

# Cannabidiol (CBD): Medical Uses

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## Purpose:

The purpose of this course is to familiarize the nurse with cannabidiol and with its modes of action, medical uses, and safety concerns.

## Goals:

Upon completion of this course, the nurse should be able to:

- Explain the difference between CBD and THC.
- Explain the difference between hemp extracts and marijuana extracts.
- Discuss how CBD and THC interact with CB1 and CB2 receptors.
- Explain the 3 types of CBD products.
- Discuss typical doses of CBD.
- Discuss 5 medical uses for CBD.
- Discuss at least 4 safety concerns regarding CBD.

## Introduction:



Cannabidiol (CBD) is derived from the cannabis plant, more commonly referred to as marijuana and hemp, comprising 40% of the plant's extracts (cannabinoids). Cannabis plants contain both CBD and delta-9 tetrahydrocannabinol (THC), the principle psychoactive constituent. Cannabis contains more than 400 different chemical components of which 61 are considered cannabinoids.

Cannabidiol, which has no psychoactive properties, is most often extracted from hemp, which is in the same plant family as marijuana. Hemp extracts have higher levels of CBD, and marijuana extracts have higher levels of THC. For example, hemp must contain 0.3% or less of THC while marijuana contains 5 to 35% of THC (depending on how it's been bred).

Cannabis extracts can be made by straining a solvent (CO<sub>2</sub>, butane hexane) through finely ground or fresh leaves, flowers, and stems or by hot pressing fresh or dry buds to extract the flower's oil. If the extract is created from fresh flowers, it may be referred to as a resin; if extracted through hot pressing (for which home kits are available), a rosin.

After CBD and THC are extracted, these components can be processed into a number of different forms, such as wax, sap, and liquid so that they can be used in various ways: applied topically, through vaping, and by ingesting in edibles or in tablet form.

CBD is now legal in some states where marijuana remains illegal, and the FDA (2018) approved the prescription use of a purified form of CBD oil (marketed as Epidiolex®) for the treatment of two types of epilepsy. Most medicinal forms of CBD are derived from hemp because marijuana plants have been selectively bred to contain high levels of THC although marijuana with low THC levels may also be used to produce CBD.

Hemp was unintentionally banned in 1970 with the Controlled Substances Act because it was a form of cannabis, despite the fact that it was not psychoactive. It was not formally legalized in all states until the Hemp Farming Act of 2018, so now hemp can again be grown in the United States for commercial purposes, including the production of CBD for medicinal uses. The FDA allowed researchers to conduct trials with CBD in 2015.

### **Action:**

The human body produces cannabinoids naturally and has two cannabinoid receptors CB1 and CB2, which are present throughout the body, including the brain. CB1 is found primarily in the brain and nervous system. THC attaches to CB1 receptors in the brain, bringing about the typical changes in mood, emotions, thought processes, appetite, and memories that occur with marijuana use.

The CB2 receptors are more commonly found in the immune system where they affect pain and inflammation. It was believed that CBD attached directly to CB1 and CB2 receptors, but subsequent studies has shown that,

instead, the CBD attaches only weakly to CB1 and CB2 receptors but directs the body to use more of its own cannabinoids by triggering the body to create additional CB1 and CB2 receptors. CBD provides an improved mood and improved tolerance to pain without the euphoric response or impaired motor skills associated with THC,

CBD has been shown in studies to have a wide variety of effects: analgesic, anticonvulsant, muscle relaxant, neuroprotective, anti-oxidant, and anti-psychotic. CBD has not been found to alter physiological parameters, such as heartrate, blood pressure, and body temperature.

CBD is absorbed fairly rapidly. If administered buccally, peak plasma concentration occurs within 2 to 4 hours, but smoking or inhaling CBD increases the plasma level more rapidly.

Both THC and CBD are metabolized by the liver and may be stored in fatty tissue for up to 4 weeks, from which they are slowly released in low levels back into the blood stream.

## Products/Dosages:



CBD products are marketed as oils, capsules, patches, creams, ointments, vaping pens, and other forms as well. CBD products may have many different formulations. Some may be combined with THC. Cannabis plants generates cannabinoids as well as terpenes and other chemical compounds that work together, so purified CBD may

have a different effect than those containing other plant components.

Types of CBD include:

- **CBD isolate:** Contains purified CBD only.
- **Full-spectrum CBD oil:** Contains CBD, trace amounts of THC (less than 0.3%), other cannabinoids, and terpenes. (Note, this amount is too low to trigger a positive finding in most drug tests.)
- **Broad-spectrum CBD oil:** The same as full-spectrum except that all of the THC has been removed.

