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CBD: Weeding Through the Controversy (255)

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Contact hours: 1.5

Course price: \$10

Course Summary

This course explains the medicinal use of cannabis, in the forms of CBD. It introduces the endocannabinoid system, addresses the legal issues, outlines therapeutic indications, and examines the claims of various products.

Course Objectives

Upon completion of this course you will be able to:

1. Explain 3 differences between CBD, marijuana, and cannabis.
2. Relate 4 unique features of the cannabis plant.
3. State 5 therapeutic uses for cannabis.
4. Discuss 3 common routes of administration of cannabis.
5. Describe elements of patient and family education regarding CBD.

Criteria for Successful Completion

80% or higher on the post test, a completed evaluation form, and payment where required. No partial credit will be awarded.

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CBD: Its Controversial Use in Medicine

Nurse Evans has been hearing more and more frequently that patients—and even her own friends—are using CBD products for various health issues. She grew up thinking that cannabis (or, as her friends called it, marijuana) was a party drug and that it was dangerous and illegal. Now she's confused about the renewed popularity of CBD and her role in guiding patients on its safe use. She knows it is legal in her own state but that cannabis manufacturing and use are still federal crimes, which is confusing.

Do you, unlike Nurse Evans, have enough information to properly educate your patients about CBD? What is CBD, anyway? What is your role in administering synthetic cannabis in FDA-approved medications? Are all CBD manufacturers the same? How is CBD regulated? What are the legitimate claims for its effectiveness? If you're like Nurse Evans, you are seeking more information for your patients and friends.

Patients are using both THC (cannabis) and CBD as medication, and it is imperative that healthcare professionals understand not only the risks and benefits of this herbal medication but also the legal issues involved in its use.

What CBD Is and Is Not

CBD is not psychoactive. It is a non-psychoactive chemical that is found in the cannabis plant. CBD is the abbreviation for cannabidiol, which is a derivative of the Cannabis sativa plant, and 1 of the 200 identified cannabinoids from this ancient plant. Up to 40% of the plant's extracts are cannabinoids (Campos et al., 2012).

CBD is not marijuana, or THC, which comes from the whole cannabis plant, but rather an extracted component from the plant that does not contain the psychoactive chemicals. Both the public and the medical community are eager to find pain medications as alternatives to the opioids that have precipitated a crisis in the United States. Thus, CBD products are currently experiencing a boom.

Sales of CBD products are expected to soar 700% in the next few years due to consumer interest prompting a forecast of about \$16 billion in sales by 2025 (Dorbian, 2019). CBD manufacturers claim to cure a myriad of conditions from the common headache and insomnia to complex issues like diabetes and even cancer. But can it really do that or is CBD just snake oil? Worse, is it dangerous?

The whole cannabis plant contains THC (tetrahydrocannabinol) and other components called flavonoids as well as chemicals that determine its color and aroma, known as terpenes. THC is the psychoactive feature of the whole plant, but CBD does not contain any THC. Without the intoxication and euphoria (high) of cannabis, CBD has demonstrated benefits for anxiety, insomnia, seizures, multiple sclerosis, post-traumatic stress disorder, and pain management.

Cannabis is currently illegal under the federal government, the DEA having listed it as a Schedule I controlled substance due to its mind-altering substances and seeming potential for addiction (found in other Category I drugs such as LSD and heroin).

CBD is not an aromatic essential oil; it is not safe because it is “natural.” It does not come in a natural form but must be extracted from the hemp portion of the cannabis plant. Both hemp and cannabis come from the same plant and the terms are often used synonymously; however, they are different and serve different purposes.

According to U.S. law, hemp is “all or part of the Cannabis sativa plant that contains no psychoactive properties,” therefore it does not include the mind-altering THC component. In Canada, they define hemp as “any part of the cannabis plant that contains less than 0.3% THC.”

The product marijuana, with the nicknames of “Mary Jane” and “weed,” comes from a cannabis plant that is grown and bred for its potent resinous glands (male portion of the plant), and its trichomes contain high THC.

In contrast, hemp is the portion of the same cannabis plant that is bred for oils and even fiber for rope, paper and clothing.

Hemp Fibers



Source: Courtesy of Wikimedia Commons.

Online Resource

Video (3:59): THC vs CBD: What’s in your weed?

<https://www.youtube.com/watch?v=1iIENII-IVo>

A Brief History of Cannabis and CBD

Recorded history and archeological remnants show that hemp fibers from the cannabis plant were used in Mesopotamia as early as 8,000 **B.C.E.** (Oláh et al., 2014). By the year 100 **A.D.** Romans were using the fiber from hemp for clothing and the Roman elite were using cannabis for analgesia and sedation. King Philip of Spain ordered the cultivation of hemp throughout the Spanish empire and introduced it to the New World in 1564 as they conquered existing civilizations. In the New World of North America, George Washington and Thomas Jefferson grew hemp for food and industrial applications.



Hemp cultivation in Europe, circa 1890. Source: Courtesy of Wikimedia Commons.

Because of its common use, cannabis and hemp were part of the U.S. Pharmacopoeia from 1850 to 1942 (do Nascimento et al., 2017). In the 1930s the U.S. Federal Bureau of Narcotics stated that “marijuana is a gate-way drug to narcotics addiction.” The Marijuana Tax Act of 1937 then placed a tax on any marijuana sold and purchased in the United States.

