ECHO IDAHO

Substance Use in Idaho

Fentanyl, Xylazine, and Kratom Updates

August 27, 2026

Dr. Annette Percy

Mental Health Clinical Pharmacist Practitioner

Department of Veterans Affairs

University of Idaho
School of Health and Medical Professions

Project ECHO

Disclosures

- No financial disclosures
- The information on these slides and content were generated by me and are not the opinion of the VA or endorsed by the VA

Learning Objectives

Review the pharmacologic profiles of kratom, xylazine/medetomidine, and fentanyl

Recognize use of these substances and determine management of dependence, withdrawal, and toxicity

Fentanyl

Fentanyl

- Potent synthetic opioid analgesic; full mu-opioid receptor (MOR) agonist
- Approved human uses: anesthesia, severe/breakthrough cancer pain in opioid-tolerant patients (Duragesic®, Actiq®, Sublimaze®, others)
- Fentanyl *is* a DEA Schedule II controlled substance, in contrast with xylazine, which is not scheduled
- Roughly 50 to 100× more potent than morphine; ~100 mcg ≈ the analgesia of ~10 mg morphine
- Illegally manufactured fentanyl (IMF) drives the illicit synthetic-opioid supply
- Used as an adulterant in heroin, cocaine, methamphetamine, and counterfeit pills, often unknowingly
- Highly lipid soluble, so it rapidly crosses the blood–brain barrier (rapid onset)

POTENCY AT A GLANCE

50–100×

more potent than morphine

~100 mcg

≈ analgesia of ~10 mg morphine

Schedule II

DEA-controlled substance

Sources: DEA Drug Fact Sheet; NIOSH/CDC; StatPearls (NIH)

University of Idaho School of Health and Medical Professions

Project ECHO

Relative Opioid Potency (vs. Morphine)

APPROXIMATE POTENCY

- Morphine: reference standard (1×)
- Heroin: roughly 2 to 5× morphine
- Oxycodone: ~1.5× morphine
- Hydromorphone: ~5 to 7× morphine
- **Fentanyl: ~50 to 100× morphine**
- **Carfentanil: ~10,000× morphine (~100× fentanyl)**

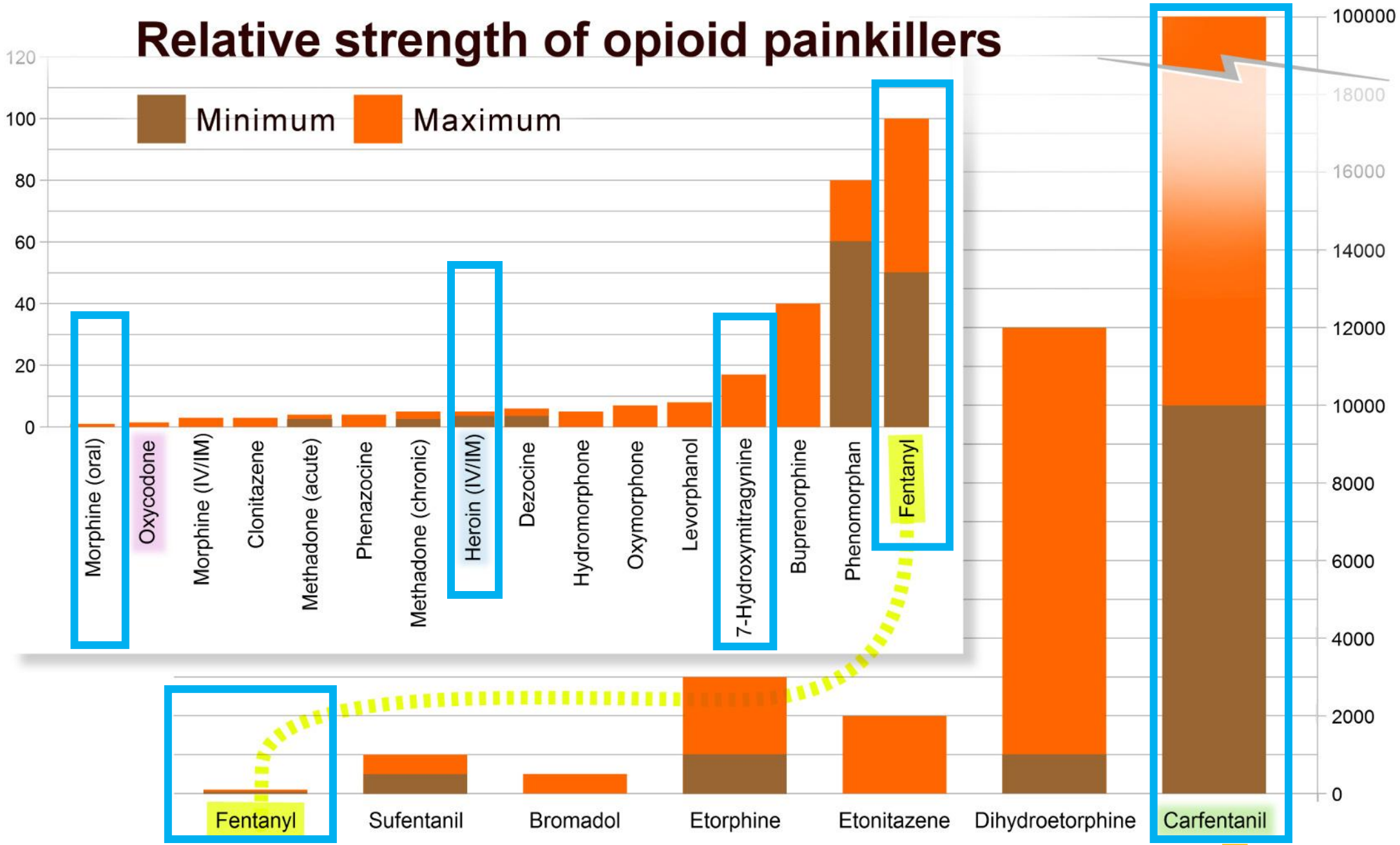
Eqipotency is approximate, source-dependent ratios for teaching context, not equianalgesic dosing conversions for prescribing.

CLINICAL IMPLICATIONS

- Potency compresses the gap between an active and a lethal dose
- Illicit product is unevenly mixed, so dosing is unpredictable
- Fentanyl lethal at ~2 mg; carfentanil active at microgram amounts
- Higher potency can mean more naloxone and longer monitoring
- Figures are approximate and vary by source, route, and study

Sources: DEA; Tennessee Poison Center; StatPearls (NIH)

Relative strength of opioid painkillers



Carfentanil & Other Fentanyl Analogs

Carfentanil: a veterinary tranquilizer for large animals, with no approved human use; roughly 10,000× morphine and ~100× fentanyl

- Increasingly pressed into counterfeit pills, not just powder; even a single pill can be fatal
- CDC reported carfentanil-involved deaths rose about 7x from 29 (Jan–Jun 2023) to 238 (Jan–Jun 2024)

Other analogs seen in the supply: acetylfentanyl (~15× morphine), acrylfentanyl, furanylfentanyl, cyclopropylfentanyl, 3-methylfentanyl, and others

Detection gap: standard fentanyl immunoassays and many test strips may *not* reliably detect carfentanil or all analogs; confirmatory testing is often required

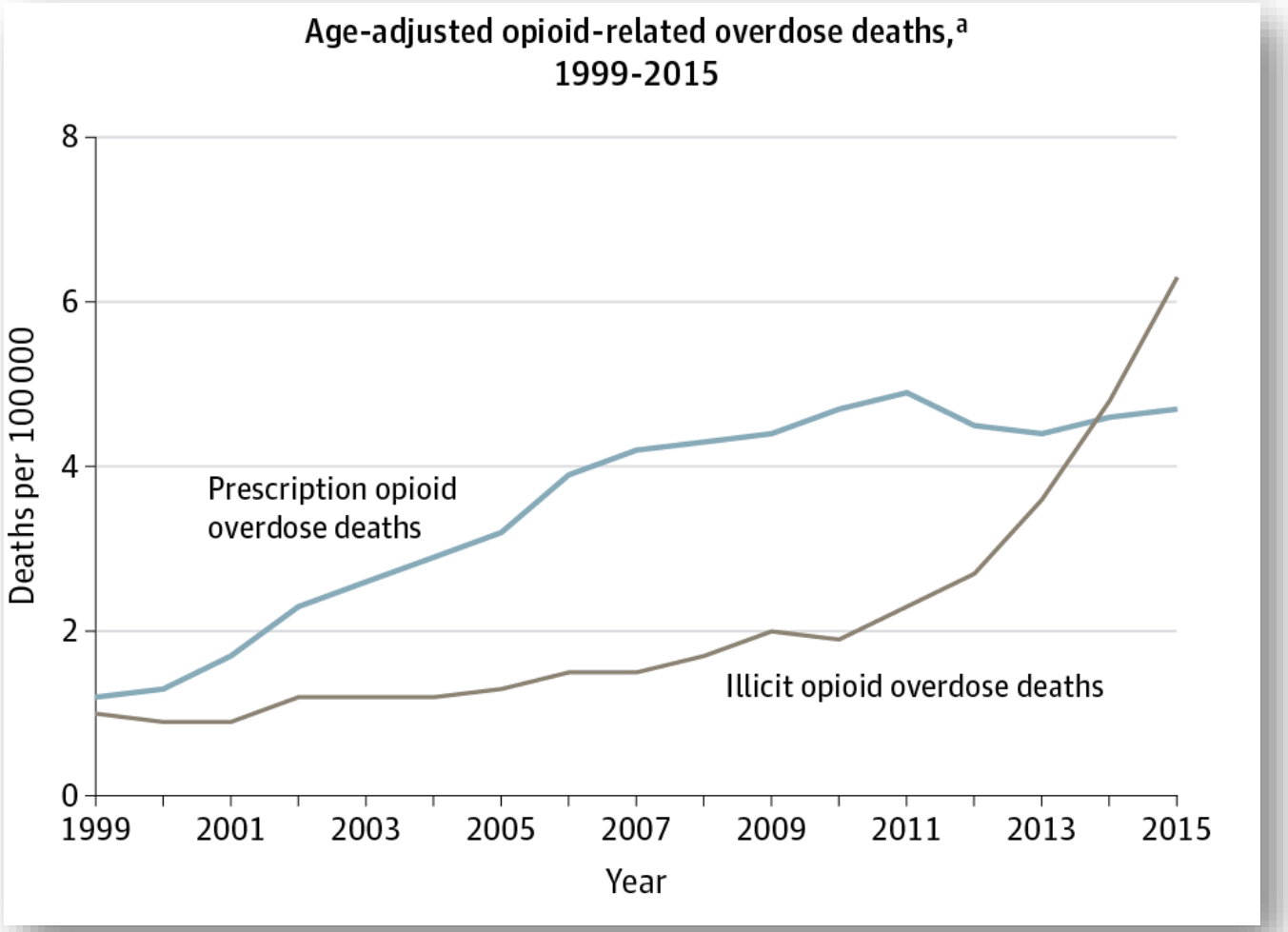
Management is unchanged: naloxone plus supportive care, but expect repeat/higher naloxone doses and prolonged monitoring given extreme potency

