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An Overview of Known Qualities, Effects and Laws of Cannabidiol (CBD)



Introduction: Recently there have been numerous reports in the media about various cannabidiol (CBD) products and their purported medicinal affects. In Denver, Colorado, where medical and recreational marijuana are legal, such products have been called a miracle cure for Dravet Syndrome, a severe form of epilepsy in the pediatric and adolescent population. Some people are uprooting and relocating their families to the Denver area to gain access to these products for the treatment of their children who are afflicted with Dravet Syndrome and other seizure disorders.¹ Unfortunately, to date there has been no animal or human testing to substantiate these claims of efficacy for such products who have not gone through Food and Drug Administration (FDA) requirements. Currently there are no standards in place for the quality or composition of these products. This report focuses on the known qualities, effects, laws, and misconceptions surrounding cannabidiol (CBD) and its relationship to tetrahydrocannabinol (THC), as well as the impact on patients and their families.

Non-approved and illegal CBD products: There are numerous companies that have bypassed the Food and Drug Administration process (FDA) and produce CBD products that are purported to cure or reduce seizures in children. However, there is only one known company to date that is undergoing FDA trials with outcomes supporting such claims. The composition of the products from the unregulated suppliers is of uncertain quality and can contain significant amounts of THC and other adulterants.

The problem with the products for seizure conditions that contain THC is that there is strong evidence that THC can be pro-convulsant (inducing seizures) in already sensitive brains. Other research indicates that THC can negatively impair IQ if taken chronically by children and adolescents.² Lately, physicians have begun to report instances where their adolescent patients experienced high anxiety, increased seizures, and insomnia due to adulterants in these non-regulated products. Recently parents have taken to the internet to voice their concerns that the batches do not have a consistent effect, that their children are becoming intoxicated or “high”, and/or that their child’s seizures are worsening.

The exact ratio of CBD to THC in all non-regulated products is unknown, however, one product reportedly contains a 20:1 CBD to THC ratio. To get an understanding of how much THC can be in one of these non-regulated products, we can look to an FDA product; Marinol, which is a synthetic form of THC developed in the 1980’s for treatment of nausea and vomiting in cancer chemotherapy patients and later for wasting disease in HIV/AIDS patients. Marinol has a standard adult dosage of 10 mg per pill. The common daily dose of CBD in FDA-approved trials for an average-size child/adolescent (110 pounds) with Dravet syndrome is 400 mg, which, at 20:1 ratio would expose a child to 20 mg of THC, the equivalent of a multiple adult dose of Marinol.

Example of Dosages of Non-approved Product

20 CBD to 1 THC =

400 mg CBD =20 mg THC

20 mg THC = 2 Marinol capsules

The graph (box) above shows the amount of THC in the dosages given to children with epileptic seizures. This amount of THC could cause seizures as indicated on the Marinol list of precautions and contraindications:

“Be sure to tell your doctor if you have a history of seizure disorders and /or seizure-like activity because this has occurred in people taking MARINOL. If you experience a seizure, stop taking MARINOL and seek medical attention immediately.”³

In a recent Wall Street Journal article titled “Marijuana Extract for Children with Epilepsy is Questioned,” by Arian Campo-Flores, it is headlined that as more states move to legalize cannabidiol, early research shows that in some cases the substance failed to help and even worsened others. Kevin Chapman, a neurologist at Children’s Hospital Colorado and co-author of a study released at an American Epilepsy Society meeting in December, said “We don’t have enough data at this point to recommend marijuana products for families.”⁴ Most anecdotal claims of the positive effects of CBD on patients have reportedly been from those who moved to Colorado for treatment and may in part be experiencing a placebo effect.

American Epilepsy Society Position on CBD: The American Epilepsy Society reports that they do not know if marijuana is a safe and effective treatment for epilepsy, which is why they support studies using well-founded research methods that all other effective treatments have undergone. Such safety concerns, coupled with a lack of evidence of efficacy in controlled studies, result in a risk/benefit ratio that does not support use of crude or adulterated marijuana products for treatment of seizures at this time.⁵

What is CBD? CBD is one of the more than 66 cannabinoids found in the (marijuana) plant.⁶ CBD does not cause THC-like psychoactivity; in fact, only THC causes intoxication. CBD has been bred out of high-potency, modern recreational cannabis, however there has been recent interest in its therapeutic qualities. As a result, a number of breeders claim to produce “high CBD” strains being used in these non-regulated CBD products. The suppliers of CBD products proclaim that THC synergizes the healing effects of CBD, but there is no valid research to support this claim. A possible reason for this claim is that it is extremely expensive and difficult to extract virtually pure CBD, leaving THC out of the product.

