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The Impact of Cannabidiol (CBD) on Sleep Quality: A Review of Mechanisms and Clinical Evidence

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ABSTRACT

Cannabidiol (CBD), a non-psychoactive component of Cannabis sativa, has garnered significant interest as a potential therapeutic agent for sleep disturbances. This review synthesizes preclinical and clinical evidence on the effects of CBD on sleep parameters, including sleep architecture, quality, and disorders such as insomnia and REM sleep behavior disorder (RBD). Preclinical studies reveal that CBD modulates sleep architecture in a dose- and region-dependent manner, influencing both slow-wave and REM sleep. These effects are mediated through complex interactions with the endocannabinoid, adenosinergic, serotonergic, dopaminergic, and GABAergic systems. Clinical trials suggest that low to moderate doses of CBD may modestly improve subjective sleep quality, particularly in individuals with co-occurring anxiety or chronic pain, although its efficacy is generally comparable to melatonin. High-dose CBD may enhance restorative sleep stages, yet the benefits are limited and inconsistently sustained. CBD demonstrates a favorable safety profile, though methodological limitations—such as small sample sizes, short follow-up durations, and product variability—impede definitive conclusions. Further research with standardized formulations, objective sleep measurements, and larger populations with diagnosed sleep disorders is needed to fully assess the therapeutic potential and clinical application of CBD for sleep-related conditions.

Keywords: Cannabidiol (CBD), Insomnia, Sleep Quality, REM Sleep, Slow-Wave Sleep, Clinical Trials, Endocannabinoid System

1. Introduction: Sleep Quality and the Role of CBD

1.1 Background on Sleep and Its Importance

Sleep is a vital, evolutionarily conserved behavior necessary for survival and optimal health. It constitutes approximately one-third of the human lifespan and plays a crucial role in neurobiological, psychological, and physiological functioning. During sleep, the brain and body engage in critical processes such as energy restoration, synaptic pruning, cellular repair, memory consolidation, emotional regulation, and toxin clearance via the glymphatic system(1,2). Sleep occurs in cycles composed of non-rapid eye movement (NREM) and rapid eye movement (REM) stages. Each stage serves specific restorative functions; for example, deep NREM sleep is associated with physical recovery and growth hormone release, while REM sleep supports cognitive processing, learning, and emotional resilience (1,2). The circadian rhythm, governed by the suprachiasmatic nucleus (SCN) in the hypothalamus, coordinates the sleep-wake cycle with environmental light-dark cues. Cortisol levels rise in the early morning, facilitating wakefulness, while melatonin is released in response to darkness, promoting sleep onset. Disruption in this balance can significantly impair the initiation and maintenance of healthy sleep (2,3). Ancient medical systems, such as Ayurveda, also emphasize the alignment of sleep with natural cycles. Texts such as the Kaiyadeva Nighantu recommend sleeping after the first two Yamas (approximately six hours after sunset) and rising before sunrise, highlighting a pre-scientific understanding of circadian harmony (1).

1.2. Prevalence and Consequences of Poor Sleep Quality

Despite its vital importance, sleep disturbances and chronic sleep deprivation are increasingly prevalent in modern society. Epidemiological data show that approximately 70 million people in the United States and 45 million in Europe suffer from chronic sleep disorders, including insomnia, sleep apnea, and circadian rhythm disruptions (3,4). In adults, the causes of poor sleep are multifactorial and include long work hours, shift work, stress, and underlying health conditions. In adolescents, excessive screen time and social media use are major contributing factors, while in children, environmental instability, familial stress, and safety concerns play substantial roles (1,3). The health consequences of inadequate sleep are profound. Short-term effects include reduced cognitive performance, emotional dysregulation, impaired memory, increased pain sensitivity, and heightened stress responsivity (2,4). Long-term sleep deprivation is associated with numerous chronic conditions, including cardiovascular disease (e.g., hypertension, atherosclerosis), metabolic disorders such as insulin resistance, obesity, and type 2 diabetes, mood disorders including depression and anxiety, immune dysfunction and increased systemic inflammation, and increased cancer risk, particularly colorectal and prostate cancers in shift workers (2,4).

