A Safety Comparison of Concentrated Synthetic 7-OH to Natural Leaf Kratom

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UConn School of Pharmacy, Storrs, CT
& Chair, Kratom Consumer Advisory Council

This talk reflects my current understanding of kratom derived products and may not reflect those of the University of Connecticut or the KCAC.

Who am I?

Media pieces with a reach >3.5 billion including NBC News, USA Today, New York Times, LA Times, Boston Globe, WNPR, DoctorRadio, Prevention, Newsweek, WebMD, CNBC, and over 100 other sites.

ASHP Award for Sustained Contributions to the Literature, ASHP Drug Therapy Research Award, ACCP Young Investigator of the Year, AACP Lyman Award, AACP Weaver Award.

UConn Distinguished Professor, CETL Teaching Fellow, Provost's Award for Public Engagement

Pharmacist and clinical pharmacologist at UConn with >500 publications and 20,280 citations

Listed on Elsevier's list of "Top 2% of Scientists Worldwide"

Investigated drug (prescription, OTC, and illicit), dietary supplement, and device or surgical procedure induced diseases for 30 years

Provided simulation training on naloxone utilization, distributed naloxone and fentanyl test strips at community events, and served as a substance use speaker and panelist

Inaugural chair of the Kratom Consumer Advisory Council, a council supported by the Global kratom Coalition that devises best practices for the safe use of kratom products in the US*

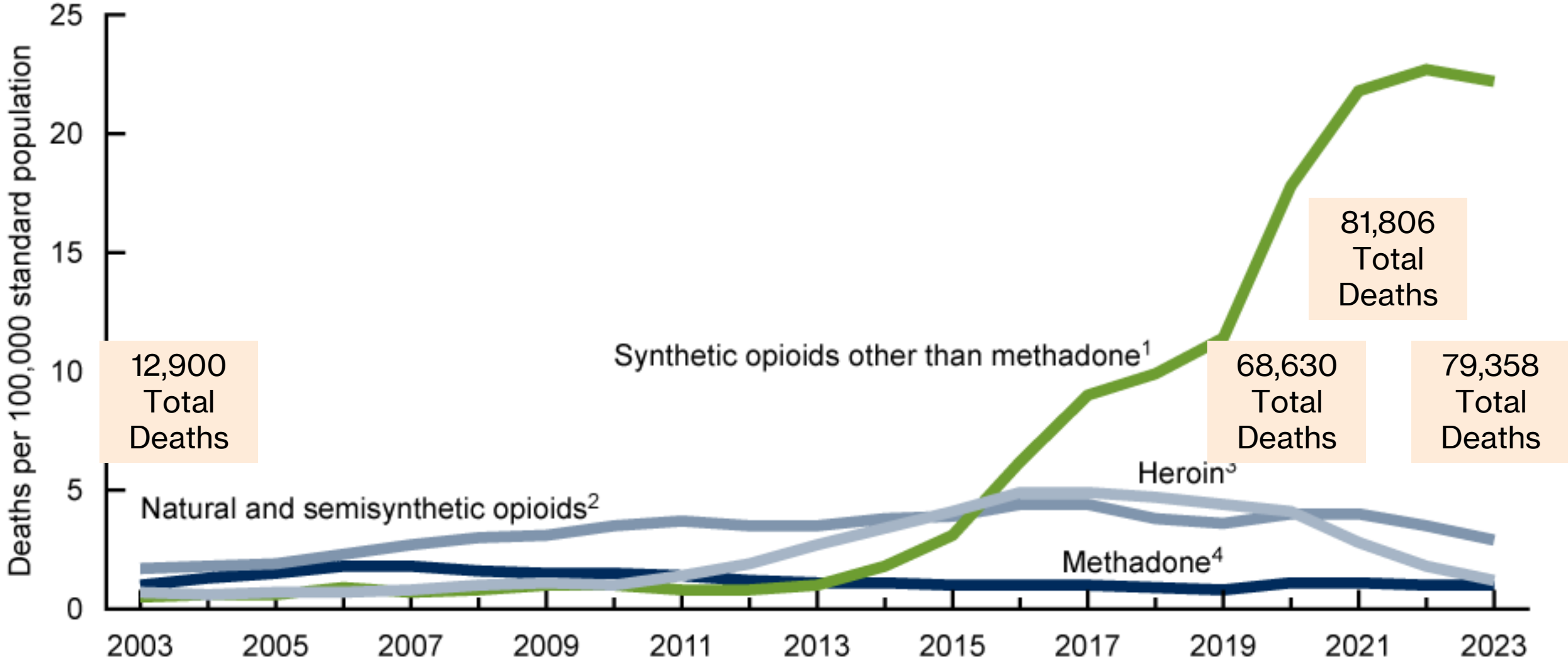
Director of one of only 14 Evidence-based Practice Centers designated by the federal Agency for Healthcare Research and Quality 2007-2020

https://theconversation.com/profiles/c-michael-white-382205

*The GKC reimburses me for the time spent leading the KCAC and educating/advocating for its position statements.

Death Due to First Three Waves of Opioid Epidemic

https://www.cdc.gov/nchs/products/databriefs/db522.htm



“Kratom” Timeline

- 1831 Dutch botanist Pieter Willem Korthals finds indigenous people in Southeast Asia commonly using leaf kratom as an herbal product
  - Use is thought to have been occurring for generations
- In the 1970s, Vietnam Veterans and immigrants from Southeast Asia bring leaf kratom with them and use it locally
- In the early 2000s, use of leaf kratom crosses over to the general population
- >25 years of leaf kratom human adverse event data and an FDA conducted tolerability study suggests the risks are generally mild
- Mitragynine extracts come out but some sellers start spiking their products with synthetic 7-OH or mitragynine pseudoindoxyl
- Concentrated synthetic 7-OH products make their debut in late 2023, sold as “kratom”
- Mitragynine pseudoindoxyl +/- 7-OH products make their debut in late-2024, sold as “kratom”
- MGM-15 and MGM-16 just starting to be sold in US in fall of 2025

https://globalkratomcoalition.org/the-evolution-of-kratom
https://katsbotanicals.com/the-origins-of-kratom-usage/#a

FDA Recommendation About 7-OH and Leaf Kratom Products

- The FDA is clear that concentrated synthetic 7-OH products pose a significant public health risk
  - They recommend that concentrated synthetic 7-OH be made a controlled substance by the Drug Enforcement Administration
  - They specifically say that this recommendation does not include leaf kratom products
    - Even though leaf kratom contains 7-OH as <2% of total alkaloids in dried leaves
    - Why is this differentiation clear to the FDA?

https://www.fda.gov/media/187898/download?attachment
https://www.fda.gov/media/187899/download?attachment

What is an Apple?

- Fiber
- Sugar
- B-Vitamins, Vitamin C
- Potassium and minerals
- Quercetin and catechin (antioxidant, anti-inflammatory)
- Amygdalin (converts to cyanide in the body)

If you extracted only the amygdalin, converted it into high doses of cyanide in the lab, and sold it in popping crystal candies, would it be an apple?

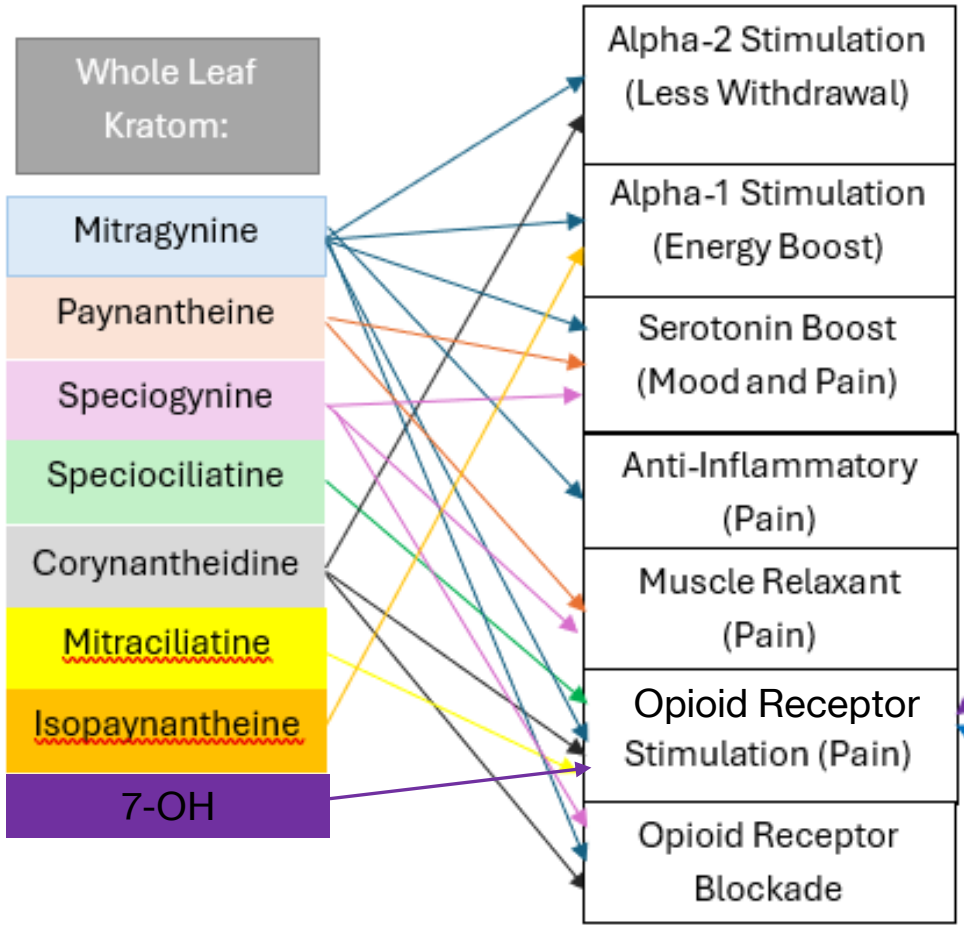
White CM. Overview if Kratom vs. Kratom Derived Products.

