CBD SIMPLIFIED
AN EASY TO UNDERSTAND GUIDE TO CANNABIDIOL

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Introduction

There’s a reason people have been using cannabis since the beginning of time. It does something to us. Whether pleasurable, pain-numbing, focusing, sedating, or relaxing, a full 5% of the global population is estimated to have used cannabis in some form in the past month. This estimate may even be low given the recent approval of cannabidiol products across the United States.

Because of legal restrictions in the United States dating back to 1930s, the amount of information on the proper use of cannabis is limited and data related to cannabis is somewhat relegated to the shadows. However, interest in cannabis, most especially CBD, has been renewed following the approval to the Agricultural Act of 2018. This has led to much misinformation online about cannabis products, how to use them, how to dose them, and whether or not there are potential interactions with medications or other natural products.

Here begins our exploration of medical cannabis and its primary chemical constituents, THC and CBD.

While many people asked me to write a book about CBD alone, I found that the highest quality evidence was related to medical cannabis that contains both THC and CBD. I also could not ignore the recreational use of marijuana which has also been researched.

Therefore, this book focuses on data related to cannabis in all its variations. When possible, data related exclusively to CBD is included. When impossible, data related to THC and CBD are discussed instead.

As always, I never claim to have all the answers. I am only here to offer interpretations of data, options, and leave the decision up to you.

You know you better than me. I trust your decision.

Lindsey
Section I

Cannabidiol Basics

The use of medical cannabis, medical marijuana and cannabidiol has exploded in the United States. Its popularity has garnered interest from clinicians, patients, regulators, and green entrepreneurs.

Cannabis sativa or marijuana has a long history of being one of the most commonly used illicit drugs in the world. According to a 2015 study, an estimated 128,480,000 to 232,070,000 people worldwide reported using cannabis in the past 12 months. This equates to roughly 2.7% to 4.9% of the worldwide population. Approximately 8.3% of people age 12 years and older report having used cannabis in the past month.

Cannabis can be used for both medicinal and recreational purposes, and because of its widespread use, the majority of Americans (66%) agree that it should be legalized. While there is not great information about the global population that is using cannabis as a medical treatment, estimates in the United States suggest that approximately 17% of the use is for medical purposes while the remaining 83% use it for recreational purposes.

Historically, cannabis has been used since ancient times, dating back 5000 years in what is now Romania and China. Cannabis was widely used as medicine in the 19th and 20th centuries in the United States, and was described as an analgesic, a sleep aid, and an anti-convulsant in the 1850 United States Pharmacopeia. Cannabis was prohibited in 1937 with the passage of the Marihuana Tax Act and was dropped from the Pharmacopeia in 1942. Legal penalties for possession increased in the 1950s, and marijuana was prohibited completely in 1970 with the passage of the Controlled Substances Act. These legislative actions not only criminalized marijuana, but also limited research and academic inquiry on the subject. Despite federal law, the majority of states across America have approved either medicinal or recreational cannabis. CBD is currently in the midst of a renaissance because of the passage of the 2018 Agricultural Improvement Act. This law made CBD legal nationwide if the product is derived from hemp and contains less than 3% THC.

Within medical cannabis, there are hundreds of physiologically active ingredients. The primary chemical constituent is tetrahydrocannabinol (THC), and there are also terpenoids, flavonoids, sterols, thiols, phenols, and waxes that have additive synergistic, or antagonistic properties. This synergism may enhance the “high” euphoric effects and analgesia or mitigate adverse effects.
Cannabidiol (CBD) is the second most abundant chemical constituent in marijuana. Relative to THC, there is dramatically less known about the pharmacology of CBD. There is also less known about effectiveness, as much of the efficacy data available is related to smoked cannabis, combination THC/CBD oral, topical, rectal, and oromucosal preparations. When possible, CBD data is discussed alone, but when impossible combination data is described.

Though they are endogenous plant oils, neither CBD nor THC are considered essential oils. Yet they are not fatty carrier oils either. They are not volatile (i.e. they do not rise rapidly into the air) and they are not aromatic in the same way that essential oils are. Furthermore, CBD and THC oils cannot be obtained via steam distillation, which is a marker of an essential oil. Of note, there is debate about whether or not steam distillation is required to constitute essential oil. But citrus oils are considered plant essences and oils extracted via solvent are absolutes. Therefore, true essential oils are obtained via distillation. Cannabis oil is heavier and thicker than an essential oil, but not quite as thick and slick as carrier oils, such as olive, coconut, or almond oil. Cannabis oils are considered to be somewhere in the middle between fatty and essential oils.
The Endocannabinoid System

The endocannabinoid system (ECS) plays a vital regulatory role in a variety of physiologic and cognitive processes. A cannabinoid is a compound that interacts with the ECS via receptor sites. There are 2 receptors in this system: cannabinoid receptor 1 (CB1), and cannabinoid receptor 2 (CB2). The difference between these two receptors is important to the understanding of how various cannabinoids affect our bodies.

Cannabinoid Receptor 1

CB1 receptors exist mainly in the brain, particularly in the substantia nigra, the basal ganglia, the limbic system, and the cerebellum. They are also expressed in the peripheral nervous system, liver, thyroid, uterus, bones and testicular tissue. The function of the CB1 receptor is to mediate neurotransmitter systems involving dopamine, gamma-aminobutyric acid (GABA), glutamate, serotonin, noradrenalin and acetylcholine. CB1 is implicated in bodily functions such as cognition, memory, neuroplasticity, and olfaction, as well as motor movements, stress response, gastrointestinal function, cardiovascular activity, drug addictions, and pain perception.

Cannabinoid Receptor 2

These receptors are mostly expressed in immune cells such as T cells, macrophages, B cells, and hematopoietic stem cells. They are also found in the spleen, throughout the gastrointestinal system, in keratinocytes, and in the peripheral nerve terminals. Within the brain, they are primarily found within microglia cells. CB2 plays a part primary in the immune system, they also have other cellular targets such as endothelial and smooth muscle cells, cardiac muscle cells, and nerves within the peripheral and central nervous systems.

Other Cannabinoid Receptors

It has long been hypothesized that there are additional cannabinoid receptor and there is evidence that they N-arachidonoyl glycine receptor G-protein coupled receptor 18 is an abnormal cannabinoid receptor that may be responsible for effects on blood pressure and inflammation.

References


There are two naturally occurring cannabinoids that are produced by the brain: anandamide and 2-arachidonoylglycerol.

Anandamide is a neurotransmitter that binds to CB1 receptors. It has been called a bliss molecule and gets its name from the Sanskrit word Ananda which means joy, bliss, or happiness. The compound is involved in neurogenesis, and this stimulation of nerve development is thought help combat anxiety of depression.

Anandamide also occurs naturally within foods. First, you can stimulate the production of anandamide by eating chocolate, as theobromine contained within chocolate causes the brain to produce anandamide. Chocolate also contains anandamide as well as compounds that slow down the metabolism of anandamide.

Until recently, chocolate was thought to be the only source of anandamide. However, it is now known that the black truffle fungus also produces anandamide. Celery, parsley, and tea may also contain small amounts of anandamide.

2-Arachidonoylglycerol

2-Arachidonoylglycerol (2-AG) is an endocannabinoid that is an endogenous agonist of the CB₁ receptor and the primary endogenous ligand for the CB2 receptor. 2-AG is the most prevalent endogenous cannabinoid ligand in the brain, and it plays a neuromodulatory role in the nervous system.

Naturally occurring 2-AG has been found in bovine and human milk.

References


Cannabidiol Receptor Genetic Variability

As with any receptor, there is genetic variation in the function of the cannabinoid receptors. There are also genetic differences in the transport and biotransformation genes that encode the receptor. Genetic differences may increase the risk of cannabis use or concomitant substance use disorder or alter response to cannabis affecting risk for psychotic symptoms, cognitive function, or memory and attention. While the entire scope of CB receptor genetics is beyond the scope of this work, you can find an excellent discussion on the matter in an article by Hryhorowicz et al. Before reading this work, you must have a firm understanding of genetic variation nomenclature.

For the Laypeople:

Most people do not know their CB receptor subtype. Therefore, it is important to monitor response to cannabis products. Excessive adverse effects, cannabis use disorder, and lack of effectiveness are all possible due to genetic variation. If a product is not working for you, change product or discontinue use of cannabis.

References

The Difference Between THC and CBD

Tetrahydrocannabinol (THC) and cannabidiol (CBD) are the two primary cannabinoids that come from the cannabis plant (Cannabis sativa). They have the exact same chemical formula (C21H30O2) with slightly different isomeric structures. CBD is typically the second most abundant cannabinoid in cannabis plants, following.

