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Review Article

Anxiolytic Activity of Several Herbs

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Anxiety disorders are among the most prevalent psychiatric conditions globally, often managed with pharmacological agents such as benzodiazepines and selective serotonin reuptake inhibitors (SSRIs). However, these conventional therapies are frequently associated with side effects, dependency, and tolerance, prompting growing interest in safer, plant-based alternatives. Herbal medicines have been used for centuries in various traditional systems and are now being scientifically explored for their anxiolytic potential. This review aims to highlight the anti-anxiety activity of selected herbal drugs, including Withania somnifera (Ashwagandha), Bacopa monnieri (Brahmi), Nardostachys jatamansi (Jatamansi), Valeriana officinalis (Valerian), Matricaria chamomilla (Chamomile), and Passiflora incarnata (Passionflower), among others. The anxiolytic effects of these herbs are attributed to their modulation of key neurotransmitter systems, particularly gamma-aminobutyric acid (GABA), serotonin, and dopamine pathways, along with their antioxidant and neuroprotective properties. Preclinical models such as the elevated plus maze and light/dark box tests, as well as clinical trials, support the efficacy of these herbal agents. While evidence is promising, issues such as standardization, herb-drug interactions, and regulatory oversight remain significant challenges. This review underscores the need for further well-designed clinical studies to validate the safety, efficacy, and mechanisms of herbal drugs in the treatment of anxiety disorders.

Keywords: Anxiety disorders, Anxiolytic activity, Herbal medicine, Phytochemicals, GABA modulation, Ashwagandha, Valerian.

INTRODUCTION

Anxiety disorders represent one of the most widespread mental health challenges, affecting millions of individuals globally and significantly impairing quality of life. According to the World Health Organization, nearly 301 million people worldwide were living with an anxiety disorder in 2019, including around 58 million children and adolescents, making them the most common mental health disorders across populations [1]. Beyond individual suffering, anxiety disorders are associated with increased risk of comorbid depression, substance abuse, cardiovascular disease, and reduced workplace productivity, contributing to a substantial socioeconomic burden [2]. Currently available pharmacological treatments, including benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), and serotonin–norepinephrine reuptake inhibitors (SNRIs), provide effective symptom relief but are not without limitations. Benzodiazepines are widely prescribed due to their rapid anxiolytic effect; however, they are associated with tolerance, dependence, cognitive impairment, and withdrawal syndromes, making them unsuitable for long-term management. On the other hand, SSRIs and SNRIs are better suited for chronic use but present challenges such as delayed onset of action, gastrointestinal side effects, insomnia, and sexual dysfunction, which frequently reduce patient adherence [3]. These limitations underscore the need for safer and more tolerable alternatives, especially for patients requiring long-term therapy. In recent decades, herbal medicines have attracted increasing attention as complementary or alternative approaches for managing anxiety. Many botanicals have been used in Ayurveda, Traditional Chinese Medicine, and Western herbal practices for centuries to reduce stress,

improve sleep, and stabilize mood. Modern pharmacological investigations reveal that herbal drugs may exert anxiolytic effects by enhancing GABAergic activity, modulating serotonergic and dopaminergic signaling, regulating the hypothalamic–pituitary–adrenal (HPA) axis, and reducing oxidative stress [4]. These multimodal mechanisms may offer therapeutic benefits with fewer adverse effects compared to conventional anxiolytics. Several herbal drugs have shown promise in both preclinical and clinical settings. For example, *Withania somnifera* (Ashwagandha) has demonstrated significant reductions in stress and anxiety scores in randomized controlled trials, likely due to its adaptogenic effects and cortisol-lowering properties. *Matricaria chamomilla* (Chamomile) has been studied in generalized anxiety disorder with encouraging results, while *Passiflora incarnata* (Passionflower) and *Valeriana officinalis* (Valerian) exhibit GABA-mediated anxiolytic activity. Conversely, *Piper methysticum* (Kava) shows proven efficacy but its clinical use is controversial due to reports of hepatotoxicity [5]. Despite promising evidence, challenges such as lack of standardization, variability in phytochemical composition, herb–drug interactions, and limited large-scale clinical trials hinder the integration of herbal drugs into mainstream therapy. This review aims to explore the anxiolytic potential of herbal medicines, summarizing their mechanisms of action, preclinical and clinical evidence, safety profile, and future research directions.

