



VALERIANA OFFICINALIS: A COMPREHENSIVE REVIEW ON ITS EFFICACY IN TREATING SLEEP DISORDERS.

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ABSTRACT:

Sleep is a crucial biological function necessary for cognitive, emotional, and physical health. Nevertheless, sleep issues like insomnia impact a considerable percentage of the worldwide population, leading to diminished quality of life and a heightened risk of chronic ailments such as heart diseases and depression. Valeriana officinalis, often referred to as valerian, has been utilized for many years as a natural treatment for issues related to sleep and anxiety. Current studies indicate that valerian's calming properties are mainly due to its adjustment of gamma-aminobutyric acid (GABA) function in the central nervous system, with components like valerenic acid and valepotriates being particularly important.

This review examines the historical importance of valerian, its pharmacological actions, clinical effectiveness, safety, and drawbacks as a therapy for sleep disorders. Although randomized controlled trials and meta-analyses have demonstrated encouraging outcomes, the evidence is still inconsistent because of differences in formulations, methodological concerns, and limited sample sizes. Valerian offers benefits compared to traditional therapies, such as being non-addictive, having few side effects, and good tolerability, positioning it as a suitable option for those wanting natural methods for managing sleep.

The evaluation also highlights the necessity for forthcoming studies employing standardized formulations and strong methodologies, incorporating objective metrics such as polysomnography. Furthermore, the possible synergistic benefits of pairing valerian with non-drug treatments, like cognitive-behavioral therapy, are emphasized. Valerian shows potential as a secure and patient-focused choice for treating mild to moderate sleep issues, necessitating additional research to clarify its place in contemporary healthcare.

KEYWORDS: Valeriana officinalis, valerian root, traditional medicine, anxiolytic effects, sedative properties, essential oil, stress management, valerenic acid, valepotriates, insomnia.

INTRODUCTION:

Sleep is a vital physiological function that is crucial for maintaining overall health, cognitive abilities, and emotional stability. However, numerous individuals worldwide suffer from sleep disorders, including insomnia, sleep apnea, and disruptions in circadian rhythms. Insomnia, which is marked by challenges in falling asleep or staying asleep, is the most common sleep disorder and is linked to diminished quality of life, decreased productivity, and a heightened risk of chronic health issues such as cardiovascular diseases, diabetes, and depression. It is estimated that between 10% and 30% of adults globally experience symptoms of insomnia, highlighting its significance as a public health issue.[1]



Valerian, derived from the dried root of the plant Valeriana officinalis L., has been utilized as a medicinal herb since ancient Greece and Rome. Hippocrates noted its sedative and anti-anxiety properties, while Galen recommended it as a treatment for insomnia. Related species within the Valerianaceae family have also been employed in traditional Chinese and Indian Ayurvedic medicine.[2]

Commonly known as valerian, *Valeriana officinalis* is a perennial herb that has historically served as a natural remedy for anxiety, restlessness, and sleep-related issues. Various traditional medicine systems, including European herbalism and Ayurveda, have long acknowledged the calming and sedative effects of valerian. In recent years, valerian has become increasingly popular as an over-the-counter supplement for insomnia and similar conditions. Despite its extensive historical use, the clinical evidence supporting valerian's effectiveness in treating sleep disorders is inconsistent, which underscores the need for a thorough review of its therapeutic potential.[3]

This review examines the pharmacological mechanisms, clinical effectiveness, safety, and limitations of valerian as a treatment for sleep disorders. By consolidating the available evidence, it seeks to offer a detailed understanding of valerian's potential role in managing sleep issues.

Historical and Traditional Use:

Valerian has served as a natural remedy for centuries, with its use documented by ancient Greek and Roman physicians, including Hippocrates and Galen, who noted its effectiveness in treating insomnia and anxiety. During the medieval period in Europe, valerian became a prevalent treatment for anxiety and sleep issues, typically consumed in the form of tea or tincture. Additionally, both Ayurvedic and traditional Chinese medicine acknowledged valerian for its soothing properties, recommending it for mental unrest and sleep disorders. This historical context underscores valerian's importance as a reliable therapeutic agent across diverse cultures and medical practices.[4]

Furthermore, valerian is a key ingredient in numerous herbal formulations commonly employed to address sleep disorders. In contemporary times, valerian extracts are marketed as dietary supplements, primarily derived from dried root or root extracts, and are available in tablet or soft gelatin capsule form. Each dosage typically contains between 50 mg and 1 gram of dried root or extract. The popularity of these dietary supplements is significant, with an estimated 210 million doses sold annually in the United States and approximately 125 million in Europe.[5]

The traditional medicinal applications of the valerian plant encompass treatment for migraines, pain relief, anticonvulsant properties, and sedative effects. Notably, its primary benefit lies in its restorative impact on the central nervous system (CNS), with the most frequent applications of *V. officinalis* being the management of insomnia and anxiety.[6]

