

EFFECT OF DIFFERENT HERBAL TREATMENT TO ALLEVIATE THE INSOMNIA

Original Research

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ABSTRACT

Background: Sleep is a complex physiological state regulated by intricate interactions among brain regions, neurotransmitters, and hormonal pathways. Insomnia, one of the most prevalent sleep-related disorders, affects up to 30% of the global population and is strongly associated with chronic medical conditions, psychiatric disorders, and significant reductions in quality of life. Its increasing prevalence among adults, particularly those aged 19–44 years, poses a major public health concern due to its linkage with cardiovascular disease, diabetes, depression, and impaired productivity. In response to the limitations and side effects associated with pharmacological treatments, there is growing interest in herbal medicine, with the World Health Organization reporting that 80% of the world's population relies on herbs for primary healthcare.

Objective: This narrative review aims to explore the effectiveness of herbal treatments in alleviating insomnia, highlighting their mechanisms of action, safety, and clinical relevance as alternative or complementary therapeutic options.

Main Discussion Points: The review discusses the classification of sleep stages, hormonal regulation of sleep, types and causes of insomnia, and the therapeutic potential of herbs such as valerian root, chamomile, and St. John's Wort. These herbs exert sedative and anxiolytic effects by modulating neurotransmitter systems, including GABA and serotonin. Evidence suggests that, when used appropriately, these agents are well-tolerated and can improve sleep latency and quality.

Conclusion: Herbal treatments present a viable, low-risk option for managing insomnia and related sleep disorders. However, further high-quality research is essential to establish standardized dosages, long-term safety, and clinical efficacy.

Keywords: Insomnia, Sleep disturbances, Herbal medicine, Neurotransmitters, GABA, Sleep quality.

INTRODUCTION

Sleep is a fundamental biological process that influences virtually every aspect of human health. It represents a reversible, physiological state of altered consciousness characterized by a reduced responsiveness to external stimuli and decreased motor activity. During sleep, both the body and brain undergo dynamic changes that are critical to physical restoration and psychological equilibrium. The human sleep-wake cycle is governed by a complex interplay of homeostatic and circadian mechanisms, with ultradian rhythms further segmenting sleep into distinct stages. These stages, particularly rapid eye movement (REM) and non-REM (NREM) sleep, are each associated with specific neurophysiological processes that contribute to memory consolidation, tissue repair, hormonal balance, and immune regulation (1). Globally, the importance of sleep is increasingly acknowledged, not only as a passive state but as a vital contributor to health, productivity, and overall quality of life. According to the World Health Organization, sleep disorders affect a significant portion of the global population, with insomnia alone impacting 10–30% of adults worldwide at any given time. Chronic sleep insufficiency has been linked to a range of non-communicable diseases including obesity, diabetes, cardiovascular disorders, and mental health conditions, thereby contributing to substantial health care costs and socioeconomic burden (2). Despite growing awareness, millions of individuals across different age groups continue to suffer from poor sleep quality or quantity, often exacerbated by modern lifestyle factors such as screen exposure, shift work, and psychosocial stressors. Extensive research in sleep medicine has elucidated various physiological underpinnings and consequences of sleep deprivation, yet significant gaps remain. While the architecture of sleep and its cyclical stages have been well-characterized, there is still incomplete understanding of how different sleep stages contribute specifically to physical recovery and cognitive functions. Moreover, current epidemiological studies often fail to capture the complexity of individual variability in sleep needs, genetic influences, and environmental determinants. The therapeutic landscape for sleep-related disorders, particularly insomnia, remains largely dominated by pharmacologic interventions, many of which carry the risk of dependence and adverse effects. In recent years, alternative approaches such as cognitive-behavioral therapy for insomnia (CBT-I), mindfulness practices, and herbal remedies have gained attention, yet the evidence supporting their efficacy and long-term benefits is still limited and often inconsistent (3,4).

