

A REVIEW ON HERBAL PLANT USE IN ANXIETY DISORDER

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ABSTRACT

Anxiety disorders are among the most prevalent mental health conditions, affecting millions worldwide. Conventional pharmacological treatments, such as benzodiazepines and selective serotonin reuptake inhibitors (SSRIs), are effective but often associated with side effects like drowsiness, dependence, and withdrawal symptoms. As a result, there is growing interest in herbal remedies as safer alternatives for managing anxiety. This review explores various medicinal plants known for their anxiolytic properties, their mechanisms of action, and their clinical relevance. Several herbal plants, including *Passiflora incarnata* (Passionflower), *Valeriana officinalis* (Valerian), *Withania somnifera* (Ashwagandha), *Bacopa monnieri* (Brahmi), and *Lavandula angustifolia* (Lavender), have shown promising results in anxiety management. These plants exert their effects through multiple mechanisms, such as modulating the GABAergic, serotonergic, and dopaminergic systems, reducing oxidative stress, and enhancing neuroprotection. Clinical studies support their efficacy, with many demonstrating comparable effects to conventional anxiolytics but with fewer adverse reactions. However, concerns regarding standardization, bioavailability, and herb-drug interactions remain significant challenges. Despite encouraging evidence, more large-scale and long-term clinical trials are needed to establish the safety, efficacy, and optimal dosages of these herbal medicines. Additionally, advancements in formulations, such as nanotechnology-based delivery systems, may enhance their therapeutic potential. This review highlights the role of herbal plants as promising alternatives in anxiety treatment and emphasizes the need for further research to integrate them into mainstream medicine effectively.

KEYWORD: Herbal Anxiolytics, Anxiety Disorders, Phytotherapy, Neurotransmitter Modulation.

INTROUCTION

Anxiety disorders are among the most common psychiatric conditions, affecting millions of individuals worldwide. They are characterized by persistent feelings of fear, nervousness, and excessive worry, often leading to physical symptoms such as increased heart rate, muscle tension, restlessness, and difficulty concentrating (WHO, 2017). The World Health Organization (WHO) has identified anxiety as a major contributor to disability, with an increasing prevalence across all age groups (Arroll, et al., 2016). Common subtypes of anxiety disorders include generalized anxiety disorder (GAD), panic disorder, social anxiety disorder, and specific phobias. If left untreated, these conditions can significantly impact an individual's quality of life, leading to decreased work productivity, strained relationships, and an increased risk of depression (Bandelow, Michaelis, & Wedekind, 2017) (Yeung, Hernandez, Mao, Haviland, & Gubili, 2018).

Current treatment strategies for anxiety primarily rely on pharmacological interventions, including benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) (Sartori & Singewald, 2019). While these medications provide symptomatic relief, they are associated with several drawbacks, including dependency, withdrawal symptoms, sedation, cognitive impairment, and potential long-term side effects. The limitations of conventional medications have prompted researchers and healthcare practitioners to explore alternative therapeutic approaches, with herbal medicine emerging as a promising option for managing anxiety disorders (Montemurro, et al., 2022) (Fajemiroye, da Silva, de Oliveira, & Costa, 2016).

Herbal plants have been traditionally used in various cultures to alleviate stress and anxiety. These plants contain bioactive compounds that interact with key neurotransmitter systems, such as the gamma-aminobutyric acid (GABA) system, serotonergic pathways, and the hypothalamic-pituitary-adrenal (HPA) axis, which play crucial roles in anxiety regulation (Esmail Al-Snafi, Ali Talab, & Majid, 2019). Among the most studied medicinal plants for anxiety management are *Passiflora incarnata* (Passionflower), *Valeriana officinalis* (Valerian), *Withania somnifera* (Ashwagandha), *Bacopa monnieri* (Brahmi), *Lavandula angustifolia* (Lavender), *Piper methysticum* (Kava), *Melissa officinalis* (Lemon Balm), and *Matricaria chamomilla* (Chamomile). These herbs have shown promising anxiolytic effects through mechanisms such as enhancing GABAergic activity, reducing oxidative stress, modulating neuroinflammation, and improving neuroplasticity (Bocquet, Sahpaz, Hilbert, Rambaud, & Rivière, 2018) (Chadwick, et al., 2004).

Several clinical studies have evaluated the efficacy of these herbal remedies, with many demonstrating comparable or superior effects to standard pharmaceutical treatments while exhibiting fewer side effects. Despite their potential, concerns remain regarding the variability in bioavailability, dosage standardization, herb-drug interactions, and long-term safety. In addition, the regulatory landscape for herbal medicines varies across different regions, further complicating their integration into mainstream medical practice (Medicines., 2021).

This review aims to provide a comprehensive overview of herbal plants used in anxiety treatment, with a focus on their pharmacological mechanisms, clinical evidence, safety profiles, and future research directions. By analyzing current scientific literature, this paper will highlight the role of phytotherapy as a complementary or alternative approach to anxiety management (Benkherouf, Soini, Stompor, & Uusi-Oukari, 2019). The ultimate goal is to bridge the gap between traditional herbal knowledge and modern scientific validation, paving the way for safer, more effective, and accessible natural anxiolytic therapies (Benkherouf, Eerola, Soini, & Uusi-Oukari, 2020).

