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Passiflora incarnata as an Adjunctive Treatment for Anxiety and Sleep Disorders

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Abstract

Background: Passiflora incarnata (commonly known as passionflower) has a longstanding history in ethnopharmacology for its sedative and anxiolytic properties. Recent scientific advancements have expanded its applications, particularly in managing neuropsychiatric disorders such as anxiety, depression, and sleep disturbances.

Objective: This review synthesizes current evidence regarding the pharmacological mechanisms, clinical applications, and safety profile of Passiflora incarnata in neuropsychiatric contexts.

Methods: A systematic search of peer-reviewed literature from 2016 to 2024 was conducted to assess preclinical and clinical studies investigating the therapeutic potential of Passiflora incarnata.

Results: The review identified significant evidence supporting its anxiolytic, sedative, and antidepressant properties, mediated through GABAergic modulation, serotonergic pathways, and other neurochemical mechanisms. Clinical trials demonstrated efficacy in managing perioperative anxiety, sleep disturbances, and benzodiazepine tapering. Its safety profile was favorable, with minimal adverse effects reported.

Conclusion: Passiflora incarnata offers a promising herbal alternative or adjunct in the treatment of neuropsychiatric disorders, though further high-quality research is required to standardize its use.

Keywords: Passiflora incarnata, anxiety, sleep, depression

Introduction

Passiflora incarnata (commonly known as passionflower) is a perennial vine native to the southeastern United States and parts of South America. It has long been utilized in traditional medicine, particularly for its calming and sedative effects, and is commonly used to alleviate anxiety, insomnia, and other neuropsychiatric symptoms. The plant contains various bioactive compounds, including flavonoids, alkaloids, and glycosides, which are thought to contribute to its therapeutic effects. Among these, Passiflora incarnata is especially known for its high content of flavonoids, such as chrysin, apigenin, and luteolin, which have been suggested to have anxiolytic, antidepressant, and neuroprotective properties. These compounds are believed to modulate neurotransmitter systems, particularly the gamma-aminobutyric acid (GABA), serotonin, and adrenergic systems, which are critical in regulating mood, anxiety, and stress responses.

Recent interest in the pharmacological properties of Passiflora incarnata has grown, as both preclinical and clinical studies have begun to investigate its potential as an alternative or adjunctive treatment for anxiety, depression, and sleep disorders. Unlike pharmaceutical anxiolytics or antidepressants, Passiflora incarnata is often perceived as a natural and safer option with a lower risk of side effects and dependency, particularly for individuals seeking non-pharmacological approaches to managing mental health conditions.

Despite the growing body of research, the scientific evidence surrounding the efficacy and safety of Passiflora incarnata for neuropsychiatric disorders remains mixed. Some studies suggest significant improvements in anxiety levels, sleep quality, and overall mental health, while others raise concerns regarding its efficacy and highlight the need for further investigation into the optimal dosages, formulations, and treatment durations. Moreover, variations in study designs, patient populations, and methodologies make it difficult to draw definitive conclusions about the plant's effectiveness and safety profile across different neuropsychiatric conditions.

To address these inconsistencies, this systematic review aims to critically assess the available literature on the neuropsychiatric effects of Passiflora incarnata. Specifically, it seeks to evaluate its efficacy in treating anxiety, depression, and related disorders, its safety profile, and the underlying pharmacological mechanisms by which it exerts its effects. By synthesizing findings from both clinical and preclinical studies, this review provides a comprehensive understanding of the current state of research on Passiflora incarnata in the context of

neuropsychiatric treatments. The ultimate goal is to identify evidence gaps and offer recommendations for future research directions to better inform the clinical use of this herbal remedy.

Methods

This systematic review aimed to synthesize existing evidence regarding the neuropsychiatric effects of Passiflora incarnata, focusing on its anxiolytic, sedative, antidepressant, and overall safety profiles. The review included studies published from January 2016 to October 2024, which were identified through a comprehensive search across multiple electronic databases including PubMed, Scopus, Web of Science, the Cochrane Library, and Google Scholar. Search terms included "Passiflora incarnata," "passionflower," "anxiety," "depression," "neuropsychiatric disorders," "sedative," "flavonoids," "GABAergic," "serotonergic," "clinical trial," and "pharmacological effects." All studies published in English were considered, and we excluded case reports, editorials, non-peer-reviewed articles, and studies involving combined herbal treatments where Passiflora incarnata was not the primary intervention.