Whole Leaf Kratom Alkaloids

Potency of Mu-opioid receptor (MOR) stimulation determined by Ki value with lower numbers meaning greater potency

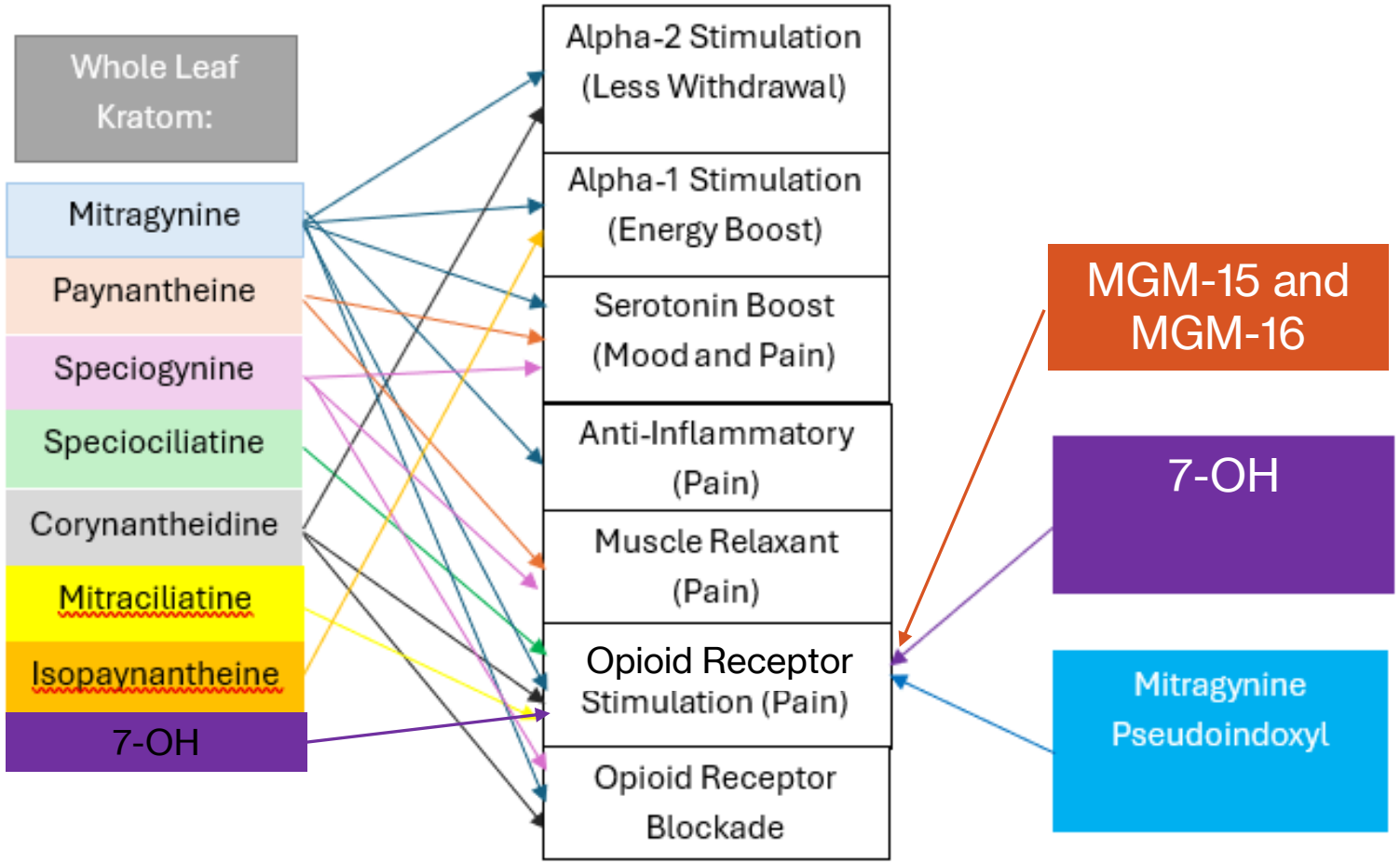
Mitragynine has a MOR Ki value of 7,800 nM
- Way below that of morphine, oxycodone, and fentanyl (1-40 nM)

7-OH is not in fresh leaves and only in trace amounts in dried leaves



https://pmc.ncbi.nlm.nih.gov/articles/PMC10846393/

Whole Leaf Kratom Alkaloids vs. Synthetic Alkaloids



Chemically converting mitragynine into 7-OH, pseudo, or MGM ingredients is not natural

Creating these products cause the creation of other unnatural alkaloids like 8-OH and 11-OH as well

MOR potency is ≥100 times that of mitragynine

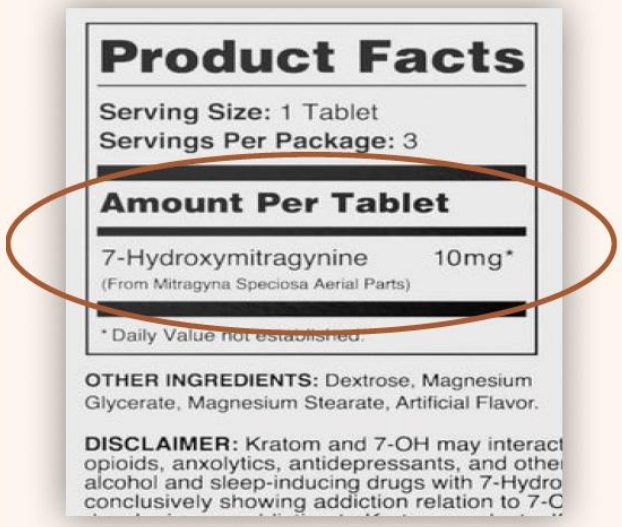
There is no entourage effect, only MOR stimulation

https://pmc.ncbi.nlm.nih.gov/articles/PMC10846393/

Synthetics vs. Natural Leaf

Synthetic 7-OH - Back Label

- 7-Hydroxymitragynine listed as the primary or most abundant alkaloid.
- Often shows high or isolated doses.



Product Facts

Serving Size: 1 Tablet
Servings Per Package: 3

Amount Per Tablet

7-Hydroxymitragynine 10mg*
(From Mitragyna Speciosa Aerial Parts)

* Daily Value not established.

OTHER INGREDIENTS: Dextrose, Magnesium Glycerate, Magnesium Stearate, Artificial Flavor.

DISCLAIMER: Kratom and 7-OH may interact opioids, anxolytics, antidepressants, and other alcohol and sleep-inducing drugs with 7-Hydro conclusively showing addiction relation to 7-C

Natural Leaf - Back Label

- Mitragynine is the most abundant alkaloid.
- Other natural alkaloids.
- 7-OH appears only in trace amounts. (<2%).

Mitragynine: 20mg/34mg = 0.59 = 59% mitragynine

Total alkaloids 34mg X 0.02 = 0.68 mg of 7-OH allowed

No mitragynine pseudoindoxyl (Red-OH), 8- or 11-OH, or MGM-15 or MGM-16

Supplement Facts

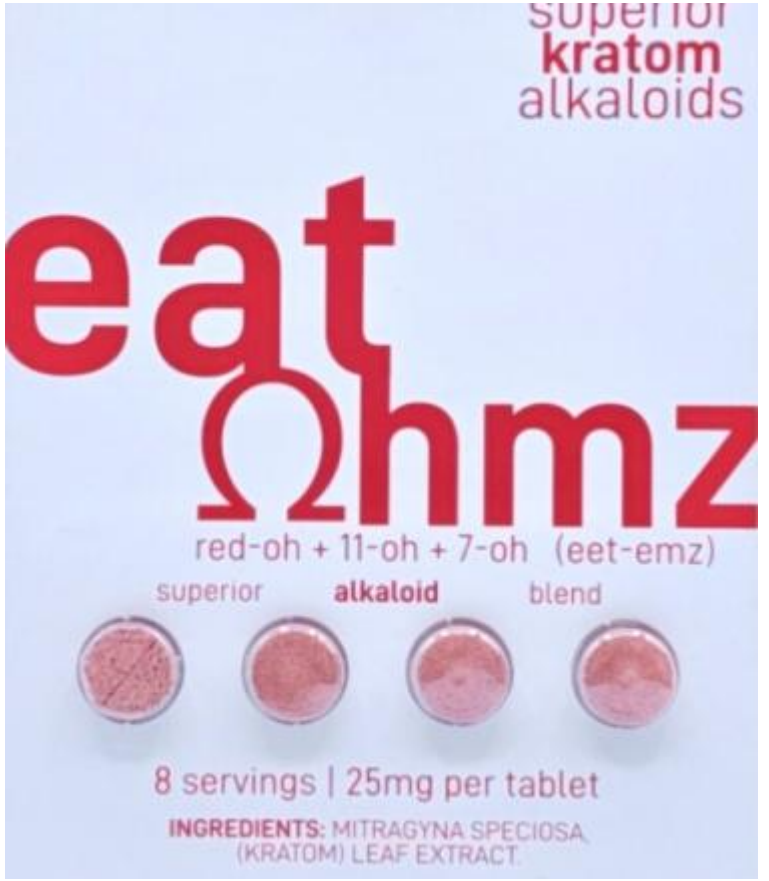
Serving Size: 2 Capsules
Servings Per Container: 30

Amount Per Serving		%DV
Ground Kratom Leaf		
Total Alkaloids	34 mg	†
Mitragynine	20 mg	†
7-hydroxymitragynine	<0.05 mg	†

* Percent Daily Value (DV) based on a 2,000 calorie diet.
† Daily Value (DV) not established.

How to Identify Synthetics: Challenge Stage!

- Doesn't Contain Mitragynine = Not a Kratom Product (see how they try to trick you in the ingredients!)
- Red-OH (Mitragynine Pseudoindoxyl) = Concentrated Synthetic Alkaloid
- 11-OH = Concentrated Synthetic Alkaloid



- Has 5 alkaloids found in natural kratom but...
- Total Alkaloids: 50mg + 35mg + 20mg + 10mg + 4mg = 119 mg
- 35mg Mitragynine/119mg = 0.29 = 29% = Not a Kratom Product
- 50mg 7-OH/119mg = 0.42 = 42% = Spiked or Enriched with Synthetic 7-OH

CONCENTRATED SYNTHETIC 7-OH PRODUCTS DATABASE

Preclinical Comparison of Mitragynine to 7-OH

	Mitragynine	7-OH	Prescription Opioids
Rapid Tolerance	+	++++	++++
Reinforcing Effects	0	++++	++++
Addiction Potential	++	+++++	+++++
Withdrawal Symptoms	++	++++	+++++
Respiratory Depression	+	++++	++++
Neurotoxicity	+	+++	+++

Rapid tolerance = you need more drug over time to get the same effects (drain bank account)
Reinforcing effects = if you use 7-OH, your tolerance to it and regular opioids goes up
Addiction potential = crave opioid euphoric effects, alter life to acquire opioids, reduced ability to hold down job, care for family or self
Withdrawal symptoms = anxiety, muscle aches, diarrhea, shaky, runny nose and eyes, intense cravings, insomnia
Respiratory depression = risk you will stop breathing or not oxygenate blood sufficiently
Neurotoxicity = risk the drug will cause impairing neurological symptoms

White CM. Overview of pharmacologic effects from animal studies.

Results of FDA Study on Kratom Dosing & Safety

Controlled servings of dried leaf kratom saw no adverse events and generally positive feelings

To gain preliminary data on kratom's effects in humans, the U.S. Food and Drug Administration (FDA) commissioned a dose-ranging and safety study:

Goals and Objectives

Primary: Evaluate the safety and tolerability of single, oral serving of kratom

Secondary: Evaluate the pharmacokinetics of kratom's alkaloids, including mitragynine, 7-hydroxymitragynine, paynantheine, speciogynine, mitraciliatine, corynantheidine, and speciociliatine, plus the pharmacodynamics of kratom

Methodology

- Single Ascending Dose (SAD) design: dosing regimen of 1, 3, 8, 10, and 12g, administered in 500 mg capsules.
- Botanical kratom (encapsulated, dried leaf from a single, reputable manufacturer) was taken orally by healthy adult males and females who are current, non-dependent, polydrug users.
- 40 subjects total (5 cohorts of 8 subjects; 2 subjects in each cohort received a placebo).
- Subjects in each cohort were required to consume between 2 and 24 500 mg capsules within five minutes.

Contextualizing the Dose

- The average serving for a kratom leaf product is between 1 and 3 grams.
- 3 out of the 5 cohorts received 3 to 4 times the normal serving of a kratom leaf product.
- Even at these high serving levels, kratom was still well tolerated by the subjects.

