KRATOM 101

What Family Physicians Need to Know About an Emerging Opioid-Like Substance

By: Austin Barnhardt MD, PGY1 MFMR

MAFP Summer Meeting

- I have no financial disclosures
- All slides are for educational purposes

A special thanks to all the faculty at Montana Family Medicine Residency and the professionals at RiverstoneHealth for guidance and resources on this topic

LEARNING OBJECTIVES

1. Describe kratom and its primary active alkaloids
   - Mitragynine
   - 7-hydroxymitragynine (7-OH)
2. Recognize common clinical presentations associated with kratom use
3. Evaluate and manage kratom-related presentations in primary care
4. Understand the current U.S. and Montana regulatory landscape

A. Never heard of it

B. Heard of it but never seen a patient using it

C. Seen 1–5 patients

D. Seen >5 patients

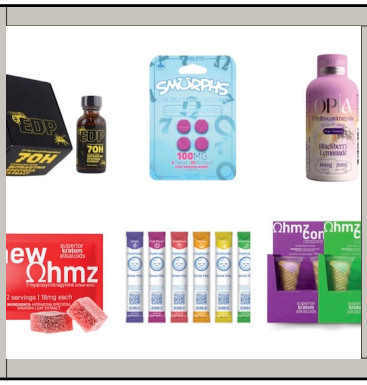
Pulse Check: Have you encounter kratom use in practice?

WHAT IS KRATOM?

MITRAGYNA SPECIOSA

- Tropical evergreen tree
- Coffee family (Rubiaceae)
- Native to:
  - Thailand
  - Malaysia
  - Indonesia
  - Myanmar
- Leaves contain 40+ of bioactive alkaloids

Traditional use: Chewed leaves or tea used for centuries in Thailand and Malaysia as a mild stimulant to increase work productivity and as folk medicine for pain, diarrhea, and opioid withdrawal



KRATOM PRODUCTS

In modern day lots of concentrated forms:

- Powders
- Capsules
- Teas
- Gummies
- Extract shots
- 7-OH products

Kratom "extracts" with increased potency found in gas stations, smoke shops, online, Kava bars and traditional dining establishments

EPIDEMIOLOGY

- Rise in recreational and commercial use in US since early 2000's
- Approximately 2 million+ users as of a 2021 cross sectional study
- Primarily in younger males with average age 35yo
- Increase in problematic use: Kratom-related poison center reports increased ~1,200% from 258 in 2015 to 3,434 in 2025
- Reported 233+ deaths to National Poison Data System
- At least 5 deaths primarily related kratom use in Montana
- High rates of concurrent substance use — 37% also misuse prescription opioids, 22% use illicit opioids, and 54% use other illicit drugs

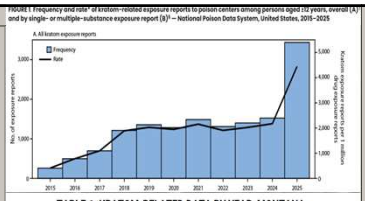
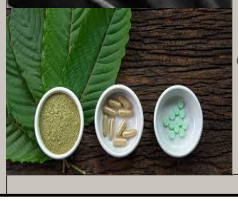


TABLE 1. KRATOM-RELATED DATA BY YEAR, MONTANA.

Indicator	2018	2019	2020	2021	2022	2023	2024	Total
Unintentional overdose deaths – Kratom detected	n/a	8	7	5	6	6	13	45
Unintentional overdose deaths – Kratom present, at least one other drug contributing to death	n/a	7	5	4	6	6	7	35
Poison Control – Kratom exposures	7	8	4	5	9	10	5	48

Why Has Kratom Become Popular?



Self-reported reasons for use:

- Pain management (most common)
- Self-treatment of opioid withdrawal symptoms
- Mood enhancement / anxiolytic effects
- Recreational "legal high"
- Self-management of depression, anxiety, PTSD

Perceived benefits reported by users:

- **Inexpensive, legal*, and accessible without prescription**
- Marketed online as a "natural" alternative to opioid replacement therapy
- See Kratomade.com or kratom.org for a consumer level perspective

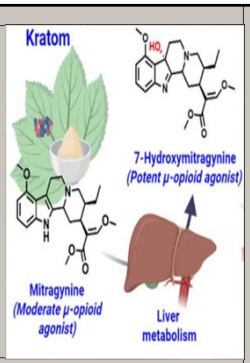
Clinical reality:

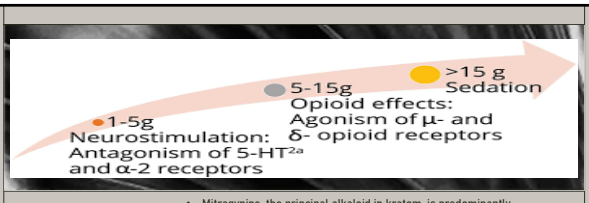
- No FDA-approved medical indications for kratom; recommended for being scheduled under CSA
- No controlled clinical trials demonstrating efficacy for any condition
- The U.S. Department of Health and Human Services has concluded kratom has no accepted medical use

