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Cannabidiol effects on Anxiety and Insomnia

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ΠΕΡΙΛΗΨΗ

One of the active cannabinoids in cannabis is cannabidiol (CBD), which does not cause euphoria or alter consciousness like tetrahydrocannabinol (THC) does. According to new research, CBD may be useful in treating several neuropsychiatric disorders, such as schizophrenia, anxiety, and epilepsy. Additionally, research indicates that CBD has a relaxing impact on the central nervous system. Clinical evidence in psychiatric research is still scarce, despite increased interest in its medicinal applications. According to a psychiatric clinic's retrospective analysis, CBD was used in conjunction with traditional therapies to assist in treating anxiety and sleep-related problems. In this chart analysis, 103 adult patients' monthly anxiety and sleep quality measurements were recorded.Of the sample as a whole, 72 people CBD,Anxiety,Cannabidiol, Sleep. stated that their main problems were anxiety (47%) or sleep issues (25%). 57 participants (79.2%) showed a decrease in anxiety symptoms during the first month of treatment, and this improvement continued during the observation period. Although there were some variations over time, 48 individuals (66.7%) saw an improvement in their sleep quality over the first month. Only three people reported negative effects, indicating that CBD was generally well tolerated. Although carefully planned controlled clinical trials are required to establish its efficacy and safety, these data imply that cannabidiol may offer therapeutic advantages for anxiety.

1. Introduction

A general definition of insomnia is the inability to fall asleep, stay asleep, or have restful, high-quality sleep that interferes with everyday functioning. A primary illness or a comorbidity of an underlying disorder can be insomnia. Women and the elderly are more likely to experience insomnia, which is frequently linked to physical andmental health issues[1]. Insomnia affects 8–40% of the general population,

depending on the criteria. While 20 to 30 percent of people have poor sleep (i.e., insomnia symptoms include difficulty falling or staying asleep, waking up early, or nonrestorative sleep at any time), 8 to 10 percent of the general population suffers with chronic insomnia.

About 4% of people say they regularly take hypnotic drugs to treat sleep issues. Even Nevertheless, it has only been in recent years that systematic studies of the connection between sleeplessness and severe medical comorbidities have surfaced. As such, sleeplessness and its associated psychological and physiological effects have always been considered rather peripheral issues in the public health debate[2]. Cardiovascular illness, hypertension, and diabetes are associated with chronic insomnia and reduced sleep duration[3]. One of the main cannabinoids obtained from the cannabis plant is cannabidiol (CBD), which is sold over the counter. The purpose of thisstudy was to critically examine the evidence supporting the therapeutic benefits of CBD inthe therapy of insomnia[4]. Examining the chronicity of insomnia in the general populationis an effective method for identifying the detrimental effects of the condition. A median of four years has been found for severe insomnia in population-based studies, andfive years after the disorder's onset, 88.2% of patients still report sleep disturbances[5]. Primary insomnia and its pathogenesis are starting to be more thoroughly investigated in terms of their clinical identification and scientifically confirmed associations, even though insomnia was previously considered a symptom and not a condition. Consequently, primary insomnia is becoming more often acknowledged as a separate condition. The precise etiology that distinguishes primary from secondary insomnia, as well as whether there are any shared etiological elements, such as a propensity for sleep disturbance, negative conditioning, or maladaptive behaviors and cognitions, is a significant unanswered question[6].

2. Disorders of Anxiety

Anxiety is a normal emotional reaction to perceived dangers or stressful circumstances that manifests as feelings of fear, concern, tension, or apprehension. It is a typical and adaptive response that keeps people vigilant and ready to tackle obstacles. However, anxiety can interfere with day-to-day functioning and general well-being when it becomes severe, chronic, or out of proportion to the real circumstance. Panic disorder, social anxiety disorder, generalized anxiety disorder (GAD), and certain phobias are all included in the clinical category of anxiety. Psychological symptoms like restlessness, irritation, and trouble focusing are frequently linked to these diseases, as are physical symptoms like perspiration, tense muscles, elevated heart rate, and gastrointestinal issues.

