



Kratom: Mitragynine & 7-hydroxymitragynine 2026

**Ari Greenberg, PAC
Community Medical Services**

Kratom & 7-OH

No Disclosures

- **Kratom Origins**
- **Mechanism of Actions**
- **Mitragynine**
 - **7-hydroxymitragynine**
 - **M. Pseudoindoxl**
- **Use risks**
- **Overdose risks**
- **Treatment options**
- **Regulations**

General Public Viewpoints

- **"It's just a plant"**

- We have patients at CMS using Kratom primarily or only Kratom who meet DSM-5 criteria for severe SUD.

- **"It's an herbal supplement"**

- Kratom may compel use up to \$100 or more per day

- **"Nobody is overdosing on it"**

- Reported OD cases w/ co-ingestion and use alone

- **"It's legal"**

- South Dakota age restriction set at 21yo.
- No age restrictions to purchase Kratom products in Montana, Idaho, Wyoming, or North Dakota.

Kratom - Mitragnyna Speciosa



Rubiaceae family (coffee plant)

Wetlands of Southeast Asia

- Workers chew leaves during the day
- Steep tea leaves for the night
- Long traditional use for medicinal, social gatherings, and cultural traditions
- ~250,000 farmers
- US popularity increased in mid-2000's

20+ identified alkaloid compounds

Psychoactive alkaloids:

- Mitragynine (66%)
- 7-Hydroxymitragynine (<2%)

(Alkaloids = morphine, cocaine, caffeine)

Kratom - Mitragyna Speciosa



Reported effects

- Stimulant
 - Mood elevation
 - Analgesic
 - Sedative
 - ED – Nature's Viagra
 - Recreational Euphoria
 - Manage opioid-related WD sx's
-
- 2-2.5 million reported users
 - Est Up to 20 million daily users – based on amount of imports and products sold.

Feel Free "energy drinks" surpassed 5Hr Energy \$\$\$

Kratom Leaf

Largest suppliers:

- Indonesia
- Vietnam

No FDA approved drugs containing Kratom or Kratom-derived products

- Powder/pills
- Resin extracts/Tablets/Teas
 - Bitter taste



Dose-Dependent Pharmacological Activity

Low (1-5g)

- Stimulatory → affects Serotonin system
- Antidepressant-like effect ¹

High (>5g)

- Sedative and analgesic properties due to opiate receptor activation²
- Counteracts opioid withdrawal

Mitragynine → [Hepatic metabolism] → 7-OH

- 7-OH greater effect as a mu-opioid agonist than Mitragynine²
- Mitragynine: alpha-2 agonist – similar to Clonidine³

