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GUIDE

KRATOM

A brief educational guide for clinicians about what Kratom is, why and how it is used, and clinical management.

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INTRODUCTION

What is Kratom?

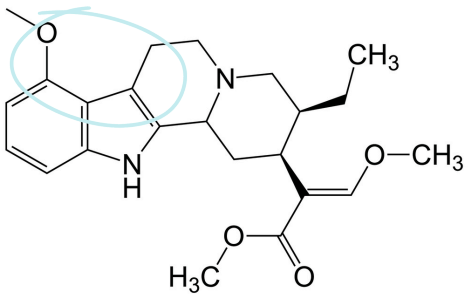
Kratom is a tropical evergreen tree native to Southeast Asia, and in the U.S. most kratom products are sourced from Indonesia.

It is a traditional folk medicine that has been used for centuries to treat several conditions, most notably musculoskeletal pain, anxiety, and depression. Kratom may be chewed, smoked, or processed into a powder that is brewed as a tea or consumed in capsules.

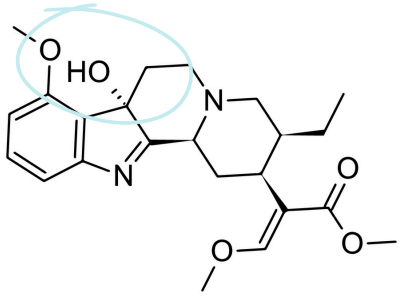
Kratom is NOT regulated by the FDA or scheduled by the DEA.

ACTIVE CHEMICALS IN KRATOM

Kratom contains over 40 identified alkaloids. Its primary active constituents are mitragynine and 7-hydroxymitragynine (7-OH), with mitragynine being the most abundant. Although present in much smaller quantities, 7-hydroxymitragynine (7-OH) is significantly more potent and is largely responsible for kratom's opioid-like effects. Both compounds act as partial agonists at μ-opioid receptors, though they differ in potency and pharmacological profile. Depending on dose, kratom can produce stimulant-like effects at lower doses and opioid-like analgesic and sedative effects at higher doses.



Mitragynine
$C_{23}H_{30}N_2O_4$



7-Hydroxymitragynine
$C_{23}H_{30}N_2O_5$

Concentrated 7-OH Risks

In recent years, some manufacturers have begun isolating, concentrating, or chemically enriching 7-OH and selling products that contain little to no whole-leaf kratom. These high 7-OH products may produce stronger opioid-like effects and carry higher risks of tolerance, dependence, and adverse effects compared to traditional kratom preparations.

This small change in chemical bonding makes a big difference!

PREVALENCE OF KRATOM USE

Estimates of Kratom use vary widely across the scientific literature and the Kratom industry.

0.7%

of Americans have used Kratom in the past year.[1]

6%

of the general population has tried Kratom.[2]

15 million

people use Kratom every year.[3]

WHY USE KRATOM?

People report using Kratom for a variety of reasons such as:

- Treat pain
- Treat opioid withdrawal symptoms
- Treat anxiety and depression
- Limit or discontinue opioid, other drug or alcohol use
- Boost concentration
- Experience euphoria

OVERDOSE RISKS

In 2018, the FDA issued a warning that kratom has a similar structure to opioids and identified 44 deaths related to kratom use. For overdose deaths reported that identified Kratom, the majority of showed multidrug ingestion. It is important to note that because testing for Kratom requires special testing and often not completed, actual overdose rates are likely underestimated.[4]

