Presented by

SOUTH CAROLINA CENTER *of* EXCELLENCE *in* ADDICTION

# Identifying and Treating 7-OH Withdrawal and Dependency

# Agenda

- Introductions
- Rescheduling 7-OH
- Kratom & 7-OH Basics
- Diagnoses and Treatment
- Care Guidelines
- Resources

# Presenters

John Emmel, MD

Medical Director, Charleston Center

Medical Director, OSUS

Lindsey Jennings, MD, MPH

Emergency Medicine, MUSC

Michelle Stone, DNP, MSN, FNP-BC, CARN-AP

Addiction Medicine, Prisma Health

# Rescheduling of 7-OH

- On July 6, 2026, the DEA filed an amendment to temporarily place 7-hydroxymitagynine (7-OH) and three related substances into Schedule I of the Controlled Substances Act (CSA)
- They recently renewed the amendment to extend the comment period
- The amendment does NOT include botanical Kratom products with a 7-OH concentration below 0.05% (dry weight)


# Anticipated Rescheduling Effects

### Local supply will dwindle

7-OH products have been widely available at gas stations and convenience stores, which will change as Schedule 1 enforcement spreads

### Online sales will slow

Currently, 7-OH and related products are widely available online; reputable retailers will no longer offer these products

### Users will experience withdrawal

Current users will experience symptoms of withdrawal and seek care, or otherwise try to self-detox or turn to other substances

# Kratom and 7-OH Basics

John Emmel MD
OSUS Medical director
Charleston Center Medical Director

# Mytragina speciosa

- Kratom is a plant product from this Southeast Asia tree, a member of the coffee family
- Used in Thailand and Malaysia in the 1800s by manual laborers for euphoria, stimulation, analgesia and to prevent withdrawal from opium and still used today all over the world for similar reasons
- Traditionally, leaves are chewed or brewed into a tea
- Now found on the internet or in stores as capsules, tablets, powder, gum, dried leaf, so ”doses” can be much higher than with the native plant
- Current use reportedly for energy and stimulant-like effects; for its anti-diarrheal, anti-inflammatory effects; to prolong sexual intercourse; to treat chronic pain; to prevent opioid withdrawal
- Therefore, some use it to try to treat their own opioid dependence

# Mytragina speciosa Chronology

- In the early 2000s, use of kratom emerges in general US population, as herbal supplement, used by 2-5 million annually (energy, pain, OUD/AUD)
- >25 years of **leaf kratom** safety data suggests the risks are generally minor-moderate (though there are cases of overdoses and addiction)
- At present FDA advises not to use kratom due to risk of serious adverse effects
- 2020: “kratom extracts” come out, contain added synthetic **7-hydroxymitragynine** (**7-OH**) or **mitragynine pseudoindoxyl** (**MP; Red-OH**)
- 2023/24: Concentrated synthetic 7-OH and MP products appear sold as “kratom”
- 2025: MGM-15 (dihydro-7-OH) and MGM-16 enter the market (even more potent)

# Whole Leaf Kratom Alkaloids vs. Synthetic Alkaloids

**Product form and concentration matter for risk!**

Whole-leaf (native leaf material) -- complex “matrix” of alkaloids acting at multiple targets (opioid, adrenergic, serotonergic)

• Effects reflect combined alkaloid profile, not a single constituent (“entourage” effects)

At lower doses stimulant effects predominate, but as dose increases mu opioid receptor effects become predominant; mu receptor affinity is high

• Unregulated markets → variable composition and labeling

Extracts / isolated alkaloids -- higher concentration → higher total alkaloid exposure is easier to reach

• Poor labelling → accidentally high doses (therapeutic index is not established)

• Higher-potency opioid-active constituents (e.g., 7-OH or MP-like compounds) may increase opioid-type toxicity