The increasing prevalence of sleep disorders, particularly in urbanized and digitally connected societies, has prompted interest in non-pharmacological and complementary treatments. Among these, the use of herbal remedies has seen a resurgence due to their historical use, perceived safety profile, and natural origin. Several plant-based compounds such as valerian root, chamomile, passionflower, and lavender have been traditionally used to promote relaxation and enhance sleep. However, despite centuries of anecdotal use, robust scientific validation of these remedies is lacking. Many existing studies are either small-scale, methodologically limited, or produce conflicting outcomes, making it difficult for clinicians to provide evidence-based recommendations. Furthermore, the lack of regulatory oversight and standardization in herbal supplement manufacturing adds another layer of complexity, posing challenges in assessing safety, potency, and potential drug interactions (5,6). Given these uncertainties, there is a pressing need to synthesize and critically appraise existing literature on the effectiveness and safety of herbal treatments for insomnia. This narrative review aims to explore the current landscape of herbal interventions used to alleviate insomnia, with particular emphasis on their mechanisms of action, clinical evidence, limitations, and future research directions. By doing so, the review seeks to bridge the gap between traditional practices and modern evidence-based medicine, providing healthcare providers with an updated understanding of the role of herbal therapies in sleep management (7,8). The review will include studies published in the last five years, focusing primarily on human clinical trials, systematic reviews, and meta-analyses evaluating the efficacy of herbal treatments for primary or comorbid insomnia. The inclusion of only recent literature ensures relevance and incorporates the latest scientific findings and regulatory updates. The discussion will encompass both monotherapy and combination formulations, with a comparative evaluation against standard treatments where applicable. This review is particularly significant in light of growing public interest in holistic and integrative health practices. Many individuals are increasingly turning to herbal treatments due to concerns over pharmaceutical side effects, accessibility issues, or personal preference for natural solutions. However, without clear evidence and clinical guidelines, this trend could result in misuse or unmet therapeutic expectations. By providing a comprehensive and critical synthesis of the most recent evidence, this review aims to inform both clinical practice and future research directions, ultimately contributing to safer and more effective management of sleep disorders.

THEMATIC DISCUSSION

Sleep stages

Sleep is organized into two major categories: rapid eye movement (REM) and non-rapid eye movement (NREM) sleep. NREM is further divided into three stages. Stage 1 represents the transition from wakefulness to sleep and is marked by a decrease in alpha activity and the emergence of theta waves (6). Stage 2 deepens this state, with the emergence of sleep spindles and K-complexes, facilitating synaptic pruning and memory processing (7). Stage 3, or slow-wave sleep (SWS), is the deepest phase of NREM, characterized by high-amplitude delta waves, physical restoration, and decreased responsiveness to external stimuli (8). REM sleep, the fourth stage, is noted for vivid dreaming and active brain patterns, playing a crucial role in emotional regulation and memory consolidation (9). Notably, disruptions in NREM Stage 3 and REM sleep have been associated with poor restorative function and increased risks of depression (10). These variations in sleep architecture emphasize the need for targeted interventions in insomnia to restore a balanced sleep cycle.

Sleep regulating hormones

Multiple hormones orchestrate the sleep-wake cycle through circadian and homeostatic control. Serotonin, a precursor of melatonin, influences REM sleep and wakefulness. A deficiency in serotonin is closely associated with insomnia and depressive symptoms, especially in individuals with low tryptophan levels (11). Melatonin, secreted by the pineal gland in response to darkness, serves as a key circadian signal that promotes sleep onset and maintenance by interacting with hypothalamic receptors (12). Orexins, also known as hypocretins, promote arousal and wakefulness, and their deficiency leads to narcolepsy (13). Cortisol, a glucocorticoid released in a circadian pattern, peaks in the early morning and declines at night. Elevated evening cortisol has been implicated in primary insomnia and hyperarousal states (12,13). Growth hormone is secreted predominantly during SWS and is essential for tissue repair and metabolic regulation (14). Gamma-aminobutyric acid (GABA), the principal inhibitory neurotransmitter, plays a critical role in sleep initiation by dampening neuronal activity, with reduced GABAergic transmission observed in individuals with chronic insomnia (15).

Types of insomnia

Insomnia can be categorized into primary and secondary types based on etiology. Primary insomnia occurs independently of other health conditions and is often linked to hyperarousal and dysfunctional cognitive patterns. It commonly affects middle-aged females and is not caused by any medical or psychiatric disorder (16). Secondary insomnia, also referred to as comorbid insomnia, is associated with medical conditions such as chronic pain, cardiovascular disease, or psychiatric disorders like depression and anxiety (16,17). These distinctions are essential for personalized treatment approaches, as primary insomnia often responds well to behavioral therapies, while secondary insomnia necessitates a comprehensive strategy targeting underlying conditions.