Anxiety disorders are the result of a complex interplay between genetic predisposition, neurobiological variables, environmental stressors, and psychological effects. Due to their effects on quality of life, productivity, and comorbidity with other mental and physical illnesses, anxiety disorders are among the most common mental health issues in the world and pose a serious public health concern. Early detection, efficient treatment, and the creation of preventative and therapeutic measures all depend on an understanding of the nature, causes, and symptoms of anxiety[7].

3. Understanding Insomnia

An inability to fall asleep, stay asleep, or wake up early are the hallmarks of insomnia, a common sleep condition that frequently impairs performance during the day. It typically presents as comorbid insomnia, which is when it co-occurs with other medical or mental health issues. However, insomnia can also appear on its own without accompanying physical or psychological symptoms, in which case it is referred to as primary insomnia. Chronic or persistent insomnia is linked to serious daytime effects, such as mood swings, cognitive decline, exhaustion, and excessive drowsiness, all of which can affect performance in the classroom and at work. Sleep that is not restorative, or trouble falling or staying asleep, are two symptoms of insomnia. Sleeplessness and a lower quality of life are strongly correlated, according to studies. Insomnia is frequently linked to depression

and pain,either as comorbid or secondary illnesses.

Additionally, those who suffer from sleeplessness are more likely to experience anxiety, alcohol and drug abuse, and cardiovascular disease. Research indicates that overactive arousal systems contribute to insomnia. In addition to elevated norepinephrine and catecholamine levels, patients with insomnia also have elevated heart rates, body temperatures, and metabolic rates. Sedating antidepressants, selective melatonin receptor agonists, and benzodiazepine hypnotics are pharmacologic treatments for treating insomnia[8].

3.1. Types of Insomnia

Acute insomnia is a short-term kind of insomnia that several different things can bring on. This type of brief sleep disturbance affects many people and typically resolveson its own without the need for medication. The term "chronic insomnia" refers to sleep disruptions that last for at least three months and happen at least three evenings every week. It is caused by a variety of reasons, including neurological ones, such as abnormalities in neurotransmitters that regulate sleep. The Pittsburgh Sleep Quality Index (PSQI) and the Insomnia Severity Index (ISI) are two standardized instruments that are frequently used to evaluate the degree and consequences of insomnia. In addition to non-pharmacological methods like dietary changes, like drinking milk that is high in melatonin, management options may include pharmaceutical therapies like benzodiazepines and some antidepressants[9].

1.1.1 Acute Insomnia

Despite being incorporated into several classification systems since at least the late 1970s, acute insomnia (AI) has not historically been clearly defined or described in the literature[10]. The fact that several names have been associated with AI during this period contributes to theissue.Adjustmentinsomnia,stress-relatedinsomnia,symptomaticinsomnia,transient

Psychophysiological insomnia, subacute insomnia, and subchronic insomnia are three classificationsof AI[11].Buildingconceptualandoperationalconsensushasbeenhampered by this terminology diversity. Another issue has been that the AI durational criteria are defined by default, using any time frame that is less than the chronic insomnia (CI) criterion[12].

1.1.2 Chronic Insomnia

The literature on chronic insomnia is more abundant than that on acute insomnia. Over the past 40 years, formal definitions have been produced and adopted, as one might expect, though not without changes[13]. There has historically been a great deal of variance in the concept of "chronic." All three of the major nosological systems presently use CI as a diagnostic category: the ICSD-3 (Chronic Insomnia Disorder), the DSM-5 (Insomnia Disorder), and the ICD-11 (Chronic Insomnia) [20]. The following factors for a sleep issue are included in all three classification systems:(1) trouble getting to sleep and/or remaining asleep; (2) severe impairment, distress, or daytime consequences; and (3) existence even when there is a sufficient opportunity for sleep[14].

