

## KRATOM: It Must Be Safe Because It Comes from a Plant, Man

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## Learning Objectives

*By conclusion participants should be able to:*

1. Describe the pharmacology of kratom and its clinical effects.
2. Understand why patients use kratom and possible risks.
3. Identify treatment options for kratom dependence and use disorder.



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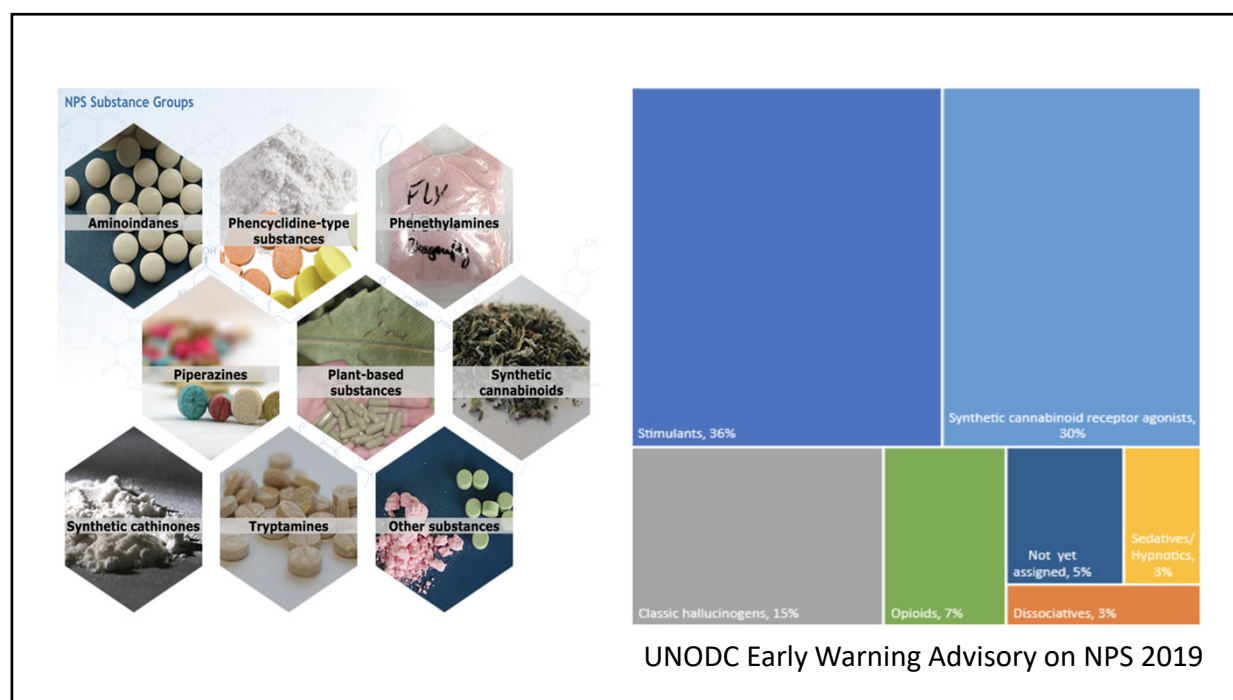
## Novel Psychotropic Substances (NPS) & Novel Benzodiazepines

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## What is a Novel Psychotropic Substance?

- Not controlled under UN drug control conventions
- Similar threats to health
- Many categories of substances
- Marketed as “legal” replacements for illicit drugs
- Large number of new substances – development and distribution
- Significant diversity of substances
- Challenging to monitor
- Challenging to develop effective and timely responses

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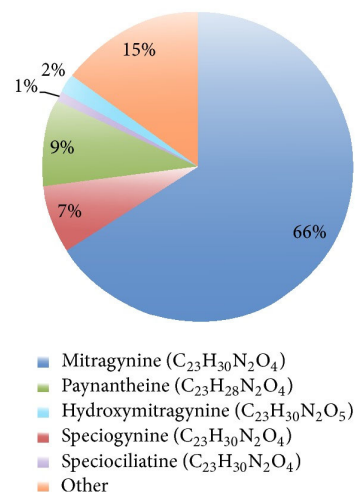
## Kratom

- Tropical tree (*Mitragyna speciosa*) native to Southeast Asia, used traditionally to combat fatigue and improve work productivity among farm populations in Southeast Asia
- Has recently become popular as a novel psychoactive substance in Western countries (Cinosi *et al*, 2015).
- FDA is concerned that kratom, which affects the same opioid brain receptors as morphine, appears to have properties that expose users to the risks of dependence and addiction
- Currently, there are no FDA-approved uses for kratom, and the agency has received concerning reports about its safety

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## Kratom: Extract Composition

- Contains varying amounts of several phytochemicals, makes pharmacological and toxicological evaluation unique and difficult.
- > 20 alkaloids have been identified in the laboratory.
- Mitragynine is classified as a kappa-opioid receptor agonist and is roughly 13 times more potent than morphine.
- Mitragynine/OH-mitragynine thought to be responsible for the opioid-like effects.



