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Foreword

It has now been 20 years since the landmark ballot initiative in the state of California that enabled patient access to cannabis for medical purposes. After litigation that was battled all the way to the 9th Circuit Court of Appeals (Conant vs. Walters), it was ruled that physicians had the right to discuss the pros and cons of cannabis, and even recommend its use to their patients. When the US Supreme Court declined to hear the case, its impact reverberated nation-wide. As is often the model with any social movement, California blazed a trail that became a model for other states and nations on this important issue. A majority of states now have legal access to cannabis for medical usage in some form. While cannabis remains an illegal, forbidden Schedule I substance under federal law, this state-by-state "experiment" is being allowed to play out, but this situation could change.

It is important to understand these developments in context. Cannabis, along with other herbal medicines, has been utilized by humans for healing purposes for millennia. It is only in the last 75 years that moral imperatives, but not science, have decreed its prohibition. Examining the issue in this light, cannabis has been the scapegoat of a historical aberration and one that may be reaching its conclusion after a long and costly "War on Drugs" both in financial respects and, more importantly, in terms of the human suffering that it has produced.

The battle is not over, however, despite the acceptance of the concept of cannabis as medicine by the overwhelming majority of the populace. Politicians are not yet fully on board with the concept and neither is the medical community, largely as the result of ignorance borne of a total lack of education on cannabis and the endocannabinoid system in medical schools. Each physician who is confronted by her first patient who asks the question, "Would cannabis help?" must decide whether to investigate the matter on her own, or merely let the question go unanswered, or be dismissed with

some snarky remark that there is simply not enough information available with which to render a decision. As you will note in this book, Bonni Goldstein, MD was confronted with the same dilemma, but chose the path of educating herself so that she could best help her patients with their intractable medical problems. The results have been amazing and have produced remarkable benefits to those afflicted and their extended families. Many of us that work with such patients are constantly struck with the fact that it is only when an individual, a family member or close friend is touched by some dire medical need that finds relief in cannabis that hardened opinions against its use are softened or morphed into acceptance.

So, what is a patient or caregiver to do? Cannabis remains a subject where it is more likely than not that the patient will need to educate their doctor first. Such a task requires good tools, and I can think of few better than this book. It is affirming and refreshing to now possess a resource that presents the scientific facts on cannabis in such an accurate and accessible form. The reader will gain the knowledge necessary not only to understand cannabis and the endocannabinoid system, but also to make informed decisions on how to apply that knowledge to the treatment of myriad conditions where "conventional medicine" has all too frequently failed. We should be clear that cannabis is not miraculous. It may or may not help treat a given condition, but what is truly remarkable is how often it is of benefit, providing just enough relief so that a patient can properly cope with the challenges of their particular situation, and get on with life again as an active participant rather than a passive observer relegated to the sidelines. That is no small achievement.

I know Bonni as a gifted and compassionate healer and it pleases me greatly to know that her knowledge and experience can now be shared on a greater stage. Read, learn and enjoy!

Ethan Russo, MD

Author's Note

First do no harm.

I don't recall exactly when I learned my mother had suffered from seizures. I think I was in high school when my mother finally talked to me about her medical history and, while I always had intimations, I felt shocked to hear about it. When I look back on my childhood I see clues, despite her keeping it a secret from just about everyone.

My parents were homebodies and devoted to their children. My mother made dinner every night, my father came home from work and played with us outside, if the weather was nice, and both were always supportive of me. I was always smaller than my peers, got good grades and aimed to please. I was consistently told I was intelligent which I think made me want to achieve even more. I wasn't interested in being social: I basically did my own thing, happily reading voraciously. I first began dreaming of becoming a doctor when I was eight years old after watching the television show *Emergency*. I decided then that medicine was going to be my career and, ever earnest, I never once questioned or varied from the path that I had to take to get there.

My mother didn't drive when I was a little girl growing up in Brooklyn. Because there was an abundance of public transportation, it didn't seem that strange, and most of my friends' mothers didn't drive either. When we moved to the suburbs in New Jersey, I noticed that my mother was the only one who didn't drive. We never talked about it, and eventually my mother did get her driver's license, but it was many years before I learned the real reason she hadn't for the early part of my childhood.

About the same time that I began dreaming about being a doctor, I also became aware that my mother took medications every night. Two big prescription bottles sat in the upper cabinet next to the kitchen sink and,

whenever I asked about them, she gave a vague answer. I remember getting a sense that this wasn't something she wanted to talk about, so I stopped asking. A few years later, when I was a teenager, I was standing next to her by the kitchen cabinet where the medicine bottles were placed and asked her again about her medications, completely unaware of the story that she finally decided to share.

That day, she told me that when my sister was two years old and I just an infant, she had her first grand mal seizure in a Brooklyn playground and then two more seizures over the next few days. She eventually went to NYU to see a neurologist and while in his office she had another grand mal seizure. Hospitalized immediately, she, my father, grandmother and uncles were told that she might die. Diagnostic studies of the brain in the early 1960s were quite limited and the doctors did not know what was causing the seizures. Started on phenytoin (Dilantin) and phenobarbital, she responded positively and was told to continue taking them for the rest of her life.