2. Pathophysiology of Anxiety Disorders

The pathophysiology of anxiety disorders is **multifactorial**, involving complex interactions among neurotransmitter systems, stress response pathways, and oxidative mechanisms. Understanding these neurobiological substrates is critical for identifying therapeutic targets of herbal anxiolytics.

1. Neurotransmitter Dysregulation

- **GABAergic system**: Reduced gamma-aminobutyric acid (GABA) activity contributes to neuronal hyperexcitability and heightened anxiety. Several herbal drugs such as *Valeriana officinalis* and *Passiflora incarnata* are reported to enhance GABAergic transmission [6].
- **Serotonergic system**: Altered serotonin (5-HT) signaling, particularly at 5-HT1A receptors, has been strongly linked to anxiety disorders. *Bacopa monnieri* and *Hypericum perforatum* are suggested to influence serotonergic modulation [6].
- **Noradrenergic and dopaminergic systems**: Dysregulated noradrenaline from the locus coeruleus and altered dopamine pathways contribute to hypervigilance and fear responses. Adaptogenic herbs like *Withania somnifera* may restore this balance [6].

2. Hypothalamic–Pituitary–Adrenal (HPA) Axis Dysfunction

- Chronic stress leads to **hyperactivity of the HPA axis**, causing elevated cortisol secretion and impaired feedback inhibition, thereby perpetuating anxiety symptoms.
- Dysregulated cortisol signaling is a hallmark of generalized anxiety and related disorders [7].
- Herbal adaptogens such as *Withania somnifera* demonstrate cortisol-lowering effects, highlighting their therapeutic potential.

3. Neuroinflammation and Oxidative Stress

- Anxiety disorders are associated with increased **oxidative stress** and elevated pro-inflammatory cytokines, which impair neuronal signaling.
- Oxidative damage affects hippocampal and amygdala function, brain regions central to fear and anxiety processing [8].
- Herbal agents like *Bacopa monnieri* and *Nardostachys jatamansi*, rich in antioxidants, may counteract these effects.

4. Structural and Functional Brain Abnormalities

- Neuroimaging studies indicate **hyperactivity in the amygdala** and reduced top-down regulation by the **prefrontal cortex**, contributing to excessive worry and fear responses [6].
- Altered connectivity within limbic circuits sustains chronic anxiety symptoms. Herbal drugs with neurotrophic and neuroprotective effects may indirectly modulate these networks.

3. Mechanisms of Action of Herbal Anxiolytics

3.1 GABAergic Modulation (9 – 12)

Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the central nervous system. Reduced GABA activity is strongly linked with anxiety disorders, as low inhibition leads to excessive neuronal excitability and heightened stress responses.

- Several herbs (e.g., **Valerian, Passionflower, Kava**) contain phytochemicals that **enhance GABAergic transmission** by binding to GABAA_AA receptors, increasing chloride ion influx, and producing calming effects similar to benzodiazepines.
- Unlike synthetic benzodiazepines, these herbal agents often exert gentler effects and may have fewer issues with dependence and tolerance.

3.2 Serotonergic Modulation

The serotonin (5-HT) system is another major regulator of mood and anxiety. Dysregulation of serotonin pathways, particularly **5-HT1A_1A1A** and **5-HT2A_2A2A** receptors, has been implicated in generalized anxiety disorder, social anxiety, and panic disorder.

- Herbal medicines like **Ashwagandha and Chamomile** have been shown in preclinical and clinical studies to **modulate serotonergic transmission**, either by acting as partial agonists on serotonin receptors or enhancing serotonin availability.
- This mechanism is somewhat similar to SSRIs but tends to involve **multiple receptor sites simultaneously**, providing a more balanced effect.

3.3 Dopaminergic and Adrenergic Pathways

Dopamine and norepinephrine are excitatory neurotransmitters that regulate arousal, motivation, and stress responses. Overactivation of these pathways is linked to restlessness, hypervigilance, and anxiety.

- Herbal extracts (e.g., **Brahmi and Jatamansi**) can **modulate dopaminergic and adrenergic signaling**, helping to restore equilibrium between excitatory and inhibitory neurotransmitters.
- By reducing excessive catecholamine activity, these herbs promote relaxation, reduce palpitations, and alleviate anxiety-related physical symptoms.

