Gas Station Highs

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Disclosure Information

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  - *No disclosures*
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  - *No disclosures*

Learning Objectives

At the conclusion of this session, attendees will be able to:

1. Identify common “gas station” or internet-accessible agents (e.g., tianeptine, alkyl nitrites, phenibut, kratom & derivatives) and describe core pharmacology and toxidromes.

2. Recognize intoxication, withdrawal, and unique complications including “poppers maculopathy,” severe tianeptine toxicity, phenibut withdrawal, and kratom-associated adverse events.

3. Apply evidence-informed strategies in the acute care and outpatient settings, including supportive care, targeted antidotes and adjuncts, and harm-reduction counseling specific to unregulated products.

Why This Matters

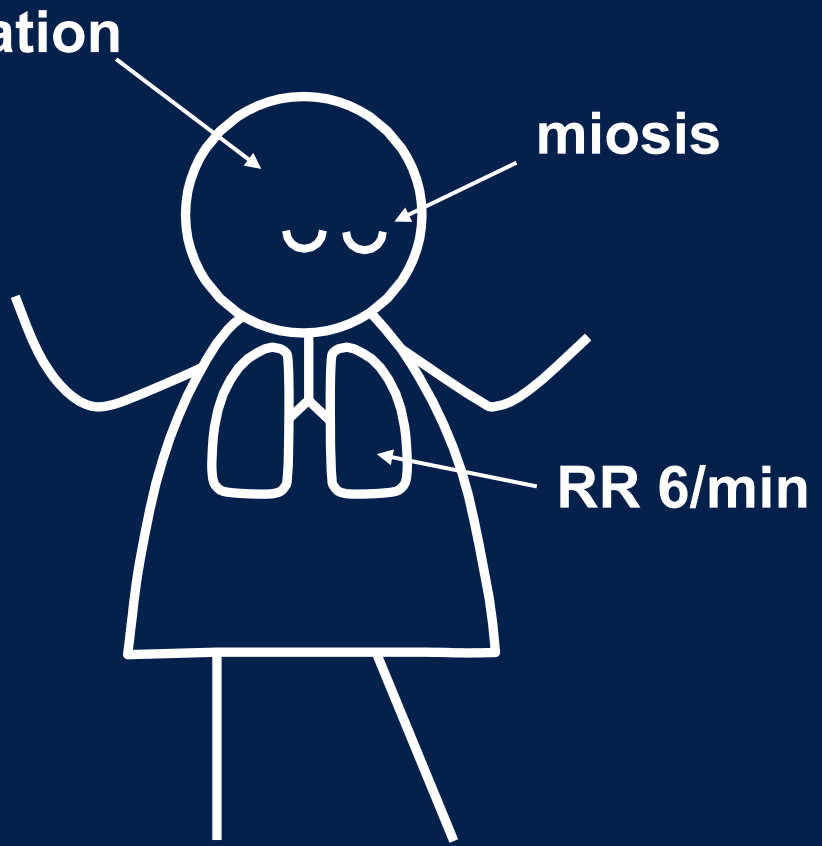
- Growing availability of psychoactive agents in unregulated, easily accessible markets: gas stations, smoke shops, and online vendors
- Product marketing: “legal,” “supplements,” “natural”
- Implications for drug testing
- Impact: increased ED visits, poison center calls, public health alerts

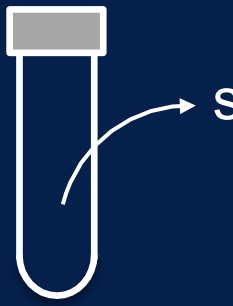
Case 1

36-year-old man is found unresponsive after injecting a powder purchased from an online vendor.

case based on: Dempsey SK, et al. (J Anal Toxicol 2017)

Case 1



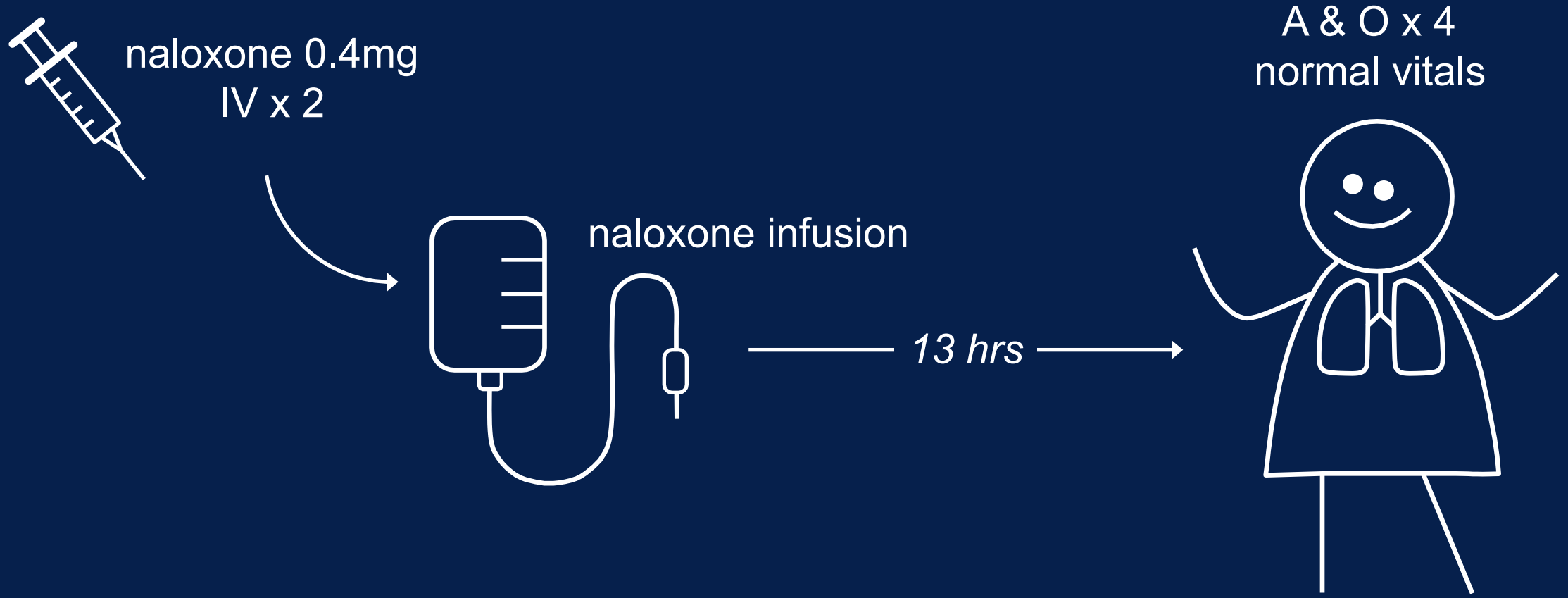


serum ethanol:
133 mg/dL

amphetamines:	*negative*
barbiturates:	*negative*
benzos:	*negative*
cannabinoid:	*negative*
cocaine:	*negative*
opiates:	*negative*
tricyclics:	*negative*

case based on: Dempsey SK, et al. (J Anal Toxicol 2017)

Case 1: Clinical Course



case based on: Dempsey SK, et al. (J Anal Toxicol 2017)

What Could This Be?

→ powder purchased online

→ sedative-hypnotic / opioid-like toxidrome → responds to naloxone

→ patient recovers in <24 hours with no sequelae

case based on: Dempsey SK, et al. (J Anal Toxicol 2017)

This Case: Tianeptine

- **atypical tricyclic antidepressant**
  - patient's urine TCA screen: *negative*
- prescribed for MDD and anxiety
  - fewer CV and anticholinergic effects compared to other TCA's
  - rapid improvement in depressive symptoms; effective in many patients with SSRI-resistant depression
  - not approved in U.S.

Available Formulations

elixir
voluntary recall 2024

capsules
online & in stores

image credit: https://feldmansheoherd.com; https://whiteoakrecovery.com

Why Use a TCA Recreationally?

- sold as a “dietary supplement” by vendors
- marketing claims:
  - “improve brain function” / cognitive enhancement
  - manage pain and OUD
  - treat anxiety and depression—without having to see a doctor
- prescribed therapeutic doses in other countries: **12.5 – 50mg** per day
- doses used by U.S. consumers of unregulated product: **150mg – 10 grams** per day

www.fda.gov; El Zahran T, et al. (MMWR 2018)

Clinical Effects

- **mechanism of action distinct from other TCA's**
  - modulates glutamate transmission (unclear mechanism)
  - efficacious full *mu*-opioid receptor agonist, potency ≈ 0.1x morphine
  - weak *delta*-opioid receptor agonist
  - no effect on 5-HT system

opioid effects at supratherapeutic doses (≥150mg / day)

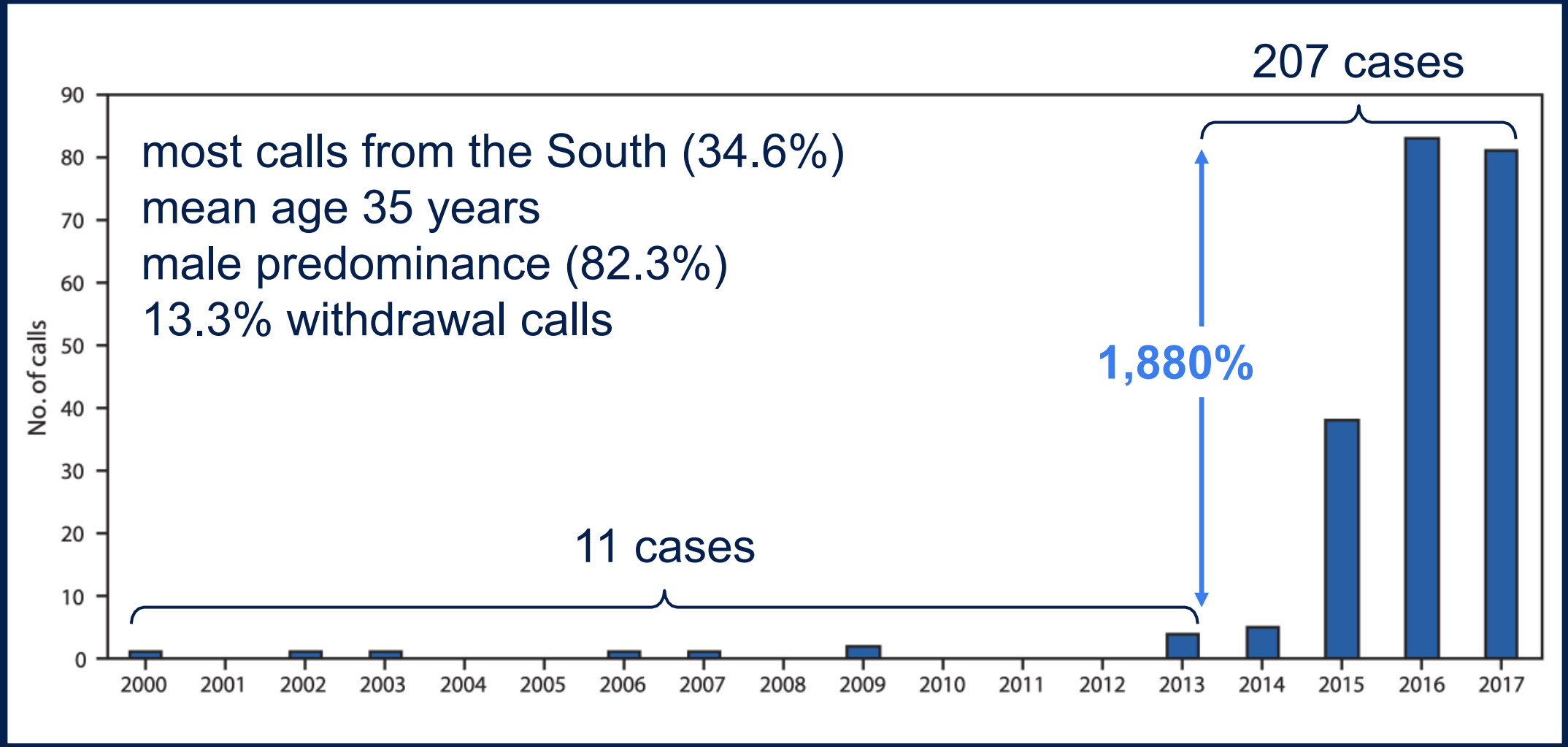
tolerance and withdrawal with long-term use

Clinical Effects

- toxicity is variable and atypical for opioid agonists
  - **neuro**: **agitation** (21.9% – 33.1%) or **sedation** (21.1% – 27.3%); confusion (13.2% – 16.7%)
  - **cardiac**: **tachycardia** (24.7%), **HTN** (11.4% – 14.7%), conduction delays (4.4%)
- respiratory depression (5.3% - 6.7%), miosis (1.8%), and seizures (2.4%) were uncommon
  - frequent co-ingestants (~44%): phenibut, ethanol, benzos, opioids