Many people to believe that THC and CBD have the same attributes and interact with the brain in the same way, but this is not true.

Though both THC and CBD are cannabinoids, and both interact with receptor sites in the brain, they do it in different ways. THC makes a person feel high by binding to CB1. It fits snugly into a special pocket, the orthosteric binding site, on the receptor.

The image of lock-and-key is apropos for orthosteric binding: THC, the molecular key, fits into the CB1 receptor lock and turns it on, which triggers a signaling cascade on a cellular level that inhibits the release of other neurotransmitters (thereby protecting the brain from too much excitation). It’s one of the many reasons why THC is such a remarkable therapeutic substance. When tetrahydrocannabinol binds directly to the CB1 receptor, it causes a release of dopamine, which creates the opioid effect of getting “high”. This causes feelings of euphoria, alterations in perception, decreased inhibitions, and other effects.

Since the CB1 receptor was discovered in 1988, it's been an article of faith among cannabinoid researchers that CBD, unlike THC, has little binding affinity for CB1. But this notion is based on old science.

New data emerging from the international cannabinoid research community indicates that CBD interacts directly with the CB1 receptor in ways that are therapeutically relevant. But CBD parks at a different docking site on CB1 that is functionally distinct from THC’s orthosteric binding site. CBD attaches to what's known as an “allosteric” binding site on the CB1 receptor.

When cannabidiol docks at the allosteric receptor, it does not initiate a signaling cascade. But it does impact how the CB1 receptor responds to stimulation by THC and...
the endogenous cannabinoids. Allosteric modulation of CB1 changes the conformation (shape) of the receptor, and this can have a dramatic impact on the efficiency of cell signaling.

Scientists at the University of Aberdeen in Scotland have synthesized a positive allosteric modulator of CB1 to treat pain and neurological disorders. When researchers at Virginia Commonwealth University tested the compound on mice, this experimental drug, known as “ZCZ011,” had no psychoactive effects of its own, but reduced neuropathic and inflammatory pain by boosting the CB1 receptor’s response to anandamide, an endocannabinoid compound.

Interestingly, CBD not only fails to bind to the CB1 orthosteric receptor, many studies show that it actually blocks the effects of THC on this receptor when the two are taken together.

References


The Difference Between Hemp and Marijuana

The classification of Cannabis genus plants is actually quite tricky. The three main types of Cannabis are: C. sativa, C. indica, and C. ruderalis. Cannabis sativa is by far the most commonly cultivated plant for THC and CBD, so this article will focus on that species.

Before we delve into the difference between hemp and marijuana, it’s important to understand what a species is. By definition, a species is a group of individuals that actually or potentially interbreed in nature. Of course, in this case, we are talking about plants.

The definition is a bit confusing because in nature, we see some creatures that seem quite different interbreed to produce offspring. For example, all domestic dogs are of the species Canis lupus familiaris, but obviously there are many varieties of dogs with very different characteristics. The same is true for other animals and even plants.

Chemical Differences of Hemp and Marijuana

In the same way, hemp and marijuana are from the same species of plant, but not the exact same plant. So, one way to think about it is as if they were different varieties (or breeds) of Cannabis sativa. These two plants do have physical and chemical differences, but because they can cross-pollinate (breed) with one another, they belong to the same species.

The Agricultural Act of 2018 provides the legal definition of hemp as having a concentration of no more than 0.3% THC. Concentrations this low are non-intoxicating and legal in all 50 states according to the farm bill. Previous legislation, namely the 1937 Marihuana Tax Act and the 1970 Controlled Substances Act, failed to make any distinction between marijuana and hemp plants. Consequently, hemp was classified as an illegal schedule 1 drug alongside marijuana, heroin, LSD, and others. With the passing of the latest farm bill, the government officially recognizes the difference and lifted the prohibition of hemp.

The defining characteristic between hemp and marijuana is their chemical compositions. Both plants produce high amounts of CBD, however, they produce THC at very different levels. While hemp can contain no more than 0.3% THC, marijuana can contain up to 30%.
Stems or Flowers?

Many people contend that hemp and marijuana look so similar as to be entirely indistinguishable. However, the two plants do have some basic differences. Hemp plants are grown primarily for their fiber and seeds. Produced to maximize size and yield, hemp plants tend to be tall, skinny and scarce in foliage. In contrast, marijuana plants are carefully cultivated to encourage more female plants with thick, lush foliage and flowers.

References

1. Understanding evolution: Defining a species. Available at: https://evolution.berkeley.edu/evolibrary/article/evo_41. Last accessed August 18, 2019


CBD and Legal Restrictions

The legalization of recreational and medicinal marijuana is such a hot topic. Currently 11 states allow the recreational use of marijuana, while a whopping 32 states allow it for medicinal purposes. It seems that everyone is touting the benefits and trying to get their hands on this supposed miracle drug.

The passing of the Agricultural Improvement Act of 2018 legalized CBD derived from hemp plants and containing less than 0.3% THC. However, marijuana-derived CBD oil remains restricted in most states. It is best to check the laws for your state for specific laws.

While it is true that you can obtain and isolate CBD from both varieties of the sativa plant, CBD obtained from the marijuana plant is still classified as illegal in most states. The 2018 Farm Bill legalized hemp-derived products, but it does not allow for CBD derived from the marijuana plant. Marijuana-derived CBD is still considered a schedule 1 substance and is therefore illegal in most states.

This is why it is very important to research and verify the source of your CBD. Unless you live in one of the states where marijuana is legal, you will want to make sure your CBD is hemp-derived.

*Accurate as of August 19, 2019*
References

1. Illinois just became the first state to legalize marijuana sales through the legislature — here are all the states where marijuana is legal. Business Insider. Available at: https://www.businessinsider.com/legal-marijuana-states-2018-1. Last accessed August 18, 2019.

CBD Extraction Techniques

With the ever-increasing popularity of CBD, the marketplace is flooded with hype-filled claims and benefits of this natural miracle drug. We can now find CBD-infused lattes at coffee shops, CBD facials at the spa, CBD candy and baked goods, and loads of lotions and potions containing CBD oil. So what exactly is CBD, and why all the hype? Is it really the miracle drug your anxious coworker and your achy mother-in-law claim it is? Here are some answers to top questions about CBD.

How is CBD Oil Obtained?

There are two main extraction methods for CBD oil.

CO2 Extraction involves the use of carbon dioxide, which is subjected to extremely low temperatures and increased pressure. This causes a phase change from a gas to a liquid. When reheated and pressurized, the CO2 becomes “supercritical”, which basically means it has properties of a gas and a liquid.

Next, the supercritical fluid passes through a chamber containing the raw cannabis material. As it does so, it gently dissolves the membrane of the plant to release its active compounds.

Then the CO2 and cannabis oil particles funnel into a pressurized cyclonic separator, where the CO2 evaporates from the mixture. The cannabis oil, waxes and resins descend into a collection vessel and are ready for further filtration and purification.

Solvent Extraction is a method of soaking raw cannabis material in ethanol to pull compounds into the solvent. Following extraction, the plant material is then removed, and the alcohol is evaporated out.

So Which Extraction Method is Better?

Well, that depends on who you ask. Because CO2 involves the use of high pressures and temperatures, some people contend that it destroys more of the chemical constituents of the plant. Others prefer the CO2 method because solvent extraction destroys the cannabis waxes, which contain beneficial flavonoids and carotenoids. Additionally, there is a limited risk that some of the solvent chemical remains in the final product.

References

Types of CBD Oil

Full-Spectrum CBD

Full spectrum, or whole plant, CBD contains all the compounds that naturally occur in the plant. This includes terpenes, essential oils, and other cannabinoids. There are over 100 different cannabinoids in the plant, with THC and CBD typically the most prevalent.

The full spectrum of constituents from the whole plant work together to magnify the therapeutic effects of each cannabinoid. This is known as the entourage effect.

Full spectrum products typically contain higher THC levels than other types of extractions. This may pose issues in some states or for users who do not want THC to show up on screenings or tests.

Broad-Spectrum CBD

Because of the concern regarding THC in full-spectrum CBD, some producers offer broad-spectrum CBD.

The product undergoes processing to remove as much THC as possible while preserving the other natural cannabinoids and terpenes. Broad spectrum CBD is an excellent choice for individuals who can't have any trace of THC in their system, whether for medical, personal, or legal reasons.

CBD Isolate

As the name suggests, CBD isolate is an extraction of the single compound of CBD. Everything else contained in the plant matter is removed, including any traces of THC, terpenes, waxes, oils, chlorophyll, etc. What remains is 99% pure CBD. This results in a very concentrated extract.