CBD was first extracted in the 1940s, and six years later studies determined the effects of the class of cannabinoids on mammals. Later, in the 1960s, the molecular structure of CBD was determined to be different from that of marijuana, which explained the different effects between two components of the same plant.

Because of misuse, poor processing, and associations with deviant behavior, the cannabis plant was declared illegal in the United States and was removed from the U.S. Pharmacopoeia; in 1970 it was classified as a Schedule 1 Controlled Substance. It was illegal to grow, harvest, transport, sell, or use the marijuana plant until new information about the chemical components of the plant were discovered.

With the movement toward evidence-based medicine, the human endocannabinoid system was identified in the 1990s, which revealed that humans have cannabinoid receptors throughout the body and especially surrounding the nervous system. In 2014 President Barack Obama signed the Farm Bill, which allowed hemp, not marijuana, to be cultivated again for further research (USDA, 2014). In 2018 the Farm Bill of 2018 allowed the cultivation of hemp and hemp-derived products, including CBD, which became legal at the federal level; on the contrary, the cannabis plant for marijuana still remains illegal federally (USDA, 2019).

States have been left to interpret the paradox of cannabis being both legal and illegal. There is no distinction yet between medicinal and recreational use. The debate continues, with some states recognizing the federal mandate against cannabis while others have approved the use of CBD on the basis that it does not have the THC component or its psychodynamic properties. Pending true clarity in the law, and in recognition of a society hungry for the products, manufacturers and marketers are moving forward to sell a plethora of CBD products in states that have legalized them.

Legal Status of CBD

Under the Controlled Substances Act (CSA), CBD is currently a Schedule I substance. It is not approved as a prescription drug or dietary supplement. Although cannabis is illegal, the Food and Drug Administration (FDA) has approved CBD for a few select health issues. Despite the federal sanction, currently 27 out of 50 states have approved cannabis, and all have approved CBD use. Four states have legalized recreational marijuana and twenty-three states have legalized medical marijuana, including CBD (Prescott, 2018).

In 2018 CBD was approved by the FDA, after CNN featured a story called Charlotte's Web. The story featured the effective use of CBD in the treatment of a rare seizure disorder for a little girl (Maa & Figi, 2014). The website Charlotte's Web remains the number 1 website for cannabis issues, public education, and product purchasing. The impressive management of these rare seizures by CBD led to an explosion of interest by the medical community—and a good excuse from recreational users of marijuana to further explore cannabis.

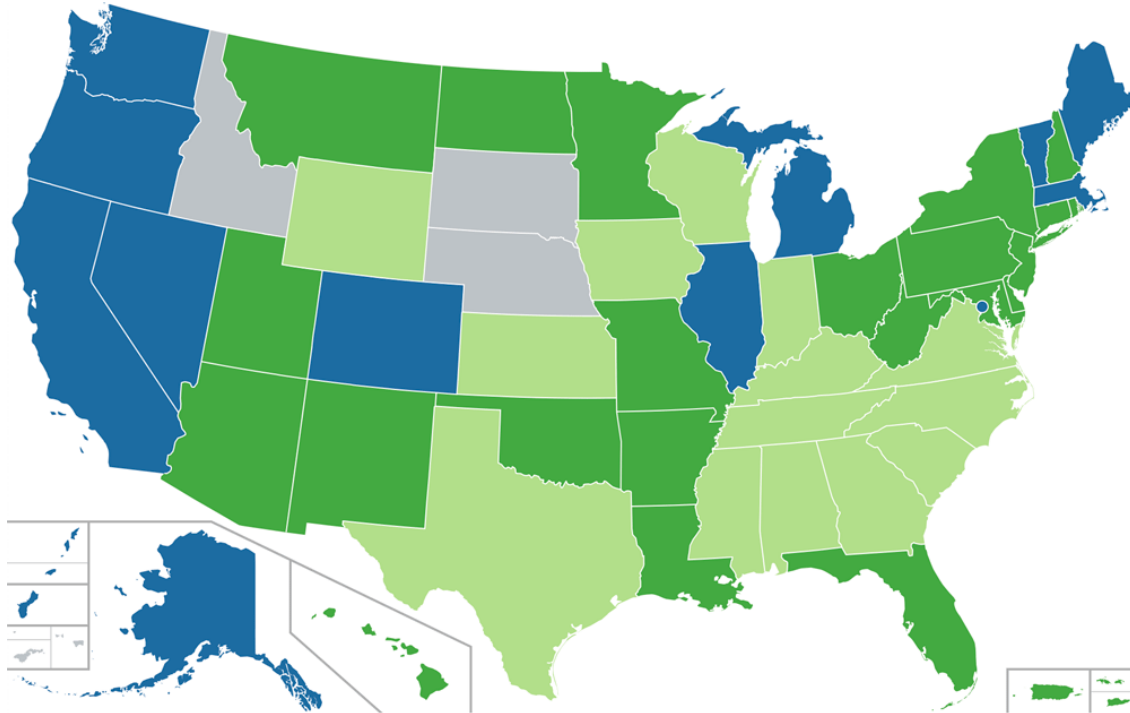
The CBD movement has found great momentum as part of the \$billion herbal supplement industry, the growing stress and anxiety in our population, and the legalization of medical and recreational cannabis throughout the country.