Conclusions

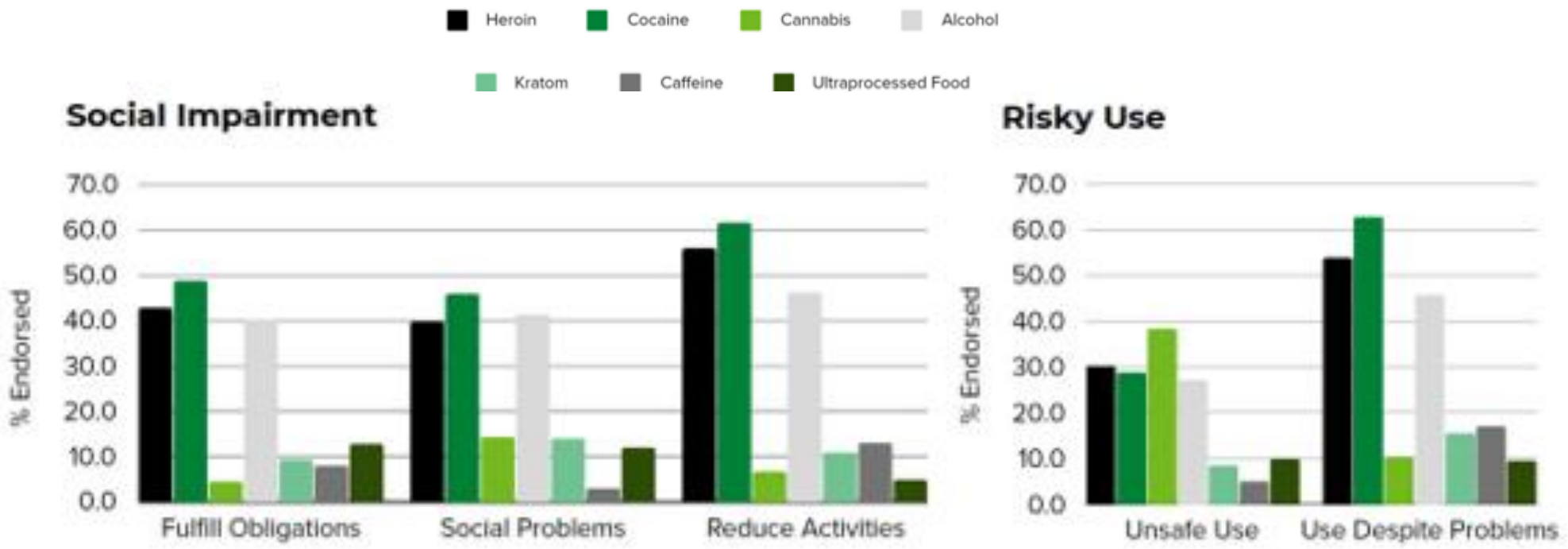
- The highest administered serving was 3 to 4 times higher than the average reported use in the US.
- At the servings tested, **kratom is well-tolerated** in humans even at the highest serving administered in the study.

FDA Conducted Clinical Trial in Normal Volunteers

Whole leaf kratom is well tolerated in humans, even when given at high doses

https://static1.squarespace.com/static/6508b3f79033221c2aa1ea17/t/662979945bb3d45d3d66f29f/1717013410023/FDA+Study+on+Kratom+Dosing+and+Safety_042424.pdf

How Addictive is Natural Leaf Kratom



White CM. J Ped Pharmacol Ther 2024, https://jppt.kglmeridian.com/view/journals/jppt/30/2/article-p289.xml

Natural Kratom for Opioid Use Disorder

- There are no CLINICAL TRIALS for this indication, so no conclusive proof of benefits
  - Thousands of anecdotal stories suggesting it is effective as opioid substitution or to wean off opioids altogether
- Three quality cross sectional descriptive studies suggest benefits
- In a cross-sectional study, 163 participants with a history of illicit opioid use who were now using kratom were recruited.
  - Participants reported that kratom initiation was associated with decreased prevalence of respiratory depression, constipation, physical pain, insomnia, depression, loss of appetite, craving, decreased sexual performance, weight loss and fatigue versus opioid use.
- In a cross-sectional study, 260 participants with a history of illicit drug use and a current use of kratom were assessed.
  - Participants reported a reduction in the illicit use of heroin, methamphetamine, amphetamine, cannabis, benzodiazepines, ketamine, methadone, and alcohol after kratom initiation
  - HIV risk behaviors such as injecting illicit drugs and sharing needles and syringes were reduced.
- In a cross-sectional study 32 HIV positive opioid users started using kratom
  - Participants reported a reduction in injecting illicit opioids and sharing syringes and needles.

https://pmc.ncbi.nlm.nih.gov/articles/PMC10846393/

Concentrated synthetic 7-OH is not natural leaf kratom

Issue 233: May 30, 2025

Public Health Impact: Reddit discussants report experiencing significant tolerance development with 7-OH products, leading to rapid dose escalation and financial strain. Users describe withdrawal symptoms from concentrated alkaloid products as more severe than traditional kratom leaf, with some comparing them to pharmaceutical opioid withdrawal. Limited awareness exists about the pharmacological differences between traditional kratom and these novel derivatives, leading to unexpected overdose-like symptoms including respiratory depression concerns.

Like oxycodone and hydrocodone

Gas station accessibility a concern for impulse control

Rapid tolerance leads to dose escalation and financial strain

Respiratory depression concerns

Reddit users frequently compare 7-OH effects to prescription opioids like oxycodone and hydrocodone, with many expressing surprise at the potency legally available at smoke shops. Discussants note high prices, ranging from $15-40, for single doses of concentrated products. The convenience of purchasing at gas stations is frequently mentioned as both an accessibility benefit and a concern for impulse use.

Community Support Group Flooded with 7-OH Users

- Certified peer support specialists, Hilary Tesluck and Decima Davis, started Kratom Quitters in 2023 to help support people with kratom use disorder.
- “Since 7-OH hit the scene, our membership just increased at a rate that we’re having a really hard time keeping up with. It’s become a full-time job,” Davis says.
- “Nearly all of the people that are joining us are 7-OH users,” Tesluck says. “I cannot remember a person joining our community that is just powder only. It’s been months since I can say that.”
- “If you just think of it as a heroin addiction, it’s the same thing. It’s the same symptoms, because it’s a powerful opioid,” Tesluck says.
- There are 10,000 total participants in the group.

https://www.thepitchkc.com/in-a-data-void-7-oh-addictions-and-contradictions-are-debated-on-social-media/

Anecdotal Experiences with 7-OH

- *“I am not sure how to proceed. Ugh, it's like I am right back on the oxy merry go round after working so hard to get off and being so happy to be free (with the exception of plain leaf kratom). I am on about 3 tablets a day now. How do we get off? Use massive doses of plain leaf?”*

- *“I take it everyday 3x a day and I wakeup in withdrawal. It really sucks I feel like a fool getting mixed up in this world. Last time I tried to wean down I got so depressed it was scary. Been using for 6 months. It's like getting hooked on oxy once you enter the everyday use and it's been a few months. It creeps up slowly but it's HARD to get off.”*

Reddit posts on 7-Hydroxymitragynine. Available at: 7_hydroxymitragynine and r/quitting7oh (reddit.com) https://www.reddit.com/r/quitting7oh/comments/1k3vl2d/11_million_views_and_2k_members_now_lets/

7-OH Human Health Risks – Poison Control Centers

- Poison control center data January through July 2025 (165 reported adverse events)
- Of patients reporting exposure to 7-OH alone, 35% had serious health problems and 67% were treated at a healthcare facility.
- Symptoms included:
  - Trouble breathing
  - Seizures
  - Agitation
  - Confusion
  - Rapid heart rate
  - High blood pressure
  - Sedation including loss of consciousness
  - Nausea and vomiting
  - Sweating

https://poisoncenters.org/news-alerts/13531044

7-OH Deaths

- LA County: Six deaths suspected to involve 7-OH and alcohol or other substances
- FDA FAERS Database: Two deaths suspected to involve 7-OH and 13 other incidences of severe adverse events
- The FDA alerts the public that these cases of harm are grossly undercounted
  - First responders, emergency personnel, coroners, medical examiners, and poison control center personnel were unaware that 7-OH came out or was not kratom
    - Misattribution of cases from 7-OH to kratom
    - Lack of attribution because 7-OH is not part of routine screenings and mitragynine screenings would come out negative for 7-OH
  - 7-OH is unstable in biological fluids so samples need to be tested within the first 14 days of refrigeration, or they can show substantially less 7-OH than was in the body at the time of death (avg time to run samples is 30-60 days)

https://www.ahpa.org/Files/Media/FDA/7-hydroxymitragynin_7-oh_an_assessment_of_the_scientific_data_and_toxicological_concerns_around_an_emerging_opioid_threat.pdf
https://www.msn.com/en-us/health/other/6-los-angeles-county-overdose-deaths-linked-to-kratom-compound/ar-AA1OsBwW?ocid=BingNewsSerp
http://www.publichealth.lacounty.gov/phcommon/public/media/mediapubdetail.cfm?unit=media&prog=media&prid=5139&start=1
https://static1.squarespace.com/static/6508b3f79033221c2aa1ea17/t/68d2bcaff487b72b1adab9a5/1758641327216/KCAC+-+Fact+Sheet_Undercounting+Death_V3.pdf

Wife blames 7-OH for husband's death as synthetic kratom ban remains on hold

Addiction Can be Deadly!

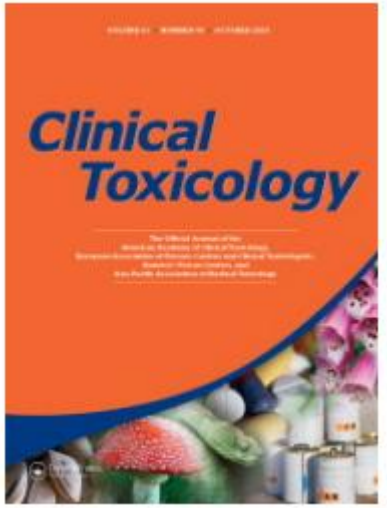
WSYX ABC 6, Ohio.

