

# NYSAM 2019

## Clinical Case Presentations

Edwin A. Salsitz, M.D., DFASAM

Mount Sinai Beth Israel, NYC

Associate Clinical Professor

[edwin.salsitz@mountsinai.org](mailto:edwin.salsitz@mountsinai.org)

No Disclosures

# 2019 NYSAM Case Presentations

## Clinical Case Presentations

Timothy J Wiegand, MD, FACMT, FAACT, DFASAM

Director of Toxicology & Associate Professor

Emergency Medicine at the University of

Rochester Medical Center

Rochester, New York, USA

**No Disclosures**

“All things are poisons, for there is nothing without poisonous qualities. It is only the **dose** which makes a thing poison.”



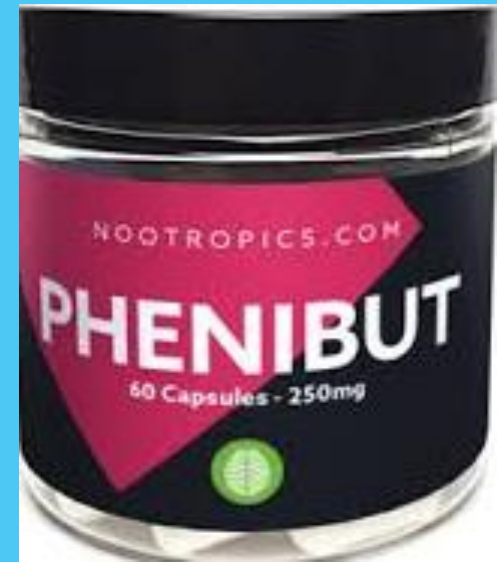
Philippus Aureolus Theophrastus Bombastus von Hohenheim, who published under the name **Paracelsus** was a Renaissance physician, botanist, alchemist, astrologer, and occultist. (1493—1541)

# Clinical Case: 1A

- 35 yo male IT Specialist
- Emigrated from Russia 5 years ago
- AUD since age 17—in remission X 2 yrs
- Hx. of anxiety and insomnia for many years
- Hx. of emotional and physical abuse by father
- Used X Drug for past 2 years for anxiety, insomnia, and alcohol craving
- Ran out of X Drug 72 hours ago
- Presented with typical sedative/hypnotic W/D

# Clinical Case: 1B

- Tremulous, Psychomotor Agitation, Tachycardia, Visual Hallucinations, Anxiety
- UDT: Neg: Opiate, Benzo, Barbiturate, Cocaine, THC, PCP, Methadone, Bupe, Methamphetamine
- ? X Drug
- Rx: Baclofen up to 60mg/day and then tapered + Tapering doses of Gabapentin
- ? X Drug
- Phenibut



**Same-Day Shipping** on most orders placed Monday-Friday by 12 PM EST. See our **Shipping and Returns Policy** for details.

[PRODUCTS](#) ▾ [SHIPPING & RETURNS](#) [FAQ'S](#) [ABOUT ZAS](#) [PRIVACY POLICY](#) [TERMS AND CONDITIONS](#) [CONTACT US](#) [ZAS BLOG](#)

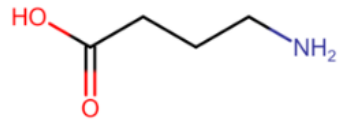
[Home](#) / [Products](#) / [Phenibut HCL](#)

Phenibut HCL

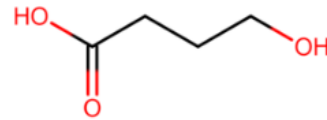
# Phenibut (1) History

- GABA analogue
- Synthesized in Russia in the 1960s
- Brand Names: Anvifen, Fenibut, Noofen
- Marketed for medical use in Russia, Latvia, Ukraine and Kazakhstan. Controlled only in Australia
- Widely available on the Internet as a supplement and nootropic(Cognitive Enhancement)
- Indications: anxiety, insomnia, depression, AUD, alcohol withdrawal, PTSD, stuttering in children,
- Soviet Cosmonauts Used in the Apollo-Sojuz Flight(1975)

