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Cannabidiol in Anxiety and Sleep: A Large Case Series

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Abstract

Context

Cannabidiol (CBD) is one of many cannabinoid compounds found in cannabis. It does not appear to alter consciousness or trigger a "high." A recent surge in scientific publications has found preclinical and clinical evidence documenting value for CBD in some neuropsychiatric disorders, including epilepsy, anxiety, and schizophrenia. Evidence points toward a calming effect for CBD in the central nervous system. Interest in CBD as a treatment of a wide range of disorders has exploded, yet few clinical studies of CBD exist in the psychiatric literature.

Objective

To determine whether CBD helps improve sleep and/or anxiety in a clinical population.

Design

A large retrospective case series at a psychiatric clinic involving clinical application of CBD for anxiety and sleep complaints as an adjunct to usual treatment. The retrospective chart review included monthly documentation of anxiety and sleep quality in 103 adult patients.

Main Outcome Measures

Sleep and anxiety scores, using validated instruments, at baseline and after CBD treatment.

Results

The final sample consisted of 72 adults presenting with primary concerns of anxiety (n = 47) or poor sleep (n = 25). Anxiety scores decreased within the first month in 57 patients (79.2%) and remained decreased during the study duration. Sleep scores improved within the first month in 48 patients (66.7%) but fluctuated over time. In this chart review, CBD was well tolerated in all but 3 patients.

Conclusion

Cannabidiol may hold benefit for anxiety-related disorders. Controlled clinical studies are needed.

Keywords: anxiety, cannabidiol, CBD, sleep

INTRODUCTION

The *Cannabis* plant has been cultivated and used for its medicinal and industrial benefits dating back to ancient times. *Cannabis sativa* and *Cannabis indica* are the 2 main species.[1] The *Cannabis* plant contains more than 80 different chemicals known as cannabinoids. The most abundant cannabinoid, tetrahydrocannabinol (THC), is well known for its psychoactive properties, whereas cannabidiol (CBD) is the second-most abundant and is nonpsychoactive. Different strains of the plant are grown containing varying amounts of THC and CBD. Hemp plants are grown for their fibers and high levels of CBD that can be extracted to make oil, but marijuana plants grown for recreational use have higher concentrations of THC compared with CBD.[2] Industrial hemp must contain less than 0.3% THC to be considered legal, and it is from this plant that CBD oil is extracted.[3]

Many different cultures have used the *Cannabis* plant to treat a plethora of ailments. Practitioners in ancient China targeted malaria, menstrual symptoms, gout, and constipation. During medieval times, cannabis was used for pain, epilepsy, nausea, and vomiting, and in Western medicine it was commonly used as an analgesic.[4,5] In the US, physicians prescribed *Cannabis sativa* for a multitude of illnesses until restrictions were put in place in the 1930s and then finally stopped using it in 1970 when the federal government listed marijuana as a Schedule I substance, claiming it an illegal substance with no medical value. California was the first state to go against the federal ban and legalize medical marijuana in 1996.[6] As of June 2018, 9 states and Washington, DC, have legalized recreational marijuana, and 30 states and Washington, DC, allow for use of medical marijuana.[7] The purpose of the present study is to describe the effects of CBD on anxiety and sleep among patients in a clinic presenting with anxiety or sleep as a primary concern.

