

REVIEW ARTICLE

CANNABIDIOL: BACKGROUND AND LITERATURE REVIEW OF POTENTIAL TREATMENTS

Beth Kolongowski, OMS-III¹; Lindsay Tjiattas-Saleski, DO, MBA, FACOEP¹

¹Edward Via College of Osteopathic Medicine – Carolinas Campus, Spartanburg, SC

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THC

ABSTRACT:

Cannabidiol, commonly abbreviated CBD, is one of the hundreds of compounds present in the flowering cannabis plant, along with its more well-known structural isomer, Δ^9 -tetrahydrocannabinol or THC. CBD can be extracted from the plant and utilized in many forms, from topical oils to smokable flowers. Recently, availability, interest in and use of CBD across the nation have grown exponentially, with internet searches for CBD increasing 160% between 2017 and 2018 and 14% of Americans citing current CBD use. Users of this compound endorse numerous perceived benefits, including anxiolysis, analgesia and much more. Most users claim to employ CBD to treat specific medical conditions spanning from autoimmune, to psychiatric, to musculoskeletal. Evidence supports some of these reported effects in recent studies, as CBD has demonstrated anticonvulsant, antipsychotic and antinociceptive properties, among others. However, the implications of these findings are still in their infancy. As of June 2018, one FDA-approved pure CBD product for seizure treatment, Epidiolex[®], is available for prescription use and many more are in various stages of testing. However, numerous safety and legal concerns remain regarding off-label and over-the-counter CBD usage. Physicians and other health care professionals are likely to encounter CBD use by their patients. As usage continues to grow, so does the duty of care providers to understand its role and serve as a source of evidence-based information for their community on this relevant health topic.

INTRODUCTION

Cannabidiol, known as CBD, is one of the hundreds of cannabinoid compounds making up the flowering cannabis plant¹ and a new entrant into the health topic spotlight. CBD's more well-known structural isomer, Δ^9 -tetrahydrocannabinol (THC),² is a source of confusion regarding the difference between these compounds and the seemingly sudden popularity and availability of CBD. The body of research regarding CBD is growing and the publicly touted benefits and cure-all promises appear to be growing even faster. The community and media presence of CBD is vast and thus, the responsibility of medical professionals to maintain awareness, follow the research and serve as a source of evidence-based information is paramount.

CORRESPONDENCE:

Lindsay Tjiattas-Saleski DO, MBA, FACOEP
Ltjiattassaleski@carolinas.vcom.edu

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PLANT SPECIES

CBD and THC, along with many other cannabinoids, coexist in various percentages within cannabis plants. Three plant species are recognized: *Cannabis indica*, *ruderalis* and *sativa*, each containing CBD and/or THC in variable, but sometimes predictable, fractions.³ CBD is created via a decarboxylation process from a cannabidiolic acid precursor and extracted for use.⁴ This compound acts on endogenous cannabinoid receptors in the human body called CB1 and CB2, affecting neurotransmission of GABA, glutamate and serotonin and demonstrating a diversity of pharmacologic actions. These include inhibition of endocannabinoid uptake, transient receptor potential vanilloid 1 activation, G protein-coupled receptor 55 activation and increased 5-HT1A receptor activity.^{5,6} CB1 receptors are located throughout the brain, including the cerebral cortex, hippocampus, basal ganglia and cerebellum, along with other organs such as the lungs, liver and kidneys. CB2 is found mainly in immune and hematopoietic cells.³ This vast distribution of potential sites of action accounts for many claims regarding CBD's effects.

THC:CBD RATIO

While THC acts as an agonist at CB1 and CB2, CBD acts as a minimal or inverse agonist and non-competitive antagonist at these sites.⁶ This accounts for a key principle in CBD's physiologic actions; pure CBD is non-psychoactive.⁷ The typical high associated with THC is not known to occur with CBD, likely due to antagonism or weak agonism at those same receptors. Therefore, the THC:CBD ratio determines the psychoactive and physical effects of the product, its legal status and even the name of the plant. Cannabis containing a high THC:CBD ratio, with THC greater than 0.3%, are those labeled as marijuana and expected to produce the sensations of intoxication, euphoria and relaxation.³ Plants containing a lower THC:CBD ratio, with less than or up to 0.3% THC, are those often known as hemp⁸ and are the focus of the CBD products that are so readily available in many states today.