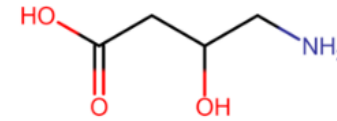
# Molecular Structures of Phenibut and Analogues



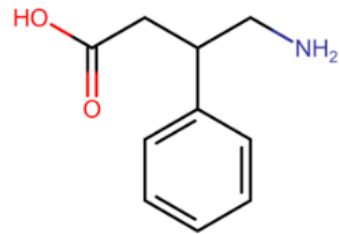
GABA



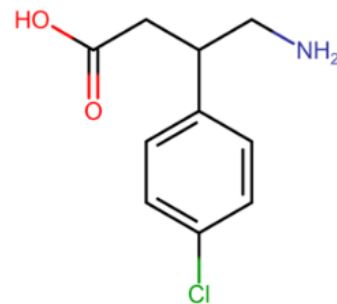
GHB



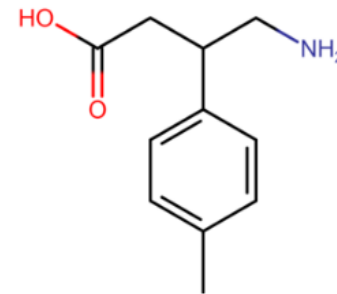
GABOB



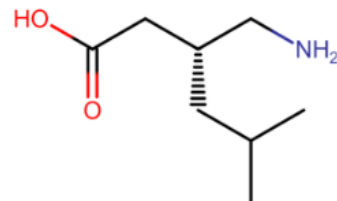
Phenibut



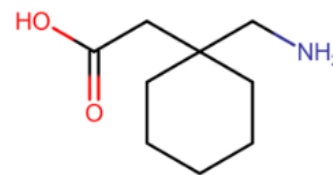
Baclofen



Tolibut



Pregabalin



Gabapentin



# Phenibut (2) Pharmacology

- Full Agonist at GABA-B Receptor (Baclofen)
- Binding to the  $\alpha 2\delta$  protein subunit of voltage gated Calcium channels in CNS/peripheral neuronal tissue  $\rightarrow$   $\downarrow$  Ca influx  $\rightarrow$   $\downarrow$  excitatory neurotransmitter release: same MOA as the Gabapentanoids
- Onset of Action 2-4 hrs: Peak Effect 6 hours
- Elimination  $\frac{1}{2}$  Life  $\sim$  5 hours
- Urinary Excretion Unchanged
- Therapeutic Dose 250-500mg/day: Misuse 1-3 gms
- Reports of Rectal Administration with Rapid Onset of Action—30 minutes

# Phenibut (3) Treatment

- Overdose: Airway, Supportive, Death: Rare
- Withdrawal: Baclofen, Gabapentanoids, Phenibut Taper. 1gm Phenibut = 10mg Baclofen
- Maintenance/Relapse: Treat Underlying Problems leading to use.
- Similar to Benzodiazepines.

Next Case

# Clinical Case 2A

- 44 yo male working in Hospitality Industry
- Past History of AUD (in remission 9mos), Tobacco Use Disorder, anxiety and depression
- Has tried different SSRIs and SNRIs with minimal +effect
- Purchased X Drug online from European source to treat anxiety
- Initially took recommended dose, then escalated dose for euphoric effect

# Clinical Case 2B

- Tried to reduce dose and taper, but developed withdrawal si/sx typical of opioid withdrawal
- Vehemently denied any opioid use
- Decided to go “Cold Turkey,” but withdrawal was severe and presented to ED.
- In the ED his COWS score was 20.
- UDT: Neg-Opiates, Oxy, Methadone, Bupe, Benzos, Barbiturates, PCP, Cocaine, Methamp, Pos: THC
- EKG: Normal      CMP: Mild elevation LFT's
- ? X Drug

# Tianeptine

Centers for Disease Control and Prevention  
**MMWR** | **TIANEPTINE, A POSSIBLE PUBLIC HEALTH RISK**