3.4 Cortisol Suppression and HPA Axis Regulation

The **hypothalamic–pituitary–adrenal (HPA) axis** is central to the body's stress response. Chronic stress leads to **excessive cortisol release**, which is associated with anxiety, sleep disturbances, and impaired cognition.

- Adaptogenic herbs like **Ashwagandha** and **Rhodiola** reduce cortisol levels and normalize HPA axis activity.
- This **neuroendocrine regulation** helps the body adapt to stress more effectively, preventing the vicious cycle of chronic anxiety.

3.5 Antioxidant and Neuroprotective Activity

Oxidative stress and neuroinflammation are increasingly recognized as important contributors to anxiety disorders. Reactive oxygen species (ROS) can damage neurons, impair neurotransmitter function, and disrupt neural circuits involved in emotional regulation.

- Herbs such as Brahmi, Chamomile, and Jatamansi contain flavonoids, saponins, and other phytochemicals with strong antioxidant and anti-inflammatory properties.
- These compounds help protect neurons from oxidative damage, support mitochondrial function, and promote neurogenesis, which may explain the long-term benefits of herbal treatments in anxiety.

Mechanism	Example Herbs	Key Action
GABAergic modulation	Valerian, Kava, Passionflower	Enhance inhibitory neurotransmission, benzodiazepine-like calming effect
Serotonergic modulation	Ashwagandha, Chamomile	Act on 5-HT1A_1A/5-HT2A_2A receptors, balance serotonin signaling
Dopaminergic/Adrenergic modulation	Brahmi, Jatamansi	Normalize excitatory signals, reduce restlessness
Cortisol suppression (HPA axis)	Ashwagandha, Rhodiola	Lower cortisol, improve stress resilience
Antioxidant & neuroprotective	Brahmi, Chamomile, Jatamansi	Reduce oxidative stress, protect neurons, promote neurogenesis

4. Major Herbal Drugs with Anxiolytic Potential

4.1 Ashwagandha (*Withania somnifera*)

Ashwagandha, commonly known as Indian ginseng or winter cherry, is a well-known adaptogenic herb in Ayurveda. It helps the body cope with stress and anxiety by **reducing cortisol levels** and normalizing hypothalamic–pituitary–adrenal (HPA) axis function. Preclinical studies show that Ashwagandha enhances **GABAergic signaling** and also influences **serotonin pathways**, leading to calming effects. Clinical trials suggest it can reduce stress, improve sleep, and lower anxiety scores in generalized anxiety disorder patients (13,14).

4.2 Brahmi (*Bacopa monnieri*)

Brahmi is a traditional Ayurvedic herb used for cognitive enhancement and anxiety. Its active compounds, **bacosides**, possess **antioxidant and neuroprotective properties**. Experimental studies reveal that Brahmi modulates **serotonin and dopamine levels**, reduces oxidative stress, and helps normalize stress-induced changes in neurotransmitters (15). Human studies suggest improved memory, attention, and reduced anxiety symptoms, making it both a nootropic and anxiolytic herb.

4.3 Jatamansi (*Nardostachys jatamansi*)

Jatamansi, a Himalayan herb, has been traditionally used as a tranquilizer and sleep aid. Animal studies show that it **enhances GABA and serotonin activity**, while also exerting strong **antioxidant effects** that protect neurons from stress-related damage. Its anxiolytic effect is believed to be similar to mild benzodiazepines, but with fewer side effects. It has also shown potential in reducing **neuroinflammation** linked to anxiety disorders (16).

4.4 Valerian (*Valeriana officinalis*)

Valerian root is widely used in Western herbal medicine for insomnia and anxiety. Its phytochemicals, such as **valerenic acid**, act on **GABAA_AA receptors**, increasing inhibitory neurotransmission. Valerian is often compared to benzodiazepines in mechanism but produces milder sedation and has less dependence risk. Clinical studies show improvements in **sleep quality and anxiety reduction**, particularly in generalized anxiety and premenstrual syndrome (17).

4.5 Chamomile (*Matricaria chamomilla*)

Chamomile is one of the most commonly used medicinal herbs for relaxation. Its flavonoid **apigenin** binds to **benzodiazepine receptors** in the brain, producing a mild sedative effect. Chamomile also has **anti-inflammatory and antioxidant properties**, which may contribute to its anxiolytic action. Clinical evidence suggests that chamomile extracts can reduce symptoms in patients with generalized anxiety disorder and improve sleep quality (14,17).