In some cases, full-spectrum CBD oil may be more effective than CBD isolate. Generally, those taking CBD isolate require higher dosages than

those taking full-spectrum CBD oil because the CBD isolate lacks the synergistic effects of full-spectrum CBD oil.

Typically, the dosage of liquid CBD products is expressed in mg per fluid ounce or per milliliter. The milligrams are designated for CBD capsules. The average adult dose range for CBD is 15 to 50 mg three times daily although some may need up to 100 to 200 mg to control pain. Creams and salves developed for topical use generally contain small amounts of CBD, but this may vary according to the product used.

Research studies have shown that patients have used up to 1500 mg of purified CBD per day without reported harmful effects and prolonged use has not shown a potential for drug abuse. However, some people can develop liver disease, so liver function tests are advised before beginning treatment, such as with Epidiolex®.

Generally, patients who wish to use CBD should begin with a low dosage and then gradually increase the dose, but full benefits may not be evident for up to two weeks.

## Medical uses:

Because of federal limitations on research into cannabis products, medical research has been limited, and use of CBD often precedes research evaluation of efficacy. Much more information will likely be gleaned about the use of CBD in the next few years. CBD is currently used by many patients for conditions for which there is little or no supporting evidence.

## Epilepsy (Epidiolex®)



The FDA (2018, June) approved Epidiolex®, which is an oral solution of CBD, to treat two different rare forms of epilepsy: Lennox Gastaut syndrome and Dravet syndrome. Studies have shown that patients treated with the drug showed significant reduction in seizures.

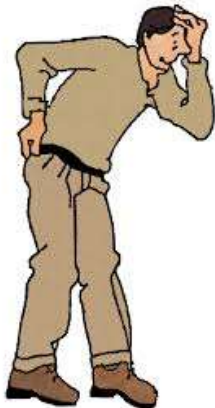
Prior to beginning treatment with Epidiolex®, the patient's liver function tests should be assessed with ALT, AST, and total bilirubin because CBD has been associated with hepatocellular injury in rare cases. Elevated ALT is greatest in patients also taking valproate and/or clobazam. Followup tests should be done at 1 month, 3 months, and 6 months after beginning

treatment with Epidiolex® and periodically afterward. ALT and AST levels greater than 3 times normal are predictive of liver damage.

Epidiolex® is administered orally in solution (100 mg/mL) at an initial dose of 2.2 mg/kg twice daily, increased to 5 mg/kg twice daily after one week. The maximum recommended dose is 10 mg/kg twice daily. Seizure control tends to be better at higher doses but adverse effects also increased

Adverse effects include hypersensitivity reaction, somnolence, sedation, and (as with other antiepileptic drugs) suicidal behavior and ideation. If Epidiolex® must be withdrawn, it should be withdrawn gradually if possible because of the risk of increased seizure activity and status epilepticus.

While CBD is used successfully to treat some forms of epilepsy, one study did show that some children with refractory epilepsy actually worsened with CBD. An Israeli study using CBD to treat 74 children with severe epilepsy found that 89% has some or total reduction of seizures but 7% reported aggravation of seizures, so CBD should be used only under the careful supervision of physicians.



### **Pain relief**

CBD is believed to block pain-conducting impulses so that the perception of pain is reduced. CBD stimulates the CB1 receptors in the brain to increase production of dopamine, which reduces pain. Additionally, CBD increases production of natural endorphins, reducing pain while avoiding the dependence and addiction associated with opioids. (Opioids, on the other hand, mimic endorphins and suppress natural production.)

CBD also modulates the 5-HT1A receptor, associated with serotonin, so CBD can produce a calming effect without sedation, and this may help to promote better

sleep.

Studies in states with legal CBD, such as Colorado, which has legalized recreational marijuana, and others that have legalized medical marijuana show that the most common medicinal reason that people seek CBD is for the treatment of chronic pain. Additionally, analyses of prescriptions show that an increase in the use of CBD decreases prescriptions of conventional pain medications, including opioids.

A review of 38 randomized trials in patients with chronic pain shows that plant-derived cannabinoids increased the odds of pain improvement by 40% over controls, and cannabinoids showed increased pain improvement over placebos.

A number of animal studies have suggested that CBD may relieve the pain of rheumatoid arthritis and osteoarthritis joint pain and inflammation, but the evidence to conclusively prove its effectiveness is lacking.