My grandmother, an uneducated and superstitious immigrant, was in complete denial that my mother had epilepsy. She was terrified and embarrassed at the same time. Because of this, my parents became tight-lipped about what had happened. It just was not discussed or shared with anyone, and for most of my childhood I was unaware of her suffering.

I learned much later that even though the medications stopped her seizures, the side effects were difficult to tolerate. She became excessively hirsute and had significant lethargy and fatigue, making the care of two small children particularly challenging. She also had severe gingival hypertrophy, an overgrowth of gum tissue and a common side effect of phenytoin, which led to a lifetime of problems with her gums that still continues. I recall being in middle school and finding out that my mother had to have oral surgery for a terrible problem she was having with her gums. She stayed in bed for days with severe pain after the procedure. I can

still see her there with ice on her swollen cheeks, black and blue, unable to talk or eat. Little did I know at the time that this was a result of her seizure medication.

After my sisters and I were in high school, my mother decided that she just couldn't tolerate the side effects of the medication any longer and that she was finished with them. She didn't consult her doctor or even gradually wean herself off the drugs, but rather just stopped taking them. Fortunately, she had no repercussions from this arguably risky decision and remains seizure free today.

Meanwhile, I continued to pursue my medical degree and eventually became a doctor working primarily in pediatric emergency medicine and urgent care. I loved my work saving lives at the county hospital and teaching medical students and residents, but once I had my son, things changed. I had thought I could manage working nights and being with my son during the days, but after a few years it grew more and more difficult as I didn't feel truly present when home with my family. Given my skills in educating and communicating, I was a very good pediatric ER doctor, but my frustrations came from the exhaustion of night work and from trying to be a caring physician in a broken system. It wore me down.

After taking a leave of absence, a sick friend asked me about medical cannabis, putting it on my radar. Once I started reading the scientific literature, I grew incredulous that despite the discovery of the endocannabinoid system, the most widespread receptor system in humans, and my years of science-based education and medical training, I knew absolutely nothing about cannabis and how it works.

Intrigued, I continued to read and study everything I could find about cannabis and soon decided to work part-time in a local medical cannabis clinic. I was surprised to find that the patients I met were just everyday normal people who went to work, who had families and who had medical conditions that were not responding to conventional medications or the

traditional Western medical interventions in which I, too, was trained. These were people who simply wanted a better quality of life.

I haven't looked back since.

Cannabis was not medically available or used as an anticonvulsant during the years that my mother took anti-seizure medications. In 1970, five years into her epilepsy diagnosis and treatment, the federal government classified cannabis as a Schedule I controlled substance with the passage of the Controlled Substance Act. Defined as a "drug or other substance that has a high potential for abuse, has no currently accepted medical use in treatment in the United States, and is lacking accepted safety for use of the drug or other substance under medical supervision," the Schedule I continues to this day. It has virtually shut down all research on the multitude of compounds in cannabis which we now know to have low risk for abuse, to have true and proven medical use, and to have an excellent safety profile, especially with medical supervision.

Scientists had started significant cannabis research in the 1960s and were gaining knowledge on the phytocannabinoids, but this act by Congress completely closed the door on advancing cannabinoid science. After the discovery of the endocannabinoid system in the late 1980's, investigations in the field have exploded over the past two decades. We are finally catching up on research that should have been completed years ago.

I am angry that my mother suffered, and continues to suffer, from the side effects of medications that she took to alleviate her epilepsy. These side effects caused problems that persisted throughout her life, even after she stopped taking the drugs. My mother's suffering was in part due to the propagation of false claims about cannabis based on ignorance and greed. The false claims continue, despite the fact that millions of patients who could be helped by cannabis continue to suffer with medical conditions that are not responding to conventional treatment, and millions more grapple with intolerable side effects of those treatments.

As a physician, I took an oath to "do no harm." After treating thousands of patients seeking relief with medical cannabis, I can assert that the compounds in cannabis relieve unnecessary suffering with little to no adverse side effects.

I have witnessed sick and desperate patients have a complete turnaround in the quality of their lives. Cannabis medicine must be available as an option or alternative to current first line treatments, especially if those treatments have harmful or potentially fatal side effects. If a pharmaceutical with the properties of cannabis were synthetically created and introduced today, the medical community would embrace it with open arms and tout it as a miracle drug.

It's been 50 years since my mother developed epilepsy when I was only a child, and I get emotional thinking about her needless suffering. Many physicians find their vocation from early experiences with ill relatives and friends. While I had little awareness of my mother's struggles with seizures and medications, I find as a physician recommending medical cannabis to my patients, that her life and experience have indeed informed mine. I wish that medical cannabis had been available to my mother.

I cannot undo what she endured. I can help others, though, by sharing the current knowledge about cannabis and cannabinoid science.