4.6 Passionflower (*Passiflora incarnata*)

Passionflower is traditionally used in Native American and European medicine as a calming agent. Its alkaloids and flavonoids enhance **GABA activity**, leading to anxiolytic and sedative effects. Studies suggest passionflower may reduce restlessness, improve sleep, and decrease physiological symptoms of anxiety such as palpitations. Some trials have even compared passionflower favorably with **oxazepam** in generalized anxiety disorder patients (13,18).

4.7 Kava (*Piper methysticum*)

Kava, native to the South Pacific, is one of the most well-studied herbal anxiolytics. Its active compounds, **kavalactones**, modulate **GABAergic and dopaminergic pathways**, producing relaxation without significant cognitive impairment. Clinical trials demonstrate significant reductions in anxiety symptoms, making it one of the best-supported herbal remedies. However, long-term or excessive use has been linked to **hepatotoxicity**, which limits its widespread clinical acceptance (14,18).

Herb	Key Active Compounds	Mechanism	Evidence Strength	Safety Notes
Ashwagandha	Withanolides	Cortisol suppression, GABA & serotonin modulation	Strong (clinical + preclinical)	Safe, mild GI upset
Brahmi	Bacosides	Antioxidant, serotonin & dopamine modulation	Moderate	Safe, mild GI effects
Jatamansi	Jatamansone, sesquiterpenes	GABA & serotonin enhancement, antioxidant	Moderate (mostly preclinical)	Safe, limited human trials
Valerian	Valerenic acid	GABAA_A receptor modulation	Strong (clinical evidence)	Safe, may cause mild drowsiness
Chamomile	Apigenin	Benzodiazepine receptor binding, antioxidant	Strong (clinical trials)	Safe, rare allergy
Passionflower	Flavonoids, alkaloids	GABAergic modulation	Moderate (some RCTs)	Safe, mild dizziness
Kava	Kavalactones	GABA & dopamine modulation	Strong (multiple RCTs)	Hepatotoxicity risk

5. Experimental Methods to Assess Anxiolytic Activity in Mice

Animal models are widely used to evaluate the anxiolytic potential of herbal and synthetic drugs. These methods allow researchers to assess **behavioral, physiological, and biochemical responses** that mimic human anxiety. Below are the most common tests applied in preclinical studies.

5.1 Elevated Plus Maze (EPM) Test

The EPM is one of the most widely used models for anxiety. It consists of two open arms and two closed arms elevated above the floor. Normally, mice avoid open arms due to fear of open spaces. Anxiolytic drugs increase the time spent and number of entries into the open arms, whereas anxiogenic agents reduce these measures (19). The test is highly sensitive to benzodiazepines and GABAergic compounds, making it useful for herbal studies such as Ashwagandha and Valerian.

5.2 Light/Dark Box Test

This test is based on rodents' natural aversion to brightly lit areas. The apparatus contains two compartments: one brightly lit and one dark. **Anxiolytic agents increase the time spent in the light box** and the number of transitions between compartments, suggesting reduced anxiety (20). Herbal extracts like chamomile and passionflower have been tested using this model.

5.3 Open Field Test (OFT)

The OFT measures both locomotor activity and anxiety. Mice are placed in a large open arena, and their movements are recorded. **Increased time in the central zone indicates reduced anxiety**, as mice typically prefer staying near walls (thigmotaxis). In addition, locomotion and grooming behavior provide insights into drug-induced sedation versus anxiolysis (21).

5.4 Hole Board Test

This test assesses exploratory behavior by counting the number of times a mouse dips its head into holes in a floor board. **Increased head-dipping is interpreted as an anxiolytic effect**, while reduced activity may indicate sedation or high anxiety. The hole board is especially useful for distinguishing

between **sedative and anxiolytic actions** of herbal drugs (22).

5.5 Vogel Conflict Test

This is a **punished drinking test** where thirsty mice are given water but punished with mild shocks for licks. Anxiolytic drugs, such as benzodiazepines, increase the number of punished responses, showing reduced anxiety. It is considered a more **pharmacologically specific model**, though technically demanding compared to maze-based tests (23).