Gradually, states passed laws allowing the use of CBD for select conditions, but physicians still cannot write the prescription, only a recommendation for use. An additional thirty states have now passed medical cannabis laws with no restrictions on THC content, and products are allowed to be purchased without a doctor's formal recommendation.

In December 2018, President Donald Trump signed a \$867 billion farm bill, which removed industrial hemp from the restricted product list and made it a lawful agricultural product. The 2014 Farm Bill defines hemp as cannabis containing less than 0.3%. Yet the FDA still determines what is food quality and has continued to enforce the ban against CBD in food and drinks.

State and federal laws are in conflict and healthcare professionals are caught in the middle. In this volatile climate, it is important that healthcare workers understand the consumer use of CBD products as an alternative or complementary treatment for select conditions. As of January 1, 2019, only three states have no legal statues about cannabis (see map below).

Medical Cannabis + CBD United States, 2020



Map showing legal status of medical cannabis in the United States.

- Blue = No doctor’s recommendation required.
- Dark Green = Doctor’s recommendation required.
- Light green = Limited THC content.
- Gray = prohibited.

Source: Courtesy of Wikimedia Commons, 2020. Jamesy0627144 / CC BY-SA (<https://creativecommons.org/licenses/by-sa/3.0>). Source: Courtesy of Wikimedia Commons.

In the past five years, scientific studies have examined the benefits of the extracted cannabidiol oil on anxiety, cognition, movement disorders, and pain. As noted earlier, in 2018 the FDA approved the drug Epidiolex for the treatment of two rare epilepsy disorders—Dravet syndrome and Lennox-Gastaut syndrome (USFDA, 2018).

The role of the FDA is to protect public health by ensuring the safety and effectiveness of human drugs, vaccines, and other biological products, including medical devices. It is also responsible for the safety of approved food supplies, cosmetics, dietary supplements, tobacco products, and even products that emit electronic radiation.

Current Worldwide Legal Status

Country	Status
Australia	Prescription only (Schedule IV) for 2% cannabinoids.
Canada	Prescription only: Nabiximol (Sativex) for neuropathic pain in MS. Approved both medical and recreational use.
European Union	Legal commerce in 2021 after safety tests.
New Zealand	By MD prescription only.
Sweden	Medical product.
United Kingdom	Prescription only, dietary supplement.
United States	Schedule 1—except Epidiolex, Schedule V—and hemp-derived.
World Health Organization	Recommends it remain unscheduled.

Through multiple studies, the FDA found CBD was statistically significant in reducing the frequency of seizures in children over the age of 2 and were able to fast-track the application for approval, which it ultimately received from the Drug Enforcement Administration (DEA). Safety studies for the drug did acknowledge and label potential side effects of this drug, which are similar for all anti-seizure medications, to include worsening agitation, depression, nausea, vomiting, abdominal pain, fatigue, anorexia, and possible liver damage.

FDA commissioner Scott Gottlieb stated, regarding the approval of this product:

Controlled clinical trials testing the safety and efficacy of a drug, along with careful review through the FDA's drug approval process, is the most appropriate way to bring marijuana-derived treatments to patients. Because of the adequate and well-controlled clinical studies that supported this approval, prescribers can have confidence in the drug's uniform strength and consistent delivery that support appropriate dosing needed for treating patients with these complex and serious epilepsy syndromes.

We'll continue to support rigorous scientific research on the potential medical uses of marijuana-derived products and work with product developers who are interested in bringing patients safe and effective, high quality products. But, at the same time, we are prepared to act when we see the illegal marketing of CBD-containing products with serious, unproven medical claims. Marketing unapproved products, with uncertain dosages and formulations, can keep patients from accessing appropriate recognized therapies to treat serious and even fatal diseases.

Proponents of legalization cite the advantageous collection of taxes on products generating state income. For example, between 2014 and 2015 the State of Colorado collected almost \$14 million in licensing, fees, and taxation from cannabis products. States that have legalized cannabis have also noted a decrease in crime rates as supplies and products are now easily available removing the dangerous underground market (Prescott, 2018).

Opposition to legalizing cannabis and its variety of products stems from caution against the psychotropic effects of marijuana and the lack of scientifically based claims for the benefits from medical marijuana. Only in the most recent years are CBD and its products beginning to receive FDA applications for research. Claims of curing cancer and chronic diseases have not been validated yet. Despite multiple efforts to move cannabis from a Schedule I drug to a lower level, it remains in the grouping with highly addictive and potentially dangerous substances.

Allegedly, the DEA won't currently inspect or prosecute people carrying CBD products, so the market flurry continues. In December 2017 the World Health Organization declared CBD was not harmful and in January 2018, the World Anti-Doping Agency removed CBD from its prohibited substances.

Apply Your Knowledge

How would you explain to a patient the difference between CBD and marijuana?

2 The Cannabis Plant

The cannabis plant has been used for thousands of years, and through those years over 700 varieties have been developed and are available.