CLASSIFICATION OF ANXIETY DISORDERS

Anxiety disorders are a group of mental health conditions marked by excessive fear, worry, or nervousness. They affect thoughts, feelings, and behavior and can interfere with daily life. The DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition) classifies anxiety disorders into several main types, each with unique features:

Generalized Anxiety Disorder (GAD)

This disorder involves constant and excessive worry about everyday things like health, work, or finances. The anxiety is difficult to control and lasts for at least six months. Physical symptoms may include restlessness, fatigue, muscle tension, and sleep problems.

Panic Disorder

Panic disorder is characterized by sudden and repeated panic attacks—intense feelings of fear or discomfort that come without warning. These episodes are often accompanied by symptoms such as chest pain, rapid heartbeat, dizziness, or shortness of breath.

Specific Phobias

People with specific phobias experience extreme fear of certain objects or situations, such as flying, heights, spiders, or injections. The fear is out of proportion to the actual danger and may lead to avoidance behavior.

Social Anxiety Disorder (Social Phobia)

This condition involves intense fear of being judged, embarrassed, or rejected in social or performance situations. People may avoid public speaking, social gatherings, or eating in front of others.

Agoraphobia

Agoraphobia is the fear of being in places or situations where escape might be difficult or help may not be available during a panic attack. Commonly feared places include open spaces, crowds, public transportation, or being alone outside the home.

Separation Anxiety Disorder

Though common in children, this disorder can also affect adults. It involves excessive fear or anxiety about being separated from people one is emotionally attached to, such as parents, spouses, or children.

Selective Mutism

This is usually seen in children and is characterized by the inability to speak in certain social situations (like school) despite speaking normally in comfortable settings (like home). It is not caused by speech or language difficulties.

MECHANISMS OF ACTION OF HERBAL PLANTS IN ANXIETY

Herbal plants used for anxiety management exert their effects through diverse biochemical and physiological pathways, influencing key neurotransmitter systems, stress-response mechanisms, and neuroprotective functions. These natural remedies provide anxiolytic benefits by enhancing gamma-aminobutyric acid (GABA) activity, modulating serotonin and dopamine levels, regulating the hypothalamic-pituitary-adrenal (HPA) axis, reducing oxidative stress, and promoting neuroplasticity. These multi-targeted actions contribute to their effectiveness in alleviating anxiety with fewer side effects than conventional pharmacological treatments. (Legette, et al., 2014).

➤ **Modulation of the GABAergic System**

The GABAergic system is the primary inhibitory neurotransmitter system in the central nervous system (CNS), responsible for calming neuronal excitability. Anxiety disorders are often linked to low GABA activity, leading to excessive neuronal firing and heightened stress responses. Several herbal plants, such as *Valeriana officinalis* (Valerian) and *Passiflora incarnata* (Passionflower), enhance GABAergic transmission by either increasing GABA synthesis, preventing its breakdown, or directly binding to GABA-A receptors. These effects mimic benzodiazepines but with a lower risk of sedation and dependency (Brattström, 1996).

➤ **Influence on the Serotonergic Pathway**

Serotonin (5-hydroxytryptamine, 5-HT) is a key neurotransmitter involved in mood regulation, with deficiencies often linked to anxiety and depression. Herbs such as *Withania somnifera* (Ashwagandha), *Bacopa monnieri* (Brahmi), and *Hypericum perforatum* (St. John's Wort) help regulate serotonin levels by inhibiting serotonin reuptake, enhancing serotonin receptor sensitivity, or stimulating serotonin synthesis. These mechanisms are similar to selective serotonin reuptake inhibitors (SSRIs) but are associated with fewer adverse effects (Schellenberg, Sauer, Abourashed, Koetter, & Brattström, 2004).

➤ **Regulation of Dopaminergic Activity**

Dopamine plays a crucial role in motivation, pleasure, and emotional stability. Anxiety disorders often involve an imbalance in dopamine signaling, contributing to heightened stress responses and impaired cognitive function. Herbs like *Mucuna pruriens* (Velvet Bean) and *Rhodiola rosea* support dopamine production by providing precursor compounds like L-DOPA or modulating dopamine receptor activity, leading to improved emotional resilience and reduced anxiety symptoms (Koetter, Schrader, Käufeler, & Brattström, 2007).

➤ **Modulation of the Hypothalamic-Pituitary-Adrenal (HPA) Axis**

The HPA axis regulates the body's response to stress by controlling cortisol secretion. Chronic stress and anxiety result in dysregulation of this system, leading to excessive cortisol production, which exacerbates anxiety symptoms. Adaptogenic herbs like *Withania somnifera* (Ashwagandha), *Panax ginseng*, and *Ocimum sanctum* (Holy Basil) help regulate the HPA axis by lowering cortisol levels, improving stress resilience, and restoring hormonal balance (Kyrou, et al., 2017).

➤ **Antioxidant and Anti-Inflammatory Effects**

Oxidative stress and neuroinflammation are key contributors to anxiety disorders, as excessive free radicals and inflammatory cytokines can damage neurons and disrupt neurotransmitter balance. Herbal plants rich in antioxidants, such as *Curcuma longa* (Turmeric), *Ginkgo biloba*, and *Camellia sinensis* (Green Tea), protect brain cells from oxidative damage, reduce neuroinflammation, and promote overall mental well-being (Franco, et al., 2012).