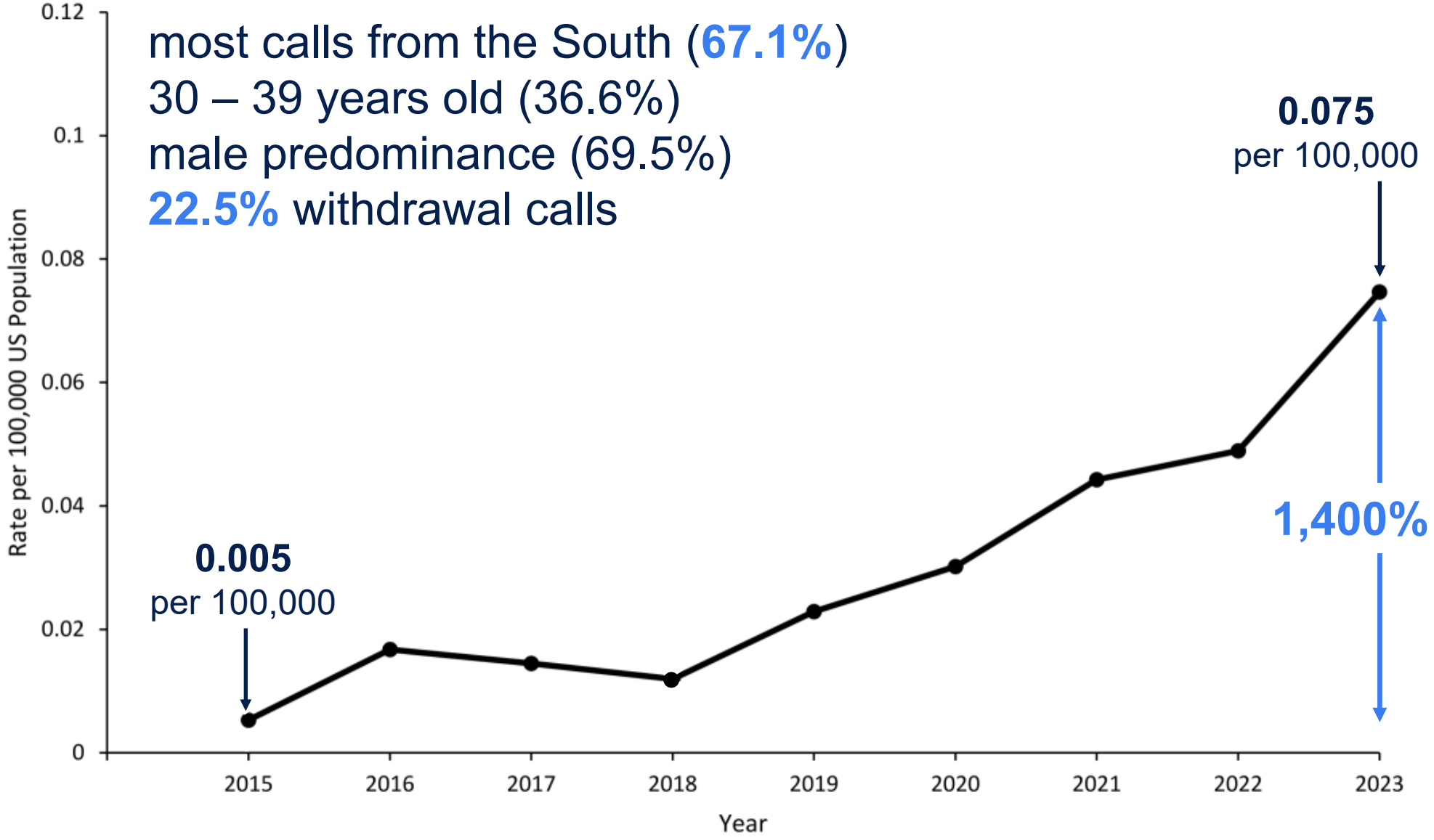
El Zahran T, et al. (MMWR 2018); Quadir M, et al. (J Med Toxicol 2025)

Tianeptine Exposure Trends



El Zahran T, et al. (MMWR 2018)

most calls from the South (**67.1%**)
30 – 39 years old (36.6%)
male predominance (69.5%)
22.5% withdrawal calls



Quadir M, et al. (J Med Toxicol 2025)

What Is Driving the Increase?

- readily available at gas stations, smoke shops, online markets
  - "gas station heroin"
  - shift from "unintentional" to "intentional" exposures

	El Zahran *et al.* (2018)		Quadir *et al.* (2025)
unintentional	54.6%	→	4.8%
intentional	10.5%	→	**65.2%**

- state-to-state variability in regulation
- not detected on routine drug screening

Can We Test for It?

✗ **Standard Immunoassay**

Not detected on routine drug screen panels

✗ **Opioid or TCA Screen**

No cross-reactivity; will not trigger a positive result

✓ **Definitive Testing**

LC/MS-MS (targeted) or HRMS (retrospective identification)

Appropriate Specimens

Urine:
preferred matrix for detection

Serum:
useful for quantification or when urine is unavailable

Krotulski AJ, et al. (J Anal Toxicol 2018)

Detection Window

Tianeptine has a **short elimination half-life**, which significantly **limits the detection window**. However, active metabolites extend the period during which the compound may be identified.

~2.5h

Half-life (parent compound)

Rapid elimination of tianeptine itself; metabolites persist longer

24–72h

Detection Window

Approximate window in urine following last use, dependent on dose and metabolite formation

Analytes: tianeptine (parent compound) ± active metabolites (MC5, MC7). Targeted LC-MS/MS assays should include metabolite panels to maximize sensitivity.

Dempsey SK, et al. (J Anal Toxicol 2017); Grislain L, et al. (Drug Metab Dispos 1990)

What Do We Do About It?

patient education

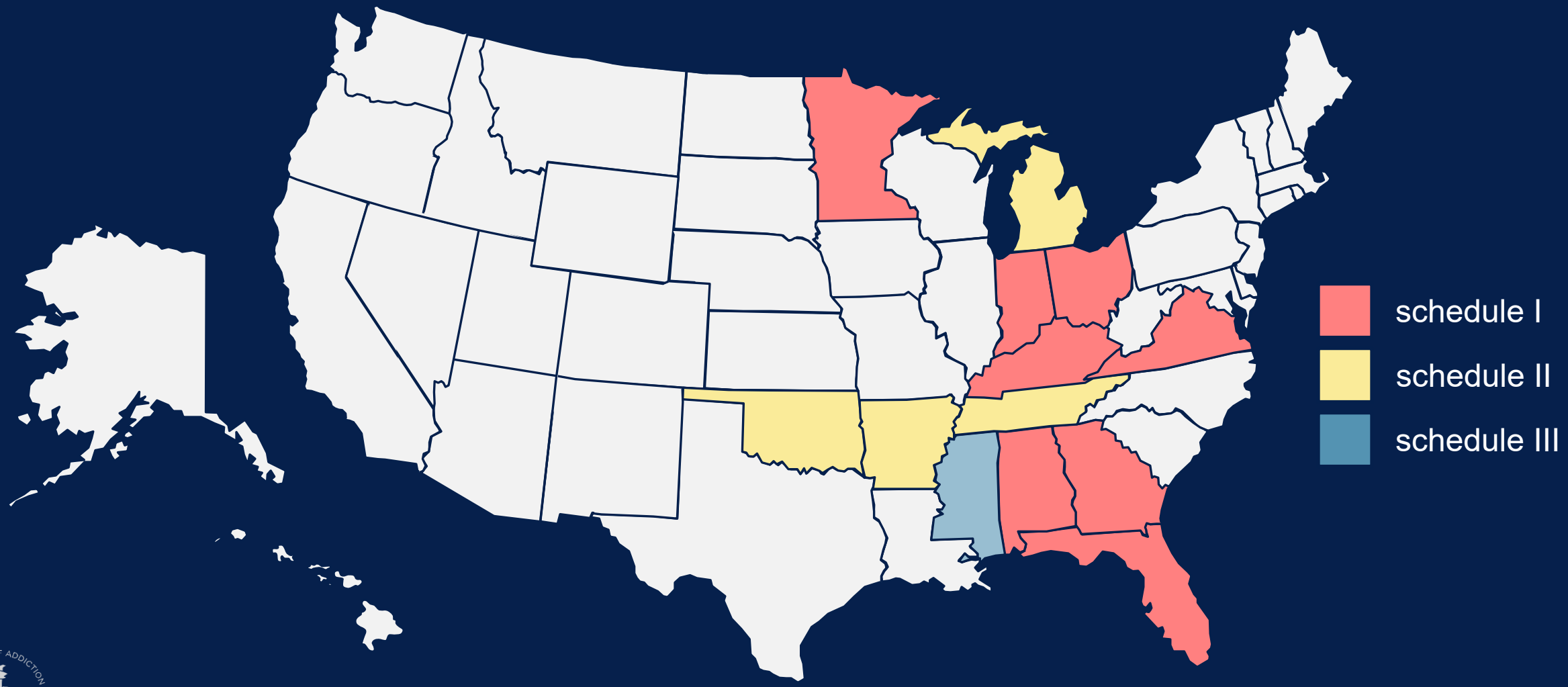
mislabeling & batch variability common
risks of co-exposures
discuss recalls & regulatory status
offer addiction treatment referral

advocacy

state example: Alabama
2018 – 2021: **1,414%** increase
Schedule I in November 2021
2021 – 2023: **75%** decrease

Quadir M, et al. (J Med Toxicol 2025)

State-Level Scheduling of Tianeptine



North Carolina General Assembly (2024)

Case 2

43-year-old woman with a history of alcohol use disorder presents to the ED with marked sedation.

Case 2

naloxone 4mg IN

naloxone 2mg IV

Case 2: The Next Day

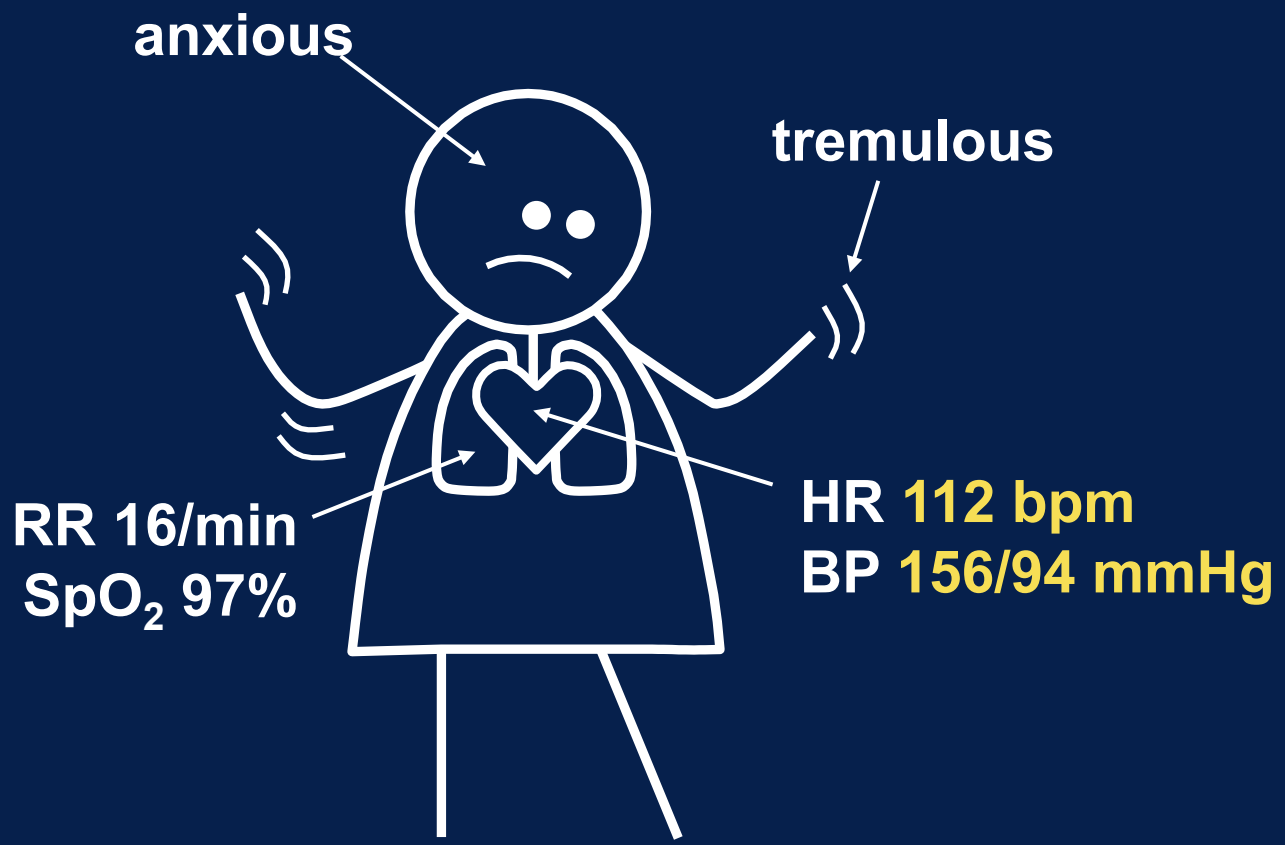


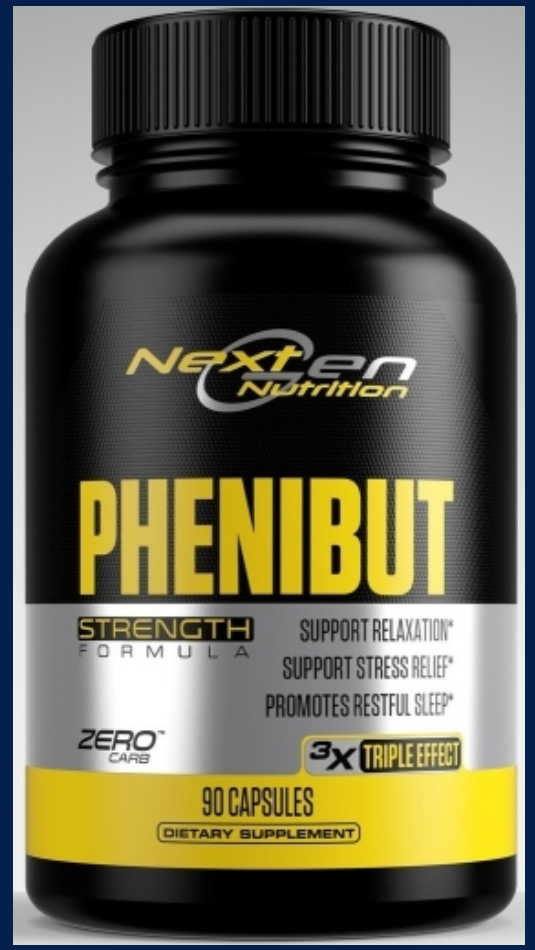
image credit: hopeharborwellness.com

What Could This Be?