Pharmaco-dynamics and -kinetics of CBD

Cannabis has hundreds of chemical components, but the active ingredients in this plant used by people are THC and CBD. When the leaves of this botanical are rolled and smoked it is generally known as marijuana. When the cannabis plant is harvested, CBD is one of the various components that are extracted out. Parts of the plant have been used throughout history: the fibrous portion, the leaves, the buds, and so on.

Botanical Drawing of Cannabis



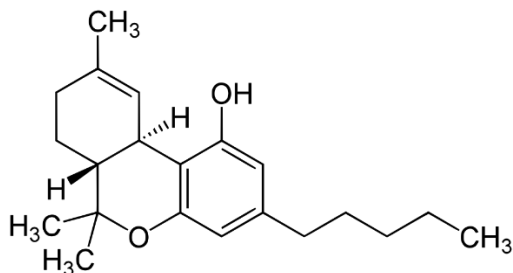
Hermann Adolph Köhler (1834–1879) / Public domain. Source: Courtesy of Wikimedia Commons.

CBD comes from a portion of the cannabis plant known as hemp. A history of hemp reveals it has been indigenous to Central and South Asia, where its fibers were used for fabric and rope. In the Neolithic age hemp was known in China and Japan. Thomas Jefferson wrote the Declaration of Independence and the U.S. Constitution using hemp paper (Price, 2015). Hemp has been used for millennia as wax, resin, paper, fuel, and clothing.

THC and CBD are similar molecules within the cannabis plant, but they act differently within the human body. Pharmacodynamics refers to the way the body reacts and pharmacokinetics to how the body impacts the drug.

Understanding the action of the cannabis plant on the human body was revealed with the discovery of the endocannabinoid system in the human body. Natural cannabinoid CB1 and CB2 receptors are located throughout the body, especially focused near the nervous system, which may explain why the psychodynamic properties are helpful for analgesia and pain control. Whereas THC binds to the CB1 receptors to produce a euphoric feeling, CBD does not. CBD has been shown to act as a serotonin receptor partial agonist, which may also explain its relaxation and sleep-inducing properties (Laun et al., 2018).

Chemical Structure of THC



Chemical Structure of CBD has a slightly different structure in the main H3C bond that prevents the psychiatric response. Source: Courtesy of Wikimedia Commons. Public domain.

Features of the whole cannabis plant are aromatic compounds known as terpenes. When the whole cannabis plant is used, it contains the cannabinoids, terpenes, and flavonoids found in fatty cells of the plant. Terpenes attract pollinators such as bees, and give flowers, herbs, and plants their unique aromas and flavors. Because of these features, terpenes are often used in cosmetics and aromatherapy. These features make CBD favorable for creams and cosmetic products. When the whole plant is used, all of these elements work together in a magnified benefit known as the entourage effect (Russo, 2011).

Because CBD is a fat-soluble chemical, it binds easily with oils and is easy to consume in a variety of products. Currently studies show promise that CBD is effective as an anti-inflammatory and anti-seizure, but we don't know enough yet about how it works in the brain and what dosages are most appropriate.

The Endocannabinoid System

Endocannabinoids were identified in the 1950s by a scientist who discovered they were internal, natural chemicals, with unique receptors (eg, brain, connective tissues, glands, immune system organs, and cells) throughout the body of mammals. Like other body systems, they work to keep the body in a state of homeostasis. It is believed that pain and inflammation result when the body is out of balance, which is why CBD has been shown to be especially helpful as an analgesic and anti-inflammatory (Kaur et al., 2016). The CBD binds with the C1 or C2 receptors to block the inflammatory response.

Endogenous cannabinoids with their receptors, mainly types 1 and 2, are known as the endocannabinoid system. It is closely related to the nervous system and impacts sensations of pain, anxiety, pleasure, and even inflammation. The distribution, synthesis, transportation, and degradation of the cannabinoids determine the effect on the body of the various cannabis products (Klumpers & Thacker, 2019).

Endocannabinoids act like keys in the locks of the receptors. The THC molecule fits nicely into the C1 and C2 receptors that respond to anxiety and stress, blocking their responses, and producing calm and even euphoria. CBD only fits the receptors blocking anxiety and stress response; it does not fit those that produce the euphoric sensation (the "high") of THC.

Research has determined that endocannabinoids have a pathology in many neurologic conditions and synthetic modulators of this system could be used in a protective role in disorders such as emesis, pain, inflammation, multiple sclerosis, anorexia, epilepsy, glaucoma, obesity, Parkinson's disease, Huntington's disease, Alzheimer's disease, and Tourette's syndrome. Much research is needed to confirm and quantify therapeutic doses. Currently, there are very limited recommendations for dosage except for Epidiolex, which is used for childhood seizures and synthetic drugs.

Apply Your Knowledge

How would you explain to your patient why CBD doesn't make someone "high" like marijuana?

3 Therapeutic Effects and Uses of CBD

Like any supplement or product being consumed and used, it is wise to do your own research to make informed and safe choices.

There are eight medical conditions for which patients can use cannabis CBD -- cancer, glaucoma, HIV/AIDS, muscle spasms, seizures, severe pain, severe nausea and cachexia or dramatic weight loss and muscle atrophy. CBD is being used as part of performance and recovery routines for athletes as CBD helps with inflammation too.