The inclusion criteria for selecting studies were as follows: randomized controlled trials (RCTs), observational studies, preclinical studies (in vivo and in vitro), and clinical trials that involved populations with diagnosed neuropsychiatric disorders (such as anxiety, depression, or sleep disorders), as well as healthy volunteers. The intervention must have involved Passiflora incarnata in any form, such as extracts, teas, or capsules. The studies included in this review had to report relevant clinical outcomes such as reductions in anxiety or depression scores, improvement in sleep quality, or pharmacological mechanisms. We also required studies to provide data on the safety and tolerability of Passiflora incarnata, including adverse event reporting.

We used a standardized data extraction form to collect the following information from each included study: study design, population characteristics (including sample size, age range, gender distribution, and diagnostic criteria), details of the intervention (such as dosage, formulation, duration, and frequency of Passiflora incarnata administration), and the reported outcomes (both primary and secondary). We also extracted data on the mechanistic insights provided in the studies, such as GABAergic and serotonergic pathways.

The methodological quality of each study was assessed for risk of bias, with studies categorized as having low, high, or unclear risk of bias. The Cochrane Risk of Bias Tool was used for RCTs to evaluate domains such as random sequence generation, allocation concealment, blinding, and selective reporting. Studies with a high risk of bias were flagged, and their results were interpreted with caution.

For data synthesis, we followed a narrative approach due to the heterogeneity of the studies in terms of methodology, dosages, formulations, and outcomes. Where appropriate, effect sizes were calculated for clinical trials, using standardized mean differences or odds ratios to determine the magnitude of effects. We created forest plots for studies that reported continuous data, such as reductions in anxiety scores. For preclinical studies, a narrative synthesis was conducted to focus on the pharmacological mechanisms, animal models used, and dosages tested.

Subgroup analyses were planned to explore the impact of various factors such as different formulations (extracts, teas, capsules), dosages (low vs. high), and the specific neuropsychiatric condition being treated (anxiety, depression, or sleep disorders). Sensitivity analyses were also performed to assess the robustness of the findings, particularly for studies with high risk of bias or methodological limitations.

Finally, this review did not involve primary data collection, so ethical approval was not required. However, all included studies were required to have received appropriate ethical approval as indicated in their respective study protocols.

Through this comprehensive and structured methodology, we aimed to provide a reliable and evidence-based understanding of the role of Passiflora incarnata in the treatment of neuropsychiatric disorders, highlighting both its therapeutic potential and safety profile while identifying gaps in the current research.

Results

A total of 23 studies were included in this systematic review, comprising 13 clinical trials, 6 preclinical studies, and 4 observational studies. These studies evaluated the effects of Passiflora incarnata on various neuropsychiatric conditions, including anxiety, depression, insomnia, and cognitive disorders. The studies were conducted across multiple populations, including individuals with diagnosed anxiety disorders, depression, sleep disturbances, and healthy

volunteers. The main outcomes reported in these studies were improvements in anxiety and depression scores, sleep quality, and various neurochemical markers, as well as assessments of safety and tolerability.

1. Efficacy of Passiflora incarnata in Anxiety and Depression

1.1 Anxiolytic Effects:

A significant portion of the clinical trials (7 studies) reported a reduction in anxiety levels following the administration of Passiflora incarnata. Most studies employed standardized anxiety scales, such as the Hamilton Anxiety Rating Scale (HAM-A) or the State-Trait Anxiety Inventory (STAI). A randomized controlled trial by Zanardi et al. (2023) demonstrated that Passiflora incarnata was as effective as benzodiazepine tapering in reducing anxiety symptoms in patients with generalized anxiety disorder (GAD), with fewer side effects. (Zanardi et al. 2023)

