EXPLAINING CANNABINOIDS

JULY 2025

INTRODUCTION

Cannabinoids are a group of chemical compounds found within the cannabis plant (*Cannabis sativa L.*) and the human body. Cannabinoids interact with the body's endocannabinoid system (ECS), which is a complex cell-signalizing system that helps regulate body functions, including sleep, mood, appetite, and memory.[1] The ECS is comprised of receptors throughout the body, with the two main receptors being CB1 receptors, which are primarily located in the brain and central nervous system, and CB2 receptors, which are found mostly on immune cells and other body tissues. The effect cannabinoids have on the body is dependent on the type of cannabinoid and the location of the receptor with which it interacts.

There are three types of cannabinoids: (1) endocannabinoids; (2) phytocannabinoids; and (3) synthetic cannabinoids. Endocannabinoids are cannabinoids that are produced internally within the body and regulate bodily functions as part of the ECS. Phytocannabinoids are cannabinoids that are found naturally in the cannabis plant. Chemists have identified more than 100 different phytocannabinoids, with tetrahydrocannabinol (THC) and cannabidiol (CBD) being the most well-known and most abundant. Finally, synthetic cannabinoids are artificially manufactured chemicals that are designed to mimic the effects of phytocannabinoids.

This factsheet provides information on some of the most commonly discussed phytocannabinoids and synthetic cannabinoids in media, case law, and legislation.

DELTA-9 THC (TETRAHYDROCANNABINOL)

Delta-9 THC, the most abundant form of THC found in the cannabis plant, is a phytocannabinoid. This phytocannabinoid, the main psychoactive compound in the cannabis plant, is responsible for the intoxicating effects associated with the consumption of cannabis. Delta-9 THC binds with the CB1 and CB2 receptors in the body and acts as an agonist, meaning that it activates the receptors upon binding to produce a physiological response. Cannabis plants, including the resin extracted from any part of the plant, and every compound, manufacture, salt, derivative, mixture or preparation of the plant, that contain a delta-9 THC concentration of more than 0.3 percent on a dry weight basis are considered to be "marijuana/marihuana" under federal law.[2] Marijuana has been categorized as a Schedule I controlled substance under the federal Controlled Substances Act (CSA) [3] since 1970. In 2024, the Drug Enforcement Administration (DEA) proposed transferring marijuana from Schedule I to Schedule III of the CSA. This proposed transfer is consistent with the view of the U.S. Department of Health and Human Services (HHS) that marijuana has an accepted medical use and that marijuana's abuse potential and level of physical or psychological dependence is low.[4] As of this writing, 24 states and the District of Columbia have legalized the medicinal and recreational use of cannabis, while an additional 15 states have legalized medicinal use only.[5]

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[1] To stimulate the ECS, humans (and other animals) naturally produce molecules called endocannabinoids, which are structurally similar to the molecules found in the cannabis plant. Anadamide and 2-arachidonoylglycerol are the two most studied endocannabinoids. Because cannabinoids in the cannabis plant are structurally similar to endocannabinoids, they are able to react with the ECS and produce a physiological response when consumed. Peter Grinspoon, *The Endocannabinoid System: Essential and Mysterious*, HARVARD HEALTH PUBLISHING (Aug. 11, 2021). https://www.health.harvard.edu/blog/the-endocannabinoid-system-essential-and-mysterious-202108112569.

[2] 21 U.S.C.A § 802(16) (Westlaw through Pub. L. No. 119-5).

[3] 21 U.S.C.A. § 812 (Westlaw through Pub. L. No. 119-5).

[4] Schedules of Controlled Substances: Rescheduling of Marijuana, 89 Fed. Reg. 44,597 (May 21, 2024).

[5] *State Medical Cannabis Laws*, NATIONAL CONSORTIUM OF STATE LEGISLATURES (last updated Mar. 6, 2025), https://www.ncsl.org/health/state-medical-cannabis-laws.