- Father of two and husband bought watermelon flavored 7-OH product from gas station because it promised increased energy
- Used it a few times and got addicted
- Escalated doses frequently to maintain the same feeling
- Trapped in cycle of addiction, spent $100-200 on 70 occasions over 2 months to buy tablets
- Tried to quit but withdrawals were horrendous, relapsed
- Couldn't function and straining family finances, the father committed suicide with a gun

https://www.bing.com/videos/riverview/relatedvideo?q=You%20Tune%20ABC%207-OH%20Caused%20Husbands%20death&mid=54315B77505467DE3A0254315B77505467DE3A02&ajaxhist=0

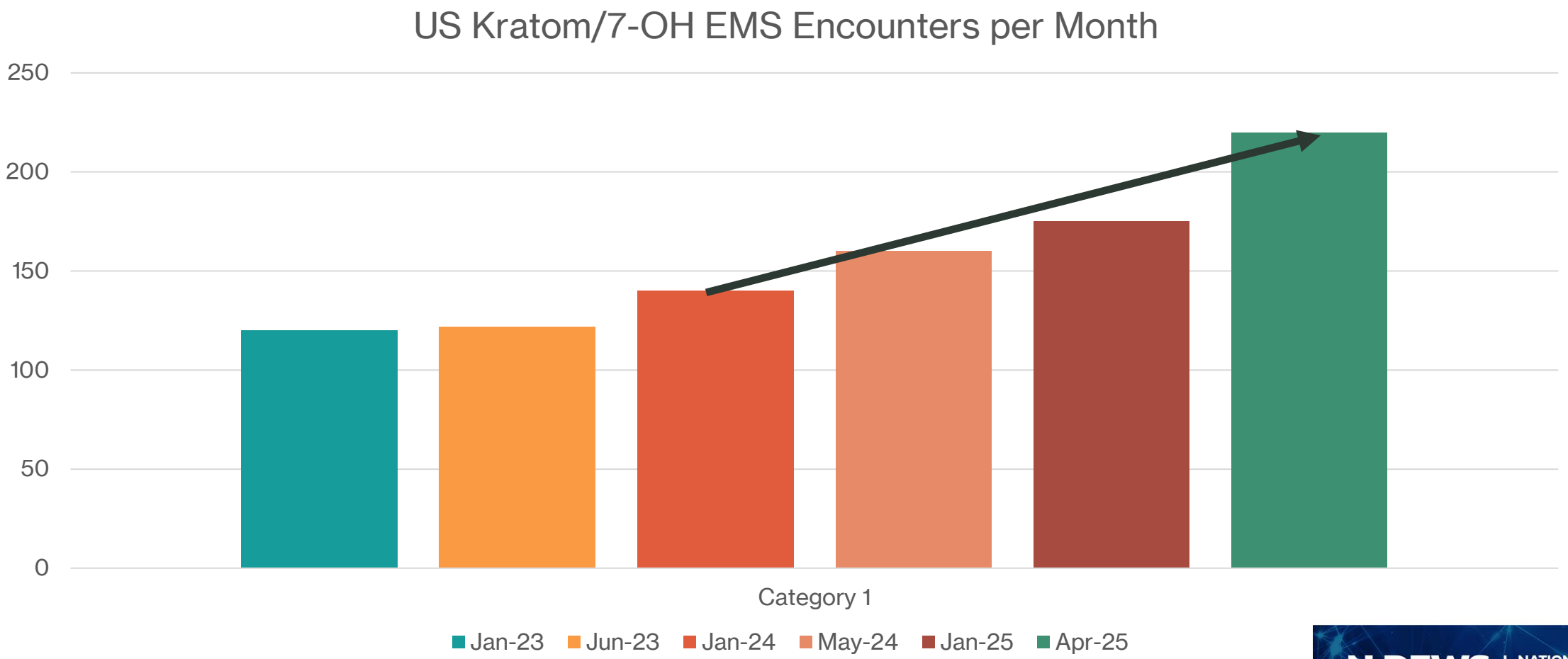
7-OH + Alcohol: Respiratory and Cardiac Arrest

- Patient found in respiratory and cardiac arrest, resuscitated with naloxone and vomits
  - States he used 4 tablets of 7-OH (~190 mg)
    - The suggested serving size was ~12.5 mg (one quarter a tablet)!
  - Patient blood positive for high alcohol (1620 mg/L), amphetamines and cannabinoids and negative for routine opioids
  - Had this patient died before naloxone was given, the case would unlikely have been attributed to 7-OH

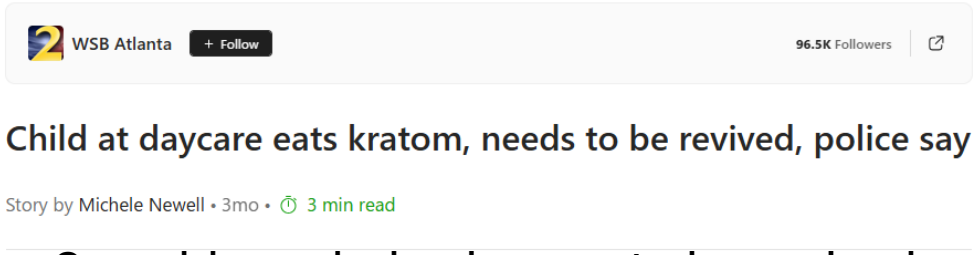


https://www.tandfonline.com/doi/pdf/10.1080/15563650.2025.2565428

After stability in EMS Calls, a sharp increase has occurred since 7-OH products were released



Many 7-OH and MPI Products are Designed to be Attractive to Children



2 yr old needed naloxone to be revived

https://www.msn.com/en-us/news/crime/child-at-daycare-eats-kratom-needs-to-be-revived-police-say/ar-AA1KPeGP

Sweetened products

Fruit flavorings and scents

Names like “Blue Raz”, “Opia”, “Perks”, “Rave” and “Smurphs”

Ice cream cone formulations

Bright coloring

Buccal pouches and sublingual strips


7-HYDROXYMITRAGYNINE
NEXTAR
MICRO
7's
BLUE RASPBERRY
5MG 7-HYDROXY


7-HYDROXY
20MG
30
RAVE
SUBLINGUAL STRIP
7-HYDROXYMITRAGYNINE
WATERMELON MINT
PREMIUM ALKALOIDS STRIPS
5 COUNT
100MG
10 SERVINGS


Ωhmz
Conez
superior kratom alkaloids
7-hydroxymitragynine (ohmz - conez)
vanilla bean cones
INGREDIENTS: MITRAGYNA SPECIOSA (KRATOM) LEAF EXTRACT.
2 cones | 6 servings | 100mg
superior kratom alkaloids


PERKS
CHILL BERRY
dozo
PERKS
MELLOW BLEND
10
dozo
PERKS


CITRUS
10 SUBLINGUAL POUCHES
7MG 7-OH POUCH
ADVANCED BOTANICAL ALKALOIDS
hyΩxi
7-OHM
HYROXI.COM


BLUE RAZZ
SMURPHS
SMURPHS
SMURPHS
100MG
100MG

Leaf Kratom Take Aways

- Leaf kratom is a natural product with centuries of use
- It is a multi-phytochemical product with an “entourage effect”, multiple non-MOR effects, very weak MOR stimulation
- Kratom seems to have benefits in uncontrolled pain and substance use disorder in some people who cannot use FDA approved therapy or do not have access to them
  - Descriptive studies suggest public health benefits over using illicit opioids
- It is not risk free, but the risks are less than that with cannabis, alcohol, and smoking which are largely regulated, not banned (similar to ultra-processed foods)
- The Kratom Consumer Advisory Counsel recommends regulations as part of a comprehensive Kratom Consumer Protection Act
  - Registration of products beforehand (COA assessment provided)
  - Packaging that does not appeal to children and proper instructions and warnings
  - No candy formulations (no scents, flavorings, fun shapes, etc) and only ingested formulations
  - No sales to people under 21 years

https://globalkratomcoalition.org/kcac-position-statements

Synthetic Concentrated 7-OH Takeaway

- 7-OH is created from a chemical process, not directly from a natural ingredient
- 7-OH is a potent opioid receptor stimulator, 100 times more potent than mitragynine
- No multi-natural alkaloid entourage effect like leaf kratom
- The risk of addiction and respiratory depression in preclinical models similar to morphine
- Tolerance leads to rapidly escalating doses and financial strain
- Products are frequently packaged in ways that would appeal to children (candy formulations, names, cartoon mascots) or suggest illicit opioid potency

https://globalkratomcoalition.org/kcac-position-statements

The End

C. Michael White, Pharm.D., FCP, FCCP, FASHP
Distinguished Professor and Chair, Pharmacy Practice
UConn School of Pharmacy, Storrs, CT
& Chair, Kratom Consumer Advisory Council

This talk and these slides are based on my current understanding of the literature base. If you have additional questions, I would be happy to answer them when I can.

Additional Slides

- The following slides convey additional nuance to the topic area and provides references for summative slides in the main presentation.
- In addition to these slides, the Kratom Consumer Advisory Council provides a number of position statements on how to make the kratom marketplace safer for consumers
  - https://globalkratomcoalition.org/kcac-position-statements

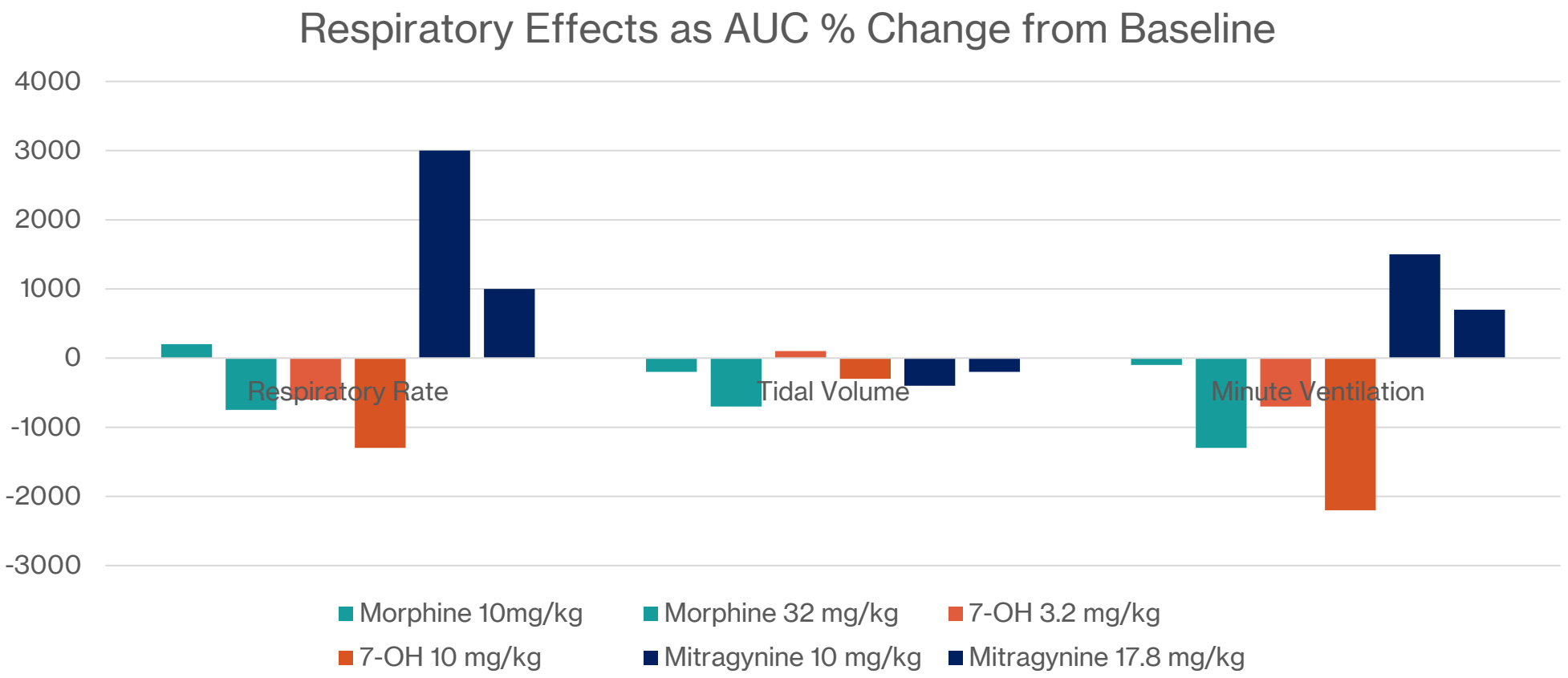
7-OH Reinforces Opioid Use Disorder, Mitragynine Does Not (Rat Study)

- Morphine addicted rats switched to either mitragynine or 7-OH for period-of-time
  - Rats readily preferred 7-OH to mitragynine
- Rats then given morphine as an option again
  - Rats using mitragynine used lower doses of morphine once it was reintroduced
  - Rats using 7-OH used higher morphine doses once it was reintroduced
- A mu-opioid receptor blocker reduced rats desire for 7-OH
- *"The present findings indicate that MG does not have abuse potential and reduces morphine intake, whereas 7-HMG should be considered a kratom constituent with high abuse potential that may also increase the intake of other opiates."*

https://pubmed.ncbi.nlm.nih.gov/29949228/

Morphine (Green) vs. 7-OH (Red) vs. Mitragynine (Blue) on Respiration

- Morphine and 7-OH produced dose-related reductions in RR and MV
- Mitragynine did not, but higher doses showed less enhancement in RR and MV



https://doi.org/10.1016/j.vascn.2025.107624.

