

Opioid Review and MAT Clinic *Augsburg PA Program Edition*

February 12, 2020

Objectives

- Identify patients who would benefit from tapering opioids, including patients with concurrent benzodiazepine use and comorbidities
- Identify signs in primary care patients of addiction and relapse (weight changes, functional changes, early refills)
- Describe morphine equivalents and opioid dose conversions
- Facilitate a team based approach to opioid tapering
- Demonstrate safe and effective tapers for opioid tapers and possible complications
- Review prescribing habits for acute pain/surgery for patients with use disorders
- Describe Kratom and its use, abuse, similarities and differences to opioids
- Describe the use, abuse, similarities and differences of synthetic opioids (Fentanyl)
- Outline metabolites of opioids and expected urine drug screen findings

Morphine Equivalents

POLL

Morphine Equivalents

Calculating morphine milligram equivalents (MME)

| OPIOID (doses in mg/day except where noted) | CONVERSION FACTOR |
|--|--------------------------|
| Codeine | 0.15 |
| Fentanyl transdermal (in mcg/hr) | 2.4 |
| Hydrocodone | 1 |
| Hydromorphone | 4 |
| Methadone | |
| 1-20 mg/day | 4 |
| 21-40 mg/day | 8 |
| 41-60 mg/day | 10 |
| ≥ 61-80 mg/day | 12 |
| Morphine | 1 |
| Oxycodone | 1.5 |
| Oxymorphone | 3 |

Morphine Equivalents

| <u>Prior Oral Opioid</u> | <u>Multiply dose by a factor of:</u> |
|--------------------------|--------------------------------------|
| Hydrocodone | 1 |
| Hydromorphone | 4 |
| Morphine | 1 |
| Oxycodone | 1.5 |
| Oxymorphone | 2 |

Methadone- not a linear relationship, exponential as dose increases

Comorbidities To Be Aware Of

Depression

- Increased risk of death in patients with depression especially at high doses
- Investigations were unable to separate unintentional OD vs. suicide
 - Turner B; Liang Y. J. Gen Intern. Med. 2015; 30: 1081-96.



History of Substance Abuse/Dependence

- 2-4x more likely to OD than patients without history of substance abuse

CDC Guidelines References (66,24,23)



Benzodiazepines

- Co-prescriptions are associated with increased risk of fatal overdose.
- Three separate studies of opioid overdose found evidence of concurrent benzodiazepine use in 31-61% of deaths *(CDC Guidelines References: 67,128,129)*

Falls/Elderly

- 4X more likely to fall on opioids than on NSAIDS



Chronic Kidney Disease

- Renally excreted opioids and metabolites can accumulate and cause life threatening symptoms
 - Tramadol preferred if needed
 - Methadone metabolizes liver- minimal accumulation in chronic kidney disease
 - Codeine- not recommended
 - Morphine- avoid if creatinine clearance <30
 - Hydrocodone- 25% renal
 - Oxycodone- can be used, dose adjusted substantial renal excretion



POLL



COPD and Opioids

- 50% of patients with COPD get opioids for chronic pain



COPD and Opioids

- Ahmed et al showed that opioids are associated with adverse outcomes, and therefore should not be given to those patients for reasons not supported with scientific evidence such as musculoskeletal pain.

- Ahmed et al. International Journal of Obstructive Pulmonary Disease. 2016 11:2651-2657)

COPD and Opioids

- COPD affects 4-10% of Canadian population
 - 5 year mortality 40-70% depending on severity
 - 2 year mortality with severe COPD- 50% when on opioids
 - Also increased risk of ER visits, hospitalization, and use of antibiotics/steroids
 - Some evidence not dose related

Nicholas t. Vozoris et al. European Respiratory Journal. July 2016. DOI 10.1183/13993003.01967-2015)

Alcohol

- ETOH: involved in 18.5% of opioid abuse ER visits and 27.2% of benzo related visits
- ETOH related to 20% of OD deaths with opioids or benzos

MMWR Oct 10, 2014. 63(40) 881-885.