1- <https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2021.696461/full>

2- <https://pmc.ncbi.nlm.nih.gov/articles/PMC6598159/>

3- <https://www.sciencedirect.com/science/article/abs/pii/S0014299924005521>

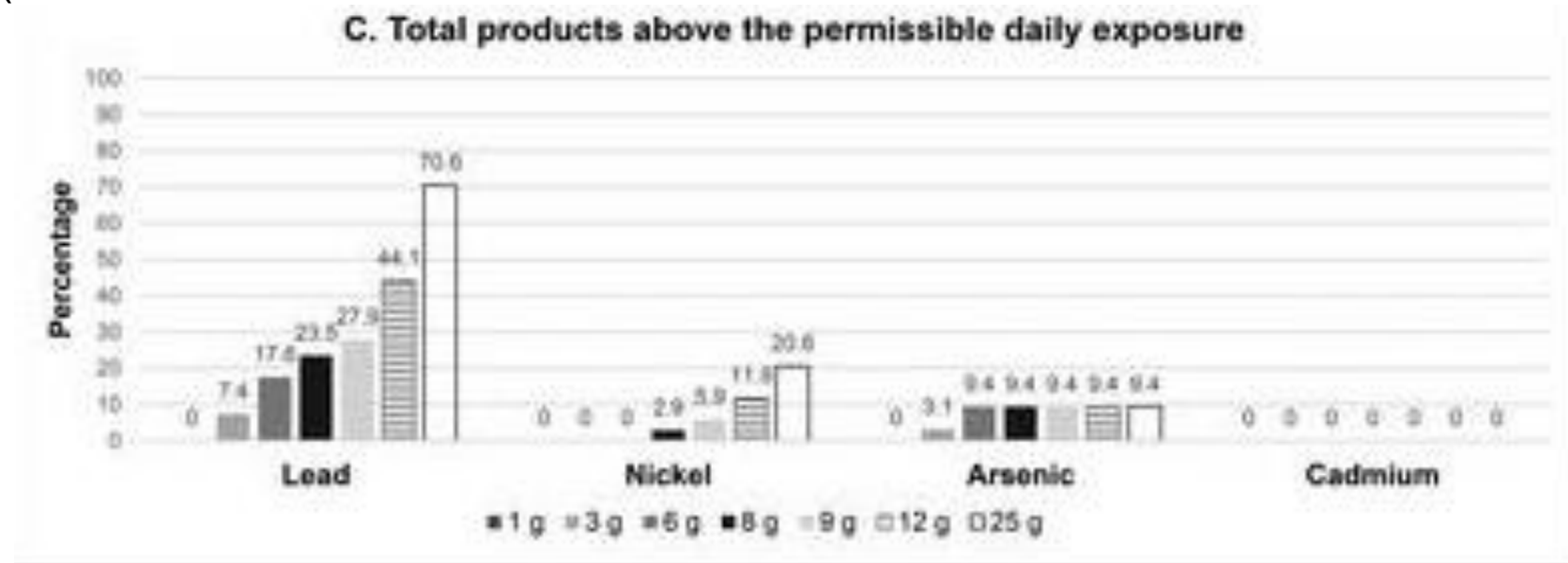
Heavy Metal Content

- Southeast Asian soil and water have high levels of heavy metals.
 - Volcanic rock is higher in heavy metals
 - Plants grown are exposed to higher conc of elemental impurities in soil
 - Harvested plants washed w/ local water
 - Use of coal, leaded gas
 - Products harvested w/ older machines or in poor repair can leach heavy metals

<https://www.tandfonline.com/doi/full/10.1080/15563650.2024.2395552>

Heavy Metal Content

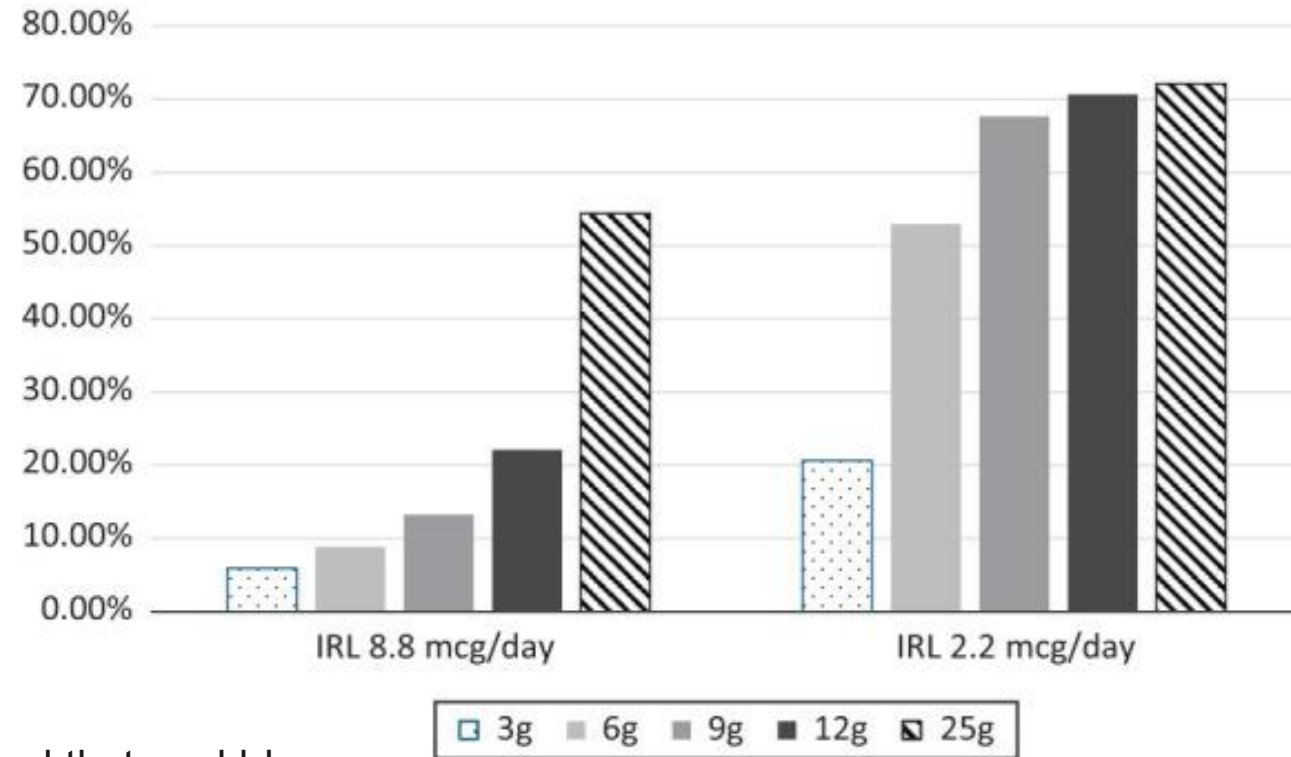
- The percentage of products that exceeded daily permissible exposure limits for lead (5 mcg/d), nickel (200 mcg/d), arsenic (15 mcg/d), and cadmium (5 mcg/d).