When evaluating an isolate, it's very important to verify the purity. While many types are 99.9%+ pure with no identifiable amounts of THC, lower purity options may still contain trace amounts. This small percentage of THC is usually negligible, but for those seeking the purest CBD, it is something to be aware of.

Enhanced CBD Isolate

Some companies, including Nature's Ultra, utilize isolate extraction for a concentrated CBD oil and then add in other compounds. For example, the addition of essential oils creates a chemical profile similar to a broad-spectrum product without the risk of THC contamination. Additionally, they bring the added therapeutic benefits of the essential oils used in the product.
Which should you choose?

As with all things Cannabis, there’s no correct answer to that question. Every person reacts differently to CBD, so you won’t know for sure what’s best for you until you try it yourself. Whatever you choose, start slowly, and gradually increase the dose after you see how it affects you.

Regardless of which type of product you choose, take a look at the company’s extraction methods. Some companies use solvent or high temperature extraction methods that can damage beneficial compounds and leave chemical residues. For this reason, many people prefer chemical-free, low temperature CO2 extraction.

References

Section 2: Cannabidiol Pharmacology

Introduction
Pharmacology is the branch of medicine concerned with the use, effects, and modes of action of drugs. We have already covered mechanism of action of THC and CBD and how they interact with cannabinoid receptors. This section will focus on dose formulations and administration, side effects, and appropriate use of cannabis. We also focus on pharmacokinetics or how rapidly or slowly cannabis enters and is eliminated from the body.

CBD Pharmacokinetics
There are many options for the self-administration of cannabis, and the most common are smoking, inhalation by vapor, and ingestion of edible products. It is important to understand that the method of administration dictates the pharmacokinetics. This governs the onset, intensity, and duration of the drug's effect, the impact on organ systems, addictive potential, and negative consequences associated with cannabis use.

Smoking combusted cannabis is a well-known method of self-administration and historically is the most important administration method. During smoking, THC gets transferred rapidly to the lungs and then to the blood. Smoking has a rapid onset, usually within minutes, and affects the brain significantly. Duration of effect is approximately 1-3 hours. There is no causal link between smoked cannabis and lung cancer, but inhalation of combusted cannabis does lead to chronic phlegm production and chronic cough.

Vaping is the use of an atomizer or heating element to heat liquid cannabis extract to a boiling point. This creates a vapor for inhalation and is an increasingly popular method for self-administration. Similar to smoking, this method of delivery has a rapid onset of action and a relatively brief duration of action of 1-3 hours. Vaping does not appear to be linked to chronic cough and phlegm production and is considered by some to be a safer option than inhaling combusted cannabis. However, this is highly controversial and there is emerging evidence that vaping may cause significant damage to the lungs, and the Centers for Disease Control and Prevention recently launched an investigation into the increase in the number of sever pulmonary disease cases have been noted in e-cigarette users.

Topical and transdermal administration avoids first pass metabolism and the potential negative pulmonary effects of smoking and vaping. Topical preparations are preferred for local symptoms and skin conditions. Depending on the site of administration and...
the formulation selected, topical administration has a rapid onset and a 2-3 hour duration of action.

Edible forms of cannabis are more commonly used in states where recreational cannabis use is legal. Oral administration is not associated with pulmonary complications, but the onset of action is much slower (30-120 minutes) and the duration of action is much longer (5-8 hours).

References


Cannabis Formulations and Dosing

Cannabis can be consumed in multiple ways, and below are some of the most common:

- Inhalation by smoking or vaporization or herbal cannabis, resins, or concentrates.
- Oral products such as oils, tinctures, prescriptions cannabinoids, and edibles.
- Topical and rectal creams, ointments, resins, concentrates and suppositories.
- Oromucosal or sublingual lozenges and lollipops.

There are also a variety of cannabis-based medications that are available via prescription.

- Dronabinol is a synthetic THC and is labeled to treat anorexia associated with weight loss in patients with AIDS as well as nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. It is a schedule III narcotic.
- Nabilone is a synthetic THC analog labeled to treat refractory chemotherapy-induced emesis. It is a schedule II narcotic.
- Epidiolex is a highly concentrated cannabidiol solution labeled to treat seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients who are older than 2 years of age or older.
- Nabiximols is a THC and CBD extract approved for use in the United Kingdom and currently in the fast track phase 3 clinical trials with the Food and Drug Administration. This medication is labeled to treat moderate to severe spasticity due to multiple sclerosis who have not responded adequately to other anti-spasticity medicines.

Medical history may be important when deciding how to administer a cannabis product. Consider underlying pulmonary disease, prior personal use of cannabis, along with state regulations, which may limit or restrict certain preparations. There is very little evidence to suggest that one delivery method is better than another, so dosage form really comes down to the side effect profile and the pharmacokinetics.

Starting Dose

There is very little guidance on the best possible dose of cannabis products. As with most natural products, it’s a good idea to start with a low dosage and go slow with increasing your dose. Recommended starting doses of CBD run the gamut, with
starting doses ranging from 10 mg to 40 mg. If you have never consumed CBD, it is prudent to start at the lower end of this range.

**Calculating Dose**

CBD formulations may come in various concentrations. While edibles, lozenges, lollipops, and suppositories will likely have a dose per unit, creams, ointments, tinctures and oils may have only a concentration per bottle.

To correctly calculate a dose, you must understand how many milliliters are in each bottle, and this allows you to figure out the dose per milliliter (a common dropper size), the dose per teaspoon (5 mL) or the dose per tablespoon (15 mL).

So, for a 30 mL bottle,

- 500 mg per bottle = 16.66 mg of CBD per 1 mL, or ~17 mg/mL
- 1000 mg per bottle = 33.33 mg of CBD per 1 mL, or ~35 mg/mL
- 1500 mg per bottle = 50 mg of CBD per 1 mL, or ~50 mg/mL

The FDA does not provide recommend dosages of CBD products, and dosage varies dramatically from person to person based on various factors. Start with a small amount, evaluate how it works for you, and increase the dosage as desired or as directed by your healthcare provider.

**Maximum Dose**

While there is no true maximum dose cannabis, there is a risk of excessive side effects at high doses. Discontinue use of cannabis if you experience escalated heart rate, headache, pale skin, paranoid thoughts, delusions or hallucinations, confusion or panic attack.

Studies have dosed up to 1280 mg without toxicity or serious adverse effects.

**References**

CBD and Drug Interactions

Drug interactions occur when a combination of medications produce a clinically significant change in pharmacologic response that is larger or smaller than the sum of effects when the drugs are administered separately. The variation relates to pharmacokinetics, which is the study of how much and how fast the body absorbs, distributes, metabolizes, and eliminates a foreign substance.

All manner of foreign substances, including essential oils, interact with the body. This leads to questions about whether people taking certain medications with certain disease states or with a history of disease should avoid using certain essential oils. As always, it is advised to consult a healthcare professional knowledgeable about essential oils before embarking on any new routine.

Drug Metabolizing Enzymes and the Liver

Many drug interactions arise from the liver. This is because the liver is the most active metabolizing organ in the body, equipped with a plethora of drug metabolizing enzymes that break down medications and foreign substances into execrable metabolites. Liver enzymes include cytochromes, CYPs (pronounced ‘sips’), and P450. Furthermore, enzymes may have more specific names (e.g. CYP3A4, 1A2, 2C9, etc.). CYP function varies based on age, race, and individual genetics.

Metabolism

Metabolism consists of three phases: phase 1, 2, and 3.

Phase 1 Metabolism

Phase 1 metabolism involves basic chemistry: oxidation, reduction, and hydrolysis. There are 2 basic types of reactions in phase 1 metabolism:

• Enzyme-dependent, such as those occurring in the liver via monooxygenase activity.
• Byproduct of pH changes, such as those occurring in the stomach.

Byproducts of phase 1 metabolism may not be immediately execrable and may undergo further transformation in phase 2. Additionally, phase 1 metabolism can activate substances (such as prodrugs to active drugs) or toxify substances (when non-toxic starting materials become toxic).

Phase 2 Metabolism

Phase 2 metabolism uses an enzyme to add a functional group to a molecule. This ensures the group is water soluble and highly execrable. Enzyme-dependent functional
groups that serve this function include sulfate, methyl, acetyl, glucuronide, glutathione, and glycine.

During conjugation to one of these groups, most products are rendered water soluble and not available for further use by the body. However, some products may proceed even further to phase 3 reactions. These reactions may take place in the liver, as well as the kidneys, lungs, central nervous system, intestine, prostate, red blood cells, and more.