Mechanistically, chronic sleep disruption activates the sympathetic nervous system and the hypothalamic–pituitary–adrenal (HPA) axis, leading to increased catecholamines, elevated cortisol, and proinflammatory cytokine release (2,4). Furthermore, circadian misalignment caused by artificial light exposure at night suppresses melatonin, which not only regulates sleep but also possesses oncostatic properties, such as DNA repair and antioxidant activity. Animal studies have shown that destruction of the SCN accelerates malignant tumor growth, highlighting the role of circadian coordination in tumor suppression (4).

The economic and social costs of short sleep are also significant, including increased workplace accidents, reduced productivity, and heightened healthcare expenditures (4).

1.3. Overview of Cannabidiol (CBD) and Its Rise in Use as a Sleep Aid

Cannabidiol (CBD), a phytocannabinoid derived from Cannabis sativa, has emerged as a promising therapeutic agent for a variety of health conditions, including sleep disorders. Unlike delta-9-tetrahydrocannabinol (THC), CBD is non-intoxicating and has a favorable safety profile, making it attractive for both clinical and over-the-counter use (5,6). Over the past two decades, public and scientific interest in CBD has surged due to its broad pharmacological properties. Preclinical and early clinical studies suggest that CBD exhibits anxiolytic, antidepressant, neuroprotective, anti-inflammatory, and immunomodulatory effects (5,7). These properties make CBD a compelling candidate for managing sleep disturbances, particularly those secondary to anxiety or chronic stress. The endocannabinoid system (ECS), which includes CB1 and CB2 receptors, endogenous ligands (anandamide and 2-AG), and associated enzymes, plays a central role in regulating sleep homeostasis, circadian rhythms, stress responses, and arousal(5,7). Recent clinical trials and pilot studies have explored CBD's effect on sleep quality, REM sleep, sleep latency, and maintenance. A 4-week randomized, placebo-controlled, crossover trial in chronic insomnia patients showed improvements in sleep quality, sleep stages, and daytime alertness following sublingual administration of CBD at a dose of 1 mg/kg. No signs of withdrawal or dependency were reported, which further supports its clinical viability (8,9). Moreover, a meta-analysis of 34 studies found that the majority reported improvements in insomnia symptoms, with CBD-dominant therapies showing positive outcomes in both subjective and objective sleep metrics(10). Still, inconsistencies in dosage, study design, and CBD:THC ratios call for more rigorous, large-scale trials (10,11). The "CANSLEEP" trial protocol describes ongoing efforts to further evaluate CBD and THC's role in chronic insomnia treatment, highlighting the need for standardized clinical research (11).

1.4. Objectives and Structure of the Study

The primary objective of this review is to provide a comprehensive and evidence-based examination of the potential role of cannabidiol (CBD) in modulating sleep quality. As growing interest in non-pharmacological and natural interventions for sleep disorders continues, it is critical to synthesize current knowledge on the biological mechanisms through which CBD may influence sleep regulation, as well as to evaluate the strength and limitations of clinical data supporting its use (5,10).

This review aims to:

- Explore the physiological basis of sleep and the pathological consequences of poor sleep quality

- Examine the endocannabinoid system's involvement in sleep regulation and the pharmacological mechanisms of CBD
- Evaluate preclinical and clinical evidence on CBD's effects on sleep outcomes
- Assess the therapeutic potential, safety profile, and comparative efficacy of CBD versus conventional sleep aids
- Identify key research gaps and propose future directions to improve the clinical application of CBD in sleep medicine

To address these aims, the study is organized into four main sections:

Section 1 (Introduction): Provides background information on the importance of sleep, the rising prevalence of sleep disorders, and introduces CBD as a potential therapeutic agent.

Section 2 (Biological Mechanisms): Describes the physiological and neurochemical pathways by which CBD may affect sleep, including its interactions with the endocannabinoid system, stress-related mechanisms, neurotransmitters, and inflammatory pathways.