Pharmacological Activity:

Barton et al. conducted a study to assess the effectiveness of *V. officinalis* supplements in improving sleep among cancer patients undergoing treatment. An additional exploratory analysis indicated that various fatigue-related outcomes, as measured by the Brief Fatigue Inventory (BFI) and the Profile of Mood States (POMS), showed significant improvement in individuals taking valerian compared to those receiving a placebo. Further exploratory analyses also indicated enhancements in certain secondary outcomes, particularly fatigue. Rezvani et al. investigated the impact of valerian extracts on a model of temporal lobe epilepsy, examining the role of the adenosine system in the effects of the aqueous extract. The findings demonstrated a notable anticonvulsant effect for the aqueous extract, while the petroleum ether extract did not exhibit similar results. Murphy et al. reported on behavioral assessments of *V. officinalis* in comparison to the benzodiazepine diazepam and analyzed the chemical composition of *V. officinalis*. Their results indicated a significant reduction in anxious behavior among subjects exposed to valerian extracts and valerianic acid when compared to the ethanol control group. This evidence supports the potential of *V. officinalis* as an alternative to conventional anxiolytics, as measured by the elevated plus maze.[7]

Research has also indicated that valerian may affect adenosine receptors, which are crucial for sleep regulation and the onset of sleep. This diverse pharmacological profile underscores valerian's potential as a natural remedy for enhancing sleep and alleviating anxiety. Nevertheless, the specific bioavailability and pharmacokinetics of these compounds continue to be subjects of ongoing investigation.[8]

Clinical Evidence from Randomized Controlled Trials (RCTs):

There exists clinical evidence that supports the efficacy of *Valeriana officinalis* (valerian) in enhancing sleep quality, as demonstrated by multiple randomized controlled trials (RCTs). One particular study involving 128 participants indicated that valerian significantly reduced sleep latency and improved overall sleep quality, especially among individuals with irregular sleep patterns. Additionally, a systematic review encompassing 21 RCTs concluded that valerian exhibited moderate effects on both subjective and objective measures of sleep. Nevertheless, despite these encouraging findings, the results are inconsistent, and there is a need for further high-quality research to establish its long-term effectiveness. A 2019 double-blind, placebo-controlled trial reported no statistically significant differences in sleep latency or quality between valerian and a placebo. The authors of this study attributed these results to high rates of placebo response and the variability in valerian formulations utilized in different studies.[9]

Meta-Analyses and Systematic Reviews:

Meta-analyses evaluated the efficacy of *V. officinalis* in enhancing sleep quality and alleviating anxiety. Due to the limited data available, all placebo-controlled studies that yielded values convertible to effect sizes were incorporated into the statistical analysis, irrespective of their quality as assessed by the Jadad scale. One author extracted outcome variables from both the *V. officinalis* treatment group and the placebo group, with verification performed by two additional authors. To evaluate the impact on sleep, we examined the changes in subjective 'sleep quality' over time with repeated use, ranging

from 5 days to 8 weeks. Given the variability in study sizes, both numerical and binary scores were converted into effect sizes for the analysis. For assessing the calming effects, studies addressing overall emotional symptoms, including anxiety, as well as those reporting binary outcomes and standard anxiety test scores, were included. In instances where multiple measurements were reported within a single study, the measure with the longest follow-up period was selected. When various doses were tested, the outcome associated with the most effective dose was chosen. Effect sizes were calculated using Hedges' *g*, based on means, standard deviations, confidence intervals, odds ratios (for binary outcomes), and sample sizes, following a specified formula. Meta-analyses were performed using Meta-Essentials, and heterogeneity was assessed through the *I*² statistic. Publication bias was evaluated by analyzing funnel plots.[10]

Safety and Tolerability:

Valerian is generally considered safe for short-term use. It has been administered in doses ranging from 300 to 600 mg daily for a duration of up to six weeks without significant issues. However, the safety of prolonged use remains uncertain. Typically, valerian is well-tolerated, though some individuals may experience common side effects such as dizziness, drowsiness, headaches, gastrointestinal discomfort, cognitive dullness, and vivid dreams. Discontinuation after extended use may lead to withdrawal symptoms. To mitigate these symptoms, it is advisable to gradually taper the dosage over one to two weeks prior to complete cessation.[11]

Furthermore, valerian may interact with other central nervous system depressants, including alcohol and sedatives, potentially amplifying their effects. Therefore, caution is recommended when using valerian in conjunction with these substances. Pregnant and breastfeeding individuals are generally advised to refrain from using valerian due to insufficient safety data regarding its effects in these groups.[12]

Valerian may enhance the effects of various medications, including:

- Anticonvulsants such as phenytoin (Dilantin) and valproic acid (Depakote)
- Barbiturates
- Benzodiazepines like alprazolam (Xanax) and diazepam (Valium)
- Insomnia medications such as zolpidem (Ambien), zaleplon (Sonata), eszopiclone (Lunesta), and ramelteon (Rozerem)
- Tricyclic antidepressants such as amitriptyline (Elavil)
- Alcohol

This interaction also applies to other herbs with sedative properties, including chamomile, lemon balm, and catnip.[13]

Limitations of Current Research:

The predominant focus of research has been on the efficacy of valerian as a sleep aid, with numerous systematic reviews conducted over the years. A systematic review from 2000 evaluated nine randomized clinical trials, uncovering inconsistent outcomes and considerable differences in patient demographics, study design, and methodologies. Similarly, a review in 2006 assessed 16 studies and identified notable methodological shortcomings. Taibi et al. (2007) conducted a review of 37 studies, which included 29 controlled trials and eight open-label trials. Their results indicated that while valerian is considered a safe herbal remedy, there is insufficient evidence to support its effectiveness in treating insomnia.

A meta-analysis of 18 trials conducted in 2010 concluded that valerian did not demonstrate significant benefits based on quantitative analysis, although it may enhance the quality of subjective sleep. The underlying reasons for these inconsistent findings remain ambiguous. Furthermore, it is still unclear whether valerian is beneficial for addressing other conditions associated with or potentially contributing to sleep disturbances. The primary objective of this study is to update the existing literature, evaluate the effectiveness of valerian in treating sleep-related issues and associated disorders, and investigate the factors contributing to the discrepancies in research findings, with a particular focus on the herbal remedies employed in these studies.[14]

Discussion:

The utilization of *Valeriana officinalis* (valerian) for the treatment of sleep disorders exemplifies a significant intersection between traditional herbal remedies and modern pharmacological approaches. A variety of studies have suggested that valerian may be effective in improving sleep quality, reducing the time it takes to fall asleep, and promoting relaxation. However, the inconsistency of findings from clinical trials highlights the challenges involved in standardizing its use for sleep management.

Clinical Efficacy and Challenges:

Valerian is commonly viewed as a suitable alternative to prescription medications for the treatment of sleep disorders, largely due to its perceived safety and gentleness. Research suggests that valerian may help individuals fall asleep more rapidly and improve their overall sleep quality. A rigorously designed study found that valerian did not show greater effectiveness than a placebo over a 14-day period; however, after 28 days, participants using valerian reported significant enhancements in their sleep patterns. This has led some researchers to suggest that a duration of several

weeks may be required for valerian to manifest its full benefits. In contrast, another study indicated that valerian was more effective than a placebo almost immediately. Additional research corroborates the idea that valerian can reduce the time taken to fall asleep and improve sleep quality. Unlike many prescription sleep aids, valerian is linked to fewer side effects, such as next-day drowsiness.[16]

While some studies indicate that valerian may be beneficial for insomnia and other sleep disorders, findings from other studies are less supportive. The interpretation of these studies is complicated by factors such as small sample sizes, varying dosages and sources of valerian, different outcome measures, and potential biases due to high participant withdrawal rates. Overall, the evidence from these trials regarding the sleep-promoting effects of valerian remains inconclusive.[15]

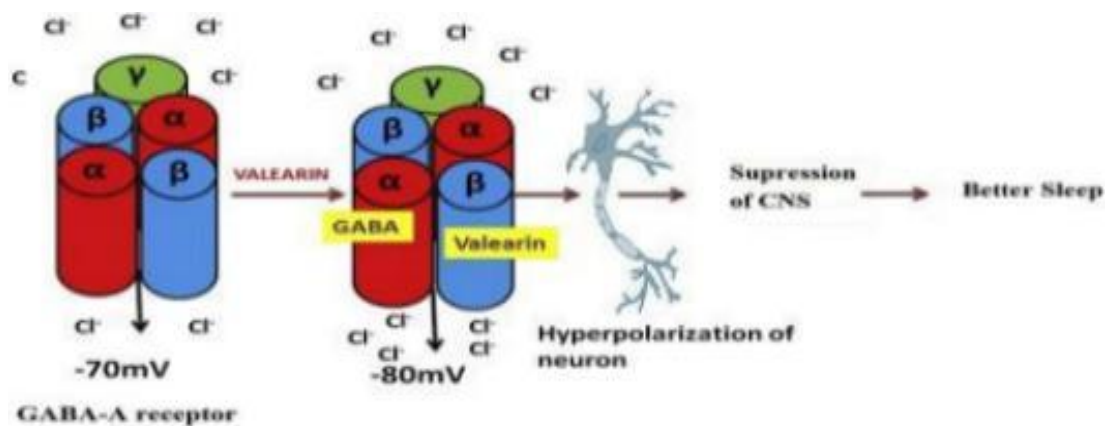
Mechanisms of Action:

Numerous chemical constituents of valerian have been identified; however, the specific compounds responsible for its sleep-inducing effects in animal models and in vitro studies remain unclear. It is probable that no single active ingredient is solely responsible, and that the effects of valerian arise from a combination of multiple constituents acting either independently or in synergy.[17, reviewed in 18].