Analogs may be present without the user's knowledge and may evade routine screening. When in doubt, treat the opioid toxidrome and support the airway.

Sources: DEA (2016; 2025); CDC MMWR; Tennessee Poison Center

University of Idaho School of Health and Medical Professions
Project ECHO

Opioid-related overdose deaths increased 4-fold from 1999 to 2020

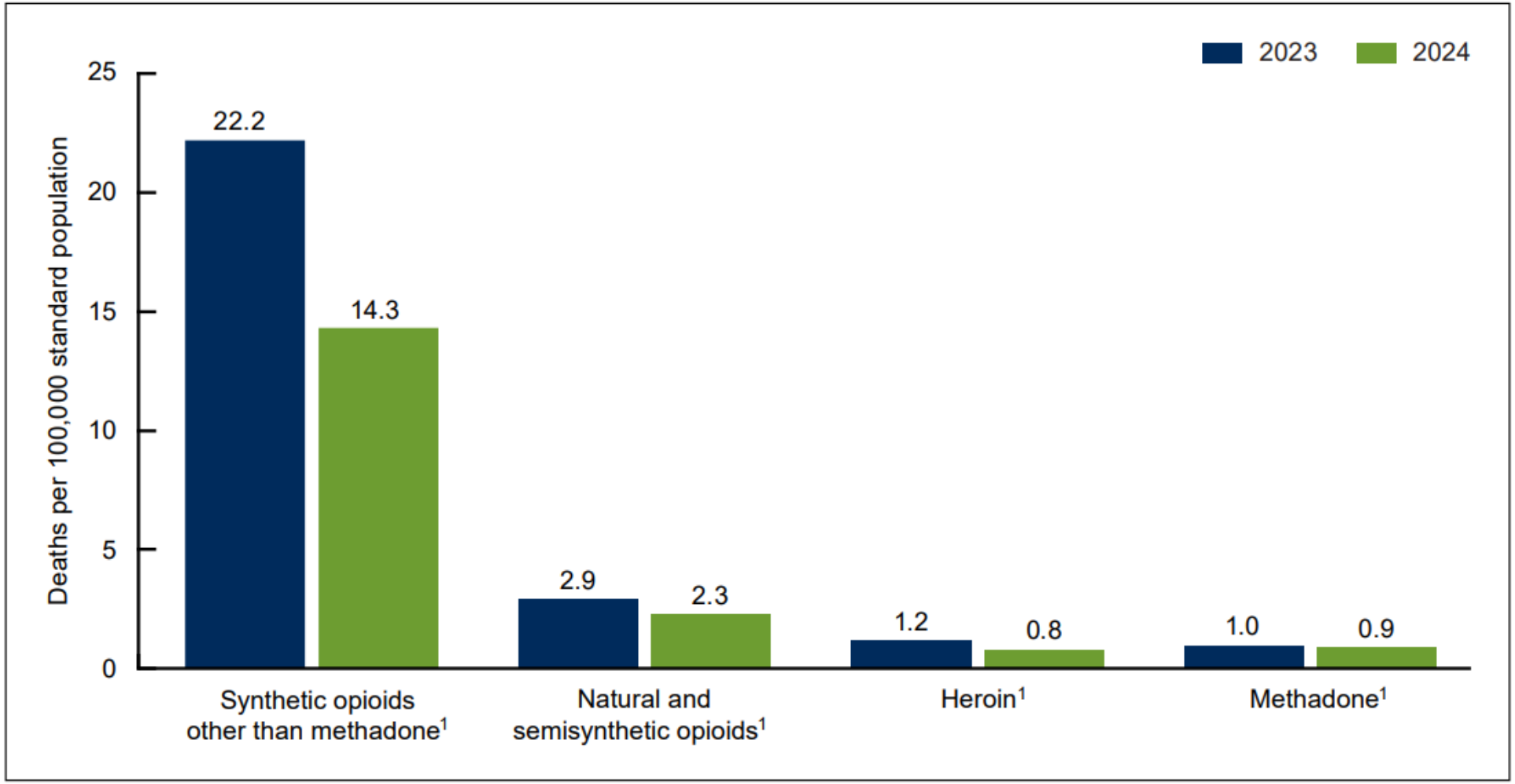


University of Idaho
School of Health and Medical Professions

Project ECHO

2023 to 2024 … Some better (?) news

Figure 4. Age-adjusted rate of drug overdose deaths involving opioids, by type of opioid: United States, 2023 and 2024



https://www.cdc.gov/nchs/data/databriefs/db549.pdf

Fentanyl: Risk and Concern

- Illegally made fentanyl (IMF) is the leading cause of U.S. overdose deaths and a persistent national threat
- Providers must recognize the threat and know how to support patients who may be exposed
- Overdose presents as the classic opioid toxidrome, but faster and more severe due to potency
- Potentiates other CNS depressants (benzodiazepines, alcohol, xylazine, other opioids)
- Among 2023 overdose deaths, ~69% involved synthetic opioids other than methadone (mainly IMF)
- Provisional CDC data: ~24% decline for the 12 months ending Sept 2024 (~87k vs ~114k)
- As little as ~2 mg can be lethal depending on tolerance and body size (DEA estimate)

Sources: CDC Overdose Prevention; CDC NCHS Data Brief (2023–2024); DEA

Physiologic Effects of Fentanyl in Humans

EFFECTS INCLUDE

- **Slowed/shallow breathing (respiratory depression), the primary cause of death**
- Bradycardia, hypotension
- Sedation, reduced consciousness, coma
- Pinpoint pupils (miosis), may dilate with hypoxia
- Euphoria, analgesia
- Muscle/chest-wall rigidity ("wooden chest")
- Nausea, vomiting, itching; ileus

TIMING & CONSIDERATIONS

- Onset can be rapid (within minutes), esp. IV/inhaled/insufflated
- Duration comparatively short, but depot effects (commercially available patch, body reservoirs) can prolong toxicity
- Effects intensify with other substances
- Not associated with xylazine-type necrotic wounds
- If wounds present, assess for co-occurring xylazine exposure (more on this later)

Onset can be rapid (minutes); potency means the margin between a euphoric dose and a fatal one is very narrow.

Sources: NIOSH/CDC; DEA; StatPearls (NIH)

Fentanyl: Routes and Detection

FORMULATIONS & ROUTES

- Pharma: transdermal patch, transmucosal lozenge/film, injectable, nasal spray
- Illicit: powder (white/off-white)
- Pressed into counterfeit pills mimicking legitimate Rx
- Mixed into heroin, cocaine, methamphetamine
- Routes: IV, IM, intranasal, inhaled/smoked, oral

DETECTION

- Standard immunoassay opioid screens may NOT detect fentanyl
- Dedicated assays / LC-MS/MS often required to confirm
- Short half-life & rapid redistribution complicate windows
- Fentanyl test strips are commercially available (harm reduction)
- Test strips may miss some fentanyl analogs

Sources: CDC; DEA; StatPearls (NIH)

Fentanyl Withdrawal: Symptoms & Management

- Symptoms: anxiety, agitation, insomnia, muscle aches, sweating, lacrimation/rhinorrhea, dilated pupils, nausea/vomiting, diarrhea, cramping, craving
- Generally **not life-threatening**, but severe discomfort drives return to use
- **MOUD is first-line:** buprenorphine, methadone, naltrexone (relapse prevention)
- **Buprenorphine caution:** high fentanyl body burden raises **precipitated withdrawal** risk
  - Consider timing, low-dose ("micro") induction, or delayed induction
- Recent fentanyl use may need adjusted strategies (fentanyl can persist ~24 to 72 h)
- Treat symptoms early; use adjunctive supportive medications as needed

KEY DISTINCTION

Fentanyl lingers in body tissue; body burden can persist 24–72 hours, raising precipitated-withdrawal risk with standard-dose buprenorphine

Sources: VA / SAMHSA MOUD guidance (template); StatPearls (NIH)

Fentanyl Intoxication & Overdose

- Presents with **respiratory depression, sedation/altered consciousness, and miosis**; may progress to hypoxia, bradycardia, hypotension, cardiac arrest, death
- **Naloxone is the reversal agent**, so give promptly for suspected opioid overdose
- Potency may require **repeat or higher naloxone doses**; IV onset 1 to 3 min
- **Supportive care first-line:** airway, ventilation/oxygenation, resuscitation as needed
- Monitor for **re-narcotization**, since naloxone may wear off before fentanyl does
- Consider co-involved substances (xylazine, benzodiazepines, stimulants); naloxone won’t reverse non-opioid components

NALOXONE QUICK SUMMARY

1–3 min

IV onset of action

Be ready to redose

Fentanyl's potency can outlast a single dose of naloxone.