Section 3 (Evidence-Based Evaluation): Reviews the current body of preclinical and clinical research on CBD and sleep, with an emphasis on study design, outcome measures, dosage considerations, and methodological limitations.

Section 4 (Clinical Relevance and Future Perspectives): Discusses the practical implications of CBD in the treatment of sleep disturbances, compares its efficacy with standard treatments, and outlines future directions for clinical research and regulatory standardization.

This structured review is intended to serve as a resource for clinicians, researchers, and healthcare professionals seeking an in-depth understanding of the potential role of CBD in improving sleep quality across diverse populations.

2. Biological Mechanisms Linking CBD to Sleep Quality

2.1. The Endocannabinoid System and Sleep Regulation

The endocannabinoid system (ECS), integrating a network of endogenous lipids such as anandamide (AEA) and 2-arachidonoylglycerol (2-AG), along with cannabinoid receptors CB1 and CB2 and associated metabolic enzymes, is increasingly recognized as an important regulator of the sleep–wake cycle (12,13).

While activation of the ECS can promote the release of wake-promoting neurotransmitters, its broader involvement in circadian regulation is supported by evidence that sleep disruption impairs ECS function, whereas enhanced ECS receptor activity facilitates the recovery of stable sleep patterns following such disturbances. (14,15).

Anandamide and 2-arachidonoylglycerol act mainly via CB1 receptors (CB1R) distributed in brain areas critical for sleep regulation, including pons and basal forebrain, where they may modulate cholinergic neurons involved in sleep induction (13). AEA exhibits circadian fluctuations, with highest plasma levels observed upon waking and lowest levels before sleep onset (16).

Individual cannabinoids like THC and CBD may have distinct effects (15). THC typically has sedative effects in the short term and may reduce sleep onset latency. However, chronic use has been associated with reduced efficacy, tolerance, disrupted circadian rhythms, and adverse

effects such as daytime sleepiness and mood alterations (14,16). Cannabidiol (CBD), a non-intoxicating cannabinoid compound, exerts dose-dependent effects on sleep. While low doses tend to have alerting properties, medium to high doses have been linked to sedative outcomes, including increased total sleep and changes in REM sleep latency in animal studies and early human trials (13,14).
Despite emerging evidence supporting the ECS's role in sleep modulation, research on the isolated effects of cannabinoids, particularly CBD, remains in early stages, with limited clinical data and inconsistent findings.

2.2 CBD's Effects on Anxiety, Stress, and Relaxation

Anxiety and stress are natural adaptive mechanisms triggered by perceived threats. However, when prolonged or excessive, they may contribute to development and progression of various mental health disorders (17,18). ECS is an important regulator of the stress response, influencing mood, appetite, pain perception, and promoting a state of relaxation (17,19).
Cannabidiol exhibits anxiolytic effects (20–22). Its anxiolytic actions involve CB1 receptors and 5-HT1A receptors in several brain regions (20). Endocannabinoids, such as N-arachidonoylethanolamine and 2-arachidonoylglycerol, are crucial in regulating the stress response (19). The CB1R is thought to inhibit the hypothalamic-pituitary-adrenal (HPA) axis, which is central to neuroendocrine stress responses (17,19). While low doses of CB1R agonists, including AEA, can be anxiolytic, higher doses may become ineffective or even anxiogenic due to the activation of TRPV1 receptors. CBD itself acts as a TRPV1 agonist at high concentrations, possibly by interfering with AEA inactivation (20). Stress rapidly decreases AEA levels, reducing the inhibitory tone on the HPA axis, while increased cortisol levels stimulate 2-AG production, which then provides negative feedback to the HPA axis, facilitating stress response termination. Chronic stress can lead to decreased CB1 expression, reducing feedback inhibition on the HPA axis (17).

