

# Clinical Characterization of Kratom: Is it a Craze or Here to Stay?

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**Translational Addiction Medicine Branch**

**National Institute on Drug Abuse Intramural Research Program**



American Society of Addiction Medicine 53<sup>rd</sup> Annual Conference

#ASAMAnnual2022

# Disclosure Information

☀️ **Focus Session: Clinical Characterization of Kratom: Is it a Craze or Here to Stay? April 2, 2022**

☀️ **Presenter 1: Kirsten E. Smith, Ph.D., M.S.W.**

☀️ **Commercial Interests: No Disclosures**

☀️ **Presenter 2: Stephanie Weiss, M.D., Ph.D.**

☀️ **Commercial Interests: No Disclosures**



# Learning Objectives

- ☀ Describe historical & current uses of kratom, including recent epidemiological data on kratom use in US.
- ☀ List clinical characteristics of kratom use, intoxication, use disorder, and possible interventions for each.
- ☀ Identify clinically relevant pharmacodynamic effects and pharmacokinetic interactions of the kratom alkaloid, mitragynine.

# What is Kratom?



















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## Self-Treatment of Opioid Withdrawal with a Dietary Supplement, Kratom

Edward W. Boyer, MD, PhD,<sup>1</sup> Kavita M. Babu, MD,<sup>1</sup> Grace E. Macalino, PhD,<sup>2</sup>  
Wilson Compton, MD, MPH<sup>3</sup>

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ADDICTION

SSA SOCIETY FOR THE STUDY OF ADDICTION

## Self-treatment of opioid withdrawal using kratom (*Mitragynia speciosa korth*)

Edward W. Boyer ✉ Kavita M. Babu, Jessica E. Adkins, Christopher R. McCurdy, John H. Halpern



*Journal of Psychoactive Drugs*, 47 (5), 360–367, 2015  
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DOI: 10.1080/02791072.2015.1096434

Routledge  
Taylor & Francis Group

## Experiences of Kratom Users: A Qualitative Analysis

Marc T. Swogger, Ph.D.<sup>a</sup>; Elaine Hart, M.S.<sup>b</sup>; Fire Erowid, B.A.<sup>c</sup>; Earth Erowid, B.A.<sup>c</sup>; Nicole Trabold, Ph.D.<sup>d</sup>; Kaila Yee, B.A.<sup>b</sup>; Kimberly A. Parkhurst, B.A.<sup>b</sup>; Brittany M. Priddy, B.S.<sup>b</sup> & Zach Walsh, Ph.D.<sup>e</sup>



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Full length article

Patterns of Kratom use and health impact in the US—Results from an online survey



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Full length article

Prevalence and motivations for kratom use in a sample of substance users enrolled in a residential treatment program



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# How many people are using kratom in the US?



Prevalence estimates vary widely

- National Survey on Drug Use and Health (2018-2019)
  - past-month rate: 0.3%
  - past-year rate: 0.8% (2.6 million)
- Covvey *et al.* (2020): 6.1% had ever tried kratom
- American Kratom Association: ~15 million



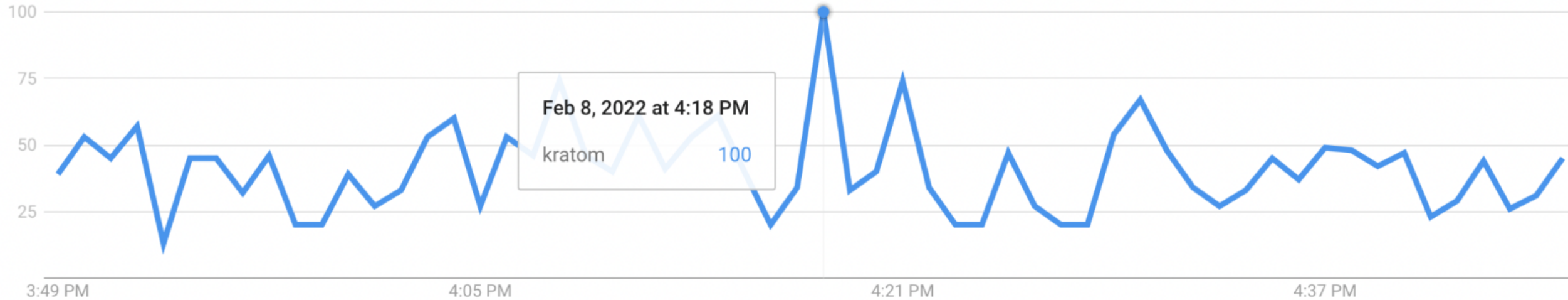
## 2004-2020



## Past 5 years






# Past *hour*, as of February 8, 2022







## Non-Prescribed Buprenorphine Use Mediates the Relationship between Heroin Use and Kratom Use among a Sample of Polysubstance Users

Kirsten E. Smith <sup>a,b</sup>, Amanda M. Bunting<sup>\*c</sup>, Robert Walker<sup>b,d</sup>, Martin T. Hall <sup>a</sup>, Oliver Grundmann <sup>e</sup>, and Olivia Castillo<sup>f</sup>



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### Kratom as a substitute for opioids: Results from an online survey

Marion A. Coe<sup>a,\*</sup>, Janine L. Pillitteri<sup>b</sup>, Mark A. Sembower<sup>b</sup>, Karen K. Gerlach<sup>b</sup>, Jack E. Henningfield<sup>a,c</sup>



## Prevalence and characteristics of self-reported kratom use in a representative US general population sample

Jordan R. Covvey, PharmD, PhD, BCPS<sup>a</sup> , Samantha M. Vogel, PharmD, BCPP<sup>b,c</sup>, Alyssa M. Peckham, PharmD, BCPP<sup>d,e</sup> and Kirk E. Evoy, PharmD, BCACP, BC-ADM, CTTs<sup>b,f,g</sup> 

ORIGINAL RESEARCH

## Self-reported Health Diagnoses and Demographic Correlates With Kratom Use: Results from an Online Survey

Rhiannon Bath, Tanner Bucholz, Amy F. Buros, PhD, Darshan Singh, PhD, Kirsten E. Smith, MS, Charles A. Veltri, PhD, and Oliver Grundmann, PhD