<b>ANTIDEPRESSANT NOT APPROVED IN THE U.S.</b>	<b>POISON CONTROL CENTER CALLS INCREASING</b>	<b>TREATING TIANEPTINE MISUSE</b>
<p><b>PEOPLE MAY BE ABUSING TIANEPTINE BECAUSE OF ITS OPIOID-LIKE EFFECTS</b></p>  <p><b>MISUSE CAN LEAD TO SEVERE ADVERSE EFFECTS, DEPENDENCE, AND WITHDRAWAL</b></p>	<p><b>218</b> CALLS FROM 2000 THROUGH 2017</p> <p><b>11</b> CALLS IN FIRST 14 YEARS</p> <p><b>207</b> IN MOST RECENT 4 YEARS</p> 	<p><b>CONSIDER TIANEPTINE MISUSE WHEN PATIENTS HAVE OPIOID-LIKE OVERDOSE OR WITHDRAWAL SYMPTOMS</b></p>  <p><b>CONSULT POISON CONTROL CENTERS (1-800-222-1222) FOR FURTHER MANAGEMENT</b></p> 

National Poison Data System data from 2000-2017 as published in El Zahran, MMWR 2018  
<https://go.usa.gsa/f/UxT4>

11/22/18

WWW.CDC.GOV

# Tianeptine (1) History

- Discovered in France 1960s
- Prescription medication in Europe, Asia, and South America:  
NOT USA, UK, Canada, NZ, Australia
- Available online as dietary supplement and research chemical
- France 2012: Tianeptine → Controlled Substance
- Studies in USA(JNJ) terminated in 2012: ? Cost Issues
- Michigan 2018: Tianeptine Schedule II
- Brand Names: Coaxil, Stablon, Tatinol
- Indications: Depression, Anxiety, Asthma, Fibromyalgia
- “Doctor Shopping” in France for Tianeptine

**Table 1.** Tianeptine brand names in respective countries.

Aneptinex	SVK HU
Atinepte	BU PL
Coaxil	BU CZ EN HU LG PL RO RS SVK HR LH
Lyxit	RO SVK
Neluptin	LH PL PO
Neptine	KS
Neptika	HR
Nobixal	RO
Salymbra	EN
Stablon	AR AU BR EG FR ID KS MT MU MY PO TH TS
Staneptine	KS
Tatinol	CH
Tialera	BK BU HU PL
Tianeptin Mylan	SVK
Tianeptin Sandoz	SVK
Tianeptina Generis	PO
Tianeptina Lupin	PO
Tianeptina Wynn	PO
Tianeptine Mylan Pharma	FR
Tianesal	PL
Tianeurax	GE
Tymogen	PL

Source: [Drugs.com](https://www.drugs.com); NATO country codes.





8 599552 090236

*Reçete ile satılır. Çocukların göremeyeceği, erişemeyeceği yerlerde ve ambalajında, kuru yerde, 30°C'nin altında, oda sıcaklığında saklayınız. Beklenmeyen bir etki görüldüğünde doktorunuza başvurunuz. Kullanmadan önce prospektüsü okuyunuz. Fiyat kupürü bulunmayan ambalajları satın almayınız.*

# STABLON® 12.5 mg

Kaplı Tablet

TIANEPTINE SODYUM 12.5 mg  
antidepresan



60 KAPLI TABLET





Same-Day Shipping on most orders placed Monday-Friday by 12 PM EST. See our Shipping and Returns Policy for details.

PRODUCTS ▾ SHIPPING & RETURNS FAQs ABOUT ZAS PRIVACY POLICY TERMS AND CONDITIONS CONTACT US ZAS BLOG

Home / Products / Buy Tianeptine Sodium Powder 90 Capsules x 12mg Each



Buy Tianeptine Sodium Powder 90 Capsules x 12mg Each

\$31.95

★★★★★ (15 reviews) [Write a Review](#)

UPC:  
680140556331

Add to Wish List ▾



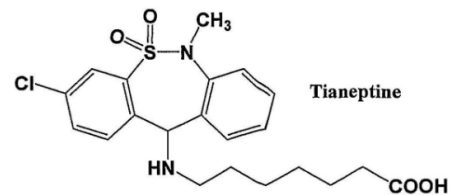
Description



WE HAVE SODIUM, FREE ACID AND SULFATE IN STOCK NOW!