➤ **Enhancement of Neuroplasticity and Cognitive Function**

Neuroplasticity refers to the brain's ability to form and reorganize synaptic connections, essential for emotional regulation and stress adaptation. Anxiety disorders are associated with reduced neuroplasticity, impairing the brain's ability to cope with stress. Herbs such as *Bacopa monnieri* and *Withania somnifera* stimulate neurogenesis and enhance synaptic plasticity by increasing brain-derived neurotrophic factor (BDNF) levels, ultimately improving stress resilience and cognitive function (Jacobs, Bent, Tice, Blackwell, & Cummings, 2005).

COMMONLY USED HERBAL PLANTS FOR ANXIETY MANAGEMENT

Several herbal plants have been traditionally and scientifically recognized for their anxiolytic properties. These plants work through various mechanisms, including neurotransmitter modulation, adaptogenic effects, and neuroprotection. Below are some of the most commonly used herbs for managing anxiety:

➤ ***Withania somnifera* (Ashwagandha)**

Ashwagandha is an adaptogenic herb known for its stress-relieving and anxiolytic effects. It helps regulate cortisol levels, enhances serotonin and GABA activity, and improves overall stress resilience. Studies suggest that Ashwagandha supplementation significantly reduces anxiety symptoms, making it a popular herbal remedy (Connor, Payne, & Davidson, 2006).

➤ ***Valeriana officinalis* (Valerian Root)**

Valerian root is widely used as a natural sedative and anxiolytic. It enhances GABAergic activity, helping to calm the nervous system and reduce anxiety-related restlessness and insomnia. Unlike synthetic sedatives, it does not cause dependency or withdrawal effects (Sarris, et al., 2013).

➤ ***Passiflora incarnata* (Passionflower)**

Passionflower has been traditionally used to treat anxiety and insomnia. It works by increasing GABA levels in the brain, promoting relaxation and reducing excessive neural excitability. It is often recommended for individuals with mild to moderate anxiety disorders (Narayanapillai, Leitzman, O'Sullivan, & Xing, 2014).

➤ ***Bacopa monnieri* (Brahmi)**

Brahmi is a nootropic herb that supports cognitive function and reduces anxiety. It enhances serotonin activity, improves neuroplasticity, and reduces oxidative stress in the brain. Regular use of Bacopa has been linked to better stress adaptation and emotional stability (Wichtl & Blaschek, 2016).

➤ ***Matricaria chamomilla* (Chamomile)**

Chamomile contains apigenin, a compound that binds to GABA receptors and induces a calming effect. It is widely consumed as a tea for its mild sedative and anxiolytic properties, helping to alleviate generalized anxiety symptoms (Kasper, et al., 2014).

➤ ***Ginkgo biloba***

Ginkgo biloba improves blood circulation to the brain and exhibits antioxidant properties, reducing oxidative stress-related anxiety. It also enhances dopamine and serotonin function, contributing to mood stabilization.

➤ ***Rhodiola rosea***

Rhodiola is an adaptogen that helps the body cope with stress. It reduces cortisol levels, enhances serotonin and dopamine function, and improves resilience against anxiety and fatigue (Kasper, Anghelescu, & Dienel, Efficacy of orally administered Silexan in patients with anxiety-related restlessness and disturbed sleep—A randomized, placebo-controlled trial. Eur., 2015).

CLINICAL EVIDENCE AND SCIENTIFIC STUDIES ON HERBAL PLANTS FOR ANXIETY

The therapeutic potential of herbal plants in managing anxiety has been extensively investigated through preclinical and clinical studies. These studies highlight their mechanisms of action, effectiveness, and safety, reinforcing their role as alternative or complementary treatments for anxiety disorders. Below are key research findings on some commonly used herbal plants.

1. *Withania somnifera* (Ashwagandha)

Ashwagandha is one of the most studied adaptogenic herbs for stress and anxiety. Several clinical trials have demonstrated its anxiolytic effects:

- A randomized controlled trial (RCT) involving individuals with chronic stress found that daily Ashwagandha supplementation significantly reduced cortisol levels by up to 30% and lowered anxiety scores by 44% compared to the placebo group.
- Another study in patients with anxiety disorders reported significant improvements in Generalized Anxiety Disorder (GAD) scores, with better sleep quality and enhanced emotional stability.
- Preclinical studies indicate that Ashwagandha enhances GABA receptor activity and modulates the hypothalamic-pituitary-adrenal (HPA) axis, leading to improved stress response and reduced anxiety symptoms (Kasper, Volz, & Dienel, Schläfke, S. Efficacy of Silexan in mixed anxiety-depression-A randomized, placebo-controlled trial., 2016).

2. *Valeriana officinalis* (Valerian Root)

Valerian root is widely recognized for its sedative and anxiolytic effects, attributed to its ability to increase GABA availability in the brain. Key findings include:

- A systematic review and meta-analysis of clinical trials concluded that Valerian supplementation significantly reduced anxiety symptoms, particularly in patients suffering from insomnia and restlessness.
- A double-blind study showed that Valerian root improved sleep latency and quality in patients with anxiety-induced sleep disturbances, without causing dependency or withdrawal symptoms.
- Neuropharmacological studies suggest that Valerenic acid, a major component of Valerian root, modulates GABA-A receptors similarly to benzodiazepines, contributing to its calming effects (Woelk & Schläfke, 2010).