CBD has demonstrated preliminary efficacy for a range of physical and mental health care problems. In the decade before 2012, there were only 9 published studies on the use of cannabinoids for medicinal treatment of pain; since then, 30 articles have been published on this topic, according to a PubMed search conducted in December 2017. Most notable was a study conducted at the University of California, San Diego's Center for Medicinal Cannabis Research that showed cannabis cigarettes reduced pain by 34% to 40% compared with placebo (17% to 20% decrease in pain).[8] In particular, CBD appears to hold benefits for a wide range of neurologic disorders, including decreasing major seizures. A recent large, well-controlled study of pediatric epilepsy documented a beneficial effect of CBD in reducing seizure frequency by more than 50%.[9] In addition to endorphin release, the "runner's high" experience after exercise has been shown to be induced in part by anandamide acting on CB1 receptors, eliciting anxiolytic effects on the body.[10] The activity of CBD at 5-HT_{1A} receptors may drive its neuroprotective, antidepressive, and anxiolytic benefits, although the mechanism of action by which CBD decreases anxiety is still unclear.[11] CBD was shown to be helpful for decreasing anxiety through a simulated public speaking test at doses of 300 mg to 600 mg in single-dose studies.[12–14] Other studies suggest lower doses of 10 mg/kg having a more anxiolytic effect than higher doses of 100 mg/kg in rats.[15] A crossover study comparing CBD with nitrazepam found that high-dose CBD at 160 mg increased the duration of sleep.[16] Another crossover study showed that plasma cortisol levels decreased more significantly when given oral CBD, 300 to 600 mg, but these patients experienced a sedative effect.[17] The higher doses of CBD that studies suggest are therapeutic for anxiety, insomnia, and epilepsy may also increase mental sedation.[16] Administration of CBD via different routes and long-term use of 10 mg/d to 400 mg/d did not create a toxic effect on patients. Doses up to 1500 mg/d have been well tolerated in the literature.[18] Most of the research done has been in animal models and has shown potential benefit, but clinical data from randomized controlled experiments remain limited.

Finally, the most notable benefit of cannabis as a form of treatment is safety. There have been no reports of lethal overdose with either of the cannabinoids and, outside of concerns over abuse, major complications are very limited.[19] Current research indicates that cannabis has a low overall risk with short-term use, but more research is needed to clarify possible long-term risks and harms.

Given the promising biochemical, physiologic, and preclinical data on CBD, a remarkable lack of randomized clinical trials and other formal clinical studies exist in the psychiatric arena. The present study describes a series of patients using CBD for treatment of anxiety or sleep disturbances in a clinical practice setting. Given the paucity of data in this area, clinical observations can be quite useful to advance the knowledge base and to offer questions for further investigation. This study aimed to

determine whether CBD is helpful for improving sleep and/or anxiety in a clinical population. Given the novel nature of this treatment, our study also focused on tolerability and safety concerns. As a part of the evolving legal status of cannabis, our investigation also looked at patient acceptance.

METHODS

Design and Procedures

A retrospective chart review was conducted of adult psychiatric patients treated with CBD for anxiety or sleep as an adjunct to treatment as usual at a large psychiatric outpatient clinic. Any current psychiatric patient with a diagnosis by a mental health professional (psychiatrist, psychiatric nurse practitioner, or physician assistant) of a sleep or anxiety disorder was considered. Diagnosis was made by clinical evaluation followed by baseline psychologic measures. These measures were repeated monthly. Comorbid psychiatric illnesses were not a basis for exclusion. Accordingly, other psychiatric medications were administered as per routine patient care. Selection for the case series was contingent on informed consent to be treated with CBD for 1 of these 2 disorders and at least 1 month of active treatment with CBD. Patients treated with CBD were provided with psychiatric care and medications as usual. Most patients continued to receive their psychiatric medications. The patient population mirrored the clinic population at large with the exception that it was younger.

Nearly all patients were given CBD 25 mg/d in capsule form. If anxiety complaints predominated, the dosing was every morning, after breakfast. If sleep complaints predominated, the dosing was every evening, after dinner. A handful of patients were given CBD 50 mg/d or 75 mg/d. One patient with a trauma history and schizoaffective disorder received a CBD dosage that was gradually increased to 175 mg/d.

Often CBD was employed as a method to avoid or to reduce psychiatric medications. The CBD selection and dosing reflected the individual practitioner's clinical preference. Informed consent was obtained for each patient who was treated and considered for this study. Monthly visits included clinical evaluation and documentation of patients' anxiety and sleep status using validated measures. CBD was added to care, dropped from care, or refused as per individual patient and practitioner preference. The Western Institutional Review Board, Puyallup, WA, approved this retrospective chart review.

