
Cannabinoids

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Disclosures

- No financial disclosures

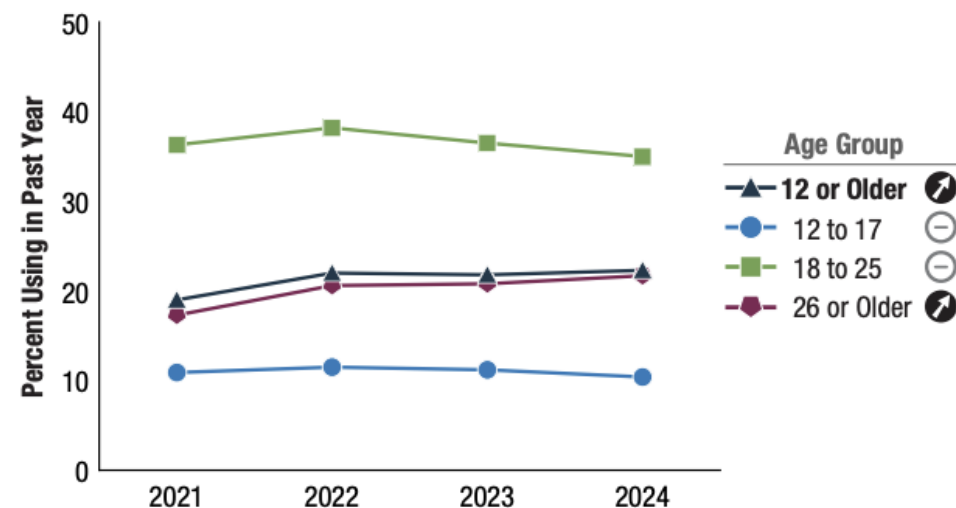
At the conclusion of this presentation, audience members should be able to:

- Recall recent epidemiology trends on cannabis use in the United States
- Describe the difference between endogenous, phyto and synthetic cannabinoids
- Understand Farm Bill implications on cannabis products
- Review cannabis products available in Virginia
- Name symptoms of cannabinoid intoxication and differences expected with new products and synthetic products
- Interpret a urine drug screen

Epidemiology

- ~52.5 million people, or about 19% of Americans used cannabis at least once in 2021
- Most commonly used “illicit” substance in the US
- ~3 in 10 people who use cannabis have cannabis use disorder (greater risk if use before 18)
- Among people 12 or older, past-year use of Marijuana increased from 19.0% in 2021 to 22.3% in 2024

Figure 15. Past Year Marijuana Use: Among People Aged 12 or Older; 2021-2024



Note: Estimates for 2021 may differ from previously published estimates because the 2021 analysis weights were updated to facilitate between-year comparisons.

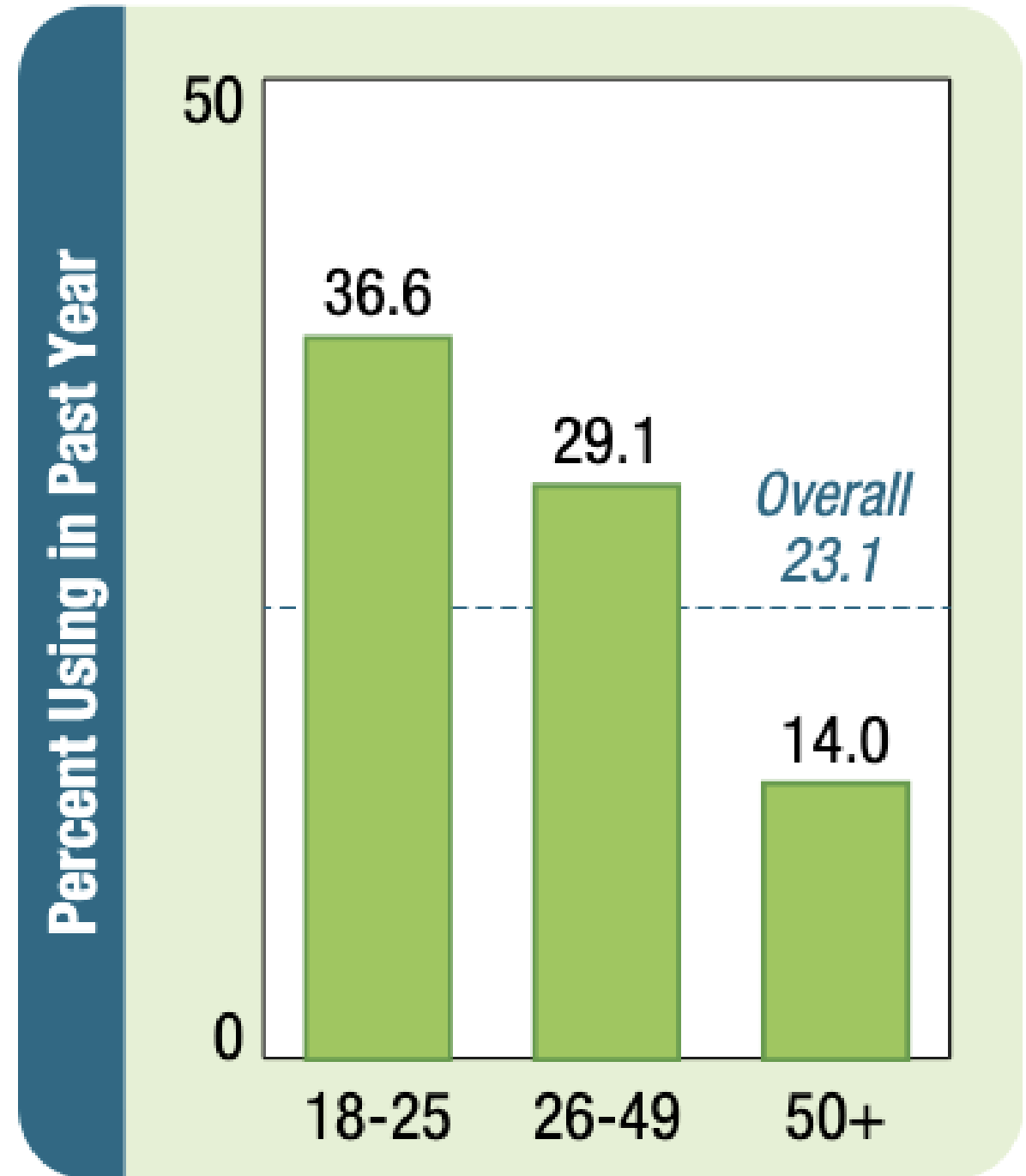
Figure 15 Table. Past Year Marijuana Use: Among People Aged 12 or Older; Percentages, 2021-2024