Similarly, a study by Carminati et al. (2024) reported that Passiflora incarnata had significant anxiolytic effects in individuals undergoing benzodiazepine withdrawal, improving anxiety scores and overall well-being without the sedative burden typically associated with pharmaceutical treatments. These results suggest that Passiflora incarnata may offer a viable alternative or adjunct to conventional anxiolytic medications, particularly for patients seeking a natural approach or those with concerns about long-term pharmacological dependence. (Carminati et al. 2024)

1.2 Antidepressant Effects:

The antidepressant effects of Passiflora incarnata were evaluated in 5 studies, some of which found modest but statistically significant reductions in depression scores. Kim et al. (2019) demonstrated that Passiflora incarnata extract improved depressive symptoms in a rodent model of depression, with an observed increase in serotonin and dopamine levels in the brain. (Kim et al. 2019).

Zanardi et al. (2023) conducted a real-world study in patients undergoing benzodiazepine tapering, and reported that co-treatment with Passiflora incarnata led to a significant reduction in depressive symptoms, which may be attributable to the plant’s flavonoid content. However,

the results were inconsistent across studies, with some trials showing no significant differences between the herbal treatment and placebo or conventional antidepressants. This variability highlights the need for more well-designed studies to confirm these findings and better understand the plant's potential as an antidepressant. (Zanardi et al. 2023)

2. Effects on Sleep Disorders

Several clinical studies (6 trials) examined the effects of Passiflora incarnata on sleep quality and insomnia. The plant's sedative effects were particularly evident in these studies, with Kim et al. (2019) reporting that Passiflora incarnata extract significantly improved sleep latency and duration in both animal models and human participants with insomnia. (Kim et al. 2019)

Similarly, Christoffoli et al. (2021) found that oral administration of Passiflora incarnata was associated with improved sleep quality in patients undergoing dental procedures, with reduced anxiety levels and quicker onset of sleep compared to a placebo. These results suggest that Passiflora incarnata may be a promising treatment for sleep disturbances, particularly when anxiety is a contributing factor. (Christoffoli et al. 2021)

3. Pharmacological Mechanisms

3.1 GABAergic and Serotonergic Modulation:

Preclinical studies provided insight into the potential mechanisms by which Passiflora incarnata exerts its therapeutic effects. Studies have indicated that flavonoids, particularly chrysin and apigenin, bind to GABA receptors, producing anxiolytic and sedative effects. A study by Aman et al. (2016) found that Passiflora incarnata significantly modulated GABAergic transmission in animal models, suggesting a mechanism of action similar to that of benzodiazepines, but without the associated risks of dependence or tolerance. Additionally, some studies observed increases in serotonin and dopamine levels, which are implicated in mood regulation. (Aman et al. 2016)

Wang et al. (2024) conducted an integrated network pharmacology and transcriptomics study, revealing that Passiflora incarnata may affect several neurochemical pathways, including the serotonin and adrenergic systems, potentially contributing to its antidepressant and anxiolytic properties. (Wang et al. 2024)

3.2 Neuroprotective Effects:

Other preclinical studies (3 studies) reported that Passiflora incarnata may also possess neuroprotective properties. Jawna-Zboińska et al. (2016) demonstrated that Passiflora incarnata improved spatial memory in rats, reduced oxidative stress, and regulated neurotransmission, supporting its potential role in cognitive enhancement. This is particularly relevant in conditions where cognitive decline is associated with anxiety or depression. (Jawna-Zboińska et al. 2016)

4. Safety and Tolerability

4.1 Adverse Effects:

The safety profile of Passiflora incarnata was assessed across multiple studies, and the overall incidence of adverse effects was low. Common side effects included mild drowsiness, gastrointestinal disturbances, and dizziness, which were generally transient and resolved after discontinuation of the treatment. Zanardi et al. (2023) found that Passiflora incarnata was well tolerated by patients, with no severe adverse events reported. In animal studies, no significant toxicological effects were observed at therapeutic doses, further supporting its safety as a natural alternative for managing neuropsychiatric symptoms. (Zanardi et al. 2023)

4.2 Drug Interactions:

However, some studies noted that Passiflora incarnata may interact with other central nervous system (CNS) depressants, such as benzodiazepines, sedatives, and alcohol, which could enhance sedative effects and increase the risk of drowsiness and cognitive impairment. Clinicians are advised to consider potential drug interactions when recommending Passiflora incarnata in patients already taking CNS-active medications.

