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CANNABIDIOL (CBD) – POTENTIAL HARMS, SIDE EFFECTS, AND UNKNOWNNS

The use of non-Food and Drug Administration (FDA)-approved **cannabidiol**, or **CBD**, has gained attention in recent years, as CBD is becoming increasingly popular and is being marketed for various health conditions.¹ A poll of American adults aged 18 years and older found that 14 percent reported using CBD products in 2019, and a similar poll conducted in 2020 found that as many as 1 in 3 adults reported using CBD products.²⁻³ However, non-**FDA-approved**, commercial CBD products marketed to the public and available over the counter differ significantly in composition from those used in clinical studies,⁴ and there is limited evidence to support their safety.⁵ The public should be aware of the misconceptions surrounding CBD products, as well as the potential harms and risks associated with their use.

Key Messages

- Cannabidiol (CBD) and delta-9-tetrahydrocannabinol (delta-9 THC) are two of many chemical compounds called cannabinoids that are found in the cannabis plant. CBD, which in its pure form does not produce any psychoactive effects,⁶⁻⁷ is typically derived from the hemp plant. Nevertheless, CBD products, except for the prescription medication Epidiolex,^{1, 8} are not FDA-approved, so despite being marketed extensively, there are no federal standards for their content, purity, or potency⁹
- The concentration of CBD may be more or less than advertised and, because of a lack of quality control, the manufacturing process may introduce harmful biological and chemical contaminants, including the psychoactive THC.⁵⁻⁶ The lack of safety standards, accuracy in labeling, and quality control may lead to additional concerns for unintended intoxication, particularly among children.
- Since federal restrictions on growing cannabis plants that contain low amounts of delta-9 THC were removed in 2018, CBD has become widely available in a range of products and formulations, including topicals, fabric, food, and beverages.¹⁰
- In 2020, as many as one-third of American adults reported using CBD products.²
- CBD has been marketed as a treatment for a range of health conditions in recent years; however, there is a lack of evidence to support many of these claims.⁵
- Potential risks and harms associated with CBD use include adverse drug interactions, liver toxicity, and reproductive and developmental effects.
- Delta-9 THC or delta-9 THC-contaminated products may be sold as CBD. Labeling of these products may be unclear or misleading, posing a potential threat to a user's current or prospective employment, produce inaccurate medical test results, or cause unintended drug interactions.
- More clinical research is needed to determine if CBD products are safe and effective treatments for the conditions for which they are marketed.¹

Definitions

Agriculture Improvement Act of 2018:

Defined cannabis plants as hemp or marijuana, depending on their concentration of delta-9 THC.

Cannabis sativa L.: A plant species used for producing hemp, marijuana, and other products; commonly referred to as cannabis.

Cannabinoids: Naturally occurring chemical compounds found in cannabis plants.

Cannabidiol (CBD): One of two main cannabinoids found in the cannabis plant; in its pure form, it has no known psychoactive effect.

Delta-8-tetrahydrocannabinol (Delta-8 THC): A cannabinoid that is typically manufactured from CBD and produces psychoactive effects. It is structurally different from delta-9 THC.

Delta-9-tetrahydrocannabinol (Delta-9 THC): One of two main cannabinoids found in the cannabis plant; it produces psychoactive effects. It is potentially more potent than delta-8 THC and may have more considerable side effects.

FDA-approved product: FDA has determined that the benefits of the product outweigh the known risks for the intended use.

Hemp: Cannabis plants and products with a delta-9 THC concentration of no more than 0.3 percent on a dry weight basis.

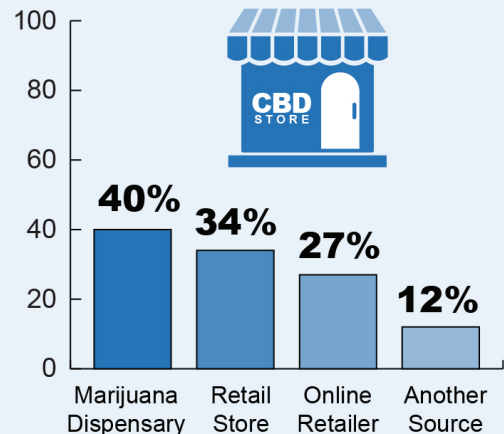
Marijuana: Cannabis plants and products with a delta-9 THC concentration greater than 0.3 percent on a dry weight basis.