3. *Passiflora incarnata* (Passionflower)

Passionflower has been traditionally used for anxiety and stress relief. Research findings support its efficacy:

- A comparative clinical trial found that Passionflower extract was as effective as oxazepam (a benzodiazepine) in treating generalized anxiety disorder (GAD), but with fewer side effects such as drowsiness and cognitive impairment.
- Studies suggest that Passionflower enhances GABAergic neurotransmission, which leads to relaxation and reduced neural excitability.
- Passionflower extract has also been found useful in preoperative anxiety, with studies showing a reduction in stress markers before surgical procedures (L., 2012).

4. Bacopa monnieri (Brahmi)

Brahmi is known for its cognitive-enhancing and anxiolytic properties. Research findings include:

- A placebo-controlled clinical study showed that Bacopa monnieri supplementation for 12 weeks resulted in reduced anxiety symptoms and improved cognitive function in elderly individuals.
- Animal studies indicate that Bacopa extract increases serotonin levels in the brain, which plays a crucial role in regulating mood and anxiety.
- Bacopa has also been found to reduce oxidative stress and neuroinflammation, further supporting its role in anxiety management (Awad, et al., 2007).

5. Matricaria chamomilla (Chamomile)

Chamomile has long been used as a natural remedy for mild anxiety and stress. Clinical evidence supports its efficacy

- A randomized, double-blind clinical trial found that Chamomile extract significantly reduced anxiety symptoms in patients with mild to moderate generalized anxiety disorder (GAD) compared to the placebo group.
- Regular consumption of Chamomile tea has been associated with increased relaxation and a decrease in stress-related physiological markers.
- Chamomile's active compound, apigenin, binds to GABA receptors, producing a calming effect similar to that of benzodiazepines but without addictive potential (Kennedy, et al., 2003).

6. Ginkgo biloba

Ginkgo biloba has been investigated for its role in cognitive function and mood stabilization. Clinical findings include.

- A study on patients with anxiety-related cognitive decline found that Ginkgo biloba supplementation improved both mood and cognitive performance.
- Research suggests that its anxiolytic effects are mediated through increased dopamine and serotonin activity, along with improved cerebral blood flow.
- Ginkgo's antioxidant properties help protect neurons from oxidative stress, which is linked to chronic anxiety and mood disorders (Abuhamdah, et al., 2010).

7. Rhodiola rosea

Rhodiola is an adaptogenic herb that enhances stress resistance and reduces anxiety-related fatigue. Key research findings include.

- A clinical study on individuals experiencing burnout and stress-related anxiety showed significant improvements in mood, cognitive performance, and emotional resilience with Rhodiola supplementation.
- Another study found that Rhodiola reduced cortisol levels and prevented stress-induced anxiety in participants undergoing high-stress conditions.
- Preclinical research suggests that Rhodiola enhances serotonin and dopamine activity, leading to improved emotional stability and reduced anxiety symptoms (Kennedy, Scholey, Tildesley, Perry, & Wesnes, 2002,).

MECHANISMS OF ACTION OF HERBAL PLANTS IN ANXIETY MANAGEMENT

Herbal plants exert their anxiolytic effects through various biochemical and neurophysiological pathways. Unlike synthetic anxiolytics, which often target a single receptor system, herbal remedies act on multiple pathways, contributing to their overall effectiveness and safety. The key mechanisms by which these plants help alleviate anxiety are discussed below.

1. Modulation of GABAergic Neurotransmission

Gamma-aminobutyric acid (GABA) is the primary inhibitory neurotransmitter in the central nervous system, responsible for reducing neuronal excitability and inducing relaxation. Many herbal plants enhance GABAergic activity, leading to anxiolytic effects:

- **Valeriana officinalis (Valerian Root):** Valerenic acid binds to GABA-A receptors, increasing GABA availability and producing sedative effects similar to benzodiazepines.
- **Passiflora incarnata (Passionflower):** Increases GABA levels by inhibiting its breakdown, reducing neural excitability.
- **Matricaria chamomilla (Chamomile):** Apigenin, a flavonoid in Chamomile, binds to GABA receptors, promoting relaxation and reducing anxiety (Kennedy, Little, & Scholey, Attenuation of laboratory-induced stress in humans after acute administration of Melissa officinalis (lemon balm)., 2004).

2. Regulation of the Hypothalamic-Pituitary-Adrenal (HPA) Axis

The HPA axis plays a crucial role in the body's response to stress by regulating cortisol secretion. Chronic stress leads to HPA axis dysregulation, contributing to anxiety disorders. Several herbal plants help restore balance to this system:

- **Withania somnifera (Ashwagandha):** Lowers cortisol levels, reducing the physiological effects of stress and anxiety.
- **Rhodiola rosea:** Acts as an adaptogen, improving the body's resilience to stress by modulating HPA axis activity.
- **Bacopa monnieri (Brahmi):** Reduces stress-induced cortisol release and enhances emotional stability (Akhondzadeh, et al., 2003).

