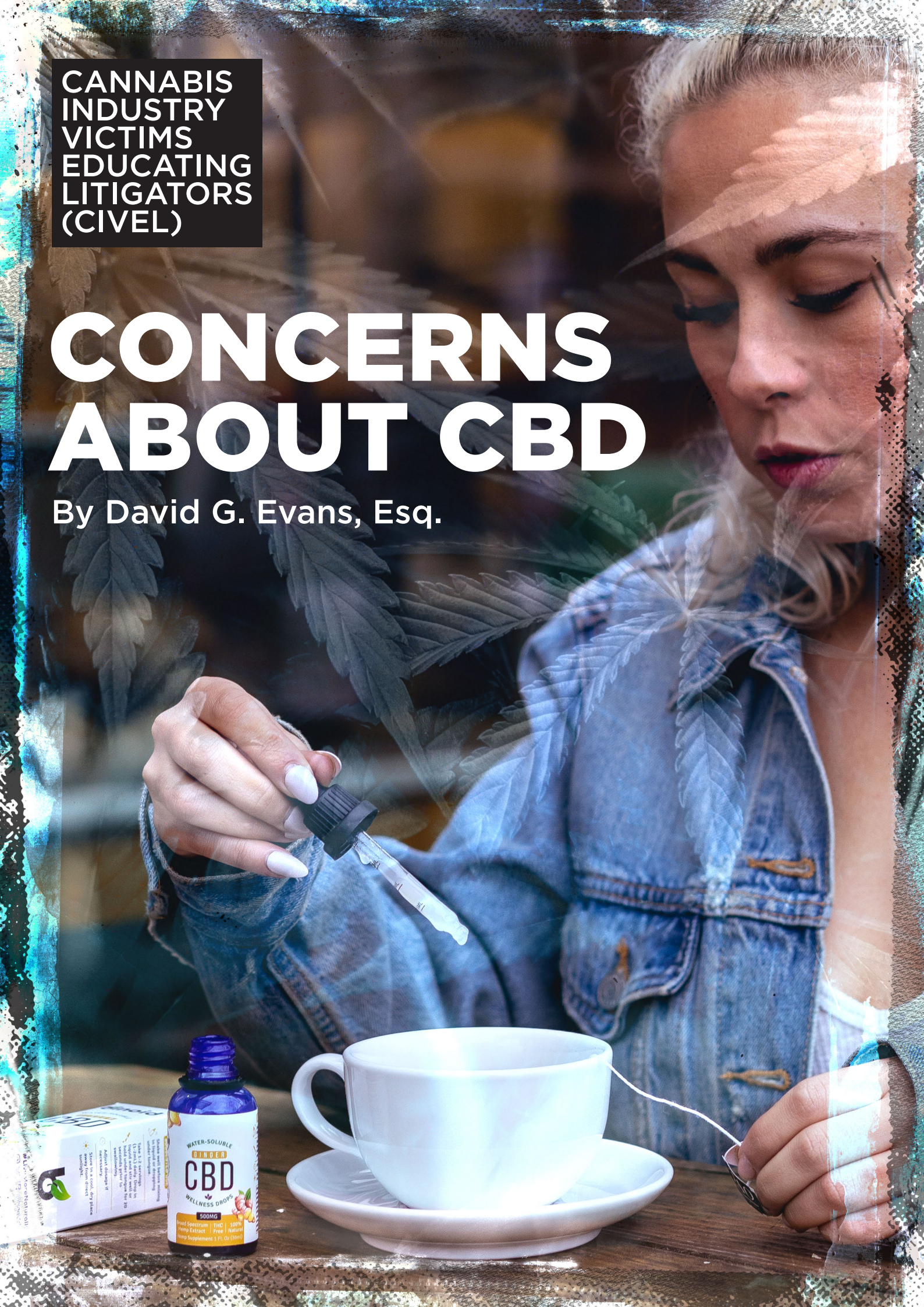


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CONCERNS ABOUT CBD

By David G. Evans, Esq.



The marijuana industry referred to here are those who illegally, negligently or fraudulently produce, market, or distribute marijuana.

WHAT IS CBD?

Cannabidiol (CBD) is a derivative of marijuana and one of the main active ingredients in the marijuana plant. There are two types of CBD. There is Epidiolex, a pure form of CBD approved by the FDA as a medicine but only for the treatment of two seizure syndromes. There is also non-FDA approved CBD that is defined as “Commercial CBD” for the purposes of this paper. Commercial CBD used as a medicine or in food is illegal under federal law and in some states.¹

The chemical in marijuana that causes the high (and many of its other effects) is delta-9 tetrahydrocannabinol, or THC. But there are over 100 other cannabinoid chemicals in the plant; CBD is one of those. Different cannabinoids can have very different biological effects.²


FALSE CLAIMS FOR CBD

The marijuana industry has touted commercial CBD as a “wonder drug.” They may claim it is perfectly safe and legal and can be used for all that ails you or makes you uncomfortable physically. People are consuming large amounts under the misapprehension that it is safe to do so. It is not safe to do so. It has negative side effects and may interfere with the functioning of other medications.

Multiple Studies Show That Commercial CBD Products May Not Be Pure and May Have Negative Side Effects

The Food and Drug Administration (FDA) has issued several warning letters to firms that market Commercial CBD that they are selling CBD illegally. These products are not approved by FDA for the diagnosis, cure, mitigation, treatment, or prevention of any disease. The FDA has also tested the chemical content of cannabinoid compounds in CBD, and many were found to not contain the levels of CBD they claimed to contain.³ Consumers should beware purchasing and using any such products.





The Journal of the American Medical Association (JAMA) published a research letter showing the results of “undercover” purchases of CBD from Internet sources. Of 84 samples obtained and tested, THC was detected in 21%. There were other defects in the mislabeled products noted by the undercover agents. For example, 26% of the 84 products contained less CBD than labeled. With respect to CBD, 42.85% of products were underlabeled 26.19% were overlabeled and only 30.95% were accurately labeled. Accuracy of labeling depended on product type, with vaporization liquid most frequently mislabeled 87.50% and oil most frequently labeled accurately 45.00%. Concentration of unlabeled cannabinoids was generally low however, THC was detected in 21.43% cannabidiolic acid 15.48% and cannabigerol 2.38%. This yielded a good deal of information suggesting that open-source CBD bought on the Internet is not a very reliable or safe product if one is planning to use it for medical purposes or in foods.⁴

On December 8, 2017, the Utah Poison Control Center (UPCC) notified the Utah Department of Health (UDOH) of reports of emergency department visits associated with reported exposure to products labeled as CBD. Patients experienced adverse reactions, including altered mental status, seizures, confusion, loss of consciousness, and hallucinations. These reactions prompted concern for potential adulteration with a synthetic cannabinoid. Sale of CBD is currently illegal in Utah, although CBD is readily available online and in shops. This investigation highlights the hazards of consuming unregulated products labeled as CBD.⁵

A Johns Hopkins researcher reports that the vast majority of edible marijuana products sold in a sample of medical marijuana dispensaries carried labels that overstated or understated the amount of THC. The results of the study suggest some medical marijuana patients could be unintentionally overdosing or are being cheated by mislabeled products.”If this study is representative of the medical cannabis market, we may have hundreds of thousands of patients buying cannabis products that are mislabeled,” says experimental psychologist Ryan Vandrey, PhD, an associate professor of psychiatry and behavioral sciences at the Johns Hopkins University School of Medicine. People could suffer from overdosing side effects, including extreme anxiety and psychotic reactions. The study collected 75 different edible marijuana products - baked goods, beverages, and candy/chocolates - representing 47 different brands from Washington state and California. Only 13 products were accurately labeled. They also tested the products for cannabidiol, or CBD, another of the active ingredients in marijuana believed to have medical benefit, which may also help reduce the side effects of THC. Testing showed 44

products (59%) had detectible levels of CBD, but the average ratio of THC to CBD was 36-to-1. Only one product had a 1-to-1 ratio, which some research suggests is associated with fewer side effects and improved clinical benefit compared with higher ratios of THC to CBD. What the testing indicates that a lot of what's available in the edible cannabis market may have very little CBD.⁶

Another report published by the National Institute of Health showed that products were mislabeled with 26% containing less CBD than labeled and 43% containing more, indicating a high degree of variability and poor standardization of online products. Notably, the oil-based products were more likely to be accurate (45% compared to 25% for tincture and 12.5% for vaporization liquid) and had a smaller percentage of deviation. Oil based products also had a higher range of concentration. In addition to CBD mislabeling, THC was detected in 21% of samples. This study also notes that products containing THC could have sufficient enough concentrations to produce intoxication in children.⁷

CBD NEGATIVE SIDE EFFECTS

Drug Contraindications

CBD oil may potentially interact in a negative way with anti-epilepsy drugs such as:

1. carbamazepine (Tegretol)
2. phenytoin (Dilantin)
3. phenobarbital (Luminal, Solfoton, Tedral)
4. primidone (anti-seizure)⁸

There are interactions with CBD and immunosuppressive drugs used in transplants or chemotherapy and there are interactions with warfarin as there may be the potentiation of anticoagulant effects with marijuana, including CBD.⁹



Common Side effects

The most common side effects of CBD can include:

- Sleepiness
- Decreased appetite
- Diarrhea
- Change in liver function
- Fatigue
- Malaise
- Asthenia (weakness or lack of energy)
- Rash
- Insomnia
- Sleep disorder
- Poor quality sleep
- Infections
- CBD also interacts with some other seizure medicines.
- Nausea or vomiting
- Dizziness
- Anxiety or depression
- Changes in appetite/weight¹⁰

Research published in the journal *Cannabis and Cannabinoid Research* shows that more than 40% of children with epilepsy who were given CBD orally had adverse events that included THC like symptoms. The research challenged the widely accepted premise that CBD is not intoxicating.¹¹

Glaucoma

A recent study suggests that CBD doesn't lower eye pressure but raises it. High eye pressure is the primary risk factor for glaucoma, a leading cause of blindness. Glaucoma damages the optic nerve at the back of the eye. Glaucoma is linked to a buildup of pressure inside the eye. The increased pressure can damage the nerve, leading to permanent vision loss.¹²

Even Epidiolex Has Negative Side Effects

In June, 2018, the FDA approved Epidiolex® (cannabidiol, CBD) oral solution for the treatment of seizures associated with two rare, severe forms of epilepsy - Lennox-Gastaut syndrome and Dravet syndrome - in people two years of age or older. The FDA approved a purified form of CBD. The FDA was quick to note however, that this is not an approval of marijuana or all of its components. This is the approval of one specific CBD medication for a specific use. And it was based on well-controlled clinical trials evaluating the use of this compound in the treatment of a specific condition. Moreover, this is a purified form of CBD. It's being delivered to patients in a reliable dosage form and through a reproducible route of delivery to ensure that patients derive the anticipated benefits. This is how sound medical science is advanced. However, use should not be taken lightly due to the number of side effects that are being seen with this product.¹³

We must assume that since it is manufactured according to FDA standards, by a reliable manufacturer, that it is free from contaminants. This purity is not guaranteed by the commercial CBD products that are not manufactured according to FDA standards.

Even Epidiolex has risks. Other CBD products share these risk but the marijuana industry has for the most part not warned about those dangers to those people who use their CBD products. The below information, unless cited otherwise, comes from the FDA-required package insert warnings and precautions for Epidiolex.¹⁴ The most common warnings are about:

1. Hepatocellular Injury (liver injury)
2. Somnolence and Sedation
3. Suicidal Behavior and Ideation
4. Hypersensitivity Reactions
5. Withdrawal of Antiepileptic Drugs

Liver Injury

Epidiolex can cause liver enzymes to be elevated. Elevated liver enzymes can indicate inflammation or damage to cells in the liver because inflamed or injured liver cells leak higher than normal amounts of certain chemicals, including liver enzymes, into the bloodstream, which can result in elevated liver enzymes on

blood tests. It is important to measure hepatic (pertaining to the liver) laboratory values and having them evaluated by the healthcare provider before treatment with Epidiolex and periodically during treatment. There may be signs or symptoms suggestive of hepatic dysfunction such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine, loss of appetite, itching, fever, feeling unwell, unusual tiredness, unusual darkening of the urine or right upper stomach area pain or discomfort. Commercial CBD that is not approved by the FDA is sold all over the United States without warnings about liver damage.¹⁵

Somnolence and Sedation

People should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that Epidiolex does not affect them adversely (e.g., impaired judgment, thinking or motor skills). Other medicines (e.g., clobazam) or alcohol may increase sleepiness. Commercial CBD is sold all over without such warnings.

Suicidal Thinking and Behavior

Use of Epidiolex, may increase the risk of suicidal thoughts and behavior. Commercial CBD is sold without warnings about this.

Hypersensitivity

Hypersensitivity reactions can occur with use of Epidiolex. This is when the body reacts with an exaggerated immune response to a foreign agent such as in anaphylaxis or allergy. People need to be warned about this.

Withdrawal of Antiepileptic Drugs

Epidiolex should be gradually withdrawn to minimize the risk of increased seizure frequency and status epilepticus.

Children

It is not known if Epidiolex is safe and effective in children under 2 years of age.



Interactions with other medications

Epidiolex may interact with other medicines, including prescription and over-the-counter medicines, vitamins, herbal supplements, and any cannabis-based products. Epidiolex may affect the way other medicines work, and other medicines may affect how Epidiolex works. People should not use CBD until they are evaluated by a health care provider.

Drug tests

Epidiolex may affect drug test results.

Adverse Reactions

Adverse reactions include:

- somnolence
- decreased appetite
- diarrhea
- transaminase elevations (liver problems)
- fatigue
- malaise
- asthenia (loss of strength and energy)
- rash
- insomnia
- sleep disorder
- poor quality sleep;
- infections.¹⁶

Pregnancy

There is not adequate data on the developmental risks associated with Epidiolex use by in pregnant women. Administration of CBD to pregnant animals produced evidence of developmental toxicity such as increased embryofetal mortality in rats and decreased fetal body weights in rabbits; decreased growth, delayed sexual maturation, long-term neurobehavioral changes, and adverse effects on the reproductive system in rat offspring.



There are not good data on the presence of cannabidiol or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Epidiolex and any potential adverse effects on the breastfed infant from Epidiolex or from the underlying maternal condition.

Geriatric Use

Clinical trials of Epidiolex did not include any patients aged above 55 years to determine whether or not they respond differently from younger patients. Dose selection for elderly persons should be cautious reflecting the greater frequency of decreased liver or cardiac function, and of concomitant disease or other drug therapy.

CONCLUSION

Epidiolex, a purified form of CBD has some risks and should only be used while medically supervised. Commercial CBD has many risks but may not have any safeguards.



ABOUT THE AUTHOR

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