Age Group	2021	2022	2023	2024	Trend
12 or Older	19.0	22.0	21.8	22.3	Increased
12 to 17	10.9	11.5	11.2	10.4	No Change
18 to 25	36.3	38.2	36.5	35.0	No Change
26 or Older	17.3	20.6	20.8	21.7	Increased

Note: Estimates for 2021 may differ from previously published estimates because the 2021 analysis weights were updated to facilitate between-year comparisons.

National Survey on Drug on Use and Health 2022-24

Use in the past year by age
18- 25 (36.6%)
26 to 49 (29.1%)
50 or older (14.0%)



National Survey on Drug on Use and Health 2022-24

Males 12-17 years were
less likely than females to
have used marijuana in the
past year (9.7% vs. 12.4%)

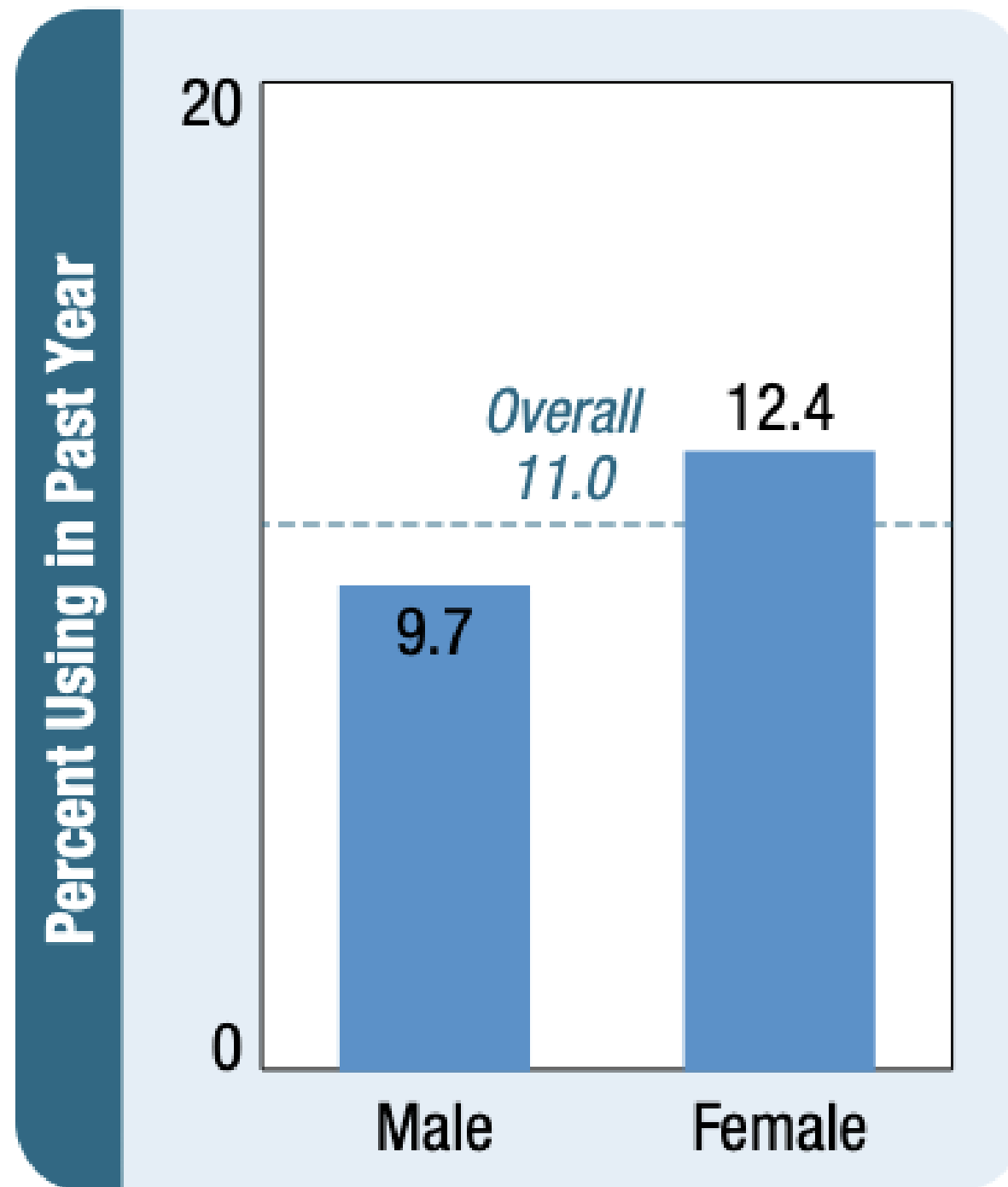
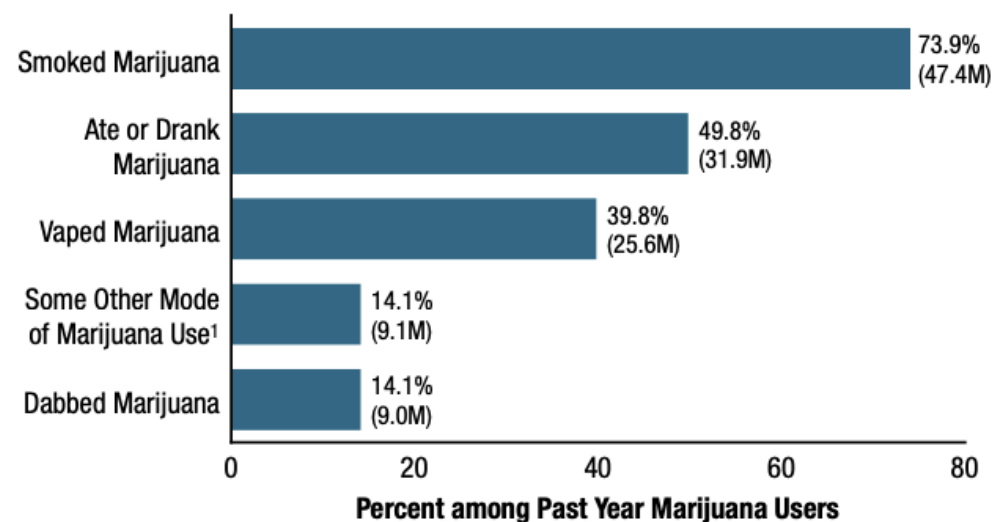