Stages of insomnia

Insomnia may be present in transient, short-term, or chronic forms. Transient insomnia lasts for a few nights to less than a month and often results from acute stress or environmental changes. Short-term insomnia persists between one and six months, while chronic insomnia extends beyond six months and is frequently associated with significant distress and functional impairment (18). The chronic form is particularly concerning due to its links with cardiovascular disease and increased mortality risks (19). Evidence suggests that untreated transient insomnia may evolve into chronic insomnia, underscoring the importance of early intervention.

Insomnia causes

The etiology of insomnia is multifactorial. Social stressors such as financial instability, family conflict, and academic pressure are significant contributors, especially among young adults and healthcare students (19). Environmental disturbances including excessive light exposure, urban noise pollution, and poor sleep hygiene interfere with melatonin secretion and disrupt circadian rhythms (20). Anxiety and stress are also strongly implicated, with general anxiety disorder (GAD) increasing vulnerability to insomnia through dysregulation of neurotransmitter pathways including GABA, serotonin, and norepinephrine (21). These causative factors are often interlinked and necessitate an integrative therapeutic strategy.

Insomnia treatments

Management of insomnia involves pharmacological, non-pharmacological, and alternative therapies. Pharmacologic treatments such as benzodiazepines, melatonin receptor agonists, and orexin receptor antagonists remain widely prescribed, but long-term use raises concerns of tolerance and dependence (21). Non-pharmacologic strategies, particularly cognitive behavioral therapy for insomnia (CBT-

I), are considered first-line treatments due to their sustained efficacy and safety profile (20,21). Alternative therapies such as herbal medicine, acupuncture, and relaxation techniques are increasingly adopted, particularly among individuals seeking holistic remedies. Despite their popularity, the clinical validation of herbal treatments remains limited, emphasizing the need for rigorous trials.

St John wort

St. John's Wort (*Hypericum perforatum*) has long been used in the management of mood disorders and more recently for insomnia due to its sedative and anxiolytic effects. Its bioactive compounds, hyperforin and hypericin, are believed to modulate neurotransmitter systems by inhibiting serotonin and norepinephrine reuptake (22). Clinical studies suggest that it may improve sleep architecture by increasing REM latency and deep sleep phases (22). However, evidence is mixed regarding its effectiveness in severe insomnia. Moreover, its potential for drug interactions, particularly with antidepressants and anticoagulants, necessitates caution in clinical use (22,23).

Mechanism of action

St. John's Wort modulates monoamine oxidase (MAO) activity and inhibits the reuptake of neurotransmitters including serotonin, dopamine, and GABA. While early in vivo studies suggested MAO inhibition, later findings indicate that hyperforin may instead act on sodium-dependent neurotransmitter transporters, indirectly elevating synaptic neurotransmitter levels (24). It also downregulates β 1-adrenoceptors and upregulates 5-HT₂ serotonin receptors, contributing to its mood-stabilizing effects. This multifaceted mechanism positions it as a viable adjunct in treating mood-related insomnia, although more controlled trials are warranted to confirm efficacy and safety.

Chamomile

Chamomile (*Matricaria recutita*) is among the most widely used herbal remedies for anxiety and insomnia. Its principal active compound, apigenin, binds to benzodiazepine receptors in the brain, enhancing GABAergic neurotransmission and promoting sedation (25). Chamomile has demonstrated modest benefits in patients with generalized anxiety disorder (GAD) and insomnia, especially at doses between 90–400 mg over several weeks (26). It is generally well-tolerated and regarded as safe, with few side effects reported. However, variability in preparation and dosage forms challenges the standardization of its clinical use.

Mechanism of action

Chamomile's effects are attributed to its action on GABA-A receptors, where apigenin enhances inhibitory neurotransmission, reducing arousal and anxiety (25). Additionally, chamomile modulates monoamine neurotransmitters and suppresses hypothalamic-pituitary-adrenal (HPA) axis activity, thus dampening cortisol-mediated stress responses (26). These actions collectively facilitate sleep initiation and maintenance, especially in anxiety-related insomnia. FDA support for chamomile's use in GAD strengthens its role as a potential natural anxiolytic and sleep enhancer.