<https://www.tandfonline.com/doi/full/10.1080/15563650.2024.2395552>

Heavy Metal Content

- Excessive lead for women of child-bearing potential (WCBP) and Children
 - They have lower interim reference levels (IRL) than men or post-menopausal women
 - WCBP (8.85mcg/d)
 - Children (2.2mcg/d)



The interim reference level (IRL), defined as the total amount of lead that could be consumed through all food, drugs, and supplements consumed daily

<https://www.tandfonline.com/doi/full/10.1080/15563650.2024.2395552>

WCBP and Children

- Why are looking at WCBP and children?
 - Kratom is used to manage women w/ opioid withdrawals
 - Promoted to help w/ getting off opiates
 - Advertised to enhance cognition for teenagers
 - Discussed as a "smart drug"
 - Helps w/ "all-nighters" or enhance academic focus
 - Athletes use it to deaden the pain and increase stamina

Kratom Impurities

Heavy Metal content

- Non-extract products (powders, capsules, tablets) generally contain greater concentrations of elemental impurities than extract products.

Microbe contamination

- Salmonella outbreak - Jan 2017 to May 2018
- 199 cases in 41 states
- 54 patients were hospitalized

<https://pmc.ncbi.nlm.nih.gov/articles/PMC12288559/>

7-hydroxymitragynine

<2% in Kratom dry mass

- Kratom 1st pass => 0.2-0.31 7-OH
- Up to 50x more potent than mitragynine

New distillates w/ up to 98% conc:

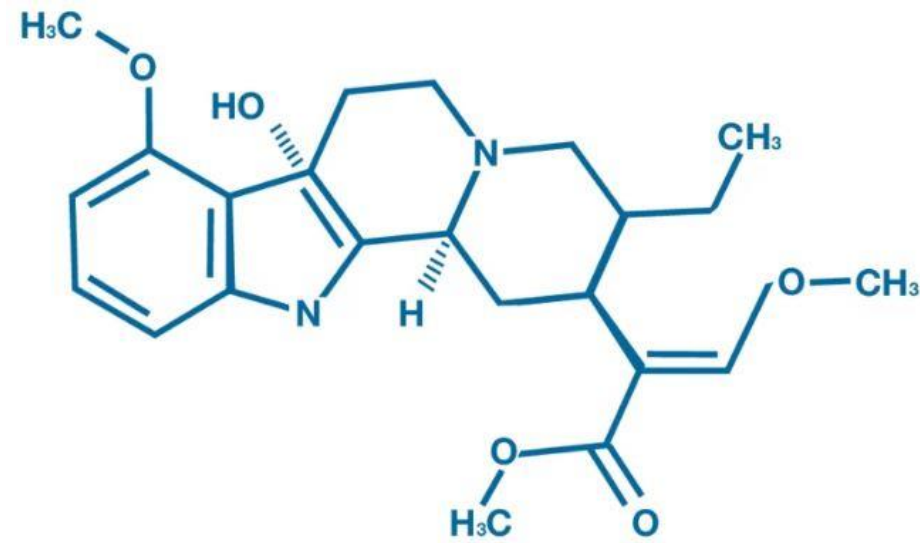
- Pills, Tablets
- Sodas, Seltzers, Teas
- Syrups
- Tinctures

Slang: 7-OH, 7-O, Hydroxy's, Om's, Mitra



7-hydroxymitragynine

7-OH



7-OH is a potent mu-opioid receptor agonist

- Potential for abuse
- **Up to 10-14-fold greater potency than morphine**
- Therapeutic effects are mediated through the same opioid pathways as other opioid agonists.¹

Clinical presentation:

- Euphoria, sedation, respiratory depression, and opioid-like withdrawal sx's¹
- **Can contribute to NOWS²**

1- https://www.kslegislature.gov/li_2024/b2023_24/committees/ctte_h_fed_st_1/documents/testimony/20230201_16.pdf

2- <https://pubmed.ncbi.nlm.nih.gov/30204686/>

Mitragynine Pseudoindoxyl MIP

First acknowledged in early 2025

- Must be synthesized from 7-OH
- Effects mu-opioid receptor
 - 100x more potent than Mitragynine

But it's promoted to be less addictive???