• Risk can be amplified by polysubstance use and adulteration/contamination

# Kratom alkaloids and μ-opioid receptor (MOR) affinity

- Whole-leaf Kratom is a multi-phytochemical product, it contains >40 alkaloids; mitragynine is the most abundant (~2/3rd of total alkaloids), and 7-OH is only 1-2%
- Kratom produces very weak MOR and multiple non-MOR effects
- 7-OH is also formed in vivo from mitragynine (CYP3A4) and has much more potent MOR effects than mitragynine itself
- Mitragynine and 7-OH bind to the MOR as a **partial agonists,** high MOR affinity
- M. pseudoindoxyl (MP) is a downstream metabolite/derivative and a very potent MOR **full agonist**
- Concentrated “semi-synthetic” 7-OH sold as tablets, gummies, edibles, drink “shots”
- Again, labeled dosages and constituents are unreliable

# Wait a minute……..

- Haven’t we read this story before?
- Oops, wrong century.  I mean – haven’t we seen this movie before?
- Oops, wrong century.  I mean – haven’t we online-streamed this before?

# See if this sounds familiar……

- Yul gi = “plant of joy”
- Yul gi = poppy plant
- Poppy derivative = opium = used for multiple symptoms:  pain, sleep, relaxation, anxiety, diarrhea, et al.
- Hippocrates advised it’s use for sleep
- Later ”Morphium” isolated as the active alkaloid
- Sir William Osler, father of modern medicine, calls it “God’s own medicine”
- Heroin (diacetylmorphine) is a derivative and marketed without a prescription for all manner of ills and felt not to be addictive
- 1914 Harrison Narcotic Act: Morphine, heroin, et al. become “controlled drugs” since they ARE addictive
- Later semi-synthetics and synthetics: oxycodone, hydrocodone, hydromorphone, fentanyl, et al.
- Illicit market and “street chemistry” allows greater concentration of, e.g., heroin or fentanyl
- Greater and greater use results in widespread health consequences, including death

# “Kratom” Effects

- Mytragynine:  stimulant effects at low dose make it attractive
- As the dose increases, MOR effects take over and produce tolerance, physical dependence, with subsequent craving, drug-seeking behavior, and possible addiction
- MOR effects include the usual euphoria, miosis, analgesia, sedation, muscle relaxation, constipation, dry mucous membranes, lowered VS including potential respiratory depression
- 7-OH: semi-synthetic, often in concentrated form so that MOR effects much more rapidly take over, increasing chances of addiction, which can occur more rapidly therefore
- These alkaloids may be referred to as atypical partial opioid agonists, though they are not classical “opioid drugs”
- Consequent to this effect at the MOR, the addiction toxidrome may reasonably be called an “opioid use disorder (OUD)”

# Toxicity

- Mytragynine may cause some respiratory depression
- Mytragynine has been associated with seizures, but without definite causal relation, especially since it is often used along with other drugs
- 7-OH, with its higher potency, is more likely to present a risk of more severe respiratory depression and death
- Both of these products have been associated with death, but rarely were the only substance present
- There have been reports of overdose death solely from 7-OH and the other more potent derivatives
- Research is ongoing

# Withdrawal

- Observed effects of stopping use of mytragynine and 7-OH in those who have developed physical dependence and addiction are typical of opioid withdrawal
- This includes dysphoria, mydriasis, insomnia, painful muscles/joints, muscle spasms, lacrimation/rhinorrhea, sweats, diarrhea, nausea/vomiting, elevated VS
- With mytragynine and its wider alkaloid profile the symptoms may be more complex, since there is also alpha-2 adrenergic withdrawal that may require additional strategies/medications for management
- There is research that suggests that the withdrawal syndrome becomes more significant when >5 grams of mytragynine daily are taken, but labeling is not reliable on the products

# In the words of Dolly Parton (more or less)

- Here it comes again…….
- ……and here we go!

EMERGENCY MEDICINE • CLINICAL UPDATE

# 7-OH & Kratom

Recognizing and treating a new potent opioid at the bedside

START HERE

# Kratom is not the same as 7-OH

## Traditional Kratom

*Mitragyna speciosa leaf*

- Main alkaloid is mitragynine; 7-OH occurs naturally at trace levels (< 0.05% of leaf)
- Mild, dose-dependent effects — stimulant at low doses, opioid-like at high doses
- Used traditionally as tea or powder; dependence develops slowly
- Not scheduled federally (as of Aug 2026)