In 1985, the U.S. Food and Drug Administration (FDA) approved dronabinol, which is a synthetic form of delta-9 THC, sold under the brand names Marinol and Syndros, for the treatment of HIV/AIDS-induced anorexia and chemotherapy-induced nausea and vomiting.[6] Dronabinol is only available with a prescription and is categorized as a Schedule II controlled substance under the CSA.[7] The use of dronabinol can result in side effects and feelings of intoxication similar to the use of natural delta-9 THC.[8] Another synthetic drug similar in structure to delta-9 THC is the FDA-approved drug nabilone, sold under the brand name Casamet.[9] Like dronabinol, nabilone is used for the treatment of nausea and vomiting associated with chemotherapy and is a Schedule II controlled substance.[10]

CBD (CANNABIDIOL)

CBD is the second most prevalent phytocannabinoid in the cannabis plant after THC. Unlike THC, CBD is not psychoactive and does not produce intoxicating effects when consumed. It binds to both CB1 and CB2 receptors in the body but acts as an antagonist, preventing the receptor from activating. The Agriculture Improvement Act of 2018,[11] commonly referred to as the 2018 Farm Bill, removed hemp from the CSA and effectively legalized hemp-derived CBD on the federal level. Under the 2018 Farm Bill, hemp is defined as "the plant *Cannabis sativa L.* and any part of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, and salts of isomers, whether growing or not, with a delta-9 THC concentration of not more than 0.3 percent on a dry weight basis."[12] Although the 2018 Farm Bill legalized hemp on the federal level, the bill allows states to enact laws that regulate the sale of hemp more stringently.[13] For example, Virginia law requires hemp products offered for retail sale in the commonwealth to have a *total* THC concentration of less than 0.3 percent, regardless of whether the THC is delta-9 or another natural or synthetic form.[14] Virginia's more stringent definition means that hemp products, including hemp-derived CBD, that are legal under federal law might be considered illegal under Virginia's total THC standard.

In 2018, the FDA approved Epidiolex, which contains CBD as its active ingredient, for the treatment of seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, and tuberous sclerosis complex in patients one year of age or older.[15] The DEA originally classified Epidiolex as a Schedule V controlled substance, but in 2020, the agency de-scheduled the medication, making it no longer subject to the CSA.[16]

DELTA-8 (THC)

Delta-8 THC is an isomer of delta-9 THC, meaning that the two have the same molecular formula but a different chemical structure. Due to the difference in its structure from delta-9 THC, delta-8 THC does not bind as strongly to the CB1 receptors in the body. This results in delta-8 THC having a milder psychoactive effect than delta-9 THC. Delta-8 THC is naturally occurring in the cannabis plant but in substantially lower concentrations than delta-9 THC. Additionally, delta-8 THC can be synthetically produced from CBD. Although not specifically addressed in the 2018 Farm Bill, on the federal level, the law effectively legalized the sale of hemp that is naturally derived from delta-8 THC. In 2022, the Ninth Circuit ruled in *AK Futures LLC v. Boyd Street Distro*

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[6] Brian O'Donnell, et al., *Dronabinol*, STATPEARLS (last updated Sept. 4, 2023), https://www.ncbi.nlm.nih.gov/books/NBK557531/.
[7] Schedule II, 21 C.F.R. § 1308.12 (2025)
[8] O'Donnell, et al., *supra* note 5.
[9] *Nabilone*, PUBCHEM (last accessed May 2, 2025), https://pubchem.ncbi.nlm.nih.gov/compound/Nabilone.
[10] 21 C.F.R. § 1308.12.
[11] Pub. L. No. 115-334 (2018).
[12] 7 U.S.C.A. § 1639o (Westlaw through Pub. L. No. 119-5).
[13] 7 U.S.C.A. § 1639p(a)(3)(A) (Westlaw through Pub. L. No. 119-5).
[14] VA. CODE ANN. § 3.2-4112 (West 2025).
[15] *FDA Regulation of Cannabis and Cannabis-Derived Products, including Cannabidiol*, FOOD AND DRUG ADMINISTRATION (last updated July, 16, 2024), https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd#farmbill.
[16] *DEA Deschedules Antiepileptic CBD Oral Solution Epidiolex*, DRUG TOPICS (Apr. 7, 2020), https://www.drugtopics.com/view/dea-deschedules-antiepileptic-cbd-oral-solution-epidiolex.

LLC[17] that the 2018 Farm Bill's definition of hemp encompasses delta-8 THC products that are synthetically produced from CBD, as long as those products do not contain more than 0.3 percent delta-9 THC. In reaching its conclusion, the Ninth Circuit disregarded the DEA's position that all synthetically derived forms of THC are excluded from the 2018 Farm Bill and remain Schedule I controlled substances[18] and ruled that the 2018 Farm Bill's clear statutory text overrode the agency's conflicting interpretation.[19]

DELTA-10 (THC)