- No human studies



Kratom Leaf Products

- Kratom dosing ranges vary widely d/t bulk packaging



7-OH Products



- 7-OH dosing ranges from 10-50mg



7-OH Products to reduce bitterness



Tinctures

Seltzers



Kratom Products to increase potency



Sublingual Strips

Disintegrating Tablets



Adverse Events

Column1	<13 years	13-19 years	>19 years
Neurological	%	%	%
Agitated	9.5	16.3	23.9
Drowsiness	9.5	18.8	14.3
Confusion	2.4	13.8	10.9
Seizures	0	11.3	9.9
Hallucinations	0	5	5.5
Syncope	0	7.5	1.6
Cardiovascular			
Tachycardia	2.4	20	22.5
Hypertension	0	8.8	10.8
Conduction	0	1.3	3.1
Chest pain	0	1.3	2.9
Gastrointestinal			
Nausea	0	18.8	14.7
Vomiting	9.5	20	12.9
Respiratory			
Respiratory Depression	0	1.3	3.9
Dyspnea	0	3.8	2.3
Tachypnea	2.4	1.3	1.8
Hepatic			
AST/ALT	0	2.5	5.5
Bilirubin	0	1.3	2.8

Hyperalgesia

Increased sensitivity to pain

Chronic Kratom Alkaloids (including MIP) exposure can induce hyperalgesia.¹

- **Similar to opioids, sometimes even greater.**

1 - <https://pmc.ncbi.nlm.nih.gov/articles/PMC12288559/>

Overdose Risk

Mitragynine and 7-OH are both **G protein-biased agonists to the mu-opioid receptor.**¹

- + Analgesic
- Less impactful on respiratory depression (β -arrestin pathway)

Kratom leaf product alone is very low OD risk, **almost always associated w/ co-ingestion**²

- Greater risk w/ 7-OH, but the overall risk is still low.
- Coingestion most common w/ OD

1- <https://www.sciencedirect.com/science/article/abs/pii/S0028390817303933>

2- <http://publichealth.lacounty.gov/phcommon/public/media/mediapubhpdetail.cfm?prid=5156>

Treatment Options

FDA-Approved MOUD

- **Methadone**
 - Same day treatment
- **Naltrexone**
 - Delay w/ initiation
- **Provide Naloxone**
- **Buprenorphine products**
 - Buprenorphine/Naloxone
 - Strips/Tablets
 - Risk for POW's
 - Micro vs Macro dosing
 - LAI's

Never Use Alone #

Never Use Alone

NEVER USE ALONE

Web : www.NeverUseAlone.com
Phone : 1-877-696-1996
FB : www.facebook.com/Neverusealone

(877)696-1996
No Judgement
No Shaming
No Preaching
Just Love!



Call us if you are going to
Use Alone!
1-877-696-1996

One of our operators will stay on the line with you while you use, to try and ensure that you don't die from fentanyl poisoning!

HOW IT WORKS

When you call, one of our volunteer operators will answer your call. You will be asked for your first name (it can be a fake name, or nickname), exact location (down to the exact room you're in), and the phone number you're calling from (in case we get disconnected).

After you've given us the required information, you can go ahead and use your substance. We ask that you let us know when you're done. If you stop responding afterward, we will notify emergency services of an "unresponsive person" at the location you've given us!

All calls are strictly confidential. We will never share your personal information with anyone other than EMS if we have to dispatch them.



CONFIDENTIAL

We don't share your personal info with anyone other than EMS, if we have to call them. We are NOT affiliated with any law enforcement agency, or treatment center!



TREATMENT RESOURCES

If you are interested in getting help, we have a large list of free/low cost, and state funded facilities throughout the country. We will never push this on you though.



HARM REDUCTION RESOURCES

If you need Narcan, or access to safe supplies, we can assist you with locating resources within your state.

Treatment Options

Macro Dosing

- >12-16h since last dose, symptomatic
- Initiate w/ 24mg dose.
- May include symptomatic mgmt.

