"GAS STATION DRUGS":

DEMYSTIFYING CORNER SHOP-BOUGHT PRODUCTS WITH ABUSE POTENTIAL

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Kentucky Pharmacy Education and Research Foundation, Inc. is accredited by ACPE as a provider of continuing pharmacy education.

ACPE UAN 0143-9999-25-065-L08-P/T

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DISCLOSURES

Faculty

Ashley Haynes, faculty for this activity, has no relevant financial relationship(s) with ineligible companies to disclose.

While Dr. Haynes works for Veteran's Affairs, positions and opinions presented are her own and do not represent the VA or Federal Government.

Planners

None of the planners for this activity have any relevant financial relationships with ineligible companies to disclose.

PRE-TEST

Question 1. A patient notes they have recently tried kratom and asks for advice. Which is the most appropriate response?

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B. Kratom has multiple drug interactions
C. Kratom has never been associated with any harm
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B. Arrhythmia
C. Chest wall rigidity
D. Death due to respiratory effects of opioid overdose

OBJECTIVES

For Pharmacists:

- Discuss common rising psychoactive products available in gas stations and corner shops
- Discuss effects of these products
- Discuss legalities of these products

For Technicians:

- Discuss common rising psychoactive products available in gas stations and corner shops
- Discuss effects of these products
- Discuss legalities of these products
- Be prepared to counsel patients regarding lack of regulation of these products
- Be prepared to counsel patients regarding addictive potential of some of these agents

DIETARY SUPPLEMENT HEALTH AND EDUCATION ACT OF 1994

- For non-tobacco non-food products intended for consumption not as a food source to gain possible health benefits, not intended for market as a pharmaceutical
  - Cannot make claims to cure
  - Are not to be misbranded or mislabeled
- Outside of FDA control, and thus onus is on FDA to prove unsafe rather than companies to prove they ARE safe

Beware Supplements!

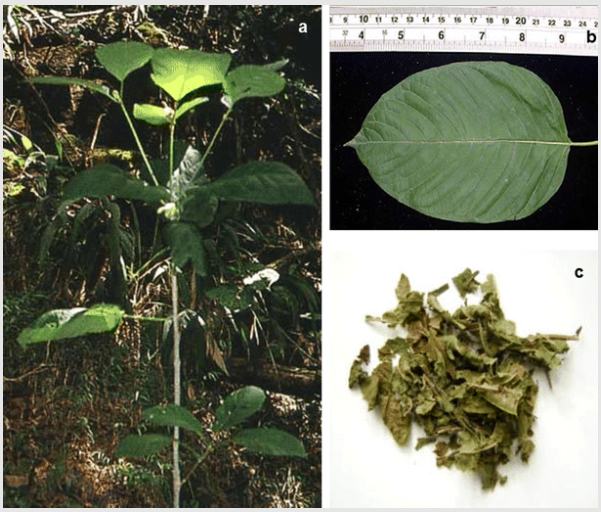
CASE EXAMPLE

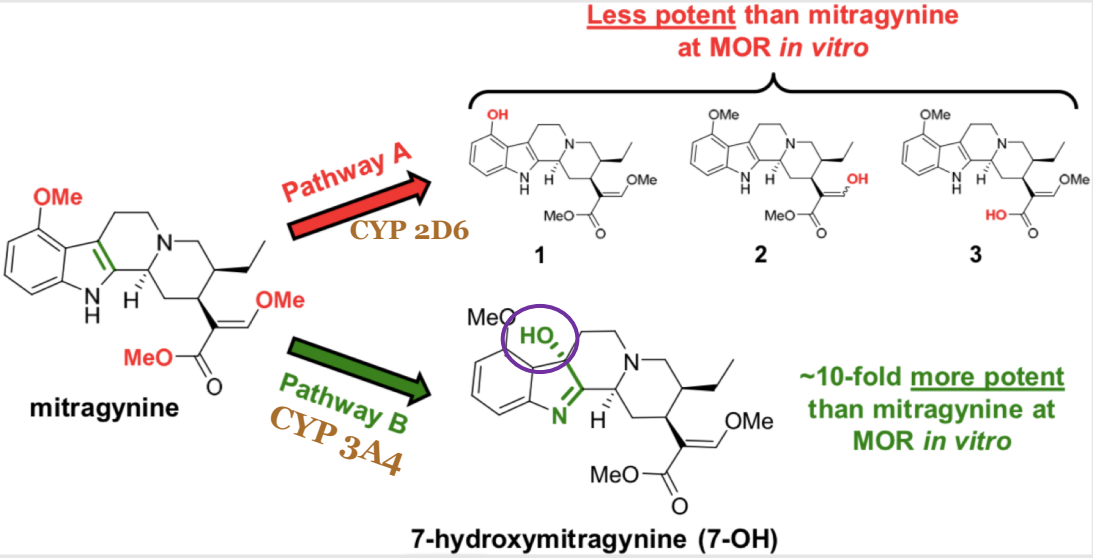
35 yo male with history of fentanyl use begins using an herbal tea from a shop near his house to help minimize withdrawal.