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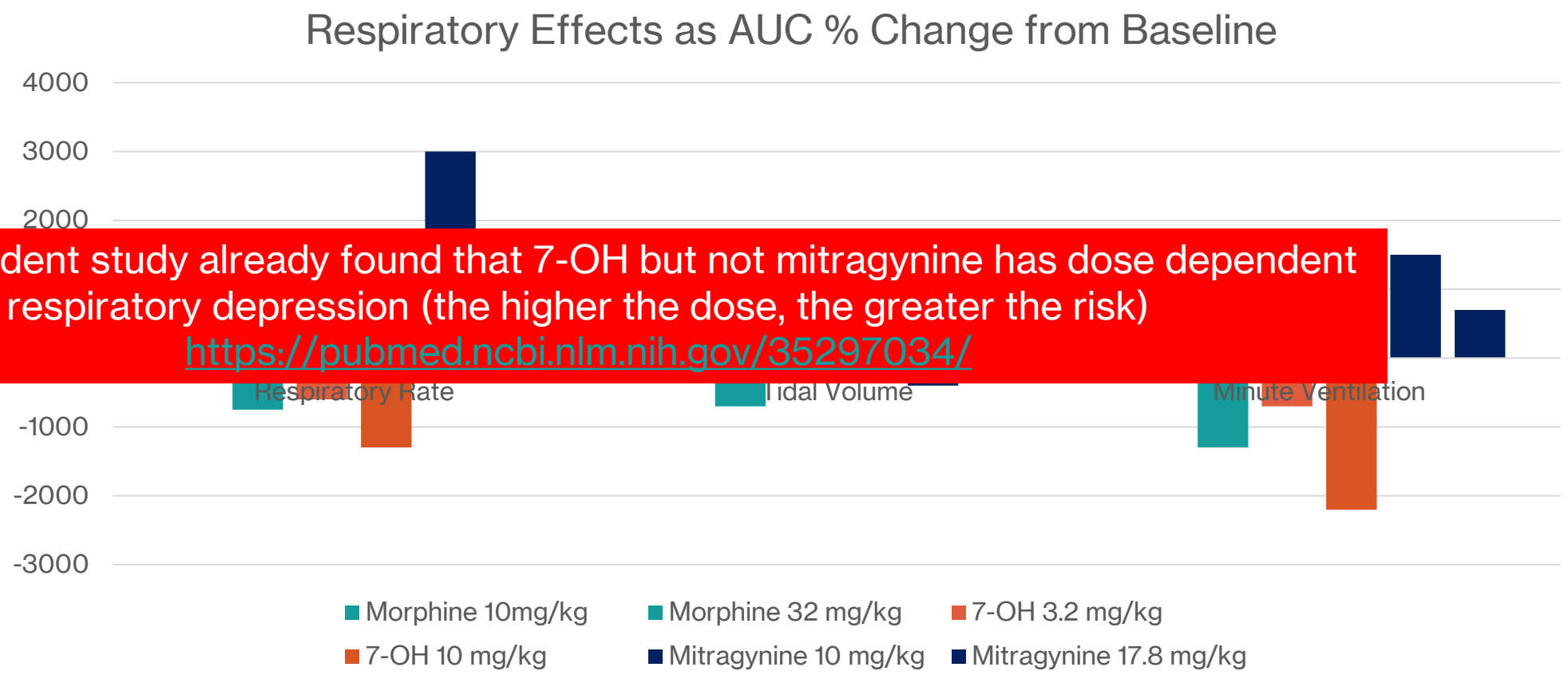


Previous rodent study already found that 7-OH but not mitragynine has dose dependent respiratory depression (the higher the dose, the greater the risk)
https://pubmed.ncbi.nlm.nih.gov/35297034/

https://doi.org/10.1016/j.vascn.2025.107624.

Beagle Study

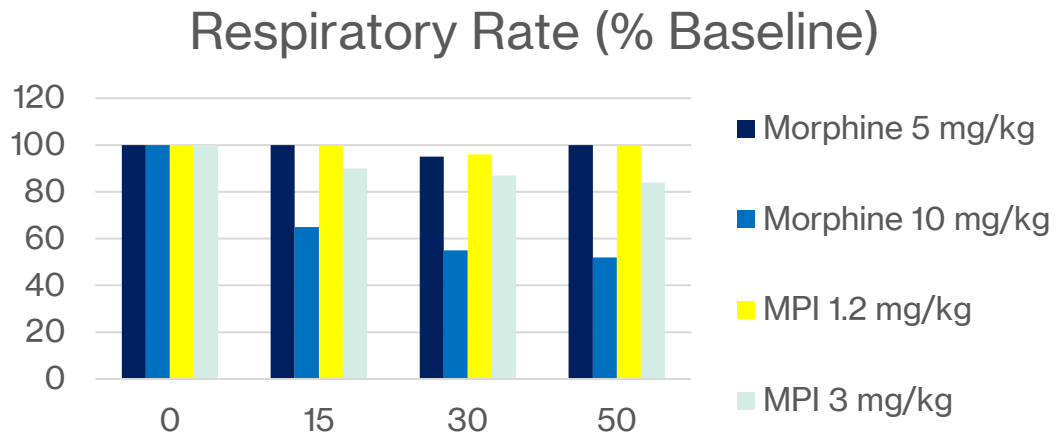
- Study in beagle dogs intending to look for neurological adverse events
  - Original dosing strategy was escalating 10mg, 20mg and 40mg doses twice daily with 7 days between each dose escalation
  - First beagle given 10mg dose had severe neurological adverse events
    - The study was paused, and the new dosing scheme was 1mg, 2mg, and 4mg once daily (1/20th the intended dose) for the study
    - Still showed significantly more adverse events than with placebo overall and dose related increases in new onset drooling (a potential neurological adverse event sign)
  - Funder put out a press release saying study showed neurological safety

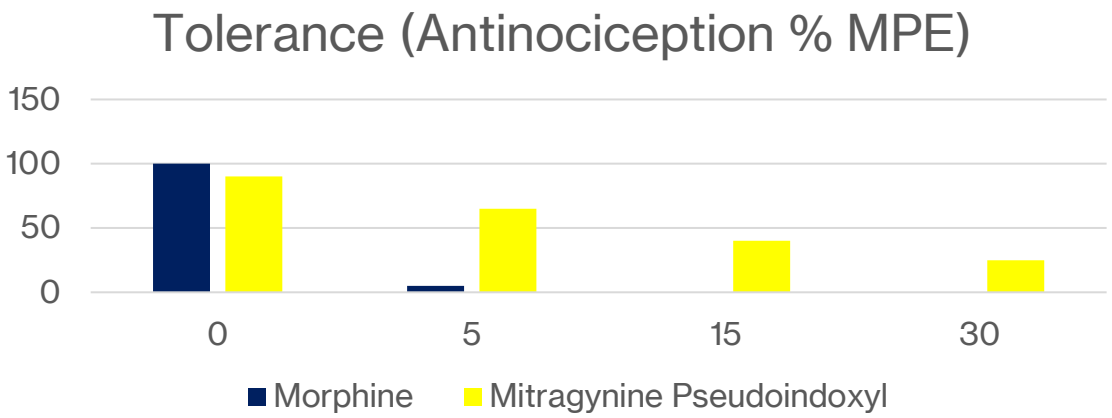
https://static1.squarespace.com/static/6508b3f79033221c2aa1ea17/t/6877f28692184750904 8f6c0/1752691335854/KCAC+-+Position+Statement_July+%2725_Animal+Safety.pdf

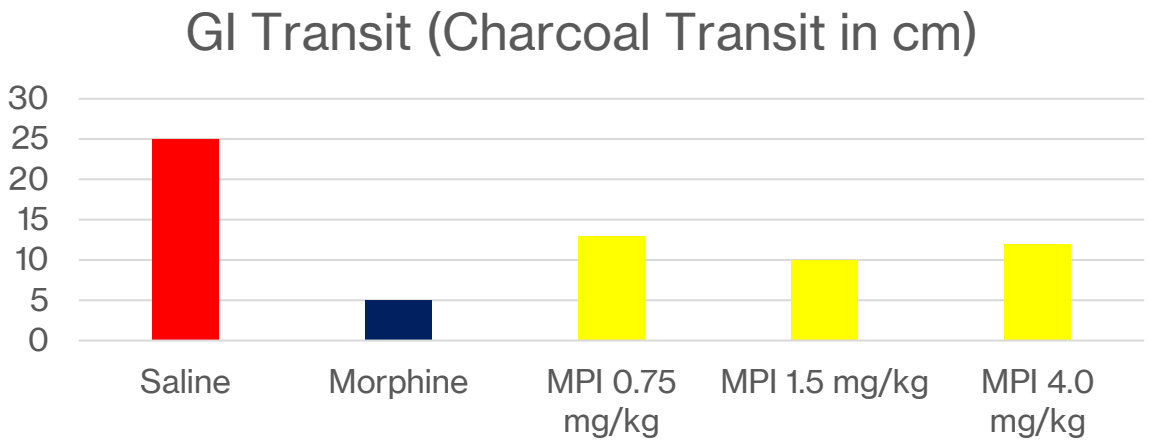
Morphine vs. Mitragynine Pseudoindoxyl

Rodent Study:

- Can cause a 15% reduction in respiratory rate, but less severely than morphine
- Rodent study: MPI causes tolerance like morphine, but it occurs more slowly
- Can cause significant constipation, but less severely than morphine







https://pmc.ncbi.nlm.nih.gov/articles/PMC5344672/#F6

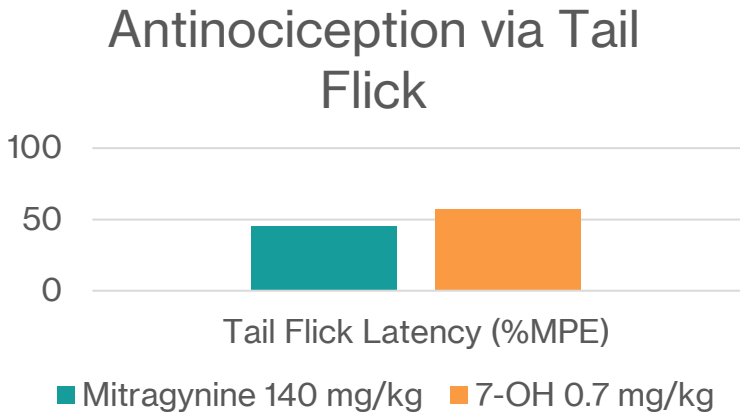
Animal or Human Data on MGM-15 and MGM-16