Micro Dosing ->

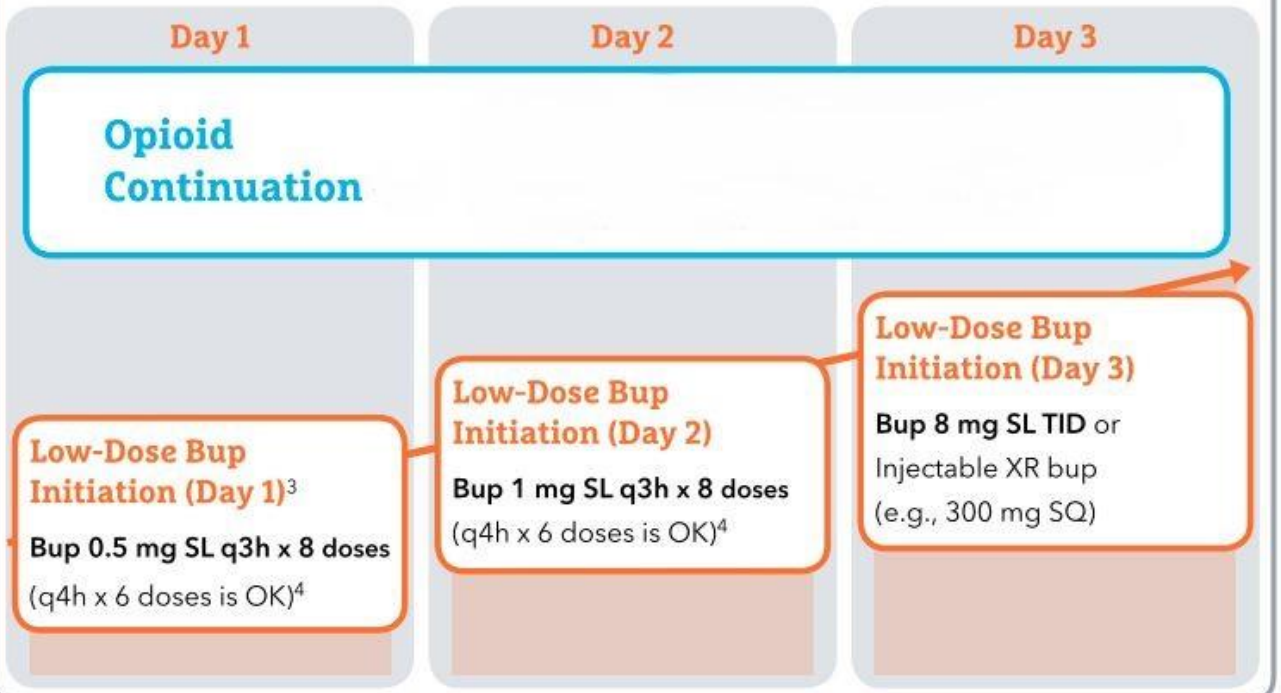
- Symptomatic mgmt.



Buprenorphine (Bup) Hospital Start: Low-Dose Bup Initiation with Opioid Continuation

Treatment Bundle Over Three Days¹

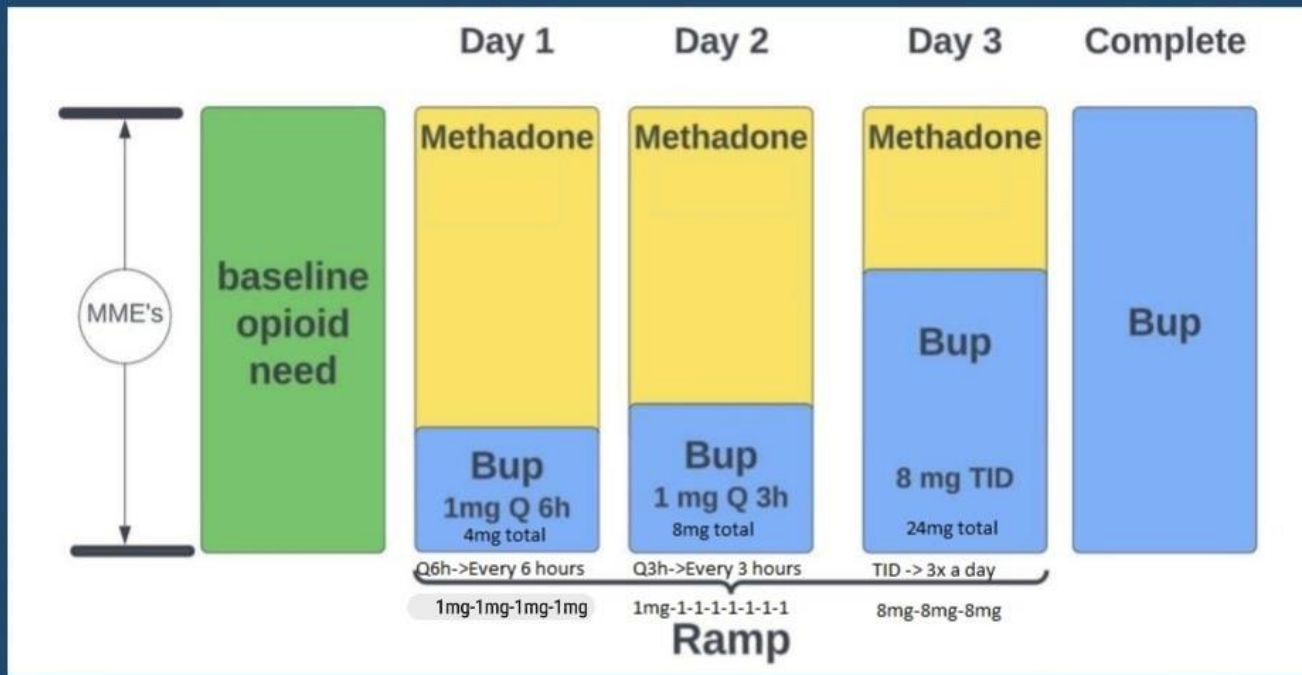
Maximize pain control & withdrawal treatment with opioid analgesics throughout bup initiation