- → presents with sedation that does not respond to naloxone
- → modest effect on vital signs (slightly decreased BP and RR)
- → recovery period marked by anxiety, tremulousness, tachycardia, and hypertension
- → not EtOH withdrawal: several months with no alcohol consumption

This Case: Phenibut

- **$GABA_B$ receptor agonist**
  - sold as a “dietary supplement”
  - structurally similar to baclofen
- purported effects:
  - nootropic
  - anxiolytic
  - **“natural” or “alternative” detox remedy for alcohol or benzo use**
  - “exercise recovery booster”



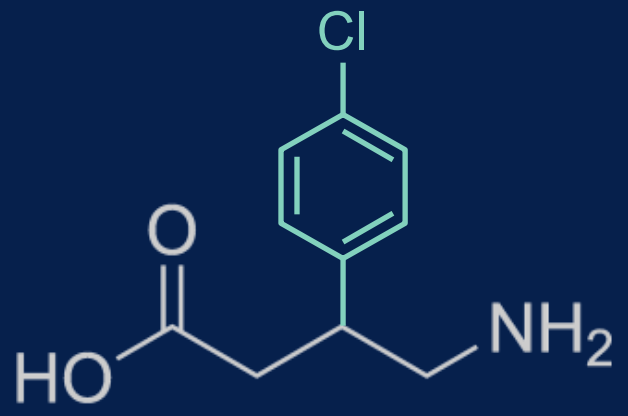
Benarroch EE (Neurology 2012); Lapin I. (CNS Drug Reviews 2001); Weleff J, et al. (J Addict Med 2023)
image credits: https:/northeastnutrition.net

Clinical Effects

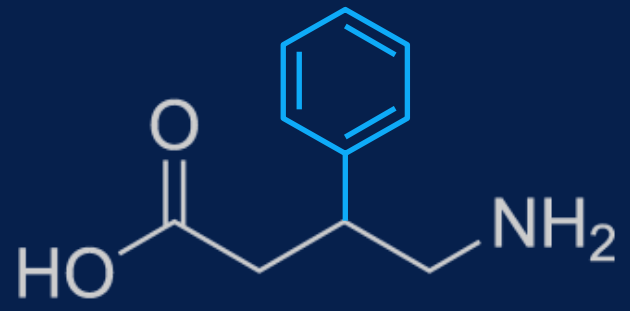
Primary mechanism: **$GABA_B$** receptor agonist

sedation, relaxation → CNS & respiratory depression

GABA



baclofen



phenibut

Clinical Effects

- Looks like baclofen overdose & withdrawal
  - agitation, confusion, CNS depression
  - seizures
  - tachycardia, hypertension

- Other GABA analogues have similar effects but different pharmacokinetics
  - GHB / GBL / 1,4-BD
  - tolibut
  - main differences are variable potencies (e.g., baclofen >> phenibut potency) and duration of action

Available Formulations

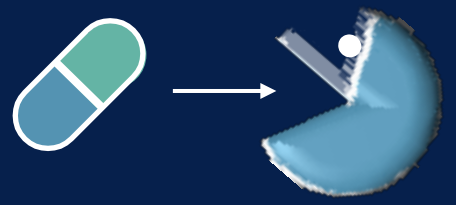
powder

capsules

Phenibut Use Patterns

75 – 81%

31 years
average age



20 – 30 grams
vs. "recommended" dose:
250 – 750mg, 2 – 3x daily

1 in 8
of exposures resulted in major effects

5 – 8 days
hospital length of stay

40 – 63%
combine use with other substances

Phenibut Exposure Trends

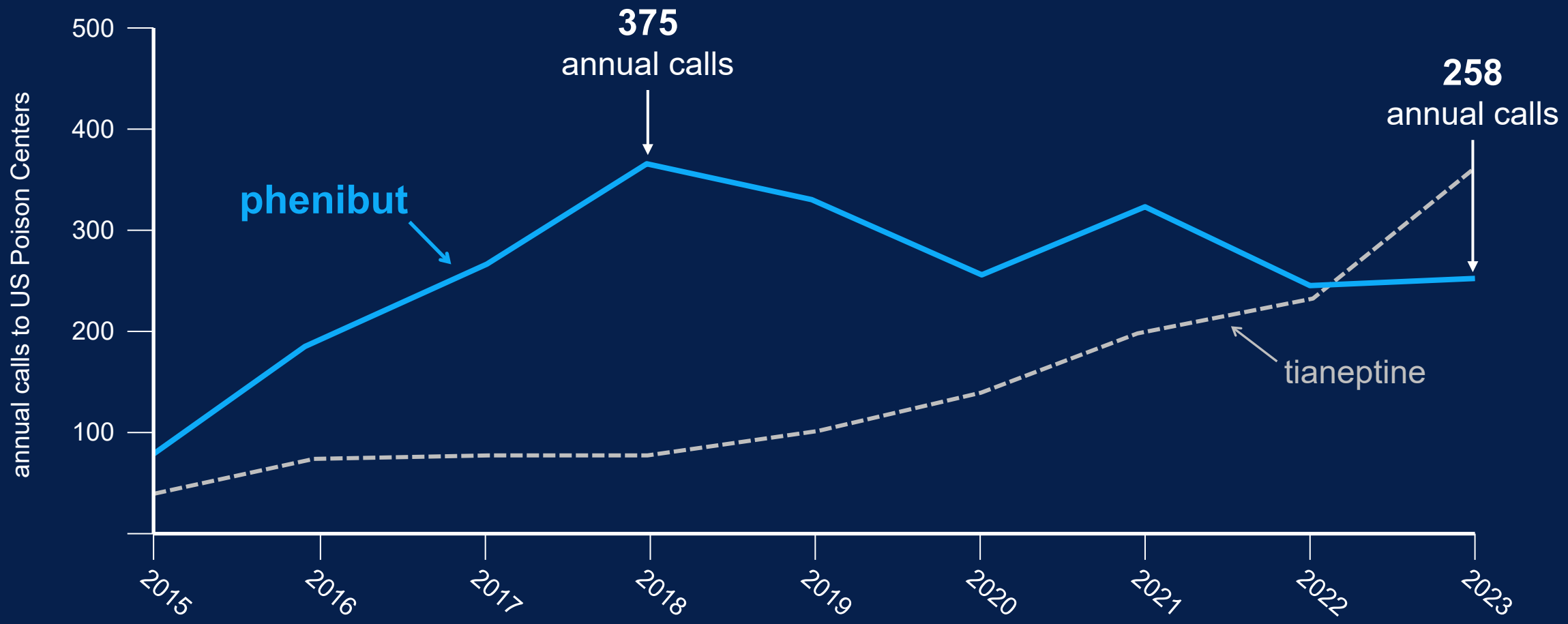


figure adapted from: Gummin DD, et al. (Clin Tox 2024)

Can We Test for It?

✗ **Standard Immunoassay**

Not detected on routine drug screen panels

✗ **“Expanded Tox Screen”**

Almost never available as an in-house test

✓ **Definitive Testing**

LC/MS-MS (targeted) or HRMS (non-targeted approach)

Appropriate Specimens

Serum / Plasma (preferred)

Urine

Gurley BJ & Koturbash I (Basic Clin Pharmacol Toxicol 2024)

Detection Window

phenibut has a half-life of about 5 hours

65% of a dose is excreted unchanged in the urine

detection relies on identifying the **parent compound** itself

12 – 24h

Serum Detection Window

possibly up to 48 hours in higher-dose exposures

24 – 48h

Urine Detection Window

estimated; limited published data available

Clinical effects may outlast measurable levels.

Most cases in clinical toxicology are managed without laboratory confirmation — awareness of testing limitations is critical for accurate clinical assessment.

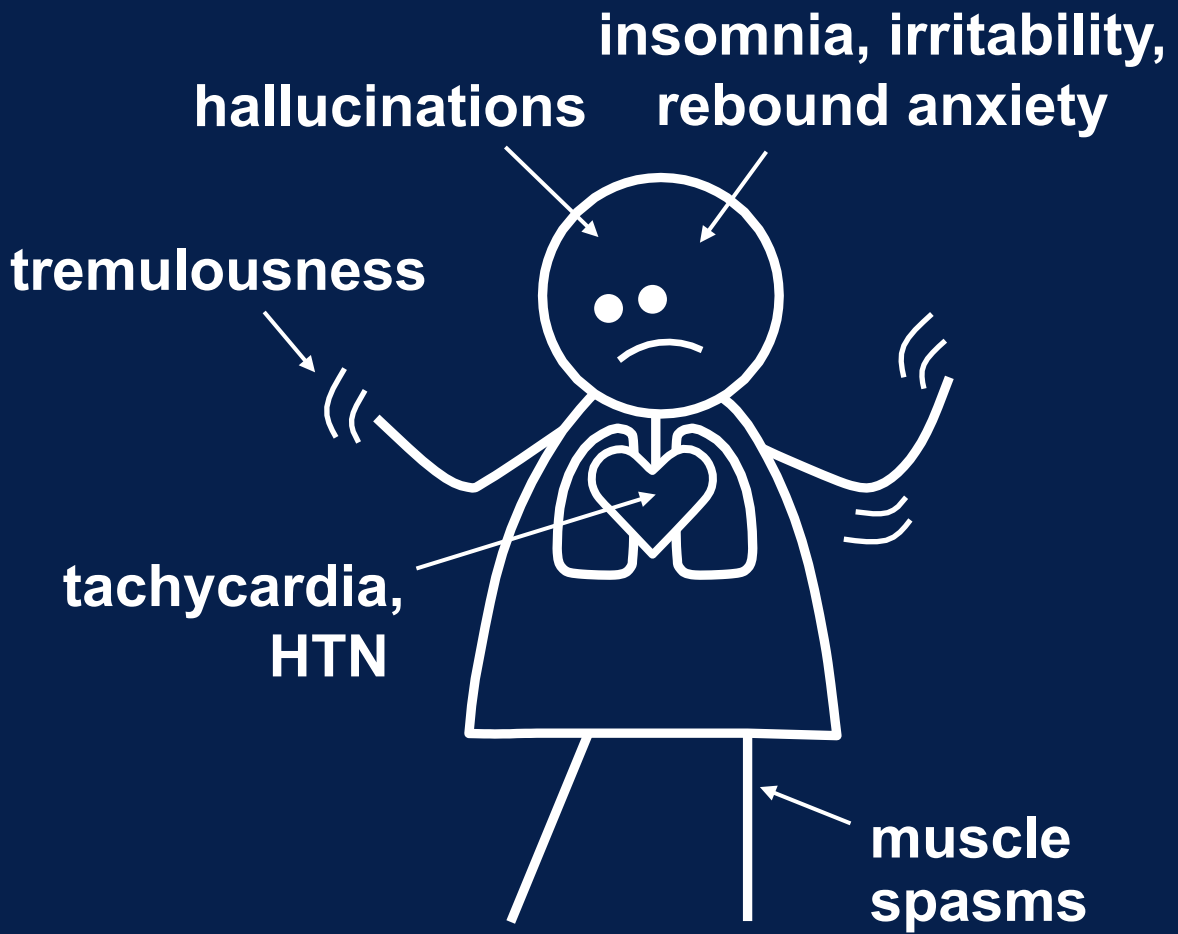
Phenibut Withdrawal

- may be severe, can last 2 – 3 weeks
- data comparing treatments limited
- case reports / series describe:
  - baclofen taper

    $GABA_B$ agonist
  - phenobarbital taper

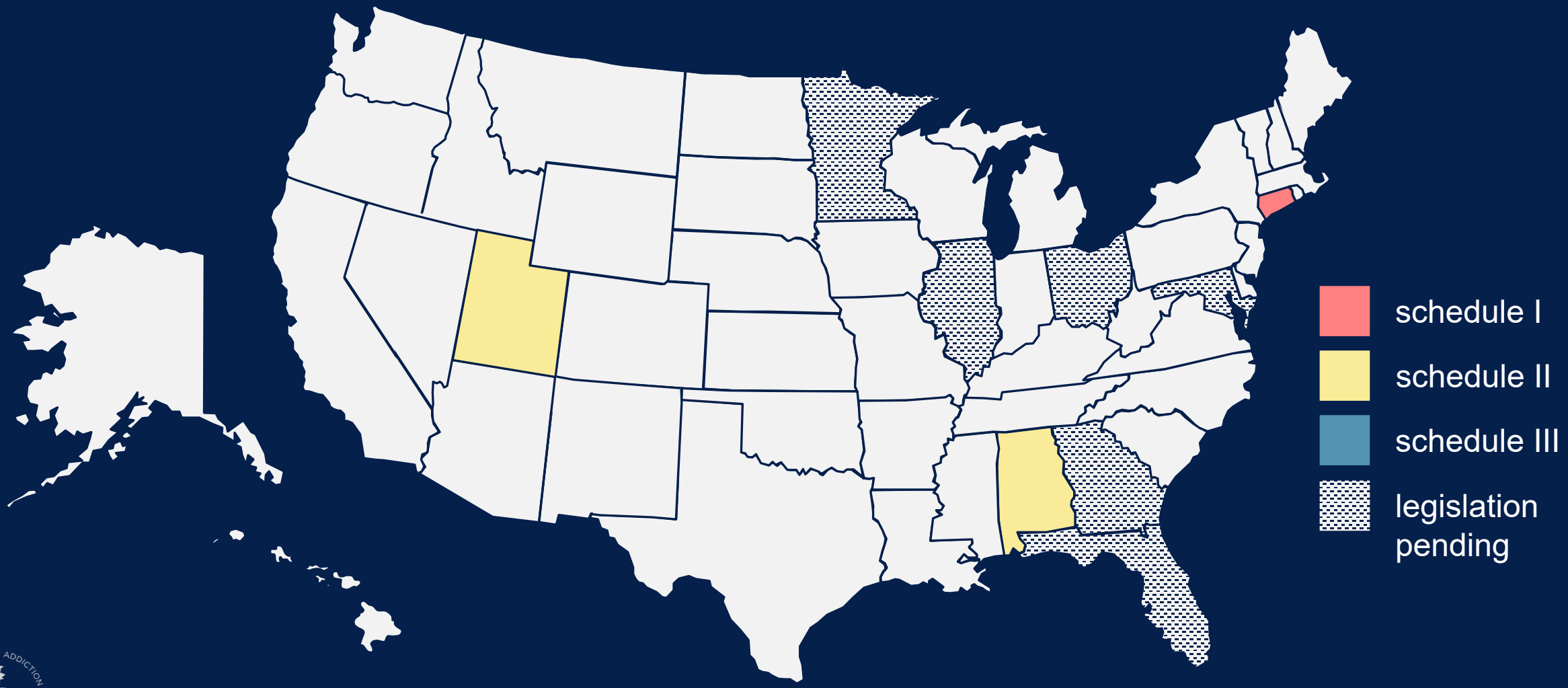
    $GABA_B$ agonist
  - benzodiazepine taper