I have written this book so that you and your loved ones, who may be suffering as my mother did, can move past the false propaganda that continues to this day and understand how cannabis is medicine.

Prologue

As a little girl, whenever I was alone – outside digging in the dirt or absent-mindedly swinging on the swing set, splashing or playing in the bathtub – I would start humming a tune. I'd start softly and then grow bolder, add in little trills and jazzy riffs, each note a bit louder than the next.

As I got older, I'd experiment with dropping my voice down to get to the lower notes and more dramatic effects. I had been exposed to singers like Judy Garland, Billie Holiday, Frank Sinatra and Nat King Cole, and then to songwriter artists like Joni Mitchell, Bob Dylan and Carole King. I listened to James Taylor, Cat Stevens and 60s Motown, and I recall at age twelve or thirteen thinking that Phoebe Snow was the ultimate in cool. Singing brought me freedom and joy, always, or at least until the pain started, and I was diagnosed with rheumatoid arthritis.

Over those years and the many that followed, in my late teens and early twenties, I didn't do that much singing, but on the occasions when I did, singing was one of the few things I could do to forget almost completely the way my body felt. During those moments, I tasted a little bit of freedom and was released from the pain and the loss of everything I used to be – all of my former life – even for a few minutes.

I have noticed lately, though, that during the process of taking my cannabis medicine that I am humming again, albeit weakly with little breath or power. The humming grows stronger as I feel the medicine move through my system and I find myself adding jazzy riffs right and left, treating my voice like a slide trombone. I can go mournfully low and tragic like Billie and then trill upwards sweet and high like Ella. I imagine myself as sultry and sassy, as confident as Peggy Lee.

It's as if cannabis has helped me to unlock the box in which I've kept my own personal songbird. This may be a small thing, but if anyone knows how it feels to be trapped in a constantly malfunctioning body, they would

realize what an enormous gift it is to feel well, to feel strong and capable at something again for the first time in over a decade. I was locked in a prison of illness and pain, and cannabis unlocked the door for me to break free.

Elise R., as told to me in February of 2016 and whose story appears on the following pages.

How To Use This Book

I have spent the greater part of the last decade educating and explaining cannabis as medicine to patients, politicians and medical professionals. In order to understand how cannabis can do all that it is touted to do, you must first understand the plant itself.

Chapter 1 discusses the many different compounds in cannabis and their medicinal properties. Chapter 2 explains our endocannabinoid system and how cannabis compounds interact with it. Diseases associated with an imbalance of the endocannabinoid system are also discussed. The safety of cannabis use is discussed in Chapter 3 with special considerations discussed in Chapter 5.

The bulk of the book is devoted to Chapter 4, How to Use Cannabis as Medicine. The goal of this chapter is to help you to understand the different cannabinoids and cannabis preparations, as well as dosing.

Chapter 6 discusses the multitude of ailments where cannabinoid medicine may play an important role. Interspersed throughout the book are incredible stories of patients who have had success with using cannabis medicine. These patients were able to overcome medical conditions that were negatively affecting their quality of life and they were all so eager to share their journey that led them to cannabis treatment.

The appendix includes a "History of Cannabis" timeline, a chart that explains the effects of cannabis by body system and the pharmacokinetics of cannabis medicine.

At the end of the book there are three charts that readers can use as references to understand the many facets of cannabis medicine. The first is a chart of phytocannabinoids, the second is a chart that explains the many terpenoids found in the cannabis plant and the third contains practical

information to help with dosing and navigating the various cannabis products available to patients.

Gavin's Story

I sensed true desperation almost immediately when I met with Gavin and his family. The despair was nearly palpable, even in Gavin's two grandmothers who had accompanied them to the office. Gavin himself appeared oblivious to his surroundings, made little to no eye contact and was very hyperactive and distracted, moving around the office the entire time. A cute child wearing a little fedora and glasses, his face showed little affect and we made no connection. "We need help so badly," the small group said to me, "we can no longer live like this."

Rebecca is a stay at home mother with a special education degree whose first child Gavin was born six weeks early. While he had low muscle tone, something you'd expect from a preemie, he also didn't reach his early milestones and, at around age two, Gavin's health and development began to really fall apart. He was nearly two when he walked and had little to no language at age three. Ultimately diagnosed with complex partial seizures, cerebral palsy and an unknown genetic anomaly, as well as cyclical vomiting and autism, Gavin was prescribed the anticonvulsant levetiracetam (Keppra) for his seizures. He was three years old, and the effects were immediate.

While the seizures stopped, Gavin's autistic behaviors increased, and within two months his meltdowns became uncontrollable. Rebecca and her husband had read about "Keppra rage," a well-documented side effect, but they wanted to control the seizures and were hesitant to take him off of the drug or add another one. During this time, Rebecca saw the CNN documentary "Weed" and began to explore cannabis as a possible treatment. When she asked Gavin's neurologist about trying cannabis, he ignorantly told her "the tar in the smoke will give him lung cancer." She was discouraged by this response but kept searching online for information and found support on Facebook. She eventually brought Gavin to my office in

early 2014. With his behavior out of control, life with Gavin had become a daily struggle.