How does CBD work? CBD works through a number of complex mechanisms. Preclinical studies indicate that CBD has analgesic (pain-relieving), anti-convulsant, anti-psychotic and neuroprotective effects. Unlike THC, it does not readily bind to the CB1 or CB2 cannabinoid receptors in the human brain, which is why it does not cause THC-like psychoactivity.⁷

What is the legal status of CBD? CBD is a cannabinoid of the cannabis/marijuana plant and is therefore a Schedule I substance under the federal Controlled Substances Act (CSA). The FDA (U.S. Food and Drug Administration) has recently confirmed that CBD is a Schedule I substance. Schedule I includes those substances that have a high potential for abuse, have no currently accepted medical use in treatment in the United States, and lack accepted safety for use under medical supervision.⁸

What is hemp and its legal status? Hemp is a variety of cannabis that is grown for its fiber, seed, or both. Under European law, true hemp has 0.3% (3/10 of 1%) THC, and very low levels of CBD (1.5-2%). The cannabinoids (including CBD) are contained in small hair-like appendages called trichomes. A few of these are found on (not in) the stalk of the hemp plant. **However, the greatest concentration of CBD is found in the flowers and leaves of the plant.** Therefore, it would take a great deal of hemp plant material to produce a meaningful amount of CBD. “High CBD cultivars” very likely contain too much THC to qualify as hemp as it is very difficult to breed a plant that has more than a 20:1 CBD to THC ratio.⁹

According to the Controlled Substances Act (CSA), marijuana is defined as: “all parts of the plant *Cannabis sativa* L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. This does not include the mature stalks of such plant fiber produced from stalks, oil or cake made from the seeds of such plant, any compound, manufacture, salt derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant is incapable of germination.”¹⁰

What is hemp seed oil? True hemp seed oil contains virtually no cannabinoids, which is why it can be sold legally in the U.S. as a dietary supplement. The US department of Agriculture indicates that hemp seeds can be used directly as a food ingredient or crushed for oil and meal. The seeds contain 29 to 34 percent oil and consist of three fatty acids: linoleic (53-60 percent), linolenic (15-25 percent), oleic (8.5-16 percent).¹¹

What is “CBD hemp oil? Is it a legal dietary supplement? Since true hemp contains very low levels of CBD and hardly any THC, so called “CBD hemp oil” is most likely produced from “high CBD” plants, which would not qualify as hemp because they would have more than 0.3% THC (or from massive quantities of hemp flowers, which still fall within the definition of marijuana). As indicated above, it is very difficult to breed a plant that has a significant amount of CBD without also having some THC; achieving ratios greater than a 20:1 CBD to THC is unlikely. These “high CBD” plants also contain varying amounts of THC (e.g., CBD to THC ratios of 1:1, 10:1, 20:1, etc.), therefore any hemp oil containing high CBD is being manufactured and sold illegally.¹² Even CBD extracted from true hemp flowers and diluted with hemp oil is still a Schedule I substance. The graphic below is an example of such a product.



The U.S. Code of Federal Regulations (CFR) provides that certain processed cannabis plant material or animal feed mixture that **contain THC** are exempted from the CSA if they are 1) made from the part of the plant excluded from the definition of marijuana and 2) **not used or intended for use for human consumption**. This clearly indicates that any products containing THC (even small amounts) that are used/intended for human consumption are illegal. **It is entirely false to claim that CBD-rich hemp oil products are legal nutraceuticals.**¹³

Are Unregulated CBD products safe? “High CBD” plant material contains varying levels of THC, sometimes significant amounts, which most simple extraction processes can’t reliably remove. Extremely complex and expensive equipment is required to adequately remove THC to produce a pure “high CBD” extract. Research demonstrates that, in many cases, large doses of CBD are needed to achieve a specific therapeutic effect, so most products made for this purpose would also include dangerously high levels of THC.