    $GABA_A$ agonist—may need higher-potency agents (e.g., clonazepam)



Esposito CM, et al. (Front Psychiatr 2021); Hardman MI, et al. (Bosnian J Med Sci 2019); Hogberg L, et al. (J Subs Use 2013); Mash JE & Leo RJ. (Prim Care Comp CNS Disorders 2020); Roopa S, et al. (Prim Care Comp CNS Disorders 2021)

State-Level Phenibut Regulation

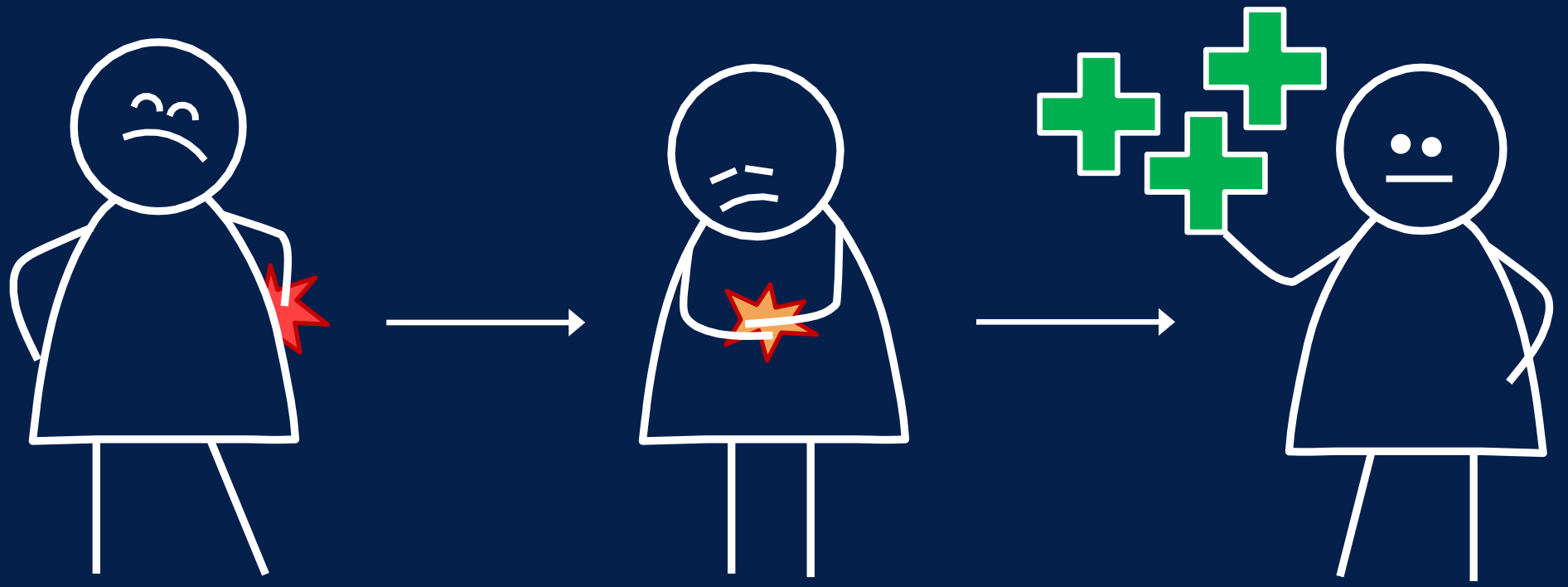


Case 3

38-year-old construction worker presents to the ED with fatigue, itching, and yellowing of the eyes.

case based on: Fernandes CT, et al. (J Investig Med High Impact Case Rep 2019)

Case 3: Additional History



3 months ago:
work injury,
Rx oxycodone

nausea, vomiting,
abdominal pain,
body aches

“natural remedy” for pain
needs escalating doses
“just to feel normal”

case based on: Fernandes CT, et al. (J Investig Med High Impact Case Rep 2019)

Case 3: Initial Evaluation

AST/ALT: 48 / 62 IU/L
Alk Phos: 259 IU/L
T Bili: 22.8 mg/dL

case based on: Fernandes CT, et al. (J Investig Med High Impact Case Rep 2019)

What Could This Be?

→ previously healthy person taking a “natural” remedy x 2 months

→ tolerance and withdrawal symptoms

→ now with itching, scleral icterus, and cholestatic hepatic injury

This Case: Kratom

- plant product: *Mitragyna speciosa*
  - active alkaloid: **mitragynine**
  - ~10 – 30 mg mitragynine / gram of leaf material
  - **7-hydroxymitragynine** (“**7-OH**”): minor component
- purported effects:
  - self-treatment of depression / anxiety
  - **“natural” treatment for opioid withdrawal**
  - pain relief

Vadiei N, et al. (Curr Psychiatry Rep 2025)

Clinical Effects

5 - 10 mg
mitragynine

kratom leaf chewed
or brewed into tea

mild stimulant effects

α_1 partial agonist (?)
α_2 antagonist (?)

μ opioid receptor
(partial agonist)

δ/κ opioid receptors
(weak antagonists)

>40 mg
mitragynine

powders or
capsules

1 – 2 grams leaf material

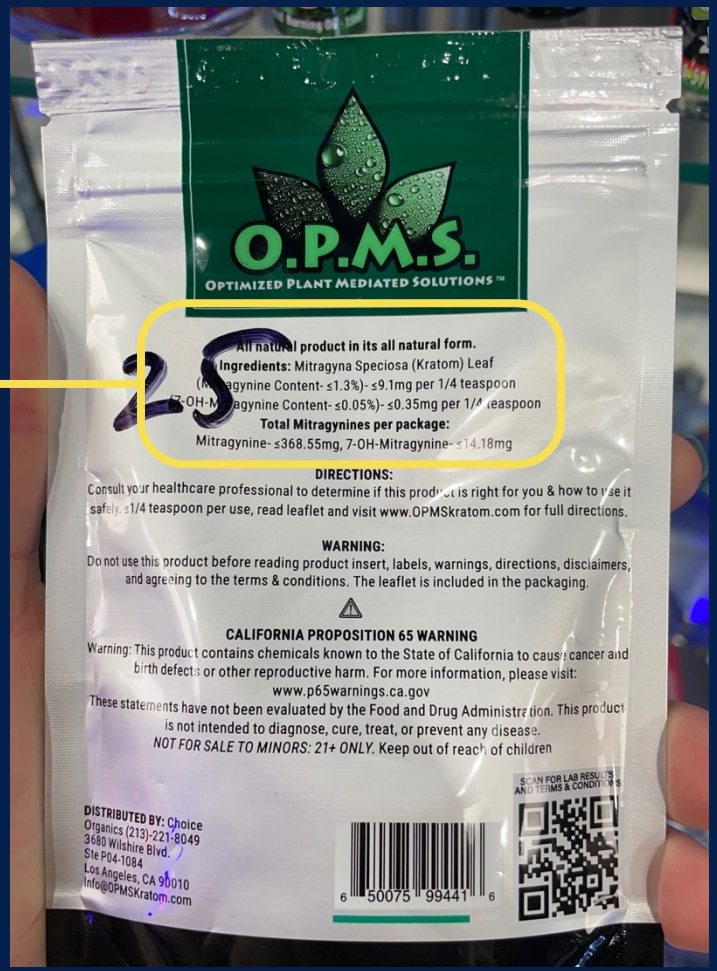
opioid effects

Available Formulations

mitragynine
100 mg / 15 mL
(1 serving)

mitragynine
≤9.1 mg / 0.25 tsp
(1 serving)

7-OH
≤0.35 mg / 0.25 tsp
(1 serving)



Kratom Use Patterns

71%

31 years
average age

5 grams

typical “recommended” dose of leaf material

(50 – 150mg mitragynine)

35%

combine use with other substances

Post S, et al. (Clin Tox 2019); Towers EB, et al. (MMWR 2026); Vadiei N, et al. (Curr Psychiatr Rep 2025)

Kratom Exposure Trends

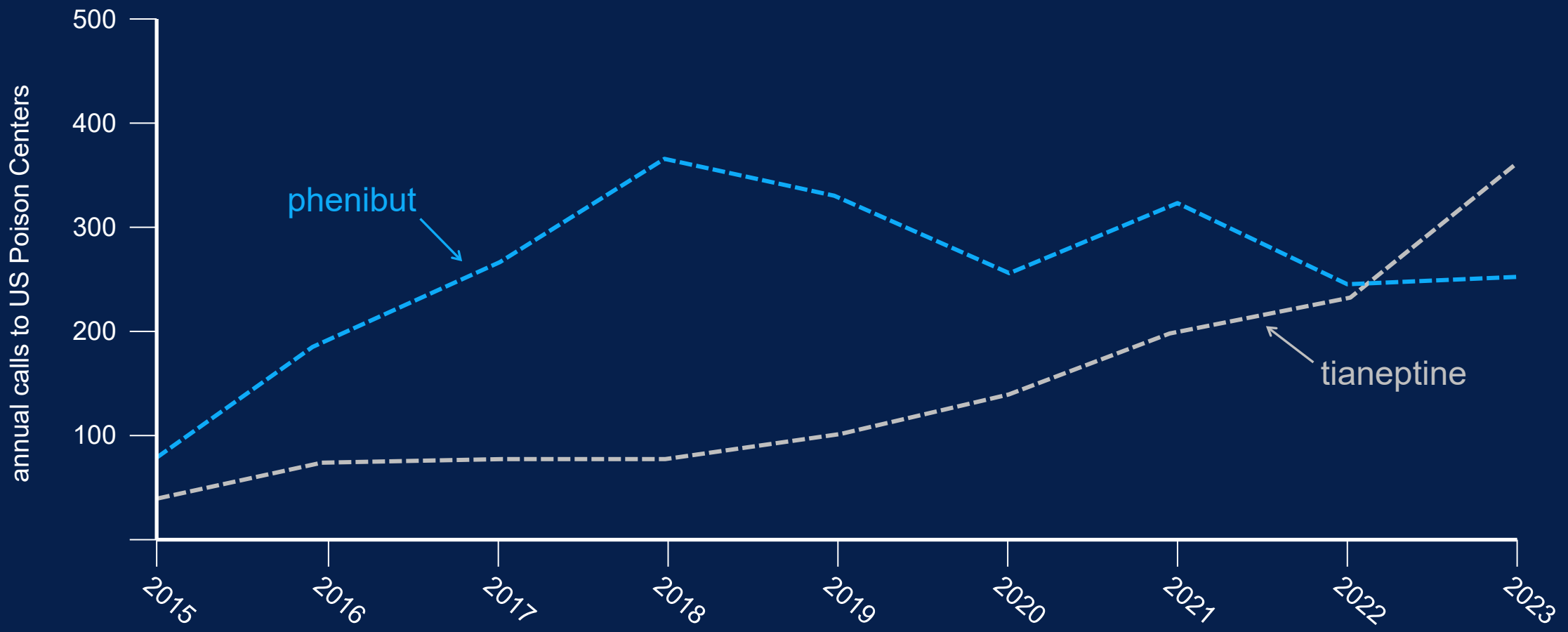
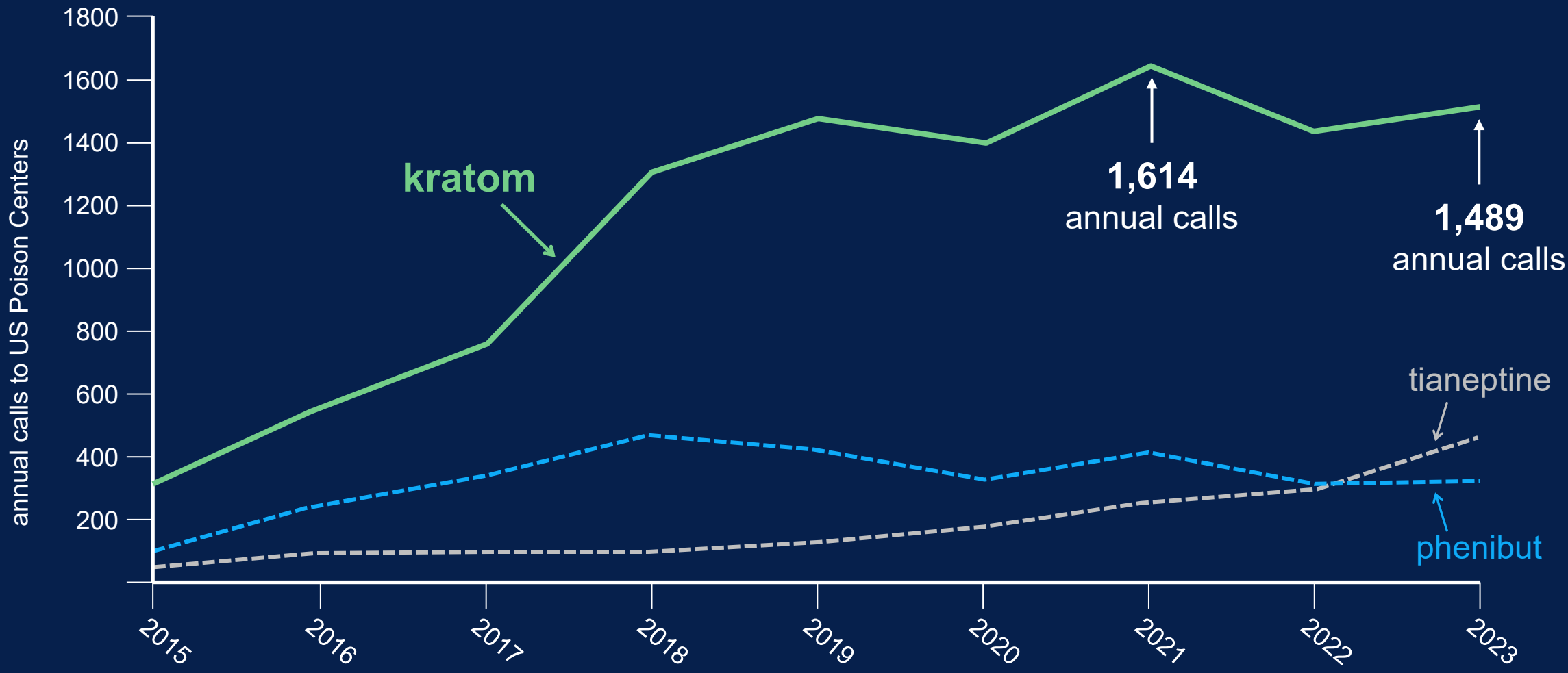


figure adapted from: Gummin DD, et al. (Clin Tox 2024)