2.3 Neurochemical Pathways

Cannabidiol exerts its neuropsychopharmacological effects through multiple neurochemical pathways, including the serotonergic system and GABA-ergic signaling. It enhances GABA-ergic transmission by acting as a positive allosteric modulator of GABAA receptors, thereby increasing inhibitory synaptic tone. Since dysfunction of GABAA receptors is implicated in several psychiatric disorders, this mechanism may contribute to CBD's therapeutic potential (23). Although further research is needed to clarify its effects in human epileptic tissue, existing evidence suggests that CBD regulates central nervous system excitability through both presynaptic and postsynaptic GABAergic mechanisms (24).
In parallel, CBD influences serotonergic signaling through multiple pathways. It functions as both orthosteric agonist and allosteric modulator of 5-HT1A receptors, with activation of postsynaptic receptors in limbic areas associated with anxiolytic and antidepressant effects. CBD additionally acts as a 5-HT3A receptor antagonist, which has been linked to neuroprotective and mood-regulating outcomes (23). Proposed mechanisms include enhanced serotonin release, inhibition of reuptake, and elevation of anandamide levels (25,26). One hypothesis suggests that CBD inhibits excitatory 5-HT3A receptors located on GABAergic interneurons, leading to disinhibition of serotonergic neurons in a way that resembles rapid antidepressant action observed with ketamine (23). CB1 receptors may also play a role in modulating serotonergic activity (13,19,25).

2.4 Anti-inflammatory and Analgesic Effects Supporting Restful Sleep

Cannabidiol demonstrates promising anti-inflammatory and analgesic properties, potentially aiding in restful sleep (13,20). Some evidence suggests that CBD has an ability to alleviate

various types of pain, including neuropathic and arthritis-related discomfort. (27). Nevertheless, effects can vary depending on the model and sometimes require co-administration with other compounds, f.e. THC, for enhanced efficacy. However, not all studies support this benefits, with some reporting no significant analgesic effects of CBD (28).
CBD appears to combat inflammation through several pathways. One key mechanism involves its ability to modulate microglia activation, which it might achieve via CB2-mediated pathways or by activating PPARγ (23). Beyond that, CBD can also shift the redox balance by impacting the levels and activity of antioxidants. This antioxidant effect often begins at the genetic level, as CBD activates Nrf2, a redox-sensitive transcription factor responsible for the transcription of antioxidant genes. Evidence from clinical studies further supports CBD's anti-inflammatory actions. These studies have shown it can reduce levels of pro-inflammatory cytokines, slow down T cell proliferation, and decrease the adhesion of immune cells genes (26,29). CBD's interaction with CB2 receptors can indirectly boost its anti-inflammatory effects by lowering reactive oxygen species (ROS) and TNF-α levels, thereby easing oxidative stress and inflammation. Additionally, CBD's influence on mammalian transient receptor potential (TRP) channels also plays a role in its impact on both redox balance and inflammation (26). Together, these anti-inflammatory and analgesic effects help reduce discomfort and physiological stress, promoting improved sleep quality and restorative rest.
Although CBD's broad pharmacological profile is well recognized, the precise mechanisms underlying its therapeutic effects remain under active investigation (24,25,30). This is particularly true in the context of sleep, where CBD's multifaceted influence on neurochemical signaling, stress modulation, and inflammation suggests potential benefits for sleep quality, yet requires further elucidation through rigorous research.

3. Evidence-Based Evaluation of CBD and Sleep Quality

3.1. Preclinical Findings Related to Sleep Parameters

Cannabidiol (CBD) has been widely investigated in preclinical studies for its role in sleep regulation. Animal research consistently demonstrates that CBD can influence sleep architecture, particularly affecting the duration and quality of slow-wave sleep (SWS) and rapid eye movement (REM) sleep, with outcomes dependent on dose, timing, and neural circuitry involved.(31,32)
Acute systemic administration of CBD in rodents has been shown to significantly alter sleep patterns.(32) For instance, doses of 10 and 40 mg/kg administered during the light phase increased total sleep time, with the higher dose also showing a tendency to prolong SWS.(32) Notably, 40 mg/kg CBD delayed REM sleep onset, while 10 mg/kg reduced REM latency on the following day, illustrating dose- and time-dependent effects on sleep stages. (32)
Additional studies indicate that CBD can modulate non-REM sleep oscillations, such as delta waves and sleep spindles, which are essential for sleep quality and memory consolidation. (33)
The site of CBD administration within the brain further shapes its impact. Direct infusion into the lateral hypothalamus has been linked to increased wakefulness and decreased REM and SWS, while intracerebroventricular administration also elevated wakefulness and reduced REM sleep, underscoring the importance of specific brain regions in mediating CBD's sleep effects. (32,34)
In models of stress- or anxiety-related sleep disturbances, CBD has been shown to prevent anxiety-induced suppression of REM sleep, suggesting that its anxiolytic actions may indirectly benefit sleep architecture. (20,35)
Mechanistically, CBD's effects are thought to involve multiple neurotransmitter systems, including the endocannabinoid and adenosinergic pathways. By altering the balance between

