

Cannabinoids 101:

UNDERSTANDING THE SCIENCE OF CANNABIS

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Cannabinoids
and cannabis:
an overview



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CHAPTER 1

Cannabinoids
and cannabis:



an overview

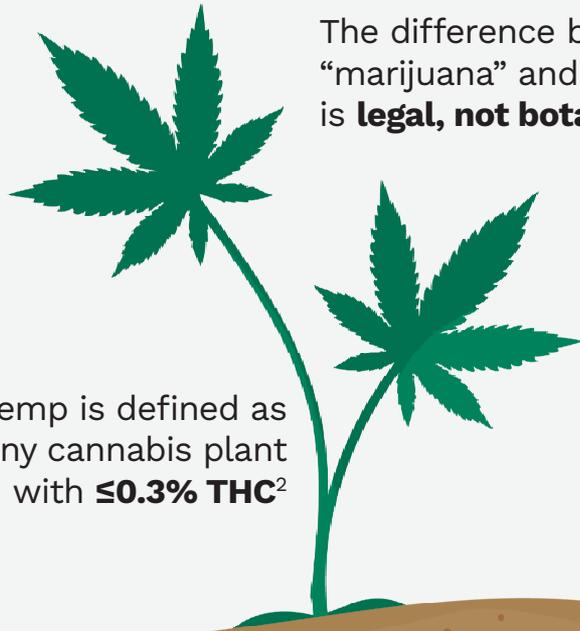
cannabis vs cannabinoids

Cannabis sativa¹:

A plant from which specific *cannabinoids* are derived

The difference between “marijuana” and “hemp” is **legal, not botanical**²

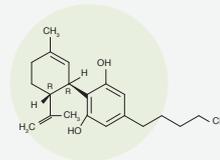
Hemp is defined as any cannabis plant with **≤0.3% THC**²



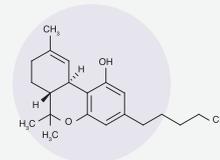
Cannabinoids¹:

Chemical compounds that can be found in cannabis plants

Cannabidiol (CBD)³



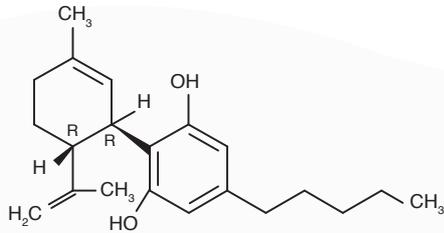
Tetrahydrocannabinol (THC)¹



Others¹

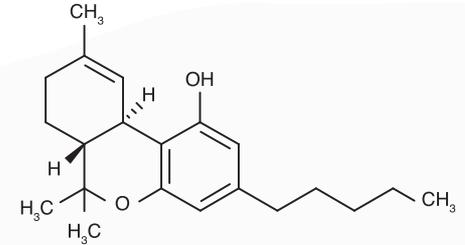
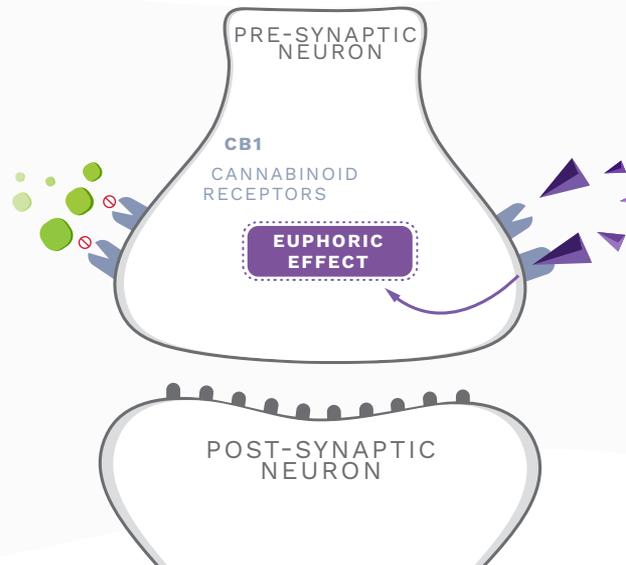
CBG
CBN
CBDA
THCV
THCA