1.1 Pathophysiology of Insomnia

Increasingsomatic,cognitive,andcerebralactivation,orhyperarousal,isgenerallythoughtto be the cause of insomnia. Both the central (cortical) and peripheral (autonomic) nervo u s systems may be physiologically hyperaroused in individuals with insomnia[15]. Cognitive and emotional processes can also be referred to as hyperarousal in insomnia. Several ideas propose that both acute and chronic insomnia may be exacerbated by cognitive and affective hyperarousal before bed[16]. Despite being frequently discussed in the literature, hyperarousalisoften not well-characterized.Forthisresearch,hyperarousalisdefinedasincreased physiological, affective, or cognitive activity that disrupts the body's natural "disengagement from the environment" and hinders sleep. EEG, heart rate variability, elevated cortisol, and even self-report can all be used to identify hyperarousal[17].

1.2 Molecular mechanisms of Insomnia

Circadian rhythmicity and sleep regulation are associated with several sleep-regulating hormones and neurotransmitters[18, 19].

Sleep-regulating molecules can be broadly divided into two groups: those that enable wakefulness, like catecholamines, orexin, and histamine, and those that encourage or maintain sleep, like gamma-aminobutyric acid (GABA), adenosine, serotonin, melatonin, and prostaglandin D2. The neurochemical underpinnings of insomnia have only been the subject of a small number of molecular investigations to date, the majority of which have concentrated on substances like cortisol and GABA. Interestingly, changes in GABA signalling in the occipital brain of insomnia sufferers have been noted; these findings are consistent with the hyperarousal concept of the condition[20].

1.3 Sleep-Wake Cycle

The main brain systems that support wakefulness are the limbic networks, the "top-down" cognitive processes, and the "bottom-up" reticular activating system. Neural circuits originating in the brainstem, thalamus, and hypothalamus make up the ascending reticular activating system[21]. The noradrenergic locus coeruleus, the parabrachial nucleus, the histaminergic tuberomammillary nucleus (TMN) in the posterior hypothalamus, the cholinergic pedunculopontine and laterodorsally tegmental nuclei, the parabrachial nucleus, the serotonergic dorsal and median raphe nuclei, and the cholinergic nuclei of the basal forebrain are some of the important structures that make up the network that controls arousal and wakefulness. These areas use the thalamus and basal forebrain pathways to project to the cerebral cortex. Furthermore, these brainstem and hypothalamic arousal-promoting areas depend on the lateral hypothalamus's orexin (hypocretin)-producing neurons to be active. The hypothalamic suprachiasmatic nuclei's intrinsic oscillatory mechanisms further regulate the circadian control of sleep propensity[22].

4. Overview of Cannabidiol

The non-psychoactive component of Cannabis sativa, cannabidiol (CBD), has drawn a lot of interest lately because of its many potential medical uses. The pharmacokinetic properties of CBD, including its bioavailability, tissue distribution, safety profile, and suitable dosage considerations, have drawn more and more attention in research. Investigations have also looked at its pharmacodynamic actions, which support its suggested therapeutic benefits. These include its modulatory effects on the endocannabinoid system and its interactions with different ion channels[23]. Cannabis sativa, also known as hemp or marijuana, is a plant that has long been used primarily for medical and recreational purposes. Numerous biological components are synthesized by it; at least 554 have been reported, including 113 phytocannabinoids, which are molecules with a typical C21 terpeno-phenolic skeleton, and 120 terpenes, which contribute to its distinctive aroma.

Cannabis was already used in19th-century medications in the US and Europe. Many formulations were sold over the counter. However, in 1937, the 'Marihuana Tax Act' was passed, and increased penalties led to a restriction on cannabis research[24].

4.1. Pharmacokinetics of Cannabinoids

Distribution.