Example From Florida

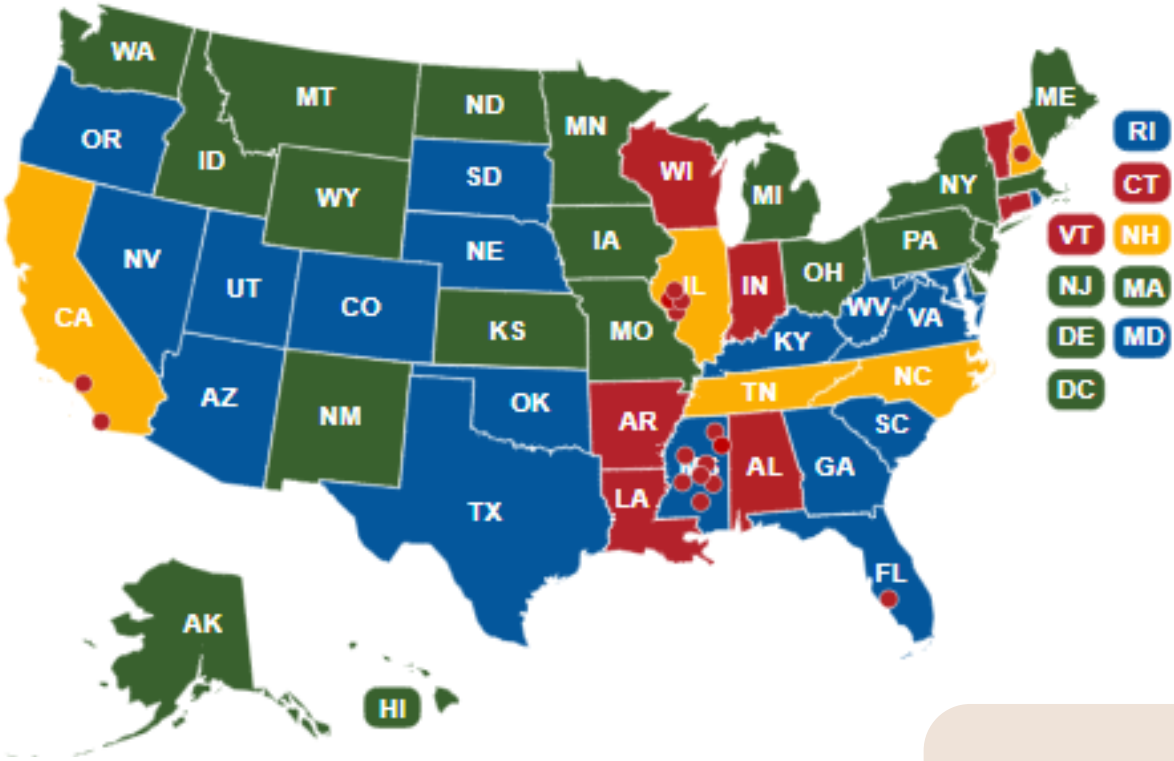
In 2020, Florida began requiring testing for Kratom as part of post-mortem toxicology. According to a review published in the Tampa Bay Times in 2023, medical examiners have identified 587 overdose deaths involving Kratom since 2013. 533 overdoses involved multi-substance overdoses involving Kratom and 46 Kratom-only overdoses.[5]

Prescribe Naloxone!

Because Kratom is not regulated by the FDA and often contains other drugs, always prescribe naloxone to patients using Kratom. Although clinical effectiveness in reversing effects of Kratom has not been proven, there is a case report of successful resuscitation of opioid toxidrome attributed to sole Kratom use.[6]

KRATOM LEGALITY

The legality of Kratom varies by state. Some states have adopted the Kratom Consumer Protection Act which requires the FDA to hold a hearing and establish a task force to look at the safety of products containing Kratom. There is no age limit to purchase Kratom in areas where it is not regulated.[7]



GREEN = Kratom is legal in the state

ORANGE = States legal but with some known local bans or with exceptions.

RED DOT = Banned city

RED = Kratom is illegal and banned in the state

BLUE = State has adopted the Kratom Consumer Protection Act bill

SCAN FOR CURRENT STATUS BY STATE

CLINICAL MANAGEMENT

Think Treatment for Opioid Use Disorder

For patients dependent on Kratom, management of withdrawal and treatment is similar to opioid use disorder.

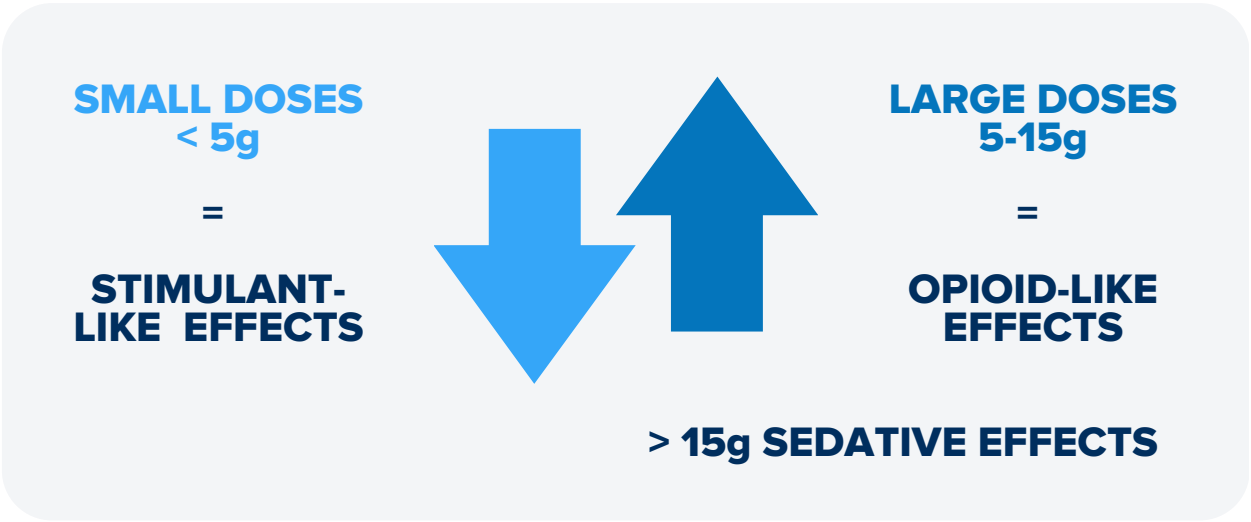
Pharmacodynamics

Kratom reaches peak concentration in approximately 2 hours. Its half-life varies greatly. Studies report a half-life of 3-24 hours.[8,9]

Pharmacokinetics

Depending on how much Kratom the person has consumed, the drug can have stimulant-like effects or opioid-like effects.