excitatory and inhibitory signaling and modulating brain oscillatory activity, CBD can affect both the duration and quality of various sleep stages. (20,31)
Overall, recent preclinical evidence supports CBD's ability to modulate sleep architecture, particularly by enhancing or restoring SWS and REM sleep under certain conditions, through complex interactions with the endocannabinoid, serotonergic, dopaminergic, and GABAergic systems.(14,20) Its capacity to counteract anxiety-related disturbances in REM sleep highlights potential therapeutic applications. (20,35) Nonetheless, the diversity and complexity of these findings emphasize the need for further research to elucidate underlying mechanisms and determine clinical relevance.

3.2. Clinical Trials and Human Studies Measuring Sleep Quality Outcomes

Cannabidiol (CBD) has emerged as a promising agent for the management of various sleep disturbances. Recent clinical research has explored its effects across a spectrum of sleep-related conditions, including insomnia, sleep disturbance, and REM sleep behavior disorder (RBD), with a focus on both efficacy and safety.(14)
Randomized controlled trials (RCTs) have been instrumental in establishing the preliminary efficacy of CBD in the management of insomnia and related sleep disturbances. For example, a study conducted by Narayan et al. enrolled 30 adult participants diagnosed with moderate to severe insomnia and randomized them to receive either 150 mg of CBD or a matching placebo, administered nightly over a two-week period.(36) Throughout the intervention, both objective sleep parameters such as sleep-onset latency, sleep efficiency, and wake after sleep onset and subjective measures of well-being were systematically assessed using validated tools.(36) The double-blind design ensured that neither participants nor investigators were aware of treatment allocation, thereby minimizing potential bias.(36) The results of this trial indicated that short-term administration of CBD may be associated with improvements in sleep quality and certain insomnia symptoms.(36) However, it is important to note that the relatively small sample size and brief duration of the intervention limit the ability to draw definitive conclusions regarding long-term efficacy or generalizability to broader populations.(36)
To address some of these limitations, larger-scale clinical trials have been conducted to compare the effectiveness of CBD with other common sleep aids. In a randomized controlled trial enrolling 1,793 adults experiencing symptoms of sleep disturbance, participants were randomized to receive a four-week supply of one of six oral capsule products.(37) These included a 15 mg CBD isolate, 5 mg melatonin, and combinations of CBD with minor cannabinoids such as cannabinol (CBN) and cannabichromene (CBC).(37) Sleep quality was assessed weekly using validated questionnaires.(37) All formulations, including pure CBD, demonstrated a favorable safety profile, with only 12% of participants reporting mild side effects and no severe adverse events were observed.(37) Statistically significant improvements in sleep disturbance were observed within all groups, with between 56% and 75% of participants experiencing clinically meaningful benefits.(37) Notably, the effect of 15 mg CBD isolate did not surpass that of 5 mg melatonin, and the addition of CBN or CBC to CBD did not enhance sleep improvement.(37) These findings suggest that while chronic use of low-dose CBD appears safe and may improve subjective sleep quality, its efficacy is comparable to that of low-dose melatonin, and the inclusion of other minor cannabinoids does not provide additional therapeutic advantage.(37)
The impact of CBD on sleep architecture appears to be dose-dependent.(14) Lower doses have been associated with stimulating effects, while medium to high doses exhibit sedative properties.(14) A double-blind, placebo-controlled crossover trial in 125 adults with insomnia evaluated a 300 mg oral CBD and terpene formulation (THC-free) over four weeks.(38) The intervention produced a modest but statistically significant increase in the percentage of time spent in slow-wave and REM sleep, particularly in individuals with low baseline restorative

sleep.(38) For some individuals, this translated to as much as 48 additional minutes of SWS and REM sleep per night.(38) However, there was no significant effect on total sleep time or cardiovascular parameters, and no adverse events were reported.(38)