Extend observation — watch for re-narcotization after wake-up.

Sources: NIOSH/CDC; DEA; SAMHSA

Fentanyl Summary Points

Potent synthetic mu-opioid agonist; leading driver of U.S. opioid overdose death, and tiny amounts can be fatal

Increasingly found as an adulterant, including in counterfeit pills, often unknowingly

Give naloxone for any suspected opioid overdose; repeat/higher doses plus prolonged monitoring

MOUD (buprenorphine, methadone, naltrexone) works; mind precipitated-withdrawal risk after recent fentanyl use

Standard opioid immunoassays may miss fentanyl; dedicated testing plus test strips aid diagnosis & harm reduction

Fentanyl field review template, modeled on the VA Academic Detailing Service Xylazine deck.

Xylazine


Rompun®
%2
25 ml
Enjeksiyonluk Çözelti
Veteriner Sedatif, Analjezik
Sadece Hayvan
Sağlığında Kullanılır
90197870
Rompun®
%2
Enjeksiyonluk Çözelti
Veteriner Sedatif,
Analjezik
25 ml
Sadece Hayvan
Sağlığında Kullanılır

Xylazine

- Non-opioid tranquilizer (sedative, anesthetic, muscle relaxant, analgesic)
- Used in veterinary medicine (Rompun ® others) → no approved human use
- Structural analog to clonidine (α2-adrenergic receptor agonist)
- Xylazine is not listed as a controlled substance
- Used as an adulterant in fentanyl, heroin, cocaine and methamphetamines
- Presence in the drug supply is likely underreported and under-identified
- Referred to as “tranq” or “tranq dope”
- Effects are thought to enhance, prolong, or modify euphoric effects of opioids

Xylazine: What Clinicians Need to Know (2023) Field Review. U.S. Dept of Veterans Affairs VA Academic Detailing Service

Xylazine: Risk and Concern

Fentanyl combined with xylazine was designated as an emerging threat to the United States in April 2023

Critical for providers become aware of emerging threat and how to support Patients who may be exposed to xylazine

Xylazine intoxication and opioid overdose present similarly → Xylazine is NOT an opioid

Can potentiate the effects of other CNS depressants (e.g., fentanyl, heroin, benzodiazepines, alcohol) and increase risk of respiratory depression and overdose

Full scope in overdose deaths is unknown → research indicates that it has been linked to overdose deaths, with the largest impact on states in the Northeast

From 2015 to 2020, xylazine was involved in 25.8% of drug overdose deaths in Philadelphia, 19.3% in Maryland, and 10.2% in Connecticut.


Administration

APRIL 12, 2023

Biden-Harris Administration Designates Fentanyl Combined with Xylazine as an Emerging Threat to the United States

ONDCP › BRIEFING ROOM › PRESS RELEASES

Xylazine's growing role in overdose deaths nationwide prompts Administration to make this designation for the first time in U.S. history

Xylazine: What Clinicians Need to Know (2023) Field Review. U.S. Dept of Veterans Affairs VA Academic Detailing Service

Physiologic Effects of Xylazine in Humans

Effects include:

- Slowed breathing
- Bradycardia, hypotension
- Loss of consciousness and physical sensation
- Constricted pupils
- Amnesia
- Little is known about the health effects of chronic xylazine exposure
- Skin ulcers, abscesses, lesions → → →

Skin and tissue wounds

- Independent of injection site or route of administration
- Can worsen quickly
- Can become severely infected
- May be slow to heal
- Look for skin lesions or abscesses. If found, refer promptly to medical services or wound care

The effects of xylazine can be rapid (within minutes) and last 8 hours or more, depending on the dose, route of administration, and if mixed with other substances

Xylazine: What Clinicians Need to Know (2023) Field Review. U.S. Dept of Veterans Affairs VA Academic Detailing Service

Xylazine: Routes and Detection

Formulations and Routes of Administration

- Available in a liquid form for veterinary use
- Can be dried into white or brown appearing powder
- Xylazine powder can be easily mixed with other powders and pressed into pills
- Routes of administration include intravenous, intramuscular, intranasal, and oral

Xylazine Detection

- Currently, VA immunoassay toxicology screens do not include tests for xylazine
- Short half-life of 23-50 minutes and rapid elimination from the body may make it difficult to detect
- Xylazine test strips currently commercially available

Xylazine: What Clinicians Need to Know (2023) Field Review. U.S. Dept of Veterans Affairs VA Academic Detailing Service

Xylazine Withdrawal Symptoms and Management

Symptoms may include anxiety, depression, nervousness/agitation, dizziness, shivering, nausea or vomiting, increased heart rate, and severe hypertension

Xylazine withdrawal may need to be managed simultaneously with opioid withdrawal

Xylazine withdrawal managed by alpha-2 agonists + meds for agitation if needed

Higher doses of buprenorphine or methadone may be needed to adequately manage withdrawal symptoms

Treat opioid withdrawal early with opioid withdrawal management strategies

Strategies may need adjustment in the context of recent fentanyl use (*e.g., 24-48 hours*)

Xylazine: What Clinicians Need to Know (2023) Field Review. U.S. Dept of Veterans Affairs VA Academic Detailing Service

Xylazine Intoxication and Overdose

Xylazine Intoxication/Overdose: Presentation and Management

- Intoxication/overdose will present with respiratory depression, hypotension, and altered consciousness, may lead to cardiac arrest
- There is no approved agent for xylazine reversal in humans
- Naloxone should be administered for respiratory depression, as xylazine and fentanyl is the combination found most often in the illicit drug supply
- Supportive care is first line recommended, including airway and blood pressure monitoring and other resuscitation efforts as needed

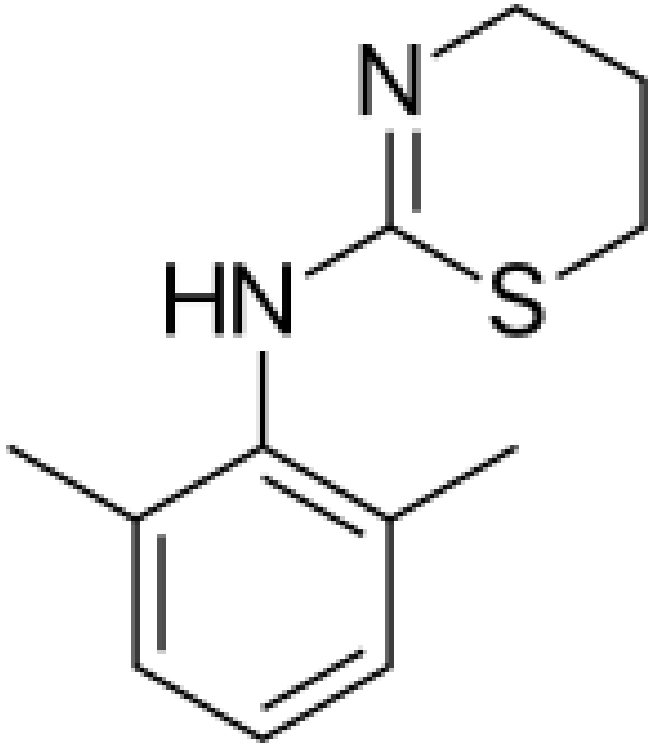
Xylazine-related wounds

- Monitor for skin lesions or abscesses that may require wound care
- Typically begin as red pinpoint blisters → untreated can develop into deeper and larger wounds
- Early treatment is essential

Xylazine: What Clinicians Need to Know (2023) Field Review. U.S. Dept of Veterans Affairs VA Academic Detailing Service

Xylazine Summary Points

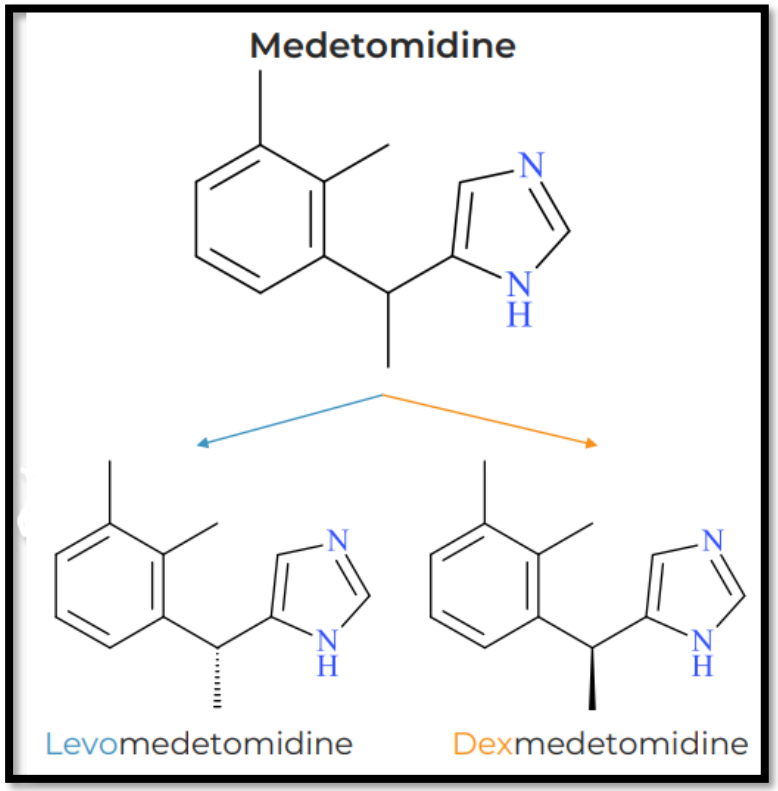
- Xylazine is a potent CNS depressant increasingly found as an adulterant in the illicit drug supply that increases the risk of respiratory depression and fatal overdose
- Naloxone should still be given in any suspected, overdose, including xylazine-involved overdoses
- Regardless of injection site or route of administration, xylazine can quickly cause severe skin wounds (e.g., necrotizing soft tissue infections) that require referral to medical services or wound care
- Not all laboratories are currently able to test for xylazine; Commercially available test strips exist and are sometimes included in harm-reduction programs