Other uses are not endorsed by the medical community but continue to be used based on anecdotal stories from people who have either received relief or improvement from CBD products. Unfortunately, the general population interested in these products are more interested in the promise of hope for relief, than they are for the real scientific studies and proof.



Cannabis sativa botanical drawing. Source: Courtesy of Wikimedia Commons. Public domain.

CBD Products

Just as olives can create a variety of products such as the whole eaten fruit to different qualities of olive oil ranging from heat-extracted, to cold-pressed, and virgin, so do CBD products vary. Because of the explosion of products, consumers largely don't really know what they're buying and the percentage of THC in the product. Many products don't fully disclose their ingredients.

In 2008 the FDA sent warning letters to eight companies producing CBD products announcing that they either had no or barely any CBD, or that some contained illegal THC that contaminated the product with potential psychoactive properties. There is no regulation of these products, which can make them dangerous for someone's health, or pocketbook by wasting money on a useless product. A later study in 2017 examined 84 CBD products purchased online and found that almost 70% were mislabeled (Penn Medicine News, 2017). Without regulation, CBD companies are policing themselves but can have wide fluctuations within their own products even in the same package.

Hemp seed oil has been used for bath oil, lamp oil, cooking oil, and a main ingredient in the food and supplement products being seen in the market today. The hemp seed oil is extracted by pressing the actual hemp seeds from the plant. It is rich in omega-6 and omega-3 essential fatty acids and a key in the claims and use for topical and ingestible products for skin and healthy tissue.

Because of the essential fatty acids, hemp seed oil was studied in 2005 by a physician in Finland for successful treatment of atopic dermatitis, known as eczema. A reduction in dryness, itching and overall skin improvement was found (Callaway, 2005).

Hemp Seeds



Source: Courtesy of Wikimedia Commons. Public domain.

CBD Product Sources

Full-spectrum CBD	Broad-spectrum CBD	CBD isolate	Hemp seed oil
Products that contain all the cannabinoids, including any THC terpenes and flavonoids in the products.	Similar to full spectrum products except the THC is removed.	This contains only CBD after an extraction process which removes other cannabinoids, terpenes and flavonoids.	Extracted from the seeds of the hemp plant. It is often used as a carrier for the CBD isolate and other CBD products.

Source: Original table by author.

Routes for CBD Delivery

The route of delivery of CBD impacts its bioavailability as oral intake of the drug is only 6% available in humans compared to 11% to 45% via inhalation (Scuderi et al., 2009). This may explain why for decades smoking marijuana has been the preferred route by recreational users. It is fat soluble and only soluble in organic solvents, which manufacturers create. Because it is lipid soluble, it can remain in the fat tissues and must be metabolized by the liver's first-pass effect. Therefore, the effect of CBD can be slow compared to an inhaled version, such as an infuse or nebulizer.

CBD doesn't appear to have psychotropic effects but conversely does show positive effects against anxiety and even PTSD (Iseger & Bossong, 2015). Medical marijuana however, does still product psychoactive effects and just because it has the name medical does not imply it is safe and without side effects.

CBD can be manufactured in oils, drops, tinctures, vaporized pens, creams, syrups, oils, lip balm, soaps, massage oils, shampoo, and foods such as gummies, drinks, and even pet foods. It may be delivered via several routes including inhalation by smoke, (vapor or aerosol spray), or buccal into the cheek, sublingual, and oral routes. It can be delivered topically such as in creams, lotions, ointments, and shampoos.

A huge concern is that the CBD products are not regulated, standardized, or certified, and so results are varied. Brands that are more reliable are difficult to determine and so consumers must be informed and do their own careful research. Unfortunately, usually the publicized and online information is originated from the manufacturers or product marketing departments themselves and not disinterested third parties using scientifically based studies.

Here are some products derived from hemp plants:

Hemp seed	Hemp oil	Hemp fiber
Baking additives	Body Care products	Animal bedding/mulch
Beer	Cooking additives	Automobile parts
Confections/candy	Detergents	Carpeting
Feed	Dietary supplements	Fabric
Fiber	Fuel	Insulation
Flour	Paint	Pulp and paper
Non-dairy milk	Salad dressing	Recycling additives
Snacks	Spreads	

Hemp used for food products have exploded to over 25,000 products in the past few years and those with CBD were introduced in 2017 (Price, 2015). Consumers must be very wary of products claiming they contain CBD as many have been found to be false. Consumers can look up cannabidiol related product reviews on the FDA website since 2015, and even read the warning letters given to these manufacturers for false claims. People are wasting money and possibly worse with unintended side effects. Beginning in October 2019, the New York City Department of Health will fine restaurants that sell foods or drinks containing CBD (LaVito & Franck, 2019).

In July 2019, the FDA stated:

Selling unapproved products with unsubstantiated therapeutic claims—such as claims that CBD products can treat serious diseases and conditions—can put patients and consumers at risk by leading them to put off important medical care. Additionally, there are many unanswered questions about the science, safety, effectiveness, and quality of unapproved products containing CBD (USFDA, 2019).