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Full length article

Kratom (*Mitragyna speciosa*): User demographics, use patterns, and implications for the opioid epidemic

Albert Garcia-Romeu<sup>a,\*</sup>, David J. Cox<sup>a</sup>, Kirsten E. Smith<sup>b</sup>, Kelly E. Dunn<sup>a</sup>, Roland R. Griffiths<sup>a,c</sup>



Drug and Alcohol Dependence

journal homepage: [www.elsevier.com/locate/drugalcdep](http://www.elsevier.com/locate/drugalcdep)

## Therapeutic benefit with caveats?: Analyzing social media data to understand the complexities of kratom use

Kirsten E. Smith<sup>a,\*</sup>, Jeffrey M. Rogers<sup>a</sup>, Destiny Schriefer<sup>a</sup>, Oliver Grundmann<sup>b</sup>

 frontiers  
in Pharmacology

ORIGINAL RESEARCH  
published: 20 December 2021  
doi: 10.3389/fphar.2021.789075



## Kratom Use in the US: Both a Regional Phenomenon and a White Middle-Class Phenomenon? Evidence From NSDUH 2019 and an Online Convenience Sample

Jeffrey M. Rogers<sup>1,\*</sup>, Kirsten E. Smith<sup>1</sup>, Justin C. Strickland<sup>2</sup> and David H. Epstein<sup>1</sup>



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ISSN: 1064-1297

Experimental and Clinical Psychopharmacology

<https://doi.org/10.1037/pha0000518>

## Social, Psychological, and Substance Use Characteristics of U.S. Adults Who Use Kratom: Initial Findings From an Online, Crowdsourced Study

Kirsten E. Smith<sup>1</sup>, Kelly E. Dunn<sup>2</sup>, Oliver Grundmann<sup>3</sup>, Albert Garcia-Romeu<sup>2</sup>, Jeffrey M. Rogers<sup>1</sup>, Marc T. Swogger<sup>4</sup>, and David H. Epstein<sup>1</sup>

# Survey (& Social Media) Self-Report: *Who is using kratom?*

- Sex/Gender split.
- Mostly Non-Hispanic White
- Late 30s-early 40s (*though this is changing*)
- Most high-school educated, many college-educated.
- Income distribution
- Most using 1-5 years
- Many use regularly, but some report having quit or used intermittently.
- Doses 2-5 times per day on average.
- Preference for kratom over other substances varies.

**Survey (&  
Social  
Media) Self-  
Report:  
*Who is using  
kratom?***

- **Use initiation Early or Late 30s**
- **Other drug use history or current substance use.**
- **Poorer psychosocial and health indicators.**