Xylazine: What Clinicians Need to Know (2023) Field Review. U.S. Dept of Veterans Affairs VA Academic Detailing Service

Medetomidine

Medetomidine



Medetomidine is a veterinary anesthetic drug with potent sedative effects

- Developed by Orion Pharma and launched in 2007
- Racemic mixtures of two stereoisomers, levomedetomidine and dexmedetomidine (alpha-2 adrenergic agonist)
- In U.S., approved for dogs as procedural sedative, distributed by Pfizer Animal Health

Medetomidine is an emerging illicit drug adulterant

- Potent sedative effects used in combination with illicit substances, most often opioid-based (e.g., fentanyl)
- Similar to xylazine, but much more potent
- First detected in U.S. illicit drug supply in 2022

Unclear supply sources to date

- Currently unclear whether sedative is diverted from medical supply or if medetomidine compounds are being formulated illegally from precursor chemicals
- Restricting access to prescription (medetomidine or dexmedetomidine) would have negative impacts on legitimate human and animal medical practice

Walton SE, Krotulski AJ. Medetomidine – An Emerging Adulterant of Concern. NPS Discovery Webinar Series – 7/11/2024. Accessed at: https://www.cfsre.org/images/Presentations/Medetomidine_NPSD_Webinar_Series_Walton_and_Krotulski.pdf

Medetomidine Fast Facts

Prescription Names:

- Medetomidine: Medetor ® Sedator ®, Domitor ® (Veterinary)
- Dexmedetomidine: Precedex ™ (human) Dexdomitor ® (Veterinary)

Nonmedical Brands and/or Street Names:

- “Tranq” (short for tranquilizer, often used for xylazine containing products)
- Selektope ® product is free-base form used in marine paint for antifouling (marine biocide)

How supplied:

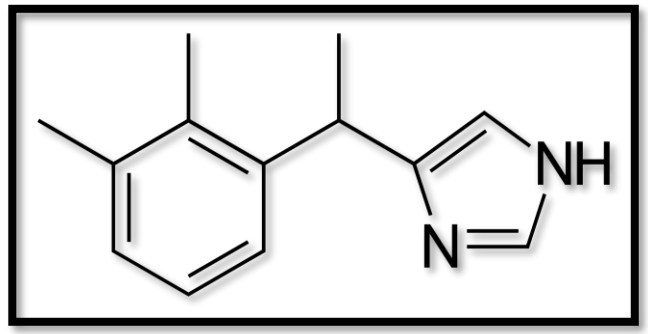
- Often supplied as hydrochloride salt (medetomidine hydrochloride), crystalline white solid that can be administered with sterile water
- Injection combinations for wildlife sedation (BAM)

Misuse or adulteration:

- Combination of α2 agonists with opioids believed to increase sedative effects; users may perceive as a better or more potent product
- Co-detected substances on laboratory samples of drug materials include fentanyl (and analogs), morphine, xylazine, diphenhydramine, caffeine, tetracaine, heroin, nitazines

Availability / Marketing:

- Commercial: Veterinary supply, Hospital supply
- Bulk laboratory chemical purposes



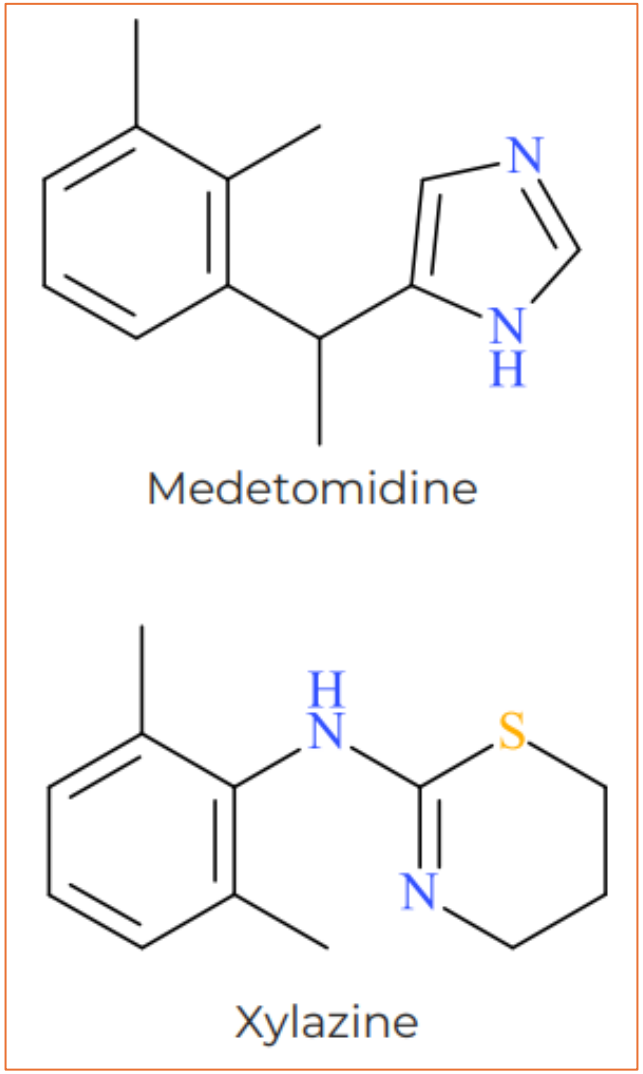
Mechanism of Action / Pharmacokinetics

Selective alpha-2 adrenoreceptor agonist	Medetomidine	Levomedetomidine	Dexmedetomidine	Route:	Half-Life (Dex):
• Anesthetic and sedative properties • Activation of G-proteins by alpha-2a receptors in brainstem = inhibition of NE release • Activation of alpha-2b receptors in periphery result in vasoconstriction	• Racemic mixture of two stereoisomers • ~50% potency of dexmedetomidine • Veterinary use (Domitor®)	• Inactive enantiomer, mild sedative and analgesic • Not used alone or prepared as single agent in veterinary or human medicine	• Active enantiomer, potent alpha-2agonist at both pre- and post-synaptic sites in CNS and PNS • Precedex™ (human) used IV sedative and anesthetic; Dexdomitor® (veterinary)	• IM, IV, SubQ, SL/Buccal	• IM – 281 +/- 177 minutes • IV – Approx up to 3 hours (prolonged in hepatic impairment)

Walton SE, Krotulski AJ. Medetomidine – An Emerging Adulterant of Concern. NPS Discovery Webinar Series – 7/11/2024. Accessed at: https://www.cfsre.org/images/Presentations/Medetomidine_NPSD_Webinar_Series_Walton_and_Krotulski.pdf

Medetomidine vs. Xylazine

Medetomidine is **~200x more potent** and **10x more selective** at alpha-2 adrenoreceptor than xylazine



Walton SE, Krotulski AJ. Medetomidine – An Emerging Adulterant of Concern. NPS Discovery Webinar Series – 7/11/2024. Accessed at: https://www.cfsre.org/images/Presentations/Medetomidine_NPSD_Webinar_Series_Walton_and_Krotulski.pdf

Pharmacologic Actions

Cardiovascular effects

- Initial short-lived hypertension (marked peripheral vasoconstriction) followed by dose-dependent hypotension and bradycardia
- Increased chance of arrythmias

Respiratory Effects

- Decreased respiratory rates and overall respiratory depression
- At high doses, hypnotic or anesthetic effects, spontaneous muscle contractions

Side effects:

- Dose-dependent sedation
- Analgesia
- Anxiolysis
- Muscle relaxation

Reversal

- Effects in dogs can be reversed using IM atipamezole (distributed as Antisedan®, Pfizer Veterinary Health)
- Synthetic alpha 2-adrenergic antagonist, competes for binding sites; not studied in humans

Walton SE, Krotulski AJ. Medetomidine – An Emerging Adulterant of Concern. NPS Discovery Webinar Series – 7/11/2024. Accessed at: https://www.cfsre.org/images/Presentations/Medetomidine_NPSD_Webinar_Series_Walton_and_Krotulski.pdf

Toxicity, Dependence, and Withdrawal

- Signs of Toxicity:
  - Respiratory depression
  - Hypnotic/anesthetic effects
  - Mydriasis
  - Hypothermia
  - Spontaneous muscle contractions
  - Bradycardia
  - Initial hypertension followed by prolonged hypotension

Complicated Presentation

- Similar to warnings with xylazine, concomitant use of medetomidine with cocaine, opioids, or a combination may potentiate or prolong the effects of these drugs, which can lead to adverse consequences

Toxicity Management

- Medetomidine/dexmedetomidine over-exposure should be treated with supportive respiratory care and management of blood pressure

Reversal?

- Medetomidine does not respond to naloxone. however, naloxone administration is recommended in illicit drug exposure because medetomidine is almost always found in combination with opioids
- Alpha 2 agonist reversal/blocking agent (atipamezole) administration not studied in humans, not recommended. Use supportive care

Toxic Adulterant Alert: Medetomidine/Dexmedetomidine. CFSRE December 2023. Accessed at: https://www.cfsre.org/images/content/reports/public_alerts/Medetomidine_Public_Health_Alert__Final.pdf

Medetomidine Summary Points

- Medetomidine is an a2-adrenergic agonist used in veterinary sedation that has been increasingly found in illicit drug supply, used to enhance effects of opioids
- Significantly more potent than xylazine
- Use is associated with severe risk of heightened sedation and profound bradycardia
- Supportive care is essential for cardiovascular and respiratory toxicities
- Naloxone administration crucial given concomitant opioid use

Kratom and 7-OH

Mitragyna speciosa

Kratom (*Mitragyna speciosa*)

Species: *Mitragyna speciosa*

- Biologically active alkaloids:
  - **Mitragynine 66%**
  - Paynantheine 9%
  - Speciogynine 7%
  - **7-hydroxymitragynine 2% ****
  - Speciophylline 1%

Appearance leaf form: See right

- Mitragynine isolated: white amorphous powder, soluble in ETOH, chloroform, acetic acid
- Drank as tea, liquid extract, powder in capsules

Origin: Tropical evergreen tree native to Indonesia, Thailand, and Myanmar

- Tree reaches heights of 50 feet; spread of 15 feet
- Member of the Rubiaceae family (Coffee!)