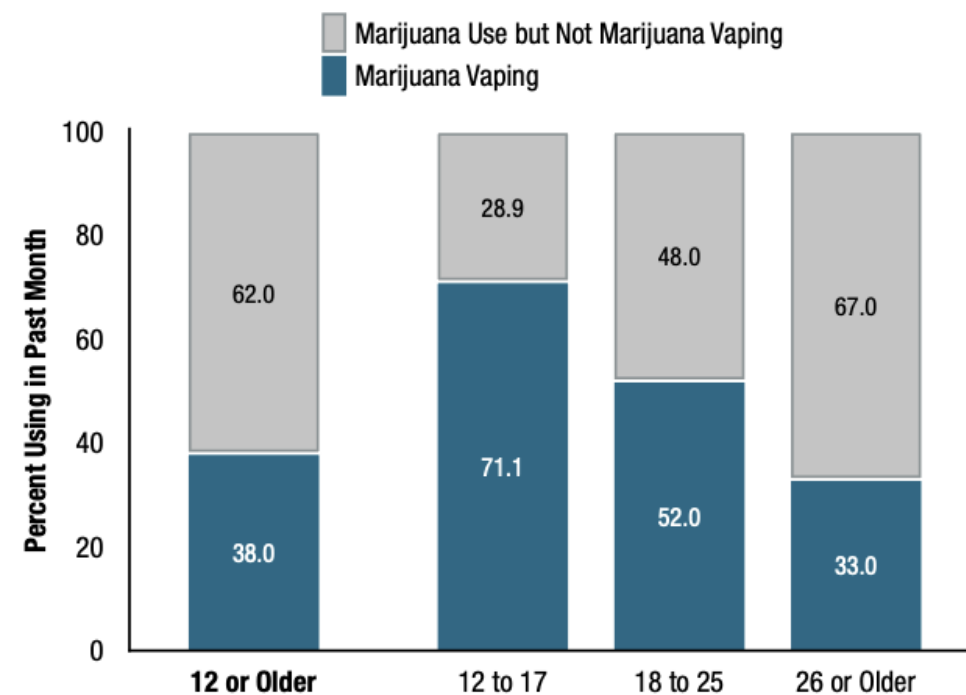
Figure 16. Mode of Past Year Marijuana Use: Among People Aged 12 or Older Who Used Marijuana in the Past Year; 2024



Note: Respondents could indicate multiple modes of marijuana use; thus, these response categories are not mutually exclusive.

¹ Includes applying lotion, cream, or patches to skin; putting drops, strips, lozenges, or sprays in mouth or under tongue; taking pills; or some other way not already listed in this figure.

Figure 12. Type of Past Month Marijuana Use: Among Past Month Marijuana Users Aged 12 or Older; 2024





Youth Cannabis Vaping

- 2021 high school aged: reported past-month cannabis vaping
 - 8th Grade – 2.9%
 - 10th Grade – 8.4%
 - 12th Grade – 12.4%
- 2021 college/young adult: reported past-month cannabis vaping
 - 19-20yr – 13.6%
 - 21-22yr – 21.8%
 - 23-24yr – 13.0%

2022 Virginia Young Adult Survey by the Virginia Department of Health (VDH)

- 45% of 18–20 year olds have used cannabis at some point in their lives
- First reported use of cannabis:
 - 2% first use before age 12
 - 14% first use between ages 12–14
 - 39% first use between 15–17



2022 Virginia Young Adult Survey by the Virginia Department of Health (VDH)

- High school age females more likely than males to use cannabis products within the past 30 days
 - All cannabis products → females (14.7%) vs males (12.1%)
 - Vape products → females (18.2%) vs males (10.6%)

2022 Virginia Young Adult Survey by the Virginia Department of Health (VDH)

2021 VDH Youth Risk Behaviour Survey 2.

Table 3. Virginia Youth Marijuana Usage and Vaping Over the Past Month (2021)