**...and we're starting to see shifts already**



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# Dosing Routines & Effects



**59.7%** Used kratom >100 times

**80.6%** Used kratom >4 times per week (regular use)

**61.9** average weeks of regular use

**41.9%** Considers themselves *current* regular kratom user

**2.7** average kratom doses per day

**65.0** Weeks spent using on typical dosing regimen

## Acute effects:

**79.8%** Felt effect every (or almost every) time kratom was dosed.

**Onset of effects (time for typical kratom dose effects to *begin*):**

**0.0%** Seconds      **82.9%** Minutes      **11.6%** Hours

**Duration of effects (time to *stop* feeling typical dose effects):**

**1.6%** Minutes                      **91.5%** Hours  
**7.0%** Unsure because I would dose before effects wore off.

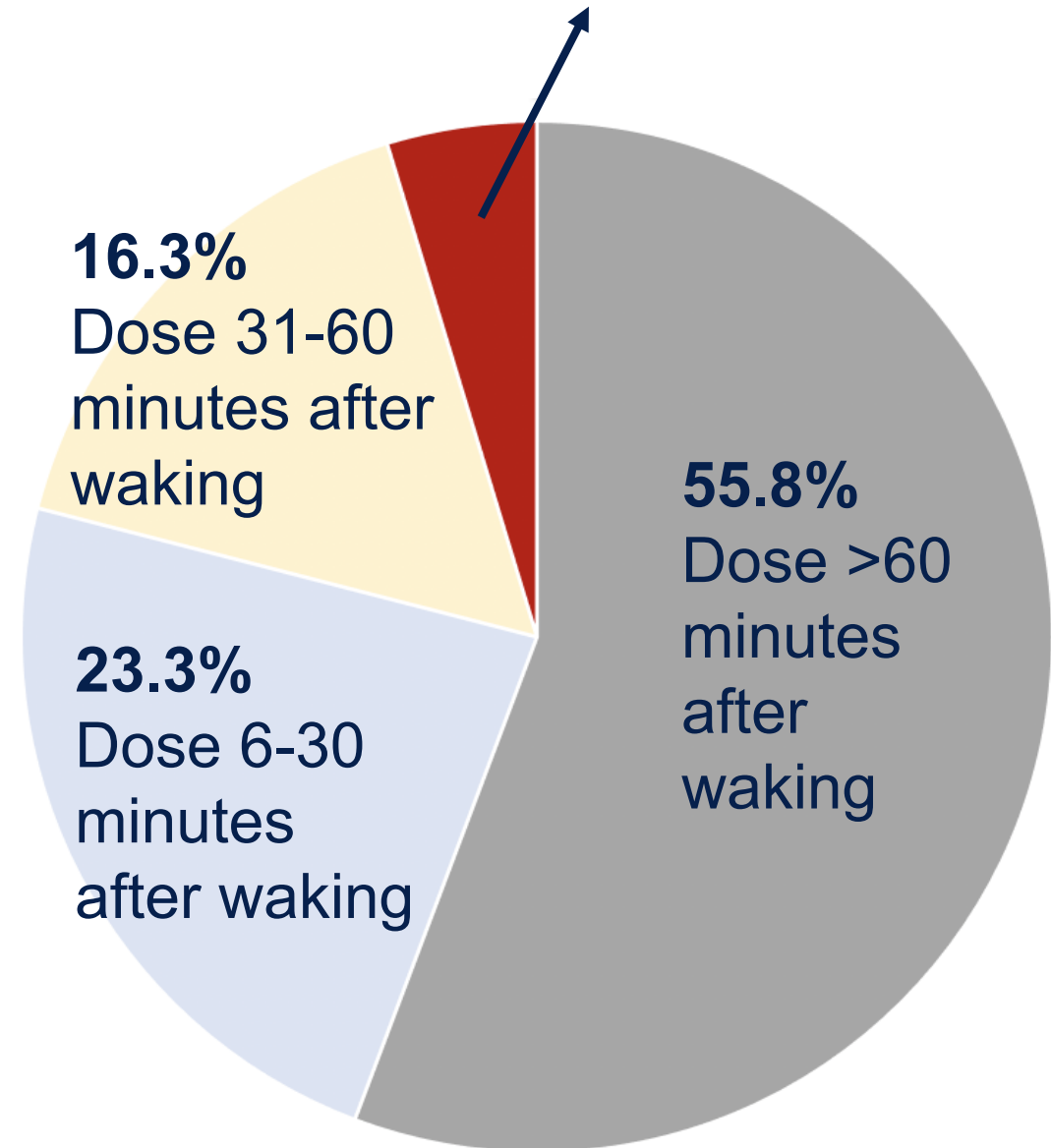
### Typical regular kratom dose

Capsules	5.38 ( $\pm$ 4.8)
Grams	4.57 ( $\pm$ 3.6)
Spoonfuls	2.52 ( $\pm$ 2.7)
Tablespoons	2.09 ( $\pm$ 1.0)
Cups of Teas	1.62 ( $\pm$ 1.1)

**41.1%** typically use *more* during the first waking hour

**54.3%** would hate to give up their first kratom dose of the day compared to other times of day.

4.7% Dose <5 minutes after waking





# Kratom Use Motivations





# The list of motivations keeps growing...

	<i>N</i>	<i>%</i>	<i>M</i> <i>effectiveness</i>	<i>(SD)</i> <i>effectiveness</i>
Just to feel less crappy in general and improve quality of life.	86	66.7	74.2	(±21.9)
Self-treat anxiety symptoms.	69	53.5	69.4	(±22.9)
Address occasional feelings of sleepiness or low energy.	65	50.4	78.0	(±21.2)
Relieve short-term pain (acute pain management)	64	49.6	71.9	(±22.1)
For recreation, fun, or to relax.	63	48.8	72.4	(±24.6)
Boost energy, stamina and/or endurance (for work, exercise).	62	48.1	77.1	(±21.8)
Reduce social anxiety.	60	46.5	75.8	(±17.4)
Self-treat depression symptoms.	54	41.8	66.6	(±22.7)
Self-treat long-term pain issues and symptoms (chronic pain management)	46	35.7	72.1	(±21.6)
Kratom is safer than other substances.	43	33.3	90.4	(±11.2)
To achieve a euphoric high.	39	30.2	70.9	(±22.3)
As a short-term substitute/replacement for opioids (rx opioids, heroin).	32	24.8	66.7	(±27.1)
Couldn't get a hold of other, more preferred drugs.	31	24.0	75.4	(±24.4)
Self-treat headaches/migraines.	31	24.0	65.3	(±22.9)

	<b>N</b>	<b>%</b>	<b>M effectiveness</b>	<b>(SD) effectiveness</b>
Relieve withdrawal symptoms from nonprescribed opioids or heroin	25	19.4	72.2	(±25.1)
Self-treat chronic fatigue syndrome.	25	19.4	72.7	(±24.4)
As a short-term substitute/replacement for alcohol.	24	18.6	66.3	(±21.9)
Doctors won't prescribe you the drugs you need.	24	18.6	82.3	(±19.8)
Self-treat ADD/ADHD symptoms.	24	18.6	61.6	(±24.4)
Self-treat post-traumatic stress symptoms.	23	17.8	61.9	(±28.3)
As a long-term substitute/replacement for opioids (rx opioids, heroin).	21	16.3	74.6	(±24.9)
Relieve withdrawal symptoms from medically prescribed opioids	20	15.5	74.2	(±22.8)
Take as part of a self-designed "stack" of drugs that help you feel good.	18	14.0	69.4	(±21.6)
Because you prefer the kratom "high" to "highs" you get from other drugs.	16	12.4	78.0	(±21.7)
To believe withdrawal symptoms from a variety of different drugs.	14	10.9	71.9	(±25.7)
As a short-term substitute/replacement for stimulants (meth, cocaine)	13	10.1	72.4	(±28.9)
Self-treat irritable bowel syndrome.	13	10.1	77.1	(±18.6)
As a long-term substitute/replacement for alcohol.	10	7.8	75.8	(±24.7)
Self-treat bipolar symptoms.	10	7.8	66.6	(±26.1)
Relieve alcohol withdrawal symptoms	8	6.2	72.1	(±29.7)

	<i>N</i>	<i>%</i>	<i>M</i> <i>effectiveness</i>	<i>(SD)</i> <i>effectiveness</i>
Relieve withdrawal symptoms for nonprescribed buprenorphine	7	5.4	90.4	(±15.3)
As a long-term substitute/replacement for buprenorphine	5	3.9	70.9	(±16.0)
As a long-term substitute/replacement for stimulants	4	3.1	66.7	(±6.9)
Relieve withdrawal from “nootropics” or cognitive-enhancing supplements.	4	3.1	75.4	(±13.7)
Relieve withdrawal symptoms from nonprescribed methadone	4	3.1	65.3	(±4.7)
Relieve withdrawal symptoms from prescribed buprenorphine	4	3.1	72.2	(±3.1)
As a short-term substitute/replacement for buprenorphine	3	2.3	72.7	(±14.0)
As a short-term substitute/replacement for methadone.	3	2.3	66.3	(±13.1)
As a long-term substitute/replacement for methadone.	3	2.3	82.3	(±4.5)
Difficulties obtaining buprenorphine or methadone.	3	2.3	61.6	(±8.5)
Relieve withdrawal symptoms from prescribed methadone	2	1.6	61.9	(±7.8)
None of these.	1	0.8	.	.