Common names: Kratom, thang, kakuam, thom, ketum, biak

Swogger M, et al. *Drug & AlcDep. 2016.*
DEA Drug Fact Sheet: Kratom

Uses of Kratom

- **Multiple varying use rationales:**
  - Analgesia, anxiolysis, attenuation of opioid withdrawal symptoms, weight loss, energy, sleep
- **Routes of administration:**
  - Oral ingestion
  - Leaves are dried or powdered, crushed and then smoked, brewed with tea, or placed in gel capsules, tablets, extracts
  - Kratom leaf may be chewed
- Different colors of veins on leaves has perceived benefits/differing potencies per users
- Purchased over internet and in smoke shops, gas stations, tea shops, bars, other boutique shops
  - Chopped leaves, capsules, compressed tablets, concentrated extracts

Swogger M, et al. *Drug & AlcDep. 2016.*
DEA Drug Fact Sheet: Kratom
Image: vietrealm.com

Examples of Kratom Commercially Available Products

https://www.brothersbotanicals.com/Premium-Kratom-Capsules-Mitragyna-Speciosa-50-Count_p_23.html

Kratom

- Leaf/powder
- Contains dozens of alkaloids with the two primary being mitragynine and 7-hydroxymytragynine (7-OH)
- When someone uses whole kratom powder, they are getting a complex mixture with relatively modest 7-OH exposure comparatively (to sole extract use)

Mitragynine

- Partial agonist at mu-opioid receptors, weaker binding than classical opioids
- Acts on adrenergic, serotonin, and dopamine receptors, which contributes in part to its stimulant effects at low doses
- Metabolized in the body *into* 7-OH, therefore some of kratom opioid agonistic effects via conversion

7-OH

- Shorthand of 7-hydroxymitragyinine
- Present in kratom leaf in very small amounts: 2% of naturally occurring alkaloid
- *Highly potent* Full or near-full mu-opioid agonist → significantly more potent than morphine at the receptor level by some estimates
- Responsible for most of the stronger opioid-like effects (analgesia, sedation, euphoria, respiratory depression risk)
- Has become available as an isolated/concentrated extract in products sold at gas stations and smoke shops

Behind the bar, Carlee Palermo, 25, keeps the kratom coming. She says she drinks the tea to help with a degenerative condition in her spine: "It completely took away my back pain."

The customers tonight at Kavasutra say they aren't aware of anyone who has been harmed by kratom. Then Palermo spills a little tea: Many of the people who come to the bar are in recovery from substance abuse.

Asked whether kratom helps with that, she says, "One hundred percent. It's done nothing but help anybody that I've seen."

npr.org/2023/07/08/1186514144/kratom-herbal-supplement-lawsuits-deaths-fda

MAYO CLINIC

Healthy Lifestyle

Consumer health

Users swear by kratom for mood enhancement and fatigue reduction, but safety issues and questions about its effectiveness abound.

If you read health news or visit vitamin stores, you may have heard about kratom, a supplement that is sold as an energy booster, mood enhancer, pain reliever and antidote for opioid withdrawal. However, the truth about kratom is more complicated, and the safety problems related to its use are concerning.

Nearly **2 million people** aged 12 and older used kratom within the past year, according to a 2022 federal estimate

https://www.mayoclinic.org/healthy-lifestyle/consumer-health/in-depth/kratom/art-20402171?p=1
https://www.samhsa.gov/data/sites/default/files/reports/rpt42731/2022-nsduh-nnr.pdf

University of Idaho School of Health and Medical Professions

Project ECHO

Pharmacologic Effects

- Onset: within 5-10 minutes
- Duration: 2 to 5 hours
- Dose-dependent effects:

Low doses → stimulant-like (1-5 grams)

- Stimulant effects, increased alertness, physical energy, talkativeness

High doses → opioid-like (>5 grams)

- Sedation; Euphoria
- 630g dose = drug-liking of 5mg IV morphine

- Adverse Effects
  - Nausea, itching, sweating, dry mouth, constipation, increased urination, tachycardia, vomiting, drowsiness
  - Anorexia, insomnia, hepatotoxicity, hallucinations with high potency extracts or chronic use

Images: Nootroholic.com
https://images.app.goo.gl/kv5HpYrjoke4Y2TX6

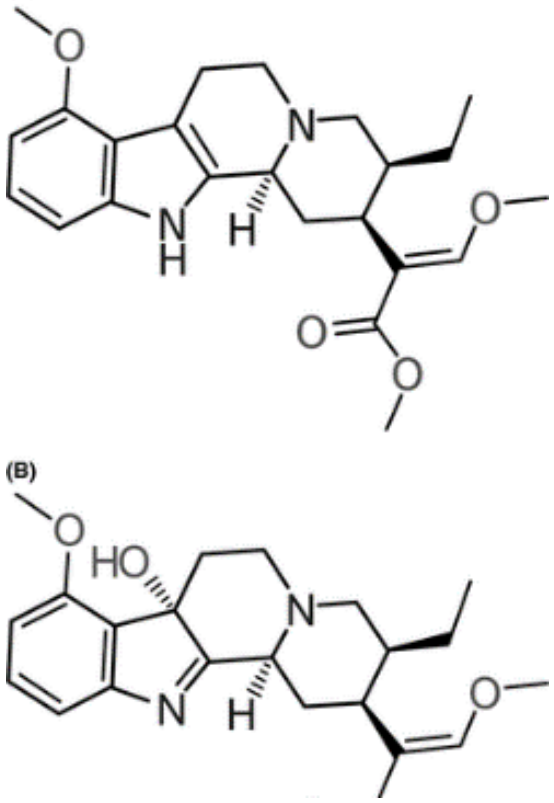
Pharmacologic Action

Kratom alkaloids *(>40 types)*

Non-Opioid Activity
- α-2 adrenergic agonism
- Potential 5HT2a-related action

Opioid Pharmacology
- MG and 7-OH-MG bind to OR
- MOR > DOR & KOR

COX-2 mRNA inhibition



White CM. Am J Health-Syst Pharm. 2017; 74:e589-95
Swogger M, et al. *Drug & AlcDep. 2018.*

University of Idaho School of Health and Medical Professions

Project ECHO

Pharmacokinetics

- In vitro, kratom extract was found to inhibit the following CYP P-450 isoenzymes:

2C9 → 2D6* → 1A2 → 3A4

**most potent inhibition*

- Using CYP system to boost effects via the “4 x 100” cocktail (common in adolescent population in Thailand):
  - Kratom leaves are boiled and mixed w/caffeine soda, dextromethorphan, codeine
  - + diphenhydramine (CYP2D6 inhibitor)

Am J Health-Syst Pharm. 2017; 74:e589-95
Swogger M, et al. *Drug & AlcDep. 2018.*
Image: http://img.medscapestatic.com/pi/features/slideshow-slide/drug-abuse-manifestations/updated/fig2.jpg?resize=645:439

Pharmacokinetics

Reminder: Rule of Five

5x the t ½ = the time at which the drug is "completely" (97%) eliminated from the body

- 1x ½ life = 50% original drug removed
- 2x ½ life = 75%
- 3x ½ life = 87.5%
- 4x ½ life = 93.75%
- 5x ½ life = 98.875%

RAT DATA:

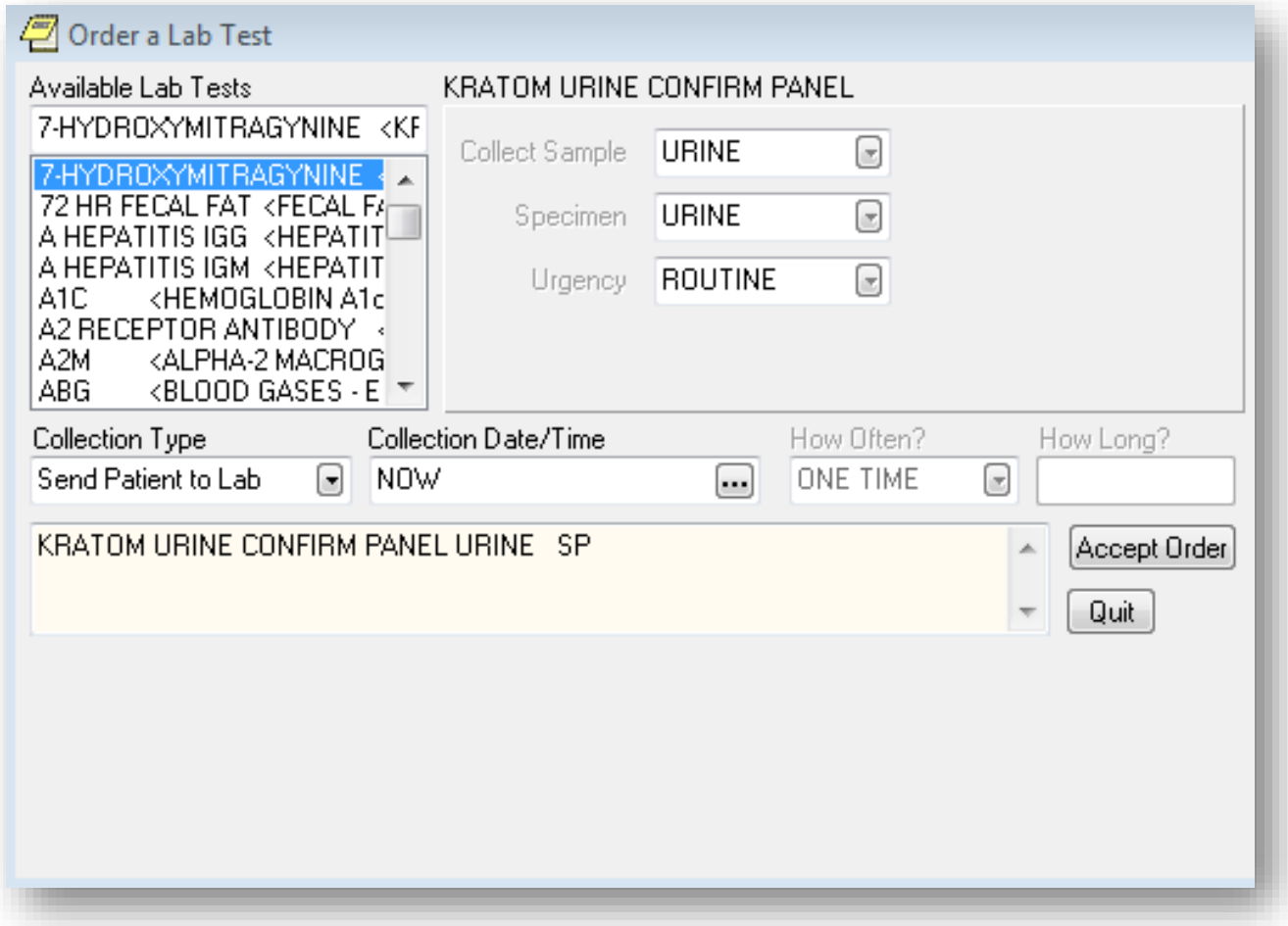
TMAX: 1.2 – 1.8 H
T ½: 3.9 – 9.4 H
VD: 37.9 – 89.5 L/KG

AVAILABLE HUMAN DATA:
(SMALL STUDIES)

TMAX: 0.83 ± 0.35 H
T ½: 23.24 ± 16.07 H
VD: 38.04 ± 24.32 L/KG

Raffa, et al. *J Clin Pharm Ther*. 2018; 43: 437– 441
White CM. Am J Health-Syst Pharm. 2017; 74:e589-95

Laboratory Detection



PROVIDER INSTRUCTIONS:

1. If positive, this panel test will quantify the following:

7-HYDROXYMITRAGYNINE

MITRAGYNINE

***A cost of $78.50 will incur if either of the above is performed.**

2. This test request 30 mLs (NLT 20) of urine.

Test Code: 791750

TAT: 6 - 11 Days

PROCESSING INSTRUCTIONS:

1. This test requires 30 mLs (NLT 20) REFRIG, Random Urine.

Please make two aliquots, one to send using the LabCorp Aliquot Tube and one backup aliquot (reserve the Primary cup if possible) and store in the walk-in.

University of Idaho School of Health and Medical Professions

Project ECHO

Kratom Withdrawal Symptoms

Hostility, Aggression, Emotional Lability

Physical Opioid Withdrawal Symptoms

Seizures and Death*

Adjunctive medications for management of uncomplicated kratom withdrawal	
Withdrawal Symptoms:	Clonidine 0.1mg q6h PRN 0.1MG PO Q2H PRN FOR KRATOM/OPIOID WITHDRAWAL - COWS >8 0.2MG PO Q2H PRN FOR KRATOM/OPIOID WITHDRAWAL - COWS >12 (Hold for SPB <90 or Pulse <56: MAX DOSE=0.6mg/24hours)
Anxiety, dysphoria, lacrimation, rhinorrhea:	Hydroxyzine 25-50mg TID PRN
Myalgias:	NSAIDS, APAP, methocarbamol 500-1500mg TID PRN
Sleep disturbance:	Trazodone 50-100mg or gabapentin 300-1800mg PRN
Nausea:	Promethazine, ondansetron, prochlorperazine
Diarrhea:	Loperamide 4mg then 2mg after each loose stool; max 16mg/day Bismuth subsalicylate 524mg q30min-1hr; max 4192/day
GI Cramping:	Dicyclomine 10-20mg q6-8hrs PRN

White CM. Am J Health-Syst Pharm. 2017; 74:e589-95
DEA Drug Fact Sheet: Kratom
VA Academic Detailing: Pain Management

Kratom Withdrawal Management

Table 1. Pharmacologic Effects of Kratom From Human Trials[2,6,9,13,20,21,24-34,a]

Adverse Events	Therapy for Adverse Events	Withdrawal Effects	Therapy for Withdrawal
Tachycardia and hypertension	Benzodiazepines, negative chronotropic drugs	Agitation and anxiety	Benzodiazepines, α-2 agonists
Nausea and constipation	Antiemetics, laxative plus stool softener	Abdominal pain and diarrhea	Nonopioid antidiarrheals
Confusion and hallucinations	Benzodiazepines, naloxone	Limb muscle spasms	Benzodiazepines
Seizures	Benzodiazepines, naloxone, anticonvulsants	Joint and muscle pain	Nonopioid pain relievers
Sedation	Naloxone	. . .	. . .

[a]Treatments for adverse events and withdrawal are general treatment suggestions and were not studied in any clinical trials of kratom.

White CM. Am J Health-Syst Pharm. 2017; 74:e589-95
Image: https://images.app.goo.gl/kv5HpYrjoke4Y2TX6

University of Idaho School of Health and Medical Professions
Project ECHO

Management of Kratom Dependency

Kratom Use Disorder (Unofficial….)

- Often using OUD Criteria for diagnosis
- Smith et al (2024) applied DSM-5 SUD criteria to kratom and found that individuals meeting criteria for KUD typically do so through tolerance, withdrawal, using more than intended, and craving → NOT function or psychosocial disruption (rare)

No guidelines or approved pharmacotherapies for KUD (OUD) available

Available evidence base is sparse, low-quality

Gradual taper recommended for discontinuation

Multiple case reports demonstrate efficacy with buprenorphine/naloxone for maintenance therapy

- Smith et al (2024) also found most clinicians treating KUD select buprenorphine formulations, acknowledge no controlled studies supporting use
- Doses up to 24mg/6mg daily appear to be effective
- May be beneficial for comorbid pain

Methadone and naltrexone may also be considered

- Considerations for comorbidities and logistical issues

Swogger MT, et al. Understanding kratom use: a guide for healthcare providers. *Front Pharmacol*. 2022;13:801855.
Shah K, et al. Kratom: an emerging issue and need for regulations in the United States. *Prim Care Companion CNS Disord*. 2021;23(1):20r02770.
Prozialeck WC, et al. Kratom use within the context of the evolving opioid crisis and the covid-19 pandemic in the united states. *Front Pharmacol*. 2021;12:729220.
Eastlack SC, Cornett EM, Kaye AD. Kratom-pharmacology, clinical implications, and outlook: a comprehensive review. *Pain Ther*. 2020;9(1):55-69
Smith KE, Epstein DH, Weiss ST. Controversies in Assessment, Diagnosis, and Treatment of Kratom Use Disorder. Curr Psychiatry Rep. 2024 Sep;26(9):487-496.. Epub 2024 Aug 13. PMID: 39134892

Kratom Toxicity and Overdose

Toxicity

- Clinical presentation: sedation, constricted pupils (miosis), sweating, dry mouth, nausea, respiratory depression
- Supportive management depending on involved organ system
  - i.e., N-acetyl-cysteine for acute hepatitis; anti-epileptics for seizures, etc.

Overdose

- Efficacy of reversal agents for kratom overdose overall unknown
- Naloxone has not been demonstrated to be highly efficacious (has not been clinically studied)

Shah K, et al. Kratom: an emerging issue and need for regulations in the United States. *Prim Care Companion CNS Disord*. 2021;23(1):20r02770.
Prozialeck WC, et al. Kratom use within the context of the evolving opioid crisis and the covid-19 pandemic in the united states. *Front Pharmacol*. 2021;12:729220.
Gorelick DA. Kratom: substance of abuse or therapeutic plant?. *Psychiatr Clin North Am*. 2022;45(3):415-430.
Eastlack SC, et al. Kratom-pharmacology, clinical implications, and outlook: a comprehensive review. *Pain Ther*. 2020;9(1):55-69

Kratom Legal Debate

- Reports of use date back to mid-1800s
- **Many clinicians had not heard of kratom prior to 2016**
  - DEA announced plan for temporary Schedule I status in August 2016
  - Scheduling withdrawn in October 2016 due to public outcry
- FDA has not approved Kratom for any medical use

AMERICAN KRATOM ASSOCIATION

"The **American Kratom Association**, the largest kratom advocacy group in the United States, helped spur an outpouring of public comments. In response, the DEA put a hold on its scheduling plans"

American Society for Biochemistry and Molecular Biology

Image: kratommarchdc.com; americankratom.org
http://www.asbmb.org/asbmbtoday/201706/Features/KRATOM/

University of Idaho School of Health and Medical Professions

Project ECHO

Kratom Le

- Reports of use date ba
- **Most clinicians h**
  - DEA announc
  - Scheduling v
- FDA has not a

The kratom industry generated
$1.3 billion
in sales in 2019

- LAPPA 2022

AMERIC
KRATOM
ASSOCIATION

American

Image: kratommarchdc.com; americankratom.org
http://www.asbmb.org/asbmbtoday/201706/Features/KRATOM/

Kratom Current Legal Status

DEA delayed ruling on scheduling of kratom and listed as "Drug and Chemical of Concern"