CBD has also been explored as a potential treatment for REM sleep behavior disorder, particularly in patients with Parkinson's disease, where RBD is a common and often distressing non-motor symptom.(39) In a phase II/III, double-blind, placebo-controlled clinical trial involving 33 patients with both RBD and Parkinson's disease, participants were randomized to receive CBD in doses ranging from 75 to 300 mg or matched placebo capsules, with follow-up for 14 weeks.(39) The use of 300 mg CBD nightly for 12 weeks did not significantly reduce the frequency of RBD episodes or improve global clinical impressions compared to placebo.(39) However, a transient improvement in sleep satisfaction was observed early in the trial, suggesting that some patients may experience short-term benefits, although these effects were not sustained over the longer follow-up period.(39)

In addition to controlled clinical trials, observational studies and retrospective chart reviews have provided valuable real-world insights into the use of CBD for sleep and anxiety in psychiatric populations. For instance, a retrospective review of 72 adult psychiatric outpatients treated with CBD for anxiety or sleep complaints found that nearly all patients received 25 mg of CBD daily in capsule form, with dosing adjusted based on whether anxiety or sleep was the primary concern.(40) Sleep quality was monitored using the Pittsburg Sleep Quality Index, while anxiety was assessed with the Hamilton Anxiety Rating Scale at monthly visits.(40) The results indicated that while 66.7% of patients reported improved sleep scores within the first month, these improvements fluctuated and were not consistently sustained over three months.(40) In contrast, anxiety scores showed a larger and more sustained decrease, suggesting that CBD may be more effective for anxiety than for sleep in this population.(40) Adverse effects were minimal, with fatigue being the most commonly reported side effect.(40)

In summary, the current body of clinical evidence suggests that CBD is generally safe and well tolerated when used for sleep disturbances, with most studies reporting only mild and transient side effects.(14) While CBD may offer modest improvements in subjective sleep quality, particularly in the short term, its efficacy does not appear to exceed that of low-dose melatonin, and the addition of minor cannabinoids such as CBN or CBC does not enhance its effect.(37) Higher doses of CBD may positively influence restorative sleep stages, such as slow-wave and REM sleep, but the overall magnitude and durability of these effects remain limited.(38) Further large-scale, long-term studies are necessary to better define the role of CBD in the management of sleep disorders, to establish optimal dosing strategies, and to identify patient populations most likely to benefit from this intervention.(14)

3.3. Limitations of Current Research and Methodological Challenges

The study of cannabinoids in relation to sleep remains a developing field, with current research facing several important limitations that restrict the ability to draw clear conclusions.(14,41) A primary concern is the predominance of small sample sizes, which restricts the generalizability of findings and reduces statistical power.(14,20) Additionally, many studies suffer from short-term follow-up periods, limiting our understanding of the long-term effects of cannabinoid use on sleep patterns and related physiological processes.(14)

Another critical methodological challenge is the frequent lack of adequate control groups in clinical and preclinical research.(14) This absence complicates the interpretation of results and raises concerns about potential biases.(31,41) Indeed, a moderate-to-high risk of bias has been identified across much of the current literature, further undermining the reliability of reported outcomes.(31,41)

The complexity of the endocannabinoid system's role in circadian regulation suggests a theoretical basis for cannabinoids influencing sleep; however, the pharmacological actions of

various cannabinoid agents remain insufficiently characterized.(14,32,41) Current research often combines different cannabinoids, doses, timing, and routes of administration, which results in heterogeneous outcomes that are difficult to compare or replicate.(14,36) This variability underscores the necessity for future studies to systematically examine the impact of specific cannabinoid ratios, dosages, administration timing, and delivery methods to elucidate their differential effects on sleep.(14,32,36,41)