POPULARITY

Despite the apparent marketplace novelty of CBD, interest and usage is massive and growing. Internet searches from 2017 – 2018 for CBD increased 160.4% nationally. In an assessment of Google searches in April 2019, CBD surpassed searches for other health topics like veganism, exercise and acupuncture, with 6.4 million CBD searches that month.⁹ A 2019 Gallup Poll reported that 14% of Americans endorsed CBD usage, with the highest density of users in the western United States. The 18- to 29-year-old group were the most frequent users, followed by 30 to 49-year-old. While no gender predilection overall was demonstrated, women used CBD more to treat anxiety and men reported use more for insomnia.¹⁰ In a 2018 cross-sectional study of CBD users, the majority noted use to treat specific medical conditions, most commonly pain, anxiety and depression. Somewhat troublingly, 76% claimed their primary knowledge of CBD stemmed from internet searches or word-of-mouth, demonstrating a potential lack of information available from more reputable sources.¹¹

ADMINISTRATION ROUTES

Administration routes encompass nearly every source of bodily entry. Sublingual is the most common route, usually as a liquid, where CBD is dissolved into sprays, oil droplets and tinctures.¹¹ While some solvents are harmless edible oils like olive, there are reports of products containing CBD dissolved into ethanol or harmful solvents such as naphtha, butane or petroleum.² The oils can be applied topically, absorbed sublingually or ingested in oral capsule form. The hemp flower is utilized like smokable tobacco and sold individually or as blends of various strains alongside effect claims. CBD products for vaporization devices are also available. Additional forms include cosmetics, infused textiles, concentrates utilized in a process known as dabbing and in food products or edibles such as gums, teas, honey, candies or spices.^{3,11,12} These products are easily available online and in CBD stores, vape or smoke shops, pharmacies, grocery stores, gas stations and even pet stores.

TREATMENTS

Interest in CBD stems from beliefs, some unfounded, about the product's benefits or safety, in addition to its massive availability and the curiosity induced by such prevalence. Users tout effects that are desirable, pleasurable or functional. CBD users may desire the believed benefits of cannabis without the high of THC.⁵ Some perceive that CBD is safer versus prescription or nonprescription drugs or that it does not have the addictive capacity. The many available forms allow users to partake via preferred route and some enjoy access to products that are odorless, efficiently dosed (such as the number of drops) or avoid the stigma of being a cannabis user.² Users may note the often legal status as a benefit or the belief that it will not be detected in drug screening. Claims exist of its efficacy as an anxiolytic, antidepressant, antiemetic, analgesic, prophylactic, anti-inflammatory, sedative, energy booster, sexual performance enhancer and natural cure-all. A casual internet search will reveal thousands of books touting CBD's infinite perceived benefits. Assertions of CBD treatment success for neurologic, psychiatric, musculoskeletal, autoimmune, endocrine, gastrointestinal, oncologic and substance abuse disorders saturate the public conversation, whether or not data has been supportive or even researched.

Despite potentially overzealous claims, CBD has demonstrated some physiologic effects due to its action at diverse tissues throughout the body. CBD does demonstrate antiemetic, anxiolytic, anticonvulsant, analgesic, antipsychotic, immunomodulatory and neuroprotective properties, but the clinical implications of these actions are still being delineated.^{3,13,14,15,16} In vitro studies have shown promising anti-tumorigenic properties, as CBD can induce apoptosis, inhibit angiogenesis, decrease free radical production and arrest the cell cycle, similar to several current treatment targets for anti-proliferative therapies.^{2,3} The compound lacks physiologic properties of an addictive substance and no cravings, withdrawal syndromes or compulsive use have been reported.⁴ Low-to-moderate doses show minimal sedation and can be stimulating, but high doses can induce sedation.¹⁷ The contraindications and adverse effects described with accuracy only refer to pure prescription CBD and further studies are needed into the effects of chronic administration.^{18,19} The only known contraindication is hypersensitivity to the compound. The adverse effects include drowsiness, sleep disturbances, skin rash, weight loss, decreased appetite, diarrhea, anemia and increased serum transaminases, infection and asthenia.¹⁹ However, as this only refers to the labeled reactions to prescription CBD, the unregulated products' potential additional effects are unknown.