The PayPal button is also the credit card processor. Choose Google pay by selecting offline payment when checking out.

SHOP NOW

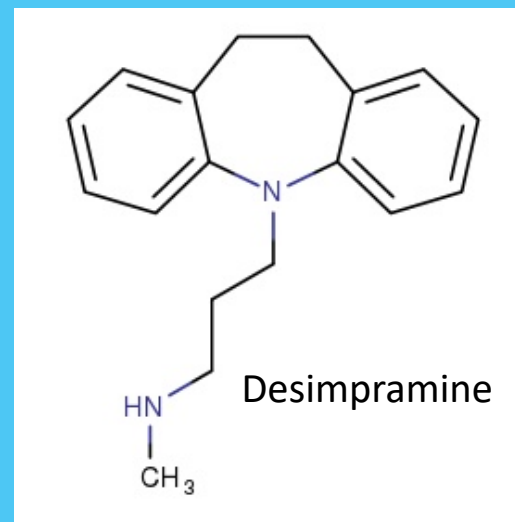
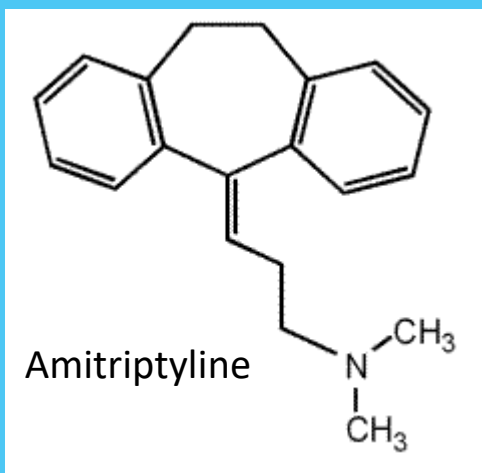


BUY TIANEPTINE

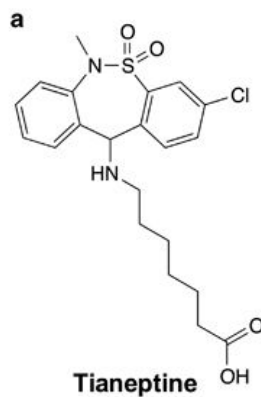
ATTENTION: WE OFFER TIANEPTINE For Research Purpose Only Not For Human Consumption

# Tianeptine (2) MOA

- Atypical Tricyclic Anti-Depressant
- Enhances Serotonin Uptake, ↑ Dopamine Signaling
- Full  $\mu$ -opioid and  $\delta$ -opioid(↓) agonist: ?Dose Dependent
- Modulation of the Glutamatergic system
- Encourage Neuroplasticity: PFC, Amygdala, Hippocampus
- Minimal Anti-Cholinergic or CV adverse effects
- Therapeutic Dose 25-50mg daily
- Misuse Doses: > 3000mg



From: The atypical antidepressant and neurorestorative agent tianeptine is a  $\mu$ -opioid receptor agonist



**b**

Receptor	K <sub>i</sub> of Tianeptine	EC <sub>50</sub> of Tianeptine (G Protein Activation)
Human MOR	383 ± 183 nM	194 ± 70 nM
Mouse MOR	-	641 ± 120 nM
Human DOR	> 10 μM	37.4 ± 11.2 μM
Mouse DOR	-	14.5 ± 6.6 μM
Human KOR	No Activity	No Activity
Rat KOR	-	No Activity

Summary of tianeptine's activity at the opioid receptors. **(a)** Chemical structure of tianeptine. **(b)** Radioligand displacement binding assay of tianeptine at  $\mu$ -opioid receptor (MOR; *n*=3),  $\delta$ -opioid receptor (DOR; *n*=4) and  $\kappa$ -opioid receptor (KOR; *n*=4). Tianeptine's functional activity at MOR, DOR and KOR are also summarized. Data represent mean±s.e.m.

