The CBD Pharmacist

Your Personal Guide to Demystifying the CBD World and Optimizing Your Health

By Sean Gale, RPh

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By Sean Gale, RPh

Dedication

I would like to dedicate this book to the love of my life, my raison de vivre, my most awesome-est wife Christine. A journey of a thousand miles begins with a single step. Thanks for being there all along the way!

With all my love,
Sean

Acknowledgements

Sean is very thankful for the insight and wisdom from his editor Steve Welch. He has been instrumental in forging this book into a literary device that will be able to hopefully impact many, many people. Thanks for jumping in with both feet Steve!

A special thank you to Dr Carl Craig, CEO at Agricor Labs for allowing me to use their COAs (I explain later) and for his clinical insight into my book. Thank you for doing your part to help keep us safe!

This book would not have been completed without the help and encouragement from my family. Countless hours were spent pouring over the early, rough versions by my Mom, Uncle Butch, and my in-house medical expert Dr Ken (stepdad). I appreciate all the time, energy, and hard work you put into helping this book become a reality! Thanks for believing in me!

I am grateful for my business partner Steve Fugiel. Thanks for keeping me from going off the rails and for being a steady, godly influence in my life.

I would be remiss for not thanking Justin Inabinette, my technology/marketing genius, for pushing me to write this book and with a sense of urgency.

And finally, a special thanks to my Lord and Savior Jesus Christ. Without God's steady, loving, and sometimes correcting hand, I wouldn't be here today.

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Foreword:

I am so excited to share the knowledge I have gained in this book that you hold in your hands! It is the culmination of a two-year journey and represents the best of all the information that is out there. Learning about CBD is a journey that can be confusing with tons of conflicting information out there. I have designed this book to help you absorb the sometimes-complicated concepts prevalent throughout this industry in an easy to read format.

You will find a mini-review at the end of each chapter affectionately called “Sean’s Summary” (I know, it’s not the most original concept you have ever heard). In this summary I break down the contents of the chapter into more simplified bullet points that are easier to digest and review. My hope is that you will use these summaries to help bolster your knowledge as you dig deeper into the book and CBD industry. I did not want to dilute the information I have provided to you in these pages so I thought a nice, concise summary at the end of each chapter would be a great way to get the best of both worlds.

I have also included a glossary of terms at the end of the book. There is so much lingo unique to the CBD world that is impossible to ignore. I do make a concerted effort to give full descriptions of the terminology in the book but sometimes it can be hard to keep it all straight. When talking about concepts such as cannabinoids, cannabidiol, endocannabinoid system, and cannabinol, it would be easy to get these concepts twisted up like a pretzel in your

brain. But no worries! As you will hear throughout this book, I am here to help guide you through the CBD maze. If you are looking for a professional, educated assessment of this market that will give you the straight poop, then you have come to the right place.

The greatest joy in my job is that I get to help people and share information that is often difficult to understand. If this book can help just one person to fully understand and utilize this revolutionary product, then all the work would be worthwhile.

Cheers to a healthier, better version of you!

Sean Gale, RPh

Chapter 1. Introduction

If you are like many people who have walked into my pharmacy over the past several years seeking information about CBD, you are wondering who to trust and why you should listen to me? In an unregulated industry like CBD, it's easy for anyone to label themselves as an "expert." Well, I'm here to tell you that as a pharmacist, I am the perfect candidate to gain expertise in the naturopathic and homeopathic market and share that knowledge with customers like you. In fact, that is what I did, and continue to do every day. It's why I wrote this book that you are reading right now!

The reality is, people like you need an independent voice that isn't trying to sell you on one brand or another. This is why pharmacy is routinely ranked as one of America's most trusted professions. You also need someone with a little grey in their whiskers. Someone who has seen homeopathic trends come and go, like ginkgo biloba and Echinacea (and both are still around, but have very specific uses), and can counsel you on what works and what doesn't. It helps that I have seen the trends and various players in the supplement industry over the past 30 years, and as a result, I know a "winner" when I see one. It also helps to have an "independent pharmacy" mindset, which differs from the big box corporations like Walgreens or CVS. In short, we independents provide more personalized service. Independents are more likely to have the time to talk to our customers, listen to their concerns, and help

craft a solution that will fit their needs the best. You just don't have the time or energy to perform such activities at the Walgreens and CVS's of the world. Believe me, I know and have tried, having worked at both.

I have been a practicing pharmacist since 1994 and have always been intrigued by the homeopathic industry. I've managed the 24-hour behemoth stores and the local neighborhood drug stores, enjoying them both. But my greatest joy comes from being able to spend the time and truly help a customer, which is much harder to accomplish when filling 1000 prescriptions per day at the big box mega-pharmacy. The personal story of my immersion into CBD unfolds in the following paragraphs. If you read beyond the basics, you will see information and expertise presented to you in a way that is balanced and fair. I use research as the foundation for the statements written in this book, and I have cited experts whenever I could. My goal is to bring a mixture of pharmaceutical knowledge and practical explanations to provide a unique view point you will find nowhere else. And who else to better understand how drugs work in your body than an expert in pharmacy and pharmacology? A clinically trained pharmacist (like me) has an in-depth understanding of how drugs work in your body and how they might interact with other medications.

If you are looking for passion, expertise, and a customer centric focus, then look no further than this book. My desire is to give you all the tools you need to make the best decisions for your health, whether it is the optimal dosage of CBD, knowing where to buy your product, or making sure you are getting quality CBD from a trusted source. Becoming an expert in CBD is more of a journey

than just memorizing and spitting out facts (which sounds really boring anyway!). I promise to be there for you, all along the twisting and winding road that is the CBD world. If you are interested in CBD, then you must read this book.

I wish that my story with CBD had started differently. If my personal journey were on display, a posted sign would quietly ask the viewer to "move along, please, nothing to see here" because there really wasn't anything exciting to see, nothing momentous happened, and my initial foray into the CBD world ended with a meek exit, stage right. And this from someone who is supposed to be an expert in over-the-counter medications!

However, we should gain encouragement from my unsuccessful entry into the CBD world. See, I sold this supplement in my pharmacy back in November 2018 because there was such a buzz around this new potential "wonder drug." Being the curious type that I am, I decided to see if it would help my chronic knee pain. Now, I am, by nature, a cheapskate (just ask my wife), so I started out with a single bottle of 250mg sublingual liquid and only used half the therapeutic dose. After taking it for a few weeks and going up to the full recommended dose (8mg CBD), I didn't feel that it was having any desired effects, and so I concluded that it did not work for me (in reality, the dose was too low to feel any kind of positive effect).

But, as time went on, I kept hearing amazing stories of CBD's positive effects from my customers and received lots of encouraging feedback about the product. I felt like I was missing something, so I gave CBD another try. Being a pharmacist, I became intrigued why others were achieving such success with the CBD product and I wasn't. Was I

taking it the right way, at the right dose, and at the right time of day? Was the manufacturer I was using supplying me with an inadequate product? All were reasonable questions, so I pushed the virtual pedal to the metal to find out more. Except this task was more difficult than I originally planned! I hit many roadblocks and struggled to find impartial sources of information that I could trust. There just wasn't enough solid information out there and I became quite frustrated with my quest.

My journey to self-knowledge was not a simple task. It was difficult to find expert information or impartial sources to learn from. See, I've never been the smartest guy in my class throughout all my schooling, but I wasn't without certain abilities. Tenacity and a determined nature have carried me well throughout my years. In fact, I used these abilities to achieve success in Cross Country and Track both in high school and in college at the University of Iowa. I continued to apply my talents as I jumped headlong into the choppy waters in the tumultuous sea of CBD to learn more about this topic.

What I found initially was pretty typical for an unregulated supplement. There were lots of testimonials and people with a vested interest in CBD that were teaching about it, but I found very few people with medical training giving conservative, professional advice. This encouraged me to look deeper, to dig through mountains of data, and to find and explore all the dead ends. The more I researched, the more I became amazed at what I found. My findings changed my opinion about this supplement, and so I took another CBD trial, but this time at a therapeutic dose of 16mg per day (double what I was using before!). The results were nearly instantaneous as I felt a lessening of

the aching in my joints (I run 5 days per week) and mentally I just felt sharper. My sleeping also improved, and I felt more refreshed in the morning. This became my "aha" moment, when I realized that there was truly something special about CBD.

I started conducting in-depth consultations with my patients and began asking for feedback on what worked and what didn't. This I believe is the role of a pharmacist; helping people make wise decisions in relation to medications, whether over the counter or prescribed. I also help people discern side effects and advise them on what they can do to mitigate these reactions. Determining optimal dose and route of administration, especially for CBD which has so many choices, is also securely in my wheelhouse.

After all my research, I can say unequivocally that CBD is unlike any drug I have encountered in my 28 years of retail pharmacy. What makes it unique is that it affects a system rather than just a specific condition. This means that while the effects vary with each person, there is great potential for amazing results. The affected "system" is the Endocannabinoid System (ECS), which acts like the conductor for the symphony consisting of all the other bodily functions and systems. The receptors for the ECS are everywhere in the body and can be found in large quantities in the brain, organs, and nerve cells. While we know how the ECS works, we still know very little about its effects and functions. This is an area I am determined to continue to research.

The more I learned about CBD, the more I realized the benefits. The thing that motivates me most in my job, and

the things that bring about the greatest amount of satisfaction, are helping other people and giving them resources to make the best decisions for their health. And with CBD, I did that in ways I had never encountered before. I was getting positive, continuous feedback on what CBD was doing for my patients. I wanted to share this information with others, so I wrote an article that appeared in the local paper, and as a result, information seekers swarmed the pharmacy. I became the #1 seller of CBD in Northern Illinois and Southern Wisconsin. I taught about CBD through the healthcare channels at my job and talked to various components of the public (cancer patients, community groups, and elderly), and professional groups too! Based on the number of questions I was asked, the lack of understanding that was out there, I realized that there was a desperate need for accurate, reliable information about CBD. People did not know how to make sense of what was happening, what was truth, and what was fiction. There are some amazing, miraculous stories out there, and many of them are true, but it's difficult to know who to believe. I have made it my mission to help people discern fact from fiction and to learn how CBD can help them change their lives for the better! And I can truly say that this research on CBD has provided as much professional satisfaction as any other thing I have done in my career.

I'm so excited to continue this learning process with you, the reader! This educating about CBD does not and will not end. We are just at the tip of the iceberg, and I hope to share this journey with you by building a foundation of knowledge with this book that will help you navigate the CBD world just as I have. I hope that you will reach out to me directly through my website with questions,

quandaries, and areas of confusion. I've always been a collaborative learner, whether in pharmacy school or managing high volume, 1000 prescriptions/day pharmacies. The more you ask the more I learn. I look forward to continuing to learn and share CBD with my readers, through my website (awakentocbd.com), monthly newsletters, and weekly posts. But, first things first. It's time to give you all the basics you need to understand what is CBD and how it might help you or your loved ones.

Chapter 2. What is CBD?

I'm guessing that most of you who are reading this book already know something about CBD but want to know how much is fact and how much is fiction or exaggeration. My role as your pharmaceutical guide through the CBD exploration process is to help clarify this conundrum. The first thing to address is, what CBD is, and what it isn't.

Because of CBD's close relations to the marijuana plant, there is a lot of confusion and misperceptions about it that I will help clarify. I designed this book to be like your roadmap. As you drive along through these pages, I will present you with the sights and sounds of the CBD world. Some stops will be more exciting than others (I really enjoyed writing about opioids and the immune system) and if you take the entire tour, I promise you will become an expert by the end. While learning about CBD might not seem that exciting, it is essential to lay the foundation for everything else we will talk about.

Differentiating CBD, Cannabis, Marijuana, and Hemp

Many of you are familiar with the terms Marijuana and Hemp, but do you really understand what they are and the difference between them? Some of the questions I hear and confusion I see revolves around understanding (or lack of understanding) these differences, and being able to answer questions like, "Is the psychoactive component of marijuana (THC) the same as CBD?" and "Will you get high from CBD?" This chapter will go a long way towards

answering those questions and giving you confidence when taking CBD.

First, let's have a brief lesson in the horticultural sciences to explain the differences between these various plants and substances:

Cannabis is a genus of flowering plants in the Cannabaceae family, which consists of the species Sativa, Indica, and Ruderalis. The flowering part of the plant is very important, and I will explain this more shortly. It is these different species which play a key role in differentiating the end product because of the higher amounts of THC.

THC stands for tetrahydrocannabinol and is the primary component associated with causing the "high" sensation that most people associate with marijuana.

Hemp refers to cannabis that is grown for non-drug use and in order to qualify as a non-drug product, it must contain less than 0.3% THC to be legal. Hemp is grown and harvested primarily for its soft fiber which is used to make clothing, paper, rope, and other products, and its seeds are often used in food and cosmetics. Most important to us as we read this book, hemp flowers are harvested for their high CBD content. Hemp primarily comes from the sativa species because it contains low levels of THC.

Marijuana refers to cannabis plants containing greater than 0.3% THC. The Indica and Ruderalis strains all have too much THC to qualify as hemp under US law, and are the primary plants used for medicinal and recreational marijuana.

The terms “hemp” and “marijuana” do not officially represent any specific species or strain of plant but are terms we have adopted into our culture. Think of these as slang terms differentiating one specific characteristic of these plants – in general, marijuana gets you high, whereas hemp does not.

Now that you understand these differences, let’s talk about the component we came here to learn about: CBD, and explain the differences between CBD and THC.
CBD is short for Cannabidiol, which is one of the largest components of the hemp plant. The highest concentrations are in the aerial parts of the plant with the stem and seeds having very little to none. We can find CBD in other plants, but it is most abundant in hemp. The hemp plant has been grown for thousands of years, and it is quite a diversified plant.

When we discuss “cannabinoid,” we are using it as a term used to describe a related group of compounds found in the hemp plant, and CBD is the most abundant of those compounds. There are over 100 different kinds of cannabinoids in the hemp plant and each one has its own unique effects on the ECS. The cannabinoid content in hemp makes it unique when compared to the marijuana plant:

- Cannabis is legal when it contains less than 0.3% THC and is legal to purchase in the United States.
- Cannabis is illegal when it contains more than 0.3% THC, which the FDA considers a controlled

substance. Many states allow dispensaries for marijuana and it is available without a prescription.

- Both THC and CBD are psychoactive (meaning they can affect the mind and behavior), but only THC can intoxicate and create a "high."
- CBD oil refers to all components of the hemp plant. In addition to the 100+ cannabinoids, you also have over 200 different kinds of terpenes and flavonoids which makes hemp a very diversified plant. This is what you buy when you go to the CBD store. All the components of the hemp plant are meant to work together, as nature intended it. We call this the "entourage effect" and will talk about it in more detail further in this chapter.
- All hemp has naturally occurring THC. The manufacturer must add an extra extraction process to remove the THC in order to produce a "THC free" product (aka broad spectrum)

The Differences Between CBD and THC

CBD and THC are like cousins with many similar attributes and functions, but with some critical differences:

- Both are psychoactive, effecting the mind and behavior, but THC can get you high and can be habit forming, and CBD will not.
    - The topic of addiction and marijuana can be controversial. I believe that THC is habit forming and represents the law of diminishing returns. Long term, habitual use causes the ECS to down regulate its normal production so more and more THC is

needed to create a similar sensation as when you first started taking it. This is not a critical topic to my book, so if you find yourself disagreeing with this last paragraph, we can still be friends. It will not affect the outcome of this book. Anecdotally, I do find myself leaning towards CBD products with THC rather than those without it, as they seem to be more effective.

- THC binds to receptors in the ECS and CBD does not. This is important because THC tends to overstimulate receptors in our ECS leading to negative side effects such as paranoia, anxiety and dependence.

In addition to its other qualities, the cannabis plant is also nutritionally dense, with over 400 components consisting of cannabinoids, flavonoids, and terpenes. It is an accepted notion that all parts of the plant work better together than apart, and this concept is called the "entourage effect." This is the basis for the different formulations of CBD that are available to the consumer.

CBD Formulations

When you purchase CBD in the store there are three different basic formulations:

- Full Spectrum: contains all parts of the plant plus trace amounts of THC (maximum amount of 0.3%)

- Broad Spectrum: contains all parts of the plant but does NOT contain THC
- Isolate: Contains CBD only

Although all the formulations contain CBD, it's important for a number of reasons to understand the difference so that you choose the product formulation that is right for you. Because full-spectrum contains trace amounts of THC, some people choose it because they believe (or are told) it may have more noticeable effects on things like anxiety and mood disorders. However, for people who are in jobs that require drug testing, it's important to weigh the risks of a potential positive test. Although it's highly unlikely it would happen with such small amounts, some companies have a zero-tolerance policy, and a positive test could result in negative implications, or at the very least, the stress over having to explain and prove what caused the positive test result.

Many people who choose the broad-spectrum formulation do so to avoid potential drug testing problems. There is some uncertainty about the difference between broad-spectrum and full-spectrum products in terms of efficacy. The debate centers on THC and if the legal amount makes any discernable difference in the therapeutic effect. For some people, it is not worth the potential risk to test positive. The anecdotal evidence, in this case, swings both ways without a clear victor in either category. As I mentioned previously, I find myself leaning toward full-spectrum CBD products, but ultimately which you choose is up to you and will also depend on your situation.

The isolate formulation has fewer uses but can be found in a prescription drug called Epidiolex, which we review in more detail in Chapter 5. Most manufacturers will also use the isolate in their gummies because it does not have any flavor to mask. The full and broad-spectrum formulations have a natural “plant-like” taste and is similar to licking a marijuana leaf. It is not an unpleasant flavor but is bitter and some do not prefer it. Most manufacturers have flavors they add to mask the bitterness, but it is a constant battle to get rid of the aftertaste. We are dealing with a plant product after all!

What Is CBD?

So, now that we’ve clarified the differences between CBD and THC, let’s talk specifically about CBD. What is CBD exactly and why is there so much hype around it? To help answer this, you also have to consider an earlier point I made, that there are over 100 unique kinds of CBD in the plant. Each of these forms of CBD has a slightly different effect on the body and helps to optimize our ECS. CBD works on the ECS like an orchestra conductor, keeping all parts of the body working in harmony to produce balance. CBD, directly and indirectly, affects certain cannabinoid receptors called CB1 and CB2. These receptors play a critical role in the body’s response to pain, inflammation, anxiety, and sleep. We will get into more detail about this in the next chapter, but it is important to understand that CBD does not work like an on and off switch similar to pain and inflammation relievers like Tylenol or Motrin. It works on a system in the body similar to how blood pressure medication works on our cardiovascular system.

CBD vs Hemp Seeds and Hemp Oil

When you look at the hemp plant, it matters where you extract the CBD. CBD is most plentiful in the leaves and buds (also known as the aerial parts), but not in the stalk or seeds. Hemp seeds and hemp oil are both very nutritious products as we see below, but they are not sources of CBD. The labeling of these products can be tricky because hemp seed and hemp oil manufacturers can make many claims similar to CBD. However, the CBD content is so low as to be negligible, so any effects felt would be from the other nutrients in the plant. Here are some of the benefits of hemp seeds and oil:

- **Hemp seeds:** rich in protein, fiber, and healthy fatty acids such as Omega-3 and Omega-6. They have antioxidant properties that may help reduce the symptoms of certain ailments and improve your overall health.
- **Hemp oil:** made from the seeds and may have trace amounts of THC and CBD but not enough to produce a therapeutic effect. This formulation is often used topically to help the skin stay healthy and reduce breakouts. It may have other benefits and help to resolve such conditions as psoriasis, dermatitis, and eczema (to name a few).

One of the best advantages of full-spectrum and broad-spectrum CBD products is you are getting all parts of the plant, which also includes flavonoids and terpenes. These additional components of the hemp plant make it unique

when compared to anything else and can provide key benefits above and beyond hemp seeds and oil.

- **Flavonoids**: a diverse group of phytonutrients which are substances found in almost all fruits and vegetables believed to have beneficial effects on our health. Flavonoids are part of the polyphenols family and have beneficial effects on the skin, blood sugar, and blood pressure regulation. They also have added benefits such as antioxidant, anti-inflammatory, and anti-carcinogenic properties. For example, the common belief that wine is healthy for the heart is because of the high content of flavonoids in the grapes. There are many effects that these flavonoids produce, and like CBD, we are still learning how they work in our bodies.
- **Terpenes:** natural compounds found in plants responsible for the plants' color, smell, and flavor. If you are familiar with essential oils, terpenes elicit a similar effect. Lavender oil, lemon oil, and peppermint oil are all examples of terpenes that have a variety of positive effects in the body. A more specific example would be D-limonene which has a fruity and citrusy smell and helps with anxiety, depression, and mood.

Hemp really is quite amazing! Hemp roots reach deep down in the soil to help hold everything together, reducing erosion and to make the plant stronger. Second, it produces high quantities of biomass from the roots and leaves that get absorbed back into the soil. Third, it is like a carbon factory and pulls all the impurities out of the soil,

which is why insecticides should not be used when growing these crops. Hemp is sturdy, grows fast, and is naturally resistant to pests and bugs, so there is little need to use chemicals when planting this crop.

When you add all this together, you can see why the effects of CBD are so varied and plentiful. Hopefully, you are starting to get the vision of how CBD can be a useful supplement for any diet. In the next chapter, we'll talk about many of the uses for CBD!

Sean's Summary:

1. Marijuana and Hemp are terms used to describe the Cannabis plant.
    a. Cannabis is legal when it contains less than 0.3% THC.
    b. Hemp naturally has a high CBD/low THC concentration. THC is the chemical responsible for causing the "high" sensation.
    c. Cannabis is illegal when it contains over 0.3% THC and is categorized as a controlled substance by the FDA (its availability by prescription varies by state).
    d. Marijuana naturally has a high THC/low CBD concentration.
2. CBD is short for Cannabidiol and is one of the largest components of the hemp plant.
    a. CBD comes from the leaves and buds from the hemp plant. You will also see this labeled as the "aerial parts" on some labels.
3. CBD oil refers to what you normally find at your local CBD store. CBD oil refers to all the various components of the hemp plant which consists of over 100 different kinds of

cannabinoids and over 200 various terpenes and flavonoids.

   a. CBD is the most plentiful of cannabinoids but each one has different effects on the body.
   b. THC naturally occurs in every hemp plant. In order to receive a THC free product, the manufacturer must go thru an extra step to remove it from the hemp plant.