I started Gavin on CBD-rich cannabis oil, given by mouth. The effects were immediate. Within 10 days, Gavin, previously non-verbal, began speaking. The change was so dramatic that Rebecca wanted to try weaning him off the seizure medication to see if his seizures might also be controlled. She switched neurologists and found a supportive physician who helped her to wean Gavin off the drug over five months. When he was completely off the drug, an initial EEG showed some seizure activity, but Rebecca asked for three months to adjust the dosage of CBD before trying other pharmaceuticals. The subsequent 48-hour EEG showed no seizure activity and Gavin hasn't needed any further antiepileptic medications.

Although the use of CBD-rich oil for a number of months resulted in seizure freedom, improved verbal ability and improved behavior, Gavin continued to have some unwanted behaviors related to his autism. It was at this point that we added THC-rich oil in the mornings and afternoons to help him to be calm and focused. As we hoped, his behavior improved significantly.

Rebecca still marvels at the dramatic turnaround in Gavin due to cannabis medicine. In addition to seizure control, Gavin's incredible improvements in speech and autistic behaviors thrill her the most. Although everyone who knew Gavin saw that he was quite intelligent (even the speech pathologist had given him an iPad with communication apps because they knew his capabilities), he had no real language or any imaginary play. One afternoon, soon after Gavin began taking CBD oil, Rebecca was in her bedroom folding laundry. She looked up to see Gavin walking in with the laundry basket. He placed it on the floor, stepped into it and declared, "Look, Mom! I'm an astronaut!"

Rebecca has had to experiment with the dose and ratio of CBD and THC and has ultimately found that a particular variety of CBD-rich oil

combined with another variety of THC-rich oil is giving him the best results. Gavin has no adverse side effects from cannabis use. He does not experience any psychoactivity. He is able to make connections in his kindergarten class, to fit in with his peers and to transition throughout the day with ease. He is happy and thriving, and reports from school are outstanding. The speech pathologist has even taken away the iPad with the communication apps because he doesn't need it anymore!

Gavin is now five years old and his story moves me as both physician and mother. When Rebecca sent me a video recently of him reciting the Pledge of Allegiance and breaking into "You're a Grand Old Flag," I was moved to tears. Although not every patient has this level of improvement, Gavin's story is an example of why cannabis treatment must be an available option for all children with severe medical conditions. His quality of life has been improved so significantly that he is able to participate in his life fully as all children deserve.

CHAPTER 1
The Cannabis Plant

In order to understand the medicinal value of the cannabis plant, you first need to learn about the many compounds that are found within it. The cannabis plant is made up of over 400 chemical compounds. When you use cannabis, you are taking a mixture of natural compounds that work together to balance each other.

The Latin name of the plant is *Cannabis Sativa*, in the family called Cannabaceae and Genus Cannabis. Other plants in this family are Humulus (hops) and Celtis (hackberries). These plants share an evolutionary origin but are quite different from one another.

The cannabis plant contains biologically active compounds called phytocannabinoids, terpenoids and flavonoids. These chemicals interact with our brain and body chemistry to give certain effects. Hundreds of different cannabis varieties, or "chemovars," are grown all over the world, each containing varying amounts of the 400 different compounds, with each strain giving different effects.

What are Phytocannabinoids?

The term "cannabinoids" is very general and refers to a group of chemical compounds that are usually made up of 21 carbon atoms in a three-ring structure. When we add the prefix "phyto" to the word, we are specifically referring to the cannabinoids that are found almost exclusively in the cannabis plant.

The main two phytocannabinoids are THC (delta-9-tetrahydrocannabinol) and CBD (cannabidiol).