Treatment Options

CA Bridge LDB-OC Induction

- Low dose Bup w/ opiate continuation



Social Media

- Bluelight.org - <https://bluelight.org/>
 - International message board that educates the public about responsible drug use by promoting free discussion, advocating harm reduction and attempting to eliminate misinformation.
- Reddit.com - <https://www.reddit.com/>
 - Online forum that functions as a vast collection of user-driven communities, known as subreddits, each centered around specific topics.
- Erowid.org - [Erowid](https://www.erowid.org/)
 - Member-supported organization providing access to information about psychoactive plants, chemicals, and related issues.

Social Media

- Anecdotal general population discussions:

"I am not a drug addict, though I have used many substances in the past. I saw 7-OH for sale at the convenience store and was told it was a good natural pain relief product. Within days of taking it, I was increasing doses and having severe issues with sleep and mood if I waited more than 5-6 hours between doses. Due to the item being legal and non-regulated I was able to buy as much as I wanted whenever I wanted. I started with 10 mg BID and increased quickly to 80 mg per day. I tried to quit in December only to give on Day 4. I immediately jumped right back to almost 100mg a day and by March I was taking 240mg a day and it only went up from there. When I quit yesterday I was averaging 400-500 mg per day"

Social Media

- Anecdotal general population discussions:

"The withdrawals and the damage done by 7oh (not so much leaf kratom) are insane."

"It is 10 times the strength of morphine. Stay far away from the stuff with pseudo. Far far away. Coming off 7oh + pseudo was the worst withdrawal I have ever gone through. I have withdrawal from oxy, methadone, alcohol, cocaine. 7oh + psedu withdrawals take the cake. User beware."

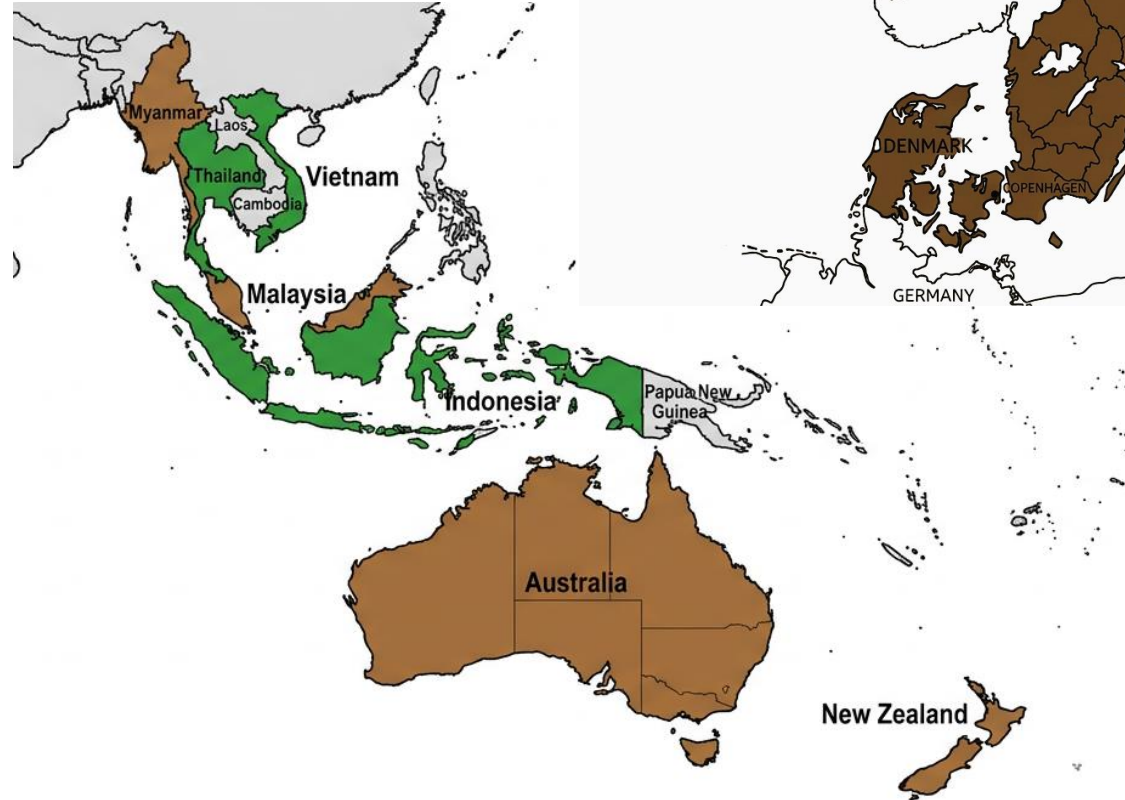
MIP - "Basically the same as 7-oh, possibly slightly stronger or more sedating. I found it enjoyable but maybe less euphoric than 7."