4. There are 3 kinds of CBD you can buy in the store:
   a. Full-spectrum: all components of the hemp plant plus a maximum amount of 0.3% THC.
   b. Broad-spectrum: all components of the hemp plant without the THC.
   c. CBD isolate: only CBD without all other components of the plants or other forms of CBD.
5. Hemp also contains over 100 unique forms of CBD, along with flavonoids, terpenes, minerals, and amino acids.

Chapter 3. Common Uses For CBD

When you look up CBD, or talk to your friends and family, the laundry list of superlatives never seems to end. I could write an entire book just on the things that CBD can do. Those of you with a cynical mindset may sit back and poke holes in any argument touting the benefits of CBD oil. I've always believed it to be an intellectual fallacy to always taking the "prove it" side of an argument. It is always much more difficult to prove something new and different than to just stay in the status quo. The placebo mindset is real, and believing that something will work is just as important as it is working. I would encourage the nay-sayers to ask questions and expect intelligent answers. We are on the early side of a steep learning curve about this naturopathic therapy, so sometimes CBD is a moving target. Information changes rapidly and we have so much to learn about the endocannabinoid system (ECS) because of all the years of prohibition and persecution of hemp and cannabis. Keep an open mind about the results that people experience on this supplement. It is not for everyone, and I do not claim it to be. We know that our bodies have an ECS (which I will discuss in depth next chapter), and that CBD does something to it. Is the effect strong enough for us to feel something? Is it effective enough to make a difference in our health? All I can say so far, is it depends, and it takes time. I recommend that you give yourself and your body at least 2-3 months to determine how well CBD works for you.

Many of my customers darken my door because they are desperate. Desperate because they have cancer, because they are in constant pain and may be addicted to opioids, because they are anxious, and because they can't sleep. But you don't have to be at the edge of your sanity to try CBD. It works best as preventative therapy in a similar way as taking your vitamins and getting good sleep. If you come to me and the nerve pain you are experiencing is at a 9 or 10, then it is difficult to have the patience to fine tune the correct dose. But it is fair to expect a reduction in that pain number, but the amount varies widely per person. My hope is that you will feel a noticeable decrease in your pain number. We'll talk more about expectations and how to dose later in the book.

I will be discussing in depth the effects of CBD on the immune system and on pain and opioid addiction in later chapters. But I wanted to take some time to address many areas where CBD may have a positive effect on your health. CBD is not a panacea, and if anyone sells it to you as such, then walk away, quickly. I've heard some amazing stories from my customers, some even miraculous. But to expect the same for every person would be presumptuous. Some conditions are more related to the ECS than others. And we have no way to measure how effective our own ECS is operating. Without any clinical benchmarks and waypoints, there can be little in the way of a sure thing with this therapy.

Take your blood pressure, for instance. When you go to the doctor and find that you have high blood pressure, we know that your cardiovascular system is not working properly. It is something we cannot see or feel (sometimes) but is something we can discreetly measure.

With a little more insight and testing, we can determine what exactly is wrong and how to fix it. You get a prescription for a medication that helps to reverse this effect along with changes in your diet and, usually, exercise. But we have no such luxury with CBD, so we have to be careful and measured when taking this supplement. Some people have a severely depressed ECS and will feel immediate results. Most people, me included, will take some time to achieve maximum benefit.

Keeping this long preamble in the forefront of your mind, let's look closely at some of the potential benefits and claims that you may or may not have heard about CBD. From personal experience and from my customers, I find most questions center around 5 or 6 issues such as: pain relief, anxiety and depression, acne, oncology, and neuroprotective effects. Let's look at each one a little more closely.

<u>Pain relief:</u>

- CBD has been shown to activate TRPV1 receptors which trigger counteractive measures to reduce pain and injuries. These receptors are also found in the bladder, lungs and in our ears, which may help modulate the progression of cystitis, asthma, and hearing loss.
- Decreases the metabolism of FAAH (more on this later) which is responsible for deactivating our own internal cannabinoids (anandamide and 2-AG). The result is an optimization of our ECS which is at the heart of CBD's most potent effects.
- Reduces the transmission of pain receptors.

- Reduction in the glutamatergic system, which is responsible for lessening pain in migraines and neuralgia.
- Reduces hyperalgesia (abnormally heightened sensitivity to pain) by inhibition of calcitonin gene-related peptide and reducing Substance P.
- Enhances effectiveness of adenosine which is a critical component to decreasing inflammation.
- CBC (3rd most prevalent cannabinoid in hemp) has shown to have anti-inflammatory effects.
- Terpenes such as myrcene and b-caryophyllene show additional pain-relieving effects and reduce inflammation.
- Flavonoids such as apigenin and cannflavin may assist with multiple sclerosis (MS), rheumatoid arthritis, and inflammation (30x stronger than aspirin).

<u>Anxiety and depression:</u>

- Enhances 5-HT 1a activity (increases serotonin, which is known as “the happy chemical”)
- Reduces acute increases in heart rate and blood pressure.
- Enhances CB1 receptor activity in the brain which increases anandamide effects and reduces stress.
- Helps to reduce recollection of fearful memories (also useful with PTSD).

<u>Acne:</u>

- Inhibits sebum production and has anti-inflammatory effects on oil-producing glands.
- Reduces excess cell growth in psoriasis.
- Reduction in itchy and dry skin.
- Reduces acne triggers.
- Activation of TRPV4 receptors which inhibits sebocytes from producing excess oils.
- Increase in adenosine levels leads to a decrease in inflammation.

<u>Cancer:</u>

- *NOTE: There is no evidence that CBD can cure cancer, so let's get that out there first. I'm not peddling false hope*. Some people claim that CBD has cured them, but until we get confirmed clinical trials, all the evidence will be anecdotal. That said, CBD may assist with a number of aspects of your body's ability to fight cancer and its side effects (pain, nausea).
- Inhibits tumor cell growth and cancer cell migration.
- Slowed tumor cell growth, reduced tumor cell invasion, and induce tumor cell death in pancreatic cancer.
- Increase in cell death and makes glioblastoma cells more sensitive to radiation therapy.
- May reduce the spread of colon cancer cells.
- Reduction of anti-tumor effects in gliomas.
- THC and other cannabinoids may stimulate the appetite (especially CBG).

- Stimulation of CB2 receptors reduces inflammation throughout the body.
- May inhibit the tumor necrosis factor, which is a similar method to prescription drugs Humira, Enbrel, and Remicade.

Neuroprotective:

- Reduced short term brain damage during hypoxia-ischemia (a condition most commonly caused by stroke or heart attack)
- Reduces damage to the brain and nervous system and encourages growth of new brain cells.
- Neuroprotective effects in Alzheimer's Disease (protects brain cells)
- Increases neuroplasticity (capacity of the brain to adapt and change in result to trauma or stress).

Sleep:

- May reduce cortisol levels at night which is a factor in causing nighttime awakenings.
- CBD reduces pain and anxiety which can have a negative effect on the quality of sleep
- The ECS plays a role in regulating circadian rhythms as it seeks to keep the body in homeostasis
- Improves quality of REM sleep
- Positive modulation of the sleep-wake cycle (promotes wakefulness during the daytime and relaxation at night.
- Increase in adenosine leads to an increase in wakefulness

Post-Traumatic Stress Disorder (PTSD):

A quick word about PTSD. PTSD is characterized by poor adaptation to a traumatic experience and is estimated to affect approximately 10% of people at some point in their life. The disorder manifests itself at different levels such as sleep disturbances, changes in cognition, decreased mood, emotional instability, and reduced social skills. This is quite the menagerie of symptoms, which is why CBD has such potential in this area!

The ECS plays an important role in the regulation of emotional behavior, especially those related to potentially traumatic experiences. The ECS has been observed to play a role in memory consolidation and retrieval. By activating CB1 and CB2 receptors throughout the body, CBD can have a positive impact on how we feel, decrease anxiety, and promote positive memories. The cannabinoids in the hemp plant play a critical role in PTSD by preventing the recall of traumatic memories and dreams.

Research has showed that many people who suffer with PTSD have very low levels of anandamide. Anandamide is one of our essential internal cannabinoids and has an important role in helping reduce anxiety and fear in addition to promoting feelings of pleasure or satisfaction.

These are all critical areas for people who suffer with PTSD, so while CBD may not cure PTSD all by itself, it helps to increase the ability of our natural resources to recover from this trauma.

I realize that the list above is quite the cornucopia of potential remedies, but that's the beauty of it. CBD

impacts an entire bodily system and has receptors all over the body. To fully understand CBD and how it works for all these things, the next chapter about the Endocannabinoid System (ECS) is vitally important. It is also my favorite subject and I am so excited to share it with you.

Chapter 4. The Endocannabinoid System (ECS)

Ah yes, the Endocannabinoid System (ECS). This is where the rubber meets the road, where we learn the basics of what helps our body stay healthy, where we see this complicated symphony in action powered by our own endocannabinoids…. well, I'm getting carried away a bit here because I am excited! It is these kinds of chapters that got me into pharmacy school, which carried me through the drudgery of the interminable study days and all-night cramming sessions. I love understanding how things work in our body. It is just the way God made me. If you like being informed and knowing how your medications work, then this chapter is for you. If you are curious about all the hype, look no further than the ECS. If you want to know how CBD imparts its effects on your body, this is the place to get started.

The 12th Body System

The discovery of the ECS is somewhat new, with cannabinoid receptors having been described first in the 1980s, as scientists were trying to better understand how THC affects the body. The more we learn about our own ECS, the more we realize we do not know. But it is exciting to be at the beginning of the learning curve as we study the 12th system in our body. Yep, you can compare the ECS to other more well-known system such as the digestive, pulmonary, or endocrine systems. If we gauge

the importance of the ECS by the number of receptors in the body, then it is VERY important. It has receptors located through your entire body in your nerve cells, organs, and immune system. The challenge this presents is there is not one symptom or response that we can isolate for how CBD works. The ECS is intertwined throughout our entire body, which makes it difficult to narrow the effects down to one action.

Most of what we have learned with scientific study is through pre-clinical trials, which are studies conducted on animals. And fortunately, the anecdotal evidence and limited human clinical trials seem to point in the same direction. So, let us enjoy that we are out in front on this one. We should appreciate that science hasn't had 100 years to slice and dice this topic into the tiniest little snippets or factoids. *What's fascinating is that there are some mechanisms of action unique to the ECS that we find nowhere else in the body*.

The Function of the ECS and Cannabinoids

Let's break down the ECS into its more functional parts to help us better understand what it does. The primary function of the ECS, above all else, is to keep our body in a state of homeostasis, which is defined as a state of internal balance. The ECS uses chemical messengers called neurotransmitters (which are specific to the endocannabinoid system, and therefore also known as endocannabinoids), to bring about this effect). The body produces two main endocannabinoids called anandamide and 2-AG (arachidonoylglycerol), which are crucial components for the effects of CBD, as we'll learn more about.

Below is a picture of the synaptic cleft which is the place where the neurotransmitters (cannabinoids) are released and exert their effect. Think of the postsynaptic neuron as the lock and anandamide and 2-AG are the keys to release the power of the ECS.

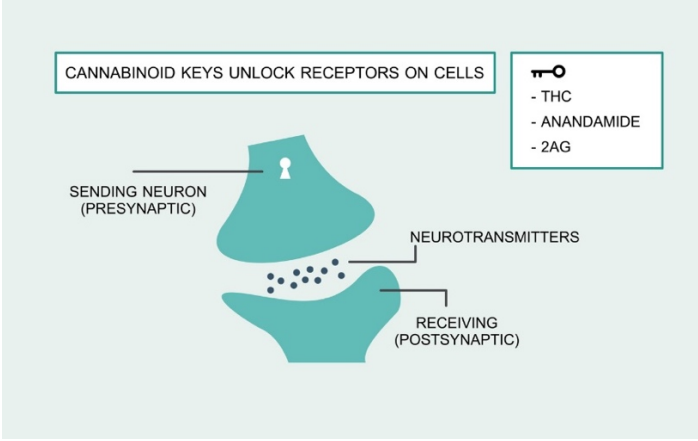


Figure: The synaptic cleft.

You will often see anandamide referred to as the "bliss molecule." This molecule works throughout the ECS to affect our appetite and memory, plus it is responsible for the "runners high" we experience after intense workouts. In contrast, 2-AG has close relations to our emotional state, contentment, and cardiovascular system. These two endocannabinoids have very powerful and important roles in keeping the body in homeostasis, and impact everything from memory to pain control to immune system function to sleep regulation. And many more!

The Cannabinoid Receptors: CB1 and CB2

It is important to understand that neurotransmitters need somewhere to exert their influence. With the ECS, their home is a group of cannabinoid receptors called CB1 and CB2. We mostly find CB1 receptors in the brain (this is important in terms of why CBD can influence mental acuity, mood, and sleep), and CB2 receptors in the nerve cells and immune system (this is important in terms of why CBD can influence pain control, inflammation, immune function, and relaxation). These receptors sit on the walls of the cells of our body, waiting for anandamide and 2-AG to come along and tell them what to do. The functions of these cells vary depending upon their location in the body and by their expected results. The ECS acts more like a complicated series of switches and levers that all work in unison to bring the body to homeostasis.

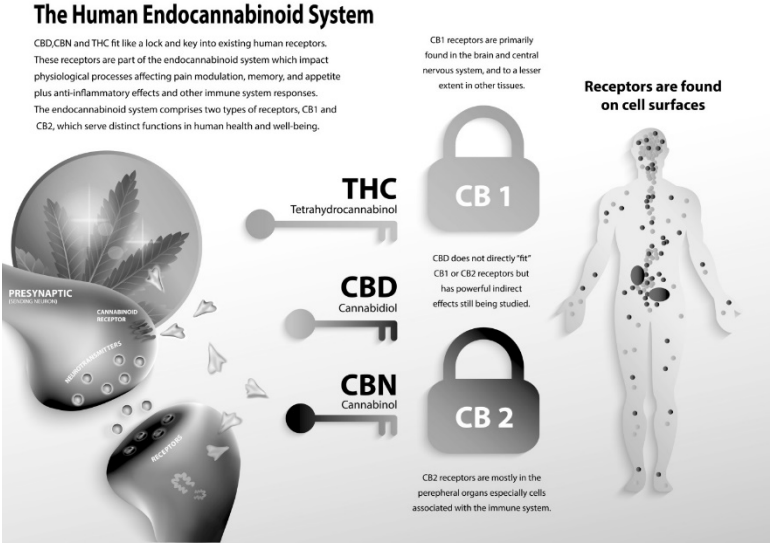


Figure: How the endocannabinoid system works, and where CB1 and CB2 receptors are found.

Let's bring this full circle and talk about how the body creates and uses these chemicals that communicate in our brain and throughout the body. We have entire systems in our body devoted to controlling when and where to make these endocannabinoids. The endocannabinoids themselves are made from fat-like molecules. They are used "on demand" and then quickly neutralized. To accomplish this, there are enzymes whose only job in the body is to quickly breakdown anandamide and 2-AG so they don't over-exert their influence on our body. The main enzyme that breaks down anandamide is FAAH (fatty acid amide hydrolase), and the enzyme MAGL (monoacylglycerol acid lipase) breaks down 2-AG.

How CBD Impacts and Influences the ECS

So where does CBD oil come into play? Well, one of CBD's most powerful effects is to delay FAAH and MAGL from deactivating, or metabolizing, anandamide and 2-AG. The result is an increase in the number of those neurotransmitters in our body, which leads to additional activation of the ECS, (which is significant!). It allows the endocannabinoids that are already naturally present in the body to work longer to exert their influence and bring balance back to our bodies. Think of it as giving the ECS and your body a boost so that it can work more effectively.

To review in a more simplified format:

- The worker bees: the messengers, anandamide, and 2-AG, which do all the dirty work.
- The gatekeepers: CB1 and CB2 receptors, which sit on the cell and wait until activated by anandamide and 2-AG.

- The clean-up crew: these bees snap into action as soon as we reach the desired effect in the cells. These guys are super cool and only go by their initials, FAAH and MAGL.
- The Queen Bee: our ECS, which directs everyone where to go and what to do to bring peace to the hive, er, body.
- The Bee Keeper: this is CBD, which exerts its effect by calming down FAAH and MAGL by allowing your cannabinoid messengers of andandamide and 2-AG to exert their effect for a longer period of time, boosting their impact on your body.

CBD vs THC

Another interesting fact about CBD is that it counteracts the psychoactive effects of THC, which create the "high" associated with marijuana use. CBD affects the CB1 and CB2 receptors in a way that makes it difficult for THC to bind to the cell. We call this "allosteric modulation" which is a fancy way of saying that it changes the CB1 and CB2 receptors enough to interrupt the ability of THC to work in our body.

Think of THC like an undercover agent to our ECS. It is sneaky because it appears to work the same as our own endocannabinoids, but in reality, it is more like a false prophet. THC forms a bond with our CB1 receptors, and does not let go. To complicate things, FAAH cannot metabolize it. So the THC creates an unnatural state in our body which leads to many of its side effects (getting "high"). CBD helps to prevent this unholy union, which reduces the negative side effects often associated with THC. Because of this, some people take CBD when using

medical marijuana, to help downplay the psychoactive effects of the marijuana.

CBD's Impact on Other Non-Cannabinoid Receptors

We now know that the major way CBD exerts its effect is to slow the metabolism of our own endocannabinoids. But there is more to CBD than just one effect. There are other receptors affected by CBD that help to explain the wide-ranging effects that we see and hear about from CBD users. These other receptors include the following:

Serotonin receptors: CBD has a direct influence on activating serotonin receptors. This is a similar mechanism of action as prescription medications such as Zoloft, Prozac, and Lexapro. We associate serotonin with such positive effects as improving mood, anxiety, and depression. In addition, activation of the 5-HT1A serotonin receptor is associated with effects on sleep, pain perception, nausea, and addiction.

Vanilloid receptors: CBD binds to TRPV1 (transient receptor potential vanilloid) receptors which have effects on pain perception and inflammation. Some of you may be familiar with capsaicin, which is a component of chili peppers and works similarly. It is often used in topical creams (Capsaicin-P) for arthritis and muscle aches.

GPR receptors (G-protein coupled receptors): are also called "orphan receptors" because they do not belong to one class in particular. CBD seems to be an antagonist of these receptors, which may have an influence in reducing bone loss and reducing cancer cell growth.

Adenosine metabolism: Part of the reason for CBD's positive effect on inflammation and pain is because it increases the amount of adenosine in our body. Adenosine plays an important role in cardiovascular health and reduces inflammation.

GABA metabolism- CBD modulates GABA receptors that have cells throughout the brain and nervous system which regulates communication between the brain cells. An increase in GABA reduces fear, anxiety, and produces a calming effect in your body.

Sean's Summary:

1. The Endocannabinoid System, or ECS, is the 12^{th} system in the body which helps to explain its wide-ranging effects. It is comparable to other bodily systems such as the pulmonary, digestive, and endocrine systems.
2. The ECS uses chemical messengers called neurotransmitters to exert its effect to promote homeostasis in the body. Homeostasis can be defined as a state of internal balance inside our body.
    a. These neurotransmitters (endocannabinoids) are produced by our body and are called Anandamide and 2-AG.
3. Our endocannabinoids work on receptors called CB1 and CB2.
    a. CB1 receptors are mainly located in the brain.
    b. CB2 receptors are strewn throughout the body and are found in all nerve cells, organs, and the immune system.

4. The final part of the ECS are the enzymes that metabolize the endocannabinoids once the appropriate effect is exerted. The main enzyme is called FAAH or Fatty Acid Amide Hydrolase.
    a. CBD inhibits this enzyme from breaking down the existing Anandamide and 2-AG that is present in the body resulting in more potent and longer lasting ECS effects.
    b. CBD also affects other receptors in the body in addition to inhibiting FAAH. These receptors have such effects as reducing pain, decreasing anxiety, decreasing inflammation, and reducing cancer cell proliferation.

Chapter 5. Potential Side Effects and Drug Interactions With CBD

Whenever you start taking a new prescription drug, over-the-counter medication, or supplement, two potential considerations to think about are (1) whether it might have any kind of side effects and/or (2) whether it might have any interaction with other drugs, medications, or supplements you are already taking.

Side effects and drug interactions are sensitive and difficult subjects in the pharmacy profession, but are of crucial importance. They are areas where pharmacists have significant experience and knowledge, but also pose a lot of challenges. Some of the difficulties are due to the large number of people who are taking multiple medications at the same time. Things get even more challenging when it comes to over-the-counter (OTC) medications and supplements, because of the lack of clinical data to guide us. They often don't think of non-prescription medications as important or potentially dangerous because they don't require a prescription. And yet, they can indeed have side effects or potential interactions with other substances we might be taking. I can't stress enough how important it is to disclose any and all medications and supplements you are taking when you discuss them with your healthcare provider and your pharmacist!

The good news is, I can speak with confidence when discussing both side effects and the potential drug interactions with CBD because of the work done with a prescription version called Epidiolex. The manufacturer performed clinical trials on the drug, which have provided us with a treasure trove of information we can use for our discussion. Kind of like stealing from the rich and giving to the poor! I don't claim to be Robin Hood, but if you take any prescription medication(s) then this chapter is a must-read for you. I'll provide the riches and you reap the benefit.