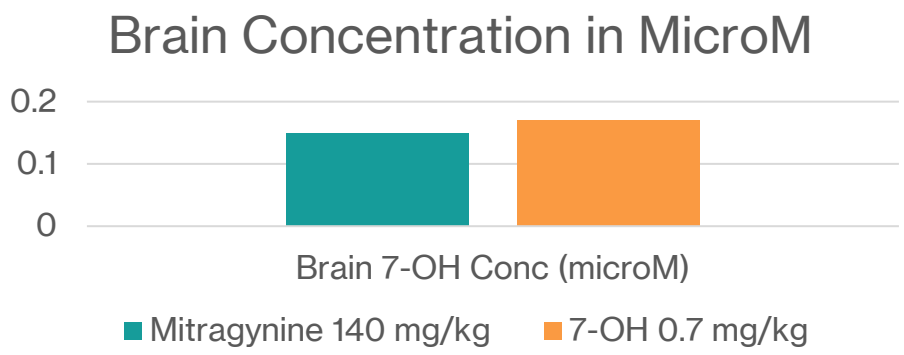
- Sorry, animal and human data are not available for MGM-15 or MGM-16
- There doesn’t need to be substantial data to ban these ingredients from products
  - They are all potent synthetic opioids with chemical structures not more dissimilar from morphine than fentanyl is
  - While they are semi-synthetic to mitragynine, they are synthetic to morphine’s core structure
- No potent MOR stimulating drug has ever been shown to be free or developing strong substance use disorders
- Mitragynine pseudoindoxyl, MGM-15 and MGM-16 are all analogues of 7-OH and if 7-OH is banned, they can also be banned as well if the DEA ruling or state laws allow for that

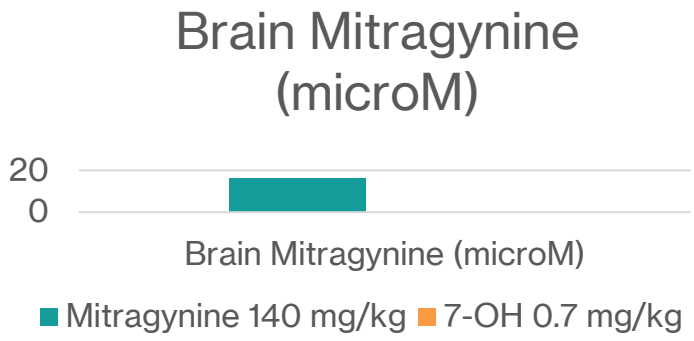
https://en.wikipedia.org/wiki/Federal_Analogue_Act

Are Kratom's Effects Only Due to 7-OH?

- Rodent study found that mitragynine converted into 7-OH is important for antinociception
- Only massive mitragynine doses will give the MOR effects seen at miniscule 7-OH doses
  - Mitragynine doses were 200X the 7-OH doses
- In kratom products, mitragynine is ~10-40mg/serving while 7-OH products are ~15-20mg/serving
  - Mitragynine doses in commercial products are only up to 2 times the 7-OH doses







https://pmc.ncbi.nlm.nih.gov/articles/PMC6598159/

Are Kratom's Effects Only Due to 7-OH?

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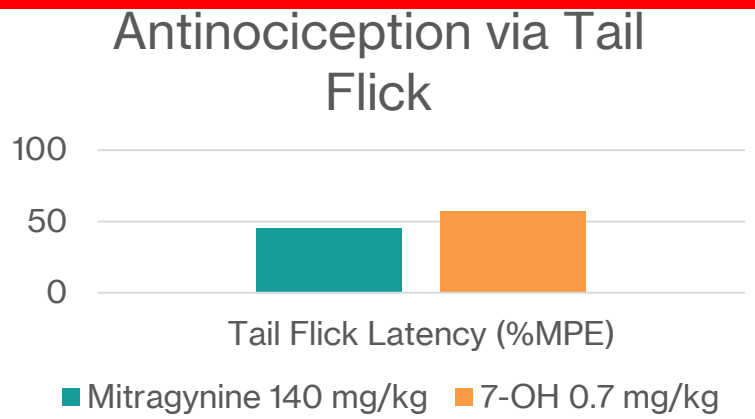
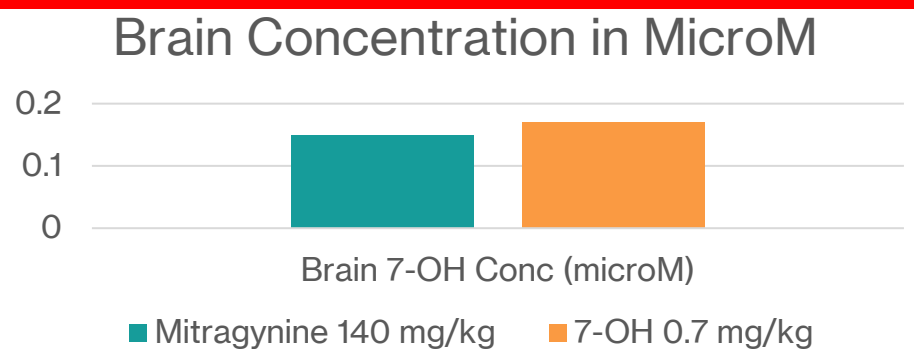
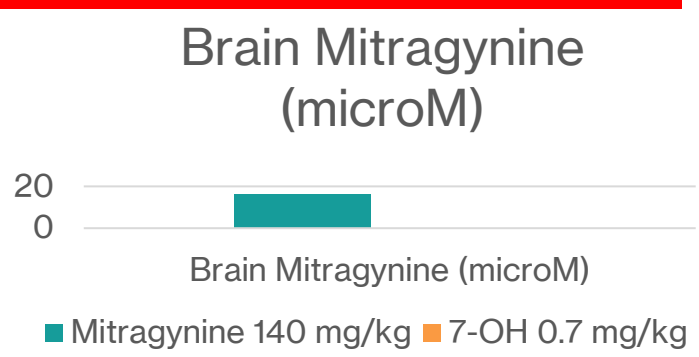
Another rodent study found equal antinociceptive effect for direct mitragynine administration and direct isolated 7-OH administration from hotplate exposure. The 7-OH concentration in the brain created by the metabolism of mitragynine was 11-fold lower than when isolated 7-OH was administered directly.
http://doi.org/10.1124/dmd.121.000640.

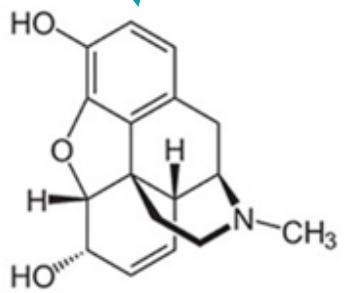






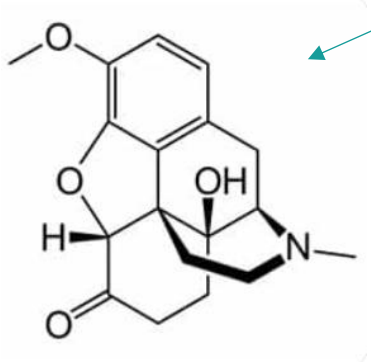
https://pmc.ncbi.nlm.nih.gov/articles/PMC6598159/

Opiate

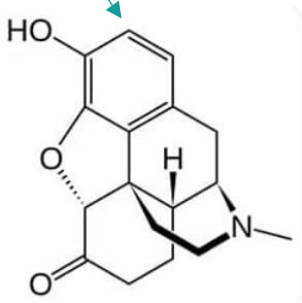


Morphine
(Ki ~ 40 nM)

Semi-Synthetic Opioids



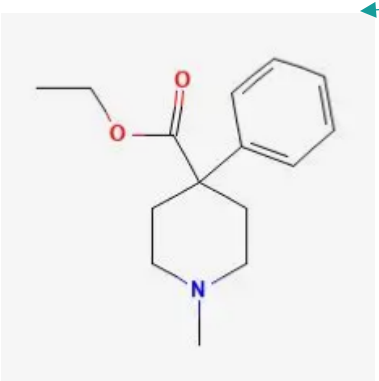
Oxycodone
(Ki ~ 20 nM)



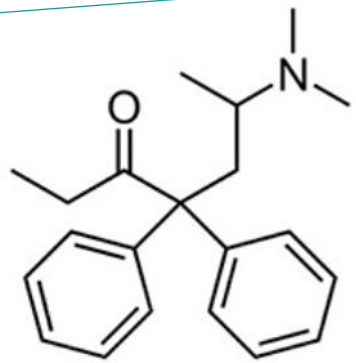
Hydromorphone
(Ki ~ 10 nM)

Semi-synthetic opioids share a common ring structure with morphine

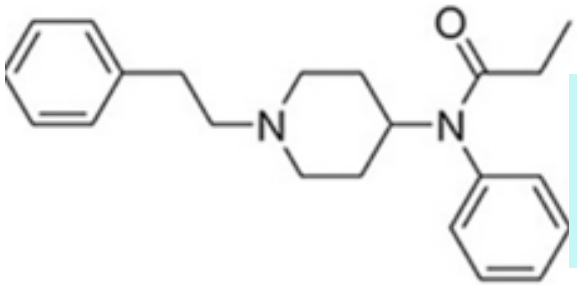
Synthetic Opioids



Meperidine
(Ki ~ 450 nM)



Methadone
(Ki ~ 3 nM)



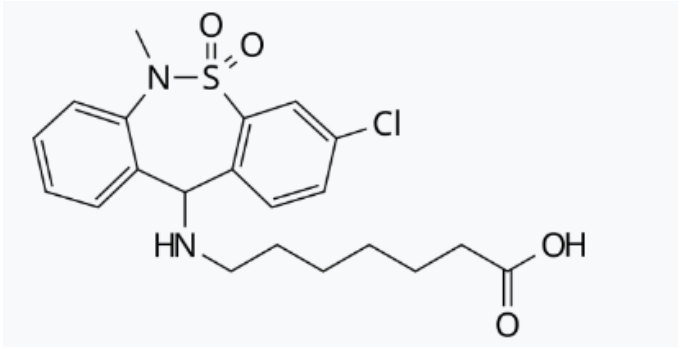
Fentanyl
(Ki ~ 1 nM)

Synthetic opioids do NOT share a common ring structure with morphine

https://pubmed.ncbi.nlm.nih.gov/21215785/

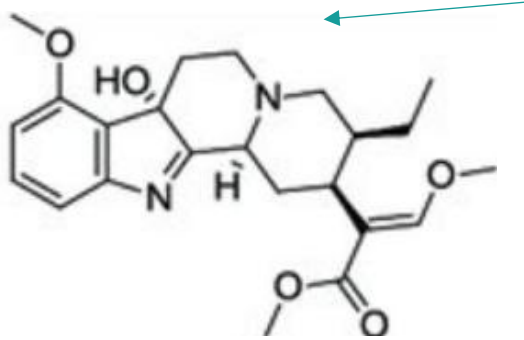
Ki is potency of mu-opioid receptor stimulation, lower number = more potent