Phase 3 Metabolism

Phase 3 takes the conjugation products from phase 2 reactions, removes the added group, and finally, acetylates them to prepare them for excretion.

Many of these metabolic processes are dependent on enzyme activity, and many foods and medications can alter enzyme function. When an enzyme becomes inhibited, metabolism of any substrate of the enzyme will decrease (meaning the medication or foreign substance will stay in the body longer). If we induce the enzyme, metabolism of the substrate will accelerate (meaning the medication or foreign substance does not stay in the body as long).

Examples of medications that can induce CYP enzymes include rifampin and carbamazepine. Medications that can inhibit include cimetidine, omeprazole, ritonavir, and many more.

**Essential Oil Drug Interactions**

Wild mountain sage, brown and yellow camphor, lemongrass, blue chamomile, blue tansy, and yarrow essential oils have been shown in vitro to interact with cytochromes. These essential oils may also interact with medications metabolized by these enzymes. Additional in vitro studies demonstrate hundreds of essential oil constituents that may interact with enzymes. The individual constituents are simply too numerous to name here.

**Other Drug Interactions**

**P-Glycoprotein**

Efflux pumps, such as P-glycoprotein in the liver, jejunum, colon, pancreas, and kidneys, effectively remove foreign substances from cells. Medications, such as proton pump inhibitors, calcium channel blockers, and certain antidepressants, can inhibit P-glycoprotein, thereby increasing the duration of time a substrate will stay in the body.

The extent to which essential oils can affect drug transport is unclear, however the effect is likely small.
CBD Metabolism

CBD is a chemical compound from the cannabis plant (Cannabis sativa). Cytochromes CYP2C19 and CYP3A4 metabolize CBD. CBD also inhibits not only these enzymes, but CYP2D6 and Pgp as well.

Each of these may lead to drug interactions. Before you dive into the rest of this post, be sure that you understand the Basics of Drug Interactions.

Drug Interactions in the Liver

Medications that May Increase the Risk of CBD Toxicity

Medications that inhibit CYP2C19 or CYP3A4 that may increase CBD activity and increase risk of adverse effects of CBD.

Medicines For:

- Antiplatelet activity (clopidogrel)
- Arrhythmias (amiodarone, diltiazem, dronedarone)
- Bacterial Infections (clarithromycin, telithromycin)
- Breast cancer (tamoxifen)
- Depression and anxiety (fluoxetine, fluvoxamine)
- Epilepsy (eslicarbazepene)
- Fungal infections (fluconazole, ketoconazole, miconazole, voriconazole)
- Hepatitis infection (simeprevir, telaprevir)
- HIV Infections (amprenavir, atazanavir, darunavir, delavirdine, ritonavir, saquinavir)
- Heartburn and gastrointestinal reflux (cimetidine, esomeprazole, omeprazole)
- Sleep Disorders (modafanil)
- Tuberculosis (isoniazid)

What are the Adverse Effects of CBD to Look Out For?

Generally, CBD is very well tolerated with minimal side effect profile. But CBD does have some adverse effects. Therefore, lookout for signs and symptoms like:

- Somnolence
- Decrease appetite
• Diarrhea
• Malaise
• Fatigue
• Rash

That said, really and truly, the risk of drug interactions causing CBD toxicity is very low. CBD is very well-tolerated in most people.

**CBD May Also Increase the Risk of Medication Adverse Effects**

Above, we describe CBD is metabolism by CYP3A4 and CYP2C19. Therefore, drugs that inhibit these enzymes may increase the risk of adverse effects of CBD.

CBD inhibits CYP2C19, CYP3A4, and CYP2D6. Therefore, you have to look out for side effects of medicines. As with any medicine, talk to your doctor or pharmacist about the side effects of your medicines.

CBD inhibits CYP2C19, CYP3A4, and CYP2D6, and may also increase medication activity and the risk of adverse medication effects.

List above, plus medicines for:

• Blood pressure (carvedilol, metoprolol, timolol)
• Cough and cold (chlorpheniramine, dextromethorphan)
• Depression (amitriptyline, fluoxetine, fluvoxamine, nortriptyline, paroxetine, protriptyline, venlafaxine)
• Nausea (dephenhydramine, palanosetron)
• Pain (codeine, duloxetine, hydrocodone, tramadol)
• Psychosis (haloperidol, risperidone)
• Sleep (trazodone)

**To Make CBD and Drug Interactions Even More Complicated**

CYP2D6 has a special property where it also activates certain drugs. These drugs are called pro-drugs, and they must go through the enzyme in order to have any biological activity.

CBD inhibits CYP2D6, meaning it slows down the activation of pro-drugs into their active form. If you are taking one of these medicines, CBD may decrease medication activity and even decrease the effectiveness of the medicine.

Medicines for:
• Arrhythmias (amiodarone)
• Depression (bupropion, fluoxetine, paroxetine)
• Nausea (diphenhydramine)
• Psychosis (haloperidol, thioridazine)

PgP Interactions

P-glycoprotein (PgP), is an enzyme that transports foreign molecules out of the blood and into the gut so they can be excreted.

CBD inhibits PgP, which may reduce the excretion of certain medicines. This may increase medicine activity and increase the risk of medicine toxicity.

Medicines for:
• Gout (colchicine)
• Heart conditions (dabigatran, digoxin, diltiazem)
• Pain (morphine)

There are a lot of unknowns when it comes to the use of CBD. While the information above sounds terrifying, keep in mind that it is almost all theoretical. There is very little reported in the literature about CBD and drug interactions, and by and large CBD is exceedingly safe at reasonable doses.

Often times with natural products, there is no black and white answer to the question of drug interactions. What is known is that you can quickly and easily learn the side effects of your medicines. Simply talk to your pharmacist or health care provider for guidance.
CBD, Drug Testing and Addiction

Drug Testing

Routine drug tests are necessary protocol for some workplaces. The majority of drug tests follow a similar 5- or 10-panel screen. Both of these models test for the presence of THC, but not CBD. So yes, if you use CBD, it could show up on a blood or urine drug screen, just as could any other medicine or supplement you use. But most drug tests are simply not designed to look for it.

Drug tests routinely screen for illegal substances, including THC. However, the tests do not screen for CBD. Whether your workplace uses a standard 5-panel or 10-panel screening, neither of them test for the presence of CBD.

You can get high from CBD. This is simply not true. As long as the product you use contains less than the legal amount of 0.3% THC, it cannot get you high. In fact, CBD has properties that actually block the effects of THC and prevent intoxication.

And this goes for drug testing as well. Drug tests are specifically designed to detect THC, not CBD.

Addiction

Though CBD and THC are both cannabinoids, they interact with the endocannabinoid system differently. THC fits into a very specific receptor site in the brain, which results in the euphoric feeling of being high. CBD doesn’t fit into the same receptor and will not cause the same sensation.

If you think you may be suffering from cannabis use disorder, or any substance use disorder, please contact Narcotics Anonymous or Alcoholics Anonymous. If you are thinking of committing suicide, taking your own life, or removing yourself from society for any reason please call 1-800-273-8255. If you are thinking of harming someone else, please call 911.
Clinical Use of Cannabis

Contraindications to Use of Cannabis

There are certain people who should not use medical cannabis, though there is not great consensus on exactly who these people are. According to some guidelines, medical cannabis should not be used in people who are less than 25 years of age, who have a personal or a family history of schizophrenia, have a current or past history of a cannabis use disorder, have another active substance use order, significant cardiovascular or respiratory disease, or are pregnant or breastfeeding.

Efficacy of Cannabis

There is more information out there on the use of medical cannabis. Although there is minimal research on CBD, the results are promising.

Pain

Chronic pain is a public health issue of massive proportions, particularly in countries with aging populations. A staggering half of all older people suffer from chronic pain. In the midst of the current opioid crisis, there is much interest in using cannabinoids to limit the use of opioid medicines.

While there is not much evidence that CBD can help with pain, there is a plethora of evidence to show that medical cannabis may reduce pain in many disease states ranging from neuropathic pain, HIV neuropathy, pain associated with multiple sclerosis, post-operative pain, Rheumatoid arthritis, and intractable cancer pain.

A review article of 31 studies evaluated the use of medical cannabis—23 randomized controlled trials and 8 observational trials—with a median duration of 2 weeks. Combined 1932 individuals received medical cannabis and 1208 received the control of either placebo or standard of care. There were 4779 total adverse events, and 96.6% were deemed not serious. The most common adverse effect was dizziness, and the most common serious adverse effect was relapsing multiple sclerosis and urinary tract infections.