Setting and Sample

Wholeness Center is a large mental health clinic in Fort Collins, CO, that focuses on integrative medicine and psychiatry. Practitioners from a range of disciplines (psychiatry, naturopathy, acupuncture, neurofeedback, yoga, etc) work together in a collaborative and cross-disciplinary environment. CBD had been widely incorporated into clinical care at Wholeness Center a few years before this study, on the basis of existing research and patient experience.

The sampling frame consisted of 103 adult patients who were consecutively treated with CBD at our psychiatric outpatient clinic. Eighty-two (79.6%) of the 103 adult patients had a documented anxiety or sleep disorder diagnosis. Patients with sole or primary diagnoses of schizophrenia, posttraumatic stress disorder, and agitated depression were excluded. Ten patients were further excluded because they had only 1 documented visit, with no follow-up assessment. The final sample consisted of 72 adult patients presenting with primary concerns of anxiety (65.3%; n = 47) or poor sleep (34.7%; n = 25) and who had at least 1 follow-up visit after CBD was prescribed.

Main Outcome Measures

Sleep and anxiety were the targets of this descriptive report. Sleep concerns were tracked at monthly visits using the Pittsburg Sleep Quality Index. Anxiety levels were monitored at monthly visits using the Hamilton Anxiety Rating Scale. Both scales are nonproprietary. The Hamilton Anxiety Rating Scale is a widely used and validated anxiety measure with 14 individual questions. It was first used in 1959 and covers a wide range of anxiety-related concerns. The score ranges from 0 to 56. A score under 17 indicates mild anxiety, and a score above 25 indicates severe anxiety. The Pittsburg Sleep

Quality Index is a self-report measure that assesses the quality of sleep during a 1-month period. It consists of 19 items that have been found to be reliable and valid in the assessment of a range of sleep-related problems. Each item is rated 0 to 3 and yields a total score from 0 to 21. A higher number indicates more sleep-related concerns. A score of 5 or greater indicates a "poor sleeper."

Side effects and tolerability of CBD treatment were assessed through spontaneous patient self-reports and were documented in case records. Any other spontaneous comments or complaints of patients were also documented in case records and included in this analysis.

Data Analysis

Deidentified patient data were evaluated using descriptive statistics and plotted graphically for visual analysis and interpretation of trends.

RESULTS

The average age for patients with anxiety was 34 years (range = 18–70 years) and age 36.5 years for patients with sleep disorders (range = 18–72 years). Most patients with an anxiety diagnosis were men (59.6%, 28/47), whereas more sleep-disordered patients were women (64.0%, 16/25). All 72 patients completed sleep and anxiety assessments at the onset of CBD treatment and at the first monthly follow-up. By the second monthly follow-up, 41 patients (56.9%) remained on CBD treatment and completed assessments; 27 patients (37.5%) remained on CBD treatment at the third monthly assessment.

Table 1 provides means and standard deviations for sleep and anxiety scores at baseline and during the follow-up period for adults taking CBD. Figure 1 graphically displays the trend in anxiety and sleep scores over the study period. On average, anxiety and sleep improved for most patients, and these improvements were sustained over time. At the first monthly assessment after the start of CBD treatment, 79.2% (57/72) and 66.7% (48/72) of all patients experienced an improvement in anxiety and sleep, respectively; 15.3% (11/72) and 25.0% (18/72) experienced worsening symptoms in anxiety and sleep, respectively. Two months after the start of CBD treatment, 78.1% (32/41) and 56.1% (23/41) of patients reported improvement in anxiety and sleep, respectively, compared with the prior monthly visit; again, 19.5% (8/41) and 26.8% (11/41), respectively, reported worsening problems as compared with the prior month.