After a few weeks, he is now using this product all day and even waking at night to take it, and develops sweats, shakes, nausea and irritability when he tries to quit.

KRATOM

- Tropical tree that is indigenous to SE Asia (Thailand, Malaysia)
- Like coca or khat, kratom leaves are chewed or prepared as a powder or juice
  - Low dose (1-5 g): stimulant effects used to reduce fatigue in laborers
  - Moderate dose (5-15 g): opioid effects
  - High dose (> 15 g): severe opioid effects including stupor





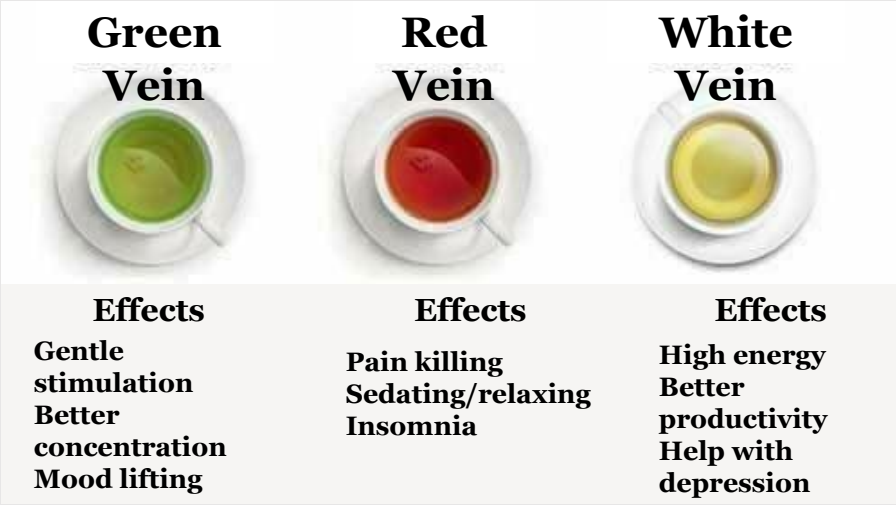
KRATOM USE IN SE ASIA

- Traditional uses
  - Laborers (stimulant activity)
  - Pain and other ailments
- Modern uses
  - Opioid withdrawal or other drug addiction issues
  - Recreational use

"4 x 100" Cocktail

https://www.cbc.ca/fifth/blog/more-on-4-x-100

KRATOM USE IN THE WEST: IMPROVE HEALTH



http://borrabnudfilms.blogspot.com/2018/07/

KRATOM USE IN THE WEST: OPIOID WITHDRAWAL

My strategic plan for using kratom for opiate withdrawal consists of obtaining the following items:

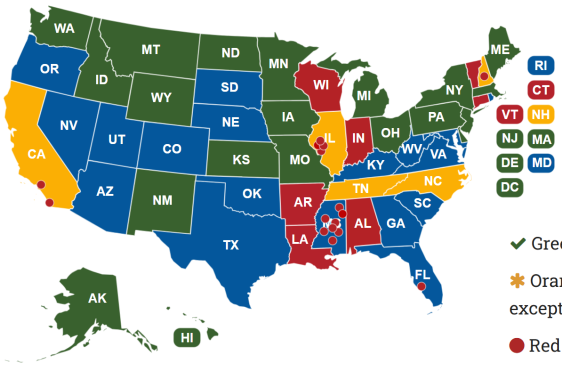
- 8 ounces of Top Extracts Classic Red Bali
- 20 grapefruits
- A cheap digital scale
- A 30-day supply of an Opiate Withdrawal Supplement

The eight ounces of kratom should be more than enough to get you through your opiate withdrawal. The grapefruits on the shopping list are going to be used to make fresh juice to mix with the kratom powder.