# Kratom Withdrawal

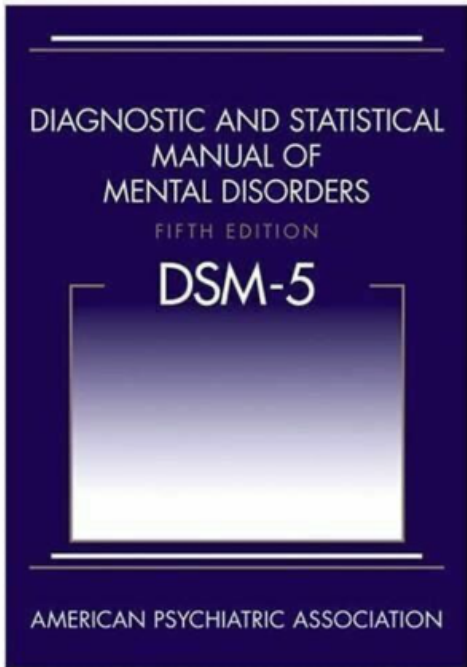




	Total (N=129)		Current KUD (N=38)		Remitted KUD (N=23)		Never KUD (N=68)	
		<i>M</i>		<i>M</i>		<i>M</i>		<i>M</i>
<b>Anxiety</b>	<b>32.6%</b>	63.2	50.0%	73.1	43.5%	70.9	19.1%	42.8
<b>Irritability</b>	<b>32.6%</b>	63.5	55.3%	74.1	34.8%	76.6	19.1%	38.4
<b>Desire to use another substance</b>	<b>28.7%</b>	67.1	52.6%	75.3	26.1%	73.0	16.2%	48.8
<b>Low energy</b>	<b>28.7%</b>	68.9	50.0%	82.6	26.1%	71.0	17.6%	46.0
<b>Difficulty Sleeping</b>	<b>22.5%</b>	74.3	42.1%	71.8	26.1%	82.5	10.3%	73.1
<b>Restlessness</b>	<b>22.5%</b>	56.2	44.7%	58.8	21.7%	65.1	10.3%	43.9
<b>Nausea</b>	<b>21.7%</b>	47.0	36.8%	52.5	34.8%	48.1	8.8%	32.8
<b>Body aches</b>	<b>21.7%</b>	63.1	44.7%	68.4	21.7%	51.2	8.8%	57.8
<b>No energy</b>	<b>20.9%</b>	75.5	36.8%	88.4	26.1%	69.3	10.3%	55.0
<b>Upset stomach</b>	<b>20.2%</b>	52.0	36.8%	58.9	21.7%	56.8	10.3%	34.9
<b>Depressed mood</b>	<b>20.2%</b>	66.1	39.5%	75.5	17.4%	69.0	10.3%	44.4
<b>Mild-moderate kratom craving</b>	<b>19.4%</b>	67.8	36.8%	69.0	17.4%	81.8	10.3%	57.6
<b>Daytime sleepiness</b>	<b>18.6%</b>	68.7	23.7%	84.0	21.7%	81.0	14.7%	48.8
<b>Hot flashes</b>	<b>15.5%</b>	54.0	36.8%	51.4	8.7%	81.5	5.9%	49.8
<b>Runny nose</b>	<b>14.7%</b>	55.9	34.2%	68.4	17.4%	24.3	2.9%	38.0
<b>Restless legs</b>	<b>13.2%</b>	65.5	21.1%	82.6	21.7%	57.8	5.9%	40.8
<b>Craving for another drug</b>	<b>13.2%</b>	77.0	36.8%	76.6	8.7%	68.0	1.5%	100.0
<b>Cold flashes</b>	<b>7.8%</b>	62.0	18.4%	63.4	4.3%	68.0	2.9%	54.2
<b>Watery eyes</b>	<b>7.0%</b>	64.2	18.4%	73.1	8.7%	33.0	0.0%	0.0
<b>Vomiting/emesis</b>	<b>6.2%</b>	22.4	10.5%	35.3	4.3%	36.0	4.4%	0.7
<b>Intense kratom craving</b>	<b>5.4%</b>	89.9	15.8%	94.2	4.3%	64.1	0.0%	0.0