KRATOM PHARMACOLOGY

AN "ATYPICAL OPIOID"

- Active alkaloids: Over 40 alkaloids identified; two primary psychoactive compounds:
- Mitragynine (~66% of alkaloid content) — partial agonist at **mu-opioid receptors; also active at adrenergic, serotonergic, and dopaminergic receptors**
- 7-Hydroxymitragynine (~2% of content but significantly more potent) — **potent mu-opioid agonist,** >10-fold greater mu-opioid receptor affinity than morphine
- Most commercial products have high and unregulated 7-OH content without standard dosing or unit measurements resulting in varying effects





MITRAGYNINE HAS G-PROTEIN BIASED AGONISM

POTENTIALLY LESS BETA-ARRESTIN RECRUITMENT & LESS RESPIRATORY DEPRESSION

- Mitragynine, the principal alkaloid in kratom, is predominantly metabolized by CYP3A4, with minor contributions from CYP2D6, CYP2C9, CYP2C19, and CYP2C18
- **The most important metabolic conversion is the CYP3A4-mediated oxidation of mitragynine to 7-hydroxymitragynine,** which has more direct u- opiod agonism; metabolic saturation at high doses caps the formation of the more dangerous active metabolite
- Both mitragynine and 7-hydroxymitragynine are subsequently cleared via CYP3A
- Kratom alkaloids inhibit CYP2D6, CYP3A4, as well as P-glycoprotein

KRATOM USE CLINICAL PRESENTATIONS

Any Examples????

IT VARIES! PATIENTS MIGHT NOT DISCLOSE USE OR KNOW THE POTENTIAL EFFECTS OF KRATOM

Common side effects:

- **Nausea, constipation**, sweating, itching, dry mouth
- Sleep disturbances, temporary erectile dysfunction
- Long-term: anorexia, **weight loss**, hyperpigmentation (mitragynine-stimulated melanocyte activity), hair loss

Serious adverse effects:

- **Hepatotoxicity**: Intrahepatic cholestasis, acute liver injury (kratom is now recognized as a cause of drug-induced liver injury)
- **Seizures** (6.1% of poison center single-substance exposures)
- Tachycardia**, agitation**, confusion, hallucinations
- Respiratory depression, coma, cardiac/respiratory arrest
- Hypothyroidism (rare)

Withdrawal syndrome (onset 12–48 hours after last use):

- Physical: Muscle spasms/pain, watery eyes/nose, hot flashes, fever, diarrhea, decreased appetite, tremors, insomnia
- Psychological: Restlessness, irritability, anger, anxiety, depressed mood, nervousness
- Generally milder than classical opioid withdrawal but can be clinically significant

Neonatal considerations: **Neonatal withdrawal symptoms** (oral intolerance, irritability, vomiting) reported in infants born to regular kratom users

ANECDOTAL ENCOUNTERS AND BARRIERS TO DIAGNOSIS

- Co-occurring use with opioids in MOUD/MAT clinic
- Primarily reason for MOUD/MAT clinic visit
- Primary reason for Rimrock admission
- Discovered use in chronic pain patients
- Started it to manage anxiety when did have insurance
- In shift workers to stay wake

Barriers to diagnosis:

- Viewed as "herbal" **only one-third (~33%) of herbal supplement users disclosed their use to a physician**
- Stigma of **opioid withdrawal self-management** (41% of users)
- Users might appear more "functional"
- Kratom is not captured on standard urine drug screens
- There is no structured EHR field for kratom use in most systems

Assessment and Diagnosis of KUD

- History and physical exam, including assessment for opioid and stimulant withdrawal
- DSM-5-based instrument to assess for KUD and other SUDs
- Confirmatory testing for kratom alkaloids (mitragynine)

Diagnosis: Comorbid KUD/OUD

- Discussion with patient about therapeutic options
- Initiate MOUD with buprenorphine, naltrexone, or methadone for KUD/OUD
- Consider initiation of adjunctive non-MOUD therapy
- Follow-up and monitoring of patient clinical course

Diagnosis: Isolated KUD

- Discussion with patient about therapeutic options
- Consider initiation of non-MOUD therapy for KUD
- Consider initiation of MOUD in appropriate patients after careful risk/benefit consideration
- Follow-up and monitoring of patient clinical course

APPROACH TO DIAGNOSIS AND MANAGEMENT OF KUD

- No formal DSM-5 diagnosis
- Can use general 11 criteria for SUD diagnosis (impaired control, social impairment, risky use, pharmacologic changes)
- No standard diagnosis for KUD used in the literature
- Mostly diagnosed due to tolerance and withdrawal
- Only 2% of users met criteria for moderate or severe use
- No RCTs for treatment at this time
- Promising algorithm proposed