## Concentrated 7-OH

*7-hydroxymitragynine — semisynthetic / enriched*

- A potent mu-opioid agonist concentrated far above natural levels (extracts up to ~98%)
- Sold as tablets, shots, and gummies — often labeled "kratom"
- Rapid, strong dependence — resembles pharmaceutical opioids
- DEA temporary Schedule I above a 0.05% threshold (effective ~Aug 2026)

***Bottom line: ask what product and what form — "kratom" on the label can mean a strong opioid inside.***

WHY THIS MATTERS NOW

# An emerging threat, hiding in plain sight

**13×**

more potent than morphine
in functional assays

**~1,200%**

rise in kratom-related poison
center cases, 2015–2025 (CDC)

**Feb 2025**

poison centers first began
coding 7-OH separately

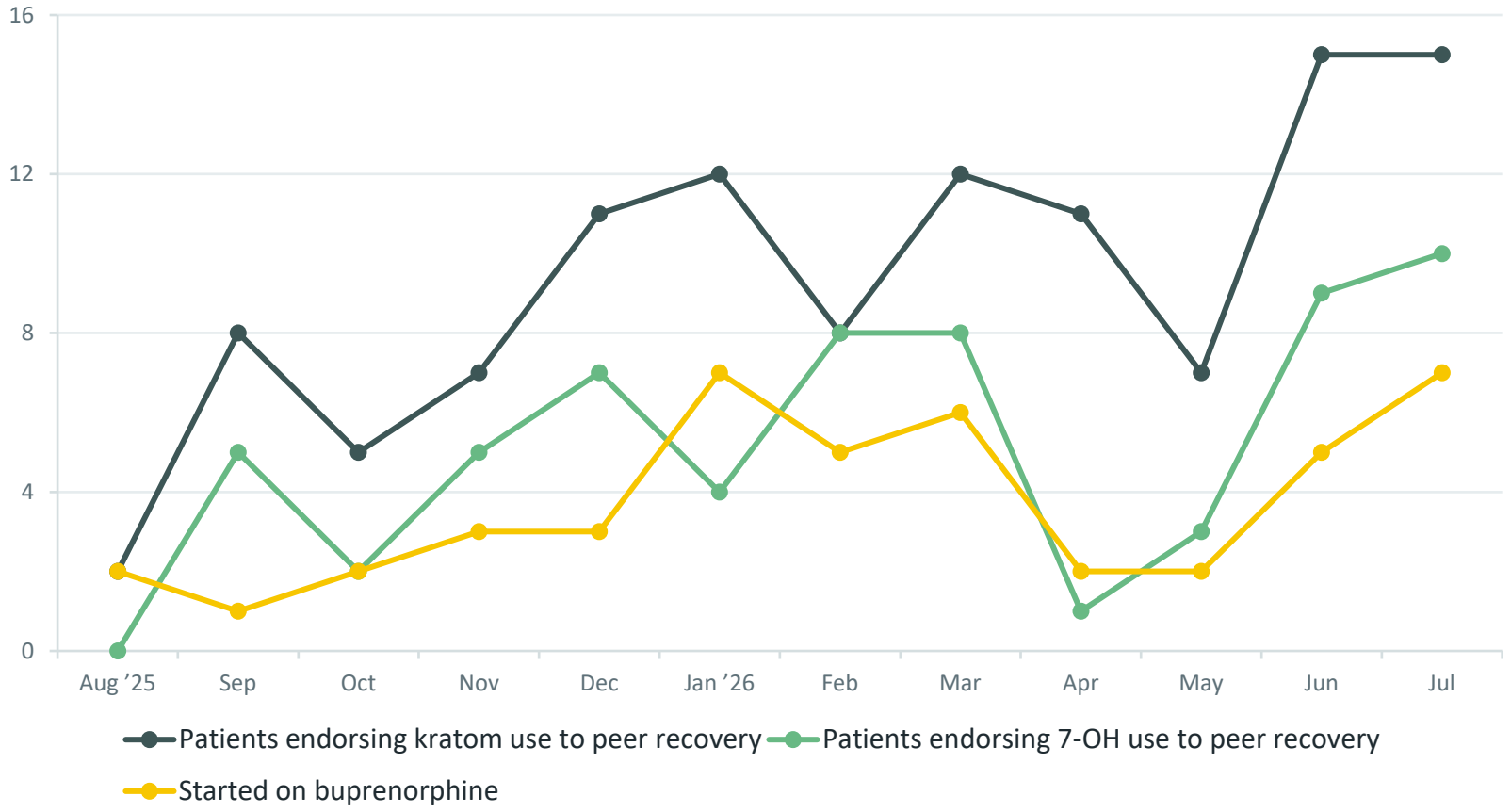
## Regulatory status — moving fast

- July 2026:  DEA announced intent to temporarily place 7-OH in Schedule I; Federal Register notice published July 6.
- Effective ~Aug 5, 2026:  applies to products above 0.05% 7-OH by weight (or >1 mg/unit); natural leaf below threshold is not scheduled.
- **Clinical implication:  a wave of patients in withdrawal is expected as products leave shelves — have a treatment plan ready.**

WHAT WE ARE SEEING

# Kratom & 7-OH across our SC EDs

*Monthly counts — Aug 2025 to Jul 2026*




**113**

patients endorsed kratom use to peer recovery

**62**

endorsed 7-OH use to peer recovery (≈ 55%)

**40%**

started on buprenorphine in the ED (45 patients)

**11 EDs**

across the network, over 12 months

*Charleston and SRMC account for the largest share. Source: our SC ED network tracking, Aug 2025–Jul 2026.*

WHAT IT DOES

# Pharmacology

## Potent mu-opioid agonist

7-OH drives most of the opioid effect; roughly 13× morphine and ~46× mitragynine in assays.

## Dose-dependent effects

Lower doses feel stimulating/anxiolytic; higher doses produce classic opioid sedation and euphoria.

## More than opioid

Also acts at adrenergic and serotonergic receptors — contributes to autonomic and neuropsychiatric symptoms.

## Why the "natural" framing is dangerous

- Marketed as a plant-based wellness aid — even as an aid to "cut down" on opioids
