With the burgeoning cannabis industry growing at an astounding rate, the familiar hemp oil products of the past are losing the spotlight to CBD oil, edible concentrates, and vape pens. These can contain a multitude of untested ingredients and mixtures, and with dubious media claims all over the internet, it is important to find accurate information about how cannabis can help your clients. To help you make an informed decision about how and when to incorporate cannabis into a health regimen, it is important to first dispel some widespread misconceptions and develop a working knowledge of the interplay between cannabinoids, terpenoids, and the endogenous cannabinoid system (ECS), which is present in all vertebrates. Once you have a basic understanding of CBD, THC, and the other constituents of cannabis, the numerous products on the market won't seem so perplexing.

Cannabis "Varieties"

Perhaps the most widespread and misleading myth surrounding the uses and effects of cannabis lies in whether the plant is a *sativa* or an *indica. Cannabis sativa*, many people believe, produces more of a head-trip effect (mind racing, heart pounding), whereas *Cannabis indica* is associated with a more sedating effect (chill on the couch and relax). This is absolutely untrue, though many products on the market today perpetuate this myth by selling "sativa" oils and "indica" oils.

In actuality, it is the mixture of phytocannabinoids and terpenoids, which interact with our own endocannabinoid system, that create these sensations. These mixtures vary widely across both species, and there is an ongoing discussion among medical researchers and botanists about whether or not the distinction between *sativa* and *indica* is even relevant anymore. To make intelligent recommendations to your clients, you must move beyond these broad and disputed categories and develop an understanding of the underlying chemovars and the effects they have on our ECS.

Phytocannabinoids

There are several chemovars found in cannabis, but the primary phytocannabinoids are tetrahydrocannabinol (THC) and cannabidiol (CBD). Prohibition has made research difficult and only now are we beginning to learn about these compounds and their complex interactions with each other and with our ECS. Until more is known, be aware that products claiming to have certain effects based on their cannabinoid profiles are unlikely to be backed by science.

THC

Delta-9-tetrahydrocannabinol (THC) is the component in cannabis that elicits the euphoric yet sometime uncomfortable "high." High-THC cultivars are in large supply as prohibition led to illicit cannabis farming and growers bred for recreational purposes, which led to a higher THC content.

Thankfully, THC has many other benefits, including bronchodilation, neuro-protective antioxidant stimulation for brain injuries and strokes, anti-inflammation without COX-1 or COX-2 inhibition, muscle relaxation, anti-emetic uses, and the reduction of the b-amyloid plaques that are found in Alzheimer's.

The appetite-stimulating effects of THC were confirmed in a long-term study of 94 AIDS patients. Of the patients who completed the trial, 25% achieved a weight gain

of 2 kg or more during a 12-month period (Beal et al., 1997). Oral THC has been found to be effective against cancer pain in doses of 15 mg and 20 mg in two clinical trials, although some participants reported intolerable side effects such as dizziness, confused thinking, and panic. (Regelson et al., 1976) A clinical trial of inhaled cannabis for neuropathic pain showed that low potency (3.5% THC) and high potency (7% THC) cannabis had equivalent analgesic properties. (Wilsey et al., 2014) The discovery that higher THC percentages are not necessary for pain reduction is significant since THC can induce uncomfortable feelings for some patients.

Despite these early and encouraging results, there is a lot of controversy surrounding the laboratory testing of THC. To date there is no standard for testing and there are large differences in THC percentages from lab to lab. The desire for high-THC strains in recreational use has spilled over into the medical field, and there is market pressure for dispensaries and edible-product companies to use laboratories with high percentages of THC in their products. But as we examine the synergy of cannabinoids and terpenoids, we will see that THC is not the only important constituent in cannabis.

CBD

Cannabidiol (CBD) is the most common phytocannabinoid in hemp or fiber plants, and unlike THC, it does not have any psychoactive properties. Research has shown its medical uses to be quite varied. It has been found to be effective against methicillin-resistant *Staphylococcus aureus* (MRSA) (Appendino et al., 2008); as an anticonvulsant (Jones et al., 2010); and as an analgesic (Costa et al., 2006). It has been shown to reduce anxiety (Russo et al., 2005) and it is cytotoxic against breast cancer (Ligresti et al., 2006).