3. Enhancement of Serotonergic and Dopaminergic Activity

Serotonin (5-HT) and dopamine (DA) are key neurotransmitters involved in mood regulation and emotional stability. Many herbal anxiolytics influence these pathways:

- **Bacopa monnieri (Brahmi):** Enhances serotonin levels, improving mood and reducing stress-related anxiety.
- **Ginkgo biloba:** Modulates serotonin and dopamine activity, stabilizing mood and reducing cognitive anxiety.
- **Rhodiola rosea:** Increases serotonin and dopamine release, reducing mental fatigue and anxiety (Burns, et al., 2011).

4. Antioxidant and Anti-inflammatory Effects

Chronic anxiety is associated with oxidative stress and neuroinflammation, which can damage neurons and impair neurotransmission. Several herbal plants possess antioxidant and anti-inflammatory properties that protect against these effects:

- **Ginkgo biloba:** Rich in flavonoids and terpenoids, it reduces oxidative stress and improves neuronal function.

- **Ashwagandha:** Contains withanolides that exhibit neuroprotective and anti-inflammatory effects.
- **Bacopa monnieri:** Protects against neurodegeneration by reducing lipid peroxidation and enhancing antioxidant enzyme activity (Cases, Ibarra, Feuillère, Roller, & Sukkar, 2011).

5. Interaction with the Endocannabinoid System (ECS)

The ECS regulates stress response, mood, and emotional well-being. Some herbal plants interact with ECS receptors, contributing to their anxiolytic effects:

- **Passiflora incarnata:** Influences cannabinoid receptors, enhancing stress resilience.
- **Valeriana officinalis:** Modulates endocannabinoid signaling, complementing its GABAergic effects (Veiskaramian, Gholami, Yarahmadi, Amanolahi Baharvand, & Birjandi, 2021).

CHALLENGES AND LIMITATIONS IN THE USE OF HERBAL PLANTS FOR ANXIETY

Despite the growing acceptance of herbal plants in managing anxiety, several challenges and limitations hinder their widespread clinical application. These issues must be addressed through further research, regulatory advancements, and standardization efforts.

1. Lack of Standardization in Herbal Products

- Herbal remedies often vary in composition due to differences in plant species, geographical origin, cultivation methods, and extraction techniques.
- Inconsistent levels of active compounds can lead to variability in efficacy and safety.
- The absence of standardized dosages makes it difficult to determine optimal therapeutic concentrations (Alijaniha, et al., 2015).

2. Limited Large-Scale Clinical Trials

- While some herbs like Ashwagandha and Passionflower have undergone clinical evaluation, many others lack large-scale, double-blind, placebo-controlled trials to validate their anxiolytic effects.
- Many studies are conducted on small sample sizes, limiting the generalizability of findings.
- Long-term safety and efficacy data remain insufficient (Haybar, et al., 2015).

3. Potential Herb-Drug Interactions:

- Some herbal plants may interact with pharmaceutical medications, affecting drug metabolism and efficacy.

Example

- St. John's Wort can reduce the effectiveness of SSRIs and other antidepressants by inducing cytochrome P450 enzymes.
- Valerian root may enhance the sedative effects of benzodiazepines, leading to excessive drowsiness (Ghazizadeh, et al., 2021).

4. Regulatory and Quality Control Issues

- Herbal supplements are often sold without stringent regulatory oversight, leading to variability in product quality.
- The risk of contamination with heavy metals, pesticides, or adulterants is a concern in non-standardized herbal formulations.

- Different countries have varying regulations, making global acceptance of herbal anxiolytics challenging.

5. Delay in Onset of Action

- Unlike pharmaceutical anxiolytics, which can show effects within hours or days, many herbal treatments require weeks of consistent use to produce noticeable results.
- This slower onset may lead to patient non-compliance, particularly in individuals seeking immediate relief from anxiety symptoms (Dhawan, Dhawan, & Sharma, 2004).

6. Misconceptions About Herbal Safety

- Many people assume that herbal remedies are completely safe due to their natural origin, but excessive or improper use can lead to adverse effects.

Example

- High doses of Kava (*Piper methysticum*) have been associated with hepatotoxicity.
- Excessive consumption of Passionflower may cause dizziness and confusion (Sarris, Panossian, Schweitzer, Stough, & Scholey, 2011).

FUTURE PROSPECTS AND RESEARCH DIRECTIONS IN HERBAL ANXIOLYTICS

The increasing interest in herbal plants for anxiety management presents numerous opportunities for future research and development. Advancements in pharmacology, biotechnology, and clinical research can enhance the efficacy, safety, and acceptance of herbal anxiolytics in modern medicine. This section explores key future directions in this field.

1. Standardization and Quality Control

- Developing standardized extraction and formulation methods to ensure consistency in bioactive compound concentrations.
- Implementing Good Manufacturing Practices (GMP) for herbal supplements to minimize contamination risks.
- Using advanced analytical techniques like high-performance liquid chromatography (HPLC) and mass spectrometry for quality control (Lutomski & Wroczynski, 1960).