First though, let me address side effects for a moment. We've all seen the TV ads for various prescription medications, and while the images show happy people living their best lives thanks to the medication they are now taking, the narrator quickly rattles off a host of often times serious and frightening potential side effects. In many cases, these are quite serious and are of utmost importance to know. In other cases, the chances of a patient experiencing these side effects are incredibly low, and are listed and mentioned as a "cya" (cover your a**) legal tactic to protect companies from potential lawsuits. In the case of CBD, the good news is that side effects are very dose dependent (meaning you'd have to take a ridiculously large amount of CBD product to prompt any of these side effects), and it's highly unlikely that anyone using CBD oil is going to experience these kinds of reactions. But it's also important to know that unwanted side effects do happen, so knowing what they might be, and warning you about it, is part of my obligation to you!

So, in the first part of this chapter, we will inspect Epidiolex, which is an FDA approved prescription form of

CBD isolate. Epidiolex has an indication to treat rare seizures in children and was approved in June 2018. We will look at the clinical work done on this drug, which gives us more insight into the positive effects and potential negative side effects of CBD.

In the second part of this chapter, I will discuss how the body metabolizes CBD in the liver. Once we understand how CBD activates certain enzymes, then we will look at potential drug interactions that are often related to these enzymes.

The Role of the FDA

Let's recap what we know, or don't know, in regard to CBD and the Food and Drug Administration (FDA). The FDA is the main governing body for approving prescription and OTC medications. The FDA has a reputation as the "Watchdog of the World" for its rigorous standards. They have the highest requirements of any country before approving medications for any disease state. As of this writing, the FDA has not approved CBD to treat any diseases, conditions, or symptoms. But that hasn't impacted the CBD market. Even though insufficient clinical data exists in the eyes of the FDA to approve it for anything, the CBD craze has caught America by storm and has forced the FDA to play catch-up.

The response by the FDA so far has been to sanction manufacturers who make (clinically) unfounded claims in regards to CBD. The reason for this approach is the FDA does not want people taking OTC medications, such as CBD, to treat medical conditions without enough clinical data to support these claims. The FDA feels, and rightly so,

that people should not delay their access to prescriptions or OTC medications that have the approval to treat a certain set of symptoms. Basically, the FDA is trying to prevent unscrupulous manufacturers from making unfounded claims about their products. The FDA does a great job of protecting the public from harmful substances by ensuring that a rigorous testing process is in place and that manufacturers have to jump through certain hoops before their product is approved. The FDA is known for moving slowly and methodically and are in no rush to wield their power in the CBD marketplace.

This push and pull with the homeopathic industry has always been in our culture but has gained more momentum with CBD. Unfortunately, our government has yet to weigh in on such crucial CBD matters as dosing, growing, and manufacturing. Without any formal FDA approval, you are unlikely to see any OTC homeopathic medication such as CBD embraced by the medical community. In my experience, I am an exception to that rule, primarily because of my own experience using CBD, as well as the exhaustive research I have performed to educate myself about CBD and the ECS.

What We Have Learned From the FDA Approved CBD Prescription Drug, Epidiolex:

Epidiolex is an FDA-approved prescription drug indicated to treat seizures associated with Lennox-Gestaut Syndrome or Dravet Syndrome in children. For an example of how this drug is changing the lives of children, type this link in your browser to read their stories: https://www.epidiolex.com/patient-stories. What I am most interested in are the studies that were conducted to

bring this drug to market. I'll discuss what we can glean from these reports shortly.

Before moving on, let me take a few sentences to explain the key differences between Epidiolex and the bottle of CBD you most commonly find at your local store. The vast majority of CBD sold today is "broad-spectrum" or "full-spectrum." Full-spectrum we know must contain 0.3% THC or less to be legal for OTC status in the USA and broad-spectrum has zero THC. Epidiolex fits in neither category as it is the rarely used form of CBD isolate. You might wonder why, for a prescription drug, they chose to use the isolate formulation, and that is a great question! The two biggest reasons are that the isolate is easier to refine which makes it easier to produce The full and broad-spectrum products have many other components that are difficult to measure and quantify and would make the manufacturing and quantification of ingredients complicated. The other reason is the isolate allows for a higher maximum dosage, which makes it safer for children who are the primary patient group for this drug. As mentioned before, CBD is the main component of the hemp plant that works on our ECS, and the testing and trials done on this drug showed that it is effective for the relief and control of seizures in children with these diseases.

Side Effects of Epidiolex (CBD Isolate)

The most common side effects of Epidiolex listed are sleepiness, decreased appetite, increase in liver enzymes, sleep disturbances, and infections. GW Pharmaceuticals (GWP) is the manufacturer of this medication and they conducted clinical trials on this CBD formulation before

launching it as a prescription medication in 2016. These trials showed that CBD has many beneficial effects (such as decreased anxiety, pain relief and improved sleep), but GWP's primary focus for the drug is on epilepsy and seizures in children, so they did nothing more to shed light in these other areas of potential benefit. You see, when you are conducting a clinical trial, it is typically completely focused on the disease or symptoms you are trying to target with your medication.

When talking about Epidiolex, GWP states some uncertainty with understanding the process with how CBD works, but their clinical trials proved to the FDA that their CBD isolate helps patients with epilepsy. GWP found that when they added Epidiolex to an existing anti-seizure drug regimen, the side effects to the medications decreased and the patients experienced a reduction in seizures. Research shows that CBD can reduce the immune cell response and anti-inflammatory effects which can be key factors when dealing with seizures. This refrain of "We know what drug X does but are not sure how" is not all that uncommon with prescription drugs.

Some theories postulated by the manufacturer about how CBD helps reduce seizure activity include:

- **Neuronal inhibition** – quiets down the nerve cells that often fire off in seizures.
- **Modulation of intracellular calcium** – helps keep the body balanced. Cellular stress responses often involve the elevation of cytosolic (or cellular) calcium levels, so CBD may help reduce the severity of damage through maintaining homeostasis in the cells.

- **Decreasing metabolism of adenosine levels** – adenosine is an inhibitory neurotransmitter that may help stabilize neurons during a seizure and stabilize our emotions.

As noted at the beginning of this chapter, side effects with CBD (and most medications) are dose-dependent. The stated guidelines for dosing of Epidiolex are high, which makes sense from the listed side effects in the drug's accompanying product literature. How high is the dosing, you might ask? Well, the recommended daily dose of Epidiolex is about 20-30 times higher than what you would normally see in most adults using an OTC CBD product. Remember, there is no set dosing chart for OTC CBD, but most adults land between 1-2 mg of CBD/10 pounds of body weight, and Epidiolex dosing is typically 40-50 mg/10 pounds of body weight. For example, a 160-pound adult would start somewhere between 16-32 mg/day of OTC CBD, and on Epidiolex he/she could take 720 mg/day. That is a significant difference and is critical when considering side effects. This is a common problem with OTC products and is seen with aspirin and its ability to thin your blood even at a low dose of 81 mg/day. A common medication like acetaminophen (Tylenol) can be toxic to the liver if taking over 6 of the extra-strength tablets per day. My point here is that taking the correct medication at a reasonable dosage is the key to success for any therapy, and it is absolutely essential with CBD.

The product insert for Epidiolex mentions elevated liver enzymes as one of the major potential side effects. We know that CBD/Epidiolex goes through extensive metabolism by the liver, so it is reasonable to look for signs of damage to this organ with such high doses given

of the prescription medication. Fatigue, drowsiness, and sleep disturbances are also more significant when compared to a placebo or control group in the trial.

Liver enzyme metabolism of CBD and potential drug interactions

Why are liver enzymes important? That is a great question, because when you ingest any kind of medication, it has to be metabolized (meaning it is used up and then deactivated once used) by your liver. There are specific enzymes in the liver that metabolize different drugs and medications. GWP found that CBD is metabolized by liver enzymes CYP3A4 (very common) and CYP2C19 (less common). CBD does not seem to have a strong affinity for these enzymes, which could be excellent news for future drug interactions. However, if you are taking prescription medications that are also metabolized by the same enzymes (and we'll talk about those in a minute), then we need to be cautious.

GWP also observed increased levels of drugs such as theophylline, caffeine, bupropion, diflunisal, propofol, fenofibrate, diazepam, clobazam, gemfibrozil, lorazepam, morphine, phenytoin, and lamotrigine when these medications were taken with Epidiolex. So, Epidiolex appears to increase the potency of the medications listed above, and therefore the manufacturer recommended reducing the dosage of any of these medications if a patient is on Epidiolex.

It is also very important to discuss CBD and potential drug interactions with your physician. Taking CBD is a team effort and everyone needs to be involved to get the best

out of this potential therapy. Each patient responds uniquely to the effects of CBD, and may report different effects in their body. This article is not a definitive guide or a recommendation that should in any manner supplant the advice of your medical provider. If I listed a medication on the drug interaction spreadsheet as a candidate for a drug interaction, it means there is a *potential* for adverse reactions but doesn't mean there is or will be one. It does mean that it's important to recognize there is a possibility and may be worth a discussion with your physician or pharmacist.

Let's get back to our liver and how it works on drugs and medications. When CBD is ingested and absorbed, the liver goes to work to detoxify the drug and protect against any unforeseen damages it could cause to the body. When you consume a medication like CBD, it occupies the enzymes CYP3A4 and CYP2C19 in the liver and reduces their effectiveness for other processes. In essence, CBD may reduce the body's ability to deactivate other medications that use these same enzymes. As a result, if you take any medications that require metabolism by those same enzymes, you may quickly experience higher potency levels of those other drugs (perhaps even toxic levels) and unknown side effects with your prescription medications.

This reduction in metabolism of a drug may not always be a negative thing, as we observe with THC. As we described before, CBD appears to reduce the impact of THC on the body and brain. The reason CBD reduces the "high" normally observed with THC is that it prevents THC from being metabolized to its active metabolite (11-OH-THC). It is a little-known fact to those outside the industry that THC itself does not cause an altered state. The drug testers of

the world are aware of this nuance and only test for 11-OH-THC which we will learn more about in Chapter 6. This is an interesting phenomenon because sometimes when our liver metabolizes a drug it is changed into an active or more active form of the drug (e.g.- Claritin, Allopurinol, Codeine, and Propranolol). In this situation, a medication like CBD would decrease the potency of such medications because less of the active metabolite means a decrease in the effect. While there are plenty of examples of active metabolites, the liver's pivotal role in our body is to deactivate medications.

These effects are also dose dependent. The more CBD you take, the harder your liver has to work to deactivate it (meaning more of those enzymes are occupied dealing with the CBD), and the higher the possibility for adverse effects with other medications. But what is considered a high dose (and thus a risky dose in terms of potential drug interactions) when it comes to CBD? When doses start to increase to over 500 mg/day, then I think we are in the realm of higher risk.

Another rule of thumb to help you on this journey is that if your prescription medication states a warning to not take it with grapefruit juice, then it's best for you to avoid CBD (or if you are set on taking CBD, talk to your physician to see if there is a comparable medication you can take that is not impacted by grapefruit juice). Why is this the case? Because grapefruit juice activates similar enzymes to CBD, so their interactions will be very similar in terms of keeping other drugs from being metabolized properly. There also has been some data from additional studies that suggest CBD may activate certain other liver enzymes and enhance their effectiveness, which would lead to

drugs being metabolized more quickly rather than more slowly (resulting in decreased potency). We still have a lot to learn in this area of drug interactions, so I recommend a cautious approach. In particular, approach such categories as blood thinners, anti-depressants, anti-rejection, and anti-seizure medications with caution.

Finally, there is another potential type of interaction to consider. Some prescription drugs may have a stronger affinity for liver enzymes than CBD (meaning they would get “priority” of the enzymes to break them down before moving on to the CBD). This could potentially cause your CBD levels to increase and stay elevated for a period of time, and potentially lead to you experiencing some of the CBD side effects described earlier. This level of detail is best handled by your pharmacist or physician and is one of the major reasons I recommend starting at a low dose with CBD, and making sure that you discuss with your physician or pharmacist any and all prescription or OTC medications that you are taking.

I have provided a chart in the Appendix which shows the liver enzymes most affected by CBD. Next to this column are the most common prescription medications affected by similar liver enzymes. I also included common drugs that the liver metabolizes into a more active form. I recommend talking with a healthcare professional first (your doctor or pharmacist) if you find one of your medications on the list or if you just want to be sure there will not be any problems. You may also reach out to me directly through my website for additional help. Taking CBD should be a team effort and I can help to provide you with many of the tools necessary to determine if CBD is right for you.

Common Prodrugs (drugs that are more potent after being metabolized by the liver): allopurinol, enalapril, famcyclovir, gabapentin, nabumetone, omeprazole, simvastatin, codeine, diazepam, morphine, prednisone, verapamil, digoxin, buspirone, ciprofloxacin, and erythromycin. This information is also found in the Appendix.

Sean's Summary:

1. Prescription drug Epidiolex is a CBD isolate used for pediatric seizures and provides us with very useful data and clinical trials to gain more insight into CBD.
    a. Epidiolex is dosed much higher than OTC CBD because of the isolate formulation so we see more side effects with Epidiolex such as elevated liver enzymes, drowsiness, infections, and sleep disturbances.
3. CBD is metabolized through the CYP450 pathway and mainly affects enzymes CYP3A4 and CYP2C19. This pathway affects thousands of drugs in addition to CBD. We discuss other prescription medications that are affected by these same enzymes to look for potential drug interactions (see Table 1 in Chapter 5).
4. CBD effects will vary depending on the person and the drug.
    a. Drugs that are deactivated by the liver may see an increase in potency when given with CBD. This would result in more of the prescription drug in our body for longer periods than normal.

   b. Drugs that are metabolized into their active metabolite will see a decrease in potency when compared to normal.
   c. It is also possible if a prescription drug has a stronger affinity for the same liver enzymes as CBD that we could see an increase in potency and side effects with CBD.
5. I have provided charts in the appendix which list prescription drugs commonly metabolized by the enzymes affected by CBD as well as medications that are metabolized into their more active form.

Chapter 6. Drug Testing: Differentiating CBD From THC

CBD has taken the US by storm. We estimate total sales in 2019 at $800 million and Nielsen has forecasted it to hit $6 billion by 2025. This market is on the cusp of exploding all across America! As CBD becomes more main-stream and gets wider exposure, some questions become more prevalent than others. Right near the top of that list is "*will CBD cause me to fail a drug test?*" This is a great question and for good reason! CBD comes from the hemp plant and is part of the Cannabis family (same as marijuana). We know that to be legal in the United States, the hemp plant must contain less than 0.3% THC. We will get to what that means later but to answer your question, yes, with certain formulations of CBD, you may be taking something with very small quantities of THC. It's not enough to get you high or give you a buzz, but you are consuming a substance that is monitored by drug tests. There are formulations of CBD that go the extra step to remove the THC (similar method to how you remove caffeine from coffee beans) and that reduces your risk. **SPOILER ALERT: No matter which form of CBD you take, a positive drug test is always a possibility.**

So why should you continue to read this chapter if I have given you the big reveal? Well, sometimes it is good to work your way backward from a problem, like a heist

movie that draws you into the penultimate scene, then takes the rest of the movie explaining the back story. There are important details to understand regarding CBD and THC that will help you make an educated decision. There are steps you can take to reduce the risk of a positive test, and some actions that are essential otherwise you are at a high risk to fail a drug test.

Hemp vs Marijuana: What's the Difference?

Let's start by differentiating between hemp and marijuana. We did this a bit in the ECS chapter, but for drug testing discussions, it's worth reiterating. Drug tests do not check for CBD because they are only interested in THC, or more specifically, its derivative 11-OH-THC. This is an important distinction that you must understand: you will not fail a drug test for taking CBD. The key focus of the drug test is to measure for the metabolite of THC which is what creates the impairment of senses described as getting "high."

Important distinctions that I mention below are the psychoactive effects of THC and CBD. The definition of psychoactive is "affecting the mind." Under this definition, I would define both phytocannabinoids as "psychoactive," which can be confusing. The distinction is that THC causes a mind-altering state and impairs our senses which would affect our ability to function normally and say, drive a car. Some people think CBD will cause a similar action because it belongs to the Cannabis family, but it simply is not true. CBD works differently inside our body and brain and does not cause a high sensation.

Hemp:

- The largest product is CBD oil
- To be legal, it must contain 0.3% or less of THC and typically has higher amounts of CBD
- Grown for agricultural products such as food, clothing, and textiles.
- CBD does not cause you to feel "high"

Marijuana:

- Largest product is THC oil
- Contains 15%-20% THC and lower amounts of CBD
- Grown for its ability to cause a "high" sensation and mind-altering effects when smoked/ingested

THC and CBD: What's the Difference?

These two plants, hemp and marijuana, are similar to each other. After all, they are both members of the *Cannabis sativa* family. CBD and THC are also incredibly similar – but there are very important differences! If you look at the molecular structures shown in the figure below (I know, it's chemistry) you see how closely related CBD and THC are to each other:

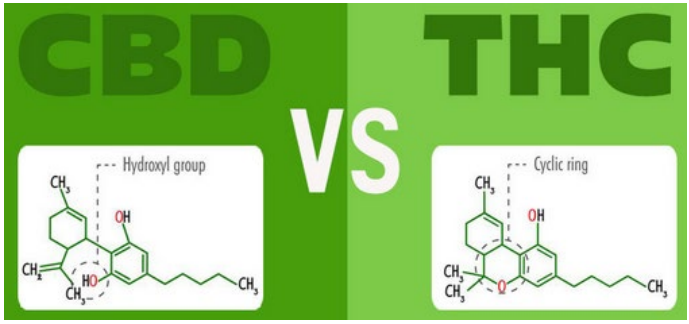


Figure. Molecular structure of CBD vs THC

It is the same basic molecular structure but with the slight differences highlighted in the picture. This makes sense, right? CBD and THC come from the same plant family, same plant species, and they even look similar at the molecular level, but the difference in their effects on the body and brain is the *pièce de résistance*. This difference, though minute, plays a huge role in how they interact with our ECS and why drug tests look for THC and not CBD. The psychoactive part of THC is the fork in the road for these two molecules: THC causes sensory impairment and CBD does not. Hard to believe that such a tiny variance in their structure can lead to such a massive difference in their function! You do not have to be a chemistry major to appreciate the subtlety and brilliance of these two molecules.

How solubility and absorption affect CBD and THC levels

Most substances like drugs and vitamins for example are either water soluble or fat soluble. The solubility characteristics determine how fast your body absorbs a drug or compound and how quickly it works. Since the body is over 60% water and your brain/internal organs are nearly 80%, it makes sense that water-soluble drugs are most easily and quickly used by the body.

CBD and THC are both fat soluble. What this means is that these substances can be dissolved in fats and stored in fatty tissues in the body. This fat solubility also affects the way and the speed with which the body absorbs and metabolizes these substances, because it also means they tend to be used more slowly than water soluble substances. Now do not go thinking fat-soluble

compounds are not as good or are bad because of this. They are equally effective but act at a different pace. Therefore, it is important to monitor and measure how much you take since fat-soluble substances are slower to absorb, and that means that toxicity is more common (this is the case with fat-soluble vitamins such as A, D, E, and K). The body has a hard time breaking down and excreting fat-soluble substances. What ends up happening is that the extra fat-soluble drugs or vitamins that your liver does not metabolize are stored in fat cells throughout your body. Again, this is not necessarily a terrible thing, but these substances will slowly get reabsorbed into the bloodstream and if not monitored, can result in higher levels than desired. THC follows a similar path where anything not immediately used can be stored in your fat cells, and released into your system down the road. So in the case of THC and drug testing, these fat-solubility properties may not work so well in your favor. You can test positive for THC long after taking it.

This biological process described above is the principal reason drug tests can detect THC consumption that occurred over 1 month ago. We definitely do not see that with alcohol (which is water-soluble)! This is a quandary for the drug testing industry, especially if conducting a field sobriety test for driving impaired on marijuana. It is difficult to get an exact picture of the amount consumed and time elapsed since the last ingestion of THC.

All of this leads to more questions like; how much CBD can one consume and not build up a detectable amount of THC? What forms of CBD are least likely to cause a positive result on a drug test? Can any or all CBD make me test

positive? These are all significant questions that we will try to answer as we dig deeper into the chapter.

Can CBD make me test positive for THC (marijuana)?

The quick answer is most likely no. It is highly unlikely, but because of hemp's close familial relationship with the marijuana plant, you will always get some THC in your product, even though it may be a microscopic amount. Even those manufacturers that claim that their CBD contains 0% THC are not 100% free of this substance. The labs have a limited ability to test for products below a certain threshold so we can say a product is virtually free of THC but cannot say it has absolutely none. This may seem like I am splitting hairs, but I just want to inform what is in your CBD and what is not, because drug testing is a very important consideration for people who want to use CBD products. The best way to ensure a negative test is to eliminate as many cannabinoids as possible and use the CBD isolate formulation. A potential problem even with the isolate can crop up when drug testing agencies use an older form of technology called gas-chromatography. This method uses an additional substance, called a reagent, to help identify the drugs it is testing. Sometimes this reagent improperly identifies CBD as THC which leads to a positive test. CBD users have successfully challenged this false positive but obviously this process can be stressful and worrisome.

The bigger question at stake here is do you know how much THC is in your CBD? It sounds like a silly question, I know, but it is not as easy as you think. Mislabeled CBD products have proliferated as they have flooded the marketplace with get-rich-quick investors and

manufacturers who do not have our best interests at heart. For example, a 2017 study in JAMA found that *18 of 84 CBD products purchased online had THC levels high enough to cause impairment or intoxication*. That is an alarming number and represents a whopping 21% of manufacturers who could put your livelihood, not to mention your safety, at risk! Some users have tested positive when consuming the 0% THC version, which tells us most likely you are dealing with a tainted product. Some tests have reported a positive result because of the cannabinoid CBN, which is also present in the hemp plant. Most of this information is anecdotal and not proven in a research laboratory with proper testing procedures.