Cinosi E, Biomed Res Int. 2015; 2015: 968786

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## Routes of Ingestion

- Capsules
- Pills
- Extract
- Leaves
  - Chewed
  - Brewed as tea
  - Smoked



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## Effects are Dose-Dependent:

- Small doses produce stimulatory effects
- Larger dosages associated with sedative-narcotic effects
- Regular kratom use is associated with addictive disorders, as evidenced by craving and compulsive use
- Opioid withdrawal symptoms upon cessation



**SOURCE:** Prozialeck W. C., Jivan J. K., Andurkar S. V. Pharmacology of Kratom: an emerging botanical agent with stimulant, analgesic and opioid-like effects. *Journal of the American Osteopathic Association*. 2012;112(12):792-799; Singh, 2014; Suwanlert, 1975; Ahmad and Aziz, 2012; Vicknasingam et al., 2010; Singh et al., 2014

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## Kratom Use in the US

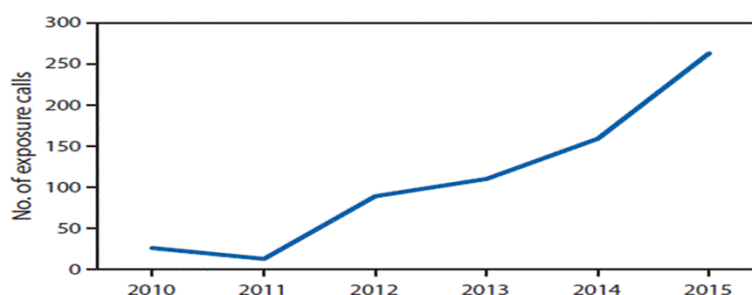
- An anonymous online survey was conducted in October 2016 of 10,000 current kratom users through available social media and from the American Kratom Association (<https://speciosa.org/home/>)
- 8,049 respondents completed the survey.
- Findings:
  - Kratom was primarily used by a middle-aged (31-50 years) males (56.91%) with income \$35,000 or higher with private insurance (61.31%).
  - Kratom was used to self-treat **pain** (68%) and **emotional or mental conditions** (66%) and for **withdrawal symptoms** associated with prescription opioid use.
  - Subjects reported dose-dependent nausea and constipation with high doses (5g) and with and frequent dosing (Q22 doses/wk).

**SOURCE:** Grundmann O.; Patterns of kratom use and health impact in the US results from an online survey. Drug Alcohol Depend. 2017; 175(5):63Y70.

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## Kratom-related Exposure Calls to US Poison Centers

National Poison Data System - United States and Puerto Rico  
January 2010–December 2015



Anwar et al. Notes from the Field. Kratom (*Mitragyna speciosa*) Exposures reported to Poison Centers – United States, 2010–2015. MMWR Morb Mortal Wkly Rep 2016;65:748–749.

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## Fatal Overdoses Involving Kratom

States	ME	NH	NM	OH	PA	RI	WV	WI	Total
Opioid Overdose Deaths	301	402	322	4,534	3,231	265	844	825	10,724
Deaths Involving Kratom	4	2	1	3	8	1	5	1	25
Percent involving Kratom	1.3%	0.5%	0.3%	0.07%	0.25%	0.4%	0.6%	0.1%	0.23%

Most kratom associated deaths appeared to have resulted from adulterated products or taking kratom along with other potent substances.

**Caution:** testing of Kratom is not uniform thus these numbers are underestimates.

CDC SUDORS Overdose Death Data

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## Concerns

- Popular for euphoric effects; marketed as a safe herbal product capable of giving a “legal” high (Swogger et al., 2015), and as an alternative to other sedative and stimulant type drugs (Warner et al., 2016).
- Reports of physical dependence on kratom in Western nations emerge from case reports from the UK (Boyer et al., 2008, McWhirter and Morris, 2010), Germany (Kapp et al., 2011) and the US (Dorman et al., 2014, Nelsen et al., 2010, Forrester, 2013, Sheleg and Collins, 2011).
- Large and growing number of internet purchase sites for kratom (cited in Cinosi et al., 2015), addiction to kratom is also likely to be growing in the Western countries.
- Neonatal abstinence syndrome (NAS) in an infant whose mother was a kratom user and who responded to opioid treatment.

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## Kratom is restricted or illegal in:

Australia	Lithuania	Romania
Denmark	Myanmar	South Korea
Finland	Malaysia	Sweden
Israel	Poland	[Thailand]
United Kingdom		

## Scheduling under consideration in U.S.

On November 14, 2017, the FDA issued a public health advisory related to mounting concerns regarding the risks associated with kratom and reported deaths with use.

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### CASE REPORT

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## Treatment of Kratom Withdrawal and Addiction With Buprenorphine

*Azin Khazaeli, MD, Jason M. Jerry, MD, and Mohsen Vazirian, MD*

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### CASE REPORT

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## Treatment of Kratom Dependence With Buprenorphine- Naloxone Maintenance

*Megan Buresh, MD*

Buresh in J Addict Med Nov/Dec 2018  
Khazaeli et al. in J Addict Med Nov/Dec 2018

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## Conclusions

- Kratom: emerging public health threat (MMWR. July 29, 2016;65(29):748Y749)
- In the West, kratom has been valued for its analgesic effects and to aid in managing opioid withdrawal. However, some of these individual attempts have resulted in cases of toxicity and fatalities.
- Providers should be aware of these herbal supplements and potential toxicity or withdrawal effects in patients including in newborns which cannot be picked up by the standard toxicology screen (Davidson et al, 2018).
- Buprenorphine-naloxone can be used to treat kratom dependence/use disorder