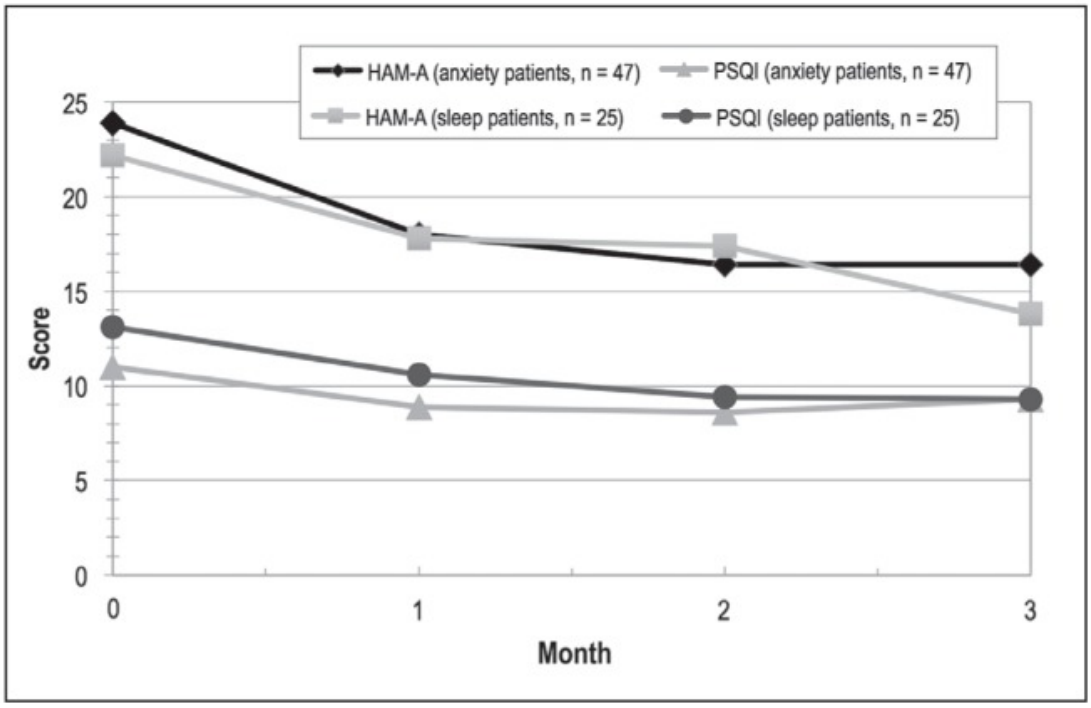

Figure 1

Mean anxiety and sleep scores for adults using cannabidiol treatment.

HAM-A = Hamilton Anxiety Rating Scale; PSQI = Pittsburg Sleep Quality Index.

Table 1

Descriptive statistics for anxiety and sleep scores among adults using cannabidiol treatment

Parameter	HAM-A, mean (SD)	PSQI, mean (SD)
Anxiety (n = 47)		
Baseline	23.87 (9.87)	10.98 (3.43)
1-month follow-up	18.02 (7.56)	8.88 (3.68)
2-month follow-up	16.35 (8.80)	8.59 (2.91)
3-month follow-up	16.36 (9.80)	9.25 (2.46)
Sleep disorder (n = 25)		
Baseline	22.18 (7.55)	13.08 (3.03)
1-month follow-up	17.82 (9.72)	10.64 (3.89)
2-month follow-up	17.36 (10.91)	9.39 (3.81)
3-month follow-up	13.78 (7.86)	9.33 (4.63)

HAM-A = Hamilton Anxiety Rating Scale; PSQI = Pittsburg Sleep Quality Index; SD = standard deviation.

These results demonstrated a more sustained response to anxiety than for sleep over time. Patient records displayed a larger decrease in anxiety scores than in sleep scores. The sleep scores demonstrated mild improvement. The anxiety scores decreased within the first month and then remained decreased during the study duration.