World Regulations

Outlawed by Thailand (1943-2021)
& Malaysia (1952)

Countries (2025):

1. Malaysia
2. Myanmar
3. Australia
4. New Zealand
5. Denmark
6. Sweden
7. Finland



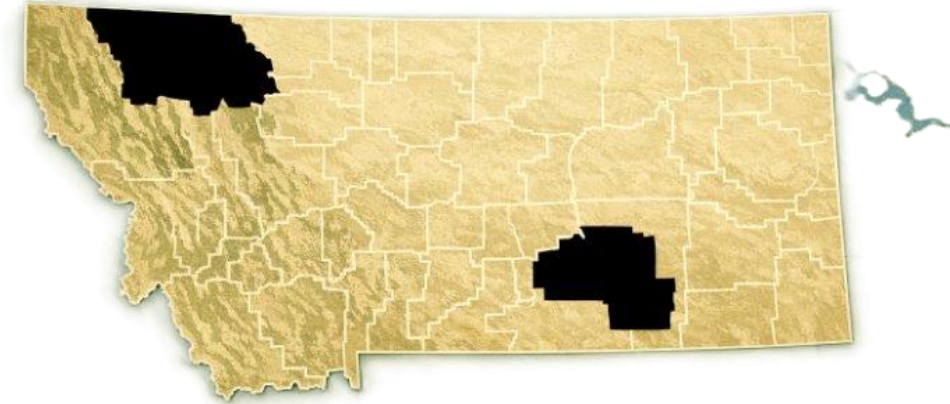
Federal Regulations

- FDA issued its 1st alert in 2012
- Consideration for control under the Controlled Substances Act suspended in 2018.
 - Incomplete science
 - Available data not adequate to support control recommendations
- Currently, HHS recommends Schedule 1 designation
 - High potential for abuse and no current accepted medical use.
 - DOD does not allow Kratom Products as an herbal supplement.
- FDA and DEA are reviewing Kratom and Kratom products again.
 - "7-OH, is more potent than morphine and abused for its ability to produce opioid-like effects."
 - "The identity, purity levels, and quantity of these substances are uncertain and inconsistent, and pose significant adverse health risks."

Montana State Regulations

Current status: No age restrictions, except local county & reservations bans

- **Blackfeet reservation**
- **Yellowstone County**
 - Licensed food & beverage establishments
 - Except gas stations, smoke shops, kava bars



Montana attempted to regulate 2025:

HB 407 – Tabled by House Appropriations Committee

- Age restrictions (21y+)
- Product testing
- Labeling

SB 461 "Kratom Consumer Protection Act" - sponsored by American Kratom Association

- Capping 7-OH to <2%

Next Montana legislative session - 2027

- Accumulating data w/ Montana Medical Association and Riverstone Health...

Kratom Support



AMERICAN KRATOM
ASSOCIATION

American Kratom Association (millions)

Non-profit consumer advocacy organization successfully campaigned for withdrawal of planned scheduling