Cannabinoids like cannabidiol (CBD), which are extremely lipophilic, have a tendency to build up in adipose tissue before dispersing into organs that are well-perfused, such as the heart, brain, liver, lungs, and spleen. They then progressively acclimate to less vascularized regions, which may explain the sharp drop in plasma concentrations seen following delivery. With an average body weight of 70 kg, the estimated volume of distribution (Vd) in adults is moderate to high, ranging from 2.5 to 10 L/kg. Similar to tetrahydrocannabinol (THC), CBD binds to plasma proteins extensively (>95%), mostly to lipoproteins[25]. The amount of unbound CBD thathas pharmacological effects is only 1% to 5% of the total content.

*Metabolism***.**

The cytochrome P450 isozymes CYP2C19 and CYP3A4 are primarily responsible for the extensive hepatic metabolism of cannabidiol (CBD), with CYP1A1, CYP1A2, CYP2C9, and CYP2D6 also playing a role. The plasma area under the curve (AUC) of 7-hydroxy-cannabidiol (7-OH-CBD), one of its main active metabolites, is around 38% lower than that of the parent chemical, suggesting less systemic exposure than that of CBD itself[26]. Following hydroxylation, these metabolites proceed through additional hepatic metabolism before being eventually eliminated in the urine and, to a lesser extent, the faeces. However, little is understood about how CBD metabolites affect humans pharmacologically[27].

Excretion.

A comparatively lengthy terminal elimination half-life is seen by cannabidiol (CBD). The plasma half-life in healthy persons receiving twice-daily dosing for seven days was found to be between 56 and 61 hours. The mean half-life after intravenous distribution is roughly 24 ± 6 hours, while the half-life after inhalation is predicted to be 31 ± 4 hours. Although minor amounts of the parent molecule and its glucuronidated derivative are also found in urine, excretion mostly takes place through the feces in its unaltered form[28].

4.2. Difference between Cannabidiol and other Cannabinoids

Plant-derived cannabinoids essentially reflect and modulate the endogenous actions of the endocannabinoid system, which naturally regulates physiological functions, including anti-inflammatory and anticancer mechanisms. Tetrahydrocannabinol (THC), cannabinol (CBN), cannabigerol (CBG), and cannabidiol (CBD) are four important representatives of the many bioactive chemicals found in Cannabis sativa that are thought to be the main phytocannabinoids of medicinal significance.While the psychological impacts of each chemical vary, they all have similar anticancer properties[29]. The sole psychotropic hallucinogenic cannabinoid is THC; the other three cannabinoids have significant anxiolytic effects but no psychotropic effects. Furthermore, by increasing the endogenous cannabinoid content, THC is the sole enzyme that directly contributes to the breakdown of cannabinoids. It has been demonstrated that the cannabis plant contains over 100 potentially active principles with both biological and psychological impacts. Furthermore, Cannabis Sativa and Cannabis Indica, the two primary Cannabis plants, vary in terms of the various concentrations of each component[30].

4.3. Safety profile of Cannabidiol

Clinical research findings largely support the positive safety profile of cannabidiol (CBD) in people. The majority of research has been on its application in diseases, including psychotic illnesses and epilepsy. Fatigue, gastrointestinal issues like diarrhoea, and changes in appetite or body weight are among the often-reported side effects. CBD exhibits a more manageable side-effect profile than many traditional pharmaceutical drugs, which may have a favourable impact on treatment compliance and patient adherence. Additionally, CBD is frequently used as an adjuvant medication to improve the effectiveness of conventional treatments[31]. Cannabis plants—aside from D9-THC—have drawn attention from researchers and policymakers. Cannabidiol is the most well-known of those (CBD). Unlike D9-THC, it has several positive pharmacological properties but is not intoxicating. It has antipsychotic, antiemetic, anti-inflammatory, and anxiolytic properties, for example. Neuroprotective qualities have also been demonstrated. Therefore, it could be used at high dosages to treat a range of ailments, including diabetes, nausea, and psychiatric illnesses, including dementia and schizophrenia [32].