Seizures

The strongest data support CBD's anticonvulsant properties and thus, it is the only treatment target with an FDA-approved CBD medication.²⁰ This topic gained attention partially due to multiple poignant anecdotal reports by parents of children with seizure disorders describing efficacy in seizure frequency reduction with CBD administration.²¹ However, the therapeutic benefit of CBD for uncontrolled epilepsy has been under evaluation since 1980.⁶ Epidiolex®, approved in June 2018, is indicated to treat the often frequent or intractable seizures associated with Lennox-Gastaut

(LGS) and Dravet (DS) syndromes in patients two years of age or older.¹⁹ This is a 99% pure CBD product,¹⁹ as THC has been shown to have both proconvulsant and anticonvulsant properties,^{22,23} while CBD alone is more consistently anticonvulsant via an only partially understood mechanism.²⁴ In a double-blind, randomized trial with DS patients, Devinsky *et al.* noted a greater reduction in seizure frequency with CBD added to standard antiepileptic therapy versus placebo.²⁵ Similarly, among LGS patients, the addition of CBD to a conventional antiepileptic resulted in greater reductions in the frequency of drop seizures than placebo.²⁶ A 2018 meta-analysis concluded that CBD, in conjunction with other antiepileptic drugs, decreased seizure frequency in patients with DS and LGS, although both had higher adverse events rates than placebo.⁶ While the mechanism is not fully understood, CBD in reviews has demonstrated efficacy as an adjunct to common antiepileptic drugs.²⁷ Epidiolex®, in its novelty, lacks long-term safety data but nonetheless represents a shift in the perspective on cannabinoids as medicine. And while many conditions have been described as targets for CBD application, this remains the only clinically validated indication.

Schizophrenia

Antipsychosis is a known CBD effect, possibly exerted via the facilitation of endocannabinoid signaling and antagonism at CB1 receptors.²⁸ The potential for CBD to reduce both the positive and negative symptoms of schizophrenia has been investigated. Cannabis CBD content has been shown to have an inverse relationship with self-reported positive psychotic symptoms in cannabis users, supporting its antipsychotic potential.²⁹ An overview of treatment prospects for the negative symptoms of schizophrenia noted that CB1 receptor density is correlated with the intensity of negative symptoms and CBD's antagonism at these receptors could account for the reduction of negative symptoms in a small trial of schizophrenic patients.³⁰ Another double-blind, randomized comparison of CBD to the atypical antipsychotic amisulpride demonstrated significant clinical improvement of schizophrenia symptoms. It was well-tolerated with fewer extrapyramidal symptoms, weight gain and prolactin release.³¹ McGuire *et al.* assessed CBD add-on therapy's safety and effectiveness to existing antipsychotic regimens in a double-blind, multicenter, randomized trial of schizophrenia patients, finding lower levels of positive psychotic symptoms at six weeks in the CBD group versus placebo, with similar rates of adverse events. The authors proposed that CBD may represent a new class of treatment for schizophrenia, as it does not appear to depend on dopamine antagonism.³² A 2018 literature review concluded that evidence suggested that CBD may exert antipsychotic effects in patients with schizophrenia. However, the authors cautioned that the antipsychotic effect appeared to be related to endocannabinoid plasma-level increase, not to CBD plasma levels. As endocannabinoid signaling facilitation was the most likely hypothesized mechanism for CBD's antipsychotic effects, continued research into the biochemical action and possible contribution to antipsychotic therapy is warranted.²⁸

Anxiety

While anxiolysis is one of the most endorsed effects of CBD by users, it remains a complex treatment target with mixed evidence-based support. Two pharmacologic mechanisms have been proposed; CBD agonizes 5-HT1A receptors and indirectly potentiates endocannabinoid transmission and both have been linked to the attenuation of defensive responses to threatening or stressful stimuli.³³ CBD has been shown to decrease the number of c-Fos positive neurons in the amygdala, thought to mark neuronal activation and play a role in expressing fear and anxiety.³⁴ Per a 2018 critical overview, CBD may exert an acute anxiolytic effect when administered in a single high dose in patients with Social Anxiety Disorder, possibly related to the modification of cerebral blood flow in the limbic and paralimbic areas or agonism of 5-HT1A receptors.²⁸ According to a recent systematic review, CBD may prove a developing role in alternative treatments for anxiety disorders, demonstrating consistent improved clinical outcomes in Generalized and Social Anxiety Disorders and anxiety related to Post-Traumatic Stress Disorder (PTSD). However, the reviewers noted that small sample sizes limited the majority of studies assessed and that few studies enrolled participants with actual anxiety disorder diagnoses and instead enrolled healthy volunteers modeling anxiety, possibly limiting the generalizability of the results.⁷ Further research evaluating the role of CBD in modulating anxiety disorders is suggested, notably in response to widespread unsanctioned use for this indication.