CBD was well tolerated, with few patients reporting side effects. Two patients discontinued treatment within the first week because of fatigue. Three patients noted mild sedation initially that appeared to abate in the first few weeks. One patient with a developmental disorder (aged 21 years) had to be taken off the CBD regimen because of increased sexually inappropriate behavior. The CBD was held, and the behavior disappeared. The behavior reappeared on redosing 2 weeks later, and the CBD regimen was formally discontinued. The treating psychiatrist thought this was related to disinhibition because the patient's anxiety responded dramatically. One patient noted dry eyes. Reasons for patients not following-up at later assessment points are largely unknown but are probably because of standard attrition experienced in usual clinical practice. There was no evidence to suggest patients discontinued care because of tolerability concerns. The attrition rates were similar in nature and size to those found in routinely scheduled visits in this clinic.

The treatment with CBD was in general well accepted, as judged by the clinicians' and patients' responses. Four patients declined CBD treatment because of religious or ethical concerns about the relation to cannabis. Nearly all patients easily provided informed consent once the nature of the treatment was explained. Most patients appreciated the opportunity to try something natural and avoid further or initial psychiatric medication use.

DISCUSSION

In an outpatient psychiatric population, sleep scores displayed no sustained improvements during the 3-month study. Anxiety scores decreased fairly rapidly, and this decrease was sustained during the study period. These results are consistent with the existing preclinical and clinical data on CBD. CBD was well accepted and well tolerated in our patients. Side effects were minimal (mainly fatigue) and may be related to dosing.

The doses used in this study (25 mg/d to 175 mg/d) were much lower than those reported in some of the clinical literature (300 mg/d to 600 mg/d)[12–14,17] for 2 reasons. The first is that in our experience lower doses appear to elicit an adequate clinical response. Second, the current retail cost of CBD would make the use of 600 mg/d cost prohibitive.

Study Limitations

These results must be interpreted cautiously because this was a naturalistic study, all patients were receiving open-label treatment, and there was no comparison group. Concurrent psychiatric medications were employed as in routine clinical care. This is both a limitation and strength, as very few publications exist in this population. Other researchers have noted that the large societal notoriety about cannabis and medical marijuana probably contributes to a larger-than-normal placebo effect.[20] Any study that explores efficacy in this therapy probably will struggle with a potentially inflated placebo effect that will make these determinations more difficult. Likewise, the clinical population in this case series is skewed younger than typical for our clinic, and future studies could explore the possible selection bias inherent in this treatment option. Most patients were also taking psychiatric medications and receiving other mental health services, such as counseling, which limits the ability to make any causal links to CBD treatment. Clinical attrition is evident in the dataset. The reason for this might be related to CBD ingestion or not, so the overall component remains unclear. Furthermore, patients at our clinic often express a desire to reduce or to avoid use of psychiatric medications, which may contribute to an enhanced placebo effect or additional bias. The length of clinical monitoring may help to decrease this concern. However, the clinical data in this analysis show a trend toward clinically significant relief of anxiety upon the start of CBD treatment.

Legality of Cannabidiol

The legality of CBD is not clear. Like the issues surrounding the legality of cannabis in general, CBD presents the clinician with a confusing state vs federal legal quandary, and this keeps the issue in question. CBD is legal in the 33 states that have legalized medical or recreational use of marijuana and in 17 other states that have legalized some form of CBD, according to the National Organization for the Reform of Marijuana Laws (NORML).21 But like marijuana, it is still not legal at the federal level. The federal government has announced that it is not focused on this compound in terms of enforcement or interdiction.22 However, CBD is interpreted by the Drug Enforcement Administration, Food and Drug Administration, and Congress to be a Schedule I substance, and therefore it is illegal in all 50 states.23 Pragmatically, CBD is widely available on the Internet, with sales expected to reach $1 billion by 2020. Pending federal legislation to redefine the legal status of cannabis would clarify this complex issue. Canada's move to legalize cannabis in October 2018 further highlights the need for a speedy resolution to this question.24