5. Cannabidiol's impact on Insomnia

It has long been known that cannabis and its pharmacologically active components, phytocan-

nabinoids, offer several health advantages. Users frequently mention the correlation betweensubjectivelyimprovedsleepandsedation.Accordingtoanumberoftheevaluated

Research suggests that cannabis may help reduce sleep disruptions, increase sleep quality, and shorten the time it takes to fall asleep. Even though cannabidiol (CBD) has been shown in numerous trials to improve sleep, there are still a number of methodological issues. Small sample sizes are common, sleep is frequently evaluated as a secondary endpoint in studies aimed at other disorders, and approved subjective and objective sleep monitoring instruments are not widely used[33].

In one study, a survey of 95 people who use cannabis medicinally for a range of symptoms and health issues provided valuable information about user preferences. The results showed a statistically significant preference for formulations of Cannabis indica, especially those that promote sedation and enhance sleep. The authors underlined the need for more study on the possibility of cannabis-based therapies in the treatment of insomnia in light of these findings [34]. Another study used a smartphone app to gather information on medicinal cannabis in a naturalistic setting, measuring the self-reported effectiveness and adverse effects of the drug[35].

1.1 Cannabis product forms and ingestion methods

Across 24,189 recorded sessions, the trends in the usage of cannabis products to treat insomnia symptoms were assessed using descriptive statistical analysis. Since there were only a few observations, the data for concentrates and vape pens were merged into one category. The findings showed that, for all age groups and genders, cannabis flower was the most widely used product for reducing the symptoms of sleeplessness, with oil-based preparations coming in second[36]. Across all monitored sessions, it displays descriptive data that looks at the prevalence of various cannabis ingestion methods, such as vaping, oil, smoking, edibles, pills, tinctures, sprays, concentrates, dabs, bubblers, portable dabs, oral, topical, or transdermal. The categories of concentrate, dab bubbler, dab portable, oral, topical, and transdermal items were combined into a single group for analysis because of the small number of observations. The results showed that vaping was the most often reported mode of cannabis intake for all genders and all age groups[37].

1.2. Evidence of Cannabidiol on Insomnia treatment

More people are aware of CBD's sedative qualities because of its promotion on social media. However, there is not much solid data to support this idea. Carlini et al. administered three dosages of CBD (40, 80, and 160 mg) and an active comparator (5 mg nitrazepam) over five different nights space done week apart in a double-blind, randomized, placebo-controlled

Study. The 15 cannabis-naïve individuals chosen for the study were already known to the researchers and had a history of taking at least an hour to fall asleep and having trouble staying asleep all night [38]. After the research medication was administered 30 minutes prior to bedtime, participants' self-reported challenges with falling asleep, staying asleep, and experiencing frequent nocturnal awakenings were used to assess the quality of their sleep. A higher percentage of individuals reported longer overall sleep duration when given 160 mg of cannabidiol (CBD) as opposed to a placebo; however, the results showed no significant differences in sleep latency or maintenance across treatment groups. Whencomparing the40 and 80 mg dosages of CBD to a placebo, there were no discernible changes in the amount or quality of self-reported sleep. It is also noteworthy that, in comparison to nitrazepam and a placebo, dream recollection was considerably decreased when using CBD, at any dosage. The authors hypothesized that CBD would impair one's ability to dream or remember dreams. Another possibility is that there was less REM sleep. Although there were no reported adverse events, consuming 160 mg of CBD did not substantially alter the number of persons who reported feeling drowsy or having trouble

focusing in the morning compared to taking a placebo[39].