- Chemistry is that of a strong opioid — respiratory depression and dependence are real
- Opioid-naïve users can develop dependence in weeks

SIGNS & SYMPTOMS — PART 1

# Acute intoxication & overdose

*Presents as a classic opioid toxidrome — often with a negative drug screen*

### Respiratory depression

Slowed/shallow breathing; the life threat. Responds to naloxone.

### Sedation & miosis

Drowsiness, pinpoint pupils, slurred speech, nodding off.

### Nausea & vomiting

Common early; risk of aspiration if obtunded.

### Agitation / confusion

Especially with high-dose or polysubstance use.

### Seizures (less common)

Reported in serious exposures and mixed ingestions.

### Polysubstance is common

Alcohol, benzos, other opioids amplify the danger.

SIGNS & SYMPTOMS — PART 2

# Withdrawal: often the reason they present

## Looks like opioid withdrawal — because it is

- Autonomic: sweating, chills, yawning, rhinorrhea, lacrimation, dilated pupils
- GI: nausea, vomiting, diarrhea, abdominal cramping
- Neuromuscular: myalgias, restlessness, tremor, involuntary jerks
- Psychiatric: severe anxiety, insomnia, dysphoria, drug craving
- **Severe cases: agitation, confusion/delirium, and even psychosis reported**

### Quantify it

Use the COWS (Clinical Opiate Withdrawal Scale) to score severity and guide treatment — the same tool you use for any opioid.

### Rapid onset

Because 7-OH is short-acting and potent, withdrawal can be intense and start within hours of the last dose — patients describe it as worse than expected for an "herbal."

THE DIAGNOSTIC TRAP

# Standard drug screens do not detect it

## 5- and 10-panel urine screens miss mitragynine and 7-OH.

A classic opioid toxidrome with a negative screen should raise — not lower — your suspicion.

## Clues that point to 7-OH

- Opioid intoxication or withdrawal that the patient attributes to "kratom" or a supplement
- Bought at a gas station, smoke shop, or online — not a pharmacy
- No history of "traditional" opioid use, yet clearly opioid-dependent

## History is your test

- What product? (brand/name on the label)
- What form — tablet, shot, gummy?
- How much and how often?
- When was the last dose?
- Other substances used with it?