"It's caveat emptor," said Barry Sample, Ph.D., senior director of science and technology for employer solutions at the nation's biggest drug testing company, Quest Diagnostics. "The actual issue is how (well) do you trust the labeling?"

Any CBD product you buy should have a *certificate of analysis* (COA) for each batch produced by the manufacturer. If you are using a full-spectrum product (one that contains THC) you should read this document to confirm how much you are consuming. For example, if you have chosen a 30 ml bottle of 1000 mg CBD you should have 3 mg of THC (or 0.1 mg per dose) in your bottle if it is at the 0.3% THC legal threshold.

The best way to confirm the accuracy of what is in your CBD product is by looking up the COA. Most of these are available by scanning a QR code on the label of the bottle (if you are looking at a product and it does not have a QR

code or any way to access a COA, I would recommend you NOT purchase that product). The COA is important to assure you are getting what you pay for, and so that you know what is actually in the product. In addition, quality CBD manufacturers should be using a state-regulated testing lab. Look for the image below on your COA, which signifies an ISO certified lab, and is considered the gold standard in the laboratory testing industry.

Granted, this label and certificate look-up requires a little extra work for you, as the consumer, to make sure you are getting what the product says on the label, but it will be worth it. I will be discussing this topic at length in Chapter 9, with step by step instructions on how to look up your product's analysis information. In the meantime, let's get back to our focus in this chapter.

Drug testing

THC is the #1 reason a worker fails a drug test and 2.3% of all drug tests came back positive for cannabis use in 2018.

If you've never been subject to a drug test, the testing process is straightforward. The first phase (for most) is a urine test where you give a urine sample, and they measure it for anything more than a trace amount of THC's active metabolite. A trace amount is 50 billionths of a gram per milliliter or 50 ng/ml, so we are talking minute amounts! What's important is for you to know your company's policies on drug testing and how strict those

policies are. Some companies, if you fail the initial test for any reason, will take immediate action that could lead to termination, especially if they have a strict zero tolerance policy. Other employers will go a step further and conduct a more detailed assay to decide what exactly is in the urine that caused the failed test. During this 2nd round of testing is where you may have an opportunity to explain that your CBD product is the reason you tested positive, and some employers will take that into account (and obviously, others will not). So if you are employed by a company that requires drug testing, it may be best to speak to your Human Resources or Legal department about their policies before embarking on your CBD journey. Views on CBD usage are starting to change but it is, and will continue to be, a slow process. This drug was illegal just a few short years ago, so be encouraged by how quickly we have progressed! I think that eventually there will be more refined testing for marijuana, THC, and CBD, because the market demands it.

Let's get back to doses and chances of a failed test. I am not telling you this to scare you, but simply to make the point that a failed test is a potential possibility. However, the chances of it are very small. How small, you might ask? Well, at a daily dose of 0.3% THC in a bottle of 160 mg CBD, which is a very large dose for most people, you would consume 0.5 mg of THC. It is estimated that this (relatively) insignificant amount would cause a failed drug test less than 0.2% of the time. Those are tiny odds! And 99% of people will never see a dose this high.

Another lab states that a 2000 mg dose of CBD may potentially cross this 50 ng/ml threshold for THC, but again, this dose is way above anything I would recommend

or that any reasonable consumer would take. It just is unnecessary for most people and CBD's effectiveness declines the larger dose you take. We will learn more about this biphasic property in the Dosing Chapter. But my point is that most people would never take enough full-spectrum CBD to ingest enough THC to cause a failed test. And, it's imperative to know exactly what % of THC is in a product you want to take.

Therefore, we must focus on quality when choosing the right manufacturers. You have the right to know what you are ingesting and what is on the label. The FDA has done very little to enforce this point, so that really leaves us on our own, but you have a friend here to help you navigate this minefield! You can check out my website www.awakentocbd.com for product reviews and links to manufacturers that you can trust. And as noted above, we'll talk about looking up product analysis certificates in Chapter 9.

In conclusion, your chances of testing positive are possible, but small if you are taking the 0.3% version of CBD. High doses over lengthy periods of time can accumulate THC in your body and possibly lead to a positive result, but such high doses are not likely at therapeutic dose ranges, and would be unlikely to be consumed if you are following an appropriate dosing regimen. If you are at an employer or in a profession that does random drug testing, then it is best to find out their status on CBD products. If a negative test means loss of employment, then I'd strongly recommend one consider using the CBD isolate version of this product, which does not have any other cannabinoids or THC.

As of the publication of this book, the military has just approved the use of CBD for its members. This is huge news and a great encouragement to me and hopefully will set the bar for other companies to follow suit. There is not a greater group of people who could benefit from this product than those that serve in the military.

Sean's Summary:

1. Because of CBD's relation to the hemp plant, a positive drug test is always a possibility.
2. Lower your risk factors by understanding the various types of CBD and make sure you know what is in your product.
    a. Full spectrum has up to 0.3% THC and broad-spectrum has 0% THC.
    b. Drug tests only monitor for the active metabolite of THC, which creates a high effect. They do not test or try to detect how much CBD is in your body.
    c. CBD and THC are very similar structurally, which is the major reason for caution. Both are psychoactive in that they affect how we act and think, but only THC can create impairment and a "high" feeling.
4. THC and CBD are fat-soluble substances. This means our body stores these substances longer, which can cause THC to be released by your fat cells later, which on very rare occasions can lead to failed drug testing months down the road.
5. There is a lot of tainted product out there, and that is the primary cause of failed drug tests.
    a. Make sure your manufacturer has a certificate of analysis for your product. This tells you everything in the bottle and the amount of THC (important to verify).

   b. Also, double-check that the lab performing the tests is ISO-certified.
6. If you take 160 mg/day of a 0.3% THC full-spectrum product, it is estimated you would fail a drug test 0.2% of the time. These odds are very low, but not zero, and results can vary because of how your body metabolizes THC.
7. If you are concerned about testing positive, then taking a 0% THC product (broad-spectrum or isolate) is the most prudent way to go.
8. If you are employed by a company that mandates drug testing, it's best to check with them on their policies on drug testing, if they are zero tolerance, and if they have any rules or recommendations on CBD products. For example, at my company, we do not perform "random" drug tests unless there is cause. If an employee is showing impairment at the job, we can request that a drug test be performed. With CBD being legalized, we changed the wording that testing positive for THC is not an automatic termination (it was in the past). Not all companies are this progressive but I think you will start to see this sort of delineation from more employers in the future.

Chapter 7. CBD and the Immune System

The Coronavirus COVID-19 has thrust us into the stormy seas of uncertainty the likes of which we have not seen in over 100 years. The last time we had a similarly widespread virus pandemic, it was called the Spanish Flu, also known as the 1918 Flu Pandemic, which was unusually lethal and unique to that day and age (and so far, until today as well!). Lasting from January 1918 to December 1920, it infected 500 million people which was about 30% of the world's population and was fatal to approximately 50 million (that's a 10% mortality rate, crazy!). One reason that mortality was so high was a lack of vaccines and antibiotics to treat secondary infections (e.g., pneumonia), both of which we have in our arsenal today. With the onset of the COVID-19 in 2020, society has been thrust back into uncertain times. Governments across the world have resorted to Draconian measures to stem the tide of this novel virus. Measures such as social distancing and stay at home orders have become commonplace. But there is more that we can do to help our own cause, especially taking better care of ourselves and strengthening our immune system. To be at optimal health, we need to be more aware of what we eat, keep our weight at healthy levels, exercise regularly, take Vitamin D, and increase antioxidants in our diet. One of the unique ways we can take care of our immune system is to add a healthy dose of CBD to our diet. But what advantage does this give us? Does CBD help with a coronavirus like COVID-19? Can CBD prevent or help manage viral infections or even the common cold? These

are some great questions to get us started! The findings we dig up may just surprise you and hopefully will encourage you.

Before we get into the fun stuff, let's have a little primer on the immune system.

Immune system: the basics

We all have heard about the immune system, but do know exactly what it does and how it does it? To put it simply, the immune system protects our body against foreign invaders and keeps us healthy. It is a collection of structures and processes whose function is to protect against disease or other unwanted foreign bodies.

To understand how CBD works with the immune system, let's first talk about how the body identifies and eliminates potential pathogens. This process is critical to determine how quickly we recover from any viral or bacterial infections. The sooner the body's immune system can successfully identify, tag, destroy, and eliminate these foreign antigens, the sooner it gets back to normal or a state of homeostasis. There is a delicate balance in the body, and the Endocannabinoid System tries to help maintain that balance as the body oversees the immune system's function. If the body cannot or does not recognize certain harmful antigens, we can develop severe conditions such as cancer or allergies. And sometimes the immune system malfunctions and goes into hyper-drive and tags our own cells as foreign antibodies, which leads to autoimmune disorders such as Hashimoto's, rheumatoid arthritis, multiple sclerosis, or Crohn's disease. So keeping the immune system in balance and

functioning properly is crucial for it to do what it does best: get rid of foreign invaders.

Generally, there are two different mechanisms by which the human body seeks and destroys these foreign intruders.

1. **Cell-mediated immunity**: This involves the use of T-cells, which are a kind of white blood cell. T-cells are a part of our immune defense system and are important for cellular immunity and activation of immune cells to fight an infection. Once activated, these T-cells rapidly multiply and secrete signaling molecules called cytokines that regulate the immune system and inflammation. They control and shape the immune response, so think of them as police officers that control the traffic, telling everyone where to go.
2. **Humoral immunity**: This includes B-cells which are responsible for producing antibodies that identify and attach themselves to a specific foreign invader to make it easier for the immune system to seek and destroy that invader. These B-cells also are a type of white blood cell just like the T-cells. Think of the B-cells as the undercover agents of the immune system, identifying the bad guys and tagging them for elimination.

To review, we have our cell-mediated immunity known as T-cells and humoral (body fluids) immunity known as B-cells. Hopefully, this overview did not turn you away! Now it's time for a dive of similar depth into CBD which will help us see why this phytocannabinoid (plant-derived version of CBD) is so useful for our body and overall health.

How CBD affects the immune system

As you may remember, we noted earlier that the primary location for cannabinoid receptor CB2 is in the immune system. This makes sense because the ECS is invested in keeping us healthy and balanced, and most of that starts in the immune system. However, this is also where the relationship between the ECS and CBD can get complicated.

The cool thing about CBD is that it has multiple effects, sometimes seeming at odds with itself. If you have done any research, you know that it suppresses the immune system to reduce pain and swelling (and if you did not know, now you do). Your body accomplishes this through inhibition of the CB2 receptors which plays a key role in regulating the inflammatory immune response. The ability of CBD to decrease swelling and inflammation is central to its most consistent, reliable effect of managing pain. So you may ask yourself, (go ahead….ask!), how can something that decreases my immune system help me stay healthy? How can CBD possibly help me combat the common cold or protect against such sinister pathogens as Covid-19? Well, I'm not going to just tell you! Read on to find out why….

One of the fundamental ways that CBD affects the immune system is by suppressing T-cell function. Pre-clinical trials (animal-based) have shown that CBD reduces the cell-surface expression of the cytokines interleukin-2 (IL-2) and interferon-y. IL-2 regulates the activity of white blood cells (leukocytes, lymphocytes) that are responsible for immunity. Interferon-y functions as a primary activator for macrophages (hunter cells) and plays a role in the

production of natural killer cells and neutrophils (the most plentiful of white blood cells and first to arrive when infection occurs). CBD also decreases Interleukin-8 which is a kind of B-cell that helps induce neutrophils to the site of infection or invasion. Now, you may be wondering how this is a good thing, because you'd think that inhibiting these things would be counter-productive. But bear with me! The reason we are discussing these details is to see the interrelation of all these components in the immune system. A primary method by which the body protects itself and limits the infection is by inducing swelling and isolating the injury. It is important to note that CBD does not inhibit this process but moderates it – and this is an important distinction. The goal of the ECS is to keep our body in a state of homeostasis, which means resolving infections as quickly as possible and getting back to a healthy state. This is important (as we'll talk about shortly).

CBD can also influence the immune system by inhibiting the reuptake of adenosine (or increase the amount of adenosine in the body) which reacts in a way to decrease inflammation, increase pain regulation and improve quality of sleep. When you add up all how CBD aids the immune system, you can see why it is easy to get excited about the potential of what CBD can do for us. This is a good thing because I promised to bring you new and promising information!

You can see here the evidence that CBD can moderate the immune system in some ways, and strengthen the immune system in others. This inhibitory effect we discussed a minute ago, explains how CBD oil may play an integral role in managing autoimmune disorders where

the body overreacts and starts attacking healthy cells in our body. As we mentioned before, what CBD does is slow the T-cell response to a perceived injury or foreign invader If CBD can help our own immune system have time to correctly identify what is foreign or what is not, the quicker the ECS can get us back to a proper state of health and balance.

A similar method has proven to be successful in some pre-clinical trials by helping the body identify and kill cancerous cells. In a way, CBD helps to accentuate the positive in the immune system and discourage the negative.

This ability for CBD to produce immune-enhancing and immune-modulating effects is related to its hermetic (biphasic) nature. CBD response may depend on such factors as CBD concentration, cell culture conditions, immune stimulation, and cellular activation. But CBD's ability to have different effects depending on the concentration is rare stuff. I won't say that it does not happen with any other drugs, but it is one of the distinguishing characteristics of CBD that makes it unique in the supplement world.

The figure below shows the biphasic nature of CBD pretty clearly. I was originally at the "low dose, low benefit" area of the graph when I started out on CBD. Once I increased my dose from 8 mg to 16 mg to 20 mg, I saw positive results and realized I had found that sweet spot. Therefore, when dosing CBD, you must pay close attention to how you are responding. There is no yellow brick road that everyone follows for the same results, but stick with me and I will get you there!

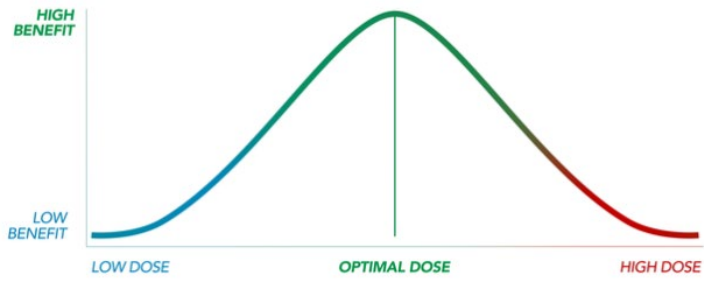


Figure. The biphasic nature of CBD dosing. Too little is not enough, and too much loses its effectiveness. Experimenting to find that optimal dose is key to success with CBD.

CBD has a unique property that enhances this bi-directional communication which is called *retrograde signaling*. To understand this concept, we need to perform a brief review. Neurotransmitters (except for 2-AG and Anandamide) always flow in one direction. From their point of release (presynaptic neuron) to their target (postsynaptic neuron) zone, it is always the same. But with the ECS, its messengers 2-AG and anandamide flow backward as the ECS seeks to bring the body back to homeostasis. To simplify, consider this: 2-AG and Anandamide are like firefighters, running into the burning building while everyone else is running out. The ECS wants to work its way back to the source of the injury rather than just to modify the side effects. It is another way that the ECS functions in a unique manner to help accomplish its goals.

This unique ability makes sense when we talk about CBD bringing our body back into homeostasis. When visualizing

the ECS, think of it like an orchestra rather than a single instrument, such as a trombone. When talking about the immune system, a more eloquent way to explain the effects of cannabinoids is they are bidirectional immunomodulators. This means when there is a hyper-immune (strong) response, CBD can down-regulate or ease our body's response to bring it back into balance. Alternatively, when the body is operating under normal conditions, CBD can help our immune system to function more efficiently. So it's interesting that CBD helps boost our immune system's response when we need it, or dampen its response when needed.

This is the crux of the issue and is why I think CBD is unique from any other homeopathic remedy. It is not a one-trick pony in the fashion of other medications because it affects an entire system in our body. The major goal of the system is to make us healthier and stronger, so why wouldn't we want to include something in our diet that enhances such positive effects? The potential is amazing, and I hope that you can glimpse it too! What's particularly exciting is that this is all fairly new information! We are just scratching the surface on discovering and understanding the role of the ECS in the body.

Let us bring this thing full circle. Does CBD help give you immunity versus Covid-19 or other viruses? No, it does not really help you develop immunity against a specific pathogen, but it does provide a positive effect in increasing the health of our immune system. Does it help your body's immune system react more readily to infections? Does it help you resist the common cold? Again, it is a yes and no answer. CBD does not give us immunity specifically, but will help our body respond more

readily to attacks by invading bacteria and viruses, and get us back to a healthy state quicker than normal.

Many people I talk to in my pharmacy come in seeking advice on how to treat a cold. The problem is, by the time they come in, it's too late, but I am consistent with my advice in these situations. Do whatever you can to boost your immune system so that you recover from your cold and do it as quickly as possible. I am a believer in taking whatever measures we can to keep our immune system strong. That includes preventative steps we can take to help us be safer from the coronavirus.

Do the obvious things like washing your hands and keep social distancing. Maybe you can start adding the not so obvious steps like getting good sleep, taking Vitamin D, exercise, increase antioxidants like Vitamin C (Emergen-C and Airborne are great options) and taking CBD. If you can start making pro-active decisions to improve your immune system, the greater chances you have of staying healthy. I would amend the popular colloquialism about apples to "a dropper a day keeps the doctor away."

Sean's Summary:
The function of the immune system is repelling foreign invaders and to keep us healthy.

1. CBD's role is to moderate or regulate the immune system response.
    a. Reduces swelling and inflammation by regulating the severity of the reaction by the immune system.
    b. It helps the body identify foreign invaders and increases immune system efficiency by

activating our natural response to kill these cells.

2. CBD's role is a balancing act to reduce swelling and pain, yet still helps the body heal more efficiently. It helps to keep in mind that CBD affects our ECS, whose principal function is to keep us in balance no matter where the receptors are located.
3. CBD also has been shown to increase adenosine levels in the body which helps to reduce inflammation and improve our quality of sleep (also very important for our healing).
4. CBD's effectiveness in our body is because of its biphasic nature. The challenge is to dose the medication at just the right balance for these positive effects to occur.
5. Retrograde signaling is a concept unique to the ECS.
    a. Retrograde means flowing in the opposite direction.
    b. Everywhere else in the body neurotransmitters such as 2-AG and Anandamide only flow in one direction
    c. This concept is important to the ECS because it can search for the source of trouble and work to stop it from getting worse rather than just responding to the injury.
6. Does CBD give immunity to Covid-19 or other seasonal colds? Not immunity exactly but it does help our immune system to work more efficiently and effectively.
        a. Control the factors you can to keep yourself healthy: eat well, manage your weight, take Vitamin C and D, exercise, wash your hands, and supplement with CBD

Chapter 8. The Opioid Epidemic: Can CBD Help?

Opioids are drugs that come from the opium poppy plant and act on receptors throughout your body. They are typically prescribed to relieve pain. These medications do not cure what is causing the pain but block your ability to feel it. Opioids are a class of narcotic drugs that includes morphine, heroin, fentanyl (e.g., Duragesic), oxycodone (e.g., Oxycontin), and hydrocodone (e.g., Norco and Vicodin). They also can become physically addictive, and this has contributed to a significant and growing problem. As you have likely heard, there is an opioid epidemic going on in the US. The mortality rate attributed to opioid addiction continues to climb and reached over 40,000 deaths in 2019. Drug overdose is now the #1 cause of accidental death in America and opioids are the biggest contributor, accounting for over 67% of these deaths. To give perspective, this trend mimics the flu death rate, which resulted in 34,000 deaths in the 2018-2019 season. Fortunately, CBD may be able to provide some relief!

Opioid Use vs Abuse

I am very well educated on this topic because opioid misuse and overuse are subjects that every pharmacist must be extremely knowledgeable about. Pharmacists are expected to maintain constant surveillance to track these medications and watch for proper and potentially improper usage. Most states have narcotic logs that help

us keep track of pain medications and observe proper usage between refills. Even with this online help, fighting the opioid crisis is an uphill battle.

On the flip side, often opioid use gets a bad rap. You see, opioids have a unique niche in the prescription drug world to help patients suffering from acute and chronic pain. Those of you who struggle with constant, untreatable pain know how difficult it can be. Chronic pain changes who we are, it alters personalities, how we eat, think, and sleep. In addition, as medical advances allow us to live longer, this longevity can come with a price, and that price can be conditions that leave a person suffering from some kind of pain, and seeking relief from it.

It's important to differentiate between use and misuse, because not everyone taking opioids is misusing them, even though there may be a physical dependence on the drug. As a pharmacist, my role is to step into this knowledge and perception gap and help people use medications in the correct manner to receive the relief that they need.

There does seem to be a tipping point where long-term use of opioids can develop into dependence on the medication. And unfortunately, for many years there was a lack of monitoring and very easy access to these drugs, which has now thrown gasoline on the fire that is the opioid epidemic. You can see the trend below showing that the death rate has ballooned since 2016. This epidemic has only increased since that data was published from 2017 and does not show any signs of slowing down.