The Canadian College of Family Physicians recently published a simplified guideline for prescribing medical cannabinoids. They recommend against the use of medical cannabis for most diagnoses except certain pain, chemotherapy induced nausea and vomiting, and spasticity due to MS and spinal cord injury. They strongly recommend against the use in the setting of acute pain, and they cite lack of evidence of effectiveness and known harms. And recommend against the use in headache due to lack of evidence, Rheumatologic pain because of a lack of evidence and known harms,
and in neuropathic pain unless patients have failed multiple therapies, understand the
risks of cannabinoids, or as adjunctive therapy to conventional therapies. They
recommend using pharmaceutically developed product as the initial therapy, and
against medical marijuana (particularly smoked cannabis) because of the risk of bias
and lack of long term safety studies. Furthermore, most medical cannabis contains
higher levels of THC and CBD than is commonly tested in studies.

On the other hand, The National Academies of Sciences, Engineering and Medicine
suggests that there is conclusive or substantial evidence that cannabis or cannabinoids
are effective for the treatment of chronic pain in adults, even if the evidence is limited
regarding dose. There is a rough approximation that medical cannabis can lead to a
30% or greater improvement in pain compared with placebo.

CBD may work as a treatment for pain as it reverses pain perception and anxious
behavior in models of neuropathic pain. It initially decreases the rate of firing of
serotonin, but repeated low dose CBD induces analgesia through activation of the
TRPV1 receptor, reduces anxiety through serotonin activation, and rescues impaired
serotonin.

Seizures

Cannabis has been used since ancient times to control seizure. With the prevalence of
seizure disorder combined with the toxicity of anti-seizure medicines has resulted in
considerable interest using cannabinoids for the treatment of seizures. A highly
concentrated form of CBD is used to treat rare seizures and treatment resistant
seizures associated with Dravet syndrome and Lennox-Gastaut syndrome.

Weight Loss Associated with HIV/AIDS

Weight loss is a common manifestation of HIV and AIDS. Nausea and vomiting may be
the cause of unintended weight loss, and cannabis use can reduce nausea and
vomiting and is effective in increasing food intake and causing weight gain.

Cancer

The National Academy of Sciences, Engineering, and Medicine report concludes that
though cannabis failed to reach statistical significance for the treatment of nausea and
vomiting, there as overall a benefit in reducing symptoms with few side effects. Of the
trials assessed, 14 studies used the drug nabilone, 6 studies used THC, 4 studies used
levonantradol, 3 studies used dronabinol, and 1 study used nabiximols.

There is also evidence that CBD can modulate breast cancer cell behavior through
interactions of epidermal growth factor-induced cell proliferation and chemotaxis.
Though the data is very preliminary, there is some promise that CBD may be a novel therapy for triple negative breast cancer.

**Sleep Disorders**

One of the most common side effects of CBD at high doses is sedation, and this has led to interest in using CBD as a treatment for sleep disorders. There is evidence that CBD can reduce sleep disturbances associated with REM behavior sleep disorder. In contrast to common prescription sleep aids, CBD does not disturb sleep cycle.

**Mental Health**

CBD has anticonvulsant, anti-anxiety, antidepressant, and antipsychotic actions, and it has been hypothesized that CBD may serve as a mood stabilizer. In an animal model of mania, CBD did not prevent amphetamine induced hyperlocomotion. In a study of 2 patients with bipolar affective disorder. There was no improvement of mania in the two patients.

There are extensive considerations when deciding whether or not to use CBD in the setting of mental health. For more information, see the special population section.

**Neuroprotection**

CBD has a pronounced neuroprotective effect in the developing brain. It can protect against hypoxic-ischemic injury.

**Immunity**

Cannabinoids regulate the immune system in several ways. First, by inducing apoptosis in immune cells. THC and CBD specifically cause cell death in T cells and macrophages, leading to immunosuppression. They also dysregulate cytokine production meaning that there are fewer inflammatory mediators. Cannabinoids also upset the balance of T-helper cell subsets, decrease tumor necrosis factor alpha, colony stimulating factors and interferon-gamma. Interestingly, the anti-inflammatory cytokine IL-10 decreases following THC treatment, while pro-inflammatory cytokine IL-8 increases. Therefore there may be multiple competing mechanisms that may lead to either an increase or a decrease in inflammation.

**Multiple Sclerosis**

Muscle spasticity in multiple sclerosis is common. Two clinical trials have investigated the use of cannabis to reduce muscle spasticity. According to the National Academy of Sciences, Engineering and Medicine, there is conclusive evidence that oral cannabinoids are effective for improving patient-reported symptoms of spasticity scores. Unfortunately, while cannabinoids can reduce spasticity associated with
multiple sclerosis, there is no evidence that it will work in the setting of spinal cord injury.

References


Cannabis Side Effects

Determining the adverse effects of CBD is complex because the data is muddied with the use of THC-containing medical cannabis. Therefore, it is important to take adverse effect data with a grain of salt. It is often not differentiated between smoked cannabis, oral cannabis or topical cannabis.

In a systematic review of trials over 40 years was conducted. Of the patients in the active cannabis arm of the study, there were 4779 adverse effects reported. 96.6% of these were deemed not serious. The most common adverse effect was dizziness with an occurrence of 15.5% among people exposed to cannabinoids.

The most common serious side effect was relapsing multiple sclerosis, vomiting, and urinary tract infection. There were more than 60 other reported adverse effects including impaired coordination and performance, anxiety, suicidal ideations, or acute psychosis. Chronic use of cannabis may lead to mood disturbances, exacerbation of psychotic disorders, cannabis use disorder, withdrawal syndrome, or neurocognitive impairment.

In other studies, the most common adverse effects were dizziness, dry mouth, nausea, fatigue, somnolence, vomiting, disorientation, drowsiness, confusion, and loss of balance.

Mental Health Effects

There are several adverse mental health effects attributed to the use of cannabis. Frequent, heavy use or the use of highly concentrated THC formulations can lead to a temporary psychotic state. This may lead to loss of control, irrational panic, paranoia, anxiety, altered perceptions, auditory hallucination, and delusions. THC also may worsen schizophrenia and other mental illnesses and may be associated with depression.

There does not appear to be the same mental health risk with the use of CBD, however more mild symptoms such as confusion and disorientation may occur.

Cannabinoid-Induced Hyperemesis

Cannabis use can be associated with cyclical vomiting known as cannabis hyperemesis syndrome. It is theorized that the condition may be attributed to the activation of the CB1 Receptor and/or the VR1 receptor inactivation. Treatment with anti-nausea medications frequently fails, and antianxiety medicines or antipsychotics may be required to break the cycles of vomiting. (Allen 2004, Galli 2011)
Drug Interactions

CBD oil may also interact with several medications. It is important to discuss with your doctor before you start using CBD oil to avoid potentially harmful interactions.

References:

Section 3: Special Populations

Introduction

The study of special populations is the investigation of how substances such as medications interact with groups with special needs. This includes, but is not limited to children, pregnant women, lactating women, elderly, LGBTQI people. In works related to humans, special populations may also extend to pets. The definition can include populations with economic, cultural, physical, or ethnic disadvantage such as lack of health literacy, lack of English literacy, deafness or blindness, and people who lack access to care.

In this section we will cover data related to medical cannabis and children, pregnant and lactating women and pets.
CBD and Kids

The ECS and Pre-natal Development

The ECS plays an important role in the earliest stages of embryonic implantation and development and throughout pre- and postnatal development and survival. This system directly impacts prenatal neural development. Research from voluntary aborted fetuses showed the development of CB1 receptors first detected at week 14 of gestation in the human embryo. This is compelling evidence of the involvement of the ECS in the maturation of the nervous system.

We know that cannabinoids affect the ECS. We know that human embryos have an active and essential ECS. Unfortunately, research about how cannabis affects the embryonic ECS does not exist. Some people contend that CBD actually helps with neurogenesis, the development of healthy brain cells. Others feel that the interference could be detrimental.

The ECS in Infants and Children

Developmental observations suggest that infants’ CB1 receptors develop gradually after birth. Because of immature CB1 receptors, infants are not as sensitive to the psychoactive effects of cannabinoids. Therefore, scientists propose that children may respond positively to medicinal applications of cannabinoids without undesirable effects. Excellent clinical results have previously been reported in pediatric oncology and in case studies of children with neurological disease or brain trauma.

The question of when the ECS reaches maturity remains unanswered. In my searches, I was unable to find any scientific study detailing this development past the early infant stages.

Cannabis in Children

Go looking for research about the safety of CBD in children, and you will find instead a slew of articles about its benefits. In my searches, I found no conclusive evidence of dangers of CBD for children, with the exception of case studies where children accidentally ingested high doses of marijuana, THC gummies, or other forms of cannabis not intended for them. Here is a brief overview of some of the research regarding the benefits of cannabis for children.

