

FAST FACTS AND CONCEPTS #370
THE ROLE OF CANNABIDIOL (OR CBD) IN PALLIATIVE CARE
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Background CBD has received public interest as an antidote for pain, epilepsy, anxiety, and nausea (1-4). In the United States (US), there is one FDA approved CBD-based medication – Epidiolex – which is indicated for refractory seizures from disorders such as Lennox-Gastaut syndrome and Dravet syndrome at a usual dose range of 2.5 to 20 mg/kg twice a day. More commonly though, CBD refers to non-regulated oil which is either derived from a marijuana plant (true CBD oil) or a hemp plant (hemp oil) (5). This *Fast Fact* addresses common clinical questions about CBD oil. For more general information on the use of cannabinoids in palliative care, see *Fast Fact* #279.

What is the difference between THC and CBD? The cannabis plant produces more than one hundred cannabinoids (1). At least two of these, delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), have potential use for symptom management (1,6). While THC is associated with CNS-altering effects, CBD oil is non-intoxicating at least in doses up to 600 mg and it does not appear to convert to THC in vivo (1,5). Most cannabinoid research has focused on THC which activates cannabinoid receptors CB1 and CB2 or THC/CBD combination products. However, CBD-only products have garnered attention as a potentially safer therapy, with some researchers even suggesting that CBD could minimize the intoxication effects of THC when used in combined formulations via CB1 receptor antagonism (5).

Is CBD legal? It depends on where you live. US laws regarding CBD oil are rapidly changing. In general, true CBD oil, meaning derived from a marijuana plant, is restricted as a type of medical marijuana. More than 30 states have legalized CBD by legalizing medical marijuana and an additional 16 states have laws specific to CBD (7). Regardless, under US federal law, true CBD oil remains a Schedule I controlled substance (7). This means that in states that have legalized medical marijuana, clinicians can only “certify” patients have a qualifying condition or “recommend” it, but they cannot prescribe it (7). In some states, clinicians can write a letter to reduce the risk of legal issues. In October 2018, Canada legalized marijuana use and thereby legalized the use of CBD.

How does hemp oil differ from true CBD oil? Hemp is a variety of the cannabis plant grown for industrial uses. It is generally a poor source of cannabinoids and has THC concentrations <0.3% (7). Because it is derived from the seeds of hemp plants, hemp oil is commercially available and is excluded from the Controlled Substances Act definition of marijuana (7). However, if CBD were to be specifically isolated from the hemp plant, even the seeds, it would then be considered marijuana (7). Hemp oil is often erroneously referred to as CBD oil commercially (7). Its CBD content is lower than true CBD oil.

What research do we have on CBD for pain? No randomized controlled trials of CBD-only products for pain management in humans exist (6,8). Most of the supporting data comes from mouse models, including studies on paclitaxel-induced pain and arthritis (9-11). One case series of seven kidney-transplant patients who requested CBD for chronic pain showed it to be effective in relieving pain in 6 of the patients and no adverse effects were reported (12). There are yet no convincing data that CBD is an opioid-sparing analgesic in humans. Published results of a combined THC/CBD oromucosal spray have been mixed. Three long-term perspective studies showed improved pain control, but neuro-psychiatric effects contributed to a discontinuation rate of 23% (13-16). A systematic review on THC/CBD did not show clinically significant benefits for neuropathic pain (13).

Besides pain, what can CBD be used for? In human observational studies, CBD appeared to reduce public-speaking related anxiety (1,17). It has also decreased nausea in rat models (1,17). Pre-clinical studies suggest that CBD oil may have anti-tumor effects, particularly in the treatment of glioma (1). THC/CBD compounds have been studied in humans for insomnia with mixed effects (2). There is anecdotal evidence of CBD oil being used to treat refractory epilepsy in children and adults.

What are the side effects of CBD oil? In general, they are mild and include nausea, dry mouth, dizziness, and drowsiness (12). A few studies raised concern for more serious side effects (9, 18-20). In a pediatric study of CBD oil for epilepsy, nearly 20% had elevated LFTs (18). Other studies have associated the use CBD oil with compromised effects on reproductive hormones (9,19). The risk of drug interactions is not firmly established, although many experts suggest this risk would be low (20).

Is CBD addictive? Animal research suggests CBD may inhibit drug-seeking behavior like craving or compulsive use (21). Systematic reviews in humans are inconclusive, although correlations have been noted between medical cannabis legalization and decreases in opioid overdose deaths (3-4,22).

Where is CBD oil available? True CBD oil is available through marijuana dispensaries. Hemp oil that contains CBD (often erroneously labeled as CBD oil) is available via the internet and many health food stores. Most CBD formulations consist of viscous extracts suspended in oil, alcohol, or vaporization liquid which can be administered either orally (often under the tongue) or topically (23).

What is the appropriate dosage? To date, no dose-confirming studies exist for pain, nausea, or anxiety. Dosages can range from 15 mg to 900 mg in various formulations (1,18,24), although many patients titrate to effect.

Are the products labeled accurately? The FDA has issued numerous warnings to vendors about mislabeling (7). A recent study examining the accuracy of online CBD products found that only 30% of products accurately labeled the CBD dose: most understated the CBD dose, a quarter overstated the dose, and some formulations contained no measurable amount of CBD (23). Approximately one fifth contained THC which raises intoxication concerns, particularly when given to children (23).

When should I recommend CBD? While CBD oil may offer some therapeutic benefits, inconsistent labelling, an unknown therapeutic window, and a lack of quality human clinical investigations supporting its use should caution clinicians from recommending CBD oil to their patients (2). Much like other untested supplements, clinicians should inquire about its use in a non-judgmental, open-minded fashion.

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