Grapefruit juice is a great "potentiator", which means that it increases the effects of kratom.

https://opiateaddictionsupport.com/how-to-use-kratom-for-opiate-withdrawal/

LEGALITY



- ✔ Green: Kratom is legal in the state
- ✱ Orange: States legal but with some known local bans or with exceptions.
- ● Red Dot: banned city for Kratom
- ⊘ Red: Kratom is illegal and banned in the state
- ♥ Blue: These states have adopted the Kratom Consumer Protection Act bill

http://speciosa.org/home/kratom-legality-map/

KRATOM CONSUMER PROTECTION ACT

- A bill to:
- Regulate the preparation, distribution, and sale of kratom products
- Prohibit the preparation, distribution, and sale of adulterated or contaminated kratom products
- Prescribe fines and penalties and allow remedies
- Provide for the powers and duties of certain state governmental officers and entities.

- American Kratom Association pushing to increase prevalence

PROPOSED KRATOM MECHANISMS OF ACTION

- Receptors Affected
  - Partial agonism of μ, κ, and δ opioid receptors
  - Agonism of α_2 receptors
  - Antagonism of 5-HT_{2A} receptors
- Ion Channels Affected
  - Blocking of K^+ channels
  - Blocking of Ca^{2+} channels
- Other Mechanisms
  - 5-HT and NE reuptake inhibition
  - Inhibition of CYP3A4 and CYP2D6

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KRATOM-ASSOCIATED TOXICITY AND DEATHS

	Southeast Asia	West (US and Europe)
Side Effects	**Weight loss, dehydration, constipation, skin hyperpigmentation**	**N/V, stomach pain, chills and sweats, dizziness, unsteadiness, visual sx**
Toxicity	**No literature reports of serious toxicity or death**	**Seizures, hepatotoxicity, coma, multiple deaths, psychosis potential**
Where Obtained	**Locally**	**Internet, head shops**
How Used	**Usually used alone (but not always)**	**Often combined with other drugs**
Legal Status	**Illegal in Thailand, Malaysia**	**Legal in most of US and Europe**

KRATOM WITHDRAWAL

- In one study, 6 months of use associated with withdrawal
- Generally similar to opioid withdrawal syndrome
- Buprenorphine, methadone, naltrexone outpatient treatment options

Voelker R. *Crackdown on false claims to ease opioid withdrawal symptoms*. JAMA. 2018;319:857.

Singh D, et al. *Kratom (Mitragyna speciosa) dependence, withdrawal symptoms and cravings in regular users*. Drug and Alcohol Dependence. 2014;139:13

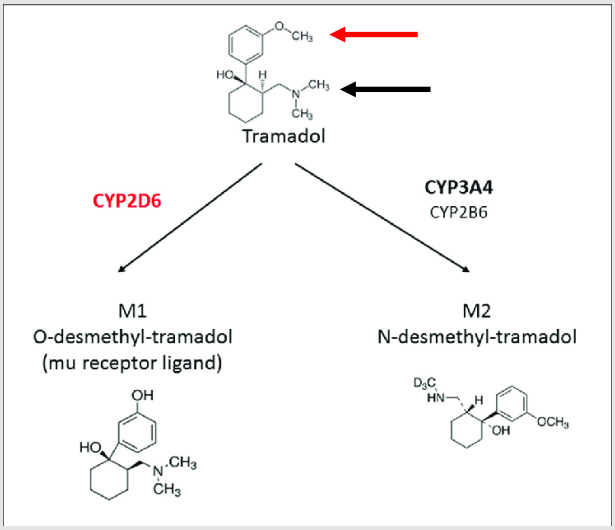
- Neonatal abstinence syndrome reported
  - Presentation similar to opioid NAS
  - Treated with opioid taper

Davidson, et al. *Natural Drugs, Not so Natural Effects*. J Neonatal Perinatal Med. 2019 (12):1.
Eldridge, et al. *Neonatal Abstinence Syndrome Due to Maternal Kratom Use*. Pediatrics. December 2018.