Epidiolex: Epidiolex is a product made by GW Pharmaceuticals headquartered in the U.K. It is an oral liquid formulation made of a highly purified extract of a high-CBD strain of the cannabis plant. The extract is passed through several complex purification steps to remove the THC. The product contains virtually pure CBD and

infinitesimal amounts of THC. Epidiolex has been tested in a wide range of rodents with epilepsy and has exhibited a substantial body of safety data. The product has also been tested on human subjects, and physicians have reported efficacy and safety data on 58 children and young adults with treatment-resistant epilepsy. This data is from three hospitals in the U.S. that have been authorized by the FDA. Recently, the FDA has approved a total of 20 hospitals to use Epidiolex to treat over 470 such patients. Epidiolex has not yet been approved by the FDA as a prescription medication and therefore is going through a program of randomized, placebo-controlled trials under an Investigational New Drug (IND) and is available free of charge for patients in FDA-approved studies.¹⁴

Conclusion: The use of marijuana in pediatric populations remains an ongoing concern due to the known medical, psychological, and cognitive side effects it can cause. In many cases, purportedly “high CBD” products may also be contaminated by pesticides, synthetic fertilizers, heavy metals, and dangerous microbes, which can also be quite hazardous. Legislators, policy makers, law enforcement and the public need to be made aware of these non-regulated CBD products that are being marketed as medication but actually contain high levels of THC. These products can be unsafe and may cause seizures and other adverse effects. Support should be given to companies that go through the FDA process such as GW Pharmaceutical, the producers of Epidiolex, which is currently available through the FDA’s (IND) program and has shown encouraging evidence of efficacy and safety.

True hemp seed oil does not contain cannabinoids and therefore is legal and can be used as a dietary supplement. CBD hemp seed oil is being fraudulently sold as a legal substance despite the fact that to contain any substantial amount of CBD, it would have to contain more than 0.3% THC or, alternatively, has been extracted from hemp flowers, which are classified as marijuana.

Please stay tuned for future reports on topics surrounding Marijuana and its impact on health, policy, and its overall impact on various U.S. populations.

¹ “When medical Marijuana Doesn’t Work”, *WEBMD Health News* by R. Scott Rappold, Reviewed by Arefa Cassoobhoy, MD, MPH.

² Solowij, N., et al (2002). *Cognitive functioning of long term heavy cannabis users seeking treatment*. Journal of the American Medical Association, 287, 1123-1131., and Scweinsburg AD, Brown, AS, & Tapert, SF (2008). *The influence of cannabis use on neurocognitive functioning in adolescents*. Current Drug Abuse Reviews, 1:99-111.

³ 1. MARINOL [prescribing n=information]. 2. MARIONOL [patient information] 1301985-1212105

⁴ <http://www.wsj.com/articles/marijuana-extra>

⁵ www.ASESNET.org

⁶ ElSohly, M.A. *Chemical Constituents of Cannabis and Cannabinoids Pharmacology, Toxicology and Therapeutic Potential* (Grotenhermen, F. and Russo, E., eds.), Haworth Press, New York, pp. 27-36. 2002.

⁷ Janet E. Joy, Stanelly J. Watson, Jr., and John A. Benson, Jr., editors, *Marijuana and Medicine – Assessing the Science Base*; Division of Neuroscience and Behavioral Health, Institute of Medicine., National Academy Press.

⁸ 21 U.S.C. 812(b)(1)(A)-(C), 74 FR 40552; 66 FR 20038

⁹ Johnson R., *Hemp As An Agriculture Commodity*, Congressional Research Service (Washington, DC: Library of Congress, July 24, 2013), pp 1-2. <http://www.fas.org/sgp/crs/misc/RP327525.pdf>.

¹⁰ The Federal Register, http://frwbgate.access.gpo.gov/cgi-bin/getdoc.cgi-bin/getdoc.cg?dbname=2001_register&docid=01-25024-filed

¹¹ ElSohly M.A., *Marijuana and Cannabinoids*, Humana Press Inc.

¹² US Code of Federal Regulations (CFR)

¹³ US Code of Federal Regulations (CFR)

¹⁴ http://www.accessdata.fda.gov/scripts/oodp/OOPD_results_2.cfm?Index_Number=408313 and more recently for treatment of Lennox-Gastaut syndrome: http://www.accessdata.fda.gov/scripts/plisting/oodp/OOP_Results_22.cfm?Index_Number=4212