# Kratom Use Disorder?





Yes  
Yes, *but not in the past year*  
No

**29.5%** Current (past-year) KUD (n=38)  
**17.8%** Remitted KUD (n=23)  
**52.7%** Never KUD (n=68)

Lifetime Severity

Mild **21.7%**

Moderate **0.5%**

Severe **0.5%**

Past-year Severity

Mild **14.0%**

Moderate **7.0%**

Severe **8.5%**

**...but something important we noticed**

# Individual Symptoms for kratom DSM-5 SUD diagnosis

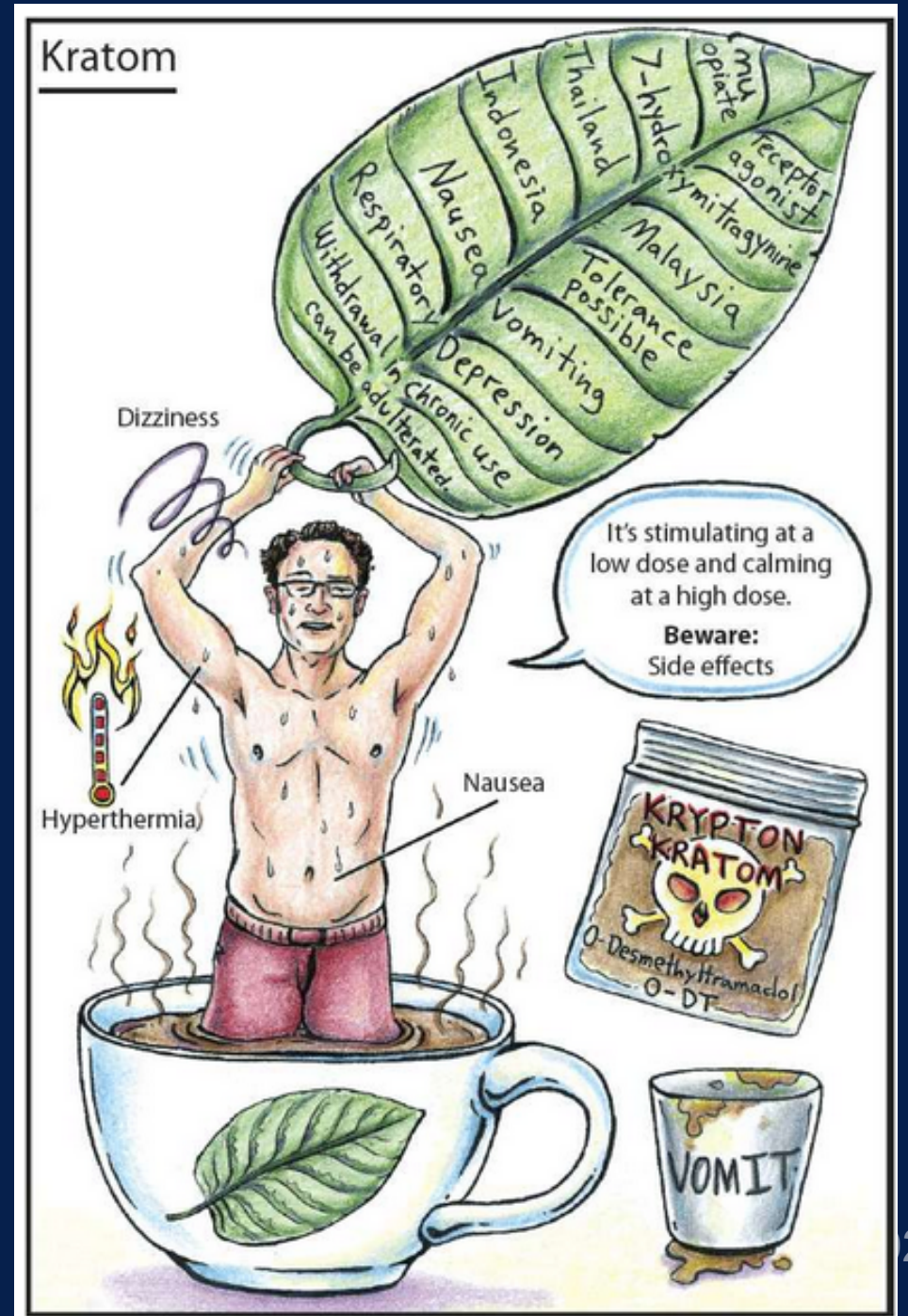
I used kratom in larger amounts and/or over a longer period than I had intended to.	45.7%
I kept using the same amount of kratom, but didn't feel it as much.	38.8%
I needed to use larger amounts of kratom just to feel the same effect.	33.3%
I had physical or psychological withdrawal symptoms during times I stopped using kratom.	33.3%
I made at least one unsuccessful attempt to cut down or control my kratom use.	32.6%
I experienced cravings, strong desires, or urges for the kratom.	31.8%
I kept using kratom in order to avoid withdrawal symptoms.	28.7%
I kept using kratom despite knowing it was causing or worsening physical or psychological problems for me.	15.5%
I spent a great deal of time on activities necessary to get kratom, use the kratom, or recover from kratom's effects.	15.5%
I kept using kratom despite knowing it was causing or worsening social or interpersonal problems for me.	14.0%
I gave up or reduced some important social, occupational, or recreational activities because of my kratom use.	10.9%
My kratom use repeatedly interfered with my major role obligations (at work, school, or home).	9.3%
I repeatedly used kratom in situations where it was physically hazardous.	8.5%



# BACK TO DOSE....

Among those who reported feeling effects from each dose (N=103)	
Effects <b>are</b> compatible with <b>and</b> help me meet my daily obligations.	54.40%
Effects <b>are</b> compatible with, but do <b>not</b> help me meet my daily obligations.	29.10%
The kratom effects are <b>not</b> compatible with my daily obligations.	3.90%
No, the effects are <b>not</b> compatible with my daily obligations, <b>and</b> they sometimes undermine my ability to meet daily obligations.	2.90%
Don't use enough to know if effects are compatible or helpful daily.	8.70%
None of those are quite true for me	1.00%

# A (Very) Brief Survey of Kratom Pharmacology, Toxicology, and Therapy



Kloss, B. T. (2014). McGraw Hill Education, NY.

# How Does Kratom Work?

- ✱ **Proposed Mechanisms of Mitragynine Activity**
  - ✱ **Partial agonism of  $\mu$  opioid receptors**
  - ✱ **Partial agonism (antagonism?) of  $\kappa$  and  $\delta$  opioid receptors**
  
  - ✱ **Agonism of  $\alpha_2$  receptors**
  - ✱ **Antagonism of 5-HT<sub>2A</sub> receptors**
  - ✱ **Serotonin and norepinephrine reuptake inhibition**

# Acute Clinical Effects of Kratom Exposures Reported to US and Thai Poison Centers

## Common Effects Uncommon

	Number of cases (%)	Effects	Number of cases (%)	Number of cases (%)
Hallucinations/ delusions	63 (8.3)		5 (3.0)	68 (7.3)
Coma	56 (7.4)		3 (1.8)	59 (6.4)
Tremor	53 (7.0)		5 (3.0)	58 (6.3)
Diaphoresis	43 (5.7)		12 (7.1)	55 (5.9)
Respiratory depression	51 (6.7)		0 (0)	51 (5.5)
Electrolyte abnormality	26 (3.4)		21 (12.5)	47 (5.1)
Muscle rigidity	7 (0.9)		32 (19.1)	39 (4.2)
Dystonia	5 (0.7)		16 (9.5)	21 (2.3)
Nausea	75 (9.9)		14 (8.3)	89 (9.6)



# Kratom-Associated Toxicity and Deaths

	Southeast Asia	West (US and Europe)
<b>Side Effects</b>	<b>Weight loss, dehydration, constipation, skin hyperpigmentation</b>	<b>N/V, stomach pain, chills and sweats, dizziness, unsteadiness, visual sx</b>
<b>Toxicity</b>	<b>Few literature reports of serious toxicity or death</b>	<b>Seizures, hepatotoxicity, coma, multiple deaths</b>
<b>Where Obtained</b>	<b>Locally</b>	<b>Internet, head shops</b>
<b>How Used</b>	<b>Often used alone (but not always)</b>	<b>Often combined with other drugs (illicit and meds)</b>
<b>Legal Status</b>	<b>Illegal in Thailand,</b>	<b>Legal in most of US and</b>



# Proposed Kratom Toxicity Mechanisms

## ☀ Behavioral Factors

- ☀ Buying kratom products online/in stores vs locally
- ☀ Mixing it with other substances vs. using it alone