Substance Abuse Disorders

Recent media reports have proposed a new tool in fighting the opioid crisis: CBD. While the medical literature has not garnered quite the same enthusiasm, there is a growing body of investigation into this hypothesis.³⁵ CBD does possess physiologic activity at addiction-linked pathways, positing a theoretical mechanism for its role in modulating substance abuse. CBD acts on the endocannabinoid system, known to influence drug-seeking behaviors and agonizes serotonergic receptors, which are already pharmacologically targeted for regulating the stress response and compulsive behavior. CBD notably is also an allosteric modulator at μ and δ opioid receptors.³⁶ The reduced amygdala activation during negative emotional processing, as discussed in the anxiety section, also holds the potential to modulate addictive behaviors through dopaminergic and serotonergic effects.⁵

In an interesting correlation, states with legalized marijuana laws report lower numbers of opioid prescriptions, opioid overdoses and opioid-positive screens in motor vehicle fatalities.³⁷ Animal studies have shown CBD to alter drug-seeking behavior and inhibit cue-induced heroin seeking behavior.³⁸ These effects persisted weeks after administration and inhibited relapse behavior even when administered during heroin intake, suggesting that CBD could affect relapse prevention after periods of abstinence.³⁷ Even in a sensitive population of polydrug abusers, administration of a therapeutic dose of CBD failed to elicit significant abuse potential versus placebo. It showed significantly less abuse-related effects than the positive controls, dronabinol and alprazolam.³⁹ In a systematic review of CBD as an intervention for addiction, the authors concluded that it might benefit opioid addiction by decreasing drug-seeking behavior and reducing the reward-facilitating effects during intoxication.³⁶

Another review revealed several studies supporting the protective effects of CBD on addiction to psychostimulants, including reduction of the detrimental neural effects of cocaine and long-lasting prevention of cocaine and methamphetamine-seeking behaviors, but with controversial consistency in the results.⁴⁰ CBD has even been implicated in reducing the number of cigarettes consumed by smokers, but no data was found supporting alcohol abuse intervention.³⁶ A notable shortcoming limiting generalizability across this body of data is the scarcity of human trials.

Alzheimer's Disease and Parkinson's Disease

Unfortunately, neurodegenerative disorders represent ideal targets for pseudoscientific claims to reverse these irreversible and debilitating disease processes. Still, evidence for CBD's effects on Alzheimer's Disease (AD) and Parkinson's Disease (PD) manifestations poses an interesting hypothesis currently being investigated. Proposed mechanisms include reducing tau protein hyperphosphorylation, attenuation of neuroinflammatory markers, reduction of reactive oxygen species, counteraction of proinflammatory cytokines and attenuation of beta amyloid peptide effects in the hippocampus, modulation of microglial cell function and reversal of iron-induced neurodegeneration.^{41,42,43,44,45} A 2014 study was the first to demonstrate that CBD prevented the development of social recognition deficits in AD in transgenic mice and hypothesized its potential to treat the devastating social withdrawal and facial recognition deficits.⁴⁶ Regarding PD, the effects of CBD on physiologic mechanisms and markers of functional improvement have been described in the literature. Pathways implicated include attenuation of oxidative stress and neurodegeneration of nigrostriatal dopaminergic neurons.⁴¹ Specific to disease morbidity, a double-blind exploratory study noted a possible improvement in the quality of life measures, including functioning and well-being, in CBD-treated PD patients versus placebo.⁴⁷ However, a mini-literature review in 2018 cited a lack of support for improvement in motor symptoms of PD following CBD treatment and noted a potential role for prevention rather than treatment based on animal studies.⁴⁸