CBD and THC are unique compounds^{1,3}



CBD

- Very low affinity for CB1 receptors and **does not cause euphoria**^{3,4}
- **Anticonvulsant properties** established in clinical trials⁵⁻⁷



THC

- Affinity for and activity at CB1 receptors; is primarily responsible for marijuana's **euphoric effects**^{4,8}

3 categories of cannabis-based products



**Pharmaceutical
formulations**



**Medical marijuana &
recreational marijuana**



Hemp



pharmaceutical formulations

- Can be plant-derived or synthetic^{3,9}
- Studied to evaluate efficacy and safety profile^{3,9}
- Controlled preparations that meet FDA standards of consistency and stability¹⁰



medical marijuana & recreational marijuana

- Cannabis products that may contain >0.3% THC²
- Medical and recreational marijuana are defined solely by intended use²:
 - **Recreational marijuana:** to induce pleasure, euphoria, relaxation, or enhance sociability¹¹
 - **Medical marijuana:** to treat disease or alleviate symptoms by patient choice, in the absence of FDA approval¹²
- Healthcare providers may “recommend” these products but do not prescribe²

hemp



- Defined as $\leq 0.3\%$ THC²
- **<0.3% THC can still cause intoxication¹³**
 - Even 5 mg/day of THC can cause side effects (feeling high, dizziness, confusion, and drowsiness)⁹
 - Can be an **inefficient source of CBD²**
- Absorbs heavy metals and chemical waste from soil²

CHAPTER 2

Non-FDA-approved
cannabis products:



**what
we
know**

Non-FDA-approved products in the news¹⁴⁻¹⁸

Pesticides and
Pot: Lab Results,
Company Statements

FEBRUARY 22, 2017



Contaminated cannabis
oil causing emergency
room visits, NC health
officials warn

MARCH 06, 2018



Fake CBD Poisoned At
Least 52 People In Utah
Last Winter, Officials Say

MAY 26, 2018



Clusters of illness
linked to CBD
vapes share second
connection

OCTOBER 21, 2019



Dangerous Chemicals
Are Found in Popular
CBD Products

NOVEMBER 19, 2018



Cannabis is often grown outdoors¹⁹

Cannabinoid quality and content can vary depending on²⁰:



Hemp is an effective “bioaccumulator” and “phytoremediator,” meaning it **absorbs heavy metals and other chemical waste from the soil²**

- The absorption of these heavy metals can impact the quality of the products and the health of those who ingest it²¹

Many non-FDA-approved CBD products may be **contaminated**^{15,18,22}

Some non-FDA-approved
CBD products have shown
concentrated amounts of
toxic pesticides²²



CBD products may be produced using
substandard manufacturing and
can be contaminated with:



**heavy
metals**²¹



**mold &
bacteria**^{23,24}



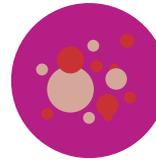
**harmful
chemicals**¹⁴

Of **47 states with medical cannabis** laws,
only **23 have testing requirements**^{25,26}



Many exclude “hemp” products
from testing requirements **completely**^{25,26}

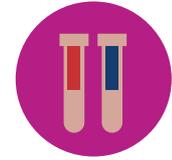
Even in state-licensed testing facilities,
there can be criticisms regarding:



**Lack of testing
for mold**²³

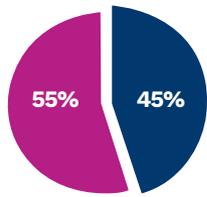


**Technical
glitches in labs**²³

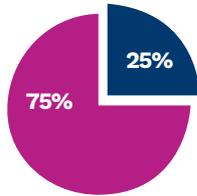


**Inconsistent
testing methods**²⁷

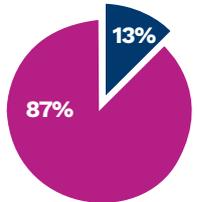
Many non-FDA-approved CBD products may be inaccurately labeled²⁸