- Risk of abuse, contaminated product, seizures upon withdrawal, neonate dependence issues, drug interactions, liver injury, etc.
- On July 29, 2025, FDA formally recommended to both HHS and DEA that synthetic or high-concentration 7-OH products be scheduled under Schedule I, citing elevated abuse risk
- Recommendation has triggered ongoing consideration by DEA, but no final scheduling has occurred
- Classifies kratom as an unapproved "new dietary ingredient" and unsafe as a food additive; issues import alerts and consumer warnings

Kratom-Summary-of-State-Laws.pdf (legislativeanalysis.org)
LSB11082 (congress.gov)
Kratom-Fact-Sheet-FINAL.pdf (legislativeanalysis.org)

Kratom Current Legal Status

Not controlled under Federal Controlled Substances Act

- **KRATOM BANS (March 2026)**: Alabama*, Arkansas, Connecticut***, Indiana, Louisiana, Rhode Island**, Vermont, Wisconsin
- **KRATOM REGULATIONS (Mixed levels)**: California, Illinois, Minnesota, Mississippi, Nevada, South Dakota, Tennessee, Texas, Virginia, Ohio (synthetic only), West Virginia
- Globally, kratom is illegal or restricted in more than a dozen countries, including parts of Europe, Japan and Russia

Kratom Consumer Protection Act

- Multiple states are considering regulating the substance under the "Kratom Consumer Protection Act," or the KCPA. Lobbying efforts to change state bans into KCPAs continue
- **KCPA enacted**: Utah (2019), Arizona (2019), Nevada (2019), Oregon (2022), Oklahoma (2021), West Virginia (2023), Virginia (2023—VCPA), Georgia (2019 + 2024 strengthening), Kentucky (2024), Maryland (2024), Colorado (2025 Daniel Bregger Act; KCPA-like), South Carolina (2025)****
- During 2023 and 2024, 33 states introduced legislation related to kratom

Federal Legislation

- **H.R. 8000 – "END 7-OH Act"** Introduced March 19, 2026 by Rep. Gus Bilirakis (R-FL)
  - Seeks to amend the CSA and classify synthetic 7-OH as a Schedule I substance, expressly excluding naturally occurring 7-OH found in plant-derived kratom

*KCPA legislation pending to replace ban
**reversed ban in April 1 2026
***Schedule I as of March 25, 2026
****2026 legislation to modify KCPA to schedule 1

Kratom-Summary-of-State-Laws.pdf (legislativeanalysis.org)
LSB11082 (congress.gov)
Kratom-Fact-Sheet-FINAL.pdf (legislativeanalysis.org)

The New York Times

Opioid Users Call Kratom a Godsend. The F.D.A. Says It's a Menace.

npr

HEALTH

Herbal supplement kratom targeted by lawsuits after a string of deaths

https://www.nytimes.com/2019/04/17/us/kratom-overdose-deaths.html
https://www.npr.org/2023/07/08/1186514144/kratom-herbal-supplement-lawsuits-deaths-fda

Kratom Legal Action

- April 2023: U.S. Marshals, at the FDA's request, seized more than 250,000 units of dietary supplements and bulk dietary ingredients that are or contain kratom, including over 1000 kilograms of bulk kratom
- Multiple recent wrongful death lawsuits
  - In July 2023, Jury in WA awarded $2.5 mil verdict in first kratom wrongful death trial in US
- 2026 and beyond expected to have multiple new cases, rise in litigation attributed to growing recognition of adverse health effects tied to kratom

"When you're selling a drug next to Skittles or energy drinks, you have no means of knowing that you're dealing with something that is exponentially more dangerous than anything else on the shelf."
– *NPR article; Atlanta attorney Matt Wetherington*

https://www.fda.gov/news-events/press-announcements/fda-roundup-april-28-2023
https://www.npr.org/2023/07/08/1186514144/kratom-herbal-supplement-lawsuits-deaths-fda
https://www.washingtonpost.com/health/2024/02/20/kratom-deaths/

Kratom Summary/Key Points

1. Pharmacologic effects are dose-dependent, ranging from stimulant- to opioid-like, and include mu-opioid agonism, COX-2 inhibition, among others
2. Used for pain, anxiety, sleep, alertness, appetite suppression, withdrawal mitigation, more
3. Drug interactions are possible and sometimes used intentionally to amplify effects
4. Federally legal substance with some state level banning/regulation; Restrictions/banning varies globally
5. Kratom is known to have a potential for addiction, and is associated with dependence and withdrawal; Withdrawal can be serious and may require medical attention

Engage in non-judgmental, open discussion about kratom/7-OH use

- Avoid abrupt dismissal of use! Acknowledge perceived benefits and autonomy
- Provide education on known risks: physical dependence and withdrawal syndrome, lack of FDA regulation, product contamination risk, limited evidence base, potential hepatotoxicity with long-term, and drug/substance interaction risk
- Discuss harm reduction strategies

Questions or Comments?

References:

(AI Disclaimer: Anthropic AI was utilized to format references into APA style and alphabetize list)

- Baird, T. R., Akbarali, H. I., Dewey, W. L., Hamid, H., Henderson, E. A., Bettinger, J. J., & Damaj, M. I. (2022). Opioid-like adverse effects of tianeptine in male rats and mice. *Psychopharmacology*, *239*(7), 2187-2199. https://doi.org/10.1007/s00213-022-06093-w
- El Zahran, T., Schier, J., Glidden, E., Kieszak, S., Law, R., Bottei, E., Aaron, C., King, A., & Chang, A. (2018). Characteristics of tianeptine exposures reported to the National Poison Data System - United States, 2000-2017. *MMWR. Morbidity and Mortality Weekly Report*, *67*(30), 815-818. https://doi.org/10.15585/mmwr.mm6730a2
- Gassaway, M. M., Rives, M. L., Kruegel, A. C., Javitch, J. A., & Sames, D. (2014). The atypical antidepressant and neurorestorative agent tianeptine is a μ-opioid receptor agonist. *Translational Psychiatry*, *4*, e411. https://doi.org/10.1038/tp.2014.30
- Han, J., Andreu, V., Langreck, C., Malagon-Vina, H., Thiele, A. M., Sargin, D., Klampfl, S. M., Traunmüller, L., Kim, C. K., Namkung, H., Dunakin, S., Galimberti, I., Cosgrove, D. M., Deisseroth, K., Lammel, S., Chevaleyre, V., Pleil, K. E., Sibille, E., Hipólito, L., ... Sahay, A. (2022). Mu opioid receptors on hippocampal GABAergic interneurons are critical for the antidepressant effects of tianeptine. *Neuropsychopharmacology*, *47*(7), 1387-1397. https://doi.org/10.1038/s41386-021-01192-2
- Kasper, S., & McEwen, B. S. (2008). Neurobiological and clinical effects of the antidepressant tianeptine. *CNS Drugs*, *22*(1), 15-26. https://doi.org/10.2165/00023210-200822010-00002
- McEwen, B. S., Chattarji, S., Diamond, D. M., Jay, T. M., Reagan, L. P., Svenningsson, P., & Fuchs, E. (2010). The neurobiological properties of tianeptine (Stablon): From monoamine hypothesis to glutamatergic modulation. *Molecular Psychiatry*, *15*(3), 237-249. https://doi.org/10.1038/mp.2009.80
- Nishio, Y., Lindsley, C. W., & Bender, A. M. (2024). Classics in chemical neuroscience: Tianeptine. *ACS Chemical Neuroscience*, *15*(21), 3863-3873. https://doi.org/10.1021/acschemneuro.4c00519
- Perić, I., Costina, V., Djordjević, S., Prekodravac, J., Stanković, S. N., Todorović, A., Horvat, A., Findeisen, P., Gass, P., & Filipović, D. (2021). Tianeptine modulates synaptic vesicle dynamics and favors synaptic mitochondria processes in socially isolated rats. *Scientific Reports*, *11*(1), 17747. https://doi.org/10.1038/s41598-021-97186-7
- Perić, I., Costina, V., Findeisen, P., Gass, P., & Filipović, D. (2020). Tianeptine enhances energy-related processes in the hippocampal non-synaptic mitochondria in a rat model of depression. *Neuroscience*, *451*, 111-125. https://doi.org/10.1016/j.neuroscience.2020.09.061
- Rawal, V. Y., Gallardo, M., Henderson, K., Malwitz, K., Janis, J., & Elefante, R. (2025). Severe tianeptine withdrawal symptoms managed with medications for opioid use disorder: A case report. *Journal of Addictive Diseases*, *43*(1), 98-103. https://doi.org/10.1080/10550887.2023.2290139
- Rushton, W., Whitworth, B., Brown, J., Kurz, M., & Rivera, J. (2021). Characteristics of tianeptine effects reported to a poison control center: A growing threat to public health. *Clinical Toxicology*, *59*(2), 152-157. https://doi.org/10.1080/15563650.2020.1781151

References (Continued):

(AI Disclaimer: Anthropic AI was utilized to format references into APA style and alphabetize list)