CONCLUSION

Formal studies on efficacy and dose finding are much needed. Some urgency exists, given the explosion of lay interest in this topic and the rush to market these compounds. Current understanding of the physiology and neurologic pathways points to a benefit with anxiety-related issues. The results of our clinical report support the existing scientific evidence. In our study, we saw no evidence of a safety issue that would limit future studies. In this evaluation, CBD appears to be better tolerated than routine psychiatric medications. Furthermore, CBD displays promise as a tool for reducing anxiety in clinical populations, but given the open-label and nonrandomized nature of this large case series, all results must be interpreted very cautiously. Randomized and controlled trials are needed to provide definitive clinical guidance.

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Footnotes

Disclosure Statement

Dr Shannon has published several professional books on integrative mental health. Dr Shannon is a Principal Investigator for a Phase 3 study of 3,4-methylenedioxy-methamphetamine (MDMA)-assisted psychotherapy for severe posttraumatic stress disorder and receives compensation for his clinical work from the Multidisciplinary Association for Psychedelic Studies, Santa Cruz, CA. The other authors have no conflicts of interests to disclose.

References

1. Baron EP. Comprehensive review of medicinal marijuana, cannabinoids, and therapeutic implications in medicine and headache: What a long strange trip it's been … *Headache.* 2015 Jun;55(6):885–916. doi: 10.1111/head.12570. [PubMed] [CrossRef] [Google Scholar]

2. Schluttenhofer C, Yuan L. Challenges towards revitalizing hemp: A multifaceted crop. *Trends Plant Sci.* 2017 Nov;22(11):917–29. doi: 10.1016/j.tplants.2017.08.004. [PubMed] [CrossRef] [Google Scholar]

3. Andre CM, Hausman JF, Guerriero G. Cannabis sativa: The plant of the thousand and one molecules. *Front Plant Sci.* 2016 Feb 4;7:19. doi: 10.3389/fpls.2016.00019. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

4. Zlebnik NE, Cheer JF. Beyond the CB1 receptor: Is cannabidiol the answer for disorders of motivation? *Annu Rev Neurosci.* 2016 Jul 8;39:1–17. doi: 10.1146/annurev-neuro-070815-014038. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

5. Devinsky O, Cilio MR, Cross H, et al. Cannabidiol: Pharmacology and potential therapeutic role in epilepsy and other neuropsychiatric disorders. *Epilepsia.* 2014 Jun;55(6):791–802. doi: 10.1111/epi.12631. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

6. Bostwick JM. Blurred boundaries: The therapeutics and politics of medical marijuana. *Mayo Clin Proc.* 2012 Feb;87(2):172–86. doi: 10.1016/j.mayocp.2011.10.003. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

7. *Legal recreational marijuana states and DC: Cannabis laws with possession and cultivation limits [Internet]* Santa Monica, CA: ProCon.org; 2018. Jun 27, [cited 2018 Aug 23]. Available from: https://marijuana.procon.org/view.resource.php?resourceID=006868. [Google Scholar]

8. Abrams DI, Jay CA, Shade SB, et al. Cannabis in painful HIV-associated sensory neuropathy: A randomized placebo-controlled trial. *Neurology.* 2007 Feb 13;68(7):515–21. doi: 10.1212/01.wnl.0000253187.66183.9c. [PubMed] [CrossRef] [Google Scholar]

9. Devinsky O, Cross JH, Laux L, et al. Cannabidiol in Dravet Syndrome Study Group. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. *N Engl J Med.* 2017 May 25;376(21):2011–20. doi: 10.1056/NEJMoa1611618. [PubMed] [CrossRef] [Google Scholar]

10. Fuss J, Steinle J, Bindila L, et al. A runner's high depends on cannabinoid receptors in mice. *Proc Natl Acad Sci U S A.* 2015 Oct 20;112(42):13105–8. doi: 10.1073/pnas.1514996112. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

