

Hemp & Cannabidiol: What is a Medicine?

by R. L. Hilderbrand PhD



The current motivation of claims and advertising appears to be the financial reward to the marijuana industry rather than the health and well-being of the consumer.



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Colorado allowed medical marijuana for debilitating medical conditions effective in 2000 by an amendment to the Colorado Constitution.¹ The *Colorado Code of Regulations (CCR) Medical Marijuana Rules*, 1 CCR 212-1, establishes the regulatory framework for medical marijuana, primarily focusing on tetrahydrocannabinol (THC) as the active drug.² Approval of retail marijuana then passed in Colorado with Amendment 64 effective December 2012.³ The references above are listed to identify three salient factors: 1) The constitutional amendments allow a variety of marijuana preparations including concentrates, mixtures, preparations and infused materials *with no restrictions on concentration*; 2) The 1 CCR 212-1 for some inexplicable reason states “Medical Marijuana-Infused Product” means a product infused with Medical Marijuana that is intended for use or consumption other than by smoking, including but not limited to edible products, ointments, and tinctures. Such products *shall not be considered a food or drug for purposes of the “Colorado Food and Drug Act.”* Thus, a marijuana extract that is widely advertised and distributed as a “medicine” and is frequently included as an infusion in a food product is exempt from Colorado food and drug rules; and 3) Industrial hemp is exempted from the rules applicable to medical marijuana and the *final extracts are not controlled* by Colorado. These three factors create a regulatory abyss that Colorado has not successfully managed. In

addition, the federal government has allowed the states with “legalized” retail marijuana to regulate and enforce the rules related to marijuana without federal interference, as long as the state has implemented strong and effective regulations.⁴ The quality, contents, and concentrations are suspect both in extracts of marijuana⁵ and hemp.⁶

In an attempt to differentiate between cannabidiol (CBD) from marijuana and CBD from hemp, some definition and limitations must be provided. Extracts from marijuana (*Cannabis sativa* with THC concentrations greater than 0.3%) produced as a “medical product” are regulated by the Marijuana Enforcement Division in Colorado and are subject to testing for contents and contaminants. Hemp (*Cannabis sativa* with a THC concentration less than 0.3%), having been excluded from medical marijuana rules, has been given to the Colorado Department of Agriculture (CDA) to manage and regulate. CDA’s regulatory role with industrial hemp is limited to cultivation; CDA registers land areas for the intended use of growing and cultivation of industrial hemp. The CDA does not have jurisdiction over the processing, sale or distribution of industrial hemp and CDA does not license or verify contents or quality of any extracted product.

CBD as an Extract from Hemp

The focus of this article is CBD extracted from hemp which is generally defined as *Cannabis sativa*

with a total THC less than 0.3% dry weight in leaves and buds. I emphasize that the only distinction between marijuana and hemp is the concentration of THC. A quick calculation for illustrative purposes shows that when hemp containing 0.3% THC and 5.0% CBD is subject to extraction the final product will contain THC as about 6% of the CBD, since the THC and CBD are removed in an essentially similar manner. The extracted product may contain other cannabinoids, residual solvents, oils from the plant, herbicides or pesticides and other organic molecules. The significant point is that an extract of hemp that is not purified

and monitored will certainly contain some concentration of THC. Effective January 13, 2017, the Drug Enforcement Agency (DEA) created a new controlled substances code number (7350) for marijuana extracts.⁷ The



DEA ruling is very clear that extracts of “any plant of the genus Cannabis, other than the separated resin” are included in Code 7350 in Schedule I of the CSA. This clearly includes extracts of hemp, which is a variety of the Cannabis plant; the US Court of Appeals for the 9th Circuit Court denied a request by petitioners to review the DEA final rule.⁸ The DEA also notes there is no way to fully separate the THC from the CBD in extracts from the hemp. As a result, the CBD extracted from hemp remains a Schedule I substance.

The hemp industry, increasingly referred to as ‘Big Weed,’ is working to make CBD much more than a purported medication and is developing it in the US market as a food supplement that is widely used. Charlotte’s Web™ is an extract of hemp that has been widely touted as an option for treating seizures as well as a range of other medical conditions.⁹ The cultivar used by the Stanley Brothers is advertised to have a high-CBD content, which was specifically cultivated for a young epileptic patient named Charlotte.¹⁰ This case is instructive as to the claims made by the Stanley Brothers

Social Enterprises, LLC, on various websites that implied their products were treatment for depression, cancer, diabetes and other conditions. On October 31, 2017, the FDA, Division of Pharmaceutical Quality Operations IV, issued a warning letter to Joel Stanley, CEO, Stanley Brothers Social Enterprises to correct the claims that the products are drugs and intended to diagnose, cure, mitigate, treat or prevent disease.¹¹ In addition to being new drugs, the products were misbranded. The company has now modified their claims and provided disclaimer statements.¹² On the same date, the FDA issued similar

letters concerning misbranding of CBD to That’s Natural! Marketing & Consulting, Pueblo, CO¹²; Natural Alchemist, El Dorado Hills, CA¹³; and Greenroads Health, Pembroke Pines, FL.¹⁴ The City of Denver has established rules that apply to all CBD products sold or manufactured in the city.¹⁵ This is a step

forward to protect consumers from contaminated CBD or CBD from uncertain origin and improper preparation.