Valerian Root (*Valeriana officinalis*)

Valerian root is another popular herbal remedy known for its sedative and hypnotic effects. It contains valerenic acid, valerenol, and other sesquiterpenes that interact with GABA-A receptors, increasing synaptic GABA availability and promoting relaxation (27). Valerian has shown to improve sleep latency and quality, especially in individuals with mild to moderate insomnia (26,27). Though generally safe, some users report gastrointestinal discomfort or vivid dreams. Importantly, its effects are cumulative, requiring consistent use over several weeks for optimal benefit.

Mechanism of action

Valerian root enhances GABA activity by inhibiting its breakdown and reuptake, leading to reduced neuronal excitability and increased sleep readiness (27). Isovalerate components may also act on adenosine A₁ receptors, which are involved in sleep promotion. This dual mechanism highlights valerian's role in promoting both onset and maintenance of sleep. Compared to pharmacological sedatives, valerian exhibits a more favorable side-effect profile, making it suitable for long-term use under clinical guidance.

Table 1: Phytochemical Profile and Sleep-Modulating Effects of Selected Herbal Remedies for Insomnia

Latin And Common Name	Known chemical Components	Known effect on sleep	Target	Reference
<i>Valeriana officinalis</i> L. (Valerian)	Alkaloids, valerenic acid, terpenes, organic acids and their derivatives, and flavones	Reduces sleep latency, Improves subjective measures	GABA receptors	(Lanje et al., 2020)
<i>Passiflora incarnate</i> (Passionflower)	Apigenin, alkaloids, flavones	Reduces sleep latency, improves sleep duration	GABA receptors	(Ingale & Hivrale, 2010)
<i>Withania somnifera</i> L. (Indian gingseng)	Withanolide A, withaferin A	Reduces sleep latency, improves sleep quality, increased (REM) and (NREM) sleep	GABA receptors	(Kulkarni & Dhir, 2008)
<i>Melissa officinalis</i> L. (Lemon balm)	Rosmarinic acid, caffeic acids, chlorogenic acid and metrillic acid	Improves sleep quality, anxiolytic effect	Decreases level of GABA transaminase	(Ghazizadeh et al., 2021)
<i>Ginkgo biloba</i> L. (Ginkgo)	Ginkgotoxin, Ginkgo flavonglycosides, ginkgo-terpenoid lactones	Improves subjective sleep quality measures	Inhibition of GAD activity	(Alsmadi et al., 2018)
<i>Hypericun perforatum</i> L. (St. John’s Wort)	Hypericin, Pseudohypericin, Hyperoside, among others	Increases REM latency and deep sleep	Inhibition of GAD and GABA transporter activity	(Kholghi et al.,2022)
<i>Piper methysticum</i> (Kava-kava)	Kavapyrones, kavalactones	Decrease sleep latency, no effect on NREM sleep	GABA receptors	(Burton et al., 2023)

CRITICAL ANALYSIS AND LIMITATIONS

Despite increasing scientific interest in herbal therapies for insomnia, a critical analysis of the existing literature reveals several methodological limitations that affect the robustness and applicability of current findings. One of the most consistent issues across the reviewed studies is the small sample size, which limits the statistical power and increases the risk of Type II errors. Most clinical trials investigating valerian, chamomile, and St. John’s Wort have involved fewer than 100 participants, often recruited from single sites, thereby limiting the generalizability of the results to broader populations (15,16). Additionally, a significant number of these studies adopt observational or quasi-experimental designs, which, while useful in hypothesis generation, do not provide the level of evidence yielded by randomized controlled trials (RCTs). Among the studies that do employ RCT methodologies, further concerns emerge regarding methodological rigor. Many trials lack blinding or use inadequate placebos, increasing the risk of performance and detection bias. For instance, in trials evaluating chamomile’s efficacy for sleep improvement, participants were often aware of the intervention, which may have influenced subjective outcome measures such as sleep latency and quality (17). Furthermore, short intervention periods—often lasting only one to four weeks—fail to capture the long-term effects and sustainability of treatment outcomes, especially important in chronic insomnia cases that may require extended management strategies (18).