Semi-synthetic to Mitragynine Ring Structure but Synthetic to Morphine

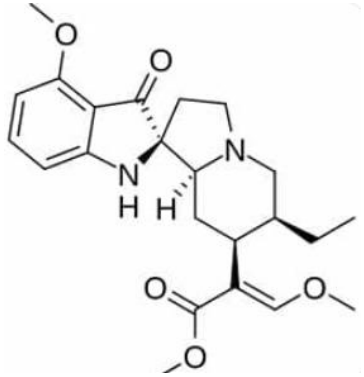


Tianeptine
(Ki = 380 nM)

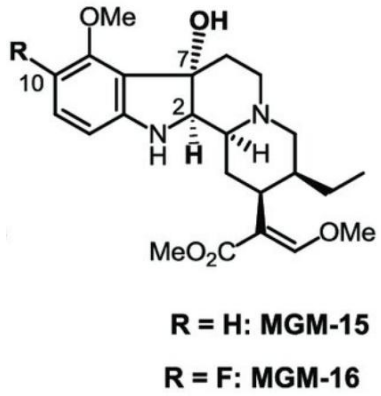
Synthetic



7-Hydroxymitragynine
(Ki = 78 nM)



Mitragynine Pseudoindoxyl
(Ki = 1 nM)



MGM-15 and MGM-16
(Ki = 6 and Ki = 2 nM)

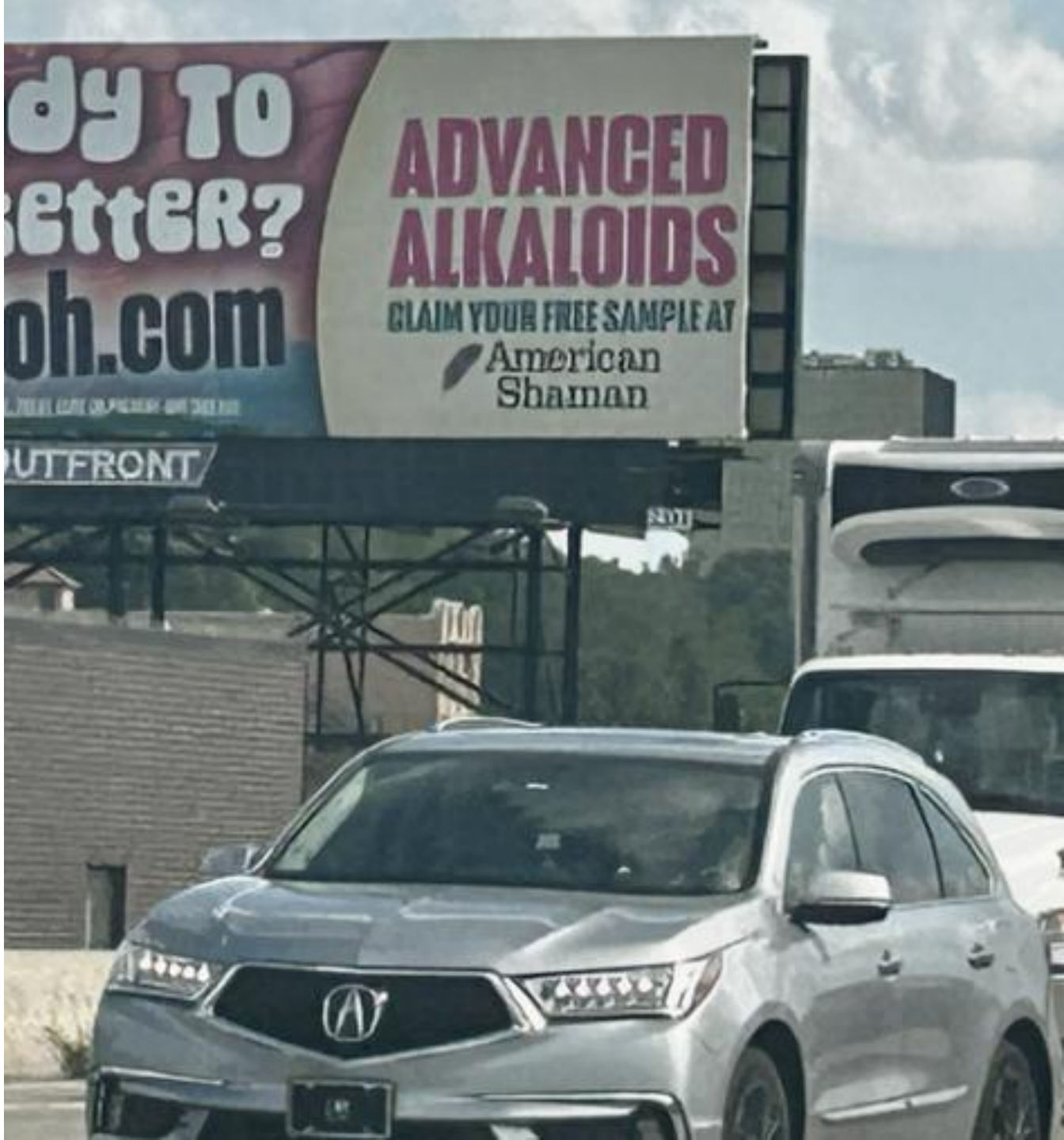
"Gas Station Heroin" Currently Being Sold

Myth: these ingredients are not opioids because they do not share the classical features of morphine or semi-synthetic opioids.
Truth: They are no different structurally than synthetics like fentanyl are to morphine.

https://www.nature.com/articles/tp201430.pdf
https://jpet.aspetjournals.org/article/S0022-3565(24)25764-5/abstract
https://jpet.aspetjournals.org/article/S0022-3565(24)27223-2/abstract

“Gas Station Heroin” Products

- Products with concentrated synthetic or semi-synthetic ingredients that potently stimulate opioid receptors
- Sold in gas stations, convenient stores, smoke shops, and over the internet
  - No medical oversight, no prescription, no quantity limits
- Multi-billion-dollar industry
- Have the potential to hook a whole new generation of people
  - The ramifications of de novo OUD, especially in young people, will take decades to fully play out



Concentrated Synthetic 7-OH vs. Natural Kratom Leaf

Concentrated Synthetic 7-Hydroxymitragynine (7-OH)		Real, Natural Kratom Leaf
AT A GLANCE COMPARISON		
7-OH (high concentration)	**Primary Alkaloid**	Mitragynine
Lab made synthetic opioid	**Origin**	Natural botanical leaf
7-OH highlighted; flashy brand names	**Label Clues**	Whole leaf, powder, natural, mitragynine most abundant alkaloid
Tabs, pills, gummies	**Format**	Leaf, powder, tea, capsules
Blue Razz, Mintopia, Baja Blast	**Taste Profile**	Bitter taste with high-fiber texture
High; similar to illicit opioids	**Risk Profile**	Low; long traditional use

Collecting Patient Data on the Concentrated Synthetic 7-OH Crisis

Read the Letter

Sign the Petition

We need better data to combat this crisis.

Because concentrated synthetic 7-OH, mitragynine pseudoindoxyl (Red-OH), or MGM-15 or MGM-16 opioid products are often falsely branded as natural kratom, clinicians may not suspect a potent synthetic agent — resulting in missed diagnoses or inappropriate treatment approaches and documentations of cases.

Take action in your clinics and communities.

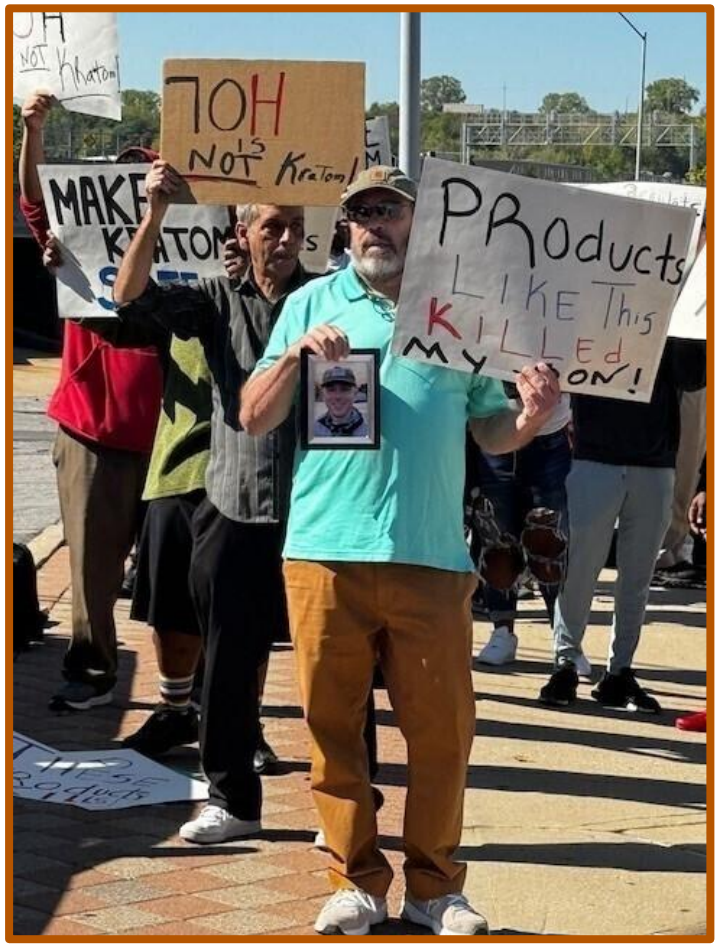
Thorough patient intake information can allow patients to self-identify as being addicted to concentrated synthetic 7-OH, mitragynine pseudoindoxyl (Red-OH), or MGM-15 or MGM-16 opioid products.

STOP
GAS
STATION
HEROIN

The Fourth Wave of America’s Opioid Epidemic

David Bregger
December 16, 2025

Why I'm Here
A Father's Journey



My Personal Mission: Safety, Clarity, and Consumer Protection

- **Protecting** families affected by misleadingly marketed products
- **Advocating** for clear, consistent kratom standards
- **Continuing** the work behind the Daniel Bregger Act

The Problem

Dangerous Street Drugs Targeting Children

Real Kid Products

Concentrated Synthetic 7-OH Opioid Products

Dangerous & Deceptive

Kid-Friendly Branding
Bright colors, cartoons, candy packaging.

Candy Lookalikes
Gummies, chewables, capsules, lollipops.

Sold Everywhere
Gas stations, smoke shops, even online.