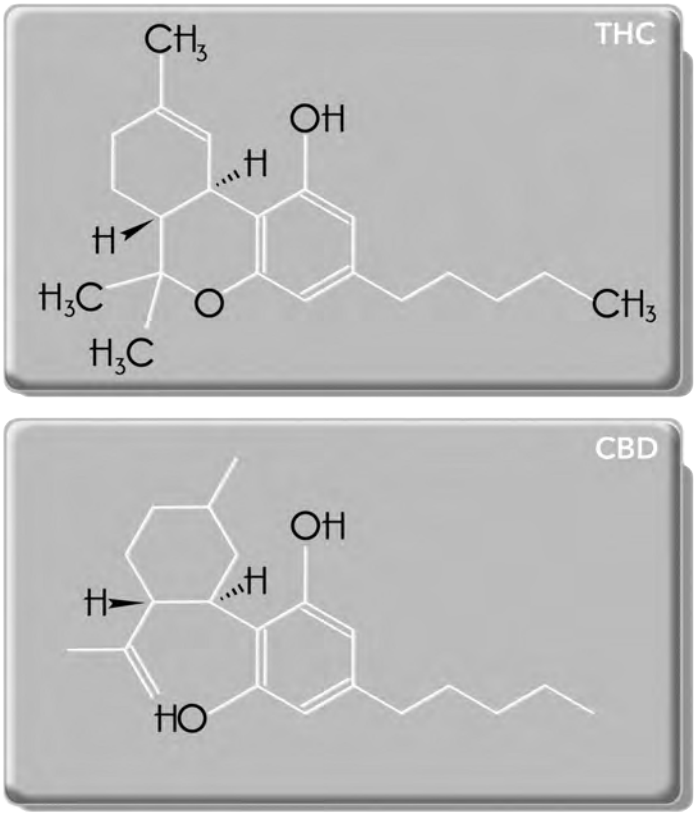


Figure 1: Molecular structures of THC and CBD

Other phytocannabinoids found in the cannabis plant, often referred to as **"minor cannabinoids,"** include cannabinol (CBN), cannabigerol (CBG), cannabichromene (CBC), cannabicyclol (CBL), cannabidivarin (CBDV), and tetrahydrocannabivarin (THCV). Future research may reveal some of these to be major cannabinoids.

The main effects of THC and CBD are summarized in Table 1.

THC effects	CBD effects
• Psychoactive	• NOT psychoactive - no "high" effects
• Sedating/relaxing	• Alerting in low doses
• Reduces pain (analgesic)	• Reduces pain
• Reduces/stops nausea/vomiting	• Relaxes muscle spasms
• Stimulates appetite	• Potent anti-inflammatory
• Induces sleep	• Stops nausea/vomiting
• Reduces anxiety & depression	• Reduces anxiety & depression
• Reduces intraocular eye pressure	• Counters psychotic thoughts
• Anti-oxidant	• Anti-oxidant
• Antiinflammatory	• Anti-convulsant
• Anti-tumor effects	• Neuro-protectant
	• Anti-tumor effects

Table 1: THC and CBD effects

The average THC content of cannabis in 1972 was 1%, increasing to 4% in the 1990s, to a national average of 13% today. California cannabis testing laboratories report a current average of 18 – 20% THC content. Cannabis currently available in California dispensaries has THC content between 15% -28% with a corresponding CBD content of <1%. Concentrated forms of THC-rich cannabis can have contents up to 90%. This increase in THC content has led to a decrease in CBD content and made CBD-rich plants rare, although this is changing.

Until 2012, the potency of cannabis tested by the government and dispensaries was based solely on THC content. Now that CBD is recognized as having significant medicinal effects, testing of various cannabis products routinely reports the potency of both compounds. As you can see in Figure 2, various chemovars (chemical varieties or "strains") of cannabis are listed with their potencies of THC, CBD, and CBN. (If you are not familiar with cannabis, the plants vary in their compounds and are often given names that may reflect their chemical makeup.) Two are high in

THC and quite low in CBD (Blue Dream and Sour OG), one is quite high in CBD and low in THC (AC/DC), and two have varying amounts of both THC and CBD (Cannatonic and Omrita). These plants will vary widely in their effects due to their different phytocannabinoid potencies. CBN stands for cannabinol, one of the minor phytocannabinoids. This compound is present only in trace amounts in freshly cut cannabis flowers and arises from the degradation of THC over time. As you can see in this chart, there is no CBN detected in these samples, which indicates that testing was likely performed on freshly cut flowers.

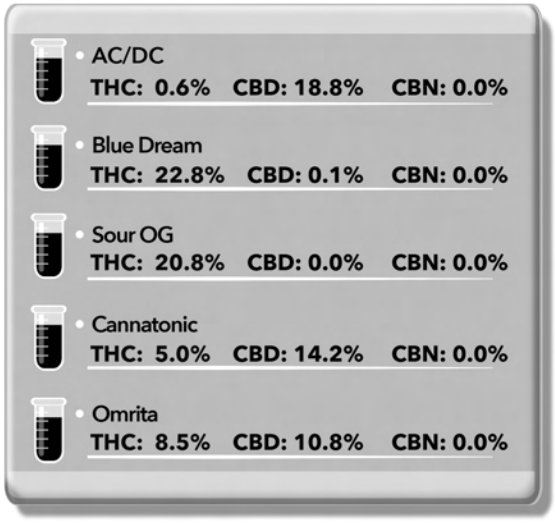


Figure 2: Cannabinoid potency test results for different cannabis chemovars

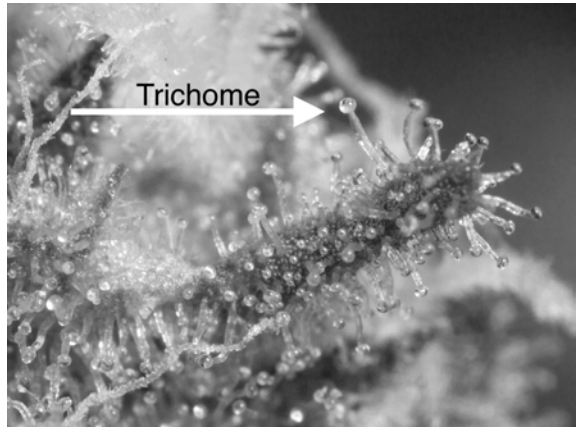
A few important notes about phytocannabinoids:

- Phytocannabinoids were initially thought to be species-specific to the cannabis plant, which meant that they were not found in any other plant species. However, phytocannabinoids other than THC have been discovered in a few other plants, namely Echinacea species, Helichysum species (sunflowers) and Radula species (liverwort).