# Tianeptine (3) Pharmacology

- Onset of action ~ 30minutes po
- Not Metabolized by CYP450.  $\beta$  – *oxidation*
- Elimination  $\frac{1}{2}$  life ~ 3hrs. Renal & Hepatobiliary
- Active Metabolite: longer  $\frac{1}{2}$  life
- ?  $\uparrow$  Hepatotoxicity > other TCAs

# Tianeptine (4) Case Reports

- Neonatal Abstinence Syndrome: Treated with Morphine: No Teratogenicity
- Overdoses: Naloxone effective
- Withdrawal Syndromes: Typical Opioid W/D
- Overdose Deaths
- IV and IN Reports
- Toxic Fatal Leukoencephalopathy:  
Tianeptine level: 3,000ng/mL Therapeutic: 300ng/mL

# Tianeptine (5) Withdrawal

- Agitation
- Nausea and Vomiting
- Tachycardia
- Hypertension
- Diarrhea
- Tremor
- Diaphoresis
  
- Tx: Benzos, Hydration, Antiemetics



# Tianeptine : US Fatalities

28 yo male with hx of AUD, TUD, anxiety and Depression. No suicide note



30 yo male on alprazolam For GAD. Syringe and needles found at the scene. Recent puncture site right antecubital fossa.



From: Case Reports of Fatalities Involving Tianeptine in the United States

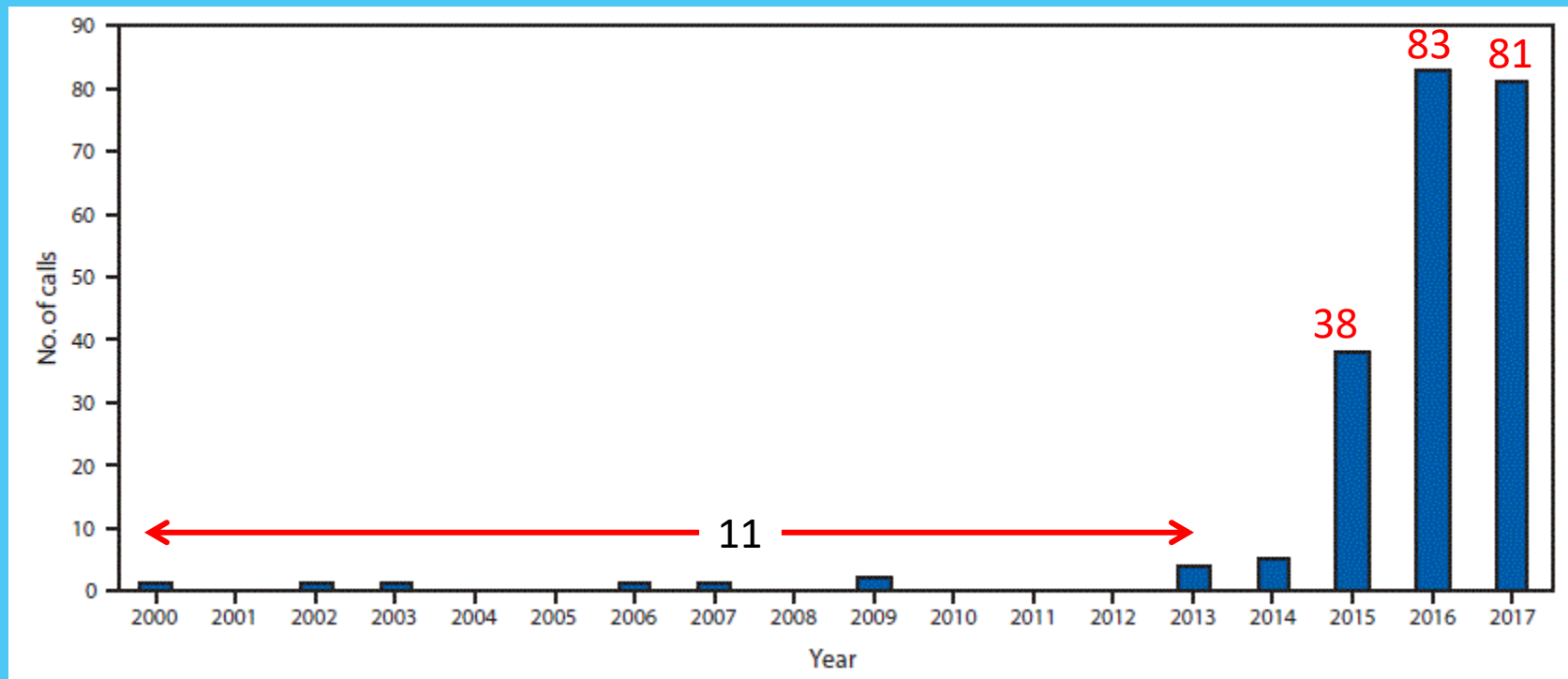
J Anal Toxicol. 2018;42(7):503-509. doi:10.1093/jat/bky023