## ☀ Pharmacological Factors

- ☀ Respiratory: Opioid respiratory depression potentiation
- ☀ Stimulatory: seizures, alpha stimulation
- ☀ Cardiotoxicity: QTc prolongation w/ torsades/sudden cardiac death
- ☀ Hepatotoxicity: different CYP2D6 isoforms

# Are there any kratom-only deaths?

- ✦ None with totally convincing evidence
  - ✦ Routine testing does not detect mitragynine
  - ✦ Most cases lack comprehensive toxicological testing
- ✦ Review of UK cases (2019)
  - ✦ 156 kratom-associated deaths
  - ✦ 129 cases with post-mortem tox data reported
  - ✦ 27 cases with mitragynine as the “sole drug” implicated
  - ✦ 6 cases reported only finding mitragynine on analysis

# Are there any kratom-only deaths?

- ☀️ **CO, USA (2019): retested blood samples from four “kratom-only” deaths using HPLC-MS**
  - ☀️ **Three of the four cases actually contained multiple drugs**
  - ☀️ **Fourth case could not be tested due to insufficient sample**
- ☀️ **Takeaways:**
  - ☀️ **Many coingestants are being missed by standard clinical and forensic testing regimens**
  - ☀️ **Most kratom-associated deaths are polysubstance ingestions**



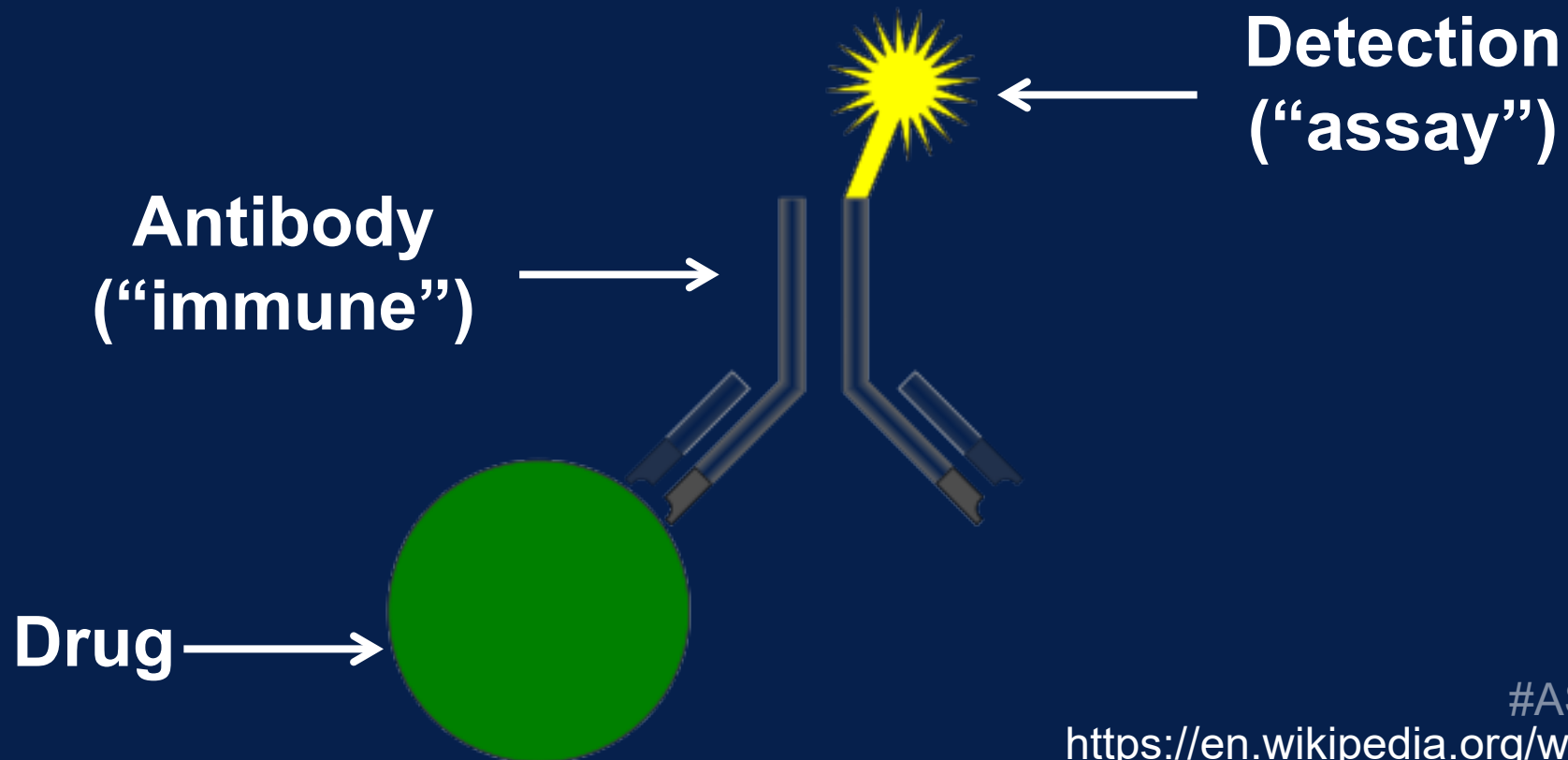
# Kratom Toxicity Workup

- ☀ **Primarily a clinical diagnosis**
  - ☀ Good history and physical exam
  - ☀ Consider withdrawal in regular users
  
- ☀ **Labs based upon clinical judgment**
  - ☀ CMP if liver toxicity suspected
  - ☀ UDS: unlikely to be helpful