- As mentioned above, the term "cannabinoids" is very general, and it refers to a specific group of chemical compounds. Cannabinoids are found naturally in two places: plants and animals. "Phytocannabinoids" refer to the cannabinoids that occur naturally in plants. "Endocannabinoids" refers specifically to the cannabinoids made by humans and other animals. Cannabinoids can also be synthesized in a laboratory setting; these are referred to as "synthetic cannabinoids" and are primarily used in research.
- Do not get confused about the acronym "CBD". CBD stands for "cannabidiol" not "cannabinoids". Many people incorrectly say "the CBDs". CBD is not plural. THC is not referred to as "THCs" because it is referring to one molecule. CBD also refers to one molecule. The acronym for the word "cannabinoid" is CB, which is used mostly in scientific papers.

How the cannabis plant makes phytocannabinoids:

The phytocannabinoids are formed and concentrated in a viscous resin in the plant's glandular trichomes, the tiny, sticky hair-like formations on the cannabis flower.



Close up of the trichome of the cannabis plant

It is inside the trichomes that the phytocannabinoids are formed.

1. Geranyl pyrophosphate is the precursor to both phytocannabinoids and terpenoids.
2. Geranyl pyrophosphate couples with olivetolic acid to produce cannabigerolic acid, which is then exposed to three enzymes – THCA synthase, which will create THCA; CBDA synthase which will create CBDA; and CBCA synthase, which creates CBDA.
3. THCA and CBDA are the acid forms of THC and CBD and are the predominant compounds in the raw flower of the cannabis plant.
4. THCA and CBDA change to THC and CBD, respectively, when they are exposed to heat. This chemical reaction is called decarboxylation.

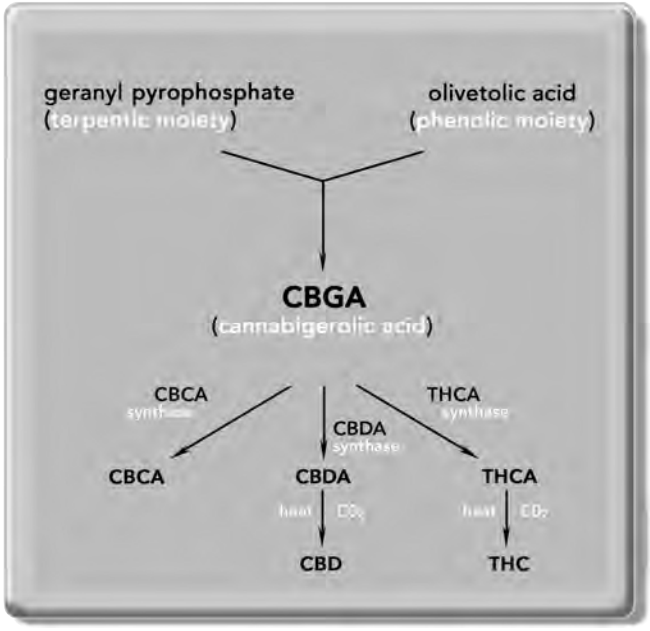


Figure 3: How the cannabis plant synthesizes phytocannabinoids

The majority of cannabis plants are genetically determined to take the pathway that leads to THCA. A small number of plants have the genetics that will lead to a higher amount of CBDA: we call these plants CBD-rich chemovars. This genetic dominance for THC explains why most cannabis is higher in THC potency and lower in CBD potency. The rampant cross-breeding of strains over the past three decades has also resulted in higher THC potency.

The Entourage Effect

Not all of the phytocannabinoids have been thoroughly studied, but those that have are found to have their own medicinal effects when isolated from the other phytocannabinoids. When used together as they occur naturally in the whole plant, they balance each other in a synergistic action first called "the entourage effect" by Raphael Mechoulam, PhD. Dr. Mechoulam, an Israeli researcher, was the first to isolate THC and CBD in the early 1960s. **The "entourage effect" means that the cannabinoids work better together than when isolated from one another. The synergy can enhance effects or modulate effects beneficially.**

Example of synergistic enhancement: both THC and CBD, when given separately, have been found to have pain-relieving properties, but studies show that CBD enhances pain relief when used together with THC, compared to THC used by itself.

Example of opposing effects: CBD can decrease psychoactivity, memory loss and the increased heart rate THC can induce.

What are Terpenoids?