- Ethanol and oxycodone cause greater ventilation depression than either alone, with the magnitude being clinically relevant. Elderly patients more affected.

Effects of Ethanol and Oxycodone. Anesthesiology (126)3: 534-542. March 2017.

Sleep Disorder Breathing

- Opioids predispose to central sleep apnea and to a lesser extent OSA
- 24% increase of CSA in long term opioid user

J. of Clinical Sleep Med. Vol 12. No. 04. Medium increased risk for central sleep apnea...in long term opioid users.

- Methadone and high dosing >200 MME and combination with benzos increases risks



Urine Drug Screens



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How to Interpret

- Have lab make available to all physicians metabolites of common medications
- Why are metabolites important



Approaching the Patient with Unexpected Urine Results

- Expected drug not present:
 - Prior to the test, you should have asked the patient what we're going to find in their urine
 - Ask the patient why the medication is not in their urine
 - Ask for an explanation
 - Ask where they got it, taper them, or give them a warning.

Approaching the Patient with Unexpected Urine Results

- Illicit substance is in the urine
 - Taper off controlled substance if in urine as well, or discontinue if not
 - See if they qualify for substance use disorder to offer treatment

Approaching the Patient with Unexpected Urine Results

- Adulterated urine
 - Bring patient back for follow up and have witnessed urine
 - Social work to meet

Approaching the Patient with Unexpected Urine Results

- Refusal to give urine
 - Patient does not get refill of medication

Approaching the Patient with Unexpected Urine Results

- Combination of a drug

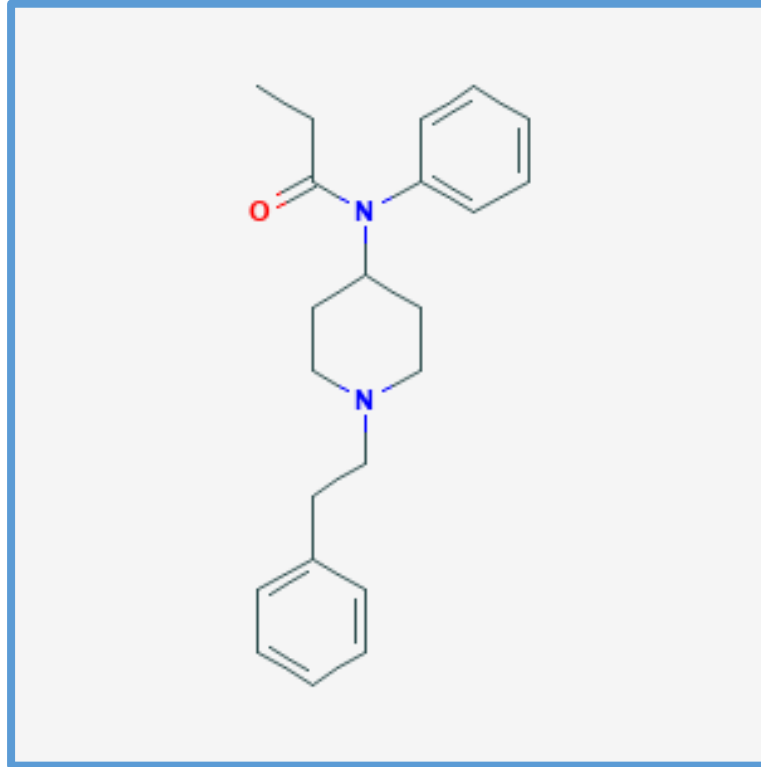
**Things that
“won’t be there”...
but be aware...**

Fentanyl

POLL



Fentanyl Structure



N-phenyl-*N*-[1-(2-phenylethyl)piperidin-4-yl]propanamide

Fentanyl

- Developed in the 1950s
- Synthetic opioid, lipophilic
- 50-100 times more potent than morphine
- 75% excreted in urine
- T $\frac{1}{2}$ - 7 hours