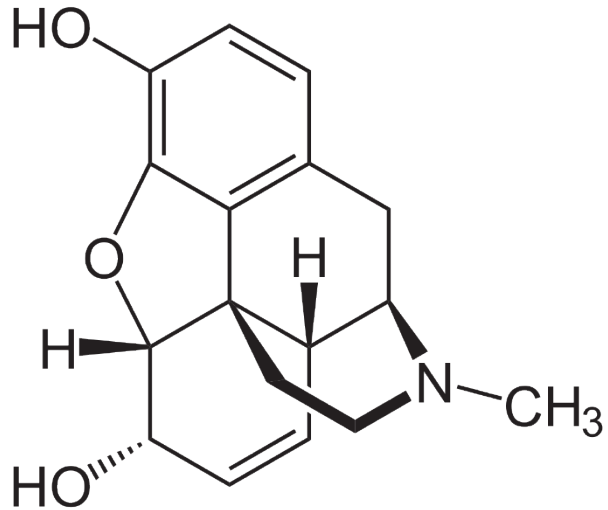


# Kratom Will Not Show Up on a Urine Drug Screen

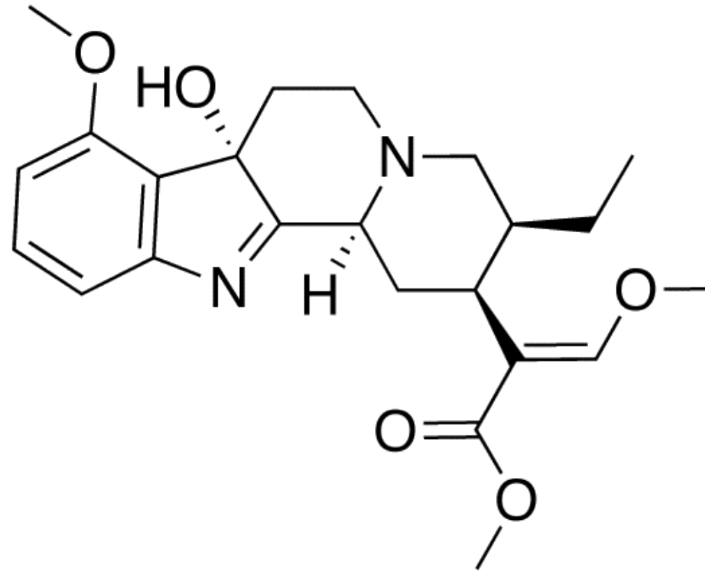
- ☀️ Immunoassay to detect common street drugs of abuse or their metabolites in urine



# Mitragynine Structure Comparison



**morphine**

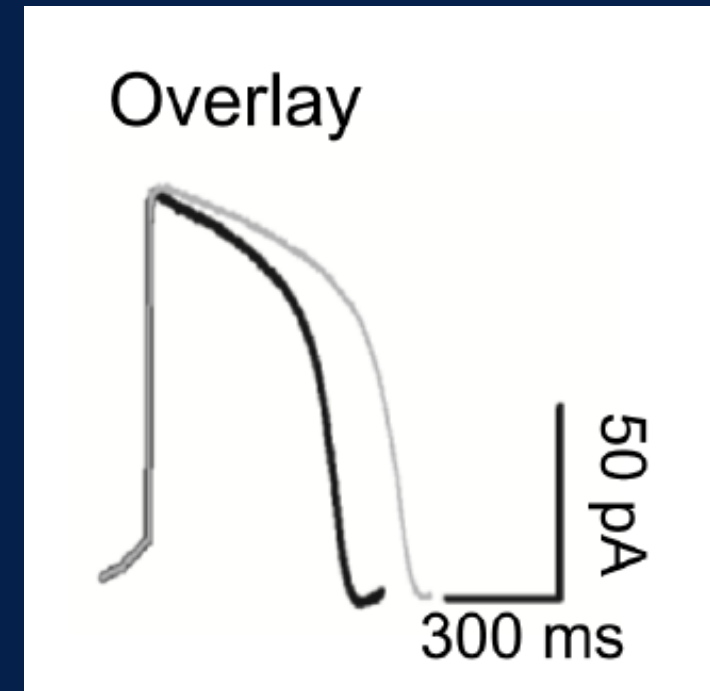
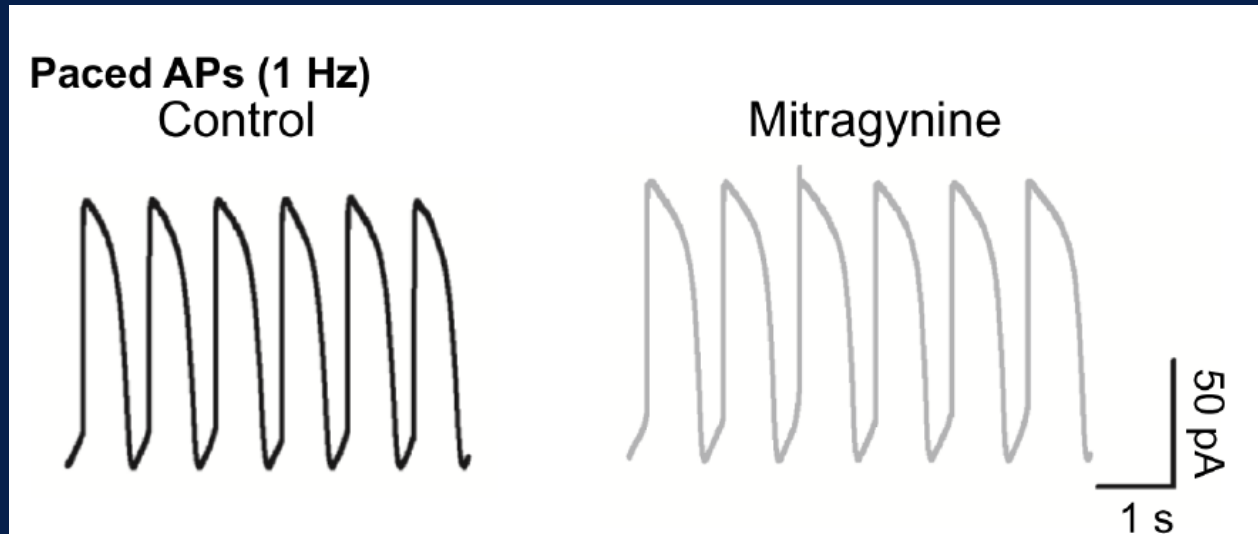


**mitragynine**

**yohimbine**

# Kratom Toxicity Workup

☀️ EKG: look for possible QTc prolongation





# Kratom Toxicity Treatment

- ☀ Primarily supportive

- ☀ Will naloxone work?