Terpenoids (also called terpenes) are the essential oils that occur naturally and exist in all plants, trees and flowers, including the cannabis plant. These

oils give cannabis its odor, color, and flavor. About 200 terpenoids occur in the cannabis plant. **The unique combination of phytocannabinoids and terpenoids in a specific cannabis plant accounts for the varying effects felt when different types of cannabis plants are used.**

Terpenoids are made up of repeating units of isoprene (C_5H_8) and include monoterpenoids (C_{10}), sesquiterpenoids (C_{15}), diterpenoids (C_{20}), and triterpenoids (C_{30}).

Some important facts about terpenoids:

- They are genetically controlled
- Production increases with light exposure
- Production decreases as soil fertility decreases
- U.S. FDA recognizes terpenoids as safe
- Terpenoids vaporize near the same temperature as THC
- Concentrating cannabis into hash or wax may reduce the terpenes content and may cause medicinal effects to change
- Terpenoid lab analysis is the only way to know about a certain product's terpenoid levels

Phytocannabinoids and terpenoids work synergistically to provide therapeutic effects. Terpenoids are also synergistic with each other, again enhancing medicinal effects.

An example of a very important terpenoid is limonene. It is a monoterpene found in lemon and other citrus fruits and is the second most common terpenoid found in nature. Limonene has potent anti-depressant and anti-anxiety activity, as well as anti-tumor effects. It has been used successfully to decrease the symptoms of gastro-esophageal reflux.

This chart explains four of the most important terpenoids in the cannabis plant.

Terpenoid	Also found in:	Effects	Aroma	Synergistic with:
Limonene	Citrus rinds Caraway seeds Dill seeds Rosemary Juniper Peppermint	Potent anti-depressant Anti-anxiety Anti-tumor Chemotherapeutic (causes breast cancer cells to die) Active against acne bacteria Suppresses GERD Anti-bacterial/anti-fungal Bronchodilator	Orange Citrus Spicy	CBD – enhanced anti-depressant and anti-anxiety effects CBD & CBG – enhanced anti-cancer effects THC – enhanced anti-GERD effects
β-Caryophyllene often found in CBD-rich chemovars	Black pepper Cloves Cotton Oregano Hops	Anti-inflammatory Analgesic Gastrointestinal Relief Anti-bacterial Anti-fungal Anti-tumor *Activates the CB2 receptor located in immune system and gut (2008, Gertsch)	Woody Spicy	THC – enhanced gastric cell protection CBD – enhanced anti-inflammatory effect
Linalool precursor ingredient in formation of Vitamin E	Lavender Citrus Birch Coriander Rosewood	Anti-anxiety Analgesic Anti-convulsant Sedating, calming Active against acne bacteria Anti-cancer	Floral Spicy Citrus	CBD – enhanced anti-anxiety and analgesic effect THC – enhanced sedation and analgesic effect CBD/THCV/CBDV – enhanced anti-convulsant effect
β-Myrcene most common terpenoid found in cannabis not found in hemp	Mango Hops Bay leaves Lemongrass Eucalyptus	Sedating Muscle relaxant Analgesic Anti-oxidant Anti-cancer Anti-inflammatory Anti-depressant Anti-bacterial	Cloves Earthy Fruity	THC – may enhance effects of THC CBD – enhanced anti-inflammatory effects CBG – enhanced anti-inflammatory effects

Some examples of known synergies between phytocannabinoids and terpenoids:

- THC + CBD + **β**-Myrcene + **β**-Caryophyllene = Pain Relief
- THC + **β**-Myrcene + **β**-Caryophyllene + Pinene = ADD relief
- CBD + CBN + Limonene + Linalool = Insomnia and Anxiety relief

Terpenoid Testing

Cannabis plants can be tested for their terpenoid profiles as well as phytocannabinoid content. The terpenoid makeup of the plant is like a "fingerprint" for the strain. Different growers may be growing the same varieties but calling them different names, or they may be calling chemovars the same names yet terpenoid testing reveals that they are different. The terpenoid profile allows for detailed comparison of varieties and is very important to patients who find relief with one particular strain. If you know which terpenoids and terpenoid combinations are helpful for your condition, you can check terpenoid testing results to see if a certain product will be likely to be effective.

What are Flavonoids?

Flavonoids are compounds that give plants their pigmentation, filter ultraviolet rays, attract pollinators, and prevent plant disease. About 20 flavonoid compounds have been found in the cannabis plant. These compounds are classified as aromatic polycyclic phenols and have a 15 carbon skeleton.