	Marijuana	Vaping²⁸
Age 15 or younger	8%	10.5%
Age 16-17	16.5%	17.0%

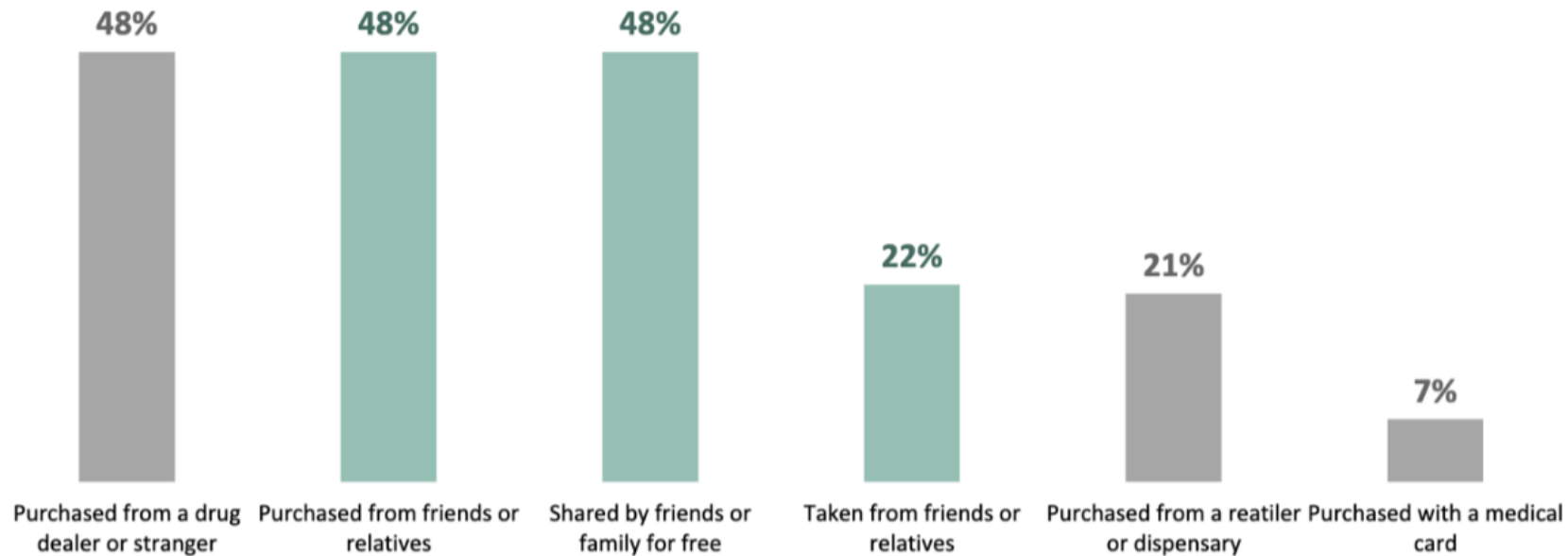
The rate of reported marijuana usage among Virginia youth roughly doubled after the age of 16, and of the youth who reported vaping, approximately 2% purchased products in a convenience store, gas station, or supermarket.

Virginia Young Adult Survey



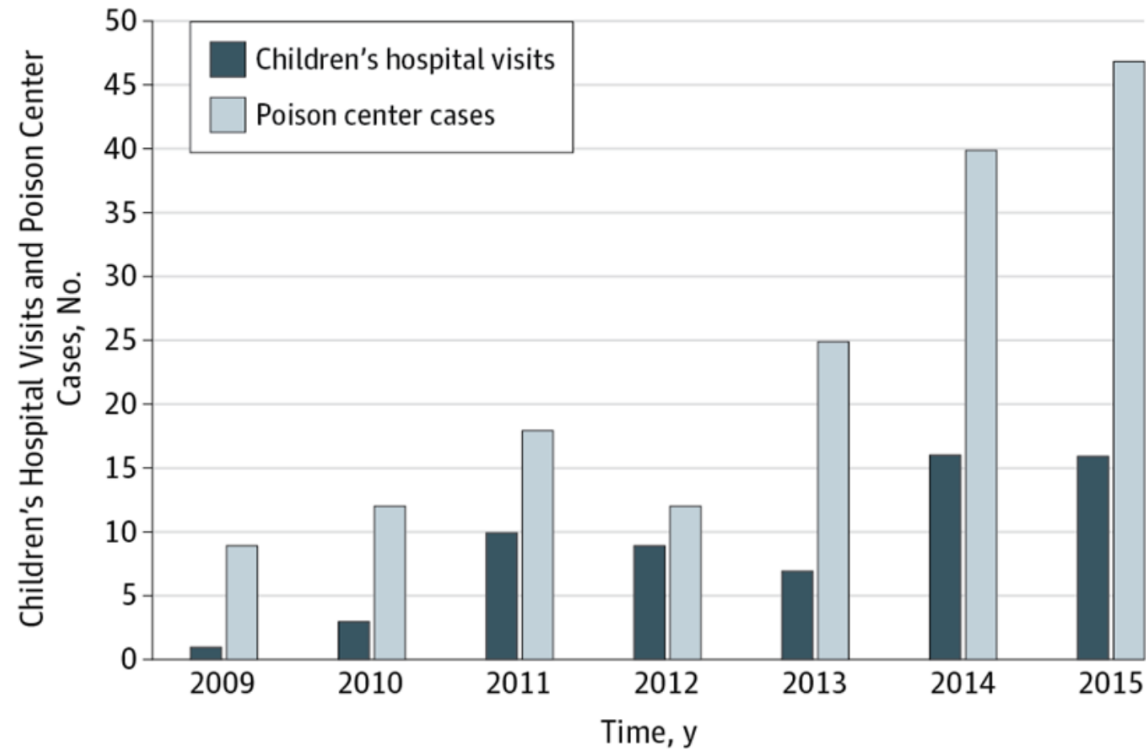
Peer Access of Cannabis Products

Young adults believe that many of their peers are accessing cannabis products through friends or family.



Hospitalizations due to cannabis

Figure 1. State Pediatric Marijuana Exposures



Annual children's hospital visits and regional poison center cases for unintentional marijuana exposures in children 9 years or younger in Colorado between 2009 and 2015. Children's hospital visits include emergency department visits, urgent care visits, and inpatient hospital admissions.