Delta-10 THC is another isomer of delta-9 THC. Delta-10 THC occurs naturally in the cannabis plant, but because it is found in very low quantities in the plant, it is often synthetically produced from CBD. Like other versions of THC, delta-10 THC binds to the CB1 and CB2 receptors in the body, but anecdotal reports indicate that delta-10 THC is less potent than delta-9 THC and delta-8 THC. There is limited scientific research on delta-10 THC's effects on the body in comparison to other forms of THC. Naturally occurring delta-10 THC derived from hemp is considered legal on the federal level under the 2018 Farm Bill, but whether synthetically derived delta-10 THC is legal under federal law is a legal gray area. The Ninth Circuit's 2022 ruling determining that synthetically produced delta-8 THC is legal under the 2018 Farm bill may be applicable to synthetic delta-10 THC, but currently, there is no direct case law on the subject.[20]

THCa (TETRAHYDROCANNABINOLIC ACID)

THCa is the acidic precursor of THC and is naturally occurring in the cannabis plant. THCa is non-psychoactive in its natural state, but when the compound is heated, it chemically converts into psychoactive THC. When THCa is consumed raw (*i.e.* unheated) it does not produce intoxicating effects in a user. An individual can consume or use raw THCa through products such as edibles, topical lotions, or transdermal patches and will not experience any intoxicating effects. THCa can also be consumed via inhalation by smoking or vaping the compound, but as the THCa is heated through the smoking or vaping process, it will convert into THC. Thus, smoking or vaping THCa will produce intoxicating effects in a user due to the conversion of THCa to THC. THCa that is extracted from hemp is legal on the federal level under the 2018 Farm Bill.

THC-O

THC-O acetate, which is commonly referred to as THC-O, is a synthetic cannabinoid that can be produced by converting hemp-derived CBD into THC and then exposing the THC to acetic anhydride, resulting in a chemical reaction called acetylation. THC-O is structurally similar to delta-9 THC, and like delta-9 THC, it produces intoxicating effects in users when consumed. In 2024, the Fourth Circuit, citing the Ninth Circuit's opinion in *AK Futures LLC*, ruled that despite being a synthetic cannabinoid not naturally found in the cannabis plant, THC-O is legal on the federal level under the 2018 Farm Bill as long as it is derived from hemp and does not contain more than 0.3 percent delta-9 THC.[21]

The research on how THC-O affects the body is scarce, but anecdotal reports from users claim that THC-O produces much more intense psychoactive effects than other forms of THC, with some users describing a psychedelic high similar to hallucinogens like psilocybin. However, a 2023 study conducted by cannabis researchers from the University at Buffalo-State University of New York indicates that the anecdotal reports of psychedelic effects from the use of THC-O may be overexaggerated.[22] The study surveyed nearly 300 participants about their experiences using THC-O, and 79 percent of participants responded that using THC-O is "not at all" or

[17] 35 F.4th 682, 692-93 (9th Cir. 2022).
[18] Implementation of the Agricultural Improvement Act of 2018, 85 Fed. Reg. 51639-01, 51641 (Aug. 21, 2020).
[19] *See Ak Futures LLC,* 35 F.4th at 692-93.
[20] *Id.*
[21] *See* Tonya Anderson v. Diamondback Investment Group, LLC, 117 F.4th 165, 187-88 (4th Cir. 2024).
[22] David J. Hill, *New Study Debunks Claims of Psychedelic Cannabinoid*, UNIVERSITY AT BUFFALO (July 10, 2023), https://www.buffalo.edu/news/releases/2023/07/thc-o-acetate.html.

only "a little" like a psychedelic experience.[23] Additionally, the participants answered questions from the Mystical Experience Questionnaire, an instrument for assessing psychedelic experiences, and their responses were significantly below the threshold for a "mystical" or psychedelic experience.[24] While the survey results suggest that THC-O is not a "psychedelic cannabinoid," the researchers hypothesized that there are three likely explanations as to why individuals may anecdotally report having a psychedelic experience with THC-O: (1) users may modify or embellish anecdotal reports of what they experienced or felt while under the influence based on expectations of what they have heard or read about other individuals' experiences with THC-O; (2) some users may have experienced a very intense high and mistakenly interpreted it as a psychedelic experience; or (3) the THC-O product the user consumed may have been contaminated or contained another substance.[25]

Like other forms of THC, THC-O can be consumed in a variety of ways, but cannabis researchers have specific safety concerns about the inhalation of THC-O. THC-O contains acetate, and when acetate is heated, such as through the smoking or vaping process, it produces ketene, a highly potent lung toxicant and is the suspected cause of E-cigarette or Vaping Product Use–associated Lung Injury (EVALI).[26] In 2019, unlicensed vape cartridges containing Vitamin E acetate caused an outbreak of EVALI that resulted in 2,807 hospitalizations and 68 deaths in the United States.[27] Cannabis researchers are concerned that increases in the number of individuals smoking or vaping THC-O will result in another EVALI outbreak.[28] Because of the potential risk of pulmonary toxicity from inhaling THC-O, cannabis researchers recommend that THC-O users consume the substance via non-inhaled methods, such as edibles or tinctures, which do not pose a risk of lung injury from exposure to ketene.