TREATMENT OPTIONS:

- **Buprenorphine-naloxone** — most commonly used; can be initiated via standard or home induction protocols. No established dosing guidelines specific to KUD; maintenance doses have varied widely across case reports.
- **Clonidine** — for symptomatic withdrawal management (autonomic symptoms)
- **Supportive care** — for mild cases, withdrawal is generally self-limited (1–3 days) and mild-to-moderate in severity; NSAIDs, anti-diarrheals, sleep aids
- **Graduated taper** — some patients successfully self-taper kratom without pharmacotherapy, though this has not been formally studied
- **Cognitive behavioral therapy** — address underlying psychiatric co-morbidities

APPROACH TO KRATOM USE IN YOUR OWN CLINIC

Screening:

- Routinely ask about kratom and other herbal supplement use during substance use screening
- Include kratom in the review of supplements, especially in patients with chronic pain, opioid use history, or unexplained liver enzyme elevations
- Consider kratom in the differential for patients presenting with opioid-like withdrawal symptoms and a negative standard urine drug screen

Counseling:

- Non-judgmental, motivational interviewing approach
- Educate patients that kratom has no FDA-approved indications and carries real risks
- Emphasize dangers of polysubstance use
- Discuss the unregulated nature of products (variable alkaloid content, potential contaminants)

Treatment:

- Use of buprenorphine, clonidine, supportive care, CBT as indicated
- Referral to addiction medicine for moderate-to-severe cases or comorbid OUD

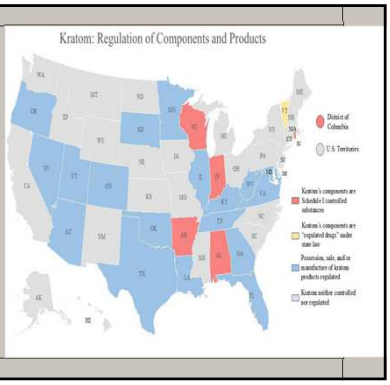
Monitoring:

- Consider liver function tests in regular users
- Assess for co-occurring substance use disorders
- Follow-up on mental health comorbidities (depression, anxiety, PTSD)

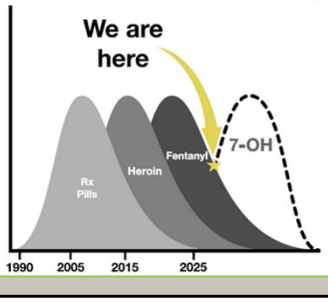
KRATOM REGULATION

LEGALITY

- DEA lists kratom as "drug of concern"
- FDA requesting DEA to schedule 1 7-OH under Controlled Substances act in 2025
- The Department of Defense prohibits service members from using kratom, citing safety concerns
- Kratom is not lawfully marketed in the U.S. as a drug product, a dietary supplement, or a food additive in conventional food
- Currently no state-level regulation in Montana



The Opioid Epidemic is Evolving with 7-OH. We Can and Must Act Now to Prevent a New Wave.



ENFORCEMENT IN YELLOWSTONE COUNTY

" RiverStone Health, the Yellowstone City-County Health Department, is responsible for enforcing food safety regulations and licensing retail food establishments under contract with the Montana Department of Public Health and Human Services (DPHHS).

Montana's food code requires that all food and beverage ingredients sold in the state are classified by the US Food and Drug Administration (FDA) as safe and suitable for consumption. The FDA has explicitly stated that kratom cannot be legally marketed as a dietary supplement and has not approved it as a food ingredient. Furthermore, the FDA does not differentiate between synthetic 7 -OH and natural leaf kratom in its analysis. Since kratom is not an FDA-approved food, beverage, or dietary ingredient, its inclusion in foods and beverages is prohibited from being sold in licensed food establishment"

Consider using your voice back home to promote public safety

1. Kratom is an unregulated botanical with real opioid-like pharmacology — treat it with the same clinical seriousness as other opioid-active substances
2. Ask about it — patients may not volunteer kratom use, and it will not appear on standard drug screens
3. Polysubstance use is the rule, not the exception, among kratom users — always assess the full substance use profile
4. Hepatotoxicity is an underrecognized risk — check LFTs in regular users
5. Buprenorphine-naloxone is the most commonly used pharmacotherapy for kratom use disorder, but evidence is limited to case reports and case series
6. Know your state's regulatory status — it affects availability and patient access
7. The landscape is evolving rapidly — the FDA's 2025 recommendation to schedule 7-hydroxymitragynine may change the regulatory environment