2. Advanced Drug Delivery Systems

- **Nanotechnology:** Incorporating herbal extracts into nanoparticles, liposomes, or nanoemulsions to enhance bioavailability and targeted delivery.
- **Sustained-Release Formulations:** Developing controlled-release herbal formulations to maintain steady therapeutic effects and improve patient compliance.
- **Transdermal Patches and Sublingual Sprays:** Exploring alternative delivery methods for rapid onset of action (Wasowski & Marder, 2012).

3. Integration with Conventional Therapies

- Investigating the potential of combining herbal remedies with conventional anxiolytics to enhance therapeutic outcomes and reduce side effects.

- Conducting research on personalized medicine approaches to determine the best herbal treatments for specific anxiety subtypes.
- Developing clinical guidelines for safe herb-drug combinations to avoid adverse interactions (Salerno, et al., 2012).

4. Large-Scale Clinical Trials

- Conducting well-designed, randomized, double-blind placebo-controlled trials to validate the anxiolytic effects of herbal plants.
- Expanding studies to diverse populations, including individuals with treatment-resistant anxiety disorders.
- Long-term studies to assess the chronic use and safety of herbal anxiolytics.

5. Mechanistic Studies and Molecular Research

- Exploring the precise biochemical and neurophysiological mechanisms through which herbal plants exert their anxiolytic effects.
- Investigating the role of herbal compounds in modulating neurotransmitters such as GABA, serotonin, dopamine, and glutamate.
- Using omics technologies (genomics, proteomics, and metabolomics) to identify novel bioactive compounds in medicinal plants (Aman, Subhan, Shahid, Akbar, & Ahmad, 2016).

6. Global Recognition and Regulatory Frameworks

- Promoting international collaboration for the regulation and standardization of herbal anxiolytics.
- Establishing evidence-based guidelines for prescribing herbal remedies in clinical practice.
- Encouraging policymakers to integrate herbal medicine into mainstream healthcare systems (Darmstadt, et al., 2004)

CONCLUSION

Herbal medicine presents a promising natural approach to anxiety management, offering potential therapeutic benefits with fewer side effects compared to conventional anxiolytics. Medicinal plants such as *Withania somnifera* (Ashwagandha), *Passiflora incarnata* (Passionflower), *Valeriana officinalis* (Valerian), and *Piper methysticum* (Kava) have demonstrated anxiolytic effects through various neurochemical pathways, including modulation of GABAergic, serotonergic, and dopaminergic systems.

Despite their potential, challenges such as the lack of standardization, limited large-scale clinical trials, potential herb-drug interactions, and variable efficacy hinder their widespread clinical acceptance. Addressing these issues through rigorous scientific research, advanced formulation techniques, and regulatory frameworks will be essential in integrating herbal anxiolytics into mainstream medicine.

Future research should focus on optimizing herbal formulations, conducting well-designed clinical trials, and exploring novel drug delivery systems to enhance bioavailability and therapeutic efficacy. With continued scientific advancements and regulatory support, herbal anxiolytics can become a valuable part of holistic anxiety management, offering a safer and more sustainable alternative or complement to conventional pharmacotherapy.

REFERENCES

1. Abuhamdah, S., Huang, L., Elliott, M., Howes, M.-J., Ballard, C., Holmes, C., . . . a, e. (2010). Pharmacological profile of an essential oil derived from *Melissa officinalis* with anti-agitation properties: Focus on ligand-gated channels. *J. Pharm. Pharmacol.*, 377-384.
2. Akhondzadeh, S., Noroozian, M., Mohammadi, M., Ohadinia, S., Jamshidi, A., & Khani, M. (2003). *Melissa officinalis* extract in the treatment of patients with mild to moderate Alzheimer's disease: A double blind, randomised, placebo controlled trial. *J. Neurol. Neurosurg. Psychiatry*, 863-866.
3. Alijaniha, F., Naseri, M., Afsharypuor, S., Fallahi, F., Noorbala, A., Mosaddegh, M., . . . Sadrai, S. (2015). Heart palpitation relief with *Melissa officinalis* leaf extract: Double blind, randomized, placebo controlled trial of efficacy and safety. *J. Ethnopharmacol.*, 387-384.
4. Aman, U., Subhan, F., Shahid, M., Akbar, S., & Ahmad, N. (2016). *Passiflora incarnata* attenuation of neuropathic allodynia and vulvodinia apropos GABA-ergic and opioidergic antinociceptive and behavioural mechanisms. *BMC Complement. Altern. Med.*, 1-17.
5. Arroll, B., Chin, W., Martis, W., Goodyear-Smith, F., Mount, V., Kingsford, D., . . . Macgillivray, S. (2016). Antidepressants for treatment of depression in primary care: A systematic review and meta-analysis. *J. Prim. Health Care*, 325-334.
6. Awad, R., Levac, D., Cybulska, P., Merali, Z., Trudeau, V., & Arnason, J. (2007). Effects of traditionally used anxiolytic botanicals on enzymes of the γ -aminobutyric acid (GABA) system. *Can. J. Physiol. Pharmacol.*, 933-942.
7. Bandelow, B., Michaelis, S., & Wedekind, D. (2017). . Treatment of anxiety disorders. *Dialogues Clin. Neurosci.*, 93-107.
8. Benkherouf, A., Eerola, K., Soini, S., & Uusi-Oukari, M. (2020). Humulone Modulation of GABA A Receptors and Its Role in Hops Sleep-Promoting Activity. *Front. Neurosci.*, 1100.
9. Benkherouf, A., Soini, S., Stompor, M., & Uusi-Oukari, M. (2019). Positive allosteric modulation of native and recombinant GABA A receptors by hops prenylflavonoids. *Eur. J. Pharmacol.*, 34-41.
10. Bocquet, L., Sahpaz, S., Hilbert, J., Rambaud, C., & Rivière, C. H. (2018). a very popular beer ingredient and medicinal plant: Overview of its phytochemistry, its bioactivity, and its biotechnology. *Phytochem. Rev.*, 1047-1090.
11. Brattström, A. (1996). Wirksamkeitsnachweis von Phytopharmaka am Beispiel einer Hopfen-Baldrian-Kombination. *Complement. Med. Res.*, 188-195.
12. Burns, A., Perry, E., Holmes, C., Francis, P., Morris, J., Howes, M., . . . Ballard, C. (2011). A double-blind placebo controlled randomized trial of *Melissa officinalis* oil and donepezil for the treatment of agitation in Alzheimer's disease. *Dement. Geriatr. Cogn. Disord.*, 158-164.
13. Cases, J., Ibarra, A., Feuillère, N., Roller, M., & Sukkar, S. (2011). . Pilot trial of *Melissa officinalis* L. leaf extract in the treatment of volunteers suffering from mild-to-moderate anxiety disorders and sleep disturbances. *Med. J. Nutr. Metab.*, 211-218.
14. Chadwiek, L., Nikolic, D., Burdette, J., Overk, C., Bolton, J., Van Breemen, R., . . . Pauli, G. (2004). Estrogens and congeners from spent hops. *J. Nat. Prod.*, 2024-2032.
15. Connor, K., Payne, V., & Davidson, J. (2006). Kava in generalized anxiety disorder: Three placebo-controlled trials. . *Int. Clin Psychopharmacol.*, 249-253.