Reduction of Seizures

For centuries, cannabis has been used to treat seizures. These studies compellingly demonstrate that cannabinoids such as CBD can be used to reduce seizures effectively, particularly in patients with treatment-resistant epilepsy.
In one study of 19 children between the ages of 2-16, “sixteen (84%) of the 19 parents reported a reduction in their child’s seizure frequency. Two parents reported that their child became seizure-free after more than 4 months of cannabidiol-enriched cannabis use. Of the remaining 14 parents reporting a change in seizure frequency, 8 reported a greater than 80% reduction in seizure frequency, three reported a greater than 50% seizure frequency reduction and three reported a greater than 25% seizure frequency reduction. Three parents reported no change.”

**Improvement of Autism Symptoms**

The use of cannabis in autistic children may help reduce aggression, hyperactivity, anxiety, and other related behavioral problems. Unlike most studies cited in this article, this one actually involves the use of CBD oil, not marijuana or other THC-containing preparations.

**Relief from Insomnia and Anxiety**

A case study looked at a single 10-year-old girl with behaviors related to a diagnosis of post-traumatic stress disorder (PTSD) secondary to sexual abuse. Her chief issues included anxiety, insomnia, outbursts at school, suicidal ideation, and self-destructive behaviors. The main finding from this case study is that CBD oil can reduce anxiety and insomnia secondary to PTSD.

**The Bottom Line for Cannabis Use in Children**

Despite lacking data regarding the safety of CBD in children, plenty of studies point to the benefits of CBD. Not to sound like a broken record, but the best advice is to speak to a trusted pediatrician or healthcare professional, do your research, talk to other parents, and make an informed decision. If you decide to try CBD with your child, start low and go slow. Monitor his/her reactions and adjust the dose slowly as needed.

**References**


CBD and Pregnancy

Cannabis in Pregnancy

Taking CBD during pregnancy may offer numerous benefits to the mother. Studies show that CBD is beneficial for supporting the emotions, including depression and anxiety, which are common complaints during pregnancy. Additionally, CBD can provide pain relief, promote better sleep, and even lower blood pressure. But is it safe for the developing baby?

Placental Barrier

Numerous studies show that cannabinoids cross the placental barrier. One study, in particular, evaluated the increased permeability of the placenta following the use of cannabidiol. It concluded that marijuana consumption enhances placental barrier permeability to xenobiotics and could endanger the developing fetus. Whether or not the use of CBD is safe for a developing fetus, this study raises the question about whether CBD makes the fetus more susceptible to the effects of other drugs and environmental toxins.

We know that CBD crosses the placental barrier, but what are the effects on the developing fetus?

Prevention of Pre-Term Labor

One study tested the efficacy of CBD to inhibit oxytocin-induced myometrial contractions. In this in vitro study, CBD relaxed uterine contractions. Researchers propose that CBD could be a viable method of preventing pre-term labor in high-risk mothers. However, keep in mind that the study involved uterine tissue in vitro.

Low Birth Weight

Maternal cannabis use during pregnancy is associated with growth restriction in mid and late pregnancy and with lower birth weight. This growth reduction was most pronounced for fetuses exposed to continued maternal cannabis use during pregnancy.

Heart Defects

A pool study from 1968 – 1980 evaluated maternal behavior and heart defects in infants. It concluded a two-fold increase in risk of heart defects with maternal cannabis use. This risk increased with regular (three or more days per week) cannabis use. The validity of this study is questionable because it is so outdated. Additionally, no details are provided about the method of exposure. It is likely that the mothers in this study
were smoking marijuana, of which the quality and source are unknown, and which may or may not have been contaminated by other substances.

Cannabis in Breastfeeding

Just as cannabis crosses the placental barrier, it also easily passes into breastmilk. The studies examined involve regular use of marijuana by nursing mothers. How this data relates to the use of CBD in topical or oral formulations is not fully understood.

Decreased Body Weight

One study involving mice resulted in lower body weights of mice of mothers who received a cannabis mixture that included THC, CBD, and other cannabinoids. The study also noted “impairment of maternal behavior”. The question this raises is whether the lower weight resulted from drug intake with mother’s milk, from decreased lactation of drugged mothers, or from a combination of both.

Decreased Motor Ability

A study involving 136 breastfed infants investigated the relationship between infant exposure to marijuana via the mother’s milk and motor and mental development at one year of age. Marijuana exposure via the mother’s milk during the first month postpartum correlated with a decrease in infant motor development at one year of age. Researchers go on to say that this decrease is a result of marijuana inhibiting the quantity and reducing the quality of breast milk.

The Bottom Line for Pregnant or Breastfeeding Moms

All of this information leaves concerned mothers-to-be in a difficult position. While the soundest advice is always to discuss your options with your obstetrician or health care provider, you will likely find yourself immediately shut down depending on your doctor’s personal opinions. Whatever you decide, do your research: Evaluate the research that exists, talk to other moms, and make sure you are confident with your decision before you proceed.

References


CBD and Pets

The Endocannabinoid System in Dogs

The vast majority of research about the ECS in pets is specific to dogs. For this reason, if you are considering giving CBD to your cat or other pets, use extreme caution. I found only one study regarding a cat who exhibited symptoms of intoxication after exposure to marijuana.

According to researchers, dogs have more cannabinoid receptors in the brain than humans. Therefore, they may be more susceptible to cannabinoids such as CBD. Many veterinary scientists claim that THC is toxic to dogs. This is also evidenced by an increase in toxicosis in dogs living in states with legalized marijuana.

The consensus on dogs seems to be that CBD is okay and even beneficial, but THC is very dangerous.

Many websites claim the numerous benefits of CBD for dogs and other animals. Unfortunately, not much research backing this data is available. A survey of veterinarians revealed that more and more recent veterinary graduates are recommending CBD to their patients.

Is it Safe for My Pets?

With all the benefits listed above, you may be tempted to slip a little CBD oil in your anxious pup's food or apply some CBD cream to an arthritic horse's joints. Veterinarians are, in fact, catching on to the CBD craze, and there are a very few promising reports. Unfortunately, there simply isn't enough research of the effects of CBD on animals at this time. The ASPCA recommends waiting on further research before using CBD with your pets.

Dosing in Pets

While there is not definitive guidance on the optimal dosing in pets, some experts contend that doses should be approximately 1-3 mg per 10 lbs of body weight. It seems reasonable to limit dosing, especially initially, to 10 mg/dose.

References


CBD and Mental Health

In the U.S. alone, mental health disorders such as anxiety and depression affect over 40 million adults annually. Even people who don't suffer from long-term emotional issues may experience occasional symptoms. And with a slew of risks associated with many prescription drugs, many people are looking for alternative ways to alleviate anxiety and depression. If you're thinking of adding cannabidiol (CBD) oil to your routine, read on to learn some of the current scientific research about CBD and emotions.

What Causes Mental Illness?

Mostly due to direct-to-consumer advertising (DTCA) from pharmaceutical companies, most people believe that depression and other emotional issues result from a serotonin deficiency in the brain. It is important to note that these advertisements do not require FDA approval. Therefore, their claims are widely unsubstantiated. In fact, when evaluating the serotonin theory, there is actually a significant body of contradictory evidence.

So, what is the root of mental illness, such as depression? To answer this, we must look into a portion of the brain known as the hippocampus. This area is responsible for memory, learning, and emotions. Studies show a direct correlation between the hippocampus and psychiatric disorders.

Serotonin (aka 5-HT) plays a role within the hippocampus as a vital neuromodulator. Its primary function might be to maintain homeostasis in the brain. A deficiency of serotonin can contribute to mental illness, but it is not often the root cause.

The hippocampus is susceptible to changes in the environment as well as inflammation in the body. This is why our physical well-being also has a profound impact on our emotional health. Inflammation, stress, trauma, and illness can actually cause hippocampal atrophy, or shrinkage.

The good news is that this area of the brain is capable of regeneration, or hippocampal neurogenesis. It is possible for new nerve connections to form and the brain to be restored to its normal, non-depressive state. (Remember this term, as we will use it throughout this discussion. Hippocampal neurogenesis = brain regeneration/restoration.)

Can CBD Help?
Although numerous studies about CBD’s effects on the brain exist, ongoing studies are being conducted to evaluate the long-term effects of its use. However, the potential of CBD to help with emotions is quite promising. Let’s look at some scientific studies.