  - ☀ A definite maybe

  - ☀ *In vitro*: effect of mitragynine alkaloids was reversed by naloxone in guinea pig ileum

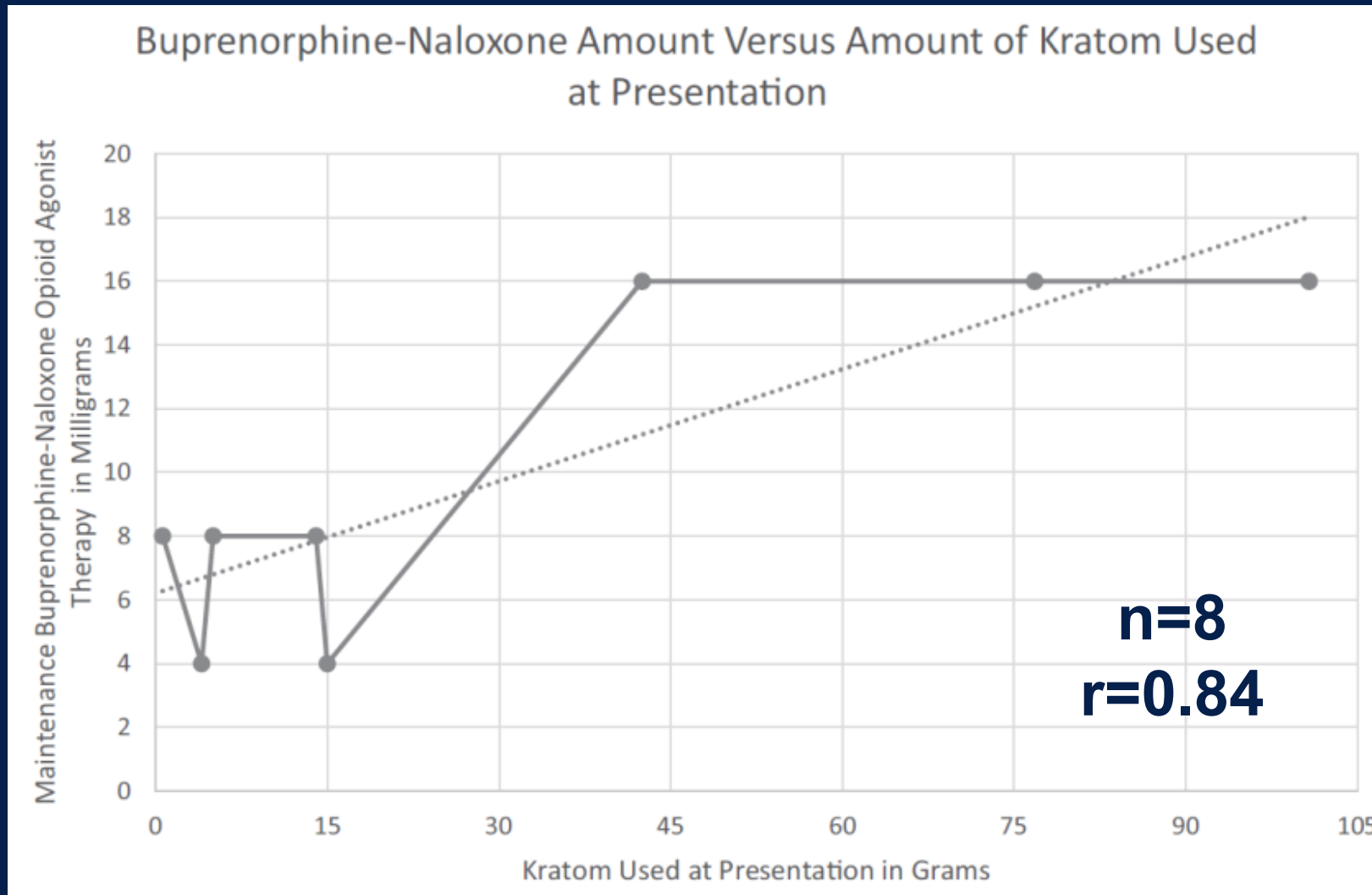
# Will naloxone work?

- ☀ ***In vivo*: One case report detailing successful resuscitation of an opioid toxidrome attributed to sole kratom use**
  - ☀ Use of other opioids was r/o by GC/MS
  - ☀ Doesn't specify which opioids were tested for
  
- ☀ **If the pt presents with an opioid toxidrome, give naloxone**
  - ☀ But use it to treat respiratory depression

# Treatment of Kratom Withdrawal/KUD

Reference	Withdrawal Treatment	KUD/Pain Treatment
Agapoff (2019)	Buprenorphine/naloxone	Buprenorphine/naloxone
Bowe (2020)	Buprenorphine/naloxone	Buprenorphine/naloxone
Buresh (2018)	N/A	Buprenorphine/naloxone
Diep (2018)	Intubation, sedation	Buprenorphine/naloxone
Galbis-Reig (2016)	Clonidine, Hydroxyzine	Naltrexone
Khazaeli (2018)	Buprenorphine/naloxone	Buprenorphine/naloxone
Mackay (2018)	Morphine	N/A
McWhirter (2010)	Dihydrocodeine, Lofexidine	N/A
Sheleg (2011)	Buprenorphine	Methadone, Oxycodone
Stanciu (2019)	Clonidine, Gabapentin	N/A
Vento (2022)	Pregabalin, Bupropion.	Tramadol, Clomipramine

# Do Doses Correlate?





# Treatment of KUD

**Table 2.** Previous Daily Kratom Use and Daily Stabilizing Buprenorphine Dose Comparisons.

Past kratom use (g/d)	No. of patients	Stabilizing buprenorphine dose
0–10	3	10 mg
11–20	4	12 mg
21–30	2	8 mg
31–40	1	16 mg
41–50	1	10 mg
51–60	7	15 mg
61–70	–	–
71–80	2	16 mg
81–90	–	–
91–100	1	12 mg
101–110	–	–
111–120	2	16 mg
>121	4	12 mg

**n=28**  
**r=0.12**

# Summary

- ☀️ Kratom has been used in the West for over a decade but has been used in Southeast Asia for centuries.
- ☀️ Kratom alkaloids have multiple pharmacological effects that are thought to cause its stimulatory and opioid properties
- ☀️ Kratom intoxication, withdrawal, and dependence is primarily a clinical diagnosis and treatment is supportive, but opioid agonist therapy appears to be useful

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# Scan for Additional References!



# Questions



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