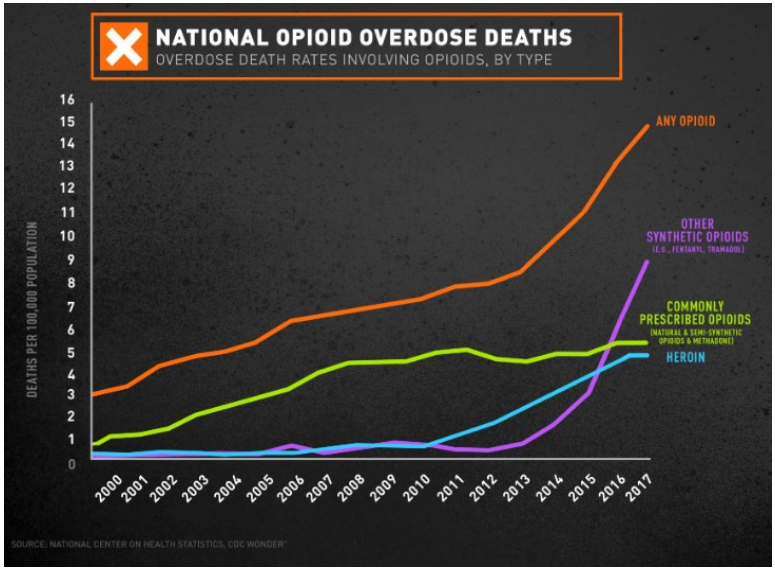


Figure 2. From "What Are Opioids?" https://www.thetruth.com/o/articles/what-are-opioids

Notable Statistics:

- In the US, 10.3 million people misused opioids in 2018, meaning they did not take them as intended or prescribed.
- 2 million of those people who misused them developed an opioid misuse disorder, which typically is characterized by a diagnosed addiction to the medication.
- Because prescription opioids are expensive and prescriptions can be limited in duration, many people who develop opioid addiction end up turning to black market or street opioids such as heroin to feed their addiction.

- 808,000 people used heroin in 2018 with it accounting for over 15,000 deaths.
- Over 32,000 deaths have been attributed to overdosing on synthetic opioids (non-methadone).

How Opioid Receptors Work

Now, time for the classroom portion common to my chapters; Yay! I know drug addiction and drug abuse is a heavy topic, but let's attempt to understand more about this addiction and the effects it has on our bodies, and where CBD might come in to play. It's one of the reasons I love talking about CBD because it has many different benefits for us.

We find opioid receptors in our brain, central nervous system, and in nerve cells throughout our body. We do produce our own opioids which act on these receptors to send signals to our brain that control feelings of pain and pleasure (reward). For example, endorphin is an opioid our body produces that elicits a natural pain killing response and makes us feel better. Opioids exert their pain-relieving effects through three opioid receptors: mu, delta and kappa. Our body's own opioid system is more complex and diverse than you might think as it not only controls pain but also reward and addictive behaviors. For example, the mu receptors are most closely related to the analgesic (pain relieving) and addictive properties with the synthetic opioid, morphine. These mu receptors also play a key role in mediating natural rewards (such as feelings of happiness and pleasure) and are thought to play a key role in infant attachment behavior. In another clinical study, mice that were bred to not have the delta opioid receptor suffered from increased levels of anxiety and depression. So, it is

not easy to put opioids in a single, negative light, as they have some very beneficial effects on the human body when properly used in appropriate doses for appropriate periods of time.

The problem with prescription opioids is that they are much more potent than the ones our body makes. Similar to what we see with THC, sometimes too much of a good thing leads to problems such as addiction, dependence, and tolerance. This is the problem with opioids that we ingest. They can be too much for our body to handle and are not meant to be a long-term solution. Too much mu receptor activation and stimulation can lead to dependence and addiction. In addition, over-stimulation is one factor that leads to other unwanted side effects such as constipation and difficulty breathing (due to opioid receptors in our GI tract and breathing centers). Suppression of breathing is particularly important because it is one of the side effects of opioids that results in overdose deaths.

Opioid therapy is meant to be short term and at the lowest dose possible to experience pain relief. The difference between a large dose and a lethal dose can be small and unpredictable. The variety of opioid receptors found in our body leads to pain relief in some areas, but dangerous side effects in others. For all its pomp and circumstance, opioid therapy often causes more problems than it solves. In addition, the longer one stays on the medication, the less effective it becomes, and requires higher doses to get the same effect. The respiratory side effects therefore can increase when this tolerance develops and more of the medication is taken to achieve the same level of pain relief.

Opioids affect nearly every single organ in the body because of the widespread nature of the receptors they bind to. Opioids can even affect the immune system and reduce its ability to fight infections. This high level of involvement throughout the body makes opioid misuse tough to battle.

The Role for CBD in Opioid Addiction and Dependence

This is where CBD enters our discussion. The encouraging news for us is that the ECS does not have receptors in our breathing centers. But the ECS does have the most prevalent receptors throughout the entire body and therefore can impose a wide variety of effects. CBD can activate the ECS and aid in the healing process from the negative actions caused by opioids. For example, CBD has natural anti-inflammatory effects which may help to reduce breathing spasms and lessen coughing or wheezing. It is not hard to see how these effects are beneficial to someone that is struggling with their breathing especially when related to conditions such as opioid overuse.

In the brain, the location of CB1 receptors and opioid (mu) receptors are very near each other. Multiple studies have found a two-way relationship exists between these receptors and the rewarding behavior and pain relief. The cool part is that CBD does not cause the “high” associated with opioid use, but provides pain relief and may lessen the addictive potential of opioids. It is like getting the best of both worlds!

Studies on CBD show it lowers overall health risk factors because of its positive effects on nausea, inflammation, and cerebral ischemia (a form of stroke).

When an individual abuses opioid medication to the point of dependency, it creates changes in their brain. CBD is able to change the way these damaged brain cells communicate with each other and even improves how they communicate. This phenomenon is called neuroplasticity which is the ability of the brain to compensate for injury, disease, and stress. The more plasticity we have, the more flexible we are in our thinking, which results in (yep, you guessed it) homeostasis.

Another potential benefit with CBD is the ability to reduce relapse when a patient is attempting to wean off or stop using opioids. There is evidence that CBD may help those with opioid abuse to reduce withdrawal symptoms such as the shakes, diarrhea, and teeth chattering. Another helpful mechanism of CBD is the positive effect on the cells that produce serotonin and dopamine (types of neurotransmitters). Our serotonin and dopamine receptors become damaged with chronic opioid overuse and lose their ability to work properly. CBD helps to reverse this trend, which helps to produce positive effects physically and in our mood.
Keep in mind when talking about the ECS that multiple levers and switches exist when trying to bring the body back into balance. CBD does not produce an all-or-nothing response in the ECS that produces instant results. Our body uses the ECS to nudge us back in the correct direction. CBD does not make us Superman so we do not feel any pain. It doesn't work like that. But if someone is

looking for multiple beneficial effects when trying to overcome addiction to opioids, CBD is an excellent place to start. Effects such as a decrease in pain, an improvement in mood, and reducing the high from opioids are all important factors that help in the physical and emotional healing from addiction. In addition, some pre-clinical animal studies have even shown that CBD can help decrease the desire for opioids. The bottom line is that CBD is worth trying because of the multi-faceted potential it has for helping with multiple aspects of opioid abuse and addiction.

Sean's Summary:

1. Drug overdose is now the #1 accidental cause of death in America, and opioids account for 67% of these deaths.
2. Opioids are a product of the opium plant and work on receptors in the brain to block the pain response in your body.
3. 20% of opioid users, or 2 million people, misused opioids in 2018.
    a. A steep increase in death rate started occurring in 2015 as the problem continues to worsen.
4. Opioids are notorious for causing breathing problems (respiratory depression)
    a. This problem worsens as tolerance develops and opioid doses increase.
5. CBD's ability to reduce inflammation and control muscle spasms is useful in treating the breathing struggles that occur with opioids.
6. Opioids affect nearly every single organ as well as the immune system.

   a. Our body does product its own opioids which aid in the moderation of how we feel pain.
   b. External opioids have a similar effect on pain but overstimulate these same receptors which leads to side effects such as constipation, dependence, and addiction.
7. CBD can help moderate addiction
   a. Increases serotonin and dopamine levels to help with a sense of well-being and alleviate anxiety.
   b. Both receptors can be damaged by excessive use of opioids
   c. Reduces the high, or the reward that is felt with opioids.
   d. Increases the ability of the brain to compensate for injury and disease by increasing the plasticity of brain cells. Plasticity means the ability to adapt to changes in the environment and maintain flexibility (helps to bring back into homeostasis)

Chapter 9. Taking CBD

If you have persisted this long and read through the book chronologically, congrats, we are finally getting to the good stuff! If you jumped ahead to get to read the finale, then no shame (well, maybe just a little, you impatient people you). But I hope you go back and read the preceding chapters, for both our sakes! This is where the rubber meets the road, where the quarterback throws the game-winning touchdown and where the gymnast sticks the perfect landing. Everything else has been leading up to this point and I am guessing some of you are still skeptical (and rightly so) and others are ready to jump into the deep end. I am a slow adopter myself, so I get those of you that like to take your time and explore all the angles. However, once I saw the light with CBD, I was all in. The potential benefits are just too great to ignore, and the risks are so small.

I'll give you an early warning, this is the longest chapter and the most complex of all the things I want to share with you. But I want to be clear about something very important before getting started: **this chapter is the only thing that stands between you and buying a potentially harmful product, or one with no CBD.** The FDA has yet to monitor this industry or provide any proper direction, so that leaves us to muddle through all the promises and false expectations that have flooded the market. The FDA has told manufacturers to stop making claims about their products that are not medically proven, but that is it. I mean, I appreciate the help brother, but seriously? How do we know how much to take, when to take it, maximum dosage, and whom to buy from? This book is your bulwark

against all the unscrupulous manufacturers out there who are looking to take advantage of your innocence and entrap your hard-earned money. But rest assured faithful reader, I will not let you fall into that trap! Once you are done reading this chapter, you will understand the pitfalls and find freedom in the CBD marketplace to find the best product that best fits your needs.

So, what is the game plan? Let us take a look at the following 6 points and see if we can make some sense of things.

1. Formulations.

When you start this process, you want to know the formulation (topical, sublingual, capsules, vaping, transdermal, etc) and what kind of CBD you will be taking (full spectrum, broad spectrum, or isolate). Here are some thoughts and considerations I suggest you make to help determine what will be best for you:

Topical: This means it is applied directly to the skin on the area that needs attention and is absorbed through the skin. Works best for yep, topical (localized) pain. It can help with issues such as arthritis and joint pain depending on the source, as well as muscle aches and strains. A surprising benefit may be for skin-cracked heels, dry skin, eczema, acne, and psoriasis, as the CBD oil also appears to have a healing or nourishing effect on those conditions.

Sublingual: This is the best absorbed and highest availability of any CBD (25-30% absorbed) that I recommend. It is also one of the most commonly used formulations. Sublingual means it is squirted into the

mouth and held and dissolved under the tongue, which allows it to be absorbed directly into the bloodstream, so it avoids metabolism by the liver. As a result, it works quickly but doesn't last as long as other formulations because of its faster absorption. Sublingual formulations work best for acute symptoms such as pain or anxiety.

Make sure to check the inactive ingredients, watching for the obvious additives that aren't healthy for you. But pay attention to the vehicle that is used to dissolve the CBD: usually it is medium chain triglyceride oil, which is a healthy fat. The biggest drawback of MCT oil is the potential for coconut allergies because many producers use coconut based MCT oil. If you are one of those people with a coconut allergy, then check the label and manufacturer information to find out if the MCT oil used is coconut oil based or not. Or you may wish to try another formulation (capsules or topical) that does not use MCT oil.

Capsules: Consuming a capsule may be easier or more convenient for some people than a sublingual formula, but the trade-off is that you will lose more of the drug to liver metabolism because the capsules are digested and metabolized by the liver. The long-acting benefit of capsules is due to slower absorption of the CBD as it works its way through your digestive system. Capsules are considered better for maintenance but can be more expensive and less efficient than sublingual formulations. You also have less flexibility in the amount of mg taken per day which may limit you in finding the "sweet spot" for your own CBD therapy.

Vaping: This one is a little controversial, but I want to discuss it. Vaping CBD has the highest absorption rate (30-40%) and the fastest effects. It may be useful for those suffering from acute symptoms such as anxiety and pain. However, I do not recommend this formulation because too many issues have cropped up lately with life-threatening side effects. To be fair, there are many manufacturers who make a quality product, but the risk for unwanted effects is still high. Without a more formal regulation process, I believe that it is not worth the risks. (#3a)

Transdermal: This is a newer technology that is slowly making its way into the CBD world. Transdermal (or absorption through the skin) patches are used for a number of pharmaceutical drugs for measured delivery. Patches offer a higher absorption rate than the capsules or the sublingual method. Patches are easy to use and there are some formulations that last up to 96 hours. This method is also safer than vaping but until the FDA steps in to help create guidelines for the manufacturers, you can't be certain that what you are getting is safe and effective. The cost tends to be much higher than other formulations and the dosages much lower. I have heard encouraging results with transdermal therapy, but I would like to see more clinical results and information about the dosing and effectiveness of transdermal CBD before making a strong recommendation about it.

Two more recent developments are liposomal and water-soluble formulations.

Liposomal: This is a drug formulation that contains the active drug in very tiny fat-like particles. They use this

technology throughout the pharmaceutical world when drugs are too large for the body to absorb. This formulation makes it easier and faster for the body to absorb and use. The manufacturers of these new liposomal CBD formulations claim a higher bioavailability and effectiveness, but because it is so new, there is not enough data for me to confidently back up this point of view. I will continue to monitor it though!

Water-soluble: This formulation is most often referred to as nano-emulsion, which makes the particles 100 times smaller than regular CBD oil. These nano-emulsified particles are so small they absorb directly into the bloodstream and result in a faster and higher peak of CBD in your body. The downside is that it the CBD is more quickly metabolized, and so people may not feel the same effect after 6-8 hours, which is when the regular oil hits its peak.

2. What kind of CBD should you take?

As mentioned before, the 3 main types are full-spectrum (contains up to .03% THC, a minute amount), broad-spectrum (contains CBD and other nutrients, but not THC), and isolate (contains only CBD and no THC or additional nutrients). Your key considerations are do you want THC or not (please take a look at the drug testing chapter for more in-depth discussion of this), and do you believe in the entourage effect (I do). There have not been enough pre-clinical or clinical trials to scientifically confirm whether THC is critical to making CBD work. My observations so far are that it can help its efficacy but isn't necessary for CBD to work.

Is the amount of THC in each dose of full-spectrum CBD enough to wake up the CB1 and CB2 receptors? It is hard to tell, but most evidence says that the 0.3% THC version may be more helpful for anxiety and social disorders. If job testing is not an issue, I would encourage you to try a couple of different formulations with and without the THC to compare effects. I have tried 4 distinct product lines and will share my results a little further down in this chapter.

CBD works best when taken regularly where you get the full range of effects for anxiety, pain, and sleep. It can be useful if only used for the occasional flare-up, but you are only harnessing a fraction of the power with this method.

3. Determine the dosage.

There are no formal guidelines issued by the FDA for dosing, and that will eventually change, but for now it is best to be conservative. There are not any hard limits recommended on the amount of CBD that a person should consume, but overall effectiveness is not linear with the dosage, in other words, more is not better, and there is a point of diminishing returns. Maximum recommendations are usually 3-4 times the starting dose, and most people do not see additional benefits beyond 100 mg/day. If the dose is too low or too high, you may find that CBD does not work well for you because of the bi-phasic nature of CBD that we talked about in Chapter 7 (see the Figure in Chapter 7 showing the dose and effect curve). You must find that sweet spot where you gain maximum effect from the minimum dosage.

Have a dose in mind when getting started so you can compare apples to apples. I like to go on a few sites that I

trust and compare prices and discounts. Just a little bit of research can go a long way!

You generally will be better off getting a higher strength tincture and cutting the dose down. To determine the dosage per dropper for the tincture, you divide the mg by ml in the bottle. Most bottles of CBD are 30 ml in volume, and the mg on the bottle represent total amount of CBD in the bottle. So here's how to calculate the dose if you have a 500 mg bottle containing 30 ml:

500 mg bottle divided by 30 ml (500/30) = 16.7 mg/ml: that is your dose!

A 1000 mg bottle would then equal 33mg per dose, and so on. So if I were taking the 16.7 mg dose, I would buy the 1000 mg bottle and take a half the dose (0.5 ml) and the bottle would last me twice as long as the 500 mg bottle at a cheaper price per dose.

I know, I know, it's math, but I promise to help you if needed! I do have a dosage chart at the back of the book in the Appendix, or you can visit my website at www.awakentocbd.com if you prefer to just click on numbers in a spreadsheet. These tools will help you figure out the ideal starting dose depending upon your weight and severity of symptoms.

I recommend "*micro-dosing*" to start, which helps to decrease potential side effects such as drowsiness, stomach upset, and vivid dreams. Everyone's ECS responds differently, so starting slow is essential to understanding how each person will respond to CBD. Do not be put off if you felt nothing at first, you aren't supposed to! I just

want to make sure you are not the 0.1% that responds poorly to CBD. Let us rule out the negative first before going to full adult dosing.

Micro-dosing implies starting at ½ the regular dose for at least 1-2 weeks and slowly increasing the dose up to a full recommended daily intake over the next 1-2 months. Doses over 33 mg/day should be divided up evenly throughout the day. I do not recommend taking at bedtime if you are naïve to therapy as this can increase the potential for the side effects I mentioned previously. CBD will help with your sleep regardless of when it is taken and will not make you drowsy during the day when taken at the right dose. It is not like some sleeping pill you take before bedtime. The uniqueness of CBD shows that it is time to change how you think about medications!

4. Know who you are buying from.

Since there has been no guidance from our government to set up purity standards or to regulate and manufacturing process, it is up to you and me to do a little research. Below are a few questions I suggest you look into when considering purchasing CBD oil from a company:

- What is the quality of their website? Is it easy to navigate and intuitive to follow? More sophisticated websites tend to show more thought and planning behind their product.
- Do they have a customer service number or a simple way to reach a representative?
- Read reviews on the company found in Google or Yelp or other online review sites. How is their customer service? How quickly do they respond

and how knowledgeable? Most companies that have been around for a while will have reviews and a history of customer service.

- Do their products list the amount of CBD on the bottle? This should be easy to find and understand. If they do not list the amount of CBD, do not purchase the product.
- Does the manufacturer make any health claims on the bottle or the website, suggesting it cures certain diseases? If so, stay away.
- Do they share information about their company or founders? Do they talk about why they got into the CBD business?

5. Look for information about where the hemp was grown and how was it cultivated.

Stick with hemp grown in the USA. We have superior cultivation standards and as we know, hemp absorbs all potential chemicals from the soil. The best manufacturers will list their affiliation and talk about how they grow their hemp.

When looking at cultivation techniques, make sure it is non-GMO (no pesticides) and whether they use best practices when growing their crops such as proper genetics for high CBD count, soil quality, and what you feed your hemp.

Look for affiliation with Hemp associations and confirmation that they follow state guidelines for growing their crops.

6. How was the CBD extracted?

This has been one of the hardest subjects for me to research. Everyone that has an opinion has an affiliation with a certain process it seems. Safety to the consumer what the strongest motivator in this category which led me to CO2 extraction as the preferred method.

CO2 extraction: The gold standard for extraction processes. CO2 extraction leaves no residue and is considered safest for consumption. Seen as safer than extraction that uses petroleum-based products such as propane and butane. It is the most expensive process because of large/complex machinery and has high labor costs.

- Positives: Low environmental impact, very safe and gives a clean end product. Extracts the good stuff like flavonoids and terpenes without the earthy-tasting chlorophyll.
- Negatives: Can extract contaminants from hemp if present which could be harmful. Expensive to purchase and to operate the machinery.

Ethanol extraction: Used primarily for full-spectrum products because the alcohol pulls away all components of the plant.

- Positives: seen as the best way to extract plant matter because it is soluble in fat- and water-soluble substances. Forms esters which make the CBD water-soluble and increase absorption.
- Negatives: Also extracts chlorophyll which can be bitter and earthy tasting. It also requires an extra step to remove the ethanol which can reduce the potency of CBD oil.

Propane/Butane extraction: Cannot manipulate through temp and pressure like CO2 but produces similar results. It's a cheaper technology to use (which increases profits for manufacturers) and gets faster extraction results while using less energy.

- Positives: Gas is seen as safe to prepare food. It does not extract water-soluble products like Chlorophyll.
- Negatives: It's difficult to work with because of a combustible nature. Concern about residue in the end product.

7. Confirm the Certificate of Analysis (COA).

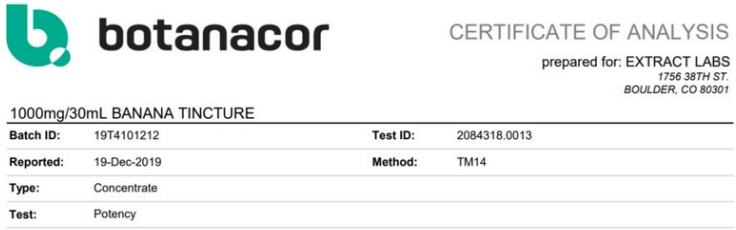
I know I'm throwing a lot at you in this chapter, but there is no easy way to make this omelet without breaking some eggs. I saved the best for last here, as the COA is critical to understanding what is in your product and what shouldn't be in your product. Since we are purchasing a by-product of a plant, especially one that pulls potential impurities out of the soil, (phytoremediation), it is vital we know if there are any contaminants or unwanted impurities and the amounts, as well as the amount of actual CBD in our product. This information should be contained on a COA.

I strongly recommend that you use a CBD product that provides a COA for every bottle or unit of product.

This information should be easy to find on the product website and the manufacturer should provide links to look up individual lot/batch numbers. You can also scan the QR code on the side of the package or bottle which contains

your CBD. The QR code is square, matrix kind of code that looks like a bunch of dots all connected together.

Date of Report: Some manufacturers only post occasional reports, but you should know what is in batch of the actual product you are taking, not what was in a batch that was manufactured 3 to 4 months ago. See the figure below, taken from a product COA from the company Botanacor (with permission). You should be able to see the date of the batch report for your product at the top left with "reported date."


botanacor

CERTIFICATE OF ANALYSIS

prepared for: EXTRACT LABS
1756 38TH ST.
BOULDER, CO 80301

1000mg/30mL BANANA TINCTURE

Batch ID:	19T4101212	**Test ID:**	2084318.0013
Reported:	19-Dec-2019	**Method:**	TM14
Type:	Concentrate		
Test:	Potency		

Accreditation: Now, not all COAs are equal. I recommend that you check to make sure the lab that is testing the product is independent and not part of the same company that made the CBD. The good ones are accredited by ISO (International Organization for Standardization) which means the lab meets specific standards is audited by a governing body. There are no regulations regarding how often CBD must be tested, so a company that posted a report from 2 years ago could say they are "lab-tested" (sneaky little buggers aren't they?). The information on the lab is normally at the bottom and should have an accreditation. The image below shows the accreditation logo at the bottom right corner.