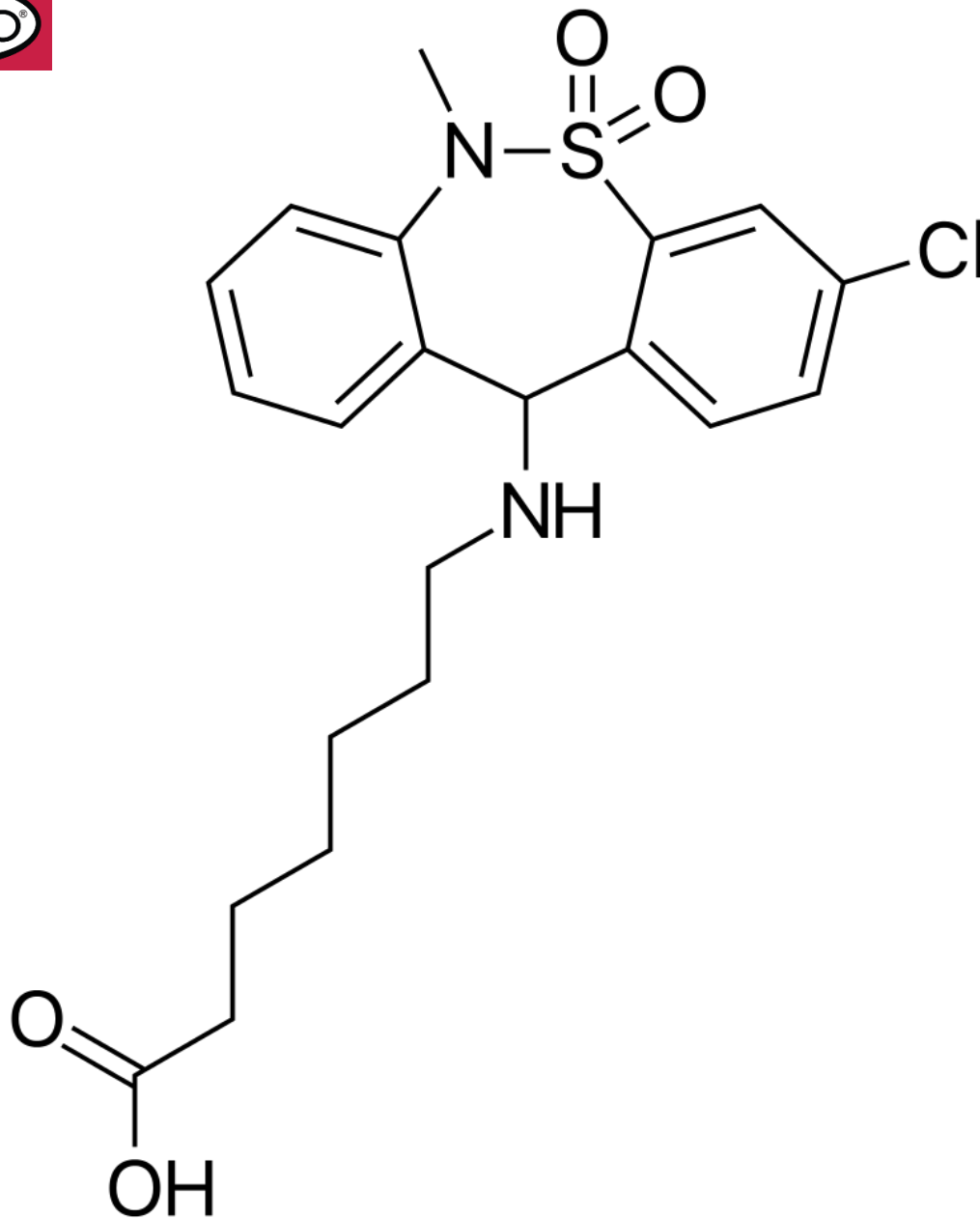
Fentanyl

- Prescription:
 - Actiq
 - Duragesic
 - Sublimaze
- Street names
 - Apache, china girl, china white, dance fever, friend, good fellas, jackpot, murder 8, tango, and cash