TREATMENT BEST PRACTICES — 1

# Acute intoxication & overdose

## Naloxone works

Reverse respiratory depression as with any opioid. Higher or repeated doses may be needed for potent, sustained exposures; re-sedation is possible — observe.

## Airway & supportive care first

Standard ABCs, oxygen, monitoring, antiemetics. Treat co-ingestants (alcohol, benzodiazepines, other opioids) on their own merits.

## Observe appropriately

Watch for recurrent sedation given potency; escalate or admit for severe symptoms or significant polysubstance use.

## Call your poison center

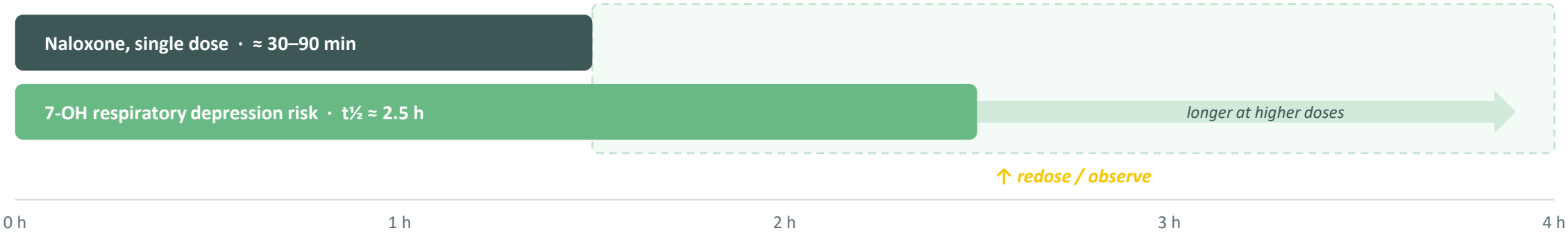
Poison Help 1-800-222-1222 for management questions and to report exposures — data are still emerging.

OVERDOSE — THE KEY NUANCE

# Naloxone reverses it — but plan for recurrence

**7-OH's respiratory depression can outlast a single dose of naloxone** — anticipate redosing and prolonged monitoring.

DURATION MISMATCH




## It does reverse it

7-OH is a μ-agonist — in animal studies it depressed breathing ~4.5× more than morphine, and naloxone fully antagonized it.

## Why it recurs

Naloxone clears fast (clinical effect ~30–90 min); 7-OH persists longer (t½ ≈ 2.5 h), and concentrated products give higher, sustained levels.

## What to do

Titrate naloxone to breathing, expect to redose, observe longer, and consider an infusion for persistent or recurrent depression.

*Human overdose kinetics are not well characterized — let clinical monitoring, not a fixed clock, guide disposition. Co-ingestants and CYP3A interactions (many drugs, citrus juice) can prolong exposure.*

TREATMENT BEST PRACTICES — 2

# Withdrawal & starting treatment

## Buprenorphine is first-line

*7-OH withdrawal responds to standard OUD treatment*

- Score severity with COWS; start buprenorphine once the patient is in moderate withdrawal (avoid precipitated withdrawal).
- Follow your usual ED-initiated buprenorphine protocol — 4–8 mg SL, may start at 4 mg (patients often do well on lower doses than chronic fentanyl users).
- Low-dose ("micro") induction is an option for selected patients where standard start is difficult.
- Adjuncts for symptoms: clonidine/lofexidine, antiemetics, antidiarrheals, NSAIDs, and something for sleep.

## What the reports show

Published cases describe patients on 7-OH stabilized with buprenorphine/naloxone (e.g., 8/2 mg twice daily), with rapid symptom control — including resolution of withdrawal-related delirium.

## Don’t just discharge

Untreated, these patients relapse quickly. The ED visit is a chance to start medication and link to ongoing care — treat dependence, don’t just manage the crisis.

ED-INITIATED BUPRENORPHINE — STEP 1

# Before you dose: timing & objective withdrawal

## See objective withdrawal

Confirm **visible signs** — not subjective complaints alone: mydriasis, gooseflesh (piloerection), GI upset, sweating, rhinorrhea, yawning.