Two main categories of constituents have been recognized as key contributors to the sedative properties of valerian. The first category comprises the primary components of its volatile oil, including valerenic acid and its derivatives, which have demonstrated sedative effects in animal studies. However, valerian extracts with low concentrations of these components still display sedative characteristics, indicating that other constituents may also play a role or that a combination of various constituents is involved. The second category includes iridoids, which consist of valepotriates. Although valepotriates and their derivatives exhibit sedative activity in vivo, their instability during storage or in aqueous conditions poses challenges in evaluating their effectiveness.[19]

One potential mechanism through which valerian extract may induce sedation is by increasing the availability of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter, in the synaptic cleft. Findings from an in vitro study utilizing synaptosomes suggest that valerian extract may facilitate the release of GABA from neuronal endings and inhibit its reuptake into nerve cells.[20]

GABA serves as the primary inhibitory neurotransmitter for the GABA-A receptor located in the central nervous system (CNS). Valerian appears to enhance the binding affinity of GABA to its receptor. It has been reported that GABA attaches to the alpha (α) subunit of the GABA-A receptor. In the absence of valerian, GABA binds weakly to the receptor, leading to the influx of chloride ions (Cl^-) into the neurons (-70 mV). Conversely, valerian enhances the binding of GABA to the GABA-A receptor, leading to an increased influx of chloride ions (Cl^-) into the neuron. This process results in hyperpolarization of the neuron, reaching a potential of -80 mV . During hyperpolarized states, neurons exhibit reduced activity in response to excitatory postsynaptic potentials, thereby suppressing the overall function of the central nervous system.[6]



Advantages Over Conventional Therapies :

Valerian offers several advantages when compared with traditional pharmaceutical interventions for sleep disorders. Unlike benzodiazepines and non-benzodiazepine hypnotics, valerian is devoid of the risks associated with dependency, withdrawal symptoms, or significant daytime sedation. Its commendable safety profile makes it an attractive choice for individuals seeking alternative or complementary therapies. Additionally, the lack of major contraindications permits its extended use without a substantial risk of tolerance development. As a result, valerian stands out as a potentially sustainable and patient-focused option for the long-term management of mild sleep disturbances.[21]

Integration with Holistic Approaches :

The effectiveness of valerian may be amplified when combined with non-pharmacological strategies such as cognitive behavioral therapy for insomnia (CBT-I). The integration of valerian with practices like sleep hygiene education or relaxation techniques could produce synergistic benefits, enhancing

outcomes for patients experiencing chronic sleep difficulties. This multi-faceted approach is in line with contemporary trends in personalized and holistic healthcare, which prioritize the customization of interventions to meet individual needs and preferences.[22,23]

Future Directions :

Future research on valerian should focus on conducting well-structured randomized controlled trials (RCTs) to rectify the methodological limitations observed in earlier studies. It is crucial to employ standardized formulations of valerian extracts that ensure consistent levels of active components, thereby providing uniformity in both dosage and efficacy. The integration of objective sleep assessment methods, such as polysomnography and actigraphy, alongside patient-reported outcomes, will offer a more comprehensive understanding of valerian's effects. Furthermore, pharmacokinetic investigations examining the absorption, metabolism, and bioavailability of valerian compounds could contribute to the optimization of dosing strategies.[24]

CONCLUSION :

Valerian demonstrates considerable potential as a natural, non-drug method for addressing sleep disorders, especially insomnia. Its capability to improve sleep quality and decrease sleep onset latency, combined with a positive safety record, makes it an attractive substitute for traditional medications. Nevertheless, the differences in clinical results highlight the necessity for additional investigation. Standardized formulations featuring uniform concentrations of active components are crucial for guaranteeing reproducibility and dependability in upcoming research. Future trials should include objective assessments like polysomnography and actigraphy, along with outcomes reported by patients, to offer a complete understanding of valerian's effects. Pharmacokinetic research examining the absorption, metabolism, and bioavailability of valerian's active substances may improve dosing methods.

Additionally, combining valerian with non-drug methods like cognitive-behavioral therapy for insomnia (CBT-I) and education on sleep hygiene may enhance treatment results. This corresponds with the increasing trend of customized and comprehensive healthcare, highlighting individualized therapies. Although valerian may not be a conclusive remedy, its traditional use, safety, and possible effectiveness renders it as a significant component of sleep management strategies.

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