Fentanyl

- Bind Mu receptors
 - Euphoria, drowsiness, nausea, constipation, sedation, problems breathing, unconsciousness
- Illegal sold as:
 - Powder, blotter paper, eye droppers/nasal spray, pressed pills

Tianeptine



Tianeptine

Marketed as:

- Stablon
- Coaxil



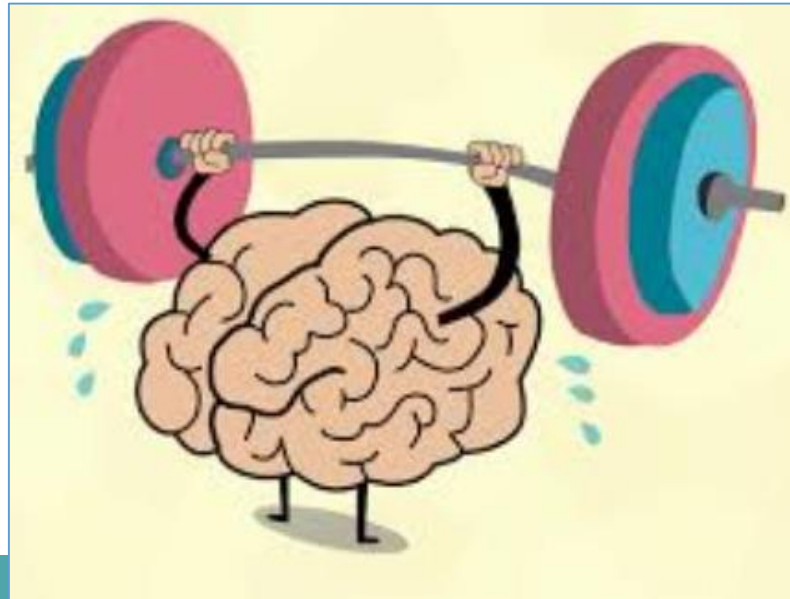
Tianeptine

**Marketed in 15 European
countries and 66 countries
world wide**



Tianeptine

Online marketing- different
“Boost working memory”
“Improve mental clarify”



Tianeptine

Toxicity

- Respiratory depression – death
- Considered initially a rare, if not unheard of problem, as abuse of this medication was felt to be < 0.3%

Tianeptine

Mechanism of Action

- First reported mechanism of action was felt to be increased serotonin reuptake which was opposite of SSRI

Tianeptine

In 2014 the article, “The atypical antidepressant and neurorestorative agent tianeptine is a μ -opioid receptor agonist” showed:

- Mu activation was likely the initial molecular event
- Possible effects to delta receptor also
- Indirectly modulates glutamate (excitatory)