FINAL APPROVAL

Daniel Weidensaul
19-Dec-2019
7:32 PM
PREPARED BY / DATE

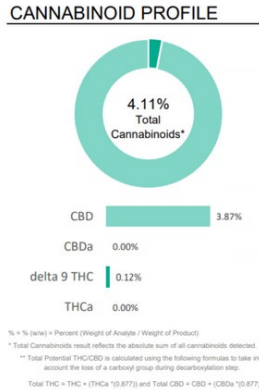
David Green
19-Dec-2019
8:59 PM
APPROVED BY / DATE

Testing results are based solely upon the sample submitted to Botanacor Laboratories, LLC, in the condition it was received. Botanacor Laboratories, LLC warrants that all analytical work is conducted professionally in accordance with all applicable standard laboratory practices using validated methods. Data was generated using an unbroken chain of comparison to NIST traceable Reference Standards and Certified Reference Materials. This report may not be reproduced, except in full, without the written approval of Botanacor Laboratories, LLC. ISO/IEC 17025:2005 Accredited A2LA Certificate Number 4329.02

ilac-MRA
A2LA ACCREDITED
Certificate #4329.02

Product Contents: Make sure you look for the amount of CBD in the product (seems obvious, but maybe it's not). The FDA considers a product misbranded if it delivers a nutrient at least 20% below or 20% above the value declared on the label. That is quite a difference in potency!! Make sure to at least take a quick gander at this number on the label and check out the THC content.

The report below shows the legal levels of THC and the total mg of CBD. In the example below regarding CBD, it is measured in mg/g, but you can convert 1 gram to 1ml to get an equivalent dose from a tincture (liquid oil) so you get the dose as we discussed in the dosing chapter. So, your product would have a minimum of 38.7 mg/ml. LOQ represents the smallest amount detectable by the lab's equipment. And you can see all the way to the left that the amount of delta 9 THC and Total Potential THC equals 0.12% which is under the legally allowable limit of 0.3%.



CANNABINOID PROFILE

% = % (w/w) = Percent (Weight of Analyte / Weight of Product)

* Total Cannabinoids result reflects the absolute sum of all cannabinoids detected.

** Total Potential THC/CBD is calculated using the following formulas to take into account the loss of a carboxyl group during decarboxylation step.

Total THC = THC + (THCa *(0.877)) and Total CBD = CBD + (CBDa *(0.877))

Compound	LOQ (%)	Result (%)	Result (mg/g)
Delta 9-Tetrahydrocannabinolic acid (THCA-A)	0.10	0.00	0.0
Delta 9-Tetrahydrocannabinol (Delta 9THC)	0.05	0.12	1.2
Cannabidiolic acid (CBDA)	0.07	0.00	0.0
Cannabidiol (CBD)	0.04	3.87	38.7
Delta 8-Tetrahydrocannabinol (Delta 8THC)	0.05	0.00	0.0
Cannabinolic Acid (CBNA)	0.13	0.00	0.0
Cannabinol (CBN)	0.06	0.00	0.0
Cannabigerolic acid (CBGA)	0.09	0.00	0.0
Cannabigerol (CBG)	0.05	0.00	0.0
Tetrahydrocannabivarinic Acid (THCVA)	0.08	0.00	0.0
Tetrahydrocannabivarin (THCV)	0.04	0.00	0.0
Cannabidivarinic Acid (CBDVA)	0.06	0.00	0.0
Cannabidivarin (CBDV)	0.03	0.00	0.0
Cannabichromenic Acid (CBCA)	0.07	0.00	0.0
Cannabichromene (CBC)	0.09	0.12	1.2
Total Cannabinoids		**4.11**	**41.10**
Total Potential THC**		0.12	1.20
Total Potential CBD**		3.87	38.70

NOTES:
N/A

Depending upon the extraction method, look for remnants of the solvent in the lab report and pesticides and soil impurities. The report should signify whether any products are out of range and might be harmful to you. They should monitor for bacteria and fungus, foreign matter, and heavy metals. The sample below shows specifics such as arsenic, cadmium, mercury, and lead. You can also look for the terms "heavy metals," "residual solvents" and "pesticides." The lab reports should give you a pass/fail rating to make it easy for you (see below).

25994-HM

Symbol	Metal	Conc.[1]	Units	MDL	Use Limits [2] All	Use Limits [2] Ingestion	Units	Status
As	Arsenic	ND	µg/kg	4	200	1500	µg/kg	PASS
Cd	Cadmium	1	µg/kg	1	200	500	µg/kg	PASS
Hg	Mercury	ND	µg/kg	2	100	1500	µg/kg	PASS
Pb	Lead	28	µg/kg	2	500	1000	µg/kg	PASS

1) ND = None detected to Lowest Limits of Detection (LLD)
2) MA Dept. of Public Health: Protocol for MMJ and MIPS, Exhibit 4(a) for all products.
3)USP exposure limits based on daily oral dosing of 1g of concentrate for a 110 lb person.

All this testing is just one factor in why you see such price differentiation between products. Most established manufacturers that have been around longer do things the right way, and you'll be able to confirm that, if you use the above criteria to monitor their claims.

8. Some other factors that are related to price and quality:

Although they can impact the price of the product you are looking at, I recommend you also look for the following aspects in a product, because they help to ensure good quality.

- Organically grown
- Extracted using the CO2 method
- Grown in the USA
- Tested for purity in 3rd party labs
- Company association with Hemp or State Agricultural societies
- Using high quality, phytocannabinoid-rich hemp (hemp that is high in CBD)

Back to my earlier comment about the different brands I have tried. The nano-emulsion typically is the best tasting for the broad-spectrum products but there are other products such as *ReThink CBD* or *RxSelect CBD* that bridge the gap as well. I personally felt the most anxiety-relieving effects from the 0.3% THC products such as *Sunny Skies CBD* but some of these nuances will have to be figured out by you. Sunny Skies uses a unique distillation procedure to process their CBD which results in a cleaner tasting product. Neither of these manufacturers were not in my original review but would rank near the top. Very often

this issue of taste is related to the amount of chlorophyll in you CBD, so the darker the color the worst the taste. The various flavors you see on the market do help to mask the taste, but it is difficult to get rid of the bitterness. I don't mind the natural taste and neither do most of my customers, but if you are finicky then I would recommend the more purified products (clearer in appearance).

I have tried capsules and tincture and found them to be similar. My wife swears by the Rethink CBD brand for the topical cream (250 mg or 500 mg). The capsule formulations usually come in one strength, but once you are established at a certain dose with the tincture, you can make it work. Cost is the primary issue when dealing with capsules, but they are much easier and more convenient to take than the sublingual liquid.

You can view more test results on my website (www.awakentocbd.com), and if you sign up for my newsletter, I will send the latest results to you in monthly emails (promise I will not spam your account or send unnecessary updates). I also have an exclusive chart on the site that reviews all the above criteria and lists out all the top manufacturers for you. This is available on my website. There are plenty of reputable companies out there despite the extensive list of criteria I have supplied above. You just have to know the pitfalls to avoid, and I hope that with this chapter I have taught you how to be a wise CBD consumer!

Sean's Summary:

1. Before making your first purchase consider the different formulations.

    a. Various options can be used together depending on the symptoms.
    b. The most common forms are tinctures, capsules, creams, and vapes.
    c. Liposomal (fat-soluble) and nano-technology (water-soluble) are both newer formulations that increase the amount of CBD absorbed by your body.
    d. Bioavailability is critical when considering which form is right for you because the liver deactivates such a large percentage of this drug.
        i. Tinctures average 25-30% bioavailability, has faster absorption and faster peak.
        ii. Capsules average 10-15% bioavailability, have slower absorption and slower peak.
        iii. Vaporizers have 30-40% available with the fastest absorption and peak.
2. What kind of CBD should you be taking?
    a. Depends on the type of pain and what is causing it
    b. The cream is good for topical pain and arthritis. Also effective for skin conditions such as acne and psoriasis.
3. Determine the amount of CBD you will take.
    a. Not a standard dosing system and this can be a trial-and-error process, but I can help you get to an ideal starting dose.
    b. The maximum dose usually 2-3 times the starting dose and most people do not go much above 100 mg. More does not always equal better with CBD.
    c. Start with micro-dosing, which means start out at half the recommended starting dose and gradually increase to the full dose.

   d. This process can take as little as 2 weeks or as long as 2 months. The duration depends on how each person responds to CBD and experiences any side effects such as drowsiness, stomach upset, or vivid dreams.
4. Know who you are buying from?
   a. How is the quality of their website?
   b. How responsive is their customer service?
   c. How are customer reviews?
   d. Are the labels easy to read? Easy to read how much CBD is in the bottle and other ingredients?
   e. Is there transparency from the founders about how and why they built their CBD company?
   f. Any claims made from the manufacturer about healing or disease states?
5. Where was the hemp grown and how cultivated?
   a. Grown in the USA should be mandatory.
   b. How are crops grown? Does grower use pesticides or any other chemicals? Insist on non-GMO, which means the hemp has not been genetically modified to produce certain crops.
   c. Look for affiliation with other hemp organizations or state farming groups.
6. How was the CBD extracted from the hemp plant?
   a. Three main methods: CO2, ethanol, and propane/butane
      i. I see CO2 as the safest but requires large machinery and experienced technicians.
      ii. Ethanol and propane/ethanol are cheaper and easier but require an extra step to remove the solvent.
7. Certificate of Analysis (COA)

a. This is a type of lab report that lists all the contents of what is in each bottle. Shows all parts of the plant along with CBD and THC.
b. Make sure reports are current and performed by a certified lab.
    i. ISO-certification is the most common standard in the industry.
c. Look for soil impurities in the product to make sure below an acceptable limit.

Chapter 10. CBD Rankings

As mentioned before, the supplement industry often flies under the radar with the FDA. As of this writing, our regulatory governmental agency for all prescription and OTC supplements has taken a fairly hands-off approach to CBD, other than monitoring for inaccurate or inflated medical claims. So, for you as a consumer, the landscape of CBD can be confusing and full of uncertainty. How do you pick the right product? Well, never fear, CBD Sean is here! I am addressing this issue through the creation of a points-based rating system which ranks CBD companies and products based on my knowledge and expertise.

CBD rankings, on the surface, seem like a plain and straightforward idea. With no shortage of topics to measure and rate, I should glide along effortlessly while plucking out the good and bad from each manufacturer. What I encountered once I created a system and began applying it, is quite different! Keep in mind my pharmaceutical background and the clinically trained need for order and balance in my research. I am used to digging through Drug Package Inserts and combing thru clinical data when trying to find answers to my questions. Trying to bring these same techniques to ranking various CBD manufacturers proved to be a much harder task.

As I mentioned earlier, there is little standing in the way of someone creating a CBD product and selling it on a website. It is scary out there, boys and girls, and we need to tread lightly. I suspect in the next 1-2 years the FDA will

issue standards concerning the manufacturers, but they are in no rush to do so. What is true for you, the reader, are these principles will still hold true today, the same as 5 years from now. In this situation, I am just doing a little more of the legwork that would normally be done by the FDA, for the benefit of you, the reader and potential CBD consumer.

I used a wide variety of categories in my rankings matrix because I do not feel a website or manufacturer should be unfairly graded on one or two criteria. It is difficult to find solid answers because there are a ton of reviews out there for CBD and it is hard to know who to trust. There are thoughtful, well thought out reviews and reviewers but there are just as many that are actually landing pages masquerading as product reviews, intended to funnel you into their site and sell you on their products. Very few of the reviews I found had more than 3 or 4 criteria on which to base their decisions, and none were as thorough as my research – I used 14 distinct categories to divine the true merit of each product. I gave thoughtful and careful consideration to each rating to offer the most exact information possible. To some people, selling CBD is their life's work, and to others they just kind of stumbled into it without really learning the industry. I am interested in the intent of the company, but also acutely attuned to how each CEO carries out his/her vision and brings top quality CBD products to market.

Accessing the rankings

You may have already noticed the absence of a spreadsheet in this book. Life moves fast in the CBD world and information becomes available at a dizzying rate. To

stay on top, you need the most current data available on the market when deciding where to buy your CBD. I will have this on my web site and and will break down all the current trends in CBD to rate the best places to buy. Allow me to do all the hard work of researching these companies to make the decision to buy easy for you. You can also view the current rankings on my website, www.awakentocbd.com.

Sean's Ranking System Criteria:

I ranked each company based on a set of 14 criteria that included multiple point-giving categories. Depending the importance of the criterion, I assigned it to a point category with a maximum of 5 points, 4 points, 3 points, and 2 points. I gave each criterion a rating and point score and totaled them up, and so you will see how various companies fared – note that it will be a moving target that I plan to update regularly online as mentioned above, so rankings may change as I review new players in the marketplace.

Here is a breakdown of the various things I judged the companies on. I will discuss some of the key ones below to ensure you understand why I chose these considerations!

- COA – Deal breaker. Must have this
- Affiliations *(up to 5 points)*
- Cost *(up to 5 points)*
- Transparency *(up to 3 points)*
- Organic Ingredients *(up to 3 points)*
- Organic Farming *(up to 3 points)*
- Website *(up to 3 points)*
- Extraction Methods *(up to 3 points)*

- Top 20 Lists *(up to 3 points)*
- Variety of products *(up to 3 points)*
- Variety of flavors *(up to 3 points)*
- Farm to shelf *(up to 3 points)*
- Donations/philanthropy *(up to 2 points)*
- Anything else unique *(up to 4 points)*

I will not go into detail on all these categories but will highlight a few that may need a little more explanation.

Certificate of Analysis:

The #1 criterion for assessing the quality and legitimacy of a product above everything else is the Certificate of Analysis (COA). I have discussed this and how to view it in Chapter 8. This is the best way for you to know what is in the product. The COA will confirm that what is labeled on the box is actually what's inside the bottle. And we also want to know what should not be in our CBD, like heavy metals and pesticides or other soil impurities. Remember that the hemp plant is very good at absorbing what is in the soil, a process normally referred to as "bio-accumulator." I implore you before ingesting any new CBD product, to make sure that each lot has its own identification number and that each lot number has its own COA. The 2nd part of this equation is ensuring that the lab is reputable and certified as mentioned in Chapters 4 and 8. I know, this sounds like a lot of work, and we are only just at the beginning, but I promise these steps are vital towards you purchasing a high-quality CBD product. If a CBD company does not test their product with an independent, ISO-certified lab, then look somewhere else. All the companies I looked at for the sake of the book passed this test, so it is a common practice. This is a

pass/fail subject with no grey area. *Do not waste your time and money with anyone who does not test their product and post the results for everyone to see.*

5-point categories:

Affiliations with local and national organizations:

I put a high emphasis on this category and gave it as much priority as any other subject (except COAs). Since there is no FDA approval process for any of these products, we have to look to local and national organizations that standardize the growing and extraction process. I gave the maximum number of points for companies that had an association with USDA organic standards, or affiliation with legitimate hemp organizations such as the National Hemp Association or Hemp Round Table. These certifications are gained by having an independent 3rd party review all the processes and procedures for the growing and harvesting of hemp. They also should monitor the extraction process and the ultimate product as they sell it to the consumer. This step is not a pass/fail but shows that the owner is striving to meet the highest standards on the market for the purity and safety of their product. Many quality companies do not have this affiliation, but it gives me confidence in the companies that have secured extra steps to ensure that things are done right.

Some companies even went the extra mile and have multiple affiliations, but it comes with a cost and often the price point on these products is slightly higher than the normal. The old adage holds true: you get what you pay for.

Organic ingredients:

This is 3-point category but I put it here because it fits in with the affiliations and cost. When recommending organic products, I try to straddle the line in my professional world. I believe that often the absorption rate is higher for vitamins when using an organic source vs synthetic. Not that anything which is non-organic is rubbish, quite the opposite! Our body does an amazing job of absorbing what it can from the nutrients we present to it. But there are certain categories such as Vitamin C, Vitamin D, and multi-vitamins where the absorption rate is important and can make a difference in your health. I believe that in herbal medications or herbal supplements like hemp, organic processing matters. For instance, if a company's hemp is grown with the help of pesticides or other chemicals, then I suggest avoiding it. It is not needed and obviously can be dangerous to your health. If a hemp farmer has gone the extra step to be certified organic, it shows purposefulness to their actions and going the extra mile to ensure quality.

I encourage you to look through the lens of practicality and bring into focus all the measures the grower and seller have put into place because, without regulatory actions by our government, all we have are words on a page. I found it frustrating at how difficult it was to confirm the "organic" claim that some producers made. I was told by one grower that they would not provide their organic certificates because it revealed too much sensitive information, whereas another grower complied with my request with no problem or hesitation. I often had to hunt for the ingredients listed anywhere on the package and some distributors didn't even list on their webpage what

was in their product. I do not know why this was such a hard step, but I have a hard time trusting any company that doesn't make it easy to confirm what is in their product.

For the purpose of this ratings scale, if a website said they used organic practices, I took them at their word. I do not know enough about organic farming and state guidelines to confirm such claims. This isn't a make or breakpoint, so I am ok with the method. I weighted more points to organic growing vs organic ingredients, but all in all, it is weighted the same as a category about affiliations. Organic ingredients show care and thought, along with extra planning and money, to bringing us a quality product that will work the way it is intended.

Cost:

Not a lot needs to be explained here. Generally, I found that the higher cost items had more organic ingredients and more refined farming practices. These sellers took the time to form affiliations and regulate their growing process. But some sellers met all my previous standards and yet were able to keep the price reasonable. The fact that they met my criteria makes me confident that their product is quality, and the fact that they kept the price low made me confident that this was not just an attempt at a cash grab. Besides, I always love finding a good bargain!

4-point category:

Anything unique: This category was more at my discretion as I looked for anything that was special such as nano-technology, extra testing, veteran discounts, or generous

return policies. This category was a place where I found other offerings unique to the manufacturer and were not included in the rankings. For example, I love the labels for Green Roads because they are easy to read and interpret, and many of the companies gave significant discounts to veterans such as Lazarus Naturals. Some even went the extra mile, such as Nu Leaf, and offered support for lower-income families.

3-point categories:

Picking up speed now, let us look at a few of the other categories that I allotted 3 points towards:

Website: I look for a quality website that is easy to navigate and intuitive to use. This was harder than I thought, and some websites were downright ornery (I'm looking at you 1 pointers). I appreciated the sellers who designed an easy-to-use experience and made it easy to find out more about their products and processes.

Transparency (company, founder, mission, etc): I am a sucker for a good story, so I weighted this category fairly high. I evaluated the backstory, and how well the seller executed their beliefs. For some, it was just background noise, but for others, their dream and vision integrated seamlessly with their product. I want to believe in people and think the best of them (I am an eternal optimist) so a convincing story helps me to feel good about what I am buying.

Extraction method: There is a lot of controversy around this subject. It is hard to determine which process is the best, so I went with what is the safest which is CO2

extraction, which I described in detail in Chapter 8. Each method has its pluses and minuses, but CO2 is consistently tested as the safest but also the most expensive. CO2 extraction requires large machinery, and the process of extraction is complex. This method favors the bigger manufacturers because of the expense and additional workers needed to run the machinery.

The other methods (alcohol, ethanol, butane, propane) all require less expertise, but they need additional refinement to remove the solvent, which can affect the overall integrity of the product. The cleanest, most effective, and safest method in my research has been CO2 extraction, so I gave it the maximum points allowed.

Top 20 lists:

It is important to me that other evaluations ratify some same criteria that I am using so sellers received extra points for hitting other "Top 20" lists. I looked at 5 other evaluations from sources I trust and found lots and lots of variety. Not one manufacturer hit all the lists, but some were listed multiple times and thus received high marks in this category.

2-point categories:

Donations: Again, this is me wanting to form a feel-good relationship with my vendor. Do they give back to any charitable organization? Is there any mention of how the company spends its profits? I found some encouragement here as some went the extra step to support causes such as Make-a-Wish Foundation.

Farm to shelf: Extra points and kudos to those sellers that also grow and harvest their own hemp. This is a small category, but I wanted to give a little benefit to the smaller players out there who are doing things right.

Sean's Summary:

1. The purpose of this chapter is to give you advice on the best places to buy your CBD.
2. I used 14 distinct categories and weighted each one differently depending upon importance.
    a. The actual spreadsheet is not included in this book because information changes so quickly in the CBD world and I want you to have the most up to date information possible.
    b. I have provided you with a link and code to access my website or you may email me directly for the rankings.
3. The most important category is the certificate of authenticity (COA) which must be present for each individual product they sell. This COA ranking is a pass/fail category, and if the manufacturer does not comply then look no further. I did not include any companies who didn't have a COA available.
4. 5-point categories:
    a. Affiliations: does the grower or distributor belong to state farming associations or national hemp organizations (e.g.-Hemp Round Table or National Hemp Association). This ensures 3rd party oversight on the growing, harvesting, and extraction of CBD.

   b. Organic ingredients or organically grown: Additional certifications are needed to promote organic practices (these are 3-point categories, but I put them in here because they tie to the affiliations etc). Shows more thought and care put into the product when using organic ingredients.
5. 4-point categories:
   a. Anything unique: any technique or method from the manufacturer that stands out from the rest.
6. 3-point categories:
   a. Website: Is it easy to use to buy a product as well as to find out more information about farming practices or information about the company?
   b. Transparency: Does the manufacturer explain who they are and why they are in the CBD industry?
   c. Extraction method: tough category to gauge but the highest scores go to CO2 extraction, which is generally viewed as the safest for consumption.
   d. Top 20 lists: Do other reputable influencers in the industry recognize these products? The more recognition, the better.
7. 2-point categories:
   a. Donations: Does the manufacturer give any portion of its profits to charitable organizations or engage in philanthropic or socially responsible activities?
   b. Farm to Shelf: Extra points given to manufacturers who grow, harvest, and sell their own product.