## Wait long enough since last use

- Short-acting opioids: 6–12 h
- Long-acting opioids: 24–72 h
- 7-OH sits between (t½ ≈ 2.5 h, but parent alkaloid lasts longer) — a reported case induced ≈ 48 h after the last dose.

COWS THRESHOLD TO START — SOURCES DIFFER


**COWS ≥ 8**

FDA / many reviews (with visible signs)

**COWS ≥ 11–12**

ASAM — mild-to-moderate withdrawal

**COWS ≥ 13**

some favor for potent 7-OH

**When in doubt, wait.** 7-OH is potent and lipophilic — a higher COWS and a longer abstinence window lower the risk of precipitated withdrawal. No trials or formal guidelines exist for kratom/7-OH; all dosing is extrapolated from OUD care — individualize and monitor.

ED-INITIATED BUPRENORPHINE — STEP 2

# The induction & discharge protocol

**Once ready to dose:** objective withdrawal confirmed on COWS and enough time since last use *(see previous slide)*

## COWS ≥ 8 — Observed ED induction

1. **Give 4–8 mg SL buprenorphine** *(may start at 4 mg)*
2. **Repeat COWS at 45 min**

**COWS < 11** → proceed to discharge

**COWS ≥ 12** → add 4–8 mg SL, then discharge

## COWS < 8 — Unobserved / home induction

- **Bup/naloxone film (not tablet)**
- Day 1: 4 mg TID PRN
- Day 2 +: 16 mg daily
- Discharge with home-induction instructions, naloxone, and referral

**Discharge (all):** bup/naloxone 16 mg daily (Rx to follow-up) · document indication as **"Opioid Use Disorder"** (not "withdrawal") · take-home naloxone · peer referral. **X-waiver no longer required** — any DEA-registered clinician may prescribe.

TREATMENT BEST PRACTICES — 4

# Close the loop: linkage & harm reduction

## Bridge & refer

Provide a buprenorphine bridge prescription and a warm handoff to addiction or MOUD follow-up.

## Naloxone to go

Prescribe/dispense take-home naloxone and teach overdose response — these are opioid users.

## Nonjudgmental care

Many arrived via "wellness" marketing. Reduce stigma; frame it as treating an opioid dependence.

## Educate & document

Name the substance clearly, counsel on product risks and mislabeling, and document the exposure.

LESSONS FROM THE ER

# What the early cases are teaching us

CASE

## The "negative screen" opioid

Classic opioid withdrawal, patient blames "kratom." UDS negative. Lesson: trust the history, treat the withdrawal.

CASE

## Withdrawal worse than expected

High-dose daily 7-OH tablets; intense, rapid withdrawal.  Lesson: don’t under-dose — use full COWS-guided buprenorphine induction.

CASE

## The "opioid-naïve" dependent

No prior opioid history, now clearly dependent from an OTC product. Lesson: anyone can be affected — ask everyone.