Psychoactive effects: The effects of a drug or other substance on the mind (i.e., mind-altering), such as changes in mood, awareness, thoughts, feelings, or behavior. Any psychoactive effect is considered intoxicating (i.e., causes a “high”) for the purposes of this advisory.

In 2019...^{2-3,11}

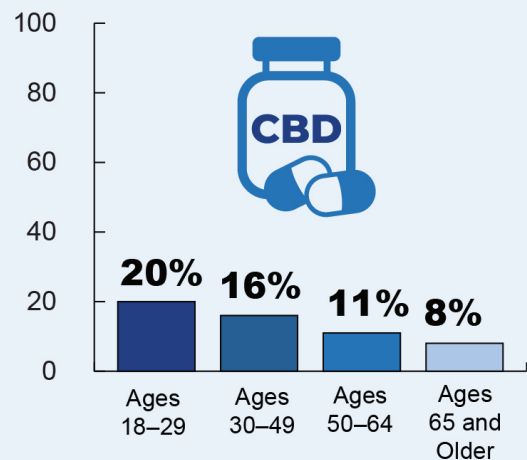
Over **270,000** U.S. retailers sold non-FDA-approved CBD products.

Percentages of CBD users who purchased it from...



64 percent of adults reported they are familiar with CBD products.

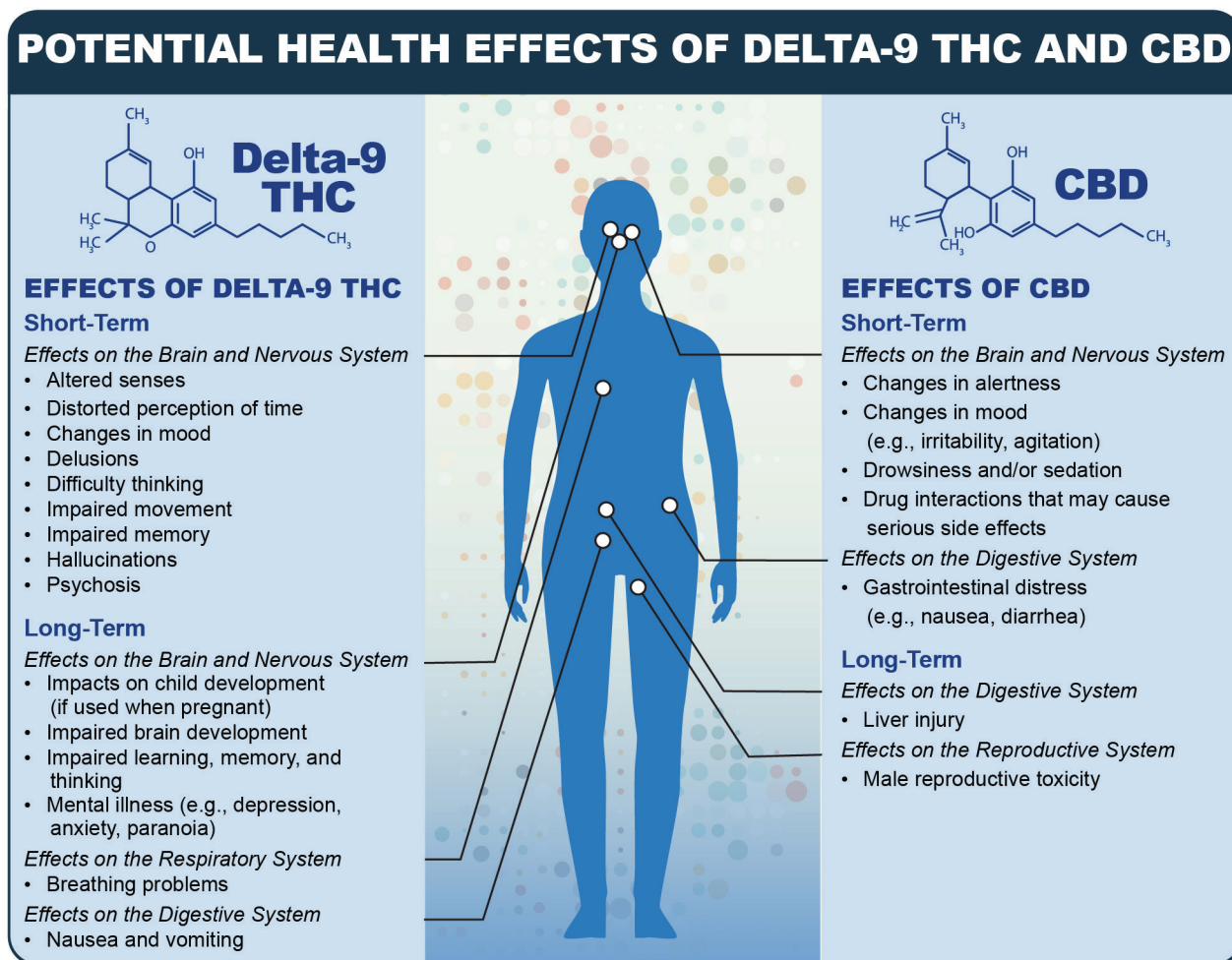
CBD use is more common in early adulthood:



Overview of Cannabis, CBD, and THC

The **cannabis** plant produces over 500 chemical compounds;¹ over 100 are **cannabinoids**—chemical compounds that produce a range of physical and mental effects.^{1, 5, 10} CBD and **delta-9-tetrahydrocannabinol (delta-9 THC)** are the two most common cannabinoids,^{1, 5, 10} with the latter having a high potential for misuse because of its **psychoactive effects**.¹² CBD and delta-9 THC both bind to receptors in the brain and body but produce different effects. Delta-9 THC disrupts many mental and physical functions and produces psychoactive effects; CBD does not produce psychoactive effects.⁶⁻⁷ Figure 1 illustrates the current understanding that CBD use is potentially associated with mostly short-term effects, whereas delta-9 THC use is associated with short- and long-term effects.^{5, 13}

Figure 1. Potential Health Effects of Delta-9 THC and CBD^{5,13}



Delta-8-tetrahydrocannabinol (delta-8 THC) is another increasingly available cannabinoid that has psychoactive effects.¹⁴⁻¹⁵ Because it is found in cannabis plants in only trace amounts, it is typically synthesized from CBD by using chemicals. The manufacturing process may introduce harmful chemical and biological contaminants.¹⁵ The health effects of delta-8 THC are not well understood,¹⁴ but adverse events have been reported to the FDA and nation's poison control centers.¹⁴⁻¹⁵

CBD versus marijuana: Legal definitions

Cannabis plants and products derived from them are divided under federal law into two broad categories, based on their delta-9 THC content: “**hemp**” and “**marijuana**”. Hemp is defined under the [Agricultural Marketing Act of 1946](#), as amended by the [Agriculture Improvement Act of 2018](#) (also known as the Farm Bill), as a cannabis plant or any part of ~~plant~~ plant with a delta-9 THC concentration of no more than 0.3 percent on a dry weight basis.¹⁷⁻¹⁹ The Farm Bill considers cannabis plants that cannot be classified as hemp, because they contain more than 0.3 percent delta-9 THC on a dry weight basis, to be marijuana.¹⁸⁻¹⁹ This law effectively permitted the legal sale of hemp and hemp-derived cannabinoid products; however, it does not affect or modify the federal authority to regulate hemp and hemp-derived products.¹⁰ Nor does it preempt or limit state or tribal laws on hemp production that are more stringent.¹⁸

Since the Farm Bill was passed in 2018, every state, except for Idaho, Mississippi, and the District of Columbia, allows for some form of hemp cultivation, which increases access to and availability of hemp products, including CBD.¹⁶

About CBD Products

Hemp and marijuana plants contain both CBD and THC. CBD is typically derived from hemp because of its low THC concentration, and THC is typically derived from marijuana plants. There is currently only one FDA-approved CBD product, Epidiolex, which is a pharmaceutical-grade CBD oral liquid used for treating rare, severe forms of seizure disorders,⁸⁻⁹ although its exact mechanism of action is not fully understood.¹⁰ This product is available only in pharmacies, with a valid prescription from a healthcare provider.

Although not FDA-approved, CBD is found in a variety of other products, including: lotions, oils, creams, and other topical products; food and beverage items like chocolate, gummies, other candy, and tea; cosmetics; fabrics; and products for pets.²⁰⁻²¹ This variety in product types has contributed to the popularity of CBD, because it can be used in many different ways.²²

Availability of CBD Products

The availability of CBD products, other than Epidiolex, varies by state, depending on its regulations. Over-the-counter CBD products are available throughout the United States, online or from “brick and mortar” retailers, including drugstores, grocery stores, convenience stores, and gas stations; however, most CBD sales—greater than 60 percent—are made online.¹¹ CBD products purchased over the counter, even from reputable retailers, are not FDA-approved.²³ Many questions about the safety, reliability, and effectiveness of CBD products remain unanswered.^{4, 24-25}

CBD products sold at cannabis dispensaries are not FDA-approved and may contain more than 0.3 percent THC, depending on the state’s definition of allowable CBD products.²⁶ In addition, although regulations and enforcement vary from state to state,²⁶ CBD products purchased from dispensaries may be subject to some form of oversight and standardization.