Chapter 11. How to Ensure You Get What You Pay For

If you follow the guidelines and rankings in the previous chapter, you will have no problems finding a quality CBD product. But there are some pitfalls to avoid, and if you spend your time looking in the wrong place it will be very difficult to complete this journey successfully.

You will find many online companies you can trust in my online ranking calculation. All companies in my top 20 can be trusted to bring you a quality hemp product with high levels of CBD. Sometimes, especially at first, it is helpful to talk to someone face to face. To ask questions and get feedback from someone else who is passionate about CBD and has a vested interest in making sure you get the right product for your needs. If I'm painting with broad strokes, which I am, then locations such as drug stores (I prefer independents), CBD stores, and organic food stores are great places to get started. I would avoid buying CBD products from places that do not sell food supplements as part of their core business model, such as gas stations and convenience stores. You see, buying CBD is not just a transaction. You need someone that can help determine the symptoms you're experiencing and/or issues you are having, and fit you with the right kind of CBD. There are details like how to take CBD and side effects to avoid. You won't get this information at your corner gas station. You also may be uncertain with the quality of product you are

receiving, so it is best to stick with those people who have a vested interest in your success with CBD.

Retail and Independent Pharmacies

CBD is starting to crop up everywhere, which is good and bad. It is good because big box pharmacies like Walgreens and CVS do sell a high-quality product, and at least you are going to be able to talk to someone about your situation and current medications. But you are going to find it hard to get the personal service you need to get started on CBD. You need more than a 2-minute conversation to go over your symptoms, health history, and to give them a chance to search for any potential drug interactions. In addition, most employees at these large retail chain pharmacies are not educated about CBD. It's just another product that they carry. That is why I prefer smaller independent pharmacies, because you will have a better chance of encountering someone who understands the products and can give you some personalized instruction and recommendations.

CBD and Vape Stores

CBD stores and even vape shops are often good sources for your CBD. People that work with this product every day are going to be your most knowledgeable sources of up to date information about CBD and the various manufacturers. Just be aware of agendas to sell you certain kinds of product that do not fit your needs or encouraging you to buy more than you need. In addition, CBD and vape shop personnel are not going to be able to help you with potential drug interactions, and they are not typically trained in healthcare. On the positive side, most

CBD stores will let you try samples while in the store which is particularly effective especially if you are trying a topical salve as results may be felt within 5-10 minutes.

Assessing the Quality of CBD Products

Remember to always look for the QR code on the bottles and you should be able to easily find what is in the bottle and where it was made (USA only). As I mentioned in the previous chapters, a reputable company will provide you with a certificate of analysis (COA) and be able to explain to you what is in their product. Equally important to the COA is how the hemp was harvested and manufactured into the form of CBD oil. Organic processes are always preferred to make sure that no chemicals or herbicides were used in the growing the crops.

Some manufacturers have been pursuing Good Manufacturing Practice certifications for their labs. This is an expensive and lengthy process but ensures a high-quality product. An excerpt from US Food and Drug Administration explains this best:

> *"Following Current Good Manufacturing Practices (CGMPs) help to ensure the safety of food. CGMP regulations generally address matters including appropriate personal hygienic practices, design and construction of a food plant and maintenance of plant grounds, plant equipment, sanitary operations, facility sanitation, and production and process controls during the production of food."*

I believe the enforcement of this regulation is one of the next steps the FDA will take in the CBD industry. It will eliminate the manufacturers who do not put safety first and will start to thin out the field (the CBD industry is overrun with manufacturers). You know that anyone who has this certification is ahead of the curve and is offering you a CBD product that you can trust. It is the same level of trust you give to someone when they manufacturer and produce the food you buy at the grocery store.

Hemp Oil vs CBD Oil

Another pitfall to avoid is buying hemp oil instead of actual CBD oil, but not because it is bad for you, but because hemp oil does not contain therapeutic amounts of CBD. Hemp oil comes from the hemp plant and is a great product in general, as many people use it as a natural source for omega fatty acids.

Confusing hemp oil and CBD oil is a common mistake, and unfortunately many unscrupulous companies try to capitalize on this confusion. CBD actually does come from hemp oil, but it's hemp oil from a different source. Hemp oil traditionally is made from the seeds and stalk of the plant, which are very low in CBD. The term "very low" is important here, because some manufacturers of hemp oil products make many of the same health claims as CBD, or may even advertise that they have CBD in their product. And although technically that may be true, hemp oil contains very little CBD. Therefore, you want to make sure that you know how much CBD is in your supplement, regardless of how it is marketed or advertised. This is why I keep going on about accessing the COA.

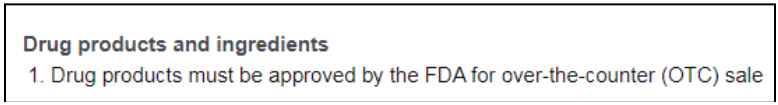
So, while hemp oil is very low in CBD, most true CBD oil products contain 80-90% CBD and are considered "phytocannabinoid rich," often abbreviated as PCR on labels and marketing materials. The highest concentration of CBD comes from the leaves and the flower of the hemp plant. Hemp oil only has trace amounts of CBD and would not have any effect on your ECS. This is an important distinction when looking at your CBD bottle. If you are purchasing a bottle of 1000 mg CBD, you are actually getting about 800-900 mg of CBD as there is no such thing as hemp extract with 100% CBD. The "1000 mg" represents raw hemp oil extract but the kind that is high in phytocannabinoids (phytocannabinoid rich, PCR). The "1000 mg" on the bottle of hemp oil means you are getting 1000 mg of hemp oil extract, but it is the kind that is low in phytocannabinoids. I know this is confusing, but **it's important to make sure you are buying CBD oil, not just hemp oil.**

A Warning About Buying CBD on Amazon

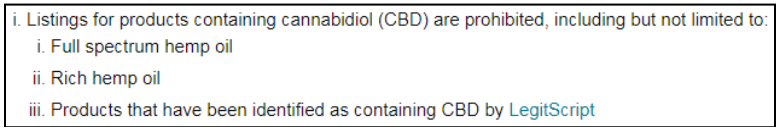
One of the reasons I am splitting hairs with these definitions is because of the proliferation of "hemp oil" being solid online claiming all the benefits of CBD, especially on Amazon. The labels on many of these products can be misleading, and I want to be sure that you are not led astray by inaccurate claims.

So here is the thing you as a consumer need to know: Amazon does not allow any items to be sold on their website that are not FDA approved. **What this means is, hemp oil can be sold on Amazon, but CBD oil can't.**

Hemp oil, by itself, DOES have FDA approval to be marketed as beneficial for pain, anxiety, and stress. So Amazon allows its sale. For more details you can visit the Amazon website. It's where I found the following definition:


Drug products and ingredients
1. Drug products must be approved by the FDA for over-the-counter (OTC) sale

There is nothing wrong with Amazon limiting what is sold on their website. It helps protect us, as the consumer, from unscrupulous products. But while we wait for the FDA to catch up to the CBD craze, we are left in limbo by the fine people at Amazon, because they do not allow *phytocannabinoid rich* (PCR) products to be sold there, because they are not FDA approved to be marketed for pain relief, sleep problems, anxiety, etc.
The final dagger comes later in Amazon's prepared statement about CBD. They go the extra step to make sure there is no confusion in this area.


i. Listings for products containing cannabidiol (CBD) are prohibited, including but not limited to:
  i. Full spectrum hemp oil
  ii. Rich hemp oil
  iii. Products that have been identified as containing CBD by LegitScript

Not much else to say after this statement. If you are looking for true CBD oil, you won't find it on Amazon. But you may very well see hemp oil being touted as a CBD product, which is not really the case.

When the day comes that CBD is approved by the FDA, it doesn't necessarily mean you can buy it on Amazon. The CBD market is a complicated one, and CBD isn't legal in all

countries, so those sellers with an international customer base may have additional restrictions.

EBAY

You will see the same issue on eBay: they allow the sale of hemp oil but not CBD oil or CBD products. Even though it is legal to sell CBD in the US, it is not in all countries world-wide, so they cite that as a reason to avoid allowing it for sale. The difference with eBay, is when you type in "CBD Oil" as a search, you aren't deluged with hundreds of manufacturers promoting their version of hemp oil and touting it as being the same as CBD. I think that eBay not allowing this kind of search-based confusion is a good thing).

In conclusion, it is easy to become disillusioned in the CBD world. Many medical and healthcare professionals either do not fully understand it, or do not want any part of it, and it seems like everywhere you go someone is trying to sell you their product and making grandiose claims about what it will cure. But fear not, I am trying to arm you with all the information you need to make informed decisions and purchase a quality product that will help you with your particular health outcomes! The CBD situation reminds me of the cell phone business. Once you commit to one vendor, you are unlikely to change as long as the service is decent, and you have a solid product that works reliably. CBD does not need to be taken for the rest of your life to be effective, but it wouldn't hurt. CBD should be considered the same as a vitamin supplement that you take to augment your natural health. The competition is intense for your loyalty which in the end is good for you and me. We do have many choices and we should not

settle on a product until we are satisfied that all the essential criteria, and improvement in your health, has been met.

Sean's Summary:

1. Where to buy your CBD
    a. Preferred locations are independent drug stores, CBD stores, and some vape shops
    b. Use caution when shopping at big box retailers and non-professional environments like gas stations or liquor stores.
2. Assessing the quality of your CBD product
    a. Insist on COA for all your products
    b. Ensure your product contains high quality PCR hemp that is grown in the USA
    c. Does your manufacturer follow GMP for their extraction and lab?
3. Know the difference between hemp oil and CBD oil
    a. Hemp oil comes from the stalk and seeds of the hemp plant and has virtually no CBD or other cannabinoids
    b. CBD oil comes from the flowering portion of the hemp plant that is grown specifically to produce high amounts of cannabinoids (80-90%). This is also called Phytocannabinoid rich hemp or PCR.
    c. Hemp oil has many uses but is not comparable to CBD
4. Buying CBD on Amazon

   a. Amazon does not sell supplements that are not approved by the FDA so you won't find CBD
   b. Specifically restricts sale of any items with PCR hemp
   c. The advertising on hemp products can be misleading so be careful when purchasing your products here.
5. Buying on EBay
   a. Similar restrictions as with Amazon because CBD is not approved in all countries outside of USA
   b. Difference is you will not be deluged with hemp oil products that make similar claims to CBD

Chapter 12. CBG

CBG, or Cannabigerol, is the new darling of the CBD/hemp world, and you may have heard mention of it. If not, well, consider this your introduction. If you are getting dizzy with the alphabet soup of this industry, (CBD, CBG, CBGA, CBDA, THC, THCA), then you are not alone! There are actually over 100 different kinds of cannabinoids in the hemp plant so it is easy to get everything confused! After reading this book, you should be most familiar with CBD and THC, which are the two most prevalent, and famous, cannabinoids found in hemp. As noted earlier, we are just beginning to understand the ECS and how these 100+ cannabinoids work. And so, as we study the amazing hemp plant, the industry is starting to dissect all the amazing components this plant produces such as flavonoids, terpenes and minerals. And the more we dig in, the more we find out how these components can benefit our health and well being!

We are starting to see special emphasis put on research of certain terpenes to ascertain how they affect things such as sleep (Myrcene shows promise for this) and anxiety (Limonene shows promise for this). Scientists are also doing the same thing with CBD as they look for other cannabinoids responsible for specific effects on the body's immune system, inflammatory pathways, and more. CBG falls neatly into this category and has a host of effects complementary, but different from, CBD.

CBG has been called the "stem cell" of the cannabinoids and for good reason, because it is the original molecule from which all other forms of THC and CBD are made.

Chapter 12. CBG

Let's take a minute to review what we know before learning more about CBG:

- Endocannabinoid System (ECS): think of this as a universal regulator of all the other systems in our body. The ECS imparts wide ranging effects on our body including impacting everything from inflammation to mood to metabolism to cancer. Helps our body to maintain and battle for homeostasis (balance).
- Endocannabinoids: cannabinoids made by the human body that work on the ECS. The two most common are Anandamide (the bliss molecule) and 2-arachidonoylglycerol (works mainly in the immune system).
- Phytocannabinoids: cannabinoids made by the hemp plant that work on the endocannabinoid system by decreasing how quickly our endocannabinoids are metabolized.
- Hemp plant: legal version of the Cannabis plant that contains less than 0.3% THC and over 100 cannabinoids along with hundreds of flavonoids and terpenes.
- THC: component of marijuana plant, in much larger quantities than hemp, that causes psychoactive impairment. One of the main components of the hemp plant but is bred in a lower percentage in order to be legal with the hemp plant.
- CBD: along with THC, CBD is the most plentiful product of the hemp plant. CBD is thought to be

responsible for many of the positive effects of CBD oil.

- Entourage effect: school of thought that all components of the plant work better together than CBD alone.

CBG fits neatly in the above explanation as a "minor" cannabinoid. This is mainly because CBG is only present at the very early stages of the plant growth. Normally, hemp strains consist of about 20% CBD, and only have 1% CBG. That means you would need 20 times the biomass for CBG to equal CBD. But CBG is hardly "minor" in any other sense. You see, CBG is essentially the source material for all other cannabinoids! But once CBD and friends start being produced in the hemp plant, the CBG concentration drops quickly. And it's this "source material" aspect that has researchers and CBD aficionados very interested in it!

How CBG Transforms Into Other Cannabinoids

Bear with me here while I explain some chemistry. Trust me, it'll all make sense! CBG, like all cannabinoids, begins in its acidic form, CBGA, and then transforms into CBG along the way. This is how things generally work in the world of botany. Under certain specific conditions like heat, light (photosynthesis) or oxidation, these chemicals are metabolized and transform into new chemicals, which sometimes even transform again (this is important in terms of how CBG is like a stem cell for cannabinoids). We can compare this process to how the liver metabolizes, or deactivates, drugs in our body. However, sometimes our liver metabolizes drugs to a more potent formulation, which is exactly what we see with THC.

When we talk about THC, the version of THC that is available in the marijuana plant is not actually THC, but its acidic form, THCA. Now what is interesting is that THCA is the non-psychoactive version of this plant compound and will not get you high. THCA is often referred to as a superfood (such as avocados, Greek yogurt, and green tea) because of its ability to help with a myriad of health conditions. The acid form needs to be changed, or decarboxylated, before it changes into its psychoactive, THC version that creates a high sensation. The point here, is that these different forms can have very different effects in the body.

This same mechanism also occurs with other cannabinoids as they change from their acid form (CBDA, CBCA, etc) to their active form (CBD, CBC). So, why all the emphasis on the chemistry and metabolism of these cannabinoids? Other than the fact that I am a chemistry nerd?? It helps to explain the role that CBG plays in the hemp world. The acidic precursor of CBG is CBGA, and I hope you are starting to see the trend here. CBGA is unique because it is the ONLY precursor for THCA, CBDA and CBCA, which then go on to form all other cannabinoids. Then the precursors all go through similar changes to transform from the acidic version to the active form. This process of conversion takes about 6-8 weeks during the plants' flowering cycle. So, think of CBGA as the mother of all cannabinoids, because without her, all the other ones do not exist!

The Role for CBG

You might be asking yourself, what makes CBG so special? Or is CBG converted into THC in my body? Will it make me

high? What specific effects does it have that make it worth getting excited about? I hope I have piqued your curiosity because I was asking myself the same questions!

I'll get the easy question out of the way first. No, CBG will not create any altered mental state, which I know for some of you is, like, a bummer. And no, it does not get converted into any other cannabinoids in your body unless you start sprouting roots and growing in the soil. It only transforms while it is in the hemp plant. CBG is like any other cannabinoid in your body, and yet it has characteristics that are unique from any of its "offspring."

The primary subject of this book, CBD, is the most abundant cannabinoid in the hemp plant, and is the heavy hitter for CBD oil. It's in the name after all! Its most prominent effect is to decrease the metabolism of anandamide and 2-AG, which leads to a greater stimulation of the ECS in your body. Now, CBG does not work this way, but rather works directly on CB2 receptors and to a lesser extent CB1 receptors. This distinction leads to a more direct impact on your ECS.
Another unique quality is the antagonism of TRPM8 channels, which plays a role in regulating and reducing chronic pain. No other cannabinoid works in this manner which is what makes CBG so intriguing. Its potential for pain relief is really fascinating, especially considering all that I discussed about the opioid epidemic in Chapter 8.

I believe that CBG is more closely related to THC than any of the other cannabinoids which may account for its ability to work directly on CB2 receptors. THC, once it is decarboxylated, fits right into the CB1 and CB2 receptors to produce an overstimulation of the ECS which leads to

many of the positive effects of marijuana (pain relieving, psychoactive high) and some of the negative (paranoia, hallucinations). The good news about CBG is that it is only a partial agonist, meaning it doesn't go hog wild and create an unnatural state in our body like THC.
Other observations and effects of CBG have a wide range of possibilities:

- May aid in the elimination of cancer cells, especially with bone and GI cancer.
- One study found that CBG was more effective than THC and CBD at relieving pain.
- Research has also shown it has antibacterial properties, especially against bacterial strains like MRSA, but also to other difficult strains of gram-positive bacteria. (same reference as above)
- Inhibits GABA reuptake to an extent greater than THC or CBD which helps to control fear and anxiety.

CBG holds a lot of promise but is years behind CBD in the amount of research to confirm the pre-clinical trial results. If you are seeking relief from any of the above mentioned issues, it might be worth trying. Most formulations are mixed with equal amounts CBG to CBD. Take for instance the 1000 mg bottle. It would contain 500 mg of CBD and 500 mg of CBG which would give you the benefit of each cannabinoid in a full or broad-spectrum tincture.

Stay tuned, because CBG is a rising star in the cannabinoid universe. There are many more minor cannabinoids that show promise for helping us with different health issues and conditions, but CBG is leading the charge at this time.

Sean's Summary:

1. CBG is the precursor for all other cannabinoids. It is the first cannabinoid present in the hemp plant and is often referred to as the stem cell for all other cannibinoids.
2. CBG is only present during the early growing stages and then disappears once converted into other cannabinoids.
    a. Often referred to as the "Rolls Royce" of cannabinoids because it is rare and very valuable. Need about 20 times the biomass of hemp to equal the amount of CBD you normally would find in the hemp plant.
3. CBG starts off as the acidic form, CBGA. Through the process of photosynthesis and oxidation inside the hemp plant does it get converted into the active formulation called CBG.
    a. CBG forms the acidic precursors for CBDA, CBCA, and THCA which then go on to create the other 100 plus cannabinoids found in the hemp plant.
4. What are the effects of CBG for you and me?
    a. Even though precursor for THCA, it will not make you high.
    b. The hemp has to be harvested earlier to obtain any noticeable amounts of CBD, but it has been found to work more directly on CB2 receptors and to a lesser extent CB1. This property makes it unique when compared to all other cannabinoids.

   c. Another unique property is that is works on TRPM 8 channels, which plays a role in regulating and lessening chronic pain.

5. Other possibilities for CBG:
   a. May aid in the elimination of GI and bone cancer cells.
   b. Strong anti-bacterial properties.
   c. Lessens fear and anxiety

Chapter 13. Summary and Parting Thoughts

My hope and goal for writing this book is to equip you with enough knowledge to pursue CBD on your own. My goal is for you to know the pitfalls that are likely to be a trap, choose a solid manufacturer, and start off at a reasonable dose. It is also important to know what CBD can and cannot do for you so that your expectations are realistic. If you are interested in learning more about the topics in this chapter, follow the links to my website to read more about this topic.
Most of my information came from published journal articles which can be more difficult to read but I do not want your (or my) opinion swayed but someone else's interpretation of results. This holds true throughout the book as I attempt to hold a clinical mindset whenever possible. Sometimes I cited opinions and articles that proved a particular point about CBD. I wanted to make sure that any claims made were at least based on pre-clinical trials and not anecdotal, or non-scientific evidence.

Even though this book is short by conventional standards, I packed a lot of information in the pages that I used. I would encourage you to look back at the pertinent chapters as you hack your way into the CBD jungle. The best place for up to date questions and answers is to visit my website, www.awakentocbd.com. I will continue to update my blog and provide relevant content for you regarding the newest updates in the industry.

With these words of encouragement, I christen you “CBD ready” for whatever this journey holds in store for you. If you read and memorize this book, (just kidding), or rather understand the concepts I have brought forth, then I am proud to welcome you into the CBD Expert Club. Use your knowledge wisely and newfound power to not only help yourself, but to help others. If each one of you shares your insights with someone else, we can shine a bright light and chase away the cobwebs of confusion that envelope this industry.

If I can help just one person, if I can just help you, then all my work and worry over this book would have been worthwhile. I would encourage to take what you can from the preceding pages. Emphasize what works for you and discard the rest (well, maybe put it gently aside). The fundamental reason that I have dove headlong into this industry, as I mentioned in the first paragraphs, is my desire to help people. I hope that CBD can make a radical difference in your life. Many of you are desperate for something, for anything, to improve the quality of your life whether it is dealing with chronic pain, anxiety, worry, and stress. I’ve seen CBD produce near miraculous results and I certainly hope the same for you.

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Glossary of Terms

11-OH-THC: The active metabolite of tetrahydrocannabinol (THC) that is responsible for the high you feel when taking marijuana.

Adenosine: A molecule that is present in all cells, and is one of the 4 building blocks for RNA. CBD reduces the metabolism of adenosine (thereby increasing the amount in your body) which can have a wide variety of positive health effects. In the brain, adenosine acts as an inhibitory transmitter which helps to promote sleep and has neuroprotective effects. When given intravenously, it can help relieve surgical pain and nerve pain, along with high blood pressure and certain kinds of irregular heartbeat.