CBD oil
(n=40)



CBD tinctures
(n=20)



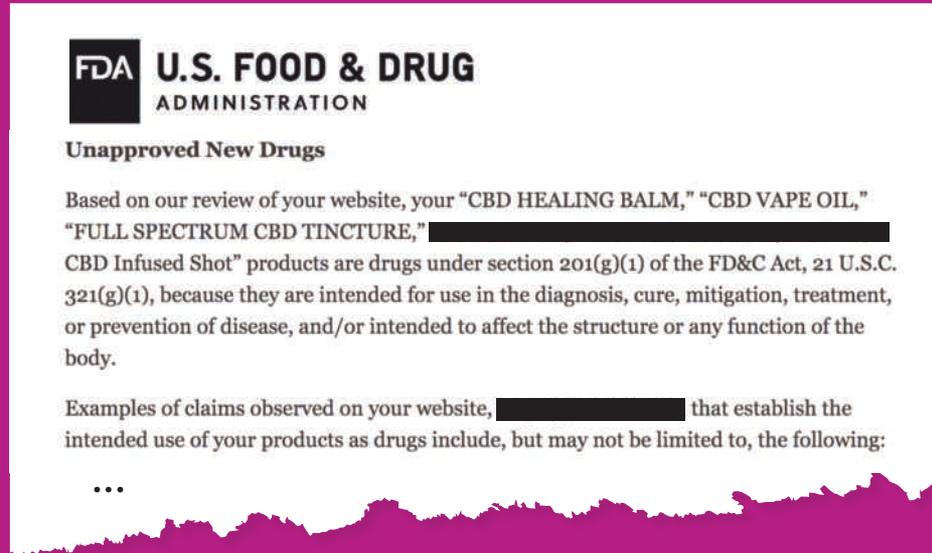
Vaporization liquid
(n=24)

- Accurate
(CBD content within 10% of labeled value)
- Inaccurate
(CBD content more than 10% higher or lower than labeled value)

Of 84 products analyzed, nearly **70%** were inaccurately labeled with respect to CBD and **21.4%** contained THC^{28,29}

Due to variable CBD and THC content, the authors concluded that these products should be avoided for pediatric patients²⁹

The FDA warns against **mislabeling and false claims**^{30,31}



The FDA continues to send warning letters to non-FDA-approved CBD companies, **noting unsubstantiated medical claims. Their analysis also found mislabeled cannabinoid content**³⁰

Oversight by healthcare professionals is vitally important

Cannabinoids can alter the effect of other medications³

Cannabinoids could decrease or increase the levels of other drugs the patient is taking³



CHAPTER 3

What's the
difference?



**treating
with
confidence**

- ✓ FDA-approved
- ✗ Non-FDA-approved



What's the difference? **Measured Quality**

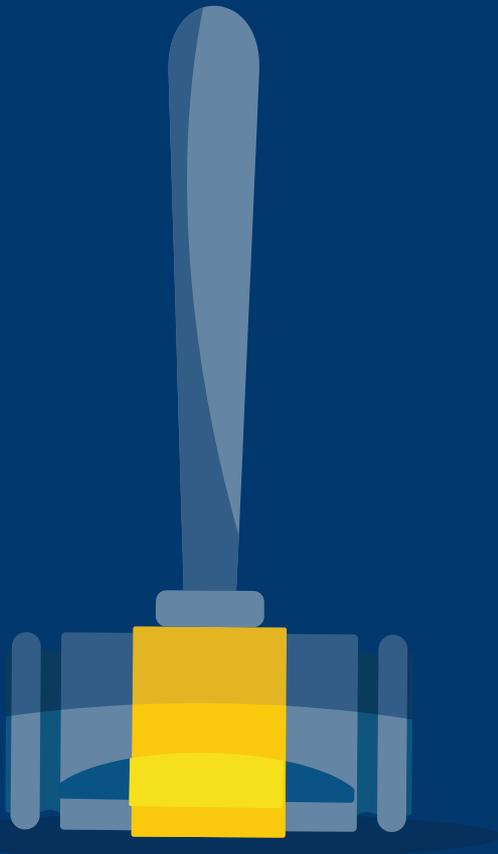
- ✓ Rigorously tested in controlled clinical trials to understand the safety profile and efficacy^{3,32}
- ✗ Have not been evaluated in clinical trials for safety; results are anecdotal, relying on parental reporting on patients taking nonstandardized dosing³³⁻³⁵
- ✓ Must meet FDA standards for quality and stability³²
- ✗ Testing standards vary from state to state and lab to lab²⁷
- ✓ Consistent concentrations of medicine ensured across every batch³
- ✗ Contents may vary between products and batches of the same brand²⁸
- ✓ Produced and federally inspected to ensure current good manufacturing practices (cGMP)³²
- ✗ Unknown inspection of manufacturing sites