Another critical concern is the variability in outcome measurements used across studies. Some trials rely solely on self-reported sleep diaries or questionnaires like the Pittsburgh Sleep Quality Index (PSQI), while others incorporate objective measures such as actigraphy or polysomnography. These inconsistencies hinder direct comparison and synthesis of results across studies. Subjective reports, although

valuable for assessing perceived benefit, are susceptible to placebo effects and recall bias, particularly in open-label designs or when participants have strong preconceptions about herbal remedies (19). Objective measurements, though more accurate, are used less frequently due to cost and logistical constraints, thereby reducing the methodological quality of many investigations. The literature is also affected by considerable heterogeneity in the dosage forms, concentrations, and preparations of herbal products. For example, studies on valerian have used varying doses ranging from 160 mg to 600 mg, with differing extraction techniques and formulations, such as capsules, teas, or tinctures (20). This lack of standardization complicates the interpretation of results and raises questions about reproducibility and clinical applicability. Moreover, many studies do not report the precise chemical composition or batch consistency of herbal preparations, making it difficult to identify which constituents are responsible for the therapeutic effects.

Potential publication bias further compounds the challenge, as studies with positive findings are more likely to be published, especially in the field of complementary and alternative medicine. The underreporting of negative or inconclusive results limits the ability to form a balanced view of the efficacy and safety of these interventions. Systematic reviews often highlight this concern, noting a skewed distribution of studies favoring herbal efficacy, which may not reflect the full scope of existing evidence (21). Generalizability remains another important limitation. Many trials focus on highly specific populations, such as women with menopausal symptoms or individuals with mild insomnia, excluding patients with comorbid medical or psychiatric conditions. As a result, the applicability of findings to more diverse and clinically complex populations remain uncertain (22). Furthermore, cultural and geographic differences in herbal usage, availability, and preparation may influence both the pharmacodynamics and therapeutic outcomes, necessitating region-specific investigations that are currently lacking. In summary, while herbal treatments like valerian, chamomile, and St. John's Wort show promise as complementary therapies for insomnia, the current body of literature is constrained by methodological weaknesses, limited sample sizes, inconsistencies in outcome measures, and potential bias. Future research must prioritize well-designed, large-scale RCTs with standardized formulations and rigorous outcome assessments to draw definitive conclusions regarding efficacy and safety.

IMPLICATIONS AND FUTURE DIRECTIONS

The findings of this review hold meaningful implications for clinical practice, especially in the context of managing insomnia with integrative and patient-centered approaches. Herbal remedies such as valerian root, chamomile, and St. John's Wort have shown promising potential in improving sleep quality and reducing symptoms of insomnia, particularly in patients seeking alternatives to conventional pharmacologic treatments. Clinicians can consider these therapies as adjuncts to cognitive behavioral therapy or as initial options in patients with mild insomnia or those who are contraindicated for sedative medications. However, it is crucial that such recommendations be individualized, taking into account patient comorbidities, concurrent medications, and the risk of herb-drug interactions, particularly with St. John's Wort, which has well-documented effects on cytochrome P450 enzymes and can reduce the efficacy of various prescribed medications (23). From a policy perspective, the evidence underscores the necessity for formal clinical guidelines that include evidence-based use of herbal therapies in the treatment of insomnia. While current insomnia guidelines emphasize pharmacologic and cognitive behavioral interventions, the inclusion of standardized herbal options, backed by well-conducted trials, could expand therapeutic choices and improve accessibility, especially in regions where traditional medicine plays a significant role in healthcare delivery. Regulatory bodies and public health agencies should also prioritize the quality control and standardization of herbal supplements to ensure consistency in composition, safety, and efficacy. This is particularly important given the current market variability in dosing and purity of over-the-counter herbal preparations (24).

Despite the promising results, there remain considerable gaps in the literature that warrant further exploration. A major limitation across existing studies is the absence of large-scale, multi-center randomized controlled trials that assess the long-term safety and efficacy of these herbal interventions. The current reliance on small sample sizes, short durations, and heterogeneous outcome measures restricts the ability to draw definitive conclusions and hampers integration into mainstream clinical guidelines. Moreover, there is limited understanding of the pharmacokinetic and pharmacodynamic interactions of these herbal agents when used in combination with conventional medications, an area that holds particular relevance in polypharmacy-prone populations such as the elderly (25). Future research should aim to address these gaps through rigorously designed randomized controlled trials that incorporate adequate sample sizes, diverse populations, and standardized herbal preparations. Trials should prioritize methodological improvements such as double-blinding, placebo control, and objective sleep measurements including actigraphy or polysomnography, which would enhance the credibility of findings and allow for reproducibility across settings (26). Additionally, dose-response studies and pharmacovigilance programs are essential to better understand optimal dosing regimens and potential adverse effects. Comparative effectiveness trials between herbal and conventional therapies could further clarify their relative benefits and inform clinical decision-making.