5.6 Social Interaction Test

This test measures the amount of time two unfamiliar mice spend interacting in a neutral arena. Normally, stress and anxiety reduce social behavior. **Anxiolytic drugs increase the duration of social interaction**, whereas anxiogenic drugs reduce it. This test is particularly relevant for herbal drugs that modulate serotonin and dopamine pathways, like Brahmi and Kava (20).

5.7 Biochemical Markers (Neurotransmitters and Stress Hormones)

In addition to behavioral models, biochemical assays are used to confirm anxiolytic mechanisms. Common markers include:

- **GABA and glutamate levels** → reflect excitatory/inhibitory balance.
- **Serotonin (5-HT) and dopamine levels** → key in mood regulation.
- **Cortisol (corticosterone in rodents)** → indicates stress response via the HPA axis.
- **Oxidative stress markers** (lipid peroxidation, antioxidant enzymes) → show neuroprotective effects of herbal drugs (21,22).

These biomarkers strengthen the link between **observed behavior** and **neurochemical mechanisms**.

Test	Principle	Anxiolytic Effect Observed	Key Usefulness
Elevated Plus Maze	Open vs closed arm exploration	↑ Open arm time/entries	Gold standard, sensitive to GABAergic drugs
Light/Dark Box	Bright vs dark compartment	↑ Time in light area	Simple, reliable for herbal extracts
Open Field Test	Center vs periphery movement	↑ Central zone activity	Distinguishes anxiolysis vs sedation
Hole Board	Head-dipping behavior	↑ Head-dips	Exploratory drive, separates sedation/anxiolysis
Vogel Conflict Test	Punished drinking	↑ Licks under punishment	Highly specific but complex
Social Interaction	Interaction between mice	↑ Interaction duration	Relevant for serotonergic drugs
Biochemical Markers	Neurotransmitters, hormones, oxidative stress	Normalized neurotransmitter & cortisol levels	Confirms mechanism of action

6. Summary of Preclinical and Clinical Evidence

6.1 Key findings from animal models

Animal studies using tests like the **elevated plus maze, light–dark box, and open field test** consistently show that herbal extracts (e.g., ashwagandha, chamomile, kava, valerian) increase exploratory behavior and reduce avoidance. These effects suggest an **anxiolytic action**, often linked to **GABAergic** and **serotonergic** pathways. However, results sometimes differ between studies due to **strain differences, test conditions, and extract variability**. Overall, preclinical evidence provides a strong foundation but requires careful interpretation before clinical translation (24).

6.2 Evidence from randomized controlled trials (RCTs)

- **Lavender oil (Silexan®):** Several well-designed RCTs show significant improvement in **Hamilton Anxiety Rating Scale (HAM-A)** scores, suggesting lavender oil may be comparable to low-dose lorazepam but with fewer side effects (25).

- **Chamomile:** Trials in generalized anxiety disorder (GAD) show **modest reductions in anxiety symptoms**, with sustained benefits in longer follow-ups (26).

- **Ashwagandha:** Meta-analyses of RCTs report **improvements in anxiety and stress**, with additional benefits in lowering cortisol (27).

- **Kava:** Early trials suggest effectiveness, but safety concerns about **hepatotoxicity** have limited its use (28).

- **Valerian & Passionflower:** Evidence is **less consistent**, with some small studies showing benefit, but larger trials are lacking.

6.3 Meta-analyses and systematic reviews

Systematic reviews highlight **lavender, chamomile, ashwagandha, and kava** as the most promising. Lavender and chamomile show consistent improvements across multiple studies, while ashwagandha shows potential but still requires larger trials. Kava demonstrates effectiveness but remains controversial due to safety warnings (25–28).

6.4 Limitations in current studies

1. **Small sample sizes** – many RCTs include fewer than 100 patients, reducing generalizability.

2. **Short durations** – trials typically last 6–8 weeks, so long-term safety remains unclear.

3. **Variability in preparations** – differences in plant species, extraction methods, and doses reduce consistency.

4. **Safety concerns** – kava is the best example, where reports of liver toxicity have restricted its approval in many regions.

7. Safety Profile and Limitations

Herbal therapies are often perceived as "safe because natural," but they carry real risks and limitations that students and clinicians must understand. The main concerns are herb–drug interactions, variability in preparations, specific toxicity signals (notably kava), and the relative scarcity of large, long-duration randomized trials.

