



Short Review

Myths and Realities about CBD as Medicine

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Abstract

The two cannabinoids from the plant *Cannabis sativa*, Linn., Cannabidiol (CBD) and delta-9 Tetrahydrocannabinol (THC) have been extensively studied for their pharmacologic activities and therapeutic potential. CBD is being extensively promoted as medicine for the treatment of a wide range of clinical conditions ranging from neurological, mental, to numerous health conditions. The available research shows that it is all a myth that CBD can safely and effectively treat health conditions involving almost every physiological system as promoted. The reality is that research from well-designed clinical studies and trials show that CBD can safely and effectively treat only one type of rare and severe type of epilepsy, known as Lennox-Gastaut/Dravet syndrome, in young children for which it has been approved by the US FDA. In combination with THC known as Sativex, it is approved in 25 countries including Canada, except the United States, for treating symptoms of multiple sclerosis including muscle spasticity, pain and sleep disturbances. Therefore, it is important that addiction psychiatrists and other addiction health care professionals play an important role in educating their patients that there is insufficient data to support CBD as medicine for treating clinical indications for which it is being promoted.

Keywords: Cannabidiol; CBD; Myths; Realities

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Introduction

Cannabis sativa Linn is a complex plant that contains 525 identified and characterized chemicals, of which 104 are classified as cannabinoids [1], while the rest are terpenes and flavonoids. Only two cannabinoids-- delta-9-tetrahydrocannabinol (THC) and Cannabidiol (CBD)-have been extensively studied for their potential therapeutic applications. In this commentary, we will present the most current data and show whether CBD as medicine, being promoted for the treatment of a wide range of clinical indications, is a myth or a reality.

CBD is a non-psychoactive chemical constituent of cannabis [2] that acts via CB2 receptors in the body. Mannucci et al., [3] reviewed the literature and concluded that for CBD's non-addictive, anti-inflammatory, neuroprotective, and antioxidant properties, this molecule alone or in combination with THC, could be beneficial in treating Parkinson's disease, Alzheimer's disease, Multiple Sclerosis (MS), Huntington's disease, Amyotrophic Lateral Sclerosis (ALS), and cerebral ischemia, but recommend additional clinical trials to confirm its use in each of these neurological conditions. Data from numerous small clinical studies and clinical trials show that CBD alone or in combination with THC also has a potential to treat anxiety, depression, and many other non-CNS conditions like heart disease, acne, inflammation, liver disease and cancer.

The reality is that CBD can be safely and effectively used for the treatment of rare and severe forms of epilepsy-Lennox-Gastaut syndrome and Dravet syndrome in children two years of age and older (<https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm611046.htm>). This was based on the anticonvulsant action of CBD that was confirmed in several small clinical studies [4] and large randomized, double-blind, placebo-controlled clinical trials [5-7]. In a survey of parents of children with treatment resistant epilepsy, it was found that CBD treatment reduced the frequency of seizures in 84% of respondents. In a randomized, dose-range safety trial in patients with Dravet syndrome, the plasma levels of CBD and its metabolites were dose-related at 2, 5, and 10 mg/kg/day doses respectively; and CBD was well tolerated with side effects like pyrexia, somnolence, decreased appetite, sedation, vomiting, ataxia and abnormal behavior [6]. Data from well planned and designed studies also clearly showed that CBD (Epidiolex) reduced the frequency of convulsions (tonic-clonic, tonic, clonic and atonic) seizures in patients with Dravet and Lennox-Gastaut syndromes [6,7]. CBD tested in a 12-wk trial in patients with treatment resistant epilepsy also reduced the frequency of seizures [8]. CBD treatment also improved the energy level, memory, control/helplessness, cognitive function, social interaction and general global quality of life of children with epilepsy [9]. It is important to note that of the 102 clinical trials registered in www.clinicaltrials.gov, 26 trials are studying the efficacy of CBD for the treatment of one or more types of seizures. In the case of movement disorders/multiple sclerosis, due to its anti-inflammatory effects, CBD could be used to treat MS-related movement disorders [10,11], and in combination with THC (Sativex [THC:CBD in a 1:1 ratio]),

and was effective in treating MS without adversely impairing driving performance [12], and improving mobility in patients with MS [13]. Incidentally, Sativex is approved in 25 countries including Canada but not in the United States for treating MS-related neuropathic pain, sleep disturbances and muscle spasticity. This is where the reality ends.

There are several myths that CBD can be used to treat a wide range of clinical conditions including neurological/mental conditions, drug use, and inflammatory disorders as mentioned above. In the case of schizophrenia, although preclinical and clinical studies show that CBD could treat schizophrenia, psychosis [14], hallucinations, delusions, negative symptoms of schizophrenia such as lack of emotion, loss of social functioning [15], and though CBD is well tolerated with no worsening of mood, suicidality, it was ineffective at 600 mg/day in treating the cognitive impairment and other neuropsychiatric complications seen in patients with schizophrenia [16]. Khoury et al., [17] reviewed the literature and concluded that there was no strong evidence to support CBD use in psychiatry at this time and those large well-designed clinical trials are required to assess the effects of CBD in psychiatric disorders. Regarding Alzheimer's and Parkinson's diseases, data from small clinical studies with a few patients show that CBD could be used to treat sleep disorders and improve the quality of life in patients with Parkinson's disease [18], and psychosis [19] without serious adverse effects. However, a significant amount of research from clinical studies and trials is needed to support its use in treating Alzheimer's and Parkinson's diseases [3]. In the case of spinal cord or traumatic brain injuries, studies in rats showed that CBD applied immediately to the damaged spinal cord minimized the extent of damage and improved the quality of movement in rats [20], but there are no clinical studies to support its use in treating spinal cord and traumatic brain injuries in humans. Similarly, because of its neuroprotective effects seen in animal studies [21] where CBD protected neurons following an injury, it could be developed to treat traumatic brain injury in humans. Similarly, research in rats [22] and mice [23] show that CBD protected against brain damage seen in stroke. However, there are no data from studies in humans that CBD would be effective in treating stroke in humans.