Its neuroprotective antioxidant properties are well established and have been found to be more potent than ascorbate (Vitamin C) or tocopherol (Vitamin E) (Hampson et al., 1998). In fact, the U.S. Health and Human Services has a patent on cannabinoids as antioxidants and neuroprotectants (US 6630507 B1; 2001)—a direct contradiction to the government's continued classification of cannabis as a Schedule I drug (no medicinal value and a high potential for abuse).

CBD has also been shown to help reduce the occurrence of seizures in infants, as with Epidiolex, a CBD drug developed by GW Pharmaceuticals for the treatment of Dravet syndrome, which is still in the clinical trial phase. Research has also discovered anti-seizure properties in vitro and in vivo and CBD has shown anti-convulsant effects in animal models of temporal lobe and partial seizures (Jones et al., 2010). The mechanism for CBD treating seizures is not fully understood.

Many other properties have been attributed to CBD, including bone-growth stimulation and the reduction and prevention of the spread of pain. As an auto-immune protectant, CBD antagonizes tumor necrosis factor, which is present in autoimmune disorders like rheumatoid arthritis. It has also been found to inhibit the activity of THC (Russo & Guy, 2006), which can reduce some of the undesirable side effects of THC reported by patients.

We are still in the early stages of understanding optimal dosing and the proper application of cannabis products. Early indications have produced a recommendation of beginning with 0.1 mg/kg/day and gradually increasing the dosage by small increments.

Further research and experimentation will help us determine better dosage information to speed healing time for our clients.

CBG, CBN, CBDV & THCV

Though less studied than CBD or THC, several other phytocannabinoids have also been identified. Cannabigerol (CBG) has been found to antagonize prostate cancer and work as an analgesic (De Petrocellis & Di Marzo, 2010). It is a GABA-uptake inhibitor (Banerjee, 1975) and antidepressant properties have also been found. Cannabinol (CBN) is an oxidative byproduct of THC and is a sedative and anticonvulsant (Turner et al., 1980). It is effective against MRSA (Appendino et al, 2008), and can be useful for treating burns. Cannabidivarin (CBDV), too, is an anticonvulsant (Jones et al., 2010), as is Tetrahydrocannabivarin (THCV), which has been shown to be effective in treating metabolic syndrome (Cawthorne et al., 2007; Riedel et al., 2009). Again, further research into these compounds and their interactions promises great potential effects.

The Endogenous Cannabinoid System

The endogenous cannabinoid system (ECS) is a network of neuro-modulation receptors within our brains, immune systems, and other parts of the body. Our ECS is a hemostatic regulatory system essential for key processes like pain, appetite, memory, and mood and pain regulation. It plays a hand in regulating mitochondrial activity and in neurogenesis. Three components of ECS are known: endogenous cannabinoids (endocannabinoids); cannabinoid receptors (CB1, CB2, TRPV1); and the enzymes that synthesize and degrade endocannabinoids.

Endocannabinoids are ligands that bind to cannabinoid receptors to stimulate and regulate a variety of functions. The two most significant endocannabinoids to date are arachidonylethanolamide (anandamide) and 2-arachidonylglycerol. Anandamide is a fatty acid neurotransmitter which has been called the “bliss molecule” because of its effects. Notably, anandamide has been shown to inhibit breast cancer cell proliferation by inhibiting DNA synthesis (De Petrocellis et al., 2011).

Cannabinoid receptors are neuro-modulating receptors that halt neurotransmitter release upon binding with an endocannabinoid. CB1 receptors, which are psychoactive, are the most abundant receptors in the brain. Most CB1 receptors are found in the limbic system, cerebellum, and cerebral cortex. Non-psychoactive CB2 receptors are found in immune tissues like leukocytes, the spleen, and tonsils, and in the heart, bones, and muscles. They are expressed in the brain when injury or disease occurs, such as multiple sclerosis (MS). As immuno-modulatory receptors, they are important in reducing pain and inflammation. CB2 agonist drugs have been shown to be effective for hepatic fibrosis and other fibrotic conditions.

CB1 and CB2 receptors are also in the gut, where they help modulate propulsion and secretion, and are distributed along the skin where they modulate pain and inflammation. TRPV1 receptors mediate pain signals and therapeutic agents that work on this receptor may reduce neuropathic pain.

The ECS is triggered by a variety of external sources, including herbs, foods, and even aerobic exercise. Metabolism and digestion are also factors in the functioning of ECS, as cannabinoid receptors affect the digestive system.