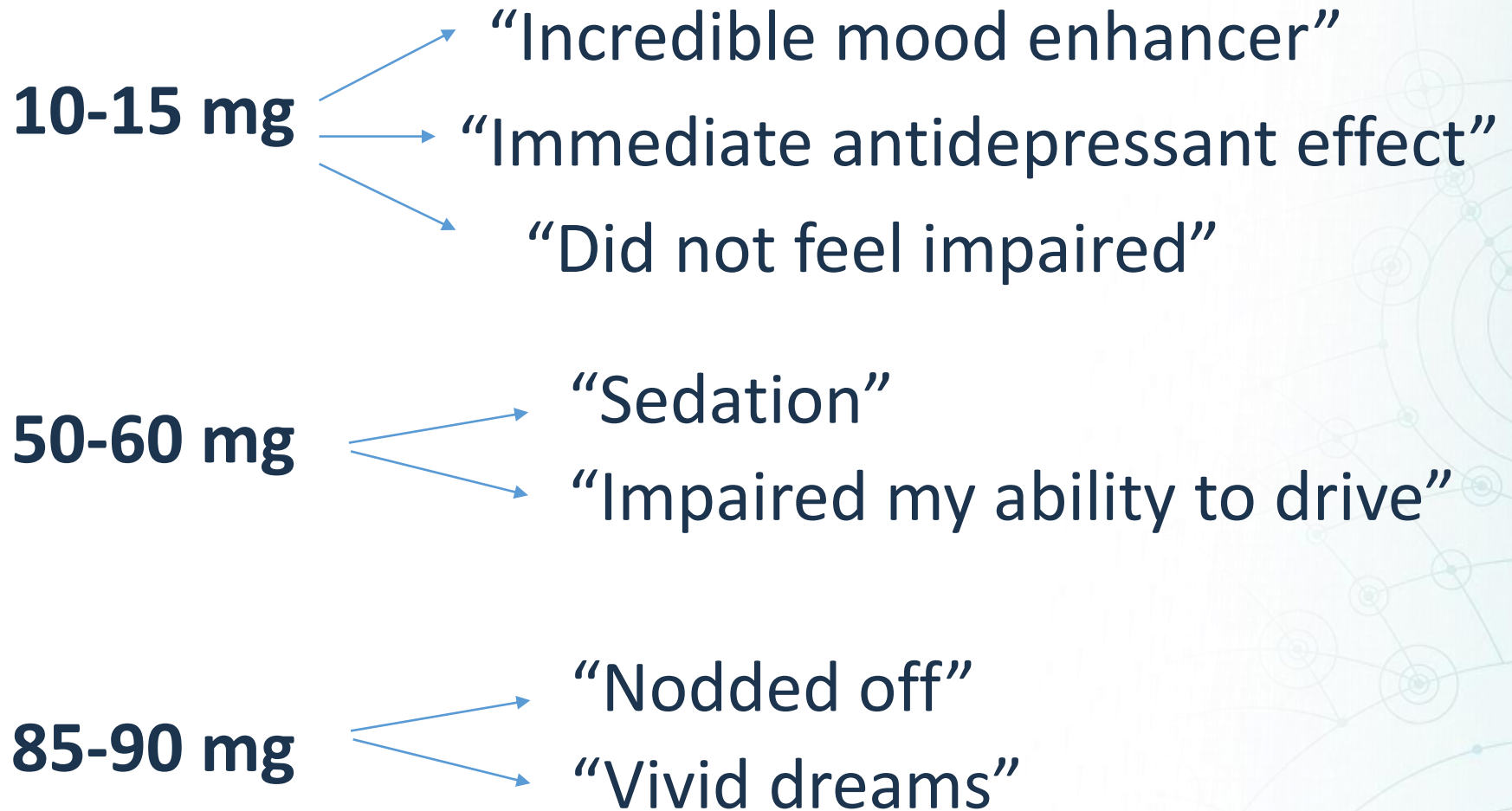
Tianeptine

Reddit- the source of all knowledge

- Tianeptine sodium- shorter acting 2.5 hours
- Tianeptine sulfate- longer acting 7.5 hours



Tianeptine



Tianeptine

Another post:

“Tolerance is quick. Kills your ability to feel any other opioids, kills effectiveness of Kratom 100%”

Tianeptine

Low dose- recommended doses

- Nausea
- Constipation
- Headache
- Dizziness



Tianeptine

High dose- when misused

- May mimic opioid OD- Naloxone effective
- Tolerance common
- NAS after delivery



Tianeptine

Use of Buprenorphine-Naloxone in the Treatment of Tianeptine Use Disorder

JUST DO IT.