Marketing and Labeling of CBD Products

The FDA has not approved CBD products to be marketed as food additives or dietary supplements and has concluded that a new regulatory pathway for CBD is needed; it is prepared to work with Congress to develop a cross-agency strategy for the regulation of these products.^{5, 28} Therefore, over-the-counter CBD products are often advertised as therapies for many health conditions, even though many of these claims are unproven and the health effects of these

products are unknown.^{5,8} The FDA has been unable to evaluate and approve these products for their marketed use, largely due to limited data to support their effectiveness.⁵ As a result, the FDA sends warning letters to companies marketing unapproved products containing CBD with unsubstantiated claims that they treat certain medical conditions.^{21, 24, 29} The FDA also regularly collects data and evaluates regulatory policies related to cannabis and cannabis-derived ingredients like CBD.

Nevertheless, the popularity of CBD products continues to grow. In 2020, CBD products generated over five billion dollars in sales,¹¹ a figure expected to increase as the market expands.³⁰

Although Epidiolex is the only FDA-approved CBD product, CBD is also marketed for other health conditions. Presently, there is insufficient evidence to support the use of CBD for many of the other health conditions for which it is marketed as treatment.^{1, 27} However, additional research evaluating the therapeutic efficacy of CBD for various medical conditions is underway. The [National Center for Complementary and Integrative Medicine](#) has summarized available findings to date.¹

Risks and Harms of CBD Use

Many concerns have been raised about CBD use, particularly with regard to over-the-counter CBD products, as there are limited data on their safety and effectiveness.⁴ These concerns include adverse events and side effects, questions about their reliability, and unproven health and wellness claims.

Adverse events and side effects. Potential side effects of CBD include decreases in alertness (e.g., drowsiness and sedation), changes in mood (e.g., irritability and agitation), decreased appetite, and gastrointestinal symptoms/distress (e.g., diarrhea).⁴⁻⁵ CBD may also produce psychotic effects or cognitive impairment in individuals who also regularly use delta-9 THC products like marijuana.⁴ In addition, CBD use has been associated with adverse events such as liver injury, interactions with other drugs, injuries following periods of sedation or drowsiness, and male reproductive harm.⁵ Factors influencing the likelihood of CBD-associated adverse events and/or side effects include the strength and purity of the product, amount used, mode of administration, concurrent substance use and misuse (such as legal and illegal drugs and alcohol), and interactions with prescribed drugs or other medications.^{9, 27}

Unreliable dosage and purity. CBD products that are not FDA-approved do not have to meet any standards for content or potency. Thus, these products may contain more or less CBD than stated on the label and, more concerning, biological and chemical contaminants due to unsafe manufacturing practices without adequate process controls.^{6, 9} Research suggests that the labeled concentrations of CBD products are unreliable.^{20, 31-34} The amount of CBD in over-the-counter products may range from very low to levels exceeding FDA-approved dosing for seizure disorders.²⁷ For example, one study found that among 84 commercial CBD extracts purchased online from 31 companies, the CBD concentration was labeled accurately in only 26 (31 percent); almost 43 percent of products were under-labeled and 26 percent over-labeled.³³ The uncertainty in composition poses significant health risks when using these products for medical conditions, particularly in children.^{33, 35}

A 2020 evidence-based review found little data to support health benefits associated with over-the-counter CBD products.⁴ Most of these products do not contain pure CBD and may contain other cannabinoids, including delta-9 THC,⁴ and contaminants, such as pesticides.⁴ The FDA has ruled that CBD products cannot be sold legally as dietary supplements and CBD is not considered a safe additive for food and beverage products.²⁷