Legal does not mean safe

CANNABIS TERMINOLOGY



Cannabis

- *Cannabis* → genus of plants
 - *C. sativa*
 - *C. indica*
 - *C. ruderalis*
- *Cannabis* contains **cannabinoids** → substances that bind cannabinoid receptors (THC, CBD etc)



Cannabinoids

Substances that bind the CB receptors

CB 1 receptors

- Centrally located
- Psychoactive symptoms
- Regulation of cognition, memory/motor, nociception
- N/V

CB 2 receptors

- Peripherally located
- Anti-inflammatory effects

Downstream effects

- Modulate neurotransmitters including GABA, serotonin, dopamine, norepinephrine, acetylcholine, glutamate

Cannabinoids

Substances that bind the CB receptors

Endogenous cannabinoids

Phytocannabinoids

Synthetic cannabinoids

CANNABINOID PRODUCTS





Phytocannabinoids

- From the Cannabis plant
- 100+ substances
 - Delta 9-THC
(tetrahydrocannabinol)
 - CBD (cannabidiol)

Regular plant → Maryjane,
MJ, pot, weed, dank, ganja,
holy weed, jazz cigarette

Pressed resin from top of
plant → hashish

Oil from resin → butane
hash oil, dab, budder, earwax

Phytocannabinoids

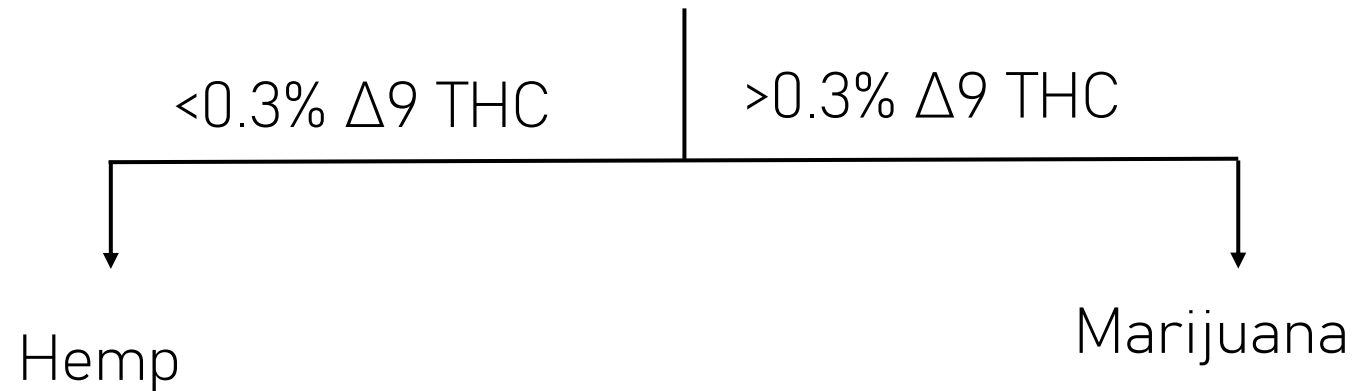
- From the Cannabis plant
- 100+ substances
 - Delta 9-THC
(tetrahydrocannabinol)
 - CBD (cannabidiol)

Farm Bill 2018

* Δ^9 THC is the main psychoactive cannabinoid in the cannabis plant

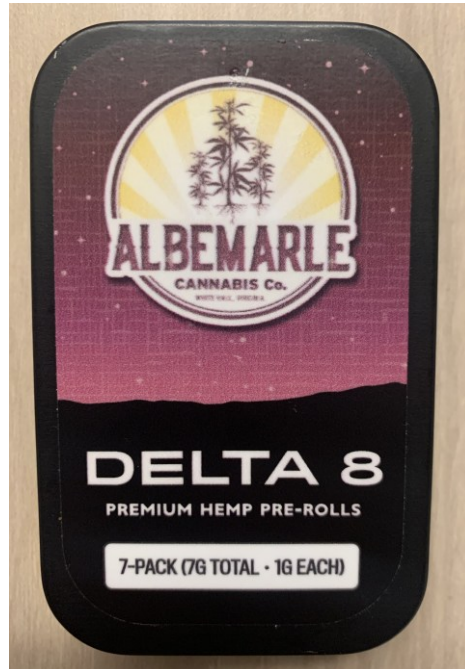


Cannabis plant



1995 ave 4% THC
2019 ave 15% THC

“Phytocannabinoids”



“Phytocannabinoids”





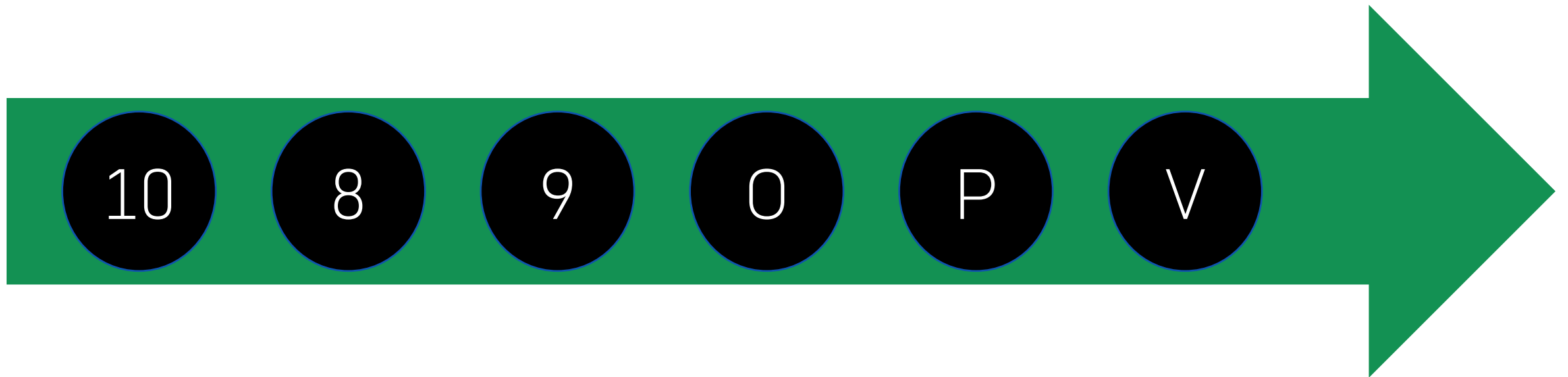
THC-A, THC-B



THC-A, THC-P, THC-M



Delta THC potency scale



Prescription “phytocannabinoids”