ADULTERATION OF KRATOM WITH OPIOIDS

- Krypton = mixture of kratom + O-desmethyltramadol, the active metabolite of tramadol
  - O-desmethyltramadol is twice as potent as tramadol
- Case series of nine deaths from Sweden from krypton
  - All had evidence of opioid overdose, including 8 with pulmonary edema
  - No parent drug (tramadol) and no other metabolites found

- Lydecker, et al. *Suspected Adulteration of Commercial Kratom Products with 7-Hydroxymitragynine*. J Med Toxicol. December 2016.



https://www.researchgate.net/publication/323556173_When_the_Safe_Alternative_Is_Not_That_Safe_Tramadol_Prescribing_in_Children/figures?lo=1

SUSPECTED ADULTERATION OF KRATOM SUPPLEMENTS

- Analysis of multiple kratom products was notable for higher-than-natural concentrations of 7-hydroxymitragynine in most products tested
  - Significant b/c 7-hydroxymitragynine is the most active component of kratom (17x higher μ opioid receptor affinity than morphine)
  - Likely a major contributing factor to the addictive potential and abuse liability of kratom
- Authors conclude that the products were likely deliberately adulterated w/ 7-hydroxymitragynine

- Lydecker, et al. *Suspected Adulteration of Commercial Kratom Products with 7-Hydroxymitragynine.* J Med Toxicol. December 2016

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WILL NALOXONE WORK?

- A definite maybe
- One case report detailing successful resuscitation of an opioid toxidrome that was attributed to sole kratom use
  - Use of other opioids was r/o by GC/MS
  - Doesn't specify which opioids were tested for

- Overbeek, et al. *Kratom (Mitragynine) Ingestion Requiring Naloxone Reversal.* Clin Pract Cases Emerg Med. Feb 2019.

- If the patient presents with an opioid toxidrome, give naloxone
  - But use it to treat respiratory depression

NEW KRATOM PRODUCT

Emerging use of "7-OH", or "7-OHM"

Containing 7-hydroxymitragynine
- MORE POTENT OPIOID
- NOT part of naturally occurring plant

FDA warning released 7/29/25
- NOT considered "lawful"

FDA Takes Steps to Restrict 7-OH Opioid Products Threatening American Consumers

Agency alerts health care professionals and consumers of 7-hydroxymitragynine risks

For Immediate Release: July 29, 2025

Hiding in Plain Sight: 7-OH Products are Designed to Look Like Everyday Treats Like Gummies, Candies and Ice Cream.

Note: These images are select illustrative examples and do not represent the full scope of 7-OH products on the market. Consumers should read packaging and labels carefully to determine whether a product contains 7-OH.

Preventing The Next Wave of the Opioid Epidemic: What You Need to Know About 7-OH 5

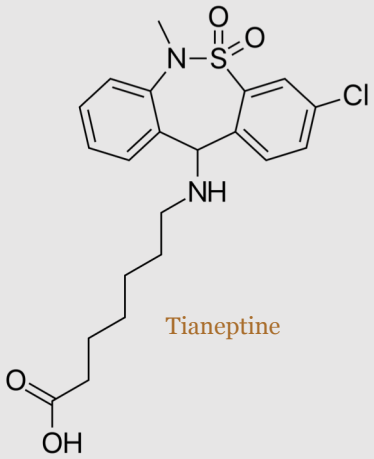
CASE EXAMPLE

44 yo male with history of opioid use disorder maintained on suboxone recently had his suboxone stopped for noncompliance.

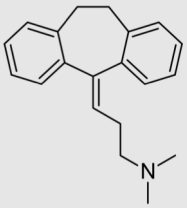
He began using a supplement sold as a "kratom booster" called "Pegasus" and is unsure of the contents.