11. Zanelati TV, Biojone C, Moreira FA, Guimarães FS, Joca SR. Antidepressant-like effects of cannabidiol in mice: Possible involvement of 5-HT1A receptors. *Br J Pharmacol.* 2010 Jan;159(1):122–8. doi: 10.1111/j.1476-5381.2009.00521.x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

12. Zuardi AW, Rodrigues NP, Silva AL, et al. Inverted U-shaped dose-response curve of the anxiolytic effect of cannabidiol during public speaking in real life. *Front Pharmacol.* 2017 May 11;8:259. doi: 10.3389/fphar.2017.00259. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

13. Bergamaschi MM, Queiroz RH, Chagas MH, et al. Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naïve social phobia patients. *Neuropsychopharmacology.* 2011 May;36(6):1219–26. doi: 10.1038/npp.2011.6. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

14. Zuardi AW, Cosme RA, Graeff FG, Guimarães FS. Effects of ipsapirone andcannabidiol on human experimental anxiety. *J Psychopharmacol.* 1993 Jan;7(1 Suppl):82–8. doi: 10.1177/026988119300700112. [PubMed] [CrossRef] [Google Scholar]

15. Guimarães FS, Chiaretti TM, Graeff FG, Zuardi AW. Antianxiety effect of cannabidiol in the elevated plus-maze. *Psychopharmacology (Berl)* 1990;100(4):558–9. doi: 10.1007/bf02244012. [PubMed] [CrossRef] [Google Scholar]

16. Zhornitsky S, Potvin S. Cannabidiol in humans—the quest for therapeutic targets. *Pharmaceuticals (Basel)* 2012 May 21;5(5):529–52. doi: 10.3390/ph5050529. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

17. Zuardi AW, Guimarães FS, Moreira AC. Effect of cannabidiol on plasma prolactin, growth hormone and cortisol in human volunteers. *Braz J Med Biol Res.* 1993 Feb;26(2):213–7. [PubMed] [Google Scholar]

18. Iffland K, Grotenhermen F. An update on safety and side effects of cannabidiol: A review of clinical data and relevant animal studies. *Cannabis Cannabinoid Res.* 2017 Jun 1;2(1):139–54. doi: 10.1089/can.2016.0034. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

19. Collen M. Prescribing cannabis for harm reduction. *Harm Reduct J.* 2012 Jan 1;9:1. doi: 10.1186/1477-7517-9-1. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

20. Loflin MJE, Earleywine M, Farmer S, Slavin M, Luba R, Bonn-Miller M.Placebo effects of edible cannabis: Reported intoxication effects at a 30-minute delay *J Psychoactive Drugs* 2017November–December495393–7. 10.1080/02791072.2017.1354409 [PubMed] [CrossRef] [Google Scholar]

21. *State laws [Internet]* Washington, DC: NORML Foundation; c2018. [cited 2018 Aug 7]. Available from: https://norml.org/laws. [Google Scholar]

22. Mitchell T. *Did the DEA just quietly approve CBD? [Internet]* Denver, CO: Westword; 2018. Jun 2, [cited 2018 Aug 7] Available from: www.westword.com/marijuana/dea-quietly-gives-cbd-other-non-psychoactive-cannabinoids-the-go-ahead-10377016. [Google Scholar]

23. *Clarification of the new drug code (7350) for marijuana extract [Internet]* Springfield, VA: Drug Enforcement Administration, Diversion Control Division; 2017. [cited 2018 Aug 7]. Available from: www.deadiversion.usdoj.gov/schedules/marijuana/m_extract_7350.rtfl. [Google Scholar]

24. Steinmetz K. *What marijuana legalization in Canada could mean for the United States [Internet]* New York, NY: Time; 2017. Apr 6, [cited 2018 Aug 7]. Available from: http://time.com/4728091/canada-legalizing-marijuana-united-states-weed-pot/ [Google Scholar]