- ✓ FDA-approved
- ✗ Non-FDA-approved

What's the difference?

Legal Status

- ✓ Federally legal in all 50 states³
- ✗ Though federally legal if less than 0.3% THC, products cannot be added to supplements or food products, nor promoted as a medicine^{2,36}
- ✓ Available with a prescription
- ✗ Cannot be prescribed, only “recommended”²
- ✓ Eligible for insurance coverage
- ✗ Not eligible for insurance coverage
- ✓ Can be legally transported between states
- ✗ Interstate transportation is federally illegal²



References: **1.** ElSohly MA, Gul W. In: *Handbook of Cannabis*. Oxford University Press: United Kingdom. 2014. **2.** Mead A. *Epilepsy Behav.* 2017;70(Pt B):288-291. **3.** EPIDIOLLEX [package insert]. Carlsbad, CA: Greenwich Biosciences, Inc.; 2018. **4.** Rosenberg EC, Tsien RW, Whalley BJ, Devinsky O. *Neurotherapeutics.* 2015;12(4):747-768. **5.** Thiele EA, Marsh ED, French JA, et al. *Lancet.* 2018;391(10125):1085-1096. **6.** Devinsky O, Patel AD, Cross JH, et al. *N Engl J Med.* 2018;378(20):1888-1897. **7.** Devinsky O, Cross JH, Laux L, et al. *N Engl J Med.* 2017;376(21):2011-2020. **8.** Pertwee RG. *Br J Pharmacol.* 2006;147(suppl 1):S163-S171. **9.** Marinol [package insert]. North Chicago, IL: AbbVie Inc.; 2017. **10.** Food and Drug Administration. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-q7a-good-manufacturing-practice-guidance-active-pharmaceutical-ingredients>. Accessed December 17, 2019. **11.** Hall W. In: *Handbook of Cannabis*. Oxford University Press: United Kingdom. 2014. **12.** National Institute of Drug Abuse. <https://www.drugabuse.gov/publications/drugfacts/marijuana-medicine>. Accessed December 17, 2019. **13.** Vandrey R, Hermann ES, Mitchell JM, et al. *J Anal Toxicol.* 2017;41(2):83-99. **14.** NBC Los Angeles. <https://www.nbclosangeles.com/news/pesticide-laced-pot-lab-results-company-statements-i-team/31337/>. Accessed December 17, 2019. **15.** The News & Observer. <https://www.newsobserver.com/news/local/article203824334.html>. Accessed December 17, 2019. **16.** Forbes. <https://www.forbes.com/sites/janetwburns/2018/05/26/officials-say-fake-cbd-poisoned-at-least-52-people-in-utah-last-winter/#c2f383c7dd3b>. Accessed December 17, 2019. **17.** The Denver Post. <https://www.denverpost.com/2019/10/21/cbd-vaping-illness-clusters/>. Accessed December 17, 2019. **18.** Consumer Reports. <https://www.consumerreports.org/cbd/dangerous-chemicals-found-in-popular-cbd-products-diamond-cbd-5f-adb/>. Accessed December 17, 2019. **19.** Caulkins JP. https://www.rand.org/content/dam/rand/pubs/working_papers/2010/RAND_WR764.pdf. Accessed December 17, 2019. **20.** United Nations Office on Drugs and Crime. https://www.unodc.org/documents/wdr/WDR_2009/WDR2009_eng_web.pdf. Accessed December 17, 2019. **21.** Girdhar M, Sharma NR, Rehman H, et al. *3 Biotech.* 2014;4(6):579-589. **22.** Subritzky T, Pettigrew S, Lenton S. *Int J Drug Policy.* 2017;42:86-96. **23.** AP News. <https://apnews.com/2cb04323f9074c1ca28001693f6e2a8a/Big-safety-testing-failure-rate-for-California-pot-products>. Accessed December 17, 2019. **24.** Thompson GR III, Tuscano JM, Dennis M, et al. *Clin Microbiol Infect.* 2017;23:269-270. **25.** GenTech Scientific. <https://cannabis.gentechscientific.com/cannabis-testing-regulation>. Accessed December 17, 2019. **26.** Norml. <https://norml.org/laws>. Accessed December 18, 2019. **27.** Jikomes N, Zoorob M. *Sci Rep.* 2018;8(1):4519. **28.** Bonn-Miller MO, Loflin MJE, Thomas BF, et al. *JAMA.* 318(17):1708-1709. **29.** Freedman DA, Patel AD. *Pediatr Neurol Briefs.* 2018;32:3. **30.** Food and Drug Administration. <https://www.fda.gov/news-events/public-health-focus/warning-letters-and-test-results-cannabidiol-related-products>. Accessed December 17, 2019. **31.** Food and Drug Administration. <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/koi-cbd-llc-593391-11222019>. Accessed December 17, 2019. **32.** Data on file. Greenwich Biosciences, Inc., Carlsbad, CA. **33.** Porcari GS, Fu C, Doll ED, et al. *Epilepsy Behav.* 2018;80:240-246. **34.** Press CA, Knupp KG, Chapman KE. *Epilepsy Behav.* 2015;45:49-52. **35.** Rosenberg EC, Louik J, Conway E, et al. *Epilepsia.* 2017;58(8):e96-e100. **36.** Food and Drug Administration. <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-signing-agriculture-improvement-act-and-agencys>. Accessed December 17, 2019.