Emerging areas of interest also include the use of herbal agents in insomnia comorbid with psychiatric or chronic medical conditions. Given the high prevalence of sleep disturbances in populations with anxiety, depression, and chronic pain, targeted trials in these cohorts may yield valuable insights into the broader therapeutic scope of herbal treatments (27). Furthermore, advances in molecular pharmacology may enable better identification of active constituents within herbal compounds and their specific mechanisms of action, supporting the development of novel, plant-derived pharmacotherapeutics for sleep disorders. In summary, this review not only highlights the therapeutic potential of herbal treatments for insomnia but also emphasizes the urgent need for structured, high-quality research to translate traditional knowledge into clinically actionable strategies. The incorporation of herbal remedies into evidence-based insomnia management may ultimately contribute to more holistic and patient-aligned models of care.

CONCLUSION

Herbal treatments have emerged as promising nonpharmacological alternatives for managing sleep disorders such as insomnia, anxiety, and depression, offering favorable safety profiles and minimal side effects compared to conventional drug therapies. This review highlights that, herbs like valerian root, chamomile, and St. John’s Wort demonstrate beneficial effects on sleep latency, quality, and emotional regulation, primarily through their interaction with neurotransmitter systems such as GABA and serotonin. However, the strength of existing evidence remains moderate due to limitations in study design, small sample sizes, and inconsistent outcome measures. Despite their widespread availability in various formulations, the lack of standardization and regulatory oversight continues to challenge their clinical integration. Therefore, it is essential for future research to prioritize high-quality randomized controlled trials with clearly defined dosages, long-term follow-ups, and both objective and subjective sleep assessments. Clinicians should remain informed about potential herb-drug interactions and individualize treatment plans accordingly, while researchers must continue exploring these natural therapies with scientific rigor to establish their role in evidence-based insomnia management.

AUTHOR CONTRIBUTION

Author	Contribution
Zikhata Amina Alleza*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Rai Muhammad Amir	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published

REFERENCES

1. Ahmad, S., Azhar, A., Tikmani, P., Rafique, H., Khan, A., Mesiya, H., & Saeed, H. (2022). A randomized clinical trial to test efficacy of chamomile and saffron for neuroprotective and anti-inflammatory responses in depressive patients. *Heliyon*, 8(10), e10774.

2. Ahmad, S. B., Ali, A., Bilal, M., Rashid, S. M., Wani, A. B., Bhat, R. R., & Rehman, M. U. (2023). Melatonin and health: Insights of melatonin action, biological functions, and associated disorders. *Cellular and Molecular Neurobiology*, 1–22.

3. Alsmadi, A. M., Tawalbeh, Loai. Issa., Gammoh, O. S., Shawagfeh, M. Q., Zalloum, W., Ashour, A., & Attarian, H. (2018). The effect of Ginkgo biloba and psycho-education on stress, anxiety and fatigue among refugees. *Proceedings of Singapore Healthcare*, 27(1), 26–32.

4. Amsterdam, J. D., Li, Q. S., Xie, S. X., & Mao, J. J. (2020). Putative antidepressant effect of chamomile (*Matricaria chamomilla* L.) oral extract in subjects with comorbid generalized anxiety disorder and depression. *The Journal of Alternative and Complementary Medicine*, 26(9), 815–821.

5. Barbato, G. (2021). REM sleep: an unknown indicator of sleep quality. *International journal of environmental research and public health*, 18(24), 12976.