Top Producers and Manufacturers

In the ever-increasing and profitable business of supplements, CBD products are exploding. Manufactures vary from those well-researched and produced with high quality and those that make false claims and promises. Following is a simple list (in alphabetical order) of the top-most popular producers and manufacturers based on social media subscribers and purchases:

- Akive, Apothecanna, Barlean's, Bluebird Botanicals, CBD Live Natural, Charlotte's Web, CBDistillery, CBDfx, CBDMD, CBD for life, CBD American Shaman, Colorado hemp honey, Corners Cannabis, Curaleaf.
- Elevate, Elixinol, Endoca, Flo Kana, Foria, Green Compass, Green Gorilla, Green Roads, Herbstrong, Hempmeds, HempWorx, Hippie Butter, Highland Pharms.
- Infinite CBD, Irwin Naturals, Joy Organics, Kannaway, Kat's Naturals, KushyPunch, Koi CBD, Lazarus Naturals, Livlabs, Lord Jones, Medterra, Moon Mother Hemp Company, nhancedcbd, Plant Therapy.
- Additionally, there are CBD oil, Procana, PureKana, Pure Hemp Botanicals, RE Botanicals, Select, Steve's Goods, Source Naturals, and Zilis.

Therapeutic Uses

Although CBD manufacturers claim many therapeutic uses, only those based on scientific studies demonstrating statistically significant benefits are legitimate. The Food and Drug Administration does randomly assess various products, but it is difficult for the consumer to know which ones are legitimate unless they go to the FDA website. Otherwise, it is left to the integrity of marketers and manufacturers to correctly educate the consuming public, which is tricky at best. The following list of uses have studies with documented therapeutic benefits for CBD.

- Anxiety and mood disorders
- Pain and inflammation
- Seizures and spasms

CBD appears to boost serotonin levels in the brain and may stimulate the production of new nerves in the hippocampus where emotions and mood evolve (Campos et al., 2013). A concern is that although preliminary studies show hopeful positive benefits, the CBD manufacturers market their products with full endorsement regardless of the truth that human studies have not been completed or are only anecdotal and not based on rigorous scientific evidence yet.

CBD has been shown in laboratory rodents (mice and rats) to reduce inflammation and neuropathic pain by suppressing the $\alpha 3$ -glycine receptors, which sense pain in the nervous system (Xiong et al., 2012). In the quest to find better alternatives for chronic pain due to the opioid crisis and legitimate concerns about side effects, CBD has the potential to deliver relief without the addictive side effects and warrants additional study.

Seizure control has been researched and became the first approved indication for CBD by the FDA. CBD has also shown promising results in relaxation and improved sleep from insomnia (Babson et al., 2017). With the caveat that more longitudinal studies are needed to determine clinical implications, cannabidiol synthetics such as nabilone and dronabinol have shown short-term benefits for sleep apnea, daytime sleepiness, and even nightmares associated with PTSD.

CBD is known to modulate the transcription of over 1100 genes that reduce inflammation in our central nervous system by up-regulating GABA receptors, which helps antiinflammation. They likewise are known to down-regulate the neurotransmitter glutamate and inflammatory biochemicals. What is difficult to assess, however, is that there are over 350 different chemicals involved in the inflammatory response, so it is not entirely clear how CBD truly impacts this process.

One noted 2017 study concluded that selective cannabinoids provided a small benefit in chronic neuropathic pain (Meng et al., 2018). They also conclude that there is a need for well designed, large, random controlled trials to better assess dosage, duration and effects on physical and psychological function before recommendations and approval for human use could be made. It is currently legal by accredited organizations with federal approval to perform cannabis studies in the United States.

A Cochrane Library review and meta-analysis done in 2018 on the use of cannabis products concluded that, collectively, all cannabis-based medicine performed better than a placebo in reducing pain intensity, providing moderate pain relief, and improving sleep and psychological distress. They recognized that high-quality evidence was lacking in these studies (Philips et al., 2018). Additionally, when looking at all cannabis-based medicine products, they believed they were no better than placebos in the conditions improving health-related quality of life. People had dropped out of the studies due to side effects of cannabis including sleepiness, dizziness, and cognitive problems.

Safe Use of CBD

Even if cannabis or CBD have real benefits for clinical use, the unreliable studies and purely anecdotal reports and claims have clouded definitive decisions by the FDA to approve CBD for many health conditions. The CBD in cannabis does show observed benefits in reducing anxiety and even tremors in patients with multiple sclerosis (Williamson & Evans, 2000). Chemotherapy-induced emesis is also reduced by cannabinoids.

The side effects of the whole cannabis plant include the mind-altering effects from smoking and the resultant lung irritants, mind impairment, and driving dangers while under the influence, but these side effects are absent when pure CBD is used.

The National Academies of Sciences, Engineering, and Medicine (NASEM) in 2017 concluded that oral cannabinoids were as effective as antiemetics in adults with chemotherapy-induced nausea and vomiting, and that adults with chronic pain experienced significant pain relief, and that adults with multiple sclerosis–related spasticity reported improvement of symptoms (NASEM, 2017). Confusion arises when results are so varied, seemingly dependent on the quality of the studies and who is funding the studies.

Is cannabis a rational solution to the opioid crisis? Proponents state that it is an excellent, less addictive alternative that will not cause death. The Alternatives to Opioids acts of 2018 (Illinois and New York) permit any condition that could be treated with opioids as a qualifying condition for medical marijuana. Those against this rationale state that use of THC products is just exchanging one addictive medication for another.