A significant challenge in current research and to any current consumer is to know and verify the composition of the material being studied or used. An anecdotal event of a study of a “pure” CBD that was sent for testing was found to be about 75% CBD. In Colorado the cannabinoids being sold at state approved dispensaries and used in oils and edibles may be augmented with CBD extracted from hemp – perhaps to reach a 1:1 ratio of CBD:THC. Testing of purity of these dispensary products should be completed; however, the CBD extracts from hemp may be sold to smoke shops or head shops with no regulation or testing. Purity and composition should be a very real concern to any investigation of CBD and certainly to any consumer.

CBD as a ‘Medicine’

The view of CBD as a medicine that is demonstrated by the claims of the companies that are producing and selling CBD on a national scale is stunning. This

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acceptance of, and advocacy for, the wildly inflated claims of benefits, seemingly by a large percentage of the general population of this country, leads to the need for an assessment of the actual benefits and adverse consequences. We have come to expect medications that are pure, of known and somewhat consistent efficacy, of a known mechanism, and from a manufacturer that is liable for the quality of the medication. At this time, most products marketed as CBD are suspect.

An exception is Epidiolex[®]. Epidiolex[®] is a pure CBD liquid formulation that is produced by GW Pharmaceuticals in the UK.¹⁶ In June 2018 this CBD formulation was approved by the FDA for the treatment of two rare, severe forms of epilepsy (Lennox-Gastaut Syndrome and Dravet Syndrome.) GW Pharmaceuticals has received a number of patents that apply to the Epidiolex[®] which has a purity of at least 98% (w/w) CBD and THC is less than 0.15% (w/w) at a dose of 10 mg/kg/day.¹⁷ As is appropriate for a medicine, the Epidiolex[®] is of known purity and concentration and the efficacy has been evaluated by studies approved by the FDA. These patients will be under the care of a physician that will monitor and determine efficacy of the treatment. Epidiolex[®] is also being evaluated as treatment for other conditions. This scientific approach to providing a medicine is in distinct contrast to the products being produced in many Colorado fields and barns by growers with no knowledge of quality control, extraction processes, contents, and quality of the final product, or the efficacy of the final product. The question is how aggressively GW Pharmaceuticals will address patent protection actions?

A basic literature search of PUBMED displays numerous articles published in the last 25 years that propose a potential benefit of CBD as a medication for many purposes. That literature is too extensive to summarize here; however, a recent publication by S. Pisanti, et al. provides extensive information and references pertaining to CBD.¹⁸ A significant concern is the proposal to use CBD as medication to treat the opioid epidemic.¹⁹ Colorado statistics show a corresponding increase in the opioid epidemic and the use of cannabinoids, but no decline in opioid use with the legalization of marijuana.

A 2017 study looking at market share of products by a Cannabis investment group finds CBD is being used to replace traditional pharmaceuticals. The top conditions being treated included anxiety (67%), insomnia (60%), joint pain and inflammation (52%) and depression

(43%). Respondents preferred CBD derived from cannabis to CBD derived from industrial hemp and only 9% of respondents indicated using hemp-derived CBD exclusively.²⁰ The preference for CBD from Cannabis is significant because, without purification, the CBD extracted from Cannabis will, most likely, contain a much higher percentage of THC than does CBD from hemp.

Summary

All physicians must be aware of the impact, not only of THC, but of CBD on treatment and prescribing of pharmaceuticals to CBD consumers. The advertisements of over-the-counter CBD product as pure, as miracle treatments for a plethora of diseases and as fully legal to sell are blatantly false. The recent approval of Epidiolex[®] for Lennox-Gastaut Syndrome, and Dravet Syndrome is the sole FDA approval of a CBD as a pharmaceutical. The efficacy of CBD for the many other proposed therapeutic uses has to be proven with legitimate scientific controlled studies. The companies that are advocating for CBD as a generally available health supplement are ignoring the Controlled Substances Act and the likely contamination with THC. CBD remains with a Schedule 1 classification and may place consumers, with no knowledge of the contents of the products, at risk. In a recent address at Institute of Cannabis Research, Dr. Di Marzo stated that the only effect of THC is to make a consumer high; thus, the CBD is the phytocannabinoid with the greatest current possibility to be useful as a medicine. Pharmaceutical preparations of CBD may ultimately be useful; however, current motivation appears to be the financial reward to the CBD industry rather than the health and well-being of the consumer.

Update

Following the Letters of Warning from the FDA, the Colorado Governor signed House Bill 18-1295 into law on May 30, 2018. This bill is significant and alarming in the attempt to prohibit the FDA from acting to control products containing industrial hemp. The bill is intended to establish, with no scientific analysis, that products are not (cannot be) adulterated or misbranded if they contain industrial hemp. HB 18-1295 defines “industrial hemp product” as a finished product containing industrial hemp that is a cosmetic, food, food additive, or herb and is for human use or consumption and contains ... any part of the hemp plant (including extracts) but the finished product contains *THC at a concentration less than*

0.3 percent. A concentration limitation does not control the dose and the actual quantity of THC consumed clearly depends on the amount of food ingested. For example, if a baked muffin weighing 3 ounces (85 grams) contains a concentration of 0.3% THC the actual total dose of THC in the one muffin is 255 mg. Having been baked, the THC would be in active form and is many times the dose that may cause impairment and is a danger to an unsuspecting consumer. This law protecting edible hemp products is of particular significance in light of the prescribing information provided for Epidiolex (essentially pure CBD) which warns of potential liver damage and developmental toxicity and other adverse effects that should be monitored by a physician.

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Discloser

None reported.

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