Chronic Pain

Another commonly endorsed reason for CBD use, chronic pain, represents a complicated and varied treatment target. Cannabis has historically been claimed to have analgesic effects, but pure CBD is a newer entrant into the conversation. CBD is touted anecdotally to treat many types of pain, but insufficient and inconsistent evidence exists for its recommendation.¹² Possible explanatory models include anti-inflammatory properties, suppression of lymphocyte proliferation, blockade of reactive oxygen burst by granulocytes, regulation of pain perception and inhibition of the lipopolysaccharide-induced increase in serum tumor necrosis factor.^{49,50} Evidence across literature reviews indicates that cannabinoids produce antinociceptive effects in inflammatory, myofascial and neuropathic pain in rodents; however, animal models dominate the body of research.^{15,51,52} CBD-induced analgesia in humans has not been extensively studied and a 2017 overview of systematic reviews on this topic consistently found insufficient evidence of any cannabis-based

medicine for pain management in patients with rheumatic disease and cancer.⁵³ A recent review also confirmed a lack of high-quality research investigating CBD for human musculoskeletal disease.⁵⁴ As there are no pure CBD pharmaceuticals approved for pain therapy, most research on this topic involves products containing THC/CBD combinations, limiting any attribution of effect to CBD alone.⁴⁹ Clinical trials on the subject are limited by small sample sizes, inconsistent cannabinoid types and dosages and variable assessments of pain.⁵⁰ Given the medical landscape shift towards non-opioid pain management options when appropriate, this area of cannabis research is deserving of future academic attention.

Sleep Disorders

While administration of medium- and high-dose CBD can cause sedation, evidence for its use as a sleep aid is mixed. The endocannabinoid system's role in the circadian sleep-wake cycle may be implicated, but an understanding of the mechanism is not complete.¹⁷ Administration of CBD has been linked to increased total sleep time in rat models and possible sleep effects in combination with THC in young adult humans.^{55,56} Isolated studies have tested specific sleep indications but reviews have not supported any broad, substantial benefit. A 2016 case study described a pediatric victim of sexual abuse, suffering from PTSD and refractory insomnia. They experienced increased sleep quality and quantity without noted adverse effects after a CBD oil administration trial.⁵⁷ Another small, non-placebo-controlled case series of PD patients demonstrated a rapid, significant and sustained reduction in the frequency of REM sleep behavior disorder symptoms after CBD treatment.⁵⁸ However, a large retrospective case series found improved sleep scores after one month of CBD treatment but the improvement was not sustained over the three-month study.⁵⁹ CBD was additionally not found to alter the sleep-wake cycle versus placebo as measured by polysomnography, subjective and cognitive measures in a randomized, double-blind crossover trial of healthy patients.⁶⁰ Again, much of the available research was conducted in animal models or with cannabis products containing THC and CBD, limiting the knowledge of CBD's effects alone.

SAFETY CONCERNS

Regardless of the evidence surrounding indications, CBD is widely available and use is increasing. Projections of retail sales of CBD products are estimated to be as great as \$1.9 billion by 2020. Therefore, a discussion of the safety concerns is necessary. Per the World Health Organization's 2018 Cannabidiol Critical Review Report, *"to date, there is no evidence of recreational use of CBD or any public health-related problems associated with the use of pure CBD."*⁴ Pure CBD is well-tolerated at up to 1500 mg per day with a favorable safety profile confirmed in a review of clinical data.^{18,19,22} However, CBD does inhibit cytochrome P450 both *in vitro* and in animals, representing a concern for many conceivable drug interactions.^{18,22,61} A case report detailed a 44-year old male on chronic warfarin therapy whose International Normalized Ratio (INR) increased with up-titration of CBD oil.⁶² Oral absorption has also been shown to increase when taken with high fat or high-calorie meals due to its high lipophilicity.^{19,22} In

laboratory animals, hepatocellular injury and developmental and reproductive toxicities have been demonstrated. CBD use is not recommended during pregnancy in response to adverse events described in animals. In humans using non-medicinal cannabis, it has been detected in the umbilical cord.^{6,63} The risk of passage into breastmilk is currently unknown.¹⁹

The most concerning risk may be the unknown production, composition and quality of non-pharmaceutical CBD. Cannabinoid analysis can differ significantly between testing labs and there are no generally accepted guidelines or laboratory certification qualifications. Contaminants have been reported, some of which could have potential health outcomes, including pesticides, synthetic cannabinoids, heavy metals, molds, bacteria and aflatoxins. Some samples have shown levels of non-decarboxylated cannabinoids, which have not undergone the typical extraction process and effects of these precursors in vivo have not been studied thoroughly.² The THC:CBD ratio often can deviate from the label, which raises many concerns, including intake of undesired THC levels, legal implications, sub-therapeutic CBD dosages or unwanted or adverse THC effects.