TIANEPTINE

- AKA: GAS STATION HEROIN
  - Zaza, Tianna, Pegasys, Neptune's Fix
- Structurally: A TCA
  - Used in Europe, Asia, Latin America
  - Various scheduling
  - In US: "supplement"
  - Not FDA approved
  - Banned in FL, GA, AL, IN, KS, KY, MI, MS, NC, OH, TN, TX



Tianeptine



Amitriptyline

STILL FOUND IN NEIGHBORING STATES AND ONLINE

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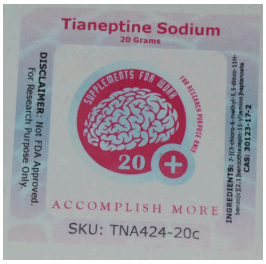

MOA:

- USUAL TCA MOA:
  - inhib
  - Also
    hista
- Howeve
  - Stabi
    recep
  - Redu
    beha

erminals

nuscarinic and

d AMPA

ss-induced

Full mu-opioid receptor agonist

Weak delta-opioid receptor agonist*[3]

* ~200-fold lower potency

- Levels of norepinephrine and dopamine levels are increased in several areas of the brain

TIANEPTINE

- FDA and CDC recommend against use
- Produces euphoric high
- OVERDOSE risk
- Short ½ life – rapid withdrawal
  - High potential for addiction/misuse
- 5mg/kg dose of morphine was equivalent to 30mg/kg of tianeptine in an animal study
  - Study to evaluate TNX-601 er monotherapy versus placebo in patients with major depressive disorder (MDD) - full text view. ClinicalTrials.gov. (n.d.). https://classic.clinicaltrials.gov/ct2/show/NCT05686408?term=tnx601&draw=1&rank=1
- NARCAN and MOUD appropriate
- Might bind TCA urine test

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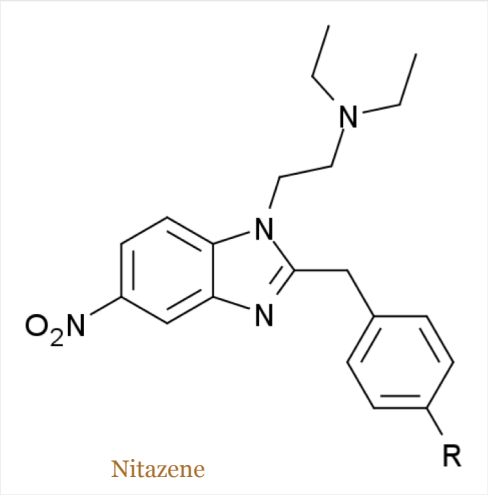
CASE EXAMPLE

27 yo female presents with opioid overdose symptoms

Friends report she used just one "anxiety medicine" she purchased online

NITAZENES

- Synthetic benzimidazole opioids
  - Mu opioid receptor agonists, varying potency
- Developed in the 1950s
- First illicit reports 2019 with isotonitazene
- Most Common
  - Isotonitazene
  - Etonitazene
  - Metonitazene
  - Protonitazene
  - N-pyrrolodino Etonitazene
  - N-pyrrolodino Protonitazene
  - N-desethyl Isotonitazene
- 100-1000x fold potency of morphine



Nitazene

Benzimidazole-Opioids Other Name: Nitazenes. DEA Diversion Control. Jan 2024.

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NITAZENES

- Little known about pharmacokinetics
- Thought to have a different orientation toward the mu-opioid receptor
- Recruit beta-arresting pathway → MORE RESPIRATORY DEPRESSION
- Very euphorigenic & cause severe withdrawal
- Some have active metabolites
- Often co-identified with benzodiazepines
- 10 are schedule 1

- Isotonitazene distributed as "pharmaceutical-grade hydromorphone"

Pergolizzi et al. "Old Drugs and New Challenges: A Narrative Review of Nitazenes". *Cureus* 2023.

NITAZENES

- Mostly in street supply, but sometimes found in online shops that sell kratom/tianeptine
- We think <<1% of circulating opioids but likely underreported

- HARD to detect - NOT DETECTED ON UDS
- Poor standards for lab detection as well
- There IS a rapid test strip on the market

- Likely will respond to naloxone but little known about dose and receptor binding