7.1 Herb–drug interactions

Herbs can interact with conventional medicines by two main routes: pharmacodynami**c** and **pharmacokinetic** interactions. Pharmacodynamic interactions occur when an herb's effects add to or oppose a drug's effects — for example, herbs with sedative/GABAergic activity (valerian, passionflower, kava) can increase central nervous system (CNS) depression when taken with benzodiazepines, opioids, sedating antidepressants, or alcohol. This additive sedation raises the risk of excessive drowsiness, impaired coordination, and respiratory depression in extreme cases. (29) Pharmacokinetic interactions alter drug absorption, metabolism or excretion. Several botanicals can affect cytochrome P450 enzymes or transporters and thereby change blood levels of antidepressants, antipsychotics, anticoagulants, and other narrow-therapeutic-**index drugs**. For example, clinically important interactions with anticoagulants (bleeding risk) have been reported with some herbal supplements; therefore, clinicians should always ask patients about supplement use and review possible interactions before starting or changing psychotropic medications (30–32).

Practical points: Always obtain a complete list of herbs/supplements during medication reconciliation, counsel patients about additive sedation, and consider closer monitoring or temporary withholding of herbal products when initiating or changing psychotropic therapy (30–32).

7.2 Variability in herbal preparations and standardization issues

A major limitation in both research and clinical use is **product heterogeneity**. The therapeutic constituents of a plant vary with species, chemotype, plant part (root, leaf, flower), cultivation conditions, harvest time, and extraction method (water vs alcohol,

standardized vs whole extract). Trials that report benefits typically use standardized extracts (i.e., preparations specified for marker compounds such as kavalactone percentage for kava or linalool/linalyl acetate for lavender), which improves reproducibility. However, many over-the-counter products are not standardized or are poorly labeled; two products sold under the same common name may contain very different active compound profiles. This variability undermines trial comparability and complicates dosing recommendations: a positive RCT using one standardized extract cannot be assumed to apply to a different, nonstandard product. Reporting guidelines (e.g., CONSORT-Herbal) and regulatory quality standards aim to improve transparency and batch-to-batch consistency, but clinical consumers should still prefer products with clear standardization data and certificates of analysis (30,32).

Practical points: Use products with explicit standardization to a known active marker and buy from reputable manufacturers; when reading trials, check the exact extract and dose used before extrapolating results to other preparations (30,32).

7.3 Toxicity concerns — the example of kava hepatotoxicity

Kava is a well-documented case showing that plant-based remedies can have serious adverse effects. Multiple randomized trials and meta-analyses have shown that certain kava extracts can reduce anxiety symptoms; however, post-marketing reports linked kava use to severe liver injury, including acute hepatitis and, rarely, liver failure. These safety signals prompted regulatory advisories in several countries and restricted use of some kava products. The exact mechanism for hepatotoxicity appears multifactorial (possible roles for extract type, concomitant drugs, or idiosyncratic reactions), and the risk has led many clinicians to avoid kava in routine practice despite its anxiolytic efficacy (33). Other herbs have less dramatic but clinically important adverse profiles: valerian can cause daytime drowsiness and interact with sedatives; chamomile may trigger allergic reactions in people sensitive to the Asteraceae family; and rare hepatic or thyroid effects have been reported with some ashwagandha products in case reports. Overall, serious toxicity is uncommon but real and sometimes unpredictable, particularly when herbs are combined or used at high doses (31–33).

Practical points: Screen for liver disease and hepatotoxic medication use before recommending kava; advise patients to stop the herb and seek medical attention if they develop jaundice, dark urine, or abdominal pain. For other herbs, counsel on sedation risk and allergy history (31–33).

7.4 Lack of large-scale clinical trials and long-term safety data

Most RCTs of herbal anxiolytics are small (often <100 participants) and short (6–12 **weeks)**. Such designs can detect short-term symptom changes but are underpowered to find uncommon adverse events or to inform long-term efficacy, relapse prevention, or comparative effectiveness versus standard pharmacotherapy. Heterogeneity in outcome measures, diagnostic criteria (GAD vs subthreshold anxiety), and product specifications further reduces the generalizability of pooled data. Systematic reviewers therefore repeatedly call for **larger, longer, well-designed trials** using standardized extracts, clear dosing, and pre-specified safety monitoring to define the risk–benefit profile more precisely (30–32).