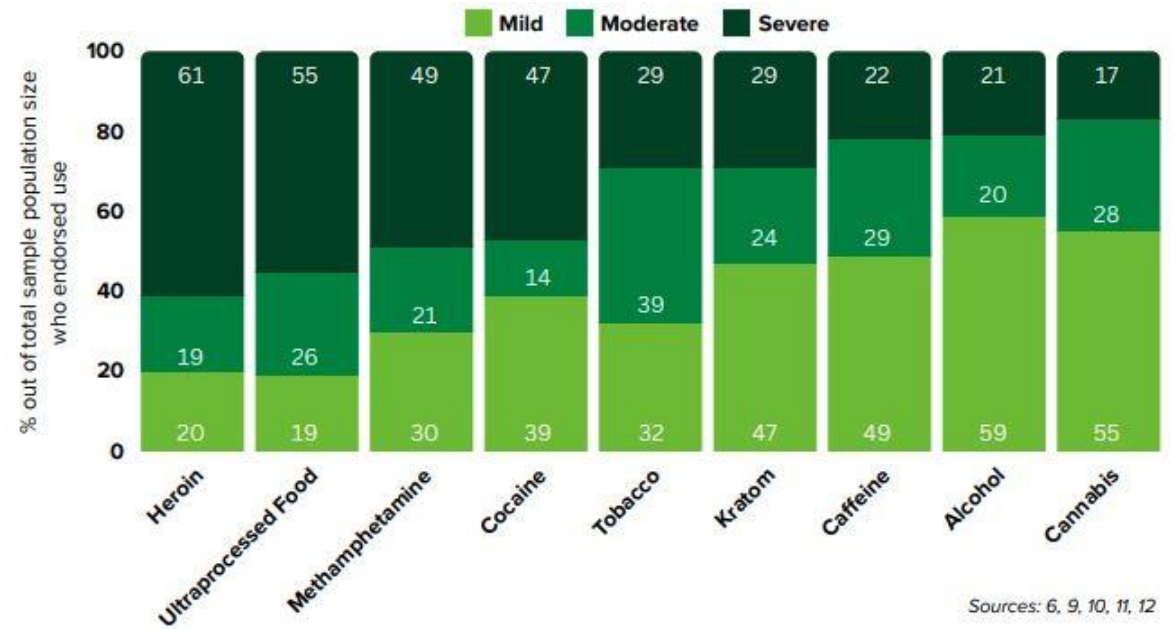
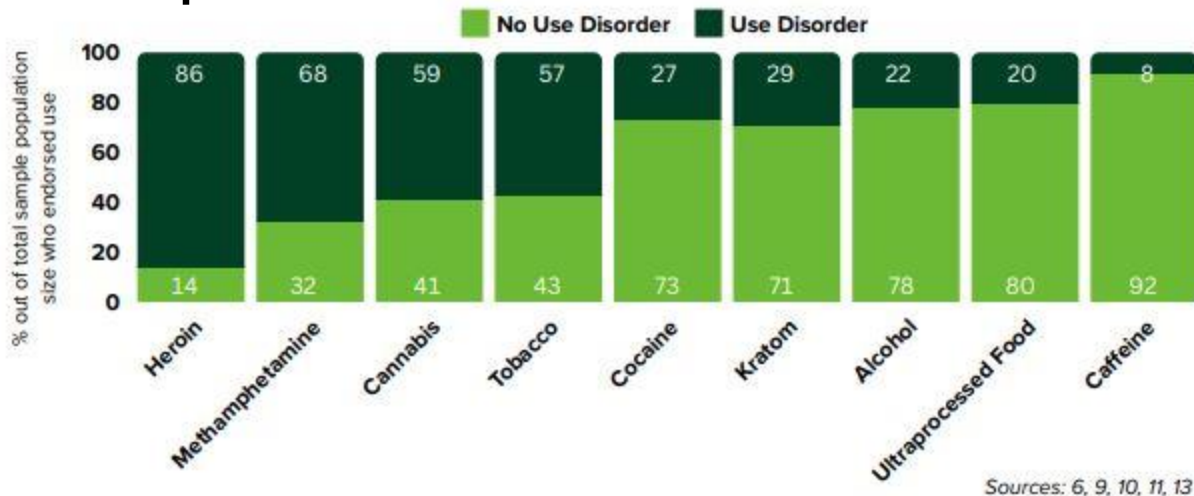
- Accuse FDA of "distributing disinformation on Kratom," as well as "misleading consumers and policy makers."
- **There is an attempt to split hairs between Mitragynine and all other synthesized products to preserve the availability of Kratom leaf.**



Kratom Support

Global Kratom Coalition

- Attempt to downplay the presence of SUD from Kratom exposure



<https://static1.squarespace.com/static/6508b3f79033221c2aa1ea17/t/66abcc0c8395076b6de4f107/1722534926845/Comparative%2BSafety%2Bof%2BKratom%2BCompared%2Bto%2BOther%2BCommonly%2BUsed%2BSubstances%2B%282%29.pdf>



New distillates on the market: 7-OH/MIP

- More potent mu-opioid agonists

Kratom leaf has multiple impacts

- Stimulant/sedation/OD
- Mitragynine => 7-OH

Impurities

- Lead, nickel, arsenic

Addictiveness - "Less is more"

- Tolerance

Adverse events/OD

- Primary or Co-ingestion

Takeaway

- Kratom may not be as dangerous as traditional opiates... but it's not without risks either.

- Similar to alcohol and cannabis, two drugs managed tightly by the states.

Need for:

- Limits of concentrations and doses
- Age restrictions
- Clear labeling
- Disclosure of risks
- Quality manufacturing expectations

Takeaway

A blue geometric shape, resembling a large triangle or a trapezoid, is positioned on the left side of the slide. It has a diagonal edge that separates it from the white background on the right.

Questions?

Thank you for listening!