Anandamide: A type of internal cannabinoid that works at the CB1 and CB2 receptor locations. This neurotransmitter is created in the brain and influences such cognitive effects as pain, appetite, pleasure, and reward. It is often called the “bliss” molecule and is partially responsible for the “runners high” you feel after an intense run or workout.

Arachidonoylglycerol (2-AG): A type of internal cannabinoid that works at the CB1 and CB2 receptor locations. Therapeutically, 2-AG has been associated with pain relief, lessening of nausea and vomiting, and inhibiting tumor growth.

B-Cells: A type of white blood cell responsible for producing antibodies.

Broad-Spectrum CBD: A product that contains all the cannabinoids, flavonoids, and terpenes that naturally occur in the cannabis plant. This product goes the extra step of removing THC from the formulation.

Cannabis: Refers to a group of 3 plants with psychoactive properties known as *Cannabis indica*, *Cannabis sativa*, and *Cannabis ruderalis*. When the flowering part of these plants produce a product with more than 0.3% THC, it is classified as the drug marijuana, which is regulated by the federal government.

Cell-mediated immunity: This involves the use of T-cells, which are a kind of white blood cell. T-cells are a part of our immune defense system and are important for cellular immunity and activation of immune cells to fight an infection. Once activated, these T-cells rapidly multiply and secrete signaling molecules called cytokines that regulate the immune system and inflammation. They control and shape the immune response, so think of them as police officers that control the traffic, telling everyone where to go.

Certificate of Analysis (COA): A report produced by a lab that evaluates the ingredients in your hemp product so that you know what you are actually buying. The COA will tell you the amount of CBD, along with other important cannabinoids, and the concentration of THC. These reports can also help to verify that your CBD product does not have high levels of pesticides or heavy metals which could be the result of impurities in the soil.

CBD: One of the most important terms of the whole book! It stands for cannabidiol which is a component of the

hemp plant. CBD belongs to a class of chemicals called cannabinoids. CBD works on the endocannabinoid system (ECS) by delaying the metabolism (*ie,* degradation) of our own internal cannabinoids (anandamide and arachidonoylglycerol or 2-AG) to maximize or prolong their effect on our ECS.
CBD also interacts with 5-HT1A receptors (serotonin), vanilloid receptors (TRPV1), and orphan receptors such as GPR55 to produce a wide variety of responses that reduce pain and decrease anxiety.

CBD Isolate: A CBD formulation that does not contain any other parts of the plant and is only CBD. We don't see this formulation much nowadays but you will find it in a prescription form called Epidiolex.

CBG: one of the minor cannabinoids but a very important one. CBG is the first cannabinoid formed in the hemp plant and is thought of as the mother of all other cannabinoids (kind of like a cannabinoid stem cell). CBG is only present in the early growing phases as it helps to form cannabinoids such as CBD and CBN.

Cannabinoids: These are a type of chemical compounds found in cannabis. Two of the most prevalent cannabinoids are THC and CBD, but there are over 100 different kinds of cannabinoids in the hemp plant.

CB1 and CB2 receptors: The main receptors found in the ECS. CB1 receptors are mainly found in the brain and central nervous system, and CB2 receptors are spread throughout the human body in nerve cells and the immune system. CBD exerts its effects upon these receptors.

CO2 extraction: One of the 3 primary methods of extracting CBD from hemp. CO2 extraction is the process of separating components from each other by using a particular kind of solvent. In particular, it is the use of supercritical fluids to separate one component of the hemp plant from another. Supercritical liquids have the ability to pass through solids and dissolve materials. This method has the ability to tune the extraction process to maximize the cannabinoids extracted, while ridding the product of chlorophyll, which adds an earthy (and unpleasant to some) taste to the product.

Endocannabinoid system (ECS): The ECS is a type of a biological system that was discovered and officially recognized as a system in the 1980s. The ECS comprises endocannabinoids and the receptors they impart their effect upon. Endocannabinoids are a type of neurotransmitter that work on cannabinoid receptors in your body called CB1 and CB2. These receptors are found throughout the human body in nerve cells, brain, and organs.
The role of the ECS is to help regulate and balance the biological systems within the body and bring it to homeostasis.

Epidiolex: The only FDA approved prescription form of CBD for juvenile seizures. Only available as the isolate formulation at doses 10-20 times higher than what would be found in a typical over-the-counter CBD product.

Ethanol extraction: One of the three primary methods of extracting CBD from hemp. The FDA categorizes ethanol as a class 3 solvent with low toxic risks and corn is the most

widely used source. Since ethanol is a plant-based substance, some experts believe it is the most efficient method for preserving the natural cannabinoid ratios as they exist in the hemp plant.
This process involves heating the hemp plant to achieve decarboxylation, then soaking the plant material in ethanol for a specific period of time. The final solution is then filtered to separate the liquids from the plant material.

Fatty Acid Amide Hydrolase (FAAH): FAAH is the enzyme responsible for breaking down the endocannabinoid anandamide inside the body. This enzyme works very quickly to deactivate our own internal cannabinoids when no longer needed. CBD works by delaying the metabolism of this enzyme, which allows anandamide to impart a more potent or prolonged effect on the body.

Flavonoids: Flavonoids are a diverse group of phytonutrients (substances found in almost all fruits and vegetables) which are believed to have beneficial effects on our health. They are one of the other types of nutrients in the hemp plant and can be found in some formulations of CBD products. Flavonoids are part of the polyphenols family and have beneficial effects on the skin, blood sugar, and blood pressure. They also have added benefits such as antioxidant, anti-inflammatory, and anti-carcinogenic properties. For example, the common belief that wine is healthy for the heart is because of the high content of flavonoids in the grapes. There are many effects that these flavonoids produce, and like CBD, we are still learning how they work in our bodies.

Full Spectrum CBD: Full spectrum CBD is very similar to broad spectrum CBD (meaning it contains CBD as well as terpenes and flavonoids) but contains less than 0.3% THC. The question has been asked, does THC have any effect at this low of a dose? We do know that it is not enough to get your high or buzzed, but whether or not it has any therapeutic effects is still up for discussion. I would say the prevailing opinion is that CBD works better when all parts of the plant are present, as nature intended it to be, in the hemp plant.

Gamma-aminobutyric acid (GABA): GABA is an amino acid that works as a neurotransmitter in your brain. It serves to reduce the activity of neurons (brain cells) to which it binds and results in a decrease in fear and anxiety. In a manner similar to adenosine, it is a neurotransmitter that works to bring calm and reduce stress to over-excited neurons.

GPR 55 receptor: A novel cannabinoid receptor that does not belong to any one category. It is thought to play a role in reducing anxiety, decreasing inflammation, and lessening neuropathic pain.

Hemp or industrial hemp: A variety of the *Cannabis sativa* plant. While hemp is naturally low in THC, to be legal in the United States it must contain less than 0.3% THC. Hemp has a rich history of being used for many industrial purposes like being made into rope, clothing, paper and building materials. The hemp we use for CBD production is bred to contain high amounts of CBD, and is frequently referred to as "phytocannabinoid rich" or PCR hemp.

Hemp seeds: Seeds of the hemp plant that are rich in protein, fiber, and healthy fatty acids such as Omega-3 and Omega-6. They have antioxidant properties that may help reduce the symptoms of certain ailments and improve your overall health.

Hemp oil: Hemp oil is made from the seeds of the hemp plant and may have trace amounts of THC and CBD, but not enough to produce a therapeutic effect. Hemp oil is often used topically to help the skin stay healthy and reduce breakouts. It may have other benefits and help to resolve such conditions as psoriasis, dermatitis, and eczema (to name a few). Unfortunately, hemp oil is often marketed as being the same as CBD oil, which is not the case, and I urge you to be careful to ensure you do not buy hemp oil as a substitute or thinking it will have the same effects as CBD oil.

Humoral immunity: This is a type of immune response involving antibodies that circulate in extra-cellular fluid. This includes B-cells which are responsible for producing antibodies that identify and attach themselves to a specific foreign invader to make it easier for the immune system to eliminate. These B-cells also are a type of white blood cell just like the T-cells that were described under cell-mediated immunity. Think of the B-cells as the undercover agents of the immune system, identifying the bad guys and tagging them for elimination. CBD's effects on humoral immunity may have promising potential for some symptom relief in autoimmune diseases. Humoral immunity is sometimes referred to as antibody immunity. The other type of immunity is called cell-mediated immunity and involves the release of T-cells and cytokines to fight pathogens, rather than antibodies.

Intracellular calcium: CBD is thought to decrease the release of intracellular calcium which decreases excitatory neurons and may help reduce seizures and improve brain wave activity.

ISO certification: The seal of approval from a third-party body that certifies a manufacturer follows standards and criteria for quality assurance.

Liposomal formulation: This is a drug formulation that diffuses the active drug in very tiny fat-like particles. They use this technology throughout the pharmaceutical world when drugs are too large for the body to absorb. This formulation makes it easier and faster for the body to absorb and use. Liposomal CBD formulations are beginning to be developed and may provide a way for the body to use CBD faster and more completely.

Monoacylglycerol lipase (MAGL): An enzyme primarily responsible for metabolizing the endocannabinoid 2-AG. This enzyme works very quickly to deactivate our own internal cannabinoids when they are no longer needed. CBD works by delaying the metabolism of this enzyme, which means the cannabinoids may have a more potent and/or longer lasting effect in the body.

Marijuana: This is defined as the leaves or flowering portion of the cannabis plant that is used as a drug in order to create a feeling of euphoria or a high. Marijuana is considered illegal by the federal government if it has more than 0.3% THC. Some states do allow for the medicinal and/or recreational use of this drug but the majority do not.

Glossary of Terms

Micro-dosing CBD: This refers to a low-dose technique used with beginners to CBD. The user starts out with a lower than average dose for the first 2-4 weeks to determine how CBD will affect the body. Also called the "low and slow" technique.

Neuroprotective: This means it serves to protect the nerve cells against damage or impairment of function during times of stress or severe trauma (ischemia, stroke).

Neurotransmitter: An internal biological molecule that carries, boosts, and balances signals between neurons (nerve cells). Billions of neurotransmitters work constantly to keep our brain and nervous system functioning and helps to manage a wide variety of effects ranging from breathing, to heartbeat, to our ability to learn. Neurotransmitters travel in the space between neurons and act like a lock and key to exert various effects on the body. What makes endocannabinoids unique is their ability to travel backwards along the neurons to the site of injury or distress. This is called retrograde transmission and is unique to the ECS.

Opioids: A class of opiate drugs that include the illegal drug heroin, synthetic opioids such as fentanyl, and prescription pain relievers such as Oxycontin, Vicodin, Norco and Dilaudid. All opioid receptors are related and react with opioid receptors on nerve cells in the brain and the body. Can also be defined as a substance resembling opium in its addictive properties or psychological effects.

Opioid receptors: Opioids exert their effects through 3 different receptors:

- Mu: these receptors influence responses to mechanical, chemical, and thermal stimuli and are located mainly in the supraspinal level.
- Kappa: modulates pain felt thru central nervous system and thru visceral pain.
- Delta: modulates pain responses with mechanical and inflammatory pain.

Our body makes neurotransmitters called dynorphins, enkephalins, endorphins, endomorphins, and nociception which act at these receptor sites.

Phytocannabinoids: These are cannabinoids that naturally occur in the cannabis plant. (Phyto = plant) There are over 100 different kinds of these plant-derived cannabinoids such as CBD, CBG and CBN. All of these have slightly different effects in the body which is why CBD is most beneficial when given all together in a full or broad-spectrum formulation.
Phytocannabinoid rich (PCR): A type of hemp bred specifically for low THC (less than 0.3% THC) and high amounts of CBD (usually 80-90%).

Propane/Butane extraction: One of the 3 primary methods for extracting CBD, also referred to as the hydrocarbon extraction process. This process starts with cannabis and liquid butane in a pressured and heated system. The vacuum turns the butane from liquid to a vapor which makes it easier to remove. The final product from this process is called shatter which is clear and contains CBD, THC, and terpenes.
This process has some risks because propane and butane are highly flammable and require careful temperature management to avoid exploding.

Retrograde transmission: A type of signaling process where a signal travels backwards from a target source to the original source. Normally, neurotransmitter flow only occurs in one direction from the original source to the target. But endocannabinoids move backwards in the ECS, making them unique in the neurotransmitter universe.

Sublingual: Latin for "under the tongue," refers to the pharmaceutical route of administration by which substances diffuse into the blood stream by being held under the tongue until they are absorbed. This form of absorption results in higher availability of the drug in the body when compared to swallowing medication.

Supercritical carbon dioxide (CO_2): When carbon dioxide is at a certain PSI and temperature, it has properties of both a gas and liquid. It is used in the extraction of CBD.

Serotonin receptor 5-HT1A: An example of g-protein coupled receptor that has a wide influence on biological and neurological processes such as anxiety, appetite, mood, sleep, and aggression. This receptor is the target for prescription drugs such as Lexapro, Zoloft, and Prozac. Research shows that CBD also has an agonist effect on the 5-HT1A receptor, and thus may impart anti-depressive or anti-anxiety effects.

T-Cell: A type of white blood cell that helps to stimulate the B-cells to produce antibodies, and helps killer cells develop. T cells also help in producing cytokines, part of the immune response. CBD is believed to help regulate T cells in certain condition to suppress inflammation and immune response.

Terpenes: Natural compounds found in plants responsible for the plants' color, smell, and flavor. If you are familiar with essential oils, terpenes elicit a similar effect. Lavender oil, lemon oil, and peppermint oil are all examples of terpenes that have a variety of positive effects in the body. A more specific example would be D-limonene which has a fruity and citrusy smell and helps with anxiety, depression, and mood.

Tetrahydrocannabinol (THC): The chemical component found in the hemp plant responsible for causing an intoxicating high. THC is one of at least 113 cannabinoids in the cannabis plant and naturally the most prevalent. Although it has been popularized and vilified because of its psychoactive properties, THC has many medicinal uses such as pain relief, anti-nausea, and appetite stimulation. THC binds directly to CB1 and CB2 receptors to produce effects equal to and greater than our own internal cannabinoids.

Vanilloid receptors (TRPV1): These receptors are found mainly in the peripheral nervous system (as opposed to the central nervous system). CBD binds with these receptors which play a critical role in the transmission and perception of pain, as well as temperature regulation, inflammation, and gastrointestinal motility.

Water soluble CBD: This formulation is most often referred to as nano-emulsion, which makes the particles 100 times smaller than regular CBD oil. These nano-emulsified particles are so small they absorb directly into the bloodstream and result in a faster and higher peak of CBD in your body. The potential downside of this

formulation is that the CBD is more quickly metabolized, and so people may not feel the same effect after 6-8 hours, which is when the sublingual oil hits its peak.

Appendix

Chapter 5: Drug Interactions

Table 1. Potential Drug Interactions (Medication Type by Enzyme)

Potential Drug Interactions for CBD	
Enzyme	**Medications affected**
CYP2C9	amitriptyline
CYP2B6	amlodipine
CYP2C8	buprenorphine
CYP2B6	bupropion
CYP1A2	caffeine
CYP1A2	cimetidine
CYP2C9	clomipramine
CYP2C9	clopidogrel
CYP1A2	cyclobenzaprine
CYP2C9	cyclophosphamide
CYP2B6	dextromethorphan
CYP2C9	diazepam
UGT1A9	diflunisal
CYP1A2	fluvoxamine
CYP1A2	fluvoxamine
CYP2B6	imipramine
UGT2B7	indomethacin
UGT2B7	ketoconazole
CYP2B6	loperamide
CYP1A2	melatonin
CYP2B6	methadone

CYP1A2	mibefradil
CYP2C8	montelukast
CYP1A2	naproxen
CYP2B6	nicotine
CYP2B6	nortriptyline
CYP2C9	proton pump inhibitor (omeprazole, etc)
UGT1A9	phenytoin
CYP1A2	quinolones (cipro, levaquin, etc)
CYP2C8	repaglinide
CYP2C8	rosiglitazone
CYP2B6	sertraline
CYP1A2	tamoxifen
CYP2B6	testosterone
CYP2C8	torsemide
CYP2B6	tramadol
CYP1A2	verapamil
CYP2C9	warfarin

Chapter 6: CBD Dosing Chart

CBD Dosing chart						
symptoms	Weight (pounds)					
	30-59	60-89	90-129	130-170	180-230	230+
Mild (1-3)	6mg	9mg	13mg	17mg	25mg	33mg
Moderate (4-	9mg	13.5mg	20mg	25mg	37mg	41mg
Severe (7-10)	12mg	18mg	26mg	34mg	46mg	50mg

Dosing with 500mg bottle in 30ml bottle						
Quality of symptoms	500mg bottle	500mg bottle	500mg bottle	500mg bottle	500mg bottle	500mg bottle
	30-59 lbs	60-89 lbs	90-129 lbs	130-170 lbs	180-230 lbs	230+
Mild (1-3)	0.4ml	0.5ml	0.8ml	1ml	n/a	n/a
Moderate (4-	0.6ml	0.75ml	1.2	1.5	n/a	n/a
Severe (7-10)	0.8ml	1.0ml	1.5	2ml	n/a	n/a

CBD Dosing chart						
Quality of symptoms	Weight (pounds)					
	30-59	60-89	90-129	130-170	180-230	230+
Mild (1-3)	6mg	9mg	13mg	17mg	25mg	33mg
Moderate (4-	9mg	13.5mg	20mg	25mg	37mg	41mg
Severe (7-10)	12mg	18mg	26mg	34mg	46mg	50mg

Dosing with 1000mg in 30ml bottle						
Quality of symptoms	1000mg bottle	1000mg bottle	1000mg bottle	1000mg bottle	1000mg bottle	1000mg bottle
	30-59 lbs	60-89 lbs	90-129 lbs	130-170 lbs	180-230 lbs	230+
Mild (1-3)	n/a	n/a	0.4ml	0.5ml	0.75ml	1.0ml
Moderate (4-	n/a	n/a	0.6ml	0.75ml	1.1ml	1.25
Severe (7-10)	n/a	n/a	0.8ml	1.0ml	1.4ml	1.5ml

CBD Dosing chart						
Quality of symptoms	Weight (pounds)					
	30-59	60-89	90-129	130-170	180-230	230+
Mild (1-3)	6mg	9mg	13mg	17mg	25mg	33mg
Moderate (4-	9mg	13.5mg	20mg	25mg	37mg	41mg
Severe (7-10)	12mg	18mg	26mg	34mg	46mg	50mg

Glossary of Terms

Dosing with 1500mg in 30ml bottle						
Quality of	**1500mg bottle**	**1500mg bottle**	**1500mg bottle**	**1500mg bottle**	**1500mg bottle**	**1500mg bottle**
	30-59 lbs	**60-89 lbs**	**90-129 lbs**	**130-170 lbs**	**180-230 lbs**	**230+**
Mild (1-3)	n/a	n/a	0.25ml	0.3ml	0.5ml	0.7ml
Moderate (4-	n/a	n/a	0.4ml	0.5ml	0.75ml	0.9ml
Severe (7-10)	n/a	n/a	0.5ml	0.7ml	0.9ml	1.0ml

Dosing Chart for all strengths						
MG per CBD	**250mg**	**500mg**	**1000mg**	**1000mg**	**1500mg**	**1500mg**
Bottle size	*30ml*	*30ml*	*30ml*	*30ml*	*30ml*	*30ml*
1ml dose	8.3mg	16.7mg	33.4mg	33.4mg	50.1mg	50.1mg
0.75ml dose	6.3mg	12.6mg	18.9mg	18.9mg	25.2mg	25.2mg
0.5ml dose	4.2mg	8.3mg	16.7mg	16.7mg	25mg	25mg
0.25ml dose	2.1mg	4.2mg	6.3mg	6.3mg	8.4mg	8.4mg

The dosages listed on this chart are starting doses only. Maximum doses are based on types of symptom and response to the medication.

For most disease states, the sweet spot for CBD is typically 2-3 times the starting dose. Most people do not derive a benefit from taking more than 100-150 mg of CBD per day.

If you are new to CBD, start at ½ the recommended starting dose and increase to full strength over 2-3 weeks.

Results may vary greatly between people, so any impact on your symptoms may start low and build up over the next 30-60 days. Be patient as results will build over time.

About the Author

Sean Gale is an American board-certified pharmacist, writer, speaker, and online course creator. He completed his clinical training at the University of Iowa (Go Hawks!) in addition to running on the Iowa Cross Country and Track team. If you attended Iowa State and purchase his book, Sean will do his best not to hold it against you!

Sean began studying CBD over 2 years ago when he started selling it in his pharmacy. The results were so encouraging that he decided to give it a try himself. His initial experience and challenges finding effective dosing exposed what he saw as a weakness in a potentially beneficial therapy, and so he dedicated himself to learning more about CBD and how it could work best of him and his customers. You are holding (or seeing) the results of his endeavor and hard work.

At his core, what gives Sean the most satisfaction in his professional life, is helping people and making a difference in the quality of their lives. By becoming the CBD expert in his medical and surrounding community, Sean is shining a beacon of light into the darkness that often surrounds the world of CBD.

By using a combination of his pharmaceutical training and 26 years of real-life experience in retail pharmacy, Sean has formulated a unique perspective on CBD that cannot be found anywhere else. His goal is to bring clear, concise, medically based information into an unregulated industry. Seeing all the potential benefits of CBD in his practice and

his own experience has spurred him on to become the source for CBD knowledge.
When not writing or researching CBD, Sean enjoys spending time with his wife and 4 girls. His passions still include running, and sometimes soccer, golf, and attending his kid's activities.

You can find Sean at www.awakentocbd.com and on Facebook at www.facebook.com/CBDseangale. You may also reach him by email at seangalerph@gmail.com.
(I will be developing more social media sites but this is it for now).