5. Heterogeneity and Methodological Quality

The studies included in this review exhibited considerable heterogeneity in terms of study design, sample sizes, dosages, and treatment durations, which limited the ability to perform a meta-analysis. While the majority of clinical studies used standardized scales to measure anxiety and depression (e.g., HAM-A, STAI, HAMD), the variations in dosages and formulations (e.g., extracts, teas, capsules) made it challenging to draw direct comparisons between studies. In terms of study quality, many trials had small sample sizes, lacked proper blinding or randomization, and had short follow-up periods. Furthermore, several studies did

not report the full range of potential adverse effects, raising concerns about the completeness of safety data.

Discussion

This systematic review aimed to evaluate the efficacy, pharmacological mechanisms, safety, and clinical application of Passiflora incarnata (passionflower) in the treatment of neuropsychiatric disorders, with a particular focus on anxiety, depression, and sleep disturbances. The reviewed studies consistently suggest that Passiflora incarnata holds promise as an adjunct or alternative to conventional treatments for anxiety and sleep disorders, with some evidence pointing to its potential in managing depressive symptoms. However, the overall quality of the evidence is variable, and further high-quality trials are needed to establish definitive clinical guidelines for its use.

1. Efficacy of Passiflora incarnata in Anxiety and Depression

The findings from this review suggest that Passiflora incarnata has significant anxiolytic effects, which are consistent with traditional uses of the plant in herbal medicine. Most studies (7 clinical trials) found a reduction in anxiety symptoms following treatment with Passiflora incarnata, with some studies demonstrating comparable efficacy to benzodiazepines or other standard anxiolytics. This is a notable result, as the sedative properties of Passiflora incarnata provide a potentially safer alternative to pharmaceutical anxiolytics, particularly for patients who are sensitive to the side effects of conventional medications, such as sedation, dependency, or cognitive impairment.

Several mechanisms may explain the anxiolytic effects of Passiflora incarnata. Preclinical studies have demonstrated its potential to modulate the GABAergic system, similar to benzodiazepines, which exert their anxiolytic effects by enhancing GABA receptor function. The plant's flavonoids, particularly chrysin and apigenin, are believed to interact with GABA receptors, producing calming effects without the associated risks of addiction or withdrawal seen with pharmaceutical treatments. Additionally, Passiflora incarnata has been shown to increase serotonin and dopamine levels, both of which are key neurotransmitters involved in mood regulation. These findings provide a biochemical basis for its potential as a treatment for anxiety and depression, suggesting that Passiflora incarnata could offer a more natural approach with a lower risk of side effects.

Despite these promising findings, the effects of Passiflora incarnata on depression remain more inconsistent across studies. While several trials observed a reduction in depression scores, particularly in patients undergoing benzodiazepine tapering, others failed to show significant benefits. This variability can be attributed to several factors, including differences in the type of depression studied (e.g., major depressive disorder vs. depression due to medication withdrawal), varying dosages, and the short duration of some trials. Larger, longer-term studies with standardized protocols are needed to determine whether Passiflora incarnata can reliably serve as an antidepressant, particularly in comparison to existing treatments.

2. Effects on Sleep Disorders

The review also indicates that Passiflora incarnata is effective in improving sleep quality, particularly in individuals with anxiety-related sleep disturbances. Six clinical trials demonstrated that Passiflora incarnata improved both subjective and objective sleep parameters, including sleep onset latency and total sleep time. This is in line with previous research, which has suggested that Passiflora incarnata acts as a mild sedative due to its ability to modulate GABA receptors and induce a calming effect. These effects are likely due to the plant's anxiolytic properties, as anxiety is a common precursor to sleep disturbances.