J Anal Toxicol | © The Author(s) 2018. Published by Oxford University Press. All rights reserved. For Permissions, please email: journals.permissions@oup.com This article is published and distributed under the terms of the Oxford University Press, Standard Journals Publication Model ([https://academic.oup.com/journals/pages/about\\_us/legal/notices](https://academic.oup.com/journals/pages/about_us/legal/notices))








# Characteristics of Tianeptine Exposures Reported to the National Poison Data System — United States, 2000–2017

Tharwat El Zahran, MD<sup>1,2</sup>; Joshua Schier, MD<sup>1,2</sup>; Emily Glidden, MPH<sup>1</sup>; Stephanie Kieszak, MPH<sup>1</sup>; Royal Law, PhD<sup>1</sup>; Edward Bottei, MD<sup>3</sup>; Cynthia Aaron, MD<sup>4</sup>; Andrew King, MD<sup>4</sup>; Arthur Chang, MD<sup>1</sup>



Number of Tianeptine exposure telephone calls reported (N = 218) — National Poison Data System, United States, 2000–2017

**TABLE 1. Characteristics of telephone calls related to tianeptine exposure (N = 218) — National Poison Data System, United States, 2000–2017**

Characteristic (no. with known information)	No.	(%)
<b>Call source (218)</b>		
Health care provider 	198	(91.2)
Caller residence	13	(6.0)
Other	7	(3.2)
<b>U.S. Census region (217)</b>		
South	75	(34.6)
West	54	(24.9)
Midwest	47	(21.6)
Northeast	41	(18.9)
<b>Sex (215)</b>		
Male 	177	(82.3)
Female	38	(17.7)
<b>Age group (yrs) (213)</b>		
<20	25	(11.7)
21–40 	121	(56.8)
41–60	59	(27.7)
≥61	8	(3.8)
<b>Exposure route (218)</b>		
Ingestion 	183	(83.9)
Parenteral	15	(6.9)
Inhalation	4	(1.8)
Unknown/Other	16	(7.4)
<b>Exposure type (218)</b>		
Intentional 	119	(54.6)
Unintentional	23	(10.5)
Withdrawal	29	(13.3)
Unknown/Other	47	(21.6)
<b>Coexposure (83)</b>		
Phenibut	26	(31.3)
Ethanol	13	(15.7)
Benzodiazepines	10	(12.0)
Opioids	10	(12.0)

**TABLE 2. Common clinical effects associated with tianeptine exposures (N = 114) and therapies received — National Poison Data System, United States, 2000–2017**