Phytocannabinoids and the ECS

The various phytocannabinoids interact with the ECS at the cannabinoid receptor sites to induce a variety of biological and psychoactive effects. THC, THCV (at higher doses), and anandamide are all CB1 agonists and elicit the euphoric effects of cannabis. CBD has the opposite effect—it antagonizes the CB1 receptors, reducing the psychoactive effects of THC. CBG has also been shown to have agonist effects on both CB1 and CB2 receptors, though its effect is weaker than THC's. This self-balancing regulatory system provided by the cannabis plant is one reason using whole plant medicine may be more beneficial than standardized extracts of phytocannabinoids.

Knowledge of the ECS and the effects phytocannabinoids have upon it can quickly help you separate fact from fiction in an unregulated marketplace where manufacturers often make dubious claims or tout measurements that have little basis in science. As you make decisions about how to incorporate new cannabis products into your practice it is important to know the correct phytocannabinoid profiles to ensure consistency in treating specific conditions. Not only is the source important, but as with any other botanical product, each harvest can yield a slightly different profile due to environmental conditions. The more information you can acquire, the better equipped you will be to help your clients.

Terpenoids

Beyond the phytocannabinoids, cannabis also contains terpenoids—over 200 have been discovered. We are already familiar with the therapeutic properties of common constituents like a-pinene in pine needles, d-limonene in citrus, and b-caryophyllene in carrot seeds, and these are among the many constituents also found in cannabis. Research into these and into the ways in which cannabis interacts with other oils and terpenoids could well yield dramatic results. According to neurologist and cannabis researcher Ethan Russo (2011), some of these phytocannabinoid-terpenoid entourage effects could well come from the interaction of cannabis with frankincense, citrus oil, lavender, spearmint, pine, black pepper, rosemary, sage, and others (Table 1). **[Insert Table 1 here]** As we learn more, terpenoids in cannabis and their effects will contribute to the plant's emerging demarcation, leading to more sophisticated products and better marketing.

Cannabis Products

There are countless cannabis products on the market today. Many of these are unregulated and the manufacturers behind them have no experience or education in phytochemical interactions. Until there is more regulation and greater understanding about the benefits and entourage effects of phytocannabinoids, it is wise to purchase only cannabis-extract products that have undergone rigorous third-party testing and provide a certificate of analysis.

CBD oil has become very popular for children and young adults with seizure disorders and is sold across the country without much regulation. Many of the claims attributed to CBD oil are not unfounded, yet it is important to remember that it is not a panacea and common sense should be applied when working with these oils. As with all herbal products, it is important to know your source and ask about growing

practices, pesticide use, and application and extraction methods.

Not only are many of the claims about cannabinoid profiles spurious, there are also significant health concerns with ingestion. Cannabis is an effective phytoremediator, which means it draws heavy metals and other toxins out of the soil. Tests have shown that THC may concentrate these heavy metals so it is very important to know the source of the cannabis in the products you purchase. Cannabis also contains iron and there is some concern about iron levels and consumption.

The lack of regulation of cannabis has allowed producers of cannabis oil to sell medical and retail cannabis products with solvent and pesticide residue, adulterants, and contaminants. Edible cannabis products are usually made with solvent-extracted hash oil. Besides the residual solvent and pesticides, they may also contain GMO ingredients, refined flours or sugar, and other unhealthy ingredients.

It is also important to remember that flavored cannabis products often contain hexane-extracted terpenoids that were added after the fact, as is popular within the food industry. A better approach would be to breed cannabis for specific terpenoid profiles instead of adding them.

Inhaled cannabis oil products like vape pen cartridges often contain propylene glycol as an additive and the cannabis oil itself is often solvent- or CO^2-extracted. Residual solvent left in the product is always a concern, as inexperienced people are making the extractions in unregulated laboratories. With CO^2 extract, it is important to know what pesticides were used to avoid contamination in the products.

Conclusion

As our understanding about phytocannabinoids and their potential interactions with other plant compounds and with our endocannabinoid system evolves, so will the marketplace for cannabis products. There is still much to discover about how phytocannabinoids and terpenoids interact with our own ECS. With the potential for pesticide and solvent residue prevalent in current products, there is a need for more education, discernment, and common sense when choosing safe products, especially for clients with debilitating conditions and weakened immune systems. The potential for cannabis to heal is evident in the regulatory pathways stimulated by this plant, but before purchasing from any supplier, make sure you learn where the plant material came from and which solvents were used for extraction, and obtain a certificate of analysis and any other laboratory testing reports available. Only with the highest standards can we realize the full healing potential of cannabis for our clients.