KEY TAKEAWAYS

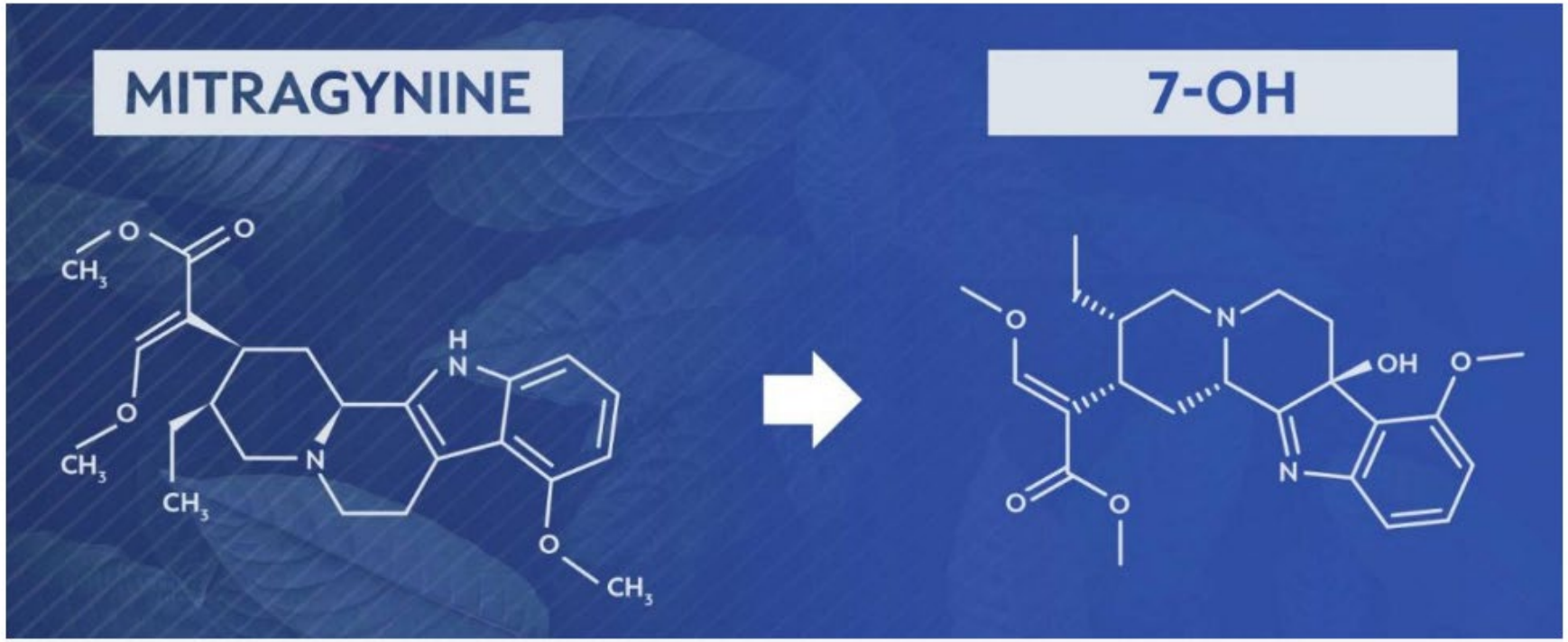
# Five things to carry to your next shift

1. **7-OH is a potent opioid sold as "kratom" — treat it as an opioid, not a supplement.**
2. It causes real intoxication, overdose, and severe, rapid withdrawal.
3. Standard drug screens miss it — the history is your diagnostic test.
4. Naloxone reverses overdose; buprenorphine treats withdrawal — use your OUD playbook.
5. Start treatment in the ED, then link to care — and give take-home naloxone.

# Guidance on 7-OH Treatment

*"Kratom and 7-OH may seem safe since they are readily available and may be marketed on social media and elsewhere. However, in reality kratom and 7-OH can be very dangerous. There is no way to know what is actually in the products sold as 'kratom' or '7-OH' or how strong they may be. The FDA has never approved a product containing kratom or 7-OH for use because of the potential significantly harmful effects it can cause."*

**DR. EDWARD SIMMER, FORMER DIRECTOR SC DPH**




*7-OH is a metabolite of mitragynine, the primary psychoactive alkaloid in kratom. 7-OH is produced once the leaf is removed from the tree and oxidizes. (Spectrum News)*

## MITRAGYNINE

Primary psychoactive alkaloid in kratom

## 7-HYDROXYMITRAGYNINE

Metabolite of mitragynine

# 7-OH WITHDRAWALS

Typically starts 6-24 hours after last use and peaks over the first few days. Resolves over a week (longer for psychological symptoms). Severity can be quantified using the COWS scale.

- Physical Symptoms: myalgias/arthralgias, rhinorrhea, lacrimation, yawning, diaphoresis, piloerection, mydriasis, nausea/vomiting, diarrhea, abdominal cramps, GI distress, and insomnia.

- Psychological Symptoms: anxiety, agitation, irritability, restlessness, dysphoria, and cravings.

- Patients report waking up in the middle of the night craving 7-OH to manage withdrawal symptoms.

* Rare but severe cases include delirium, rhabdomyolysis, and complex withdrawal with neurologic/electrolyte/hepatic derangement.

# Assessment

- Current use patterns
  - Frequency, amount, length of use
- History of substance use / opioid use or dependence
- Treatment goals and needs
  - Long term medication management
  - Symptomatic withdrawal focused management

# Single Question Assessment

Do you currently take anything that you get from a gas station or a smoke shop?