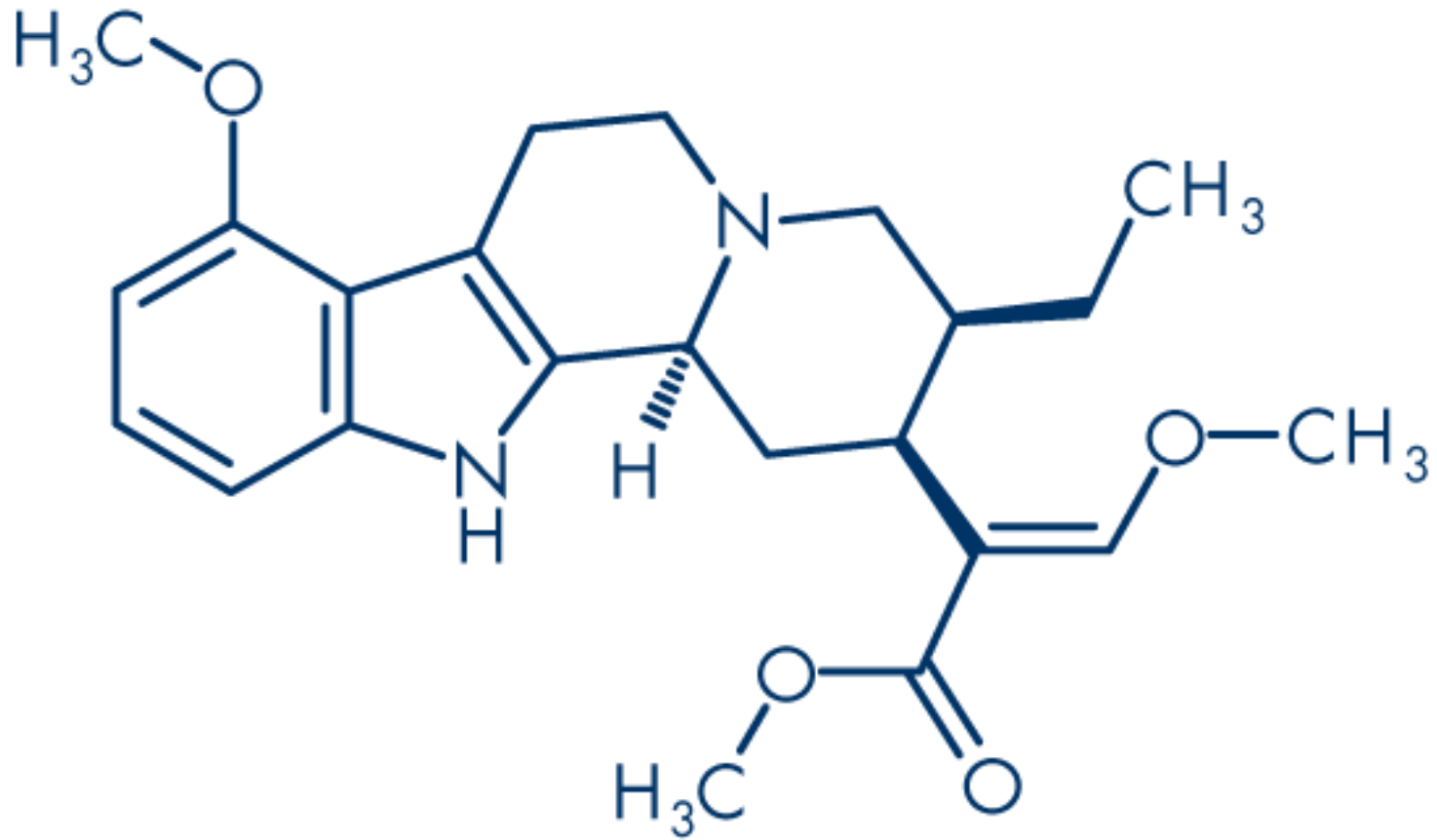


Kratom

Kratom



Kratom



Kratom

- DEA - *Mitragyna speciosa* (*Rubiaceae* family)
- Indigenous to Thailand, Malaysia, Myanmar, Papua New Guinea, others



Kratom tree



Leaf of kratom tree



Kratom capsules


Kratom

- **Formulations**

- Leaves
- Powder
- Pills
- Leaves
- Liquid extract/tinctures

- **Route**

- Drink
- Chew leaves
- Smoke
- Ingest pills



DrugFacts


www.drugabuse.gov

Kratom

What is kratom?