Take Home Points

QUESTIONS

1. Bin Abdullah MFIL. Kratom dependence and treatment options: a comprehensive review of the literature. Curr Drug Targets. 2020;21(15):1565-1579. doi:10.2174/1389450121666200719011653

2.Boness CL, Votaw VR, Schwebel FJ, Moniz-Lewis DIK, Witkiewitz K. An evaluation of cognitive behavioral therapy for substance use disorder: a systematic review and application of the Society of Clinical Psychology criteria for empirically supported treatments. Clin Psychol. 2023;30(2):125-142. doi:10.1037/cps0000131

3.Comstock G, Engstrom AK, Hojat LS, et al. Association between state-level kratom regulations and poison center-reported severe medical outcomes. Addiction. Published online 2026. doi:10.1111/add.16789

4.Foley H, Steel A, Cramer H, Wardle J, Adams J. Disclosure of complementary medicine use to medical providers: a systematic review and meta-analysis. Sci Rep. 2019;9(1):1573. doi:10.1038/s41598-018-38279-8

5.Garcia-Romeo A, Cox DJ, Smith KE, Dunn KE, Griffiths RR. Kratom (Mitragyna speciosa): user demographics, use patterns, and implications for the opioid epidemic. Drug Alcohol Depend. 2020;208:107849. doi:10.1016/j.drugalcdep.2020.107849

6.Kiyokawa M, Tokash JM, Gannon BM. Kratom use disorder case reports on successful treatment with home induction of buprenorphine-naloxone. Fam Pract. 2023;40(4):595-598. doi:10.1093/fampra/cmad003

7.Kopczynski A, Engel SS, Engstrom AK, et al. Kratom use trends within the Mass General Brigham system from 2017 to 2024. JAMA Netw Open. 2026;9(3):e262037. doi:10.1001/jamanetworkopen.2026.2037

8.Kruegel AC, Grundmann O. The medicinal chemistry and neuropharmacology of kratom: a preliminary discussion of a promising medicinal plant and analysis of its potential for abuse. Neuropharmacology. 2018;134(Pt A):108-120. doi:10.1016/j.neuropharm.2017.08.026

9.Kruegel AC, Uprety R, Grinnell SG, et al. 7-Hydroxymitragynine is an active metabolite of mitragynine and a key mediator of its analgesic effects. ACS Cent Sci. 2019;5(6):992-1001. doi:10.1021/acscentsci.9b00141

10.Palamar JJ. Past-year kratom use in the U.S.: estimates from a nationally representative sample. Am J Prev Med. 2021;61(2):240-245. doi:10.1016/j.amepre.2021.02.004

11.Prozialeck WC, Avery BA, Boyer EW, et al. Kratom policy, pharmacology, and toxicology: a comprehensive review. Biomed Pharmacother. 2024;170:116003. doi:10.1016/j.biopha.2024.116003

12.Singh D, Müller CP, Vicknasingam BK, Kronstrand R. Kratom (Mitragyna speciosa) liver injury: a comprehensive review. Drugs. 2020;80(3):263-283. doi:10.1007/s40265-019-01242-6

13.Ujam BK. Kratom (Mitragyna speciosa) dependence, withdrawal symptoms and craving in regular users. Drug Alcohol Depend. 2014;139:132-137. doi:10.1016/j.drugalcdep.2014.03.017

14.Tanna RS, Nguyen JT, Engel SS, et al. Clinical assessment of the drug interaction potential of the psychotropic natural product kratom. Clin Pharmacol Ther. 2023;113(6):1315-1325. doi:10.1002/cpt.2901

15.Towers EB, Hojat LS, Engstrom AK, et al. Increases in kratom-related reports to poison centers—National Poison Data System, United States, 2015-2025. MMWR Morb Mortal Wkly Rep. 2026;75(11):139-145.

16.U.S. Food and Drug Administration. FDA and kratom. Updated July 2025. Accessed June 2, 2026. https://www.fda.gov/news-events/public-health-focus/fda-and-kratom

17.Montana Department of Public Health and Human Services. Kratom fact sheet. Montana DPHHS. Published 2024. Accessed June 2, 2026. https://dphhs.mt.gov/assets/publichealth/EMSTS/Data/Kratom_Fact_Sheet_condensed.pdf

18.RiverStone Health. Kratom fact sheet. RiverStone Health. Published March 14, 2024. Accessed June 2, 2026. https://riverstonehealth.org/wp-content/uploads/Final_KratomFactsheet_2024.03.14-1.pdf

19.RiverStone Health. Kratom enforcement update. RiverStone Health. Published December 2025. Accessed June 2, 2026. https://riverstonehealth.org/wp-content/uploads/Kratom_Enforcement_12.15.pdf

20.Grover C. Kratom and the US opioid crisis: a help or a harm? Addiction Medicine Made Easy podcast. Published 2024. Accessed June 2, 2026.

References