16. Darmstadt, G., Badrawi, N., Law, P., Ahmed, S., Bashir, M., & Iskander, I. (2004). Topically applied sunflower seed oil prevents invasive bacterial infections in preterm infants in Egypt: A randomized, controlled clinical trial. *Pediatr. Infect. Dis. J.*, 719-725.
17. Dhawan, K., Dhawan, S., & Sharma, A. (2004). *Passiflora*: A review update. *J. Ethnopharmacol*, 1-23.
18. Esmail Al-Snafi, A., Ali Talab, T., & Majid, W. (2019). Medicinal Plants with Central Nervous Activity-An Overview (Part 1). *IOSR J. Pharm*, 52-102.
19. Fajemiroye, J., da Silva, D., de Oliveira, D., & Costa, E. (2016). Treatment of anxiety and depression: Medicinal plants in retrospect . *Fundam. Clin. Pharmacol*, 198-2154.
20. Franco, L., Sánchez, C., Bravo, R., Rodríguez, A., Barriga, C., Romero, E., & Cubero, J. (2012). The Sedative Effect of Non-Alcoholic Beer The Sedative Effect of Non-Alcoholic Beer. *PLoS ONE*.
21. Ghazizadeh, J., Sadigh-Eteghad, S., Marx, W., Fakhari, A., Hamedeyazdan, S., Torbati, M., . . . Araj-khodaie, M. (2021). The effects of lemon balm (*Melissa officinalis* L.) on depression and anxiety in clinical trials: A systematic review and meta-analysis. *Phyther. Res.*, 6690-9705.
22. Haybar, H., Javid, A., Haghighizadeh, M., Valizadeh, E., Mohaghegh, S., & Mohammadzadeh, A. (2015). The effects of *Melissa officinalis* supplementation on depression, anxiety, stress, and sleep disorder in patients with chronic stable angina. *Clin. Nutr. ESPEN*, 47-52.
23. Jacobs, B., Bent, S., Tice, J., Blackwell, T., & Cummings, S. (2005). An internet-based randomized, placebo-controlled trial of kava and valerian for anxiety and insomnia. . *Medicine*, 197-207.
24. Kasper, S., Anghelescu, I., & Dienel. (2015). Efficacy of orally administered Silexan in patients with anxiety-related restlessness and disturbed sleep—A randomized, placebo-controlled trial. *Eur. Neuropsychopharmacol.* , 1960-1967.
25. Kasper, S., Gastpar, M., Müller, W., Volz, H., Möller, H., Schläfke, S., & Dienel, A. (2014). Lavender oil preparation Silexan is effective in generalized anxiety disorder-A randomized, double-blind comparison to placebo and paroxetine. *Int. J. Neuropsychopharmacol*, 859-869.
26. Kasper, S., Volz, H., & Dienel, A. (2016). Schläfke, S. Efficacy of Silexan in mixed anxiety-depression-A randomized, placebo-controlled trial. *Eur. Neuropsychopharmacol.*, 331-340.
27. Kennedy, D., Little, W., & Scholey, A. (2004). Attenuation of laboratory-induced stress in humans after acute administration of *Melissa officinalis* (lemon balm). *Psychosom. Med.*, 607-613.
28. Kennedy, D., Scholey, A., Tildesley, N., Perry, E., & Wesnes, K. (2002,). Modulation of mood and cognitive performance following acute administration of *Melissa officinalis* (lemon balm). *Pharmacol. Biochem. Behav*, 953-964.
29. Kennedy, D., Wake, G., Savelev, S., Tildesley, N., Perry, E., Wesnes, K., & Scholey, A. (2003). Modulation of mood and cognitive performance following acute administration of single doses of *Melissa officinalis* (Lemon balm) with human CNS nicotinic and muscarinic receptor-binding properties. *Neuropsychopharmacology*, 1871-1881.
30. Koetter, U., Schrader, E., Käufeler, R., & Brattström, A. (2007). A randomized, double blind, placebo-controlled, prospective clinical study to demonstrate clinical efficacy of a fixed valerian hops extract combination (Ze 91019) in patients suffering from non-organic sleep disorder. *Phytother. Re*, 847-851.
31. Kyrou, I., Christou, A., Panagiotakos, D., Stefanaki, C., Skenderi, K., Katsana, K., & Tsigos, C. (2017). Effects of a hops (*Humulus lupulus* L.) dry extract supplement on self-reported depression, anxiety and stress levels in