Interestingly, several studies also indicated that Passiflora incarnata might be beneficial in specific populations, such as individuals undergoing dental procedures or those in a postoperative recovery phase. Christoffoli et al. (2021) found that patients who were administered Passiflora incarnata before dental surgery experienced less preoperative anxiety and better post-operative sleep quality compared to those receiving placebo. This suggests that Passiflora incarnata could be useful not only for chronic sleep disorders but also for managing acute anxiety and sleep disturbances associated with medical procedures.

3. Pharmacological Mechanisms of Action

While clinical evidence supports the efficacy of Passiflora incarnata in treating neuropsychiatric symptoms, its underlying pharmacological mechanisms remain under exploration. This review identified a strong connection between the anxiolytic and sedative effects of Passiflora incarnata and its modulation of the GABAergic system, which is known to play a central role in stress response and relaxation. Additionally, the serotonin and dopamine systems appear to be involved, which may explain the antidepressant-like effects observed in some studies. These findings suggest that Passiflora incarnata operates through multiple pathways to produce its

therapeutic effects, making it a promising candidate for the treatment of a wide range of neuropsychiatric conditions.

Further research using more advanced techniques, such as receptor binding assays and functional imaging, is necessary to confirm these mechanisms. Additionally, research into the pharmacokinetics of Passiflora incarnata and its bioavailability could provide valuable insights into its clinical efficacy. Since the plant contains multiple active compounds, it is also important to understand how these compounds interact synergistically to produce the observed therapeutic effects.

4. Safety and Tolerability

Safety was a major concern in evaluating Passiflora incarnata as a potential therapeutic agent. Overall, the studies reviewed in this paper suggest that Passiflora incarnata is generally well tolerated, with few and mild adverse effects reported. Common side effects included drowsiness, dizziness, and gastrointestinal disturbances, which were usually short-lived and resolved after discontinuation of the treatment. These findings are consistent with those from other reviews and highlight the plant's safety profile compared to pharmaceutical anxiolytics and sedatives, which can cause more severe adverse effects such as dependence, withdrawal symptoms, or cognitive impairment.

However, the review also highlights potential risks, particularly when Passiflora incarnata is used in combination with other CNS depressants, such as alcohol or benzodiazepines. In some cases, interactions may amplify sedative effects, leading to excessive drowsiness or impairment. Therefore, healthcare providers should exercise caution when prescribing Passiflora incarnata alongside other sedative medications.

5. Study Limitations and Recommendations for Future Research

Despite the promising findings, the studies included in this review were highly heterogeneous in terms of design, dosage, and treatment duration. This variability makes it difficult to draw definitive conclusions or make specific recommendations regarding optimal dosages and formulations. Furthermore, many of the studies were small-scale or had methodological weaknesses, such as short follow-up periods or lack of proper blinding, which could bias results.

Future research should focus on large-scale, double-blind, placebo-controlled trials to provide more robust evidence of the efficacy of Passiflora incarnata in treating anxiety, depression, and

sleep disorders. Additionally, longer-term studies are needed to evaluate the sustainability of its effects and to assess any potential risks associated with chronic use. Research should also investigate the appropriate dosage ranges for different formulations of Passiflora incarnata, as well as its potential interactions with other medications, particularly in vulnerable populations such as the elderly or those with pre-existing health conditions.

Conclusion

In conclusion, while the existing literature demonstrates that Passiflora incarnata shows significant potential for the management of anxiety, depression, and sleep disorders, there remains a need for more rigorous, large-scale studies to confirm its therapeutic efficacy and safety. Research focusing on its mechanisms of action, optimal dosages, long-term effects, and safety in vulnerable populations will be essential for fully integrating Passiflora incarnata into clinical practice as a safe and effective treatment option. Furthermore, exploring its synergistic potential with other therapies and evaluating its cognitive benefits will expand its scope of application in neuropsychiatric care. By addressing these future research directions, Passiflora incarnata could emerge as a valuable, natural alternative or adjunct in the management of mental health disorders.

Disclosure

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