Moreover, there is a pressing need for research employing well-defined cannabinoid products alongside validated and objective measures of sleep quality, including assessments of next-day cognitive function and performance.(14,31,41) Such rigorous methodologies would help clarify the safety and efficacy profiles of cannabinoids, particularly cannabidiol (CBD), which has shown promise due to its favorable safety profile and lack of dependence potential.(31) Maintaining the uniformity and purity of cannabinoid products, especially cannabidiol (CBD), is essential to prevent interference from contaminants such as psychoactive substances.(31)

Finally, the current literature lacks sufficient replication studies and long-term investigations into chronic cannabinoid use.(14,20) This is particularly important for understanding whether ongoing use of cannabinoids like CBD can consistently reduce anxiety and improve sleep over time.(20,32) To advance the field, future research must prioritize large, well-controlled studies with extended follow-up periods, standardized cannabinoid formulations, and comprehensive assessments to fully understand the therapeutic potential and limitations of cannabinoids for sleep disorders.(14,32,36,41)

4. Clinical Relevance and Future Perspectives

The growing public interest in cannabidiol (CBD) as a sleep aid, driven by its non-psychoactive nature and wide availability, stands in contrast to the current state of clinical evidence (10,42). While preliminary findings are promising, significant gaps remain in understanding CBD's therapeutic role, safety profile, and comparative efficacy for sleep disturbances. This section will explore the clinical relevance of CBD for insomnia, compare it to existing treatments, discuss safety considerations, and outline critical directions for future research.

4.1. CBD as a Potential Therapeutic for Insomnia and Low Sleep Quality

Emerging evidence suggests that CBD may be a beneficial therapeutic agent for individuals with insomnia and poor sleep quality (10). The potential for CBD to improve sleep is often linked to its anxiolytic, anti-inflammatory, and analgesic properties, with evidence pointing toward a calming effect on the central nervous system (42,43). A large retrospective case series involving 72 adults with primary concerns of anxiety or poor sleep found that sleep scores improved in 66.7% of patients within the first month of CBD treatment, although these improvements tended to fluctuate over time (43).

More robust evidence comes from a large-scale, double-blinded, randomized controlled trial which demonstrated that chronic use (4 weeks) of a low dose of CBD (15 mg) was associated with significant improvements in sleep disturbance (42). In this study, a majority of participants (between 56% and 75%) across all CBD and melatonin formulations experienced a clinically important improvement in their sleep quality [4]. In populations with comorbid conditions, such as chronic neuropathic pain, cannabinoids have been shown to produce a significant, albeit small, improvement in sleep quality compared to placebo (44,45).

Despite these positive signals, systematic reviews of the literature conclude that there is currently insufficient evidence to support the routine clinical use of cannabinoids for any specific sleep disorder (41). This is largely because very few studies have focused on populations with a primary diagnosis of insomnia, and much of the existing research is hampered by methodological limitations (10,46).

4.2. Comparative Efficacy vs. Conventional Treatments

A significant gap in the literature is the lack of research comparing CBD to conventional treatments for insomnia (42). Standard pharmacologic interventions, particularly GABA-A receptor agonists like benzodiazepines, have strong evidence of efficacy but are accompanied by concerns over side effects such as cognitive impairment, abuse potential, and a considerable risk of dependence (42). This has spurred interest in safer therapeutic alternatives like CBD (42).

Similarly, many patients turn to complementary and alternative medicines (CAM), with melatonin being one of the most common and well-studied for improving sleep quality (42). Until recently, no clinical study had directly compared the effects of CBD and melatonin on sleep (42). A large randomized trial addressed this gap, investigating the relative effects of formulations containing 15 mg of CBD and 5 mg of melatonin (42). The findings suggest that while chronic use of low-dose CBD could improve sleep quality, its effects do not exceed that of 5 mg of melatonin (42). There were no statistically significant differences in the improvement of sleep disturbance between the CBD isolate group and the groups receiving melatonin, either alone or in combination with cannabinoids (42). Further comparative effectiveness research is needed to position CBD accurately among the array of available treatments for sleep disorders (46).