A meta-analysis study in 2017 found that when THC products were used in combination with morphine, the desired relief could be achieved with 3.6 times lower dose than with morphine alone. Likewise, the dose of codeine administered in combination with delta-9-THC was 9.5 times lower than of codeine alone (Nielsen et al., 2017).

In states where medical cannabinoid use has been enacted, there has been a statistically lower opioid overdose mortality rates of 24.8 % lower compared to states without medical cannabis laws (Bachhuber et al., 2014).

Health Risks

Like any prescription medication, there are always risks and side effects that need to be considered to determine if the benefits outweigh the risks. The psychodynamic properties of THC are always a concern for products that come from the whole cannabis plant. Although CBD has been approved if it contains less than 0.3% THC component, not all products on the market disclose their full ingredients and consumers may be unaware of the additional components, which may impact side effects.

Common adverse effects from cannabis include anticholinergic effects of dry mouth, blurred vision, urinary retention, tachycardia, constipation, and hypertension. Other CNS effects include ataxia, cognitive dysfunction, and even hallucination with any THC components.

Risks for Specific Populations

Cannabis can have serious side effects for special populations, including children and teens, pregnant and lactating women, and elders, who are also at risk for polypharmacy. Because the quantity of CBD varies from producer to manufacturer to product, amounts that exceed safety or are toxic are unknown. There are no studies on using CBD during lactation but the whole cannabis plant is known to pass through breast milk. CBD has been used for hyperemesis gravidarum but is not officially prescribed by physicians due to the lack of safety guidelines. An edible brownie or cookie with CBD may be therapeutic for an adult; however, there are no studies to confirm or warn regarding safety consumption in children.

Teenagers who are exposed to edible CBD products in their own home may also unknowingly consume THC products, which has shown to increase antisocial behaviors and pose a safety risk. One reason cannabis continues to remain on the Schedule 1 drug list is the unexplored potential for psychotic behavior, which can be dangerous for children and elders. Finding willing participants in research studies of infants, children, teens, and elders becomes challenging due to national research safety guidelines.

Another population at risk are those with mental illness, who may experience a worsening of their illness with cannabis products. Because cannabinoids with THC appear to affect the same internal reward system as alcohol, cocaine, and opioids, patients may also develop a dependence on cannabis with worsening irritability, anxiety, sleep disturbances, and food cravings.

Apply Your Knowledge

What guidance can you give a patient who is looking to buy a CBD cream to decrease pain or inflammation?

4 Dosage and Administration of CBD

Currently the FDA has approved three isolated synthetic CBD products, which include Marinol, Syndros, and Cesamet (Porter, 2017). The FDA is also aware of the many cannabis and CBD products in use by the general public. Because the major purpose of the FDA is public safety using pharmaceuticals and ingestible products, they will only approve CBD for therapeutic use after extensive, peer-reviewed research. When the FDA approves or registers a product it does not guarantee the drug's effectiveness but only its reasonable safety if taken within defined parameters, which still includes common side effects.

Orally ingested products are weaker than inhaled products, but inhaled products are not metabolized by the liver. Nevertheless, recommendations are that smoking any product is potentially damaging to the lungs.

Marinol (dronabinol) is a synthetic derivative of THC and was approved in 1985 for the treatment of weight loss in anorexia, vomiting, and weight loss associated with cancer chemotherapy and AIDS patients. Side effects and warnings include anaphylaxis if: allergic to sesame oil, seizure-like activity, hypotension, syncope, addiction for those with addiction disorders or dependence, and depression, all of which are serious side effects. Marinol alone has become a \$150 million product; Syndros is liquified dronabinol, and sales have been estimated to be \$400 million.

Cesamet (nabilone) was approved in 1985 and is a synthetic drug that works on the CB1 receptor to inhibit nausea and vomiting and stimulate appetite. Because its effects are on the central nervous system (CNS), the negative side effects are seen in the CNS and include euphoria, depression, anxiety, panic disorders, and paranoia. Both Marinol and Cesamet still have components of THC, which explains these side effects. CBD products should have less than 0.3% and create no CNS psychotic effects.

Although these two products contain THC, which is federally illegal, the FDA has taken the rare step of approving these botanicals. While the FDA may approve the drugs for specific therapeutic uses, it is still up to the DEA to lower the schedule of marijuana. Currently insurance does not cover the cost of medical cannabis, but some plans do cover FDA-approved drugs.

Epidiolex studies show that side effects include fatigue, diarrhea, changes in appetite, and dry mouth. Most of the safety research is in animal studies. Epidiolex dosages is 5 mg/kg oral BID with a max of 20 mg/kg/day.

The average adult dosing of CBD is 300–1500 mg/day for desired effects.

The average adult dosing of THC varies from 2.5 to 5 mg for a beginning cannabis user, up to 20 mg/day. Dosages above 20–30 mg/day may increase the adverse effects or induce tolerance without improving efficacy, and should be discontinued (Lee, 2018).

Regardless of the CBD product, the effects of cannabis are dependent on:

- Dose
- Variety
- Route
- Timing
- General health
- Age of the patient
- Use of other medications
- Chronic use or naïve user

The **L.E.S.S. Method** is a measured approach to oral cannabis and CBD dosing to start low, establish potency and efficacy, go slow and supplement as needed.