In a Dutch study,⁴⁶ cannabis oil samples, obtained online or from home stores, were tested versus their labeled THC and CBD percentages. Seven samples were devoid of any cannabinoids and several drastically diverged from their labeled concentrations, with percentage differences of CBD up to 100%. Others contained more THC than indicated by their packaging, with one sample containing 57.5% more.⁶⁴ An American analysis of 84 CBD products from 31 online retailers reported equally disconcerting mislabeling, where 42.9% were under-labeled for CBD content, 26.2% over-labeled and 21.4% had THC content sufficient to potentially induce intoxication or impairment.⁶⁵ These results not only pose potential health risks but also raise concern for implications in drug screening. While pure CBD intake is not known to result in a positive urine drug test by federal workplace guidelines, CBD products that include THC, perhaps unknown to the user, can produce positive urine screening results.⁶⁶

Cannabis has a long and convoluted history with the legal system, the intricacies of which are beyond the scope of this discussion. Per the *Controlled Substances Act*, marijuana and its compounds and derivatives, including cannabinoids, are classified as Schedule 1 substances. However, the Agriculture Improvement Act of 2018, the so-called Farm Bill, removed hemp, defined as the cannabis plant or any part thereof containing less than or equal to 0.3% THC, from the definition of marijuana and categorization as a controlled substance under federal law.²¹ This largely accounts for the noticeable expansion in CBD availability, but individual state cannabis access laws vary widely. They range from the prohibition of all cannabis, including CBD, to full adult and medical cannabis use programs, adding to the ambiguity about purchase and consumption. Regulatory concerns further complicate the dialogue, especially regarding its status as a medicine or natural food product.

This classification changes the regulation, as medicines are considered unsafe until proven safe, but food products are considered safe until shown otherwise.² Per the FDA, under the *Federal Food, Drug and Cosmetic Act*, CBD is excluded from the

definition of a dietary supplement and unsubstantiated medical claims are prohibited. The FDA issued *Warning Letters* in 2015 and 2016 to online vendors in violation of these terms for misbranding CBD products with medical claims or mislabeled contents.⁶⁷ However, enforcement depends on resources to do so and the threat posed to public health, explaining some of the widespread accessibility.⁸ Age limit to purchase is variable depending on the state and individual vendor policies.

CLINICAL TRIALS

Clinical trials abound in this time of massive influx of CBD information and prevalence of use. Pharmaceuticals are in various testing phases for a diverse list of new indications. Pure CBD in tablet, transdermal gel, sublingual oil, powder, aerosolized inhalant and intravenous formulations are facing research scrutiny for future potential medical application. Trials are underway for expanding the anticonvulsant indications, including other treatment-resistant epilepsies, absence seizures, Sturge-Weber Syndrome, Tuberous Sclerosis and infantile spasms.^{4,27,68} The list of additional medicinal CBD products in development is expansive and includes hypothesized indications for Fragile X Syndrome, marijuana adverse event prevention, Graft-Versus-Host Disease prevention, schizophrenia, encephalopathy and Prader-Willi syndrome.^{4,69,70} Theoretical proposed treatment targets based on preliminary studies represent an even larger body of intriguing future research directions, including many psychiatric disorders, autism spectrum disorders, diabetes mellitus complications, inflammatory bowel disease, post-ebola syndrome and pain management.^{71,72,73,74,75} The body of evidence is growing and represents an area of necessary attention for health care professionals to provide current and informed evidence-based medicine.

CONCLUSION

The advice for clinicians remains to be vigilant for high-quality studies and evidence. The current body of research on cannabinoids is ever-changing and it is the duty of practitioners to follow and critically evaluate the data. Consider asking patients about their CBD use, specifically when obtaining a social history. Document quantity, frequency and route if known. Ask patients their purpose for the use, as it may facilitate discussion of a formerly unrevealed medical concern. Offer alternatives if a patient is using CBD to treat a specific symptom and utilize the conversation as an opportunity to educate and discuss potential effective therapies. Inform patients of potential risks, including adulteration of CBD products, scarcity of evidence for non-pharmaceutical use, drug interaction risks and potential legal concerns due to inconsistent labeling. Remain non-judgmental and unbiased to better facilitate a patient-physician partnership to approach their concerns and rationale for use. As more evidence becomes available, being a source of reputable information for patients remains a high priority and a necessity to protect and improve the health of the community.

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