Kratom Exposure Trends



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Kratom Exposure Trends

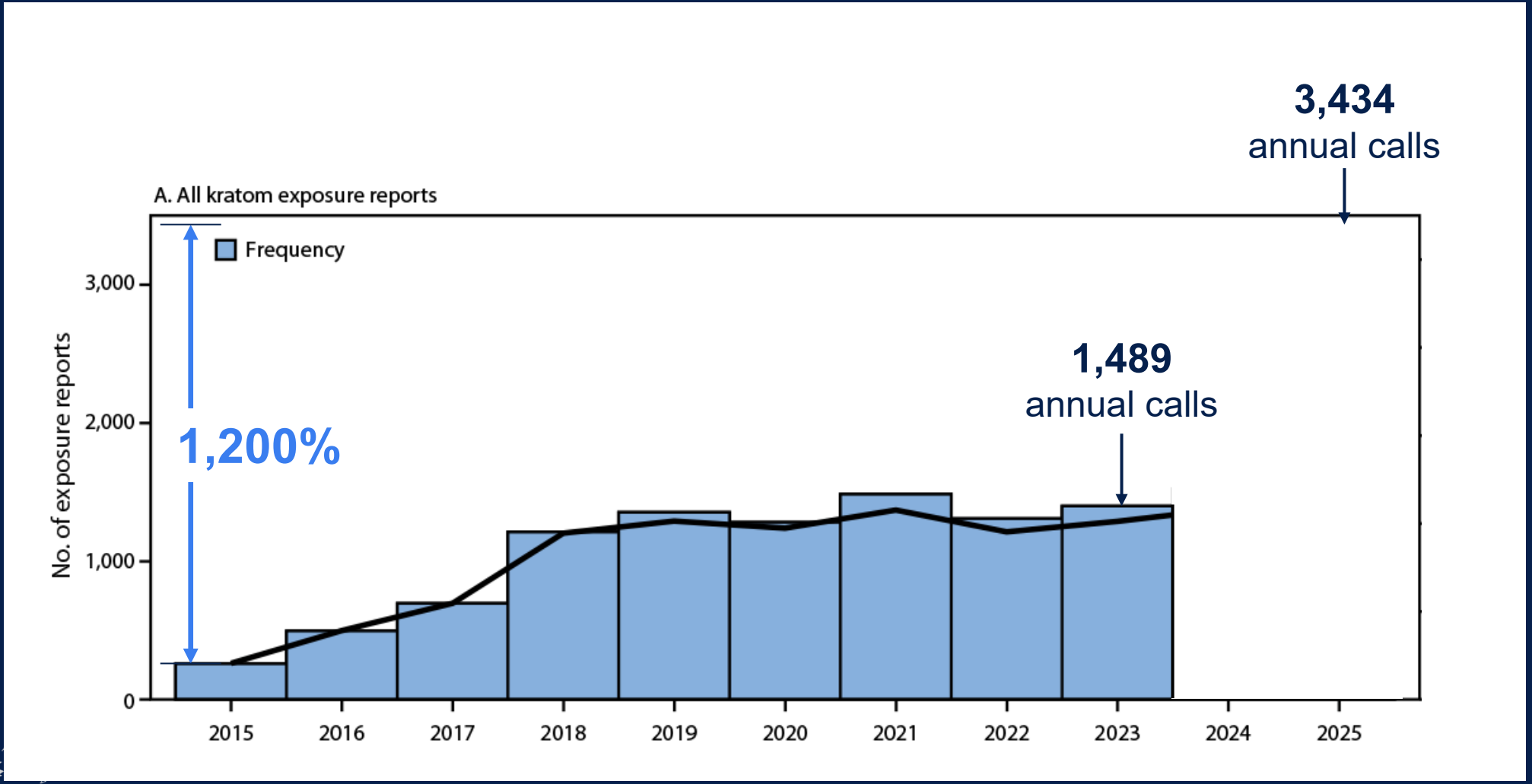
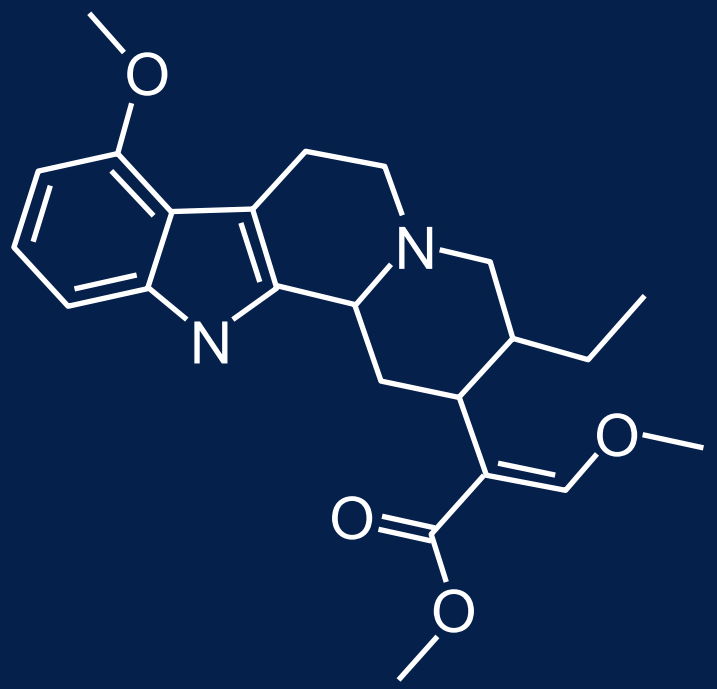
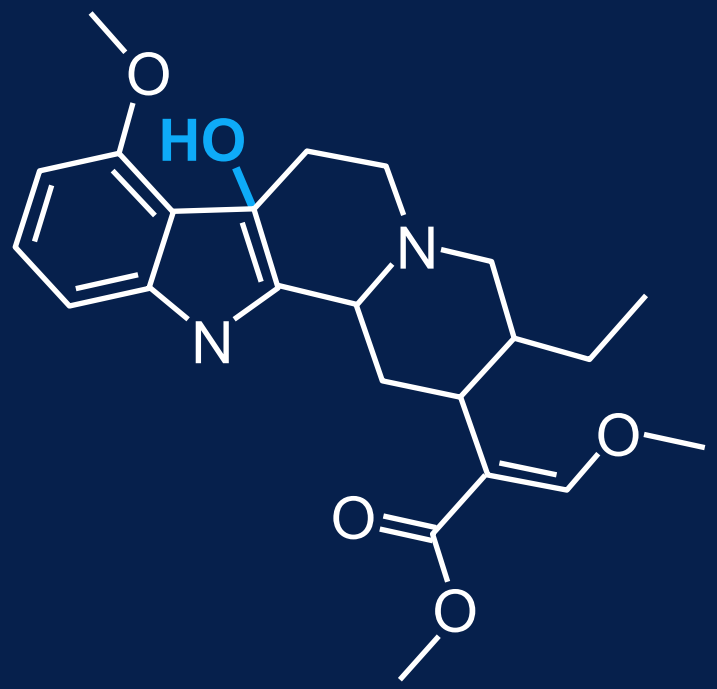


figure adapted from: Towers EB, et al. (MMWR 2026)

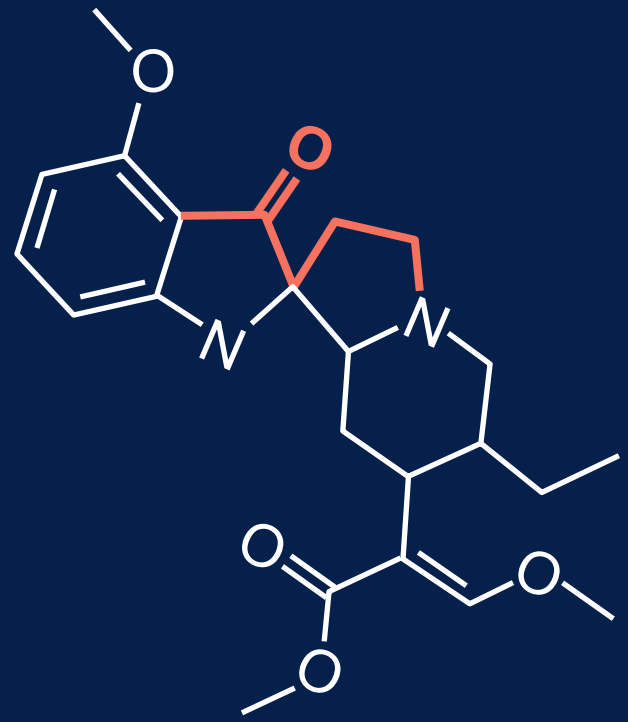
Newer Products



mitragynine



7-OH-mitragynine
("7-OH")

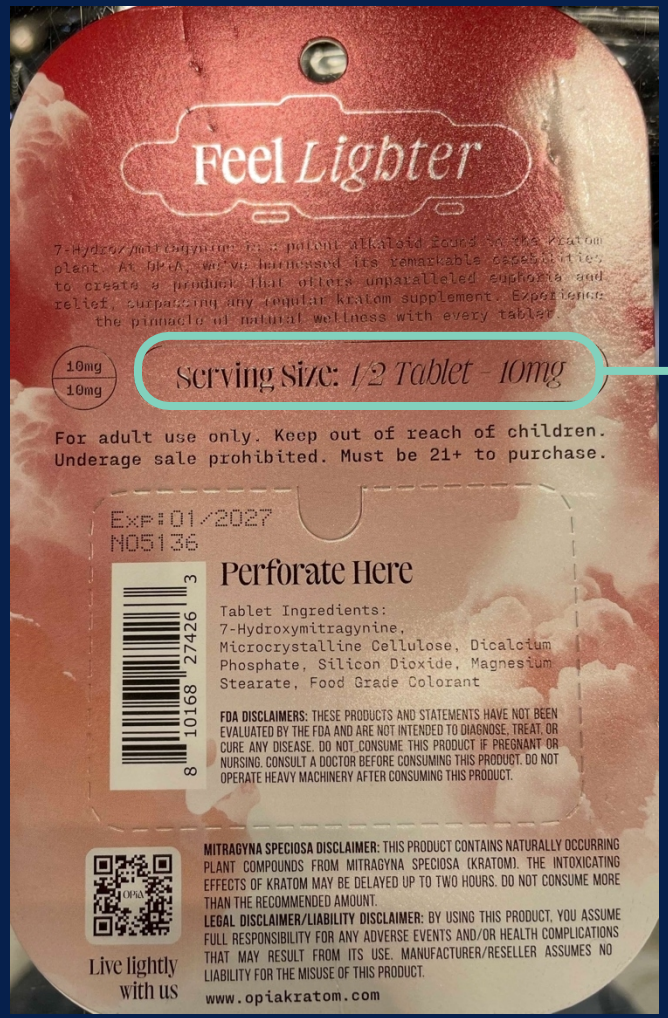


mitragynine pseudoindoxyl
("pseudoindoxyl")

Vadiei N, et al. (Curr Psychiatry Rep 2025); White CM, et al. (Subst Use Misuse 2025)

Available Formulations

7-OH
80 mg
(per package)



7-OH
½ tab (10 mg)
(1 serving)

White CM, et al. (Subst Use Misuse 2025)

Can We Test for It?

✗ **Standard Immunoassay**

Not detected on routine drug screen panels

✗ **Opioid Immunoassays**

Does not cross-react despite mu-opioid agonist activity

✓ **Definitive Testing**

LC/MS-MS (targeted) or LC-HRMS (non-targeted)

Appropriate Specimens

Urine (most common)

Blood (forensic)

Oral Fluid (some labs)

Helander A & Rylski A (Drug Testing Anal 2023); Rhee J, et al. (J Anal Toxicol 2024)

Detection Window

mitragynine: wide variability in reported $t_{½}$ (3 – 24 hours)

highly lipophilic, accumulates with chronic use

after cessation, redistribution may prolong detection window

24h

Serum Detection Window

possibly longer with chronic use

1 – 3d

Urine Detection Window

chronic use may extend detection window to >5 days

analytes: mitragynine ± 7-hydroxymitragynine

much less information on 7-OH and pseudoindoxyl kinetics / testing

7-OH from dried kratom leaf: $t_{½}$ 5 – 25 hours, depending on chronicity of use

Huestis MA, et al. (Molecules 2024); Trakulsrichai S, et al. (Drug Des Devel 2015); Ya K, et al. (Asian J Psychiatr 2019)

Other Kratom Concerns

FDA Investigated Multistate Outbreak of Salmonella Infections Linked to Products Reported to Contain Kratom

FDA adds heavy metals contamination to its list of concerns about kratom

LiverTox

Clinical and Research Information on Drug-Induced Liver Injury

Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-.