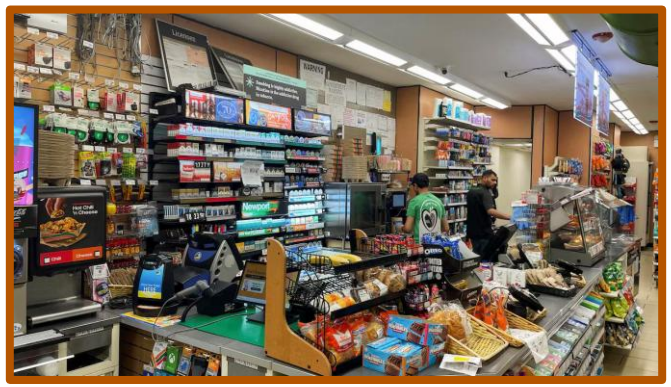
Opioid Strength
Up to **13x stronger than morphine.**

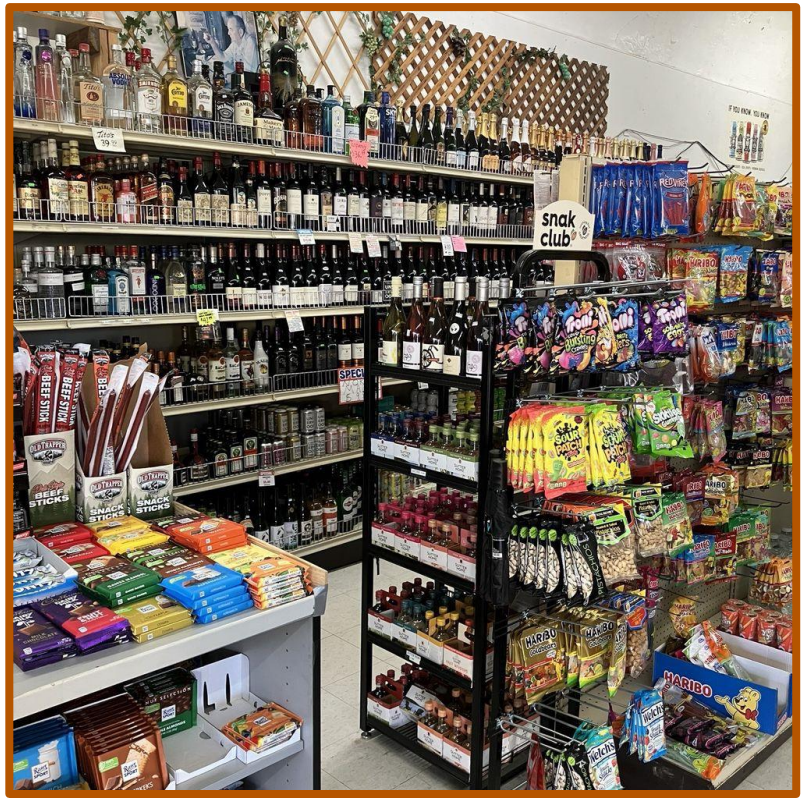
The FDA is concerned about the rise of concentrated synthetic 7-OH products, which "may be especially appealing to children and teenagers, such as fruit-flavored gummies and ice cream cones."

Concentrated synthetic 7-OH opioid products are "13 times more potent than morphine," according to FDA Commissioner Marty Makary.

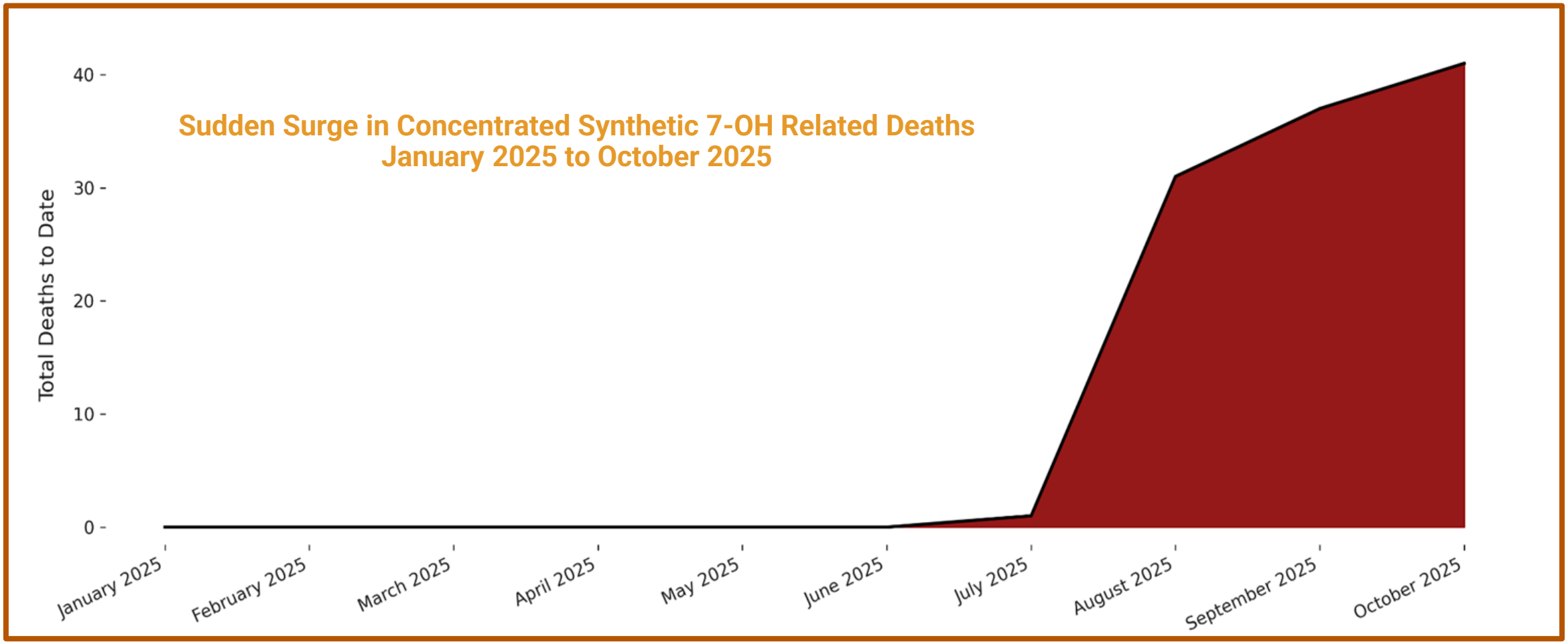
The Product
Lab-Made Opioids on Retail Shelves

Concentrated synthetic 7-OH opioid products are sold in gas stations, vape shops, and convenience stores across America.





The Impact
American Consumers at Risk



The Impact
Fourth Wave of Opioid Epidemic

Wave 1 - 1990 to 2011

OPIOID MEDICATION PRESCRIBING

- Pain made a “Fifth Vital Sign” and “Performance Measure”
- Subjective patient reports of pain above 4 of 10 triggered expectations for new pain medications or increased doses.

Wave 2 - 2005 to 2015

ILLICIT HEROIN CONVERSION

- Some prescription users “outgrew” prescription opioids and wanted something stronger.
- Many prescription opioid users were abruptly shut off from the legitimate supply chain.

Wave 3 - 2015 to Present

ILLICIT FENTANYL

- Fentanyl supplemented heroin or fentanyl substituted heroin.
- Fentanyl sought out as its own potent illicit opioid.

The Solution
Responsible Kratom Regulation

Banning →
Concentrated synthetic 7-OH opioid products

Preserving →
Access to lawful, all-natural kratom leaf products

Creating →
Clear labeling and transparency standards

Aligning →
State action with federal policy and gguidance

Enabling →
Enforcement against illegal manufacturers

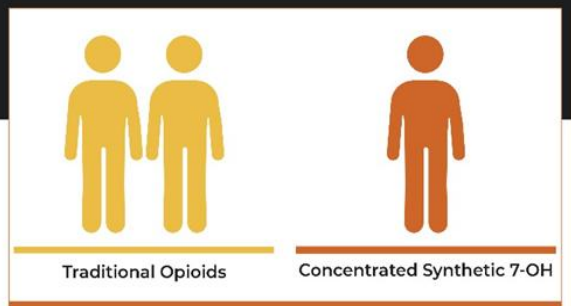
The Solution
Federal Scheduling Action

- In July, the FDA **recommended scheduling** concentrated synthetic 7-OH as a Schedule I substance.
- FDA Commissioner Martin Makary said concentrated synthetic 7-OH "is an opioid that can be **more potent than morphine**," underscoring the need for "regulation and public education to prevent **another wave of the opioid epidemic**."
- Agency officials emphasize they are "specifically targeting 7-OH, a concentrated byproduct of the kratom plant … [We are] **not focused on natural kratom leaf products**."
- The DEA **still has not adopted** the FDA's recommendation.

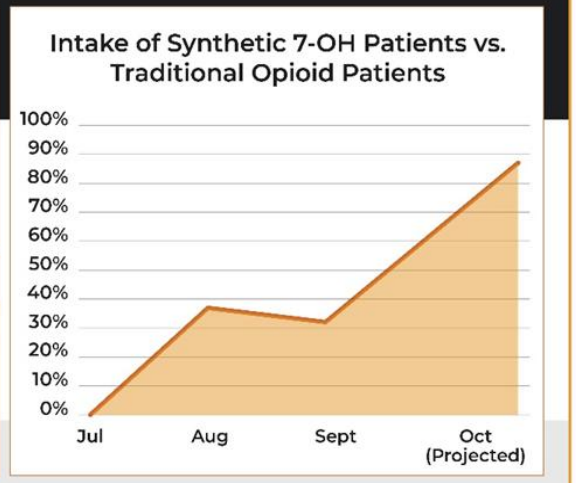
The Solution
Partnering to Prevent Deaths

Treatment Centers See Surge of Concentrated Synthetic 7-OH Patients

New data from treatment providers indicate a national increase in concentrated synthetic 7-OH opioid admissions, underscoring the urgent need for DEA intervention.



Since August, one in three opioid patients has been admitted for concentrated synthetic 7-OH use disorder, and that number is expected to grow.



"The surge in synthetic 7-OH patients is the biggest shift we've seen since the rise of fentanyl. Before August, we did not have any patients with a concentrated synthetic 7-OH use disorder. Now, they represent an average of **36% of intakes every month**. Even more alarming, **October intakes are expected to be up 100-150%** from August."

- Phil Atteberry, Chief Executive Officer of BRIGHTSIDE

STOP GAS STATION HEROIN

BRIGHTSIDE®

Clinic and Recovery, Treatment Center

Brightside partner with CMS

Number of Brightside and CMS Locations

- CMS has 73 clinics in 12 states
- Brightside has 6 clinics in 2 states

States where Brightside and CMS Are Located

- CMS: Alaska, Arizona, Colorado, Illinois, Indiana, Michigan, Minnesota, Montana, North Dakota, Ohio, Oregon, Texas, Wisconsin
- Brightside: Illinois, Ohio

Number of Patients across Brightside and CMS

- CMS current census is 24,669
- Brightside current census is 750

Relationship between Brightside and CMS

- The services that both CMS and Brightside provide offer treatment options that directly address the opioid epidemic, with the goal of improving quality of life and enabling those with OUD to regain control of their lives, reducing the possibility of overdose. This partnership allows for expansion of services to even more people in need in the Midwest and fuels growth in opioid treatment to those in need.

Researchers →
Continuing to study effects and risks

Clinicians →
Tracking encounters and reporting trends

Advocates →
Pushing for targeted, evidence-based policy

Regulators →
Enforcing against concentrated synthetic 7-OH opioid products

The Solution
Collecting More Patient Data

Read the Letter	Sign the Petition

We need better data to combat this crisis.

Because concentrated synthetic 7-OH opioid products are often falsely branded as natural kratom, clinicians may not suspect a potent synthetic agent — resulting in missed diagnoses or inappropriate treatment approaches and documentations of cases.

Take action in your clinics and communities.

More thorough patient intake information could prompt overdue scheduling action and help save lives. Commit now to adding an option to your intake forms for patients to self-identify as being addicted to concentrated synthetic 7-OH opioid products.

STOP GAS STATION HEROIN

We need to STOP GAS STATION HEROIN -

Join the Fight!

stopgasstationheroin.com