- Samuels, B. A., Nautiyal, K. M., Kruegel, A. C., Levinstein, M. R., Magalong, V. M., Gassaway, M. M., Grinnell, S. G., Han, J., Ansonoff, M. A., Pintar, J. E., Javitch, J. A., Sames, D., & Hen, R. (2017). The behavioral effects of the antidepressant tianeptine require the mu-opioid receptor. *Neuropsychopharmacology*, *42*(10), 2052-2063. https://doi.org/10.1038/npp.2017.60
- Smith, K. E., Rogers, J. M., Strickland, J. C., & Epstein, D. H. (2021). When an obscurity becomes trend: Social-media descriptions of tianeptine use and associated atypical drug use. *The American Journal of Drug and Alcohol Abuse*, *47*(4), 455-466. https://doi.org/10.1080/00952990.2021.1904408
- Springer, J., & Cubała, W. J. (2018). Tianeptine abuse and dependence in psychiatric patients: A review of 18 case reports in the literature. *Journal of Psychoactive Drugs*, *50*(3), 275-280. https://doi.org/10.1080/02791072.2018.1438687
- Szczesniak, L., & Sullivan, R. (2022). Microdose induction of buprenorphine in a patient using tianeptine. *Journal of Addiction Medicine*, *16*(5), 591-593. https://doi.org/10.1097/ADM.0000000000000994
- Svenningsson, P., Bateup, H., Qi, H., Takamiya, K., Huganir, R. L., Spedding, M., Roth, B. L., McEwen, B. S., & Greengard, P. (2007). Involvement of AMPA receptor phosphorylation in antidepressant actions with special reference to tianeptine. *The European Journal of Neuroscience*, *26*(12), 3509-3517. https://doi.org/10.1111/j.1460-9568.2007.05952.x
- Szegedi, V., Juhász, G., Zhang, X., Barkóczi, B., Qi, H., Madeira, A., Kapus, G., Svenningsson, P., Spedding, M., & Penke, B. (2011). Tianeptine potentiates AMPA receptors by activating CaMKII and PKA via the p38, p42/44 MAPK and JNK pathways. *Neurochemistry International*, *59*(8), 1109-1122. https://doi.org/10.1016/j.neuint.2011.10.008
- United States Drug Enforcement Administration, Diversion Control Division. (n.d.). *Tianeptine*. https://www.deadiversion.usdoj.gov/drug_chem_info/tianeptine.pdf
- Uzbay, T. I. (2008). Tianeptine: Potential influences on neuroplasticity and novel pharmacological effects. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *32*(4), 915-924. https://doi.org/10.1016/j.pnpbp.2007.08.007
- Wagstaff, A. J., Ormrod, D., & Spencer, C. M. (2001). Tianeptine: A review of its use in depressive disorders. *CNS Drugs*, *15*(3), 231-259. https://doi.org/10.2165/00023210-200115030-00006

Web Resources

- Cleveland Clinic. (n.d.). *Gas station heroin (Tianeptine)*. https://health.clevelandclinic.org/gas-station-heroin-tianeptine
- Center for Forensic Science Research & Education. (n.d.). *Tianeptine public health alert*. https://www.cfsre.org/images/content/reports/public_alerts/TIANEPTINE_Public_Health_Alert_Final.pdf
- Krewel, L. (2024, July 12). *Tianeptine gas station heroin drug*. NPR. https://www.npr.org/2024/07/12/nx-s1-4865955/tianeptine-gas-station-heroin-drug

References

- National Center for Complementary and Integrative Health. Health Information: Kava. National Center for Complementary and Integrative Health website accessed at https://www.nccih.nih.gov/health/kava. April 10, 2024.
- Becker MW, Lourençone EMS, De Mello AF, et al. Liver transplantation and the use of kava: case report. Phytomedicine. 2019;56:21-26.
- Kava kava. LiverTox: clinical and research information on drug-induced liver injury. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases; 2018.
- Kava. Natural Medicines website. Accessed at https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=872 on January 22, 2024.
- Pittler MH, Ernst E. Kava extract for treating anxiety. Cochrane Database Syst Rev. 2003;2003(1):CD003383. doi: 10.1002/14651858.CD003383. PMID: 12535473; PMCID: PMC6999799.
- Sarris J. Herbal medicines in the treatment of psychiatric disorders: 10-year updated review. Phytotherapy Research. 2018;32(7):1147-1162.
- Sarris J, Stough C, Bousman CA, et al. Kava in the treatment of generalized anxiety disorder. A double-blind, randomized, placebo-controlled study. Journal of Clinical Psychopharmacology. 2013;33(5):643-648.
- Smith K, Leiras C. The effectiveness and safety of kava kava for treating anxiety symptoms: a systematic review and analysis of randomized clinical trials. Complementary Therapies in Clinical Practice. 2018;33:107-117.
- White CM. The pharmacology, pharmacokinetics, efficacy, and adverse events associated with kava. Journal of Clinical Pharmacology. 2018;58(11):1396-1405.

References

- Henningfield JE, Fant RV, Wang DW. The abuse potential of kratom according the 8 factors of the controlled substances act: implications for regulation and research. Psychopharmacology (Berl). 2018 Feb;235(2):573-589. doi: 10.1007/s00213-017-4813-4. Epub 2017 Dec 23. Review. PubMed PMID: 29273821; PubMed Central PMCID: PMC5813050.
- Tatum WO, Hasan TF, Coonan EE, Smelick CP. Recurrent seizures from chronic kratom use, an atypical herbal opioid. Epilepsy Behav Case Rep. 2018 Apr 17;10:18-20. doi: 10.1016/j.ebcr.2018.04.002. eCollection 2018. PubMed PMID: 30062086; PubMed Central PMCID: PMC6063981.
- White CM. Pharmacologic and clinical assessment of kratom. Am J Health Syst Pharm. 2018 Mar 1;75(5):261-267. doi: 10.2146/ajhp161035. Epub 2017 Dec 18. Review. PubMed PMID: 29255059.
- Diep J, et al. Kratom, an Emerging Drug of Abuse: A Case Report of Overdose and Management of Withdrawal. A Case Rep.2017 Oct 26. doi: 10.1213/XAA.0000000000000658. [Epub ahead of print] PubMed PMID: 29077662.
- Fluyau D, Revadigar N. Biochemical Benefits, Diagnosis, and Clinical Risks Evaluation of Kratom. Front Psychiatry. 2017 Apr 24;8:62. doi:10.3389/fpsyt.2017.00062. eCollection 2017. Review. PubMed PMID: 28484399; PubMed Central PMCID: PMC5402527.
- Warner ML, Kaufman NC, Grundmann O. The pharmacology and toxicology of kratom: from traditional herb to drug of abuse. Int J Legal Med. 2016 Jan;130(1):127-38. doi: 10.1007/s00414-015-1279-y. Epub 2015 Oct 28. Review. PubMed PMID: 26511390.
- Tayabali K, Bolzon C, Foster P, Patel J, Kalim MO. Kratom: a dangerous player in the opioid crisis. J Community Hosp Intern Med Perspect. 2018 Jun 12;8(3):107-110. doi: 10.1080/20009666.2018.1468693. eCollection 2018. PubMed PMID: 29915645; PubMed Central PMCID: PMC 5998276.
- Olsen EO, O'Donnell J, Mattson CL, Schier JG, Wilson N. *Notes from the Field:* Unintentional Drug Overdose Deaths with Kratom Detected — 27 States, July 2016–December 2017. MMWR Morb Mortal Wkly Rep 2019;68:326–327. DOI: http://dx.doi.org/10.15585/mmwr.mm6814a2
- Trakulsrichai S, Sathirakul K, Auparakkitanon S, et al. Pharmacokinetics of mitragynine in man. Drug Des Devel Ther. 2015 Apr 29;9:2421-9. doi: 10.2147/DDDT.S79658. eCollection 2015. PubMed PMID: 25995615; PubMed Central PMCID: PMC4425236.
- Raffa, RB, Pergolizzi, JV, Taylor, R, Ossipov, MH. Nature's first "atypical opioids": Kratom and mitragynines. *J Clin Pharm Ther*. 2018; 43: 437– 441. https://doi.org/10.1111/jcpt.12676
- Meireles V, Rosado T, Barroso M, et al. *Mitragyna speciosa*: Clinical, Toxicological Aspects and Analysis in Biological and Non-Biological Samples. *Medicines (Basel)*. 2019;6(1):35. Published 2019 Mar 4. doi:10.3390/medicines6010035
- Eldridge WB, Foster C, Wyble L. Neonatal Abstinence Syndrome Due to Maternal Kratom Use. Pediatrics. 2018 Dec;142(6). pii: e20181839. doi: 10.1542/peds.2018-1839. Epub 2018 Nov 7. Review. PubMed PMID: 30404789.

References

- Prozialeck WC, Avery BA, Boyer EW, et al. Kratom policy: The challenge of balancing therapeutic potential with public safety. Int J Drug Policy. 2019 Aug;70:70-77. doi: 10.1016/j.drugpo.2019.05.003. Epub 2019 May 16. PubMed PMID: 31103778.
- Veltri C, Grundmann O. Current perspectives on the impact of Kratom use. Subst Abuse Rehabil. 2019 Jul 1;10:23-31. doi: 10.2147/SAR.S164261. eCollection 2019. PubMed PMID: 31308789; PubMed Central PMCID: PMC6612999.
- Henningfield JE, Grundmann O, Babin JK, Fant RV, Wang DW, Cone EJ. Risk of death associated with kratom use compared to opioids. Prev Med. 2019 Nov;128:105851. doi: 10.1016/j.ypmed.2019.105851. Epub 2019 Oct 21. PubMed PMID: 31647958.
- Gutridge AM, Robins MT, Cassell RJ, et al. G protein-biased kratom-alkaloids and synthetic carfentanil-amide opioids as potential treatments for alcohol use disorder. Br J Pharmacol. 2019 Nov 8. doi: 10.1111/bph.14913. [Epub ahead of print] PubMed PMID:31705528.
- 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 Jun 26;5(6):992-1001. doi: 10.1021/acscentsci.9b00141. Epub 2019 May 29. PubMed PMID: 31263758; PubMed Central PMCID: PMC6598159.
- Ismail I, Wahab S, Sidi H, et al. Kratom and Future Treatment for the Opioid Addiction and Chronic Pain: Periculo Beneficium? Curr Drug Targets. 2019;20(2):166-172. doi: 0.2174/1389450118666170425154120. PubMed PMID: 28443503.
- Davidson L, Rawat M, Stojanovski S, Chandrasekharan P. Natural drugs, not so natural effects: Neonatal abstinence syndrome secondary to 'kratom'. J Neonatal Perinatal Med. 2019;12(1):109-112. doi: 10.3233/NPM-1863. PubMed PMID: 30149482; PubMed Central PMCID: PMC6484255.