Likelihood Score: B (likely cause of clinically apparent liver injury).

LiverTox (NIDDK / NIH 2026)

Back to Case 3: Hospital Course

- admitted for further evaluation
- next morning, patient is experiencing:
  - anxiety
  - insomnia
  - diaphoresis
  - *“I feel like I have the flu”*

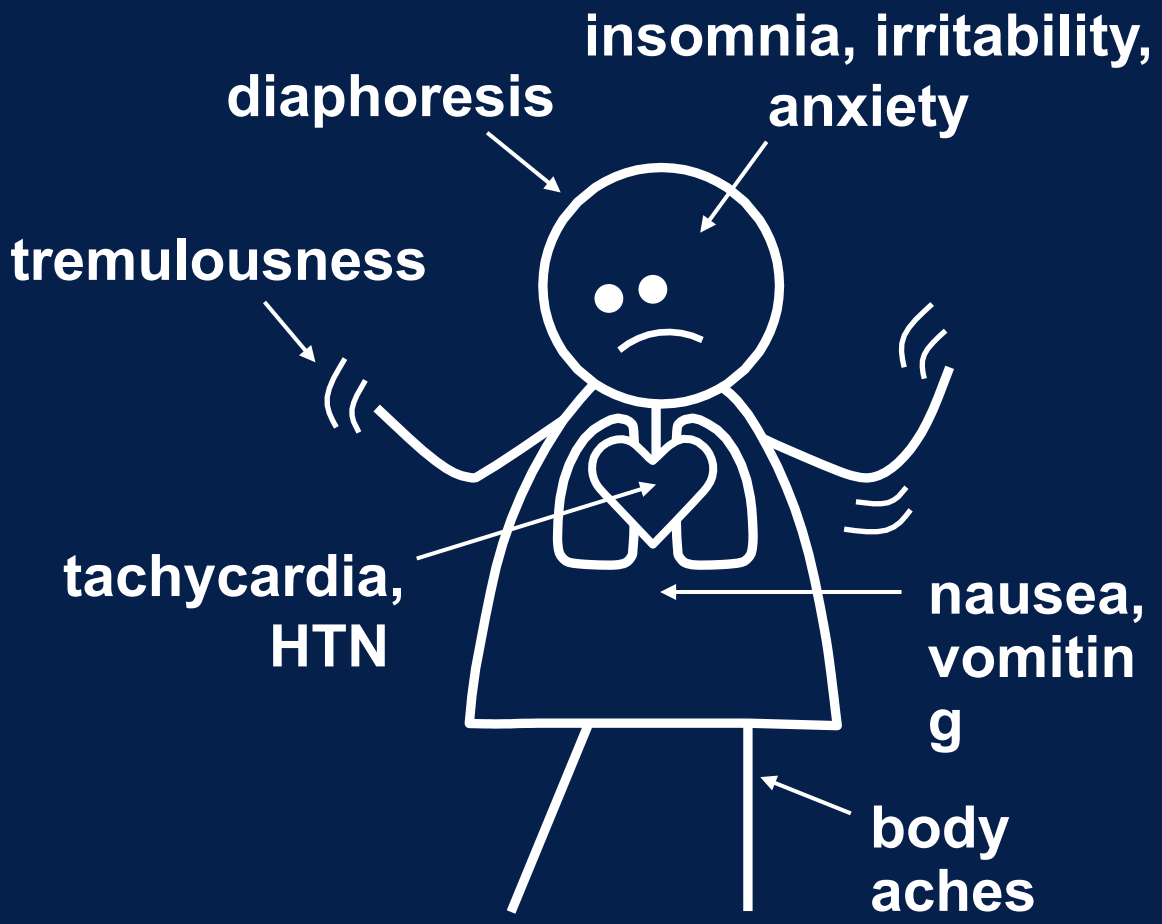
Kratom & Derivatives: Withdrawal

typical opioid withdrawal symptoms

±

heightened adrenergic state

(from α_1/α_2 receptor effects)



Some Management Options

acute opioid withdrawal

- **buprenorphine**
  2– 8mg SL based on initial COWS
- **methadone**
  10 – 20mg PO x 1
  reassess 2 hours later
  may give 10mg additional prn
- **adjunct therapies**
  (e.g., clonidine, hydroxyzine, ondansetron, NSAIDs, acetaminophen, dicyclomine)

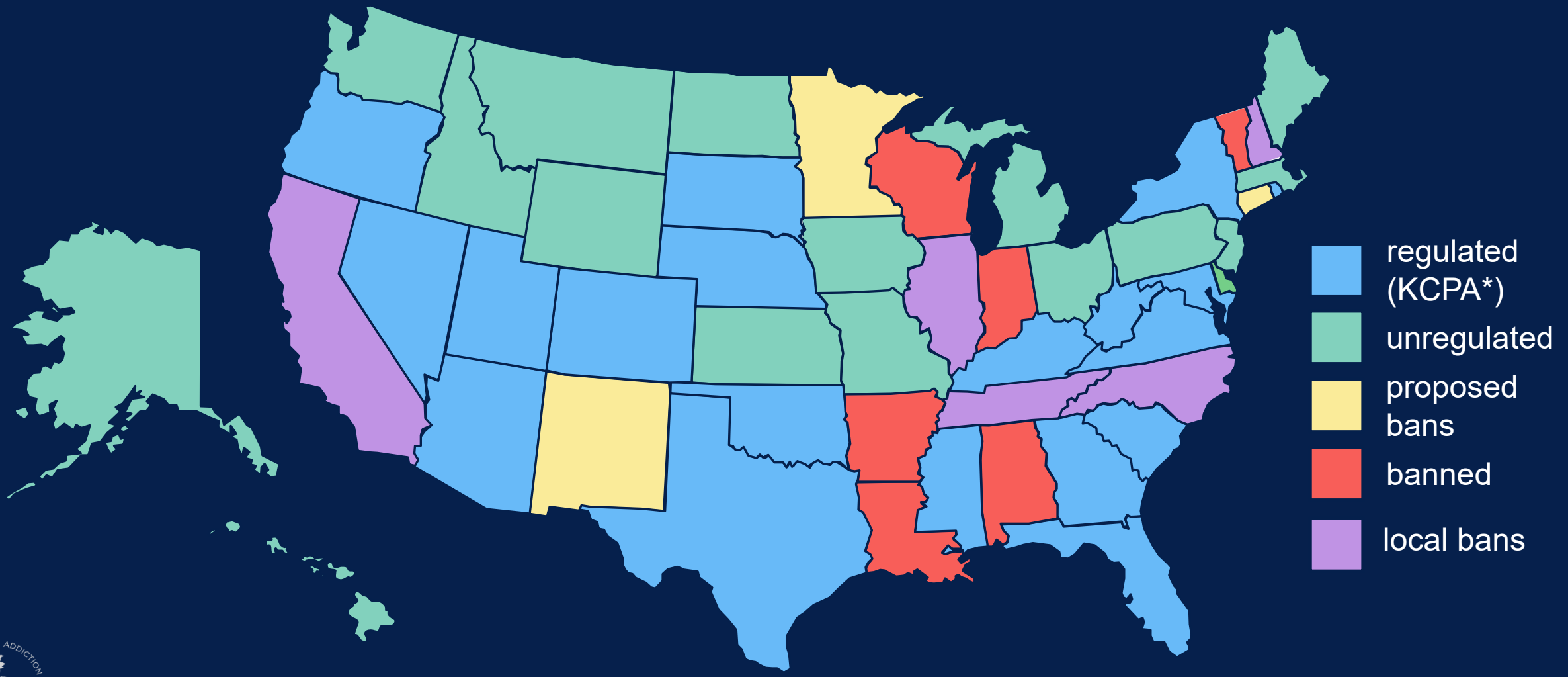
long-term management

limited data

- **buprenorphine**
  *patients taking **7-OH** or **pseudoindoxyl** may need doses at the upper end of typical dosing range*
- **methadone**
  usual dose titration and engagement in OTP

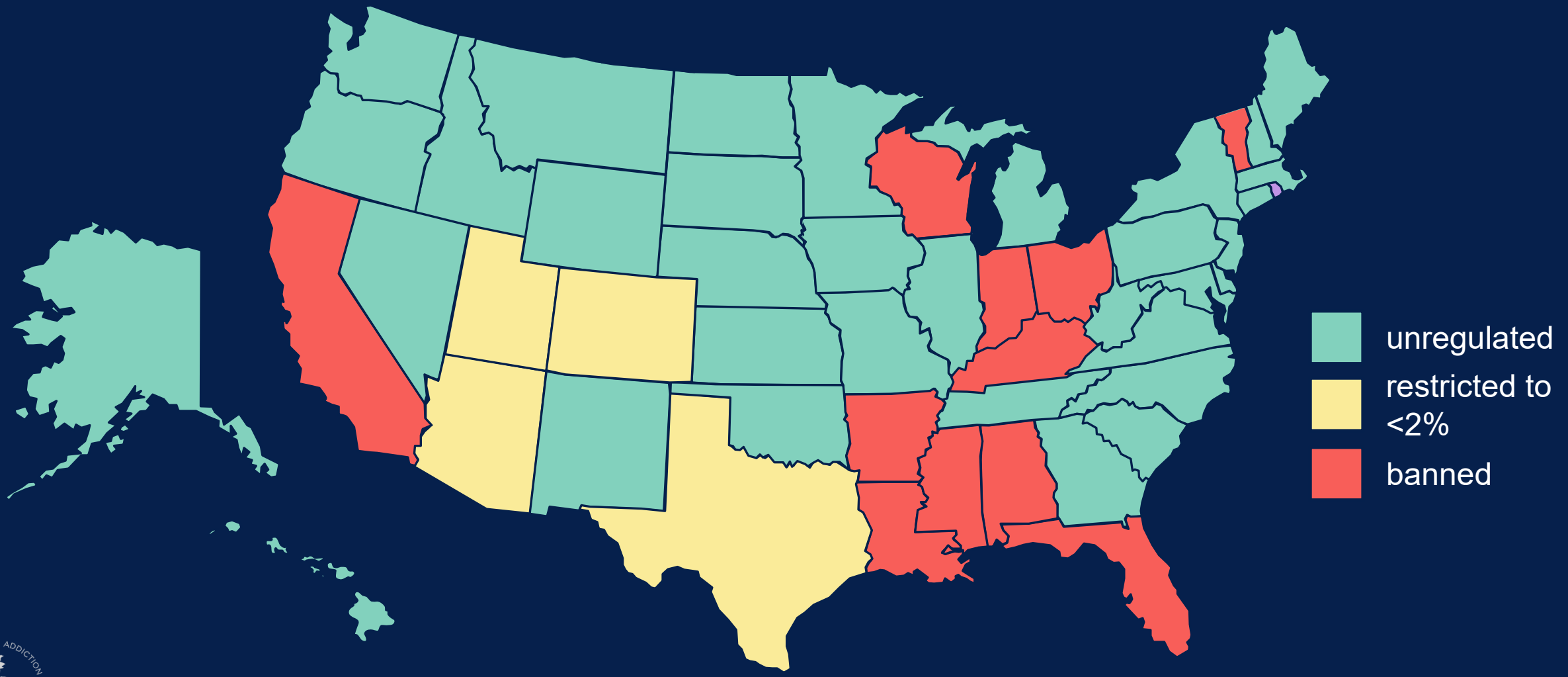
Broyan VR, et al. (Subst Abuse 2022); Sherrick RC (J Addict Med 2026)

State-Level Kratom Regulation

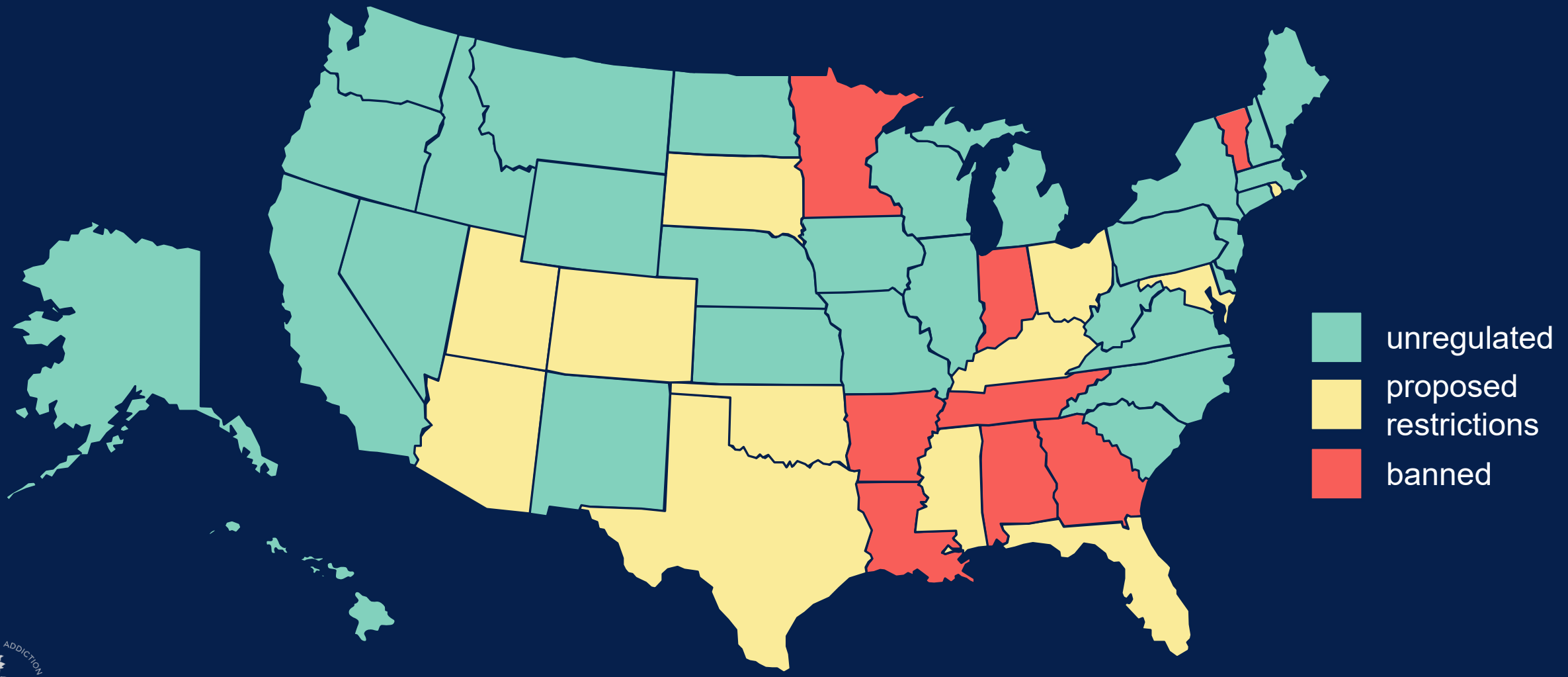


*Kratom Consumer Protection Act

State-Level 7-OH Regulation



State-Level Pseudoindoxyl Regulation



Case 4

23-year-old man with no medical history presents to the ED with cyanosis after ingesting a substance that he believed to be alcohol at a concert.