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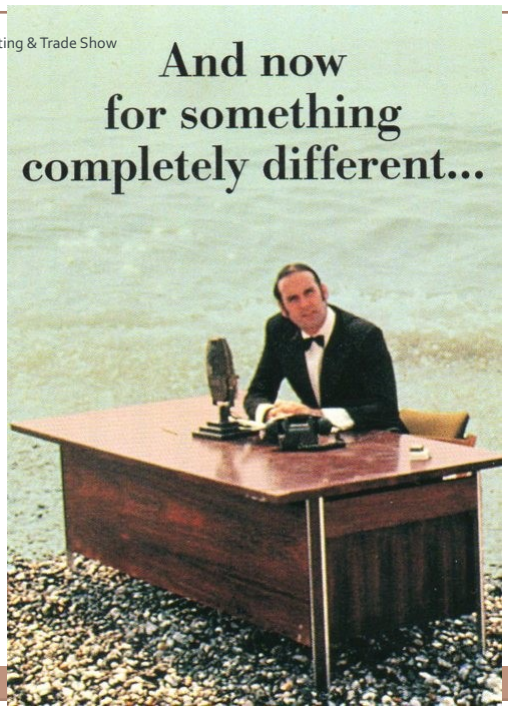

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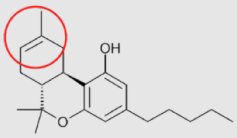
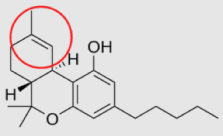
"THE DELTAS"

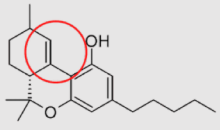
Delta 8 vs. Delta 9 vs. Delta 10 THC



Delta 8 THC



Delta 9 THC



Delta 10 THC

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THE FARM BILL

- 2018 – Agriculture Improvement Act – removed hemp from controlled substances
- Defined as cannabis species with "low THC" content (<0.3% delta-9 THC)
- Delta-8 and Delta-10 – not FDA approved, less psychoactive properties
  - Derived from the CBD in hemp
- Delta-9 – IS FDA approved for chemo-induced n/v and appetite in AIDS

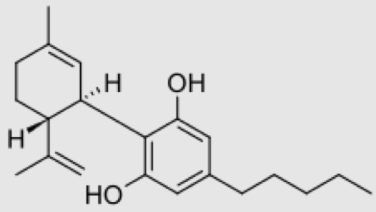
CONTAMINANTS

- Analysis of Delta-8 THC products have shown:
  - 25% with heavy metals
  - 15/16 products with illegal levels of Delta 9-THC
  - 68% different concentrations than labeled
  - Concentrations up to 15.2% delta-9 THC in some products (>23% in a vaping pen)

Meehan-Atrash, J. and Rahman I. Novel Δ^8-tetrahydrocannabinol vaporizers contain unlabeled adulterants, unintended byproducts of chemical synthesis, and heavy metals. *Chem Res Toxicol*. 2022.

CANNABIDIOL (CBD)

- Second most prevalent cannabinoid
- Derived from low-THC hemp species



- WHO: "In humans, CBD exhibits no effects indicative of any abuse or dependence potential…. To date, there is no evidence of public health related problems associated with the use of pure CBD"
- Unlikely to impair daily functioning or workplace performance

Lo, L.A., Christiansen, A.L., Strickland, J.C. *et al.* Does acute cannabidiol (CBD) use impair performance? A meta-analysis and comparison with placebo and delta-9-tetrahydrocannabinol (THC). *Neuropsychopharmacol.* **49**, 1425–1436 (2024). https://doi.org/10.1038/s41386-024-01847-w

USES

- In 2015, FDA eased restrictions to allow research
- Best data for childhood epilepsy syndromes (Dravet syndrome and Lennox-Gastaut syndrome)
- Under investigation:
  - Anxiety
  - Insomnia
  - Chronic pain – inflammation, arthritis, neuropathic pain
  - Addiction --- HIGH doses

SIDE EFFECTS

- Nausea, diarrhea, fatigue, irritability, mood, insomnia
- Hepatotoxicity reported
- Inhibition of CYP2C hydroxylation, CYP3A4 and CYP3A5 – may lead to drug interactions
- May reduce THC clearance
- 2022 FDA reports possible harm to male reproductive system

CBD PRODUCTS

Wikipedia Commons

CDC

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QUESTIONS?

POST-TEST

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- Drug Enforcement Agency 2025 National Drug Threat Assessment. https://www.dea.gov/sites/default/files/2025-07/2025NationalDrugThreatAssessment.pdf
- FDA News Release. FDA Takes Steps to Restrict 7-OH Opioid Products Threatening American Consumers. US Food & Drug Administration. https://www.fda.gov/news-events/press-announcements/fda-takes-steps-restrict-7-oh-opioid-products-threatening-american-consumers

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THANK YOU!

Questions?

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