Dronabinol (Marinol, Syndros)

- Synthetic form of **delta 9 THC**
- FDA approved for chemotherapy induced N/V and as an appetite stimulant for patients with AIDS
- Schedule III substance

Nabilone (Cesamet)

- Oral mucosal spray with chemical structure similar to **delta 9 THC**
- FDA approved for chemotherapy induced N/V
- Schedule II substance

Epidiolex

- **CBD**, oral solution
- FDA approved for epilepsy from Dravet, Lennox-Gestaut syndromes, and tuberous sclerosis
- Schedule V substance



Synthetic cannabinoids

- 2004 Germany
- Sold as "herbal incense"
- JWH-018 was first isolated structure
- Bind to CB receptors with 100x potency of phytocannabinoids

Spice in prison

Synthetic cannabinoids in prisons – invisibly impregnated paper sheets as a Trojan horse

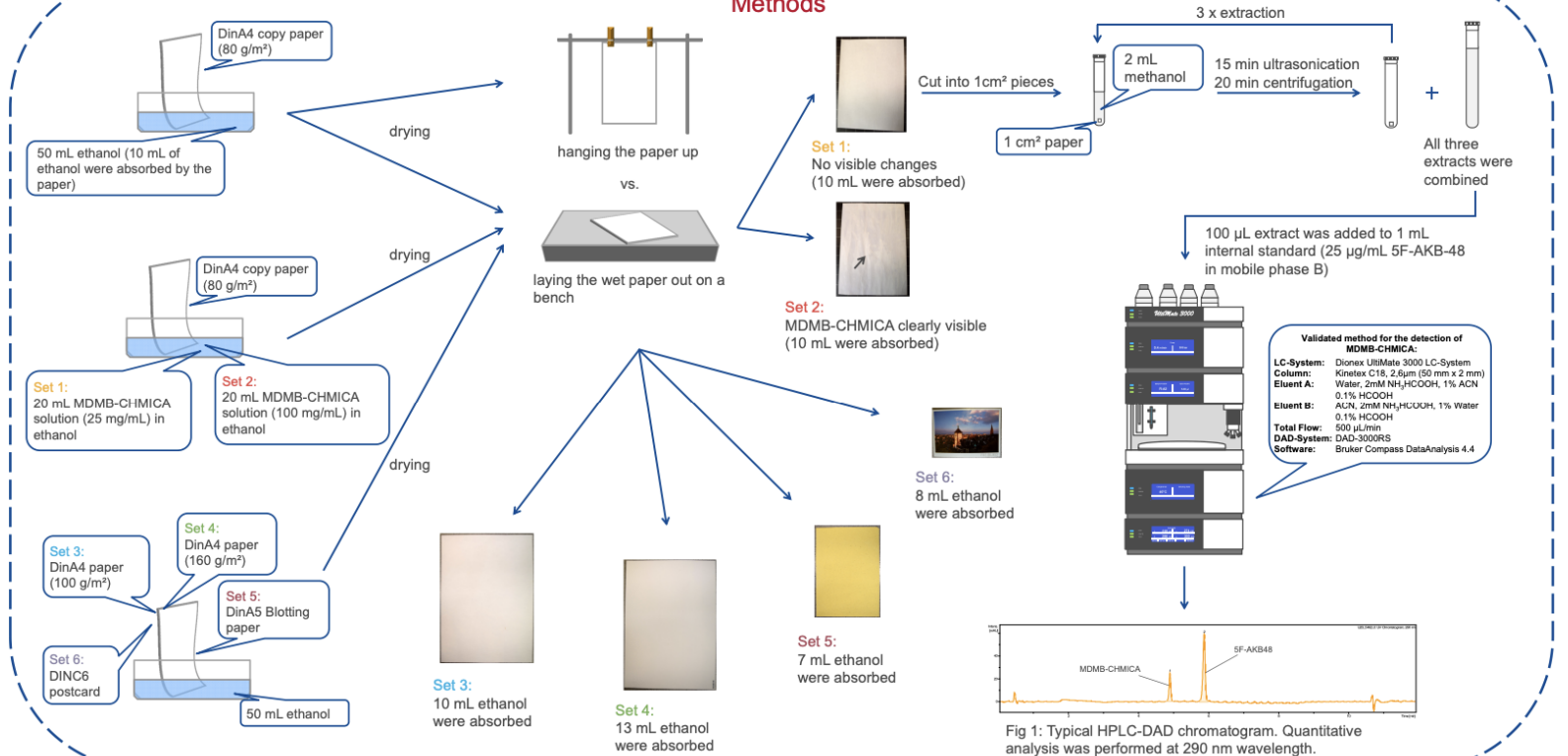
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Background and Objectives

Synthetic cannabinoids (SCs) have been among the most prevalent new psychoactive substances for many years. Due to the non-detectability of most SCs with commercially available rapid test systems SCs are highly prevalent in prisons and in general among people regularly tested for drug abstinence. Often SCs are smuggled into prisons in the form of paper sheets impregnated with SCs (e.g. letters or paintings). The aim of this study was to investigate preparation techniques of soaking paper with SC solutions with a focus on visibility of this manipulation.