When evaluating the brain-healing potential of CBD oil, the studies refer to CBD’s ability to protect living neurons (neuroprotection), to help form new connections (neuroplasticity), and to trigger the formation of new neurons (neurogenesis). Most of the findings indicate that CBD is key for neuroplasticity in that it directly affects neurotransmitters.

**Neuroprotection**

A study evaluating CBD’s effects on epileptic seizures showed that cannabinoids provide neuroprotection against brain excitability and induce at least partial restoration of neurotransmitter dysfunction.

In an animal study, CBD demonstrated a fast and sustained antidepressant-like effect. Thus, the authors of the study propose that CBD is a promising compound with large-spectrum therapeutic potential.

**Neuroplasticity**

Similar to the actions of anti-anxiety drugs, CBD activates serotonin receptors, which control a variety of neurological communications and increase neurogenesis of the brain.

One extensive review of CBD also concluded that CBD activates 5-HT1 receptors. This has a direct impact on learned fear and phobias, implicating that it may be an effective treatment for anxiety disorders, including post-traumatic stress disorder (PTSD).

**Neurogenesis**

Decreased adult hippocampal neurogenesis has been associated with psychiatric disorders such as anxiety, schizophrenia, and mood disorders. CBD’s positive effect on neurogenesis was first observed in 2005 and many other studies have also demonstrated similar results.

**Specific Mental Illness Studies**

**Psychosis**

Though there is evidence that cannabis can trigger new onset psychosis, CBD may actually alter disease trajectory when used in newly onset psychosis. When given acutely to healthy volunteers, oral CBD has been reported reverse the
psychotomimetic effects of THC, reduce anxiety as well as other subjective effects of THC.

**Schizophrenia**

Though schizophrenia is a contraindication to the use of medical cannabis, there is some evidence that CBD has beneficial effects in patients with the disease. Patients who receive CBD have fewer psychotic symptoms compared to the placebo group, were more likely to have been rated as improved, and as not severely unwell when evaluated by a physician.

**Depression and Anxiety**

CBD is an anxiolytic and antidepressant compound that improves nervous behaviors in animal models.

**Post-Traumatic Stress Disorder**

In the setting of PTSD, CBD may be a treatment for inappropriate retention of aversive memories.

References:


Section 4: CBD Recipes

Introduction

In this section, you will find ways to cook with CBD and do it yourself recipes for everything from bath bombs to love lube. When creating recipes and DIYs, it is very important to remember just how fatty cannabis oils are. You must mix them into water with much force, and it is easier to use another, thinner carrier oil to facilitate blending.

Combining essential oils and CBD is a great way to add a therapeutic aroma to your bath experience, as well as to get the benefits of both the essential oil and the CBD oil.

Choose your oils based on the desired fragrance or action. For example, you may choose a relaxing essential oil, such as lavender, if you want a bedtime bath bomb. Or you may choose wintergreen or peppermint if you want a soothing after workout soak. Alternatively, you can make bath bombs sans essential oils and just add the desired oils directly to the bath water with the bombs. A third option is to use essential oil-infused CBD oil in the recipe.

Have you made a DIY with CBD or cannabis? Submit your recipe to hello@lindseyelmore.com.
Vegan CBD Brownies

Cannabidiol (CBD) is everywhere these days. You can find it infused into soaps, lotions, and muscle rubs, but you can also cook foods and mix up beverages that include CBD. Try these Vegan CBD Brownies for a unique way to enjoy a treat and wind down from a stressful day at the same time!

These Vegan CBD Brownies are perfect for mellowing out and helping you relax after a long day. Try bringing them to your next gathering and share with your friends the benefits of CBD oil.

Vegan CBD Brownies

Ingredients

4 cups chickpea flour
3 cups coconut sugar
2 cups cocoa powder
1 ½ teaspoons salt
1 tablespoon baking powder
2 cups organic applesauce
½ cup agave nectar
1 cup almond milk
1 ½ cups coconut oil
100-250 mg high-quality CBD in oil
1 tablespoon vanilla extract
2 cups mini dark chocolate chips
6 tablespoons cocoa nibs
Fresh mint, for garnish

Instructions

1. Preheat oven to 325° F. Grease and flour two 9" X 12" inch baking dishes.
2. Combine chickpea flour, coconut sugar, cocoa powder, salt, and baking powder in a medium mixing bowl.
3. In a separate bowl, combine and mix applesauce, agave, almond milk, coconut oil, CBD oil and vanilla extract in a large mixing bowl.

4. Add the wet ingredients into the dry and stir with a hand whisk until smooth. Add the chocolate chips and mix again.

5. Pour the batter onto prepared baking pans. Top with the cocoa nibs.

6. Bake for 12-14 minutes, until rich and dark and a cake tester comes out clean.

7. Allow brownies to cool and cut each sheet into 12 portions.

8. Garnish with freshly chopped mint.
CBD Infused Lemon Garlic Dressing

Servings: 4  
Prep Time: 5 minutes

Ingredients

1 Tablespoon Dijon Mustard  
¼ cup lemon juice  
¼ cup white wine vinegar  
4 cloves crushed garlic  
2 tablespoons freshly chopped parsley  
50 mg cannabidiol oil, or to preference  
Salt and pepper, to taste  
¼ cup extra virgin olive oil

Instructions

1. Combine mustard, lemon juice, vinegar, garlic, parsley, CBD, and a pinch of salt and pepper in a medium sized bowl.
2. Slowly drizzle in olive oil to mixture while rapidly whisking.
3. Taste and season again with salt and pepper.
4. Serve as a salad dressing, use as a quick fish marinade, serve over hummus or a block of feta, or use as a bread dip.
Mint Chocolate Chip Smoothies with CBD Oil

Ingredients

1 ¼ cup vanilla pea milk or other plant milk
1 avocado, halved with pit removed
1 frozen banana
1 handful fresh baby spinach
3-4 drops peppermint essential oil
1/2 teaspoon spirulina
25 mg CBD oil
1 tablespoon chocolate chips or cacao nibs
Fresh chopped mint, to garnish

Instructions

1. Add pea milk, avocado, banana, spinach, essential oil, spirulina, and CBD oil to a blender.
2. Add chocolate chips. Pulse to roughly chop chips and combine mixture.
3. Garnish with fresh mint and serve with a metal straw.
Lavender Chamomile CBD Tea

Your bedtime routine has a new best friend. This relaxing, sleep inducing blend will have you drifting off to Lalaland in no time.

Ingredients

1 chamomile tea bag
1 teaspoon lavender flowers
5 ounces boiling water
5 ounces vanilla pea milk, or other plant milk
1 teaspoon maple syrup
10 mg cannabidiol tincture or oil
1 drop lavender essential oil, optional

Instructions

1. Steep the chamomile and lavender in the hot water for 5 minutes and then discard the tea leaves.

2. While it steeps, warm the milk of choice almost to a boil. When the tea is done steeping add in the milk, maple syrup and CBD. Add lavender essential oil, if desired.
Chickpea Pasta with Pesto Sauce Infused with CBD

CBD oil has a grassy intense aroma and flavor that doesn't always lend itself to savory recipes. But when you combine it with big, bold flavors like basil, garlic, and pungent olive oil, you can get the soothing effects without the unpleasant grassiness.

Yield: 3-4 servings
Prep Time: 10 minutes
Cook Time: 20 minutes

**Ingredients**

For the Pesto

- 1/3 cup high quality olive oil
- 40 mg cannabidiol
- 1 cup fresh basil
- 1/2 cup spinach
- 1/4 cup pine nuts
- 3 garlic cloves
- 1/4 teaspoon sea salt
- Juice of 1/2 a lemon

For the Pasta

- 1 box chickpea spaghetti
- Salt
- Basil, chiffonade, for garnish

**Instructions**

1. In a bowl, whisk together the olive oil and CBD until well combined. Set aside.

2. In a food processor, add basil, spinach, pine nuts, garlic, salt and lemon juice. Pulse to roughly combine. Slowly drizzle in CBD and olive oil mixture.

3. Heavily salt a large pot of water over high heat. Bring to a boil and add chickpea spaghetti; boil for 8-10 minutes, according to package instructions. Drain pasta, reserving 1 cup of pasta water.

4. Add cooked pasta to a warmed skillet over medium heat. Add pesto, and just ½ cup of pasta water. Toss to combine pasta with sauce and add additional water if needed.

5. Serve immediately garnished with basil.
CBD DIYS

CBD Bath Bombs

Try these simple-to-make CBD Oil Bath Bombs for a way to relax and unwind after a stressful day.