Flavonoids have been shown in laboratory studies to have anti-inflammatory and antioxidant properties. They also have anti-fungal, anti-bacterial, anti-viral, anti-cancer and anti-allergic activity. Several studies in humans report the following benefits of flavonoids:

- Dietary flavonoid intake in the form of green tea decreased the risk of gastric cancer in women
- Intake of flavonoids were protective against smoking-related cancers
- Intake of flavonoids (anthocyanidins from berries and flavanols from green tea and cocoa) may lower the risk of type 2 diabetes and cardiovascular disease

Three of the main flavonoids that have been found in the cannabis plant and their properties:

Flavonoid	Medicinal Properties	Also found in
Quercetin	Potent antioxidant Anti-viral Anti-cancer effects	Red wine Green tea Berries Onions Buckwheat tea
Apigenin	Anti-anxiety Anti-inflammatory	Parsley Celery Chamomile tea Celeriac
Cannaflavin A	Potent anti-inflammatory	Unique to cannabis

Sativa versus Indica?

You may have noticed I have not mentioned the terms "sativa" and "indica" in the discussion of the plant. These terms are used frequently in the cannabis industry to designate the "two" types of cannabis plants that can have different effects. Currently cannabis growers and suppliers continue to use these terms, albeit incorrectly, referring to sativa plants as "uplifting and stimulating" and indica plants as "relaxing and sedating." Some say sativa plants cause a "brain high" and indica plants cause a "body high." Most

experts agree that due to extensive hybridization over the last three decades, these designations no longer apply.

If one uses the correct scientific nomenclature, *Cannabis sativa, variety sativa* refers to the hemp (fiber) variety of the plant, meaning that the genetics of this particular plant promote the growth of the fiber with very little THC production. These fiber varieties also carry the gene that allows the plant to synthesize CBD over THC. *Cannabis sativa, variety indica* scientifically refers to the variety of the plant that carries the genetics to synthesize THC instead of fiber, so called "drug" variety plants.

Aside from their genetics, cannabis plants are living entities that respond to their environment. Growing conditions, harvest time and other factors play an enormous role in the final product. This is why the same strain grown in different places by different growers under different conditions can result in different phytocannabinoid and terpenoid content. For instance, a chemovar grown outdoors in Northern California is likely to have a different profile than the same variety grown in a greenhouse in Colorado.

The best way to determine the effects of a particular plant or product is to first evaluate the content of CBD and THC, calculate the ratio of CBD to THC, and then look at the dominant terpenoids. This assessment will be much more informative than the simple and often incorrect terms "sativa" and "indica."

Hemp-Derived CBD

There are numerous products made from industrial hemp that claim to contain CBD for medicinal purposes. It can be very confusing to patients and caregivers who see products available online that claim to be CBD products that are legal in all states.

Martin Lee from Project CBD (ProjectCBD.org) explains that there are two types of cannabis plants: hemp plants that are used for fiber and seed

oil, and drug plants that are used for medicine and recreational purposes, what I prefer to call the "medicine" plants. As Lee explains, the main difference between the hemp variety and the drug variety is the content of resin. **High-resin plants contain the phytocannabinoids, terpenoids and flavonoids – all the compounds that have proven beneficial medical effects. Industrial hemp is low-resin and therefore typically low in cannabinoid content. Hemp is not an optimal source of CBD or other medicinal compounds.**

The US government has defined industrial hemp as containing less than 0.3% THC. The majority of high-resin plants, including CBD-rich plants, contain over 0.3% THC and therefore are still illegal federally and in most states. These high-resin plants are much preferred as medicine when compared to low-resin industrial hemp.

A large number of hemp plants are required in order to obtain a small amount of CBD. This increases the risks of contamination since hemp is a "bioaccumulator", which means it accumulates toxic substances from the soil. These plants can contain metals, pesticides, gasoline and solvents and, during the CBD extraction process, these contaminants may be concentrated and can be toxic. In fact, there are anecdotal reports of people getting ill from so-called "CBD" products made from industrial hemp.

The Hemp Industries Association in a press release in 2014 stated that:

> *CBD is not a product or component of hemp seeds, and labeling to that effect is misleading and motivated by the desire to take advantage of the legal gray area of CBD under federal law. Hemp seed oil does not contain any significant quantity of CBD. Hemp fiber and seed cultivars contain relatively minimal CBD and CBD production from such plants should not be considered a primary product. There are high CBD cultivars that may qualify as "hemp" under federal law, however the genetics for such cultivars are closely held by various parties, and generally hemp cultivars available to American farmers are not suitable for producing CBD.*
>
> *Source: http://www.thehia.org/HIAhemppressrelease/3346474*

In 2015, the FDA tested products obtained through the Internet, which claimed to contain CBD. They found these products to contain either no CBD or tiny amounts of CBD that would not be effective as medicine.

I encourage my patients to avoid products that come from industrial hemp as I have found that the drug (medicine) variety of cannabis is a much more effective product when treating most illnesses. That means patients should use whole plant cannabis that is labeled properly, lab-tested, and safely extracted. There are some products that are labeled as hemp but they contain THC, other cannabinoids and terpenoids. These products may have medicinal value. Unfortunately there is still a fair amount of confusion even within the cannabis industry. Hemp products, such as hemp milk, hemp oil, and hemp seeds, which are available in most grocery stores are a beneficial dietary source of balanced omega-3 and omega-6 fatty acids and should be a part of your diet.

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