CANNABINOIDS 101



Cannabis sativa:

A plant from which specific cannabinoids (such as THC and CBD) are derived¹

THC and CBD are unique compounds with different effects on the brain

CBD has been shown to reduce seizures in clinical studies and does not cause a “high”^{3,4}

THC is responsible for the “high” marijuana causes^{3,8}

3 categories of cannabis-based products



Pharmaceutical formulations^{3,9,10}

- Studied for safety and efficacy
- FDA standards ensure consistency and stability



Medical & recreational marijuana²

- Defined by intent of use
- “Recommended” but not prescribed in the absence of FDA approval



Hemp²

- No more than 0.3% THC (can be enough to cause intoxication)
- Inefficient source of CBD
- Absorbs heavy metals and chemical waste from soil

NON-FDA-APPROVED PRODUCTS

Products may be produced with substandard manufacturing and can be contaminated with^{14,21,23,24:}



Mold & bacteria



Heavy metals



Harmful chemicals

**ONLY
23/47**

states with medical cannabis laws have testing requirements^{25,26}

Of 84 products analyzed,
~70%
were inaccurately labeled
with respect to CBD and

21.4%
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The FDA continues to send warning letters, noting **unsubstantiated medical claims and mislabeled cannabinoid content²⁹**

FDA-APPROVED MEDICINE



Produced and inspected to ensure current good manufacturing processes (cGMP)³²



Safety and efficacy **rigorously tested** in controlled clinical trials^{3,32}



Consistent dosing and medication concentration in every batch³



Federally legal and available in all 50 states³



Available with prescription



Eligible for insurance



Can be **legally transported** between states

