Mechanism**: Beta-blockers reduce the physical symptoms of anxiety (e.g., rapid heartbeat, trembling) by blocking beta-adrenergic receptors, which helps to decrease the effects of adrenaline.
- **Examples**: Propranolol, Atenolol.
- **Considerations**: They are often used for performance anxiety or specific situations rather than for generalized anxiety disorder.

- **Antihistamines**:

Mechanism: Some antihistamines have sedative properties that can help with short-term anxiety relief by blocking histamine receptors in the brain.

Examples: Hydroxyzine.

Considerations: They are usually used for short-term relief and not for chronic anxiety (19).

Evaluation of putative anxiolytic effects of medicinal plants

In all fields of biomedical research, animal models are essential. To investigate anxiolytic effect of crude extract or active principles from medicinal plants, a wide range of behavioural testing has been developed . Some well-established tests of anxiety include open field test. This test was originally introduced as a measure of emotional behaviour in rats and later adapted to mice . Parameters such as ambulation, time and crossing at the centre of the open field, grooming, freezing and rearing are often measured. Light–dark box (LDB) has also been used to investigate anxiolytic properties. The underlining principle of LDB model is based on the aversion of rodents to brightly

illuminated areas, novel environment and light-induced mild stress. The number of transitions between the two compartments and the time spent in the light area are recorded over a specified period . Elevated plus maze is another widely used behavioural model with a strong predictive validity to measure the anxiolytic-like effect of a novel compound . The time spent and the number of entries with all four paws inside the open arms are well-established parameters for assessing anxiolytic or anxiogenic property of new drugs. The open and closed arms are considered to evoke the same exploratory drive; therefore, avoidance of Since the open and closed arms are thought to elicit the same exploration urge, avoiding the open arms is thought to be the result of higher degrees of fear being induced . Other models such as marbleburying and hole board tests with repetitve tendency have been used to evaluate anxiolytic- or anxiogenic-like effects(20).

TREATMENT OF ANXIETY WITH EXERCISE AND PHYSICAL ACTIVITY

In treating anxiety, exercise has been shown to alleviate anxious feelings. Exercising at 70%– 90% of maximum heart rate for 20 minutes three times a week has been shown to significantly reduce anxiety sensitivity . Following a recommended exercise program, there is a decrease in self-reported worries of anxiety sensations, fears of respiratory and cardiovascular symptoms, fears of publically viewable anxiety symptoms, and fears of cognitive dyscontrol. In a study by Cox and colleagues , the most substantial decrease in state anxiety occurred 90 minutes following 20 minutes of aerobic exercise at 80% of maximal oxygen uptake. While useful in treatment, exercise has not been shown to reduce anxiety to the level achieved by psychopharmaceuticals. In a study of patients suffering from moderate to severe panic disorder, both a 10-week protocol of regular aerobic exercise and clomipramine were associated with significant improvement of symptoms compared to placebo . In comparison with exercise, clomipramine alleviated anxiety symptoms more effectively and significantly earlier. In general, exercise does appear to be effective in reducing symptoms associated with anxiety . Furthermore, symptoms improve following both an acute episode of physical activity as well as following a program of routine exercise

Conclusion

This review emphasizes the historical significance and current applicability of medicinal herbs in the treatment of anxiety disorders, highlighting their promising potential. Herbs with possible anxiolytic qualities include chamomile, lavender, passionflower, and ashwagandha. These effects are mostly due to their pharmacological actions on neurotransmitter systems. When compared to conventional medications, the evidence from observational research and clinical trials suggests that these herbal therapies may successfully reduce anxiety symptoms, frequently with a positive side effect profile.

Even with these positive results, more research is still necessary because of the variations in herbal preparation, dosages, and patient responses. In order to maximize the use of medicinal herbs in the management of anxiety, future research should concentrate on standardizing methodology and developing evidence-based recommendations. A comprehensive treatment plan that improves patient outcomes may be created by combining various complementary and alternative therapies. In the end, more research into medicinal herbs can make a big difference in the growing field of mental health treatment by providing dependable and safe options for those with anxiety problems.

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