6. Burton, N., Sneed, K., & Pathak, Y. (2023). *Systemic Review of the Use of Kava Kava for the Reduction of Anxiety Disorder*.
7. Calvert, M. E., Molsberry, S. A., Kangarloo, T., Amin, M. R., Genty, V., Faghih, R. T., Klerman, E. B., & Shaw, N. D. (2022). Acute sleep disruption does not diminish pulsatile growth hormone secretion in pubertal children. *Journal of the Endocrine Society*, 6(11), 146.
8. Chaput, J. P., Dutil, C., Featherstone, R., Ross, R., Giangregorio, L., Saunders, T. J., ... & Carrier, J. (2020). Sleep duration and health in adults: an overview of systematic reviews. *Applied Physiology, Nutrition, and Metabolism*, 45(10), S218-S231.
9. Chennaoui, M., Leger, D., & Gomez-Merino, D. (2020). Sleep and the GH/IGF-1 axis: Consequences and countermeasures of sleep loss/disorders. *Sleep medicine reviews*, 49, 101223.
10. Chan, N. Y., Chan, J. W. Y., Li, S. X., & Wing, Y. K. (2021). Non-pharmacological approaches for management of insomnia. *Neurotherapeutics*, 18(1), 32-43.
11. Ingale, A. G., & Hivrale, A. U. (n.d.). Pharmacological studies of *Passiflora* sp. and their bioactive compounds. *African Journal of Plant Science*.
12. Kulkarni, S. K., & Dhir, A. (2008). *Withania somnifera*: An Indian ginseng. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 32(5), 1093–1105.
13. Ghazizadeh, J., Sadigh-Eteghad, S., Marx, W., Fakhari, A., Hamedeyazdan, S., Torbati, M., Taheri-Tarighi, S., Araj-khodaei, M., & Mirghafourvand, M. (2021). The effects of lemon balm (*Melissa officinalis* L.) on depression and anxiety in clinical trials: A systematic review and meta-analysis. *Phytotherapy Research*, 35(12), 6690–6705.
14. Grandner, M. A., & Fernandez, F. X. (2021). The translational neuroscience of sleep: a contextual framework. *Science*, 374(6567), 568-573.
15. Guadagna, S., Barattini, D. F., Rosu, S., & Ferini-Strambi, L. (2020). Plant extracts for sleep disturbances: A systematic review. *Evidence-Based Complementary and Alternative Medicine*, 2020.
16. Hauri, P. J. (2021). Sleep disorders. In *Handbook of psychology and health* (pp. 211–260). Routledge.
17. Knoop, M. S., de Groot, E. R., & Dudink, J. (2021). Current ideas about the roles of rapid eye movement and non-rapid eye movement sleep in brain development. *Acta Paediatrica*, 110(1), 36-44.
18. Kovalzon, V. M. (2021). Serotonin, sleep and depression: A hypothesis. *Serotonin and the CNS-New Developments in Pharmacology and Therapeutics*.
19. Kholghi, G., Arjmandi-Rad, S., Zarrindast, M. R., & Vaseghi, S. (2022). St. John's wort (*Hypericum perforatum*) and depression: what happens to the neurotransmitter systems. *Naunyn-Schmiedeberg's Archives of Pharmacology*, 395(6), 629-642.
20. Law, R., & Clow, A. (2020). Stress, the cortisol awakening response and cognitive function. *International review of neurobiology*, 150, 187-217.
21. Lanje, C. N., Patil, S. R., & Wankhade, A. M. (2020). Medicinal natural drug of Valerian (*Valeriana Officinalis*): An-over review. *Am J PharmTech Res*, 10(01), 148–173.
22. Lightman, S. L., Birnie, M. T., & Conway-Campbell, B. L. (2020). Dynamics of ACTH and cortisol secretion and implications for disease. *Endocrine reviews*, 41(3), bnaa002.
23. Manzar, M. D., Salahuddin, M., Pandi-Perumal, S. R., & Bahammam, A. S. (2021). Insomnia may mediate the relationship between stress and anxiety: a cross-sectional study in university students. *Nature and Science of Sleep*, 31-38.
24. Madari, S., Golebiowski, R., Mansukhani, M. P., & Kolla, B. P. (2021). Pharmacological management of insomnia. *Neurotherapeutics*, 18, 44-52.
25. Morin, C. M., & Jarrin, D. C. (2022). Epidemiology of insomnia: prevalence, course, risk factors, and public health burden. *Sleep Medicine Clinics*, 17(2), 173-191.
26. Nicolussi, S., Drewe, J., Butterweck, V., & Meyer zu Schwabedissen, H. E. (2020). Clinical relevance of St. John's wort drug interactions revisited. *British journal of pharmacology*, 177(6), 1212-1226.
27. Jiang, J., Li, Z., Li, H., Yang, J., Ma, X., & Yan, B. (2024). Sleep architecture and the incidence of depressive symptoms in middle-aged and older adults: A community-based study. *Journal of Affective Disorders*.