Clinical effect*	No.	(%)
<b>Cardiovascular effect</b>	<b>37</b>	<b>(32.5)</b>
Tachycardia	29	(25.4)
High blood pressure	13	(11.4)
Conduction delays	5	(4.4)
<b>Neurologic effect</b>	<b>55</b>	<b>(48.3)</b>
Agitation	25	(21.9)
Drowsiness	19	(16.7)
Confusion	15	(13.2)
Coma	5	(4.4)
<b>Gastrointestinal effect</b>	<b>12</b>	<b>(10.5)</b>
Nausea	9	(7.9)
Vomiting	5	(4.4)
Diarrhea	3	(2.6)
<b>Dermal effect</b>	<b>10</b>	<b>(8.8)</b>
Pallor	3	(2.6)
Pain	3	(2.6)
Cellulitis	2	(1.8)
<b>Constitutional effect</b>	<b>10</b>	<b>(8.8)</b>
Diaphoresis	8	(7.0)
Fever	3	(2.6)
Pain	1	(0.9)
<b>Respiratory effect</b>	<b>8</b>	<b>(7.0)</b>
Respiratory depression	6	(5.3)
Dyspnea	3	(2.6)
Tachypnea	1	(0.9)
<b>Ocular effect</b>	<b>6</b>	<b>(5.3)</b>
Mydriasis	4	(3.5)
Miosis	2	(1.8)
<b>Renal effect</b>	<b>5</b>	<b>(4.4)</b>
Urinary retention	3	(2.6)
Creatinine abnormality	2	(1.8)
Kidney failure	1	(0.9)
<b>Metabolic effect</b>	<b>5</b>	<b>(4.4)</b>
Electrolyte disturbances	3	(2.6)
Acidosis	2	(1.8)
<b>Musculoskeletal effect</b>	<b>5</b>	<b>(4.4)</b>
Muscle weakness	2	(1.8)
Rigidity	1	(0.9)
<b>Psychiatric effect</b>	<b>2</b>	<b>(1.8)</b>
Delusions	2	(1.8)
<b>Therapy</b>		
Fluids	40	(35.1)
Benzodiazepines	31	(27.2)
Oxygen	12	(10.5)
Naloxone	11	(9.7)
Antibiotics	11	(9.7)
Sedation	9	(7.9)
Antiemetics	7	(6.1)
Intubation	5	(4.4)
Ventilator support	5	(4.4)
Antihistamine	3	(2.6)



## News & Events

Home > News & Events > Newsroom > Press Announcements

### FDA News Release

# FDA warns marketers of products labeled as dietary supplements that contain tianeptine for making unproven claims to treat serious conditions, including opioid use disorder



SHARE



TWEET



LINKEDIN



PIN IT



EMAIL



PRINT

**For Immediate  
Release**

November 20, 2018

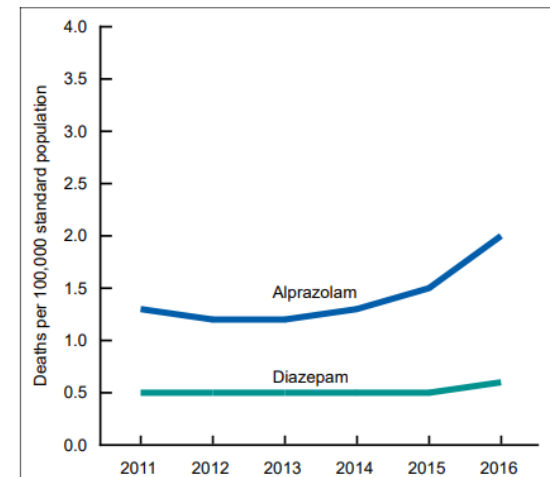
### Release

The U.S. Food and Drug Administration today posted [warning letters](#) issued to two companies for the illegal marketing of products labeled as dietary supplements that contain tianeptine, a chemical compound that companies are illegally claiming treats opioid use disorder (OUD), pain and anxiety, and other unlawful and unproven claims. These actions follow reports to the FDA of serious adverse events associated with the use of products containing tianeptine.