Methods





CANNABINOID TOXICITY SYMPTOMS

Cannabis symptoms

Smoking

- Symptoms within minutes
- 10-35% of available THC absorbed

Eating

- Symptoms 1-3 hours
- 5-20% of available THC absorbed

Phytocannabinoid acute symptoms

Vital sign changes

- Tachy/bradycardia
- Hyper/hypotension

General

- N/V
- Bloodshot eyes

Neuro/psych

- Impaired judgement, high, anxiety, paranoia, psychosis
- Drowsiness, fatigue
- Ataxia
- Decreased coordination, slow reaction time

Phytocannabinoid chronic symptoms

Rome Criteria for Cannabis Hyperemesis

Required criteria [8]	Comments
1. Symptoms present for past 3 months (with onset at least 6 months prior) 2. Stereotypical episodes lasting <1 week 3. At least 3 episodes in last 1 year and 2 episodes in last 6 months (occurring at least 1 week apart) 4. No vomiting between episodes. Milder symptoms can be present during this. All these criteria should be associated with chronic use of cannabis and stop after its cessation	Definition of chronic use needs more elaboration Cessation of cannabis use needs to be defined for an exact period

- Psychosis (acute and chronic)
- COPD
- Increased risk of coronary artery disease
- Reduced fertility
- Cannabis hyperemesis syndrome
 - Downregulation of CB receptors

Seiz

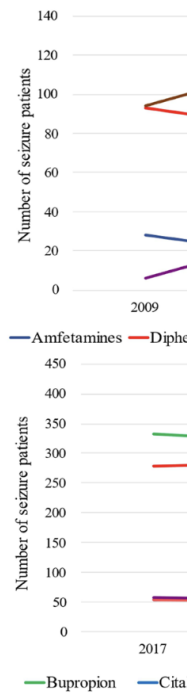
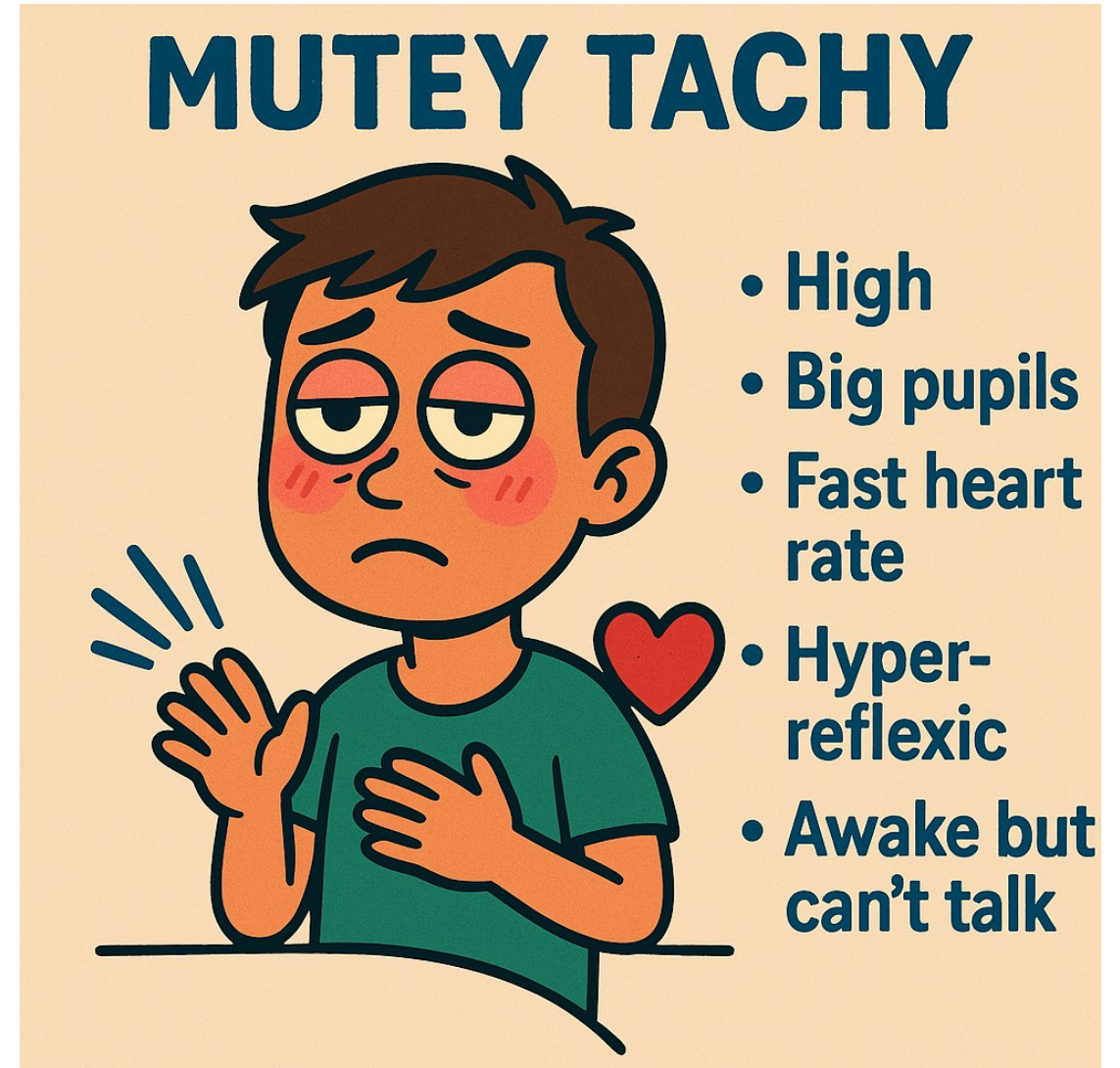


Figure 3. Trends in seizure patients grouped by four ti



“Phytocannabinoids”

- Delta 8 THC → “mutey tachy”
 - Tachycardia
 - Clonus
 - Temporary mutism
- Most common symptoms reported to poison centers for delta 8, delta 10, THC-O
 - CNS depression
 - Tachycardia
 - Agitation
- THC-P causing severe altered mental status and intubation

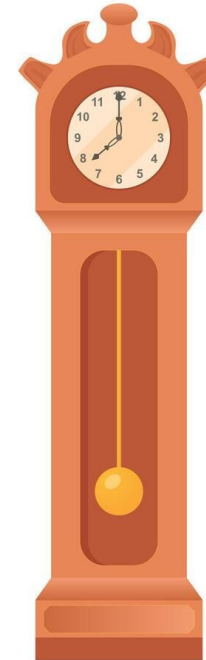




Synthetic cannabinoids

- Most commonly reported symptoms
 - Tachycardia, agitation, drowsiness, nausea, vomiting and hallucinations
- Other reported symptoms
 - Seizures, psychosis, delusions, depressed mood, catatonia, mania, headache, dizziness, chest pain
- Rare but serious symptoms
 - Stroke, MI, AKI, rhabdo, death