Kratom is a tropical tree (*Mitragyna speciosa*) native to Southeast Asia, with leaves that contain psychoactive (mind-altering) opioid compounds. The tree's bitter leaves are consumed for mood-uplifting effects and pain relief and as an aphrodisiac.

Kratom is not currently an illegal substance and has been easy to order on the Internet in recent years. It is sometimes sold as a green powder in packets labeled "not for human consumption." It is also sometimes sold as an extract or gum.



In recent years, some people have used kratom as an herbal alternative to medical treatment in attempts to control withdrawal symptoms and cravings caused by addiction to other opioids or to other addictive substances such as alcohol. There is no scientific evidence that kratom is effective or safe for this purpose (see "Medication-Assisted Treatment").

Kratom sometimes goes by the following names:

- Herbal Speedball
- Biak-biak
- Ketum
- Kahuam
- Ithang
- Thom

Photo by DEA/www.dea.gov/pr/multimedia-library/publications/drug_of_abuse.pdf#page=84

Kratom

• Adverse Effects

- Dry mouth
- Nausea
- Weight loss
- Constipation
- Seizure
- Hepatic injury
- QT prolongation
- Tolerance
- Withdrawal

Kratom

- **Withdrawal**
 - Similar to opioid withdrawal
 - Starts at about 6-12 hours
 - Lasts about 2-3 days

Other “No-Showers”

- Gabapentin
- Clonazepam/alprazolam
- “Z-drugs”
- Synthetics

Screen vs. Confirmatory

Decisions on care
should not be based
on a screening test
alone

Taper Considerations

POLL

Concerning Patients

- Aware of family history of SUD
- Known associates of people with use disorder
- Jail list, notification of law enforcement

“Red Flags”

- Weight changes- unexplained
- Drug seeking behavior
- Unexplained symptoms of “withdrawal”
 - Diarrhea, abdominal pain, nausea, vomiting
 - Meth- teeth
- Overall appearance: disheveled/ dirty/ etc.

Behavior Problems

- Signs/symptoms of use disorder
- Early refills
- Unexpected urines
- Doctor shopping
- Erratic behavior
- Significant mental health issues
- Suicidality
- History of overdose

Guidelines

- MME > 90, or > 50 with benzos
- Concurrent opioid use disorder
- Encouraged if no meaningful improvement in pain and function (at least 30% improvement)
- Misuse/diversion

Taper How To

- 10% decrease per month for longer history
- Utilize pharmacist
- Involve patient
- +/- long acting transition with a fixed schedule
 - 50% dose as long acting
 - 50% as short acting

References

- Gassaway MM, Rives ML, Kruegel AC, Javitch JA, Sames D. The atypical antidepressant and neurorestorative agent tianeptine is a μ -opioid receptor agonist. *Transl Psychiatry*. 2014;4(7):e411. Published 2014 Jul 15. doi:10.1038/tp.2014.30
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Case Presentation

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Meet John Doe

- 29 yo man who called the Little Falls clinic asking about suboxone
- Significant polysubstance use history starting at age 14
- Prior heroin use, has been on Suboxone in the past
- Most recently using a “natural” product he buys in bulk online
- You have a few minutes between other patients to ask questions

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logo here



GO



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logo here



Plan of action

- Given amount of Kratom use, figured he would end up needing between 16 and 24mg of suboxone daily
- Initial COWS of 18 -> given 4mg dose of suboxone
- Half hour later COWS 10 -> given another 4 mg
- Felt good enough to go home, discussed further dosing options (he is used to suboxone, having

Insert your
logo here



Next visit

- Settled on 8mg three times daily for total daily dose of 24mg daily
- “Night and day difference,” slight headache, no constipation or nausea
- Able to quit smoking marijuana - he had been using this to fend off nausea that came on when he went too long between Kratom doses