Practical points: Treat current evidence as provisional for long-term use; use herbs as adjuncts rather than replacements for evidence-based treatments in severe anxiety, and advocate for post-marketing surveillance and registry data to capture rare harms.

FUTURE PERSPECTIVES

Although herbal medicines show promising results in managing anxiety disorders, several scientific and clinical gaps remain. Addressing these will be crucial for their safe and effective integration into modern healthcare.

8.1 Need for standardized extracts

One of the biggest limitations in herbal research is the lack of **standardized extracts**. Active compounds in herbs can vary depending on species, cultivation, harvest season, and extraction method. Without standardization, two products sold under the same

name (e.g., "valerian extract") may contain very different concentrations of bioactive molecules, resulting in inconsistent outcomes across studies. Future research should focus on producing extracts with defined concentrations of known **active ingredients** (e.g., kavalactones in kava, withanolides in ashwagandha) and ensuring batch-to-batch consistency. This will improve reproducibility, allow dose–response studies, and facilitate regulatory approval (34,35).

8.2 Combining herbal drugs with conventional therapy

A growing interest exists in **adjunctive use of herbs with standard anxiolytics or antidepressants**. Preliminary evidence suggests that some herbs (such as chamomile or ashwagandha) may enhance treatment response, reduce medication side effects, or allow for dose reduction of conventional drugs. However, rigorous clinical trials are required to define **synergistic benefits versus risks** (e.g., additive sedation or pharmacokinetic interactions). Rational combinations, guided by pharmacological profiles, may eventually yield integrative treatment regimens that are both safer and more effective than monotherapy (35,36).

8.3 Integrative medicine approaches

The future of anxiety management may lie in **integrative medicine**, where herbal medicines are combined with psychological therapies, lifestyle interventions, and conventional pharmacotherapy. Such models are already being explored in fields like oncology and chronic pain management. Integrative approaches recognize that herbal treatments are rarely "standalone cures" but may provide **holistic benefits**, such as improved sleep, stress resilience, and mood stabilization. Patient-centered care, incorporating cultural practices and patient preferences, can also increase **adherence and satisfaction** with therapy (35,37).

8.4 Advances in pharmacognosy and phytochemistry

Modern advances in pharmacognosy and phytochemistry are expanding our understanding of herbal anxiolytics. Techniques such as metabolomics, molecular docking, and high-**throughput screening** can help identify novel bioactive compounds and their molecular targets. For example, studies have shown that many herbs act on multiple neurotransmitter systems (GABA, serotonin, dopamine)**, along with** anti-inflammatory and antioxidant pathways. (34)

CONCLUSION

Herbal medicines represent an important area of research in the management of anxiety disorders. Unlike conventional anxiolytic drugs, which often act on a single receptor or neurotransmitter, herbal remedies typically exert multifaceted effects involving GABAergic, serotonergic, dopaminergic, and neuroendocrine pathways. In addition, many herbs demonstrate antioxidant and anti-inflammatory actions, which contribute to their neuroprotective potential and may improve resilience against stress-related neuronal damage (38,39). Preclinical studies in animal models consistently show anxiolytic-like effects of herbal extracts such as *Ashwagandha*, *Brahmi*, *Valerian*, and *Passionflower*. These findings are supported by several randomized controlled trials that report reductions in generalized anxiety symptoms and improvements in overall well-being when using herbal therapies either alone or as adjuncts to standard treatment. Furthermore, meta-analyses and systematic reviews suggest moderate but consistent benefits, reinforcing the therapeutic promise of herbal medicine in anxiety management (39,40). Despite encouraging evidence, significant limitations remain. Variability in herbal preparation, dosage, and phytochemical composition makes it difficult to generalize results across studies. Safety concerns, such as kava-related hepatotoxicity and potential herb–drug interactions, also warrant caution. Most importantly, the lack of large-scale, well-controlled clinical trials limits the strength of current conclusions. Future research must focus on standardization of extracts, rigorous clinical validation, and long-term safety monitoring to establish herbal medicines as reliable therapeutic options (41). In conclusion, herbal medicines hold great potential as alternatives or adjuncts to conventional anxiolytic drugs. Their multimodal mechanisms, favorable safety profiles, and cultural acceptance make them promising candidates for integrative approaches in psychiatry. However, robust

clinical evidence is still required before they can be fully incorporated into mainstream medical practice.

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