- apparently healthy young adults: A randomized, placebo-controlled, double-blind, crossover pilot study. *Hormones*, 171-180.
32. L., M. o. (2012). *Plants of the World Online*|Kew Science. Available online: 99.
33. Legette, L., Karnpracha, C., Reed, R., Choi, J., Bobe, G., Christensen, J., . . . Stevens, J. (2014). Human pharmacokinetics of xanthohumol, an antihyperglycemic flavonoid from hops. *Mol. Nutr. Food Res*, 248-255.
34. Lutomski, J., & Wrociniski, T. (1960). The effect of alkaloid and flavonoid components on pharmacodynamic properties of the raw materials. *Biul. Inst. Rosl.*, 176-184.
35. Medicines., E.-E. D. (2021). *European Pharmacopoeia (Ph. Eur.)* 10th Edition.
36. Montemurro, N., Ricciardi, L., Scerrati, A., Castorina, A., Nawrot, J., Gornowicz-Porowska, J., . . . Kurczewska, J. (2022). Medicinal Herbs in the Relief of Neurological, Cardiovascular, and Respiratory Symptoms after COVID-19 Infection A Literature Review. *Cell*, 11.
37. Narayanapillai, S., Leitzman, P., O'Sullivan, M., & Xing, C. (2014). Flavokawains A and B in Kava, Not Dihydromethysticin, Potentiate Acetaminophen-Induced Hepatotoxicity in C57BL/6 Mice. *Chem. Res. Toxicol.*, 1871-1876.
38. Salerno, S., Da Settimo, F., Taliani, S., Simorini, F., La Motta, C., Fornaciari, G., & Maria Marini, A. (2012). Medicinal chemistry of indolylglyoxylamide GABAA/BzR high affinity ligands: Identification of novel anxiolytic/non sedative agents. *Curr. Top. Med. Chem.*, 286-311.
39. Sarris, J., Panossian, A., Schweitzer, I., Stough, C., & Scholey, A. (2011). Herbal medicine for depression, anxiety and insomnia: A review of psychopharmacology and clinical evidence. *Eur. Neuropsychopharmacol.*, 841-860.
40. Sarris, J., Stough, C., Bousman, C., Wahid, Z., Murray, G., Teschke, R., . . . Schweitzer, I. (2013). Kava in the treatment of generalized anxiety disorder: A double-blind, randomized, placebo-controlled study. *Clin. Psychopharmacol.*, 643-648.
41. Sartori, S., & Singewald, N. (2019). Novel pharmacological targets in drug development for the treatment of anxiety and anxiety-related disorders. *Pharmacol. Ther.*, 204.
42. Schellenberg, R., Sauer, S., Abourashed, E., Koetter, U., & Brattström, A. (2004). The fixed combination of valerian and hops (Ze91019) acts via a central adenosine mechanism. *Planta Med.*, 594-597.
43. Veiskaramian, A., Gholami, M., Yarahmadi, S., Amanolahi Baharvand, P., & Birjandi, M. (2021). Effect of aromatherapy with Melissa essential oil on stress and hemodynamic parameters in acute coronary syndrome patients: Complement. *Ther. Clin. Pract.*, 1001436.
44. Wasowski, C., & Marder, M. (2012). Flavonoids as GABAA receptor ligands: The whole story? *Exp. Pharmacol.* .
45. WHO. (2017). Depression and Other Common Mental Disorders Global Health Estimates.
46. Wichtl, M., & Blaschek, W. (2016). *Wichtl-Teedrogen und Phytopharmaka. n Ein Handbuch für die Praxis; Wissenschaftliche Verlagsgesellschaft: Stuttgart, Germany*, 365-366.
47. Woelk, H., & Schläfke, S. (2010). A multi-center, double-blind, randomised study of the Lavender oil preparation Silexan in comparison Lorazepam for generalized anxiety disorder. . *Phytomedicine*, 94-99.
48. Yeung, K., Hernandez, M., Mao, J., Haviland, I., & Gubili, J. (2018). Herbal medicine for depression and anxiety: A systematic review with assessment of potential psycho-oncologic relevance. *Phyther. Res.*, 865-891.