Yield: 5-6 bath bombs (7 cm diameter)

Ingredients

1 cup baking soda
1/2 cup citric acid
1/4 cup Epsom salts
1/2 cup cornstarch
1 tablespoon coconut oil, melted
20 mg CBD oil
20-30 drops desired essential oils
1/2 – 1 teaspoon water (if needed for consistency)

Bath bomb molds

Instructions

1. Combine baking soda, citric acid, Epsom salt, and cornstarch in a medium bowl.
2. In a separate bowl, combine coconut oil, CBD oil, and desired essential oils.
3. Slowly add wet ingredients to dry ingredients, stirring constantly.
4. Test the consistency by squeezing some of the mixture in your hand. If it packs together, it is ready to place in molds. If it is still too dry and crumbly to hold its shape, add 1/2 teaspoon water at a time until the consistency is correct. Be careful as you add water, though, because too much will cause the mixture to start fizzing.
5. Once thoroughly combined, scoop mixture into molds and press together firmly. Allow to set for one hour.
6. After an hour, gently remove bombs from molds. They will be fragile and not completely set, but if you wait longer, they will be more difficult to remove from the molds.
7. Allow bombs to dry completely overnight.
8. Store in airtight glass container until ready for use.

CBD Love Butter

While the effects of CBD on reproductive health are relatively unknown, some cultures consume cannabis while trying to get pregnant and throughout pregnancy. We do know that the ECS is critical during pregnancy, and that cannabis consumption may negatively impact male fertility. Review articles have failed to show a statistical difference in time to pregnancy in people who use cannabis. Whether or not you choose to use this Love Butter, remember that essential oils and fatty oils break down latex condoms. Be sure to use polyurethane or lambskin to protect against sexually transmitted infections and pregnancy.

Ingredients

1 cup unrefined cocoa butter
¼-½ cup coconut oil
¼ cup grapeseed oil
20-25 mg CBD oil
15 drops aphrodisiac essential oils (e.g. ylang ylang, jasmine, orange, rose)

Instructions

5. Melt the cocoa butter over medium low heat on the stove. Once melted, add ¼ cup coconut oil and grapeseed oil and whisk until smooth. Add more coconut oil if you want a firmer finished product.

6. Remove from heat and add CBD oil and essential oils.

7. Quickly pour into 4 oz salve jars. Store one container near bedside, and the others either in the refrigerator or in a cool, dry place.
Blueberry Dog Treats

Ingredients
2 Tablespoons coconut oil, plus more for greasing
1 ¼ cups mixed gluten-free flour
½ cup Just Egg replacer, or 2 eggs
½ cup dried blueberries
CBD oil, dosed according to dog’s size. Add 1-3 mg per every 10 lbs of body weight, Max dose of 10 mg

Instructions
1. Preheat oven to 350 degrees Fahrenheit. Grease a silicon molded baking mold or mini muffin tin with coconut oil. Bonus points for making them in bone shapes.
2. Pour warm water over blueberries and allow to sit for 10 minutes to reconstitute.
3. In a large bowl, combine together coconut oil, flour, and egg substitute and stir until well-blended. The mixture will be a bit crumbly. Fold in blueberries. Add CBD oil by dropping at many points in the batter and stir thoroughly to combine.
4. Rub coconut oil on your hands, and fill molds half-way with dog treat mixture. Press down to make sure that the mixture is packed down. When
5. Drop the appropriate amount of CBD oil drops into each mold.
6. Bake for 15-20 minutes until the top is firm and lightly browned.
7. Once the biscuits are cool enough to handle, remove from mold or tin. Serve to the doggies! If they have never tried edible CBD, start with a quarter or half of a treat.
CBD Boo Boo Salve

Ingredients
1 cup olive oil
1-ounce beeswax
1-ounce shea butter
50 mg CBD oil

Instructions
1. Place a large stockpot containing about two inches of water over high heat, and bring water to a boil. Place a stainless-steel bowl on top of the pot containing boiling water.
2. Add beeswax, olive oil, and shea butter and melt. Whisk or stir to combine.
3. Remove pot from heat and add CBD oil and stir to combine.
4. Pour into 4 oz jars and bring to room temperature. Then, place them in the refrigerator to firm up. Once firm, store at room temperature.
CBD Sleep Balm

There's nothing worse than climbing into bed ready for a restful night and not being able to catch those precious z's. Whether your mind is racing, or your body just doesn't get the message to wind down, wrestling with sleep stinks. Instead of reaching for sleeping pills, try something natural to help you drift off to dream land. This Sleep Balm combines the power of CBD and the calming aroma of essential oils to help you get a better night's rest.

**Ingredients**

1 tablespoon beeswax or carnauba wax pellets
1 tablespoon jojoba oil
2 tablespoons coconut oil
30 drops lavender essential oil
30 drops cedarwood essential oil
200 mg CBD oil

**Instructions**

1. Combine beeswax or carnauba wax, jojoba oil, and coconut oil, in a mason jar.
2. Create a double boiler by pouring a few inches of water in a small saucepan, and carefully set the jar of ingredients in the water.
3. Next, gently heat the pan over medium-low heat.
4. Once the mixture is completely melted, remove from heat. (Be careful, the glass will be very HOT!)
5. Finally, add essential oils and CBD oil and gently stir to incorporate.
6. Allow to cool completely and solidify before using.

**To Use**

About 30 minutes before bedtime, apply Sleep Balm to bottoms of feet, chest, neck, or arms. (You can really apply it just about anywhere you desire.)
About

Dr. Lindsey Elmore is a speaker, author, world-renowned wellness expert, and founder and owner of Lindsey Elmore enterprises. She analyzes data and translates complicated science into understandable stories. A chemist and a clinical pharmacist, she travels the world educating audiences about natural wellness.

Education

She obtained an undergraduate degree in chemistry from the University of Alabama, Birmingham and a doctorate in pharmacy from the University of California San Francisco. She completed her first-year post-doctoral residency in pharmacy practice at Princeton Baptist Medical Center in Birmingham, AL and her second-year specialty residency in ambulatory care at New Hanover Regional Medical Center in Wilmington, NC. She is a Board-Certified Pharmacotherapy Specialist and licensed to practice in three American states.

She served as a visiting scholar at the University of Zambia, Department of Medicine and provided direct patient care inpatient and outpatient in family medicine and community pharmacy for years before changing course to embrace true health and wellness.

Speaking, Publications, Media, and Affiliations

Dr. Elmore has spoken to audiences on five continents and more than 30 countries. Her educational materials have been translated into more than 25 languages. She is the author of Essentials: 75 Answers to Common Questions about Essential Oils and Supplements, the Clean Slate Cleanse Cookbook and Workbook series, and now CBD Simplified.

She is published in a wide variety of pharmacy and medical journals including Annals of Pharmacotherapy, American Journal of Health System Pharmacy, Currents in Pharmacy Teaching and Learning, Evidence Based Practice, Natural Medicine Journal, Journal of Pharmacy Technology, and more. She has been quoted in Bustle, Elite Daily, Reader’s Digest, Yahoo News, Parade, Brit + Co, Best Life, Medium, She Knows, Well + Good, Woman’s World, Business Insider and many more. She has appeared on news segments on ABC, CBS, NBC, CW, Fox, and The Daily Buzz, and is a regular on a wide variety of podcasts.

Dr. Elmore reaches millions of women on social media. Her Facebook content reaches more than 85 countries, and more than 15 million minutes of education have been
watched on Facebook alone. Her sassy stories and heartfelt writings also touch the 
lives of many on Instagram.

Dr. Elmore serves as a brand ambassador for Young Living Essential Oils.

**Additional Certifications**

Dr. Elmore is passionate about mindful wellness. She is a Certified 250-hour vinyasa, 
yin, and Aroma Yoga® Instructor, an Aroma Freedom practitioner, and the creator of 
the Clean Slate Cleanse. She has been a patient of Chinese medicine and acupuncture 
for over a decade and blends Eastern and Western concepts of health in all her 
teaching.

**The Club**

From all of her travels and diverse learnings, she created The Club, a hub for health, 
wellness, and business education. She has more than 200 videos on essential oils and 
supplements inside The Club, teaches exclusive live events online regularly, and 
constantly creates content requested by her audience.

**Find Out More**

Dr. Elmore inspires people to take ownership of their health and wellness. Join her on 
her journey: @lindseyelmore on Facebook and Instagram and online at 

Share your Essentials journey #essentialsbook on social media.

You can also follow along with her gluten-free, vegan foodstagram @cleanslatecleanse 
on Instagram and @thecleanslatecleanse on Facebook.

In her spare time, Dr. Elmore enjoys giving thanks and showing kindness, swimming, 
singing, dancing, and watching her brother play professional baseball. She is from 
Alabama and lives in New York City.