1.3. Cannabidiol as an Extract from Hemp

Hemp, which is commonly defined as Cannabis sativa leaves and buds with a total THC level of less than 0.3% dry weight, is the source of CBD. IstressthattheTHCcontent is the single factor that separates hemp from marijuana[40].A straightforward illustration calculation demonstrates that when hemp having 0.3% THC and 5.0% CBD is extracted, the THC level would represent roughly 6% of the CBD concentration because THC and CBD have similar elimination mechanisms.Other cannabinoids, residual solvents, plant oils, pesticides, herbicides, and other organic compounds may also be present in the extracted product[41]. The important aspect is that an unpurified and unmonitored hemp extract will undoubtedly have some THC in it[42]. The U.S. Drug Enforcement Administration (DEA) created a new prohibited substances code number, 7350, for marijuana extracts on January 13, 2017. Extracts from cannabis plants fall under this classification under Schedule I of the Controlled Substances Act (CSA), with the exception of separated resin, as the DEA's decision makes clea[43].A petition against the DEA's final rule was dismissed by the U.S. Court of Appeals for the Ninth Circuit, which upheld the rule's applicability to extracts made from hemp, a type of cannabis plant. The DEA further stressed that it is not technically possible to separate THC and CBD completely in hemp extracts. Consequently,hemp-derivedCBDcontinues to be classified as a Schedule I substance [44].

1.4 Side effects of Cannabidiol

Cannabidiol, a substance derived from cannabinoids, may help patients with epileptic encephalopathies, including Dravet syndrome and Lennox-Gastaut syndrome, who have seizures that are resistant to treatment. Clinical research that led to the approval of cannabidiol has established its well-known short-term adverse effects, generally mild to moderate, dose-dependent side effects, such as diarrhoea, decreased appetite, or somnolence, and is a well-tolerated medication. Serious, perhaps fatal side effects are also possible, and they are frequently linked to the uncontrolled hazardous combination with other antiseizure medications that are frequently prescribed to these individuals, such as clobazam or sodium valproate[45].

According to research, CBD does not substantially change typical physiological processes like heart rate, blood pressure, or body temperature and is generally non-toxic to healthy, non-transformed cells. Furthermore, it doesn't seem to affect food intake, cause catalepsy, disrupt gastrointestinal motility, or affect psychomotor or psychological function[46]. Additionally, it has been shown that individuals tolerate high doses of CBD—up to 1,500 mg/day—and chronic use effectively[47]. On the other hand, some research has shown that this cannabinoid may have several adverse consequences, including decreased p-glycoprotein and other drug transporter activities, changes in in vitro cell viability, suppression of hepatic drug metabolism, and impaired fertilization capacity[48]. According to recent studies on the administration of cannabinoids in humans, controlled CBD consumption is probably safe for both humans and animals[49].

5.5 Cannabidiol for moderate-severe Insomnia

When compared to a placebo in people with moderate to severe primary insomnia, this randomized, placebo-controlled pilot study shows that nightly supplementation with 150 mg of cannabidiol (CBD) for two weeks does not significantly improve core insomnia symptoms, such as insomnia severity, sleep-onset latency, wake after sleep onset, or total sleep time. Nonetheless, CBD was consistently well tolerated and linked to modest but significant improvements in secondary outcomes, including short-term gains in alertness and functioning upon waking, as well as long-term gains in general well-being and specific objective sleep efficiency measures. These results imply that rather than having strong sleep-promoting effects, CBD may primarily have psychological or quality-of-life advantages at this

dose and duration. In order to better characterize the therapeutic role of CBD in the management of primary insomnia, bigger, longer-duration trials with a variety of dose techniques and subgroup analyses are required. Overall, the study emphasizes the safety of short-term nightly CBD use[50].