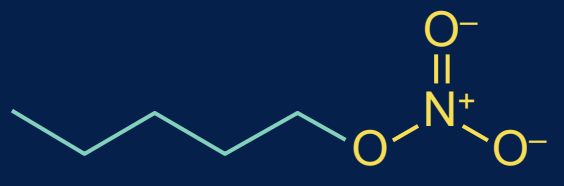
Case 4

What Could This Be?

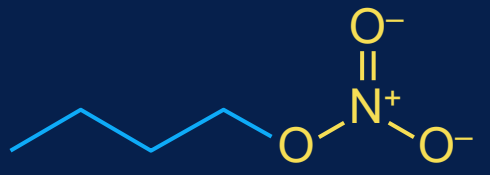
- → previously healthy young man drinks an unknown substance
- → cyanosis and low SpO_2 without significant respiratory distress
- → hypotension
- → normal mental status

This Case: Akyl Nitrite "Poppers"

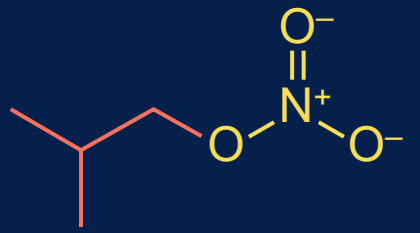
- volatile, inhaled compounds
  - rapid pulmonary absorption and conversion to nitric oxide (NO)
  - vasodilation & smooth muscle relaxation
  - originally used to treat angina (pre-1960's)
- now used for:
  - euphoric effect
  - relaxation of the anal sphincter during intercourse



amyl nitrite

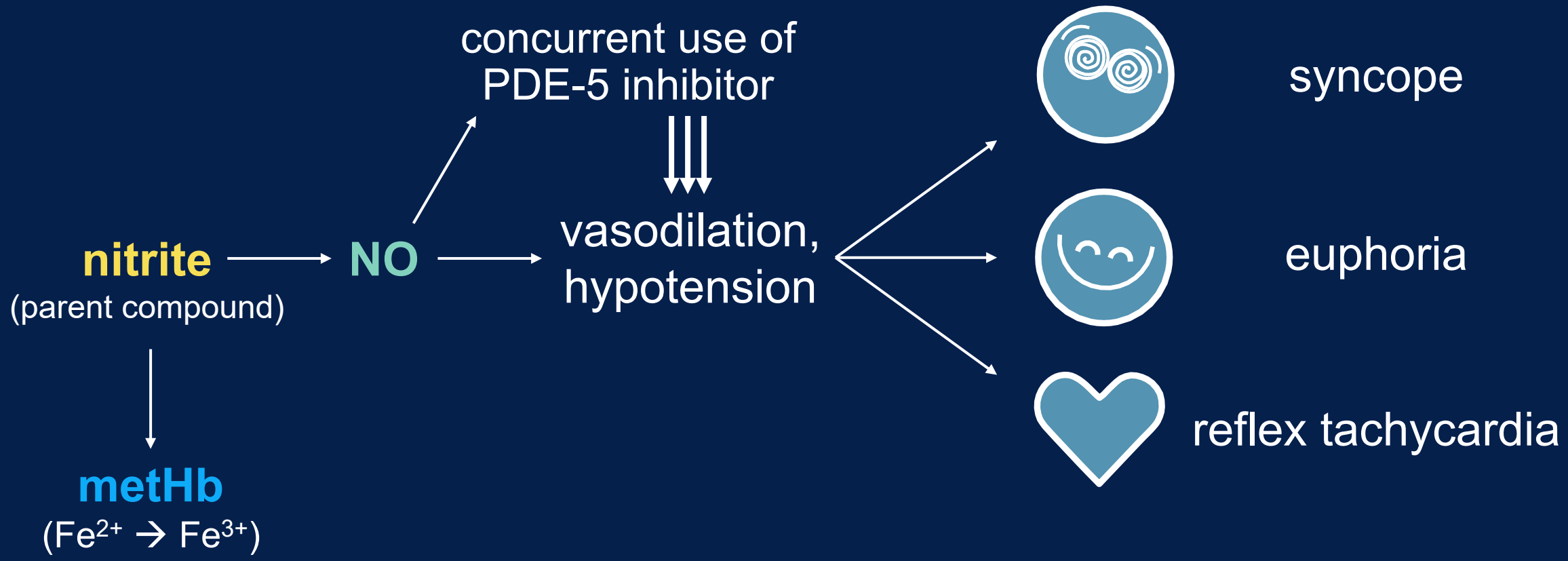


butyl nitrite



isobutyl nitrite

Clinical Effects



Available Formulations

image credits: https://talktofrank.com; www.menage.cz

Akyl Nitrates: Use Patterns

80 – 89%

18 – 25 years old

46%
inhalational use

56%
ingestion

Alkyl Nitrates Exposure Trends

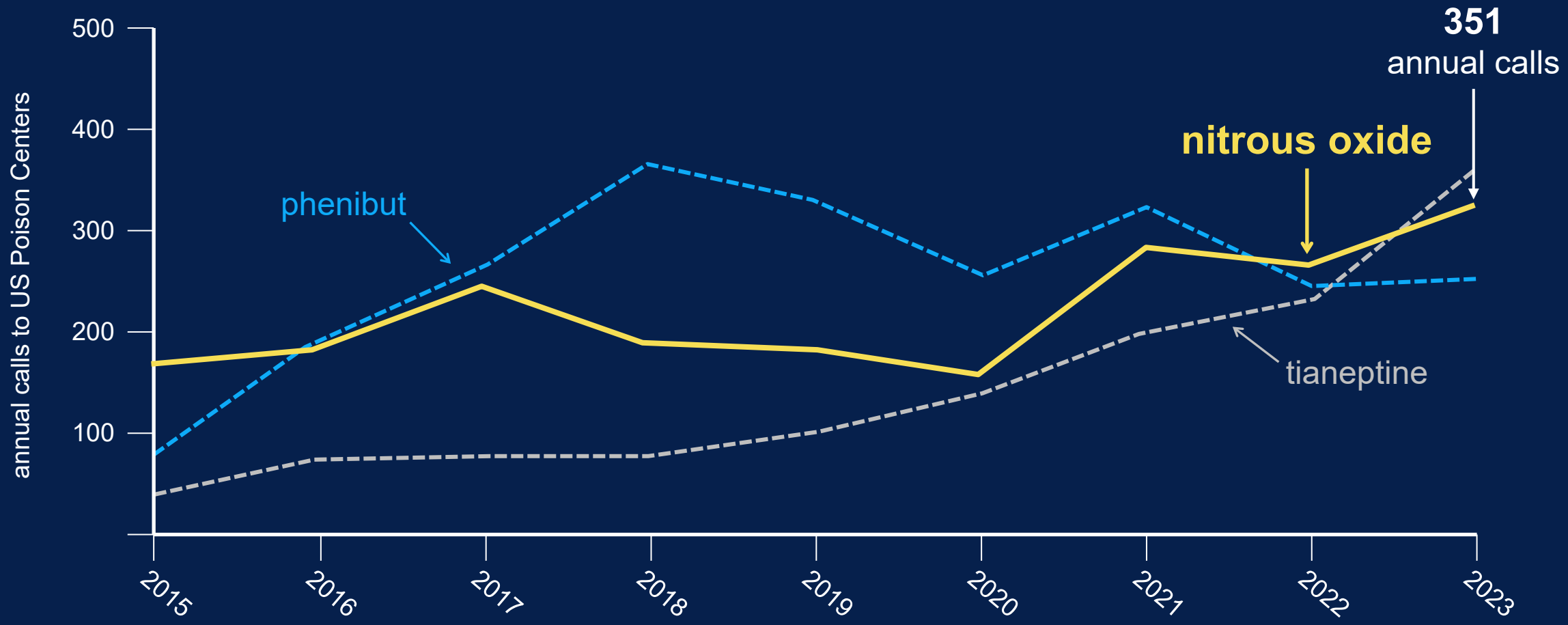


figure adapted from: Gummin DD, et al. (Clin Tox 2024)

Can We Test for It?

✗ **Standard Immunoassay**

Not detected on routine drug screen panels

✓ **Definitive Testing**

headspace GC-MS (primarily in forensic laboratories)

Appropriate Specimens

Blood

Vogt S, et al. (Toichem Krimtech 2015)

Detection Window

extremely difficult to detect

volatile, rapid metabolism to NO → very short $t_{½}$

minutes

Detection Window

parent compound rarely detected

12 – 36h

metHb may persist
12 – 36 hours
without treatment

*Diagnosis usually **clinical**, without confirmatory testing.*

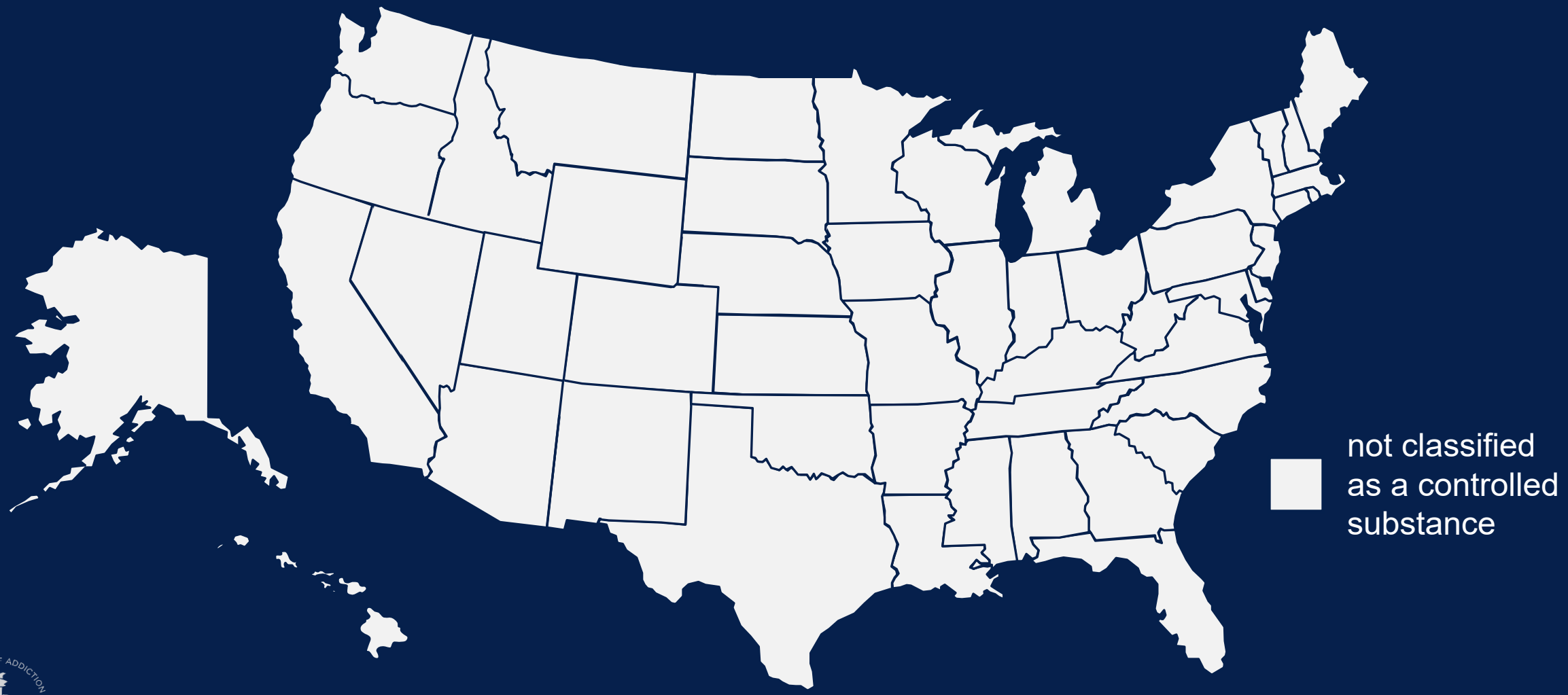
Clues: vasodilation and/or methemoglobinemia after ingestion or inhalational exposure.