4.3. Safety, Tolerability, and Long-Term Use Considerations

CBD is generally regarded as having a favorable safety profile and being well-tolerated across a range of doses (43,46). Studies have reported good tolerability for doses up to 1500 mg per day (43). A large clinical trial found that a low daily dose of 15 mg CBD was safe, with only 12% of participants reporting any side effect, none of which were severe (42). The most frequently reported adverse events in this trial were mild cases of heartburn, diarrhea, constipation, and dizziness (42). Similarly, a large case series noted that CBD was well-tolerated in all but three of the 72 participants (43).

However, some adverse effects have been consistently associated with cannabinoid use. Meta-analyses have shown that improvements in sleep may be associated with a higher likelihood of experiencing daytime somnolence, dizziness, dry mouth, fatigue, and nausea (44,45). A primary safety consideration for clinicians is the potential for drug-drug interactions (46). CBD is a potent substrate and inhibitor of the cytochrome P450 enzymatic pathway, which is critical for the metabolism of many commonly prescribed medications (46,47). Healthcare professionals should therefore exercise caution and familiarize themselves with potential interactions relevant to a patient's medication history (46). While short-term use appears to carry a low overall risk, more research is required to clarify the possible long-term risks and harms of chronic CBD administration (43).

4.4. Future Research Directions and Standardization Needs

There is a clear and consistent call across the literature for more rigorous, large-scale, randomized, placebo-controlled trials to definitively establish the efficacy and safety of CBD for sleep disorders (10,43,46). The current body of evidence is limited by significant methodological issues, including high risk of bias, small sample sizes, a lack of control for confounding factors, and inconsistent findings (46,48).

Future research should prioritize several key areas. First, studies must focus on populations with formally diagnosed insomnia to assess direct therapeutic effects, rather than sleep as a secondary outcome to other conditions (10). Second, there is a critical need for standardization in terms of product formulation, dosage, and purity (42). Most clinical trials have evaluated high doses of CBD (300-1500 mg), whereas commercially available products contain much lower doses; the effects of these lower, more commonly used doses warrant further investigation (42). Research should also explore dose-dependent effects, as some evidence suggests a potential bell-shaped dose-response curve for CBD (42).

Third, the contribution of minor cannabinoids like cannabinol (CBN) and cannabichromene (CBC) remains unsubstantiated. A large trial found that the addition of low doses of CBN and CBC did not improve the effects of CBD or melatonin formulations, challenging marketing claims about the "entourage effect" for sleep (42). Fourth, future trials must incorporate validated objective measures of sleep, such as polysomnography or actigraphy, in addition to subjective patient-reported outcomes(10,46) . Finally, to ensure comprehensive safety assessment, studies should include measures of next-day function, including cognition and driving performance (46). Addressing these gaps is essential before definitive clinical inferences can be made and CBD can be confidently integrated into therapeutic regimens for insomnia.

CONCLUSSIONS:

CBD exhibits potential as a well-tolerated, non-addictive therapeutic option for individuals with insomnia and poor sleep quality, particularly when associated with anxiety or chronic pain. Preclinical evidence supports its role in modulating sleep architecture, while clinical studies indicate modest improvements in subjective sleep quality and minimal adverse effects. However, current findings do not establish CBD as superior to conventional agents such as melatonin, and evidence for the efficacy of added minor cannabinoids (e.g., CBN, CBC) remains weak. The lack of high-quality, long-term randomized controlled trials, combined with variability in dosing, product purity, and outcome measures, highlights the need for rigorous future research. To clarify CBD’s clinical relevance, studies must prioritize standardization, focus on insomnia as a primary condition, and incorporate both objective and subjective sleep assessments. Until such evidence is available, CBD should be considered a potentially helpful adjunct but not a first-line therapy for sleep disorders.

DISCLOSURE

AUTHOR'S CONTRIBUTION:

Conceptualization: [AM], [MK], [JP], [MJ], [AZ]

Methodology: [MK], [MJ], [DZ], [KK]

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