# Case Presentations in Russia

- X Drug Approved by the FDA in 1981
- Highly misused: Obtained on Internet
- Often combined with opioids: ODs
- W/D: Seizures, Delirium, Tachycardia

6 National Vital Statistics Reports, Vol. 67, No. 9, December 12, 2018



NOTES: Drug overdose deaths are identified using *International Classification of Diseases, Tenth Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the referent drug (i.e., the one listed). Deaths involving more than one drug (e.g., a death involving both heroin and cocaine) are counted in both totals. Caution should be used when comparing numbers across years. The reporting of at least one specific drug in the literal text improved from 73% of drug overdose deaths in 2011 to 85% of drug overdose deaths in 2016.

SOURCE: NCHS, National Vital Statistics System, Mortality files linked with death certificate literal text, 2011–2016.

**Figure 2. Age-adjusted rates for drug overdose deaths involving selected benzodiazepines, 2011–2016**

**NEXT CASE**

# Clinical Case 3A

- 26 yo pregnant female delivers a term male neonate
- Patient has a past hx of OUD: oxycodone and IN heroin
- Successful Rehab Treatment 2 years ago. No MAT
- Attends evening outpatient rehab 2X week.  
UDTs: Neg → opiates, methadone, oxy, bupe, cocaine, benzos, amphetamines +/- → THC No Alcohol/Tob 9mos
- Works fulltime as administrative assistant
- Admission UDT → Neg
- At 24 hours of age neonate developed si/sx of opioid NAS
- Mother denied use of prescription and/or illicit opioids

# Clinical Case 3B

- Interview of the Father revealed that the mother was drinking tea 2-3 X daily, which she had purchased on the Internet. He thought it was a healthy herbal tea.
- Neonate UDT → Neg
- ↑ Finnegan Score: Rx Morphine → Resolution

? What Substance



# Neonatal Abstinence Syndrome Due to Maternal Kratom Use

Whitney B. Eldridge, MD, Cherie Foster, MD, Lance Wyble, MD

Neonatal abstinence syndrome (NAS) is increasing in incidence and most commonly associated with maternal opioid use during pregnancy. Nonopioid alternatives to treat opioid dependence are highly sought after in the country's current opioid epidemic. Whether Kratom, a legal, widely available herbal supplement, should be classified as an opioid is contentious. Although the US Food and Drug Administration has recently addressed this controversy, Kratom continues to be marketed as a nonopioid remedy for opioid withdrawal. Its use is increasing in the United States. We describe an infant with NAS born to a mother with daily Kratom tea ingestion to self-treat opioid dependence. Pediatricians and parents should be aware of the risk of NAS due to Kratom use during pregnancy.

abstract

# KRATOM POWDER & EXTRACTS



GUARENTEED HIGHEST QUALITY ON POWDERS AND EXTRACTS



o Red  
★★  
- \$119.99

♡ Borneo White  
★★★★★  
\$9.99 - \$119.99

♡ Green Bali  
★★★★★  
\$9.99 - \$119.99

♡ Green Malaysian  
★★★★★  
\$14.99 - \$179.99

♡ Maeng Da  
★★★★★  
\$16.99 - \$203.99



WE'RE HERE TO ANSWER YOUR QUESTIONS  
**PHONE SUPPORT NOW AT KRAKEN**  
 Our Customer Service Reps are ready to help!  
 9 - 5 ET, Monday - Friday  
**503-877-1200**



- HOME
- BUY KRATOM TEA
- BUY KAVA TEA
- ACCESSORIES
- REWARDS
- COUPONS
- CONTACT US
- ORDER STATUS
- WHOLESALE

Home / Kratom Tea Capsules



[Share now to receive a 10% discount.](#)



### BUY KRATOM CAPSULES FROM THE MOST REPUTABLE BRAND ONLINE

Our vegetable capsules consist of only two ingredients: 100% natural vegetable cellulose and purified water. These capsules contain preservatives, gelatin, wheat, animal by-products, or starch and are made from pure cellulose of pine or poplar. All capsules are Kosher and Halal certified.

### CATEGORIES

- BUY KRATOM TEA POWDER & LEAF
- BUY KAVA TEA
- ACCESSORIES

Sort By

Show  
 per page

**FREE**  
**SAME-DAY**  
**SHIPPING**  
 ON ALL ORDERS



Bali Kratom