Treatment





CANNABINOID DRUG DETECTION

Urine drug screen (UDS)



Things that turn UDS positive for marijuana

- Cannabis plant
- Delta 9 THC products
- Delta 8 THC products

Things that don't turn UDS positive for marijuana

- Pure CBD
- Synthetic cannabinoids

Things that may turn UDS positive for marijuana

- Delta 10 THC, THC O, THC V, THC P, HHC
- Second hand smoke (rarely, need very high exposure)

Immunoassay drug screen for "marijuana"

- Common method of UDS screens
- Screening for Delta 9-THC metabolite 11-nor-9-THC carboxylic acid (THC-COOH)
- Stays positive 2 weeks – 2 months
- Positive screen does NOT equal acute intoxication

Confirmation testing with GCMS for THC-COOH

- Not done at every hospital
- Highly specific



Mayo Labs #FCSC: Synthetic Cannabinoids

REFERENCE VALUES ⓘ

Reporting limit determined each analysis.

<u>Test</u>	<u>Result</u>	<u>Units</u>
5F-PINACA 3-methylbutanoic acid	None Detected	ng/mL
4F-BINACA 3,3-dimethylbutanoic acid	None Detected	ng/mL
5F-PICA 3,3-dimethylbutanoic acid	None Detected	ng/mL
5F-PINACA 3,3-dimethylbutanoic acid	None Detected	ng/mL
MDMB-4en-PINACA butanoic acid	None Detected	ng/mL
FUBINACA 3-methylbutanoic acid	None Detected	ng/mL
FUBINACA 3,3-dimethylbutanoic acid	None Detected	ng/mL
4-carboxy-NA-PIM	None Detected	ng/mL

Analyte(S)
4-fluoro-BINACA 3,3-dimethylbutanoic acid
4-fluoro-MDMB-BINACA
5-fluoro-MDMB-PICA / 5-fluoro-EMB-PICA
5-fluoro-MDMB-PINACA / 5-fluoro-EMB-PINACA
5-fluoro-PICA 3,3-dimethylbutanoic acid
5-fluoro-PINACA 3,3-dimethylbutanoic acid
5-fluoro-PINACA 3-methylbutanoic acid
ADMB-CHMINACA
ADMB-FUBINACA
APP-BINACA
FUBINACA 3,3-dimethylbutanoic acid
FUBINACA 3-methylbutanoic acid
MDMB-4en-PINACA
MMB-FUBINACA



LAWS AND REGULATIONS

FEDERAL LAWS

Drug Enforcement Administration (DEA) Scheduling definitions

Schedule I	Substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse	Heroin Ecstasy LSD Psilocybin Tetrahydrocannabinoids
Schedule II	Substances, or chemicals are defined as drugs with a high potential for abuse, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous.	Oxycodone Cocaine Dextroamphetamine
Schedule III	Substances, or chemicals are defined as drugs with a moderate to low potential for physical and psychological dependence. Schedule III drugs abuse potential is less than Schedule I and Schedule II drugs but more than Schedule IV.	Ketamine Buprenorphine/naloxone Acetaminophen with codeine
Schedule IV	Substances, or chemicals are defined as drugs with a low potential for abuse and low risk of dependence.	Lorazepam Barbital
Schedule V	Substances, or chemicals are defined as drugs with lower potential for abuse than Schedule IV and consist of preparations containing limited quantities of certain narcotics. Schedule V drugs are generally used for antidiarrheal, antitussive, and analgesic purposes	Pregabalin Codeine preparations < 200mg/100mL



What is legal in Virginia?

- Medical cannabis sold by a licensed pharmaceutical processor or dispensing facility
- Possession of cannabis for personal use in your private residence
- Public possession of up to 1 oz. of cannabis for personal use
- Home cultivation of up to four cannabis plants.
- Adult-sharing – the private transfer of 1 oz. or less of cannabis between people 21 years or older without exchanging anything else of value.
- Per VA Hemp Law in 2023– can sell delta 9 THC retail if the ratio of CBD to total delta 9 THC is at least **25:1**



VIRGINIA DEPARTMENT
OF AGRICULTURE AND
CONSUMER SERVICES

What is not legal in Virginia?

- Delta 8 THC
- THC product with more than 2 mg per package unless the CBD:THC ratio is 25:1

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Virginia mother arrested, charged in child's death after 4-year-old ate THC gummies, police say

By Claudia Dominguez and Raja Razek, CNN

🕒 2 min read · Published 7:47 PM EDT, Fri October 21, 2022

Medical dispensaries

- VA Cannabis Control Authority regulates cannabis products sold from medical dispensaries since 2021
- Divide state into 5 health service areas → each area has a licensed pharmaceutical processor
- RISE Dispensaries owned by Green Thumb Industries service southwestern VA
 - Abingdon, VA
 - Bristol, VA

Key Takeaways on Cannabinoids and Cannabis

- Cannabis use is rising
- Cannabinoids include endogenous, phytocannabinoids, and synthetic types affecting CB1 and CB2 receptors
- The Farm Bill created a loophole for the sale of non delta 9 THC products (delta 8/10, THC-P/O/A/M/B/V)
- Products at medical dispensaries are regulated by the Virginia Cannabis Control Authority
- Recreational cannabis products are unregulated
- Cannabinoid intoxication symptoms range from mild to severe, with synthetic cannabinoids posing additional risks
- "Marijuana" urine drug screens detect the delta 9 THC-COOH metabolite and may cross react with "phytocannabinoids" but do not detect synthetic cannabinoids



1-800-222-1222



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