# Patient Subgroups Using 7-OH

- No history of OUD/SUD
  - “accidental” use patients
    - Friend told them it would help with pain
    - Picked it up at a gas station for more energy

- Have complex histories of OUD/SUD
  - May include previous fentanyl/opioid or polysubstance use
  - May have used 7-OH products to minimize or manage opioid withdrawal symptoms and

# Treatment and Management

- Varied buprenorphine dosing 8-32mg/day
  - Assess COWS score
    - Focus on OBJECTIVE signs vs SUBJECTIVE symptoms
    - Seems to be lower anecdotal risk of precipitated withdrawal due to short half life
  - Encourage or offer frequent dosing intervals in addition to other adjuvants for symptomatic management
- Shared decision making to assess treatment goals and consider length of treatment
  - Withdrawal management support / short term MOUD use
  - Long term medication management

# Treatment and Management

- Varied buprenorphine dosing 8-32mg/day
  - Assess COWS score
    - Focus on OBJECTIVE signs vs SUBJECTIVE symptoms – looking for moderate withdrawal symptoms to dose
    - Seems to be lower anecdotal risk of precipitated withdrawal due to short half life
  - Encourage or offer frequent dosing intervals in addition to other adjuvants for symptomatic management and support
    - 2-8mg with repeat dosing

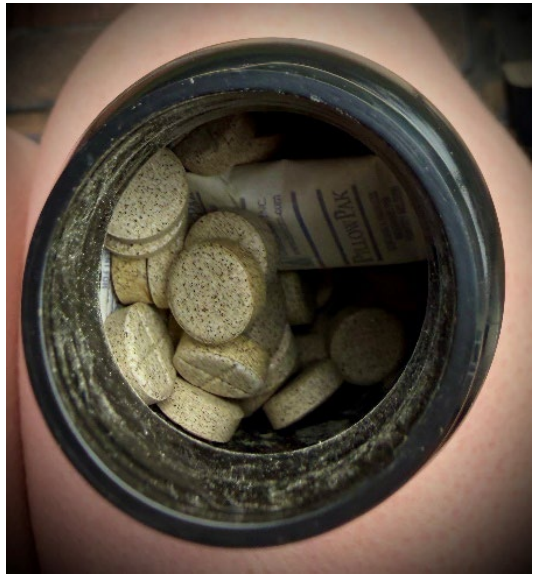
# Predatory Marketing



# 7-OH Products


Fresh Pressed Labs
M2
Dual Alkaloid Formula
Sour Apple
25MG MIT/5MG MGM-15
PER TABLET
EQUAL TO 30MG OF 7-OH
3000MG TOTAL-100 TABLETS


Supplement Facts
Amount per tablet
% Daily Value




dopium
180MG
180MG
ZOHM
PERKS
PERKS
FOCUS


Tabz
7-Hydroxymitragynine
Pure Extract Tablets
15mg
8
15mg
feel free.

# Key Clinical Points

- 7-OH has 10-22 times the μ-receptor affinity of morphine.
- Reported complications of heavy use include hepatic and renal injury, seizures, cardiac arrest, overdose, and death.
- Naloxone can/should be given for suspected overdose.
- 7-OH is **not** found on routine urine drug screens

# Takeaways

Self-Report of 7-OH use is **CRITICAL** to accurate diagnosis

7-OH has a short **half-life** – withdrawals may begin within hours of discontinuing use

Variable/high dose of buprenorphine required to address symptoms

# RESOURCES

## South Carolina Clinician Warmline

**864-914-1301**

Free, confidential, clinician-to-clinician consultation on SUD/OUD evaluation and management.

Open 9 am - 5 pm, Monday – Friday

https://addictioncenterofexcellence.sc.gov/

SOUTH CAROLINA
CENTER *of*
EXCELLENCE *in*
ADDICTION

# Thank you for attending!

This webinar has been recorded and will be posted for unrestricted access on the S.C. Center of Excellence in Addiction website at

addictioncenterofexcellence.sc.gov

SOUTH CAROLINA
CENTER *of*
EXCELLENCE *in*
ADDICTION