One major problem with studies conducted in the United States is that the products available at a federal level have been either vaporized or smoked, but products that are commonly used, such as transdermal patches, creams, and capsules have a different delivery system. Thus, there is little accurate information available about efficacy, dose, administration routes, and side effects of commercially available preparations.

### **Immunomodulation**

CBD reduces inflammation, so research is being carried out to determine if CBD may provide benefits for those with diseases associated with immune dysfunction, such as fibromyalgia, chronic fatigue syndrome, Crohn's disease, and ulcerative colitis.

### **Multiple sclerosis**

In the UK, Europe, and Canada a formulation of 1:1 CBD to THC (marketed as Sativex® in Canada), has been approved for use as an adjunctive treatment to relieve muscle spasticity and pain associated with MS but also pain associated with cancer. This drug is still undergoing clinical trials in the United States (as Nabiximols). However, some patients are using personalized or pre-packaged combination of CBD and THC for treatment as these cannabinoids are available in some states without prescription.

A recent study indicates that CBD (CBD:THC combination of 1:1 or greater CBD) reduces fatigue, pain, inflammation, depression and spasticity in MS patients, allowing them to increase their mobility. The decreased depression appears to be dose-related but the exact mechanism by which that occurred is unclear.



### **Chemotherapy-induced nausea and vomiting**

Two cannabinoids are FDA-approved for the treatment of chemotherapy-induced nausea and vomiting: Dronabinol (Marinol®) and nabilone (Cesamet®). However, dronabinol is a synthetic form

of THC and nabilone a synthetic form of a cannabinoid that is similar to but more potent than THC.

CBD is also sometimes used to control nausea and vomiting. Animal studies suggest that its antiemetic effects are produced by indirect activation of 5-HT (1A) receptors. Anecdotal reports suggest that CBD relieves nausea and vomiting, but there are few research studies at present to support this use as most preparations studied include or are limited to THC.

## **Safety concerns/Adverse reactions:**

While adverse effects are usually mild, nurses should be aware of concerns:

- While CBD does not alter consciousness, it is not without some safety concerns. When ingested, it may result in nausea, fatigue, and irritability in some patients. However, **adverse reactions** tend to be relatively mild.
- CBD can also **affect other medications**, by the same mechanism that grapefruit interacts, so patients taking other medications should be aware of possible interactions. CBD is known to increase the level of coumadin, for example, when taken concurrently.
- CBD may **impact the activity of liver enzymes**, such as cytochrome P450, and at high doses, CBD may temporarily deactivate these liver enzymes, thereby altering the metabolism of a wide range of compounds. Greater than 60% of current drugs are metabolized by this group of liver enzymes.
- One concern is that many forms of CBD are marketed as dietary supplements and, therefore, **not currently regulated by the FDA** so the consumer has no way of knowing if the labeled ingredients are correct. One study showed that tested products purchased online contained 26% less CBD than indicated on the label, seriously effecting the dosage.
- Some manufacturers of CBD have made **extravagant claims**, such as that CBD can cure cancer, or made other claims regarding benefits that have not been demonstrated through research studies.
- Additionally, some **CBD products contain THC** as well as CBD, and these products can affect long and short-term memory and attention as well as mood and mental health (the same as marijuana), so it's

important for consumers to discuss the use of CBD with a physician, to obtain CBD products from reliable sources, and to fully understand the components.

- Limited research has been carried out regarding the safety of CBD during **pregnancy**, so women who are pregnant should discuss use with their physicians. However, CBD is generally believed to be safer than THC during pregnancy. Some pregnant women take CBD to reduce nausea. Animal data suggests that CBD may cause fetal harm.

## Conclusion:

CBD has potential uses in many areas of medicine by itself or in combination with THC and other cannabinoids, but research is ongoing and has not yet begun in some areas because of longstanding restrictions on research with cannabis products.

Most production of CBD products is unregulated by the FDA, much current use is not supported by research, and the most effective dosages and drug formulations are not clear. Production is simply outpacing regulations in the United States; however, the industry should expect more regulations as times pass. It's likely that many of the regulations regarding food processing will eventually apply to the production of CBD oil.

Many of the claims regarding CBD at present are anecdotal or simply false, so those who wish to try CBD should proceed with caution and consult a healthcare provider familiar with CBD. While CBD has relatively mild side effects for most people, CBD can interfere with the metabolism of many drugs and can, in some cases, result in liver damage. Patients should consult with a pharmacist about drug interactions before using CBD.

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