What Can We Do About It?

mostly acute management

- **hypotension**
  supportive care: IVF, vasopressors
- **methemoglobinemia**
  methylene blue, 1 – 2 grams IV
- **ocular toxicity**
  can see partial to complete improvement with cessation of use

State-Level Regulation of Alkyl Nitrates



www.fda.gov; https://prowlerpoppers.co.uk; https://destiny-rc.com

Final Takeaways

- → consider “gas station products” when routine tox screens are negative
- → use of these agents is increasing overall, with wide variability in state-to-state regulation
- → patient counseling: risks of tolerance, withdrawal, contamination, and unique complications (e.g., hepatic injury, maculopathy)
- → definitive testing requires LC-MS/MS, GC-MS, or other techniques that may only be available in forensic or specialty labs

References

- *Abukahok N, Palamar JJ. Trends in Past-Year Use of Poppers Among New York City Nightclub Attendees, 2017-2024. Subst Use Addctn J, 2026; 47(2):409-417. doi: 10.1177/29767342251372314.*
- *Benarroch EE. GABAB receptors: structure, functions, and clinical implications. Neurology, 2012;78(8):578-84. doi: 10.1212/WNL.0b013e318247cd03.*
- *Bowery NG, Hill DR, Hudson AL. Characteristics of GABAB receptor binding sites on rat whole brain synaptic membrane. British Journal of Pharmacology. 1983;78(1):191–206.*
- *Broyan VR, Brar JK, Allgaier Student T, Allgaier JT. Long-term buprenorphine treatment for kratom use disorder: A case series. Subst Abus. 2022;43(1):763-766. doi: 10.1080/08897077.2021.2010250.*
- *Chen Y, Seto J, Obeng S, Mottinelli M, Mukhopadhyay S, Tyagi R, Hampson AJ, McCurdy CR, McMahon LR, Moniri NH, Canal CE. In Vitro Pharmacology of Mitragynine at α-Adrenoceptors. ACS Chem Neurosci, 2025;16(23):4531-4545. doi: 10.1021/acschemneuro.5c00719.*
- *Dempsey SK, Poklis JL, Sweat K, Cumpston K, Wolf CE. Acute Toxicity From Intravenous Use of the Tricyclic Antidepressant Tianeptine. J Anal Toxicol. 2017 Jul 1;41(6):547-550. doi: 10.1093/jat/bkx034.*
- *El Zahran T, Schier J, Glidden E, et al. Characteristics of Tianeptine Exposures Reported to the National Poison Data System — United States, 2000–2017. MMWR Morb Mortal Wkly Rep 2018;67:815–818. doi: http://dx.doi.org/10.15585/mmwr.mm6730a2*

References

- *Esposito CM, Mandolini GM, Delvecchio G, Fiorentini A, Brambilla P. Psychomotor Agitation Non-responsive to Treatment: A Case Report of Phenibut Withdrawal Syndrome. Frontiers in Psychiatry, 2021; 12:688147. doi: 10.3389/fpsyt.2021.688147.eCollection 2021*
- *"FDA Advises Consumers Not to Purchase or Use Nitrite 'Poppers'." https://www.fda.gov/food/alerts-advisories-safety-information/fda-advises-consumers-not-purchase-or-use-nitrite-poppers#:~:text=FDA%20Advises%20Consumers%20Not%20to%20Purchase%20or,Polish%20Remover%20and%20Premium%20Ironhorse%2C%20among%20others. Accessed 4-8-26.*
- *"FDA warns consumers not to purchase or use any tianeptine product due to serious risks." https://www.fda.gov/drugs/drug-alerts-and-statements/fda-warns-consumers-not-purchase-or-use-any-tianeptine-product-due-serious-risks. Updated 5/8/2025.*
- *https://www.fda.gov/consumers/consumer-updates/tianeptine-products-linked-serious-harm-overdoses-death*
- *Fernandes CT, Iqbal U, Tighe SP, Ahmed A. Kratom-Induced Cholestatic Liver Injury and Its Conservative Management. J Investig Med High Impact Case Rep. 2019 Jan-Dec;7:2324709619836138. doi: 10.1177/2324709619836138.*
- *Gassaway MM, Rives M-L, Kruegel AC, Javitch JA, Sames D. The atypical antidepressant and neurorestorative agent tianeptine is a μ-opioid receptor agonist. Transl Psychiatry. 2014;4:e411. doi: 10.1038/tp.2014.30.*

References

- *Graves JM, Dilley J, Kubsad S, Liebelt E. Notes from the Field: Phenibut Exposures Reported to Poison Centers—United States, 2009-2019. Morbidity and Mortality Weekly Report, 2020; 69(35):1227–1228.*
- *Grislain L, Gele P, Bertrand M, Luijten W, Bromet N, Salvadori C, Kamoun A. The metabolic pathways of tianeptine, a new antidepressant, in healthy volunteers. Drug Metab Dispos. 1990 Sep-Oct;18(5):804-8. PMID: 1981739.*
- *Gummin DD, Mowry JB, Beuhler MC, Spyker DA, Rivers LJ, Feldman R, Brown K, Pham NPT, Bronstein AC, DesLauriers C. 2023 Annual Report of the National Poison Data System® (NPDS) from America's Poison Centers®: 41st Annual Report. Clin Toxicol (Phila). 2024 Dec;62(12):793-1027. doi: 10.1080/15563650.2024.2412423.*
- *Gurley BJ and Koturbash I. Phenibut: A drug with one too many "buts". Basic & clinical pharmacology & toxicology, 2024; 135(4):409-416.*
- *Hardman MI, Sprung J, Weingarten TN. Acute phenibut withdrawal: A comprehensive literature review and illustrative case report. Bosnian Journal of Basic Medical Sciences, 2019; 19(2):125-129. doi: 10.17305/bjbms.2018.4008.*
- *Helander A. & Rylski A. Drug testing for mitragynine and kratom: Analytical challenges and medico-legal considerations. Drug Testing and Analysis, 2023; 15(2): 213-219.*
- *Hogberg L, Szabo I, Ruusa J. Psychotic symptoms during phenibut (beta-phenyl-gammaaminobutyric acid withdrawal. Journal of Substance Use, 2013; 18(4):335-338. doi: 10.3109/14659891.2012.668261*
- *Krotulski AJ, et al. Detection of tianeptine in biological specimens by LC–HRMS. J Anal Toxicol. 2018;42(7):e33–e37.*

References

- *Huestis MA, Brett MA, Bothmer J, Atallah R. Human Mitragynine and 7-Hydroxymitragynine Pharmacokinetics after Single and Multiple Daily Doses of Oral Encapsulated Dried Kratom Leaf Powder. Molecules. 2024 Feb 23;29(5):984. doi: 10.3390/molecules29050984.*
- *Kerester S, Bloom J, Schwartz L, Mercurio-Zappala M, Palamar JJ, Su MK. Alkyl Nitrite ("Poppers") Exposures in the US. JAMA Netw Open. 2025 Jul 1;8(7):e2523408. doi: 10.1001/jamanetworkopen.2025.23408.*
- *Lapin I. Phenibut (beta-phenyl-GABA): a tranquilizer and nootropic drug. CNS Drug Reviews, 2001; 7(4):471-81. doi: 10.1111/j.1527-3458.2001.tb00211.x.*
- *"The Legal Status of Poppers." Published 4-10-25. https://prowlerpoppers.co.uk/blogs/guides/the-legal-status-of-poppers-uk-vs-us#:~:text=US:%20A%20More%20Complicated%20Picture,specific%20medical%20and%20industrial%20uses. Accessed 4-8-26.*
- *LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012 -. https://www.ncbi.nlm.nih.gov/books/NBK547852/. Accessed 4-7-26.*
- *Mash JE and Leo RJ. Phenibut: A Novel Nootropic With Abuse Potential. The Primary Care Companion for CNS Disorders, 2020; 22(4):19l02587. doi: 10.4088/PCC.19l02587.*
- *North Carolina General Assembly: "Regulation of Tianeptine—State by State Overview." https://webservices.ncleg.gov/ViewDocSiteFile/84838. Accessed 4/6/26.*

References

- *Huestis MA, Brett MA, Bothmer J, Atallah R. Human Mitragynine and 7-Hydroxymitragynine Pharmacokinetics after Single and Multiple Daily Doses of Oral Encapsulated Dried Kratom Leaf Powder. Molecules. 2024 Feb 23;29(5):984. doi: 10.3390/molecules29050984.*
- *Kerester S, Bloom J, Schwartz L, Mercurio-Zappala M, Palamar JJ, Su MK. Alkyl Nitrite ("Poppers") Exposures in the US. JAMA Netw Open. 2025 Jul 1;8(7):e2523408. doi: 10.1001/jamanetworkopen.2025.23408.*
- *Lapin I. Phenibut (beta-phenyl-GABA): a tranquilizer and nootropic drug. CNS Drug Reviews, 2001; 7(4):471-81. doi: 10.1111/j.1527-3458.2001.tb00211.x.*
- *"The Legal Status of Poppers." Published 4-10-25. https://prowlerpoppers.co.uk/blogs/guides/the-legal-status-of-poppers-uk-vs-us#:~:text=US:%20A%20More%20Complicated%20Picture,specific%20medical%20and%20industrial%20uses. Accessed 4-8-26.*
- *LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012 -. https://www.ncbi.nlm.nih.gov/books/NBK547852/. Accessed 4-7-26.*
- *Mash JE and Leo RJ. Phenibut: A Novel Nootropic With Abuse Potential. The Primary Care Companion for CNS Disorders, 2020; 22(4):19l02587. doi: 10.4088/PCC.19l02587.*
- *North Carolina General Assembly: "Regulation of Tianeptine—State by State Overview." https://webservices.ncleg.gov/ViewDocSiteFile/84838. Accessed 4/6/26.*

References

- *"Overview of Current 7-OH Regulations in the United States." https://www.kratomanonymous.com/about-kratom/overview-of-current-7-oh-regulations-in-the-united-states-9sgxj. Accessed 4-7-26.*
- *Parnia S, Jain L, Ali M, Sarfraz Z, et al. Gas station heroin—tianeptine and its impact: a systematic review and exploratory analysis. BMC Public Health, 2025; 25:3591. doi: https://doi.org/10.1186/s12889-025-24666-0.*
- *Post S, Spiller HA, Chounthirath T, Smith GA. Kratom exposures reported to United States poison control centers: 2011-2017. Clin Toxicol, 2019; 57(10):847-854. doi: 10.1080/15563650.2019.1569236.*
- *Quadir M, Rine NI, Badeti J, Hays HL, Michaels NL, Yang J, Smith GA. Tianeptine Exposures Reported to United States Poison Centers, 2015-2023. J Med Toxicol. 2025 Jan;21(1):30-41. doi: 10.1007/s13181-024-01053-6. Epub 2024 Dec 26. PMID: 39724478; PMCID: PMC11706824.*
- *Roopa S, Ravishankar DA, Nagireddy R. Phenibut Dependence and Withdrawal. The Primary Care Companion for CNS Disorders, 2021; 23(1):19l02457. doi: 10.4088/PCC.19l02457.*
- *Sherrick RC. Treatment of Kratom Use Disorder With Methadone in an Opioid Treatment Program. J Addict Med. 2026 Feb 12. doi: 10.1097/ADM.0000000000001666.*
- *Towers EB, Thomas YT, Holstege CP, Farah R. Increases in Kratom-Related Reports to Poison Centers — National Poison Data System, United States, 2015–2025. MMWR Morb Mortal Wkly Rep 2026;75:139–145. DOI: http://dx.doi.org/10.15585/mmwr.mm7511a1*

References

- *Trakulsrichai S, Sathirakul K, Auparakkitanon S, Krongvorakul J, Sueajai J, Noumjad N, Sukasem C, Wananukul W. Pharmacokinetics of mitragynine in man. Drug Des Devel Ther. 2015 Apr 29;9:2421-9. doi: 10.2147/DDDT.S79658.*
- *Vadiei N, Evoy KE, Grundmann O. The Impact of Diverse Kratom Products on Use Patterns, Dependence, and Toxicity. Curr Psychiatry Rep. 2025 Oct;27(10):584-592. doi: 10.1007/s11920-025-01631-7.*
- *Vogt S, Angerer V, Kempf J, Auwärter V. Analysis of "poppers" products and analytical detectability of a single use of "poppers"." Toxichem Krimtech, 2015; 82: 218-219.*
- *Weleff J, Kovacevich A, Burson J, Nero N, Anand A. Clinical Presentations and Treatment of Phenibut Toxicity and Withdrawal: A Systematic Literature Review. J Addict Med. 2023 Jul-Aug 01;17(4):407-417. doi: 10.1097/ADM.0000000000001141.*
- *White CM, Belcourt J, Sedensky A. A Descriptive Assessment of Products Containing the Opioid Receptor Stimulator Mitragynine Pseudoindoxyl. Subst Use Misuse. 2025;60(12):1950-1954. doi: 10.1080/10826084.2025.2522162.*
- *Ya K, Tangamornsuksan W, Scholfield CN, Methaneethorn J, Lohitnavy M. Pharmacokinetics of mitragynine, a major analgesic alkaloid in kratom (Mitragyna speciosa): A systematic review. Asian J Psychiatr. 2019 Jun;43:73-82. doi: 10.1016/j.ajp.2019.05.016.*
- *Zvejniece L, Vavers E, Svalbe B, Veinberg G, Rizhanova K, Liepins V, et al. R-phenibut binds to the α2-δ subunit of voltage-dependent calcium channels and exerts gabapentin-like anti-nociceptive effects. Pharmacology, Biochemistry, and Behavior. 2015;137:23–9.*