KRATOM USE AND EFFECTS



Kratom acts as an agonist at the mu-opioid receptor and as an antagonist at the kappa and delta opioid receptors in vitro. It has less affinity for opioid receptors than morphine. Because it has a broad affinity for receptors including serotonergic, adrenergic, and GABAergic pathways, Kratom can be linked to stimulant effects:[9]

MEDICATION INTERACTIONS

Kratom inhibits multiple cytochrome P450 isoforms (CYP) including CYP2D6 and CYP3A. CYP3A4 is responsible for the metabolism of more than 50% of medicines. Potent inhibitors of CYP3A4 include: clarithromycin, erythromycin, diltiazem, ketoconazole, ritonavir, verapamil, and grapefruit. Many websites advise "potentiating" the Kratom experience with grapefruit juice. Inducers of CYP3A4 include phenobarbital, phenytoin, rifampicin, St. John's Wort and glucocorticoids.[9]

ADVERSE EFFECTS

The most common adverse effects experienced are:[10]

- Agitation
- Tachycardia
- Nausea
- Vomiting
- Fatigue/drowsiness
- Hypertension
- Hypertension
- Confusion
- Seizures are common
- Psychotic symptoms[11]
    - Hallucinations
    - Delusions

TESTING FOR KRATOM USE

Testing can be done for mitragynine which is one of the main active ingredients. However, it requires advanced tests like liquid chromatography-tandem or mass spectrometry. It is unclear how long the drug is present in the urine but likely is dose dependent.[12]

DIAGNOSIS

Currently, ICD-10 diagnosis code, F19. 99 “Other psychoactive substance use, unspecified with unspecified psychoactive substance-induced disorder” is the most applicable. Treating Kratom use disorder and subsequent withdrawal is similar to how opioid use disorder is managed.

There is not an ICD-10 diagnosis for Kratom use disorder.

WITHDRAWAL SYMPTOMS

Withdrawal from Kratom can be similar to opioid withdrawal. Someone may experience these symptoms:[8,9]

- Anxiety
- Irritability
- Cravings
- Restlessness
- Body aches
- Fatigue
- Insomnia
- Nausea
- Depressed mood
- Hot or cold flashes
- Runny nose
- Watery eyes
- Vomiting

TREATMENT FOR KRATOM USE

Treating Kratom or 7-OH dependence and subsequent withdrawal is similar to how opioid use disorder is managed. Medications like buprenorphine can be used to manage withdrawal and dependence. Dosing for buprenorphine is similar to opioid use disorder management. In our experience, most patients transitioning from Kratom or 7-OH to buprenorphine have significant anxiety requiring supportive alpha-2 agonists like clonidine. These symptoms are secondary to sympathetic overactivation.[12,13]

SPECIFIC POPULATIONS

Considerations for young or pregnant people.

ADOLESCENTS

Kratom use in adolescents is a concern due to:

- Wide availability
- Ease of access
- No age restriction to purchase in places where it is not regulated

The majority of young people who try Kratom are between the ages of 17 to 19 years old.[14]

OPEN RESOURCES

OPEN's Youth Engagement Initiative frequently has new resources for tackling tough topics. Check back often for newly expanded content.

Cannabis Use and Addiction Education Guide for Teens and Young Adults
Use this guide to educate teens and young adults on cannabis use and addiction.

Naloxone Saves Lives Youth Flyer
Dispel myths around naloxone and share resources for accessing this life-saving medication with a flyer aimed at youth audiences.

PREGNANT PERSONS

From a peer literature review conducted in 2021, there were five published case reports that met inclusion criteria. There were six pregnant persons included who used Kratom during pregnancy. All deliveries were full term.

- Polysubstance use was reported in four out of six persons
- Treatment plans for the pregnant persons was similar to typical opioid treatment plans
  - All reported successfully weaning off of Kratom
- Five out of six infants experienced neonatal abstinence syndrome (NAS) including the two that were only exposed to Kratom
  - Additional research is needed to understand the timing of withdrawal compared to prenatal Kratom exposure

OPEN RESOURCES

OPEN's Substance Use Disorder Initiative frequently has new resources for tackling tough topics. Check back often for newly expanded content.

Comprehensive Care of Patients with Opioid Use Disorder in Pregnancy Guide

Use this guide as a prenatal care roadmap, guiding clinicians from core principles and screening through tailored counseling, medication management, and added supports to deliver comprehensive, coordinated care throughout pregnancy and beyond.

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