Apply Your Knowledge

What patient education instructions would you give to a patient receiving dronabinol?

Patient Education

Do-it-yourself healers and athletes looking for the next chemical advantage for healing and performance comprise a large group of consumers of CBD products. The market has exploded with products claiming numerous benefits from CBD, many of which have not been substantiated. Those suffering from chronic illness and pain not relieved by traditional pharmacologic products tend to try hemp and whole cannabis plant products. The concern is getting consumers honest information that doesn't come from the marketers. Because there are no prescribing limitations and guidelines, consumers also use products without medical guidance, which may interfere with prescribed medications.

General guidance

- Look for full spectrum CBD (100% pure without THC)
- Use a CBD product made from organically grown hemp
- Require transparency from your CBD company
- Keep CBD and cannabis products out of reach of children
- Ask for test results and studies from manufacturers
- Avoid products that make unfounded health claims
- Avoid vaping products that contain propylene glycol (which degrades to formaldehyde)
- Utilize independent certifications when comparing product companies
- Look for companies that test for pesticides and heavy metals

When CBD products are offered in edibles such as baked goods and candy, children may be in danger from such products. These edibles may also be dangerous when eaten in unlimited quantities by adults because the CBD component varies and may become toxic.

Unfortunately, cannabis is often marketed as a nutritional supplement and marketers claim that people are deficient in cannabinoids, which is false. The extremely popular market of CBD products demonstrates that the lack of scientific evidence doesn't prevent people from buying and using a product.

The Center for Food Safety is a national nongovernmental, non-profit public environmental advocacy organization that grades products for safety. An example of their contribution to public safety is their Hemp CBD Scorecard.

HEMP CBD SCORECARD	
MARCH 2020	
GRADE	COMPANY
A	
B	
C	
D	No companies in this category.
F	



CENTER FOR
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www.centerforfoodsafety.org

Source: Center for Food Safety, 2020. Used with permission.

Role of the Healthcare Professional

It is the duty of the healthcare professional to ask nonjudgmental assessment questions about CBD and cannabis product use, provide unbiased information and help guide them to use it wisely. Physicians currently cannot write a prescription, however the better informed they are can help improve adherence to healthy living behaviors.

Important conclusions about this topic about CBD product use in medicine includes the following:

- Be open and non-judgmental in the dialogue with patients.
- Explain that driving and operating heavy machinery should not be done under the influence of any cannabis product.
- Be aware of the legal issues in your state.
- Provide access to legitimate and fair websites.
- Provide information about drug to plant interactions, side effects, and risks of addiction.
- Explain the reasons for getting a medical marijuana card.
- Educate patients about recreational marijuana use.
- Set goals and safety guidelines for the use of CBD products.
- Consider a treatment agreement.
- Remember that cannabis is illegal on a federal level.

Apply Your Knowledge

Has your opinion of CBD use changed? What issues must be addressed for patients taking CBD products?

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Post Test

1. The Controlled Substances Act lists cannabis (marijuana) as a:

- a. Schedule IV substance.
- b. Schedule III substance.
- c. Schedule I substance.
- d. Cannabis is no longer a controlled substance.

2. What is the difference between CBD and marijuana?

- a. Nothing, they are two names for the same thing.
- b. They are both from the cannabis plant but have different molecular structures and act differently in the body.
- c. CBD is when the cannabis plant is in pill form, and marijuana is when its smoked.
- d. CBD is the oil and marijuana is the leaf.

3. What is a cannabinoid?

- a. It is the active part of the cannabis plant found in CBD.
- b. It is the psychoactive component of the cannabis plant.
- c. It is what gives the plant its color and aroma for aromatherapy.
- d. It is a natural receptor in the human body that causes inflammation.

4. What is the endocannabinoid system?

- a. It is the same as the endocrine system.
- b. It is part of the vascular system that impacts vasodilation and constriction.
- c. It is a chemical found only in the brain for psychodynamic actions.
- d. It is a system of chemicals and receptors found throughout the body and works with the nervous and inflammatory systems.

5. Which of the following conditions have been shown to improve with CBD?

- a. Nausea and vomiting
- b. Anxiety
- c. Inflammation
- d. All of the above

6. Which product is federally illegal?

- a. Hemp seed
- b. THC and whole cannabis plant
- c. Hemp oil
- d. Hemp fiber

7. Which drug is not approved by the FDA?

- a. Dronabinol
- b. Nabilone
- c. Syndros
- d. THC pills

8. What condition is dronabinol approved for?

- a. Nausea and appetite stimulation
- b. Seizures
- c. Anxiety
- d. Schizophrenia

9. What safety guidelines should you teach patients who are interested in using CBD products?

- a. Look for a product without THC
- b. Do not use in children without a physician's knowledge
- c. Let your physician know to avoid drug interactions
- d. All of the above

10. What is your role as a healthcare professional in dealing with patients who take CBD or are interested in using these products?

- a. Report them to the Federal government as it is illegal.
- b. Inform and educate them about safety and adverse effects.
- c. Issue a medical marijuana card.
- d. Nothing, it's none of your business.

Answer Sheet

Name (Please print) _____

Date _____

Passing score is 80%

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____

*How long did it take you to complete this course, posttest, and course evaluation?

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