5.6. Effectiveness of Cannabinoids on Subjective Sleep Quality in People with and without Insomnia or Poor Sleep

Cannabinoid-based therapies are linked to a moderate improvement in subjective sleep quality in people with insomnia, insomnia symptoms, or poor sleep, as well as in those without comorbid medical illnesses, according to this comprehensive review and meta-analysis. While CBD-only treatments did not significantly enhance sleep quality, formulations comprising cannabinoids other than or in addition to cannabidiol (CBD), such as THC and/or CBN, appear to be the main source of the therapeutic impact. Significantly, there was a discrepancy between perceived and physiological sleep outcomes, as these subjective gains were not consistently accompanied by changes in objective sleep measurements, insomnia severity, anxiety, or well-being. Despite the fact that cannabinoids were usually well tolerated, cautious interpretation is required due to the significant heterogeneity among studies, formulation variations, short treatment durations, and potential unblinding effects. Overall, the results encourage more thorough, long-term, and carefully monitored clinical trials to elucidate the precise functions, ideal formulations, and therapeutic applicability of cannabis in the treatment of insomnia and disturbed sleep[51].

5. Cannabidiol for Anxiety in women with Breast Cancer

This phase II, double-masked, placebo-controlled, randomized clinical trial shows that a single 400 mg oral dose of pharmaceutical-grade cannabidiol (CBD) is safe and well-tolerated in women with advanced breast cancer who are anxious about scans. Participants receiving CBD reported significantly lower anxiety levels 2 to 4 hours after ingestion compared with placebo, despite the study's primary endpoint of a statistically significant difference in pre- to post-ingestion anxiety change scores between the CBD and placebo groups not being met.These results point to a possible acute anxiolytic effect of CBD without significant side effects. All things considered, the study offers significant initial proof of the viability and safety of CBD as a potential substitute for traditional anxiolytics in oncology settings. It also emphasizes the necessity of more extensive, long-term studies concentrating on patients with moderate to severe anxiety in order to more precisely define its clinical efficacy[52,53].

6.1 Impact of cannabidiol treatment for anxiety disorders

Although cannabidiol (CBD) has a generally favourable safety profile and may have anxiolytic effects in certain anxiety-related diseases, the overall data from randomized controlled trials is still conflicting, according to this comprehensive review. Many trials reported no meaningful benefit or even anxiogenic effects at larger or suboptimal doses, despite the fact that certain research reports anxiety reduction, especially in particular experimental models like public speaking or anxiety connected to substance withdrawal. The large variation in CBD dosage, single-dose versus repeated administration, the variety of anxiety disorders examined, the heterogeneity of outcome measures, and methodological constraints like small sample sizes and uncertain risk of bias all seem to have an impact on these discrepancies.All of the results point to the fact that CBD is not yet a dependable, stand-alone treatment for anxiety disorders. To precisely characterize the therapeutic role of CBD in the management of anxiety disorders, well-designed, large-scale RCTs with standardized dosage regimens, disorder-specific populations, extended treatment durations, and reliable anxiety assessment methods are crucial[54].

6. Conclusion

The most thorough clinical data on the use of can-

nabinoids to treat sleep disturbances to date have been included in this review. The majority of the evidence currently available comes from short-term, uncontrolled, and unblinded trials and case series, as there have been relatively fewer randomized controlled trials. Currently, there is insufficient evidence to support the effectiveness of any therapeutic option for sleep problems. Nonetheless, the results from the current research are encouraging and call for more research on cannabis' potential to cure all of the sleep disorders covered in this review. The need for carefully monitored clinical research is underscored by the lack of clarity about the effects of cannabis use on lung health. Subsequent investigations ought to concentrate on cannabis formulations that are standardized, permit dosage modification, and may be delivered via less hazardous, safer methods. Validated evaluations of symptoms related to sleep as well as objective measures of sleep quality should be included in such investigations. A number of variables may affect the effectiveness of treatment, including the mode of administration, food intake before usage, previous cannabis exposure, age, sex, body composition, and the use of a single or combination of cannabinoids. Investigations should also look into the long-term efficacy and safety of using cannabinoids, taking into account potential withdrawal symptoms, tolerance, and dependence. It's equally critical to assess the effects on day-to-day functioning, including driving abilities, and weigh these risks against the outcomes of untreated sleep problems.

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