CBD appears to be a promising drug to treat anxiety disorders including opiate use disorder, panic disorders, generalized anxiety disorder, PTSD, and social anxiety disorder and opiate withdrawal [24]. Several anecdotal reports also support the benefits of CBD for treating anxiety. Since CBD activates the endocannabinoid system by increasing levels of naturally occurring cannabinoids, such as anandamide, research suggests that changes in the endocannabinoid system may be involved in depression and therefore, CBD could treat depression. Further, CBD acts as an antidepressant by acting on serotonin pathways in the brain [25] and it can specifically reduce anhedonia, a symptom of depression that makes people unable to feel joy or happiness [26]. Since anxiety and depression occur in bipolar disorder, CBD may stabilize mood in bipolar disorder too [27]. However, CBD failed to improve acute manic episodes of bipolar in patients with mania [26], even though animal research suggested that CBD could protect mania-related brain damage [27]. Additional research is needed to support the use of CBD for treating depression.

Regarding sleep disorders, although CBD was effective in promoting wakefulness in rats via triggering increased levels of dopamine in areas of the brain responsible for wakefulness [28]

suggesting that CBD could promote wakefulness in disorders causing excessive sleepiness, such as narcolepsy. But in only one case report, CBD improved the quality and quantity of sleep in a 10-year-old young patient with PTSD, most likely due to its anxiety-relieving benefits [29]. Therefore, more clinical research is needed to support its use in treating sleep disorders in humans.

Preclinical research suggests that CBD could treat inflammatory diseases of the gut such as colitis, inflammatory bowel disease and Crohn's disease. CBD at 10 mg/d, po, was safe but not effective in treating Crohn's disease, possibly due to small dose of CBD, the smaller number of patients, or lack of synergism with other cannabinoids, and suggested further investigation. CBD may be effective in treating chronic pain, arthritic pain, cancer-related pain, but the potential benefits of cannabis-based medicine in chronic neuropathic pain might be outweighed by their potential harms [30], and there is inadequate evidence for supporting the use of cannabinoids (dronabinol, nabilone, medical cannabis, or THC/CBD spray) in the treatment of cancer pain, pain of rheumatic or GI origin [31].

Preclinical research showing antiemetic effects of CBD in animals suggests that CBD may stop nausea and vomiting in patients that are not getting relief from prescribed anti-nausea drugs. But additional research is needed to support CBD use in treating nausea and vomiting in humans. Although smoked cannabis increases appetite and weight gain in patients with HIV/AIDS without affecting viral load [32], and the oral THC also increased the weight gain in patients with cachexia (extreme loss of weight), there are no studies to show that CBD stimulates appetite in humans.

CBD has been tested to treat tobacco, opiate, and/or cannabis use disorders. CBD decreased the number of cigarettes smoked [33] and reduced the salience and pleasantness of cigarette cues at a single dose of 800 mg but did not influence tobacco craving or withdrawal or any subjectively rated side effects [34]. CBD plus THC (Sativex) combined with Motivational Enhancement Therapy and Cognitive Behavioral Therapy (MET/CBT) was well tolerated and reduced cannabis use and craving but not withdrawal symptoms in chronic cannabis users [35]. Additional research is needed to determine if CBD alone or as an adjunct could be used to treat cannabis dependence. In a small clinical trial, CBD reduced the cue-induced craving and anxiety in people with opiate use disorder [36], but the investigators suggested that large clinical trials are needed to confirm the efficacy of CBD in treating opiate use disorder. The National Academy of Sciences (2018) [37] also suggests that CBD has a potential to treat a wide range of health ailments.

Conclusion

There is no doubt that CBD has a great potential to treat a wide range of clinical conditions/diseases, but as discussed above and elsewhere [38,39], the only reality is that CBD can safely and effectively treat a rare and severe form of epilepsy in young children, and in combination with THC, treat MS-related neuropathic pain. Whether it has been demonstrated to be effective for any and all clinical conditions as promoted, is all a myth. As recommended by National Academy of Sciences (2018) [37] and others, more systematic research and clinical trials are needed to further develop CBD as medicine by conducting well-designed clinical trials and get it approved by a regulatory agency like the US Food and Drug

Administration for its clinical use. It is also of paramount importance that the addiction physicians and psychiatrists play a role in educating their patients regarding the insufficient data to support the prescription of CBD for treating any of their mental, neurological or any other health ailment [40].

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Conflicts of Interest

None for JK, GB and SBM.

Contributions

Conceived by JK, then all authors contributed equally to the manuscript.

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Disclaimer

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