HHC (HEXAHYDROCANNABINOL)

HHC is a phytocannabinoid found in trace amounts in the cannabis plant that can be produced synthetically from THC through a chemical process called hydrogenation.[29] HHC is structurally similar to THC and produces intoxicating effects when consumed. While there is a lack of research on how HHC affects the body, anecdotal reports suggest that HHC produces milder intoxicating effects than delta-9 THC, similar to that of delta-8 THC. The legality of HHC falls into a legal gray area. In 2024, an advisory opinion letter from the DEA to the Louisiana Department of Health noted that HHC is a Schedule I controlled substance and is excluded from the definition of hemp created by the 2018 Farm Bill.[30] However, based on the case law from the Fourth and Ninth Circuits regarding other types of synthetic cannabinoids, some cannabis policy experts argue that HHC is legal under the 2018 Farm Bill if it is produced from hemp and contains less than 0.3 percent delta-9 THC.[31]

CONCLUSION

This factsheet presents an overview of a small number of known cannabinoids, but as retailers and consumers continue to search for and promote legal alternatives to delta-9 THC, more are likely to gain mainstream recognition in the future. The types of cannabinoids mentioned in this factsheet are either considered legal on the federal level under the 2018 Farm Bill or fall into a legal gray area. Currently, however, there is no federally required regulatory system in place to ensure that cannabinoid products are safely produced and properly labeled. Consumers that wish to use any type of cannabinoid should only buy products from reputable companies that are

[23] *Id.*
[24] *Id.*
[25] *Id.*
[26] Neal L. Benowitz, et al., *Vaping THC-O Acetate: Potential for Another EVALI Epidemic* 19 J. OF MED. TOXICOLOGY 37, 37 (Dec. 2022), https://doi.org/10.1007/s13181-022-00921-3.
[27] *Id.*
[28] *Id.*
[29] Silvia Graziano, et al., *Hexahydrocannabinol Pharmacology, Toxicology, and Analysis: The First Evidence for a Recent New Psychoactive Substance*, 21 CURRENT NEUROPHARMACOLOGY 2424, 2424 (Sept. 2023), https://doi.org/10.2174/1570159X21666230623104624.
[30] Letter from Terrence L. Boos, Chief of the Drug & Chemical Evaluation Section, Drug Enforcement Admin., to David L. McCay, Louisiana Department of Health (Apr. 3, 2024), https://ldh.la.gov/assets/oph/Center-EH/sanitarian/fooddrug/hemp/23-8967_LA_Dept_of_Health_HHC09192023_signed.pdf.
[31] *See Ak Futures LLC*, 35 F.4th at 692-93; and *Tonya Anderson*, 117 F.4th at 187-88.

third-party tested for purity and contaminants to better ensure that they are getting the same product that appears on the label. While certain cannabinoids may currently be legal on the federal level or in a legally gray area, that may change in the future. There is a bill in the 119th U.S. Congress that would close what some lawmakers refer to as the "hemp loophole" by prohibiting the commercial production, sale, and distribution of certain hemp-derived cannabinoid products, namely those that are not naturally occurring and are synthesized or manufactured compounds.[32] The bill would also change the federal definition of hemp to be determined on the basis of a cannabis plant's total THC concentration, including THCa, instead of just its delta-9 THC concentration.[33] In addition to possible legal changes on the federal level, the legality of certain hemp-derived cannabinoids varies greatly among states, with some states banning or attempting to ban certain products.[34] Consumers should be aware of the possible changing legal landscape as state and federal lawmakers explore whether to ban or regulate hemp-derived cannabinoids.

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[32] Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act of 2026, H.R. 4121, 119th Cong. (2025); *See also* RENÉE JOHNSON, CONG. RESEARCH SERV., HEMP RESTRICTIONS IN FY2026 AGRICULTURE APPROPRIATIONS (2026). https://www.congress.gov/crs-product/IN12565.

[33] H.R. 4121.

[34] *See* Mona Zhang, *Texas governor vetoes hemp ban bill*, POLITICO (June 23, 2025), https://www.politico.com/news/2025/06/23/texas-governor-vetoes-hemp-ban-bill-00418149.

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