The purity of commercial CBD is also highly questionable, with contaminants including the intoxicant THC.^{6, 32, 34} For example, in the previously mentioned study on 84 commercial CBD extracts, 21.4 percent of the samples contained unlabeled delta-9 THC;³³ another study found that 3 out of 25 (12 percent) hemp oil products available commercially exceeded the 0.3 percent concentration limit.³² Thus users of CBD products that claim to not contain delta-9 THC may still screen positive for marijuana,^{25, 32, 35-36} even at a delta-9 THC concentration as low as 0.02 percent by weight;³⁶ it is unlikely that pure CBD will produce a positive urine drug test.³⁷⁻³⁸ Individuals should be aware that delta-8 or delta-9 THC-contaminated products may be sold as pure CBD. Unclear or misleading labeling may pose work-related, legal, and health risks, given that use of unsuspected delta-9 THC may threaten an individual's current or prospective employment, including athletics, produce inaccurate medical test results, potentially involve law enforcement, and cause unintended drug interactions.^{20, 25, 32, 34-36, 39}

Unproven health and wellness claims. Over-the-counter CBD products are marketed for various health conditions, despite limited evidence of effectiveness or safety.¹⁰ Nevertheless, the marketing claims may lead individuals to purchase these products without consulting a healthcare provider or being aware that they may contain impurities and different CBD doses than used in clinical studies with pharmaceutical-grade CBD.^{4-6, 32, 34} Moreover, these individuals may assume that they are effectively treating their medical condition and therefore not seek medical care, which can delay receipt of accurate diagnosis and treatment. The FDA recommends that individuals discuss any medical concerns with a healthcare provider before taking CBD.⁵

Unknown health effects. Available evidence suggests that pure (i.e., uncontaminated) CBD, when used by itself, does not produce any psychoactive effects; however, it does affect the body, whether ingested or used topically (i.e., placed on skin) and may produce observable side effects.²⁷ Uncertainties around CBD use include unknown long-term health effects, proper dosing, effects on the developing brain, and developmental impacts on fetuses and infants when used by pregnant and breastfeeding people.⁵ The FDA therefore strongly advises against the use of CBD in any form during pregnancy or while breastfeeding.⁴⁰

Other concerns. Like CBD, products containing delta-8 THC are now available for purchase online and in stores and are being marketed for a range of health conditions;¹⁴ however, these products have not been evaluated by the FDA and are not considered safe to use.¹⁵ One of the greatest concerns around delta-8 THC products is that individuals who use them may be misled to believe that they do not have any psychoactive properties because they are labeled as a hemp product.¹⁵ There are also concerns around product formulations, purity and dosage, unintentional product exposure to children and pets, and potential adverse events, such as vomiting, hallucinations, and loss of consciousness.¹⁵

Tips and Action Steps

Tips and Action Steps for Community Coalitions and Substance Use Prevention and Treatment Leaders

- Work with local health departments, regulatory agencies, and medical providers to disseminate the latest evidence on the risks and therapeutic potential of CBD, including that which is unknown.
- Educate community partners and community members, including adolescents and young adults, about the short- and possible long-term effects associated with CBD use.
- Implement evidence-based programs to prevent any non-FDA-approved CBD use, particularly among adolescents and young adults.

Tips and Action Steps for Healthcare Providers

- Encourage additional clinical research on the effects of CBD.
- Learn about potential interactions of CBD with alcohol and prescription and over-the-counter medications.
- Educate patients on the potential risks and harms associated with CBD use, including interactions with prescription drugs, dietary supplements, alcohol, and illicit drugs.

Tips and Action Steps for Parents, Caregivers, and the General Public

- Talk with children about the risks and harms of using products that contain CBD.
- Do not allow children to use over-the-counter CBD products.
- Consult a healthcare provider before using any CBD product.
- Be aware that the risk of CBD products containing delta-9 and/or delta-8 THC is unknown, and their use may affect employment drug screenings and interactions with law enforcement.
- Do not use CBD concurrently with medications, alcohol, or illicit drugs.
- If you experience adverse events as a result of using CBD products, report them to the FDA through their [MedWatch Safety Information and Adverse Event Reporting Program](#).⁴¹

Resources

About Cannabis Policy in the United States	Information about cannabis policy, including the history of cannabis policy in the United States, issues treated by cannabis-related law, and federal laws.
FDA Regulation of Cannabis and Cannabis-Derived Products	FDA resources on CBD policy, including consumer information and several regulatory resources.
Conversation Goals: Talking with Teens About Alcohol and Other Drugs	Conversation goals for parents talking to children about alcohol and other drugs that can be used to also discuss CBD.
SAMHSA's National Helpline 1-800-662-HELP (4357)	A free, confidential, 24/7, 365-day-a-year treatment referral and information service (in English and Spanish) for individuals and families facing mental and/or substance use disorders.
Prevent Coalition	Prevent Coalition is a community coalition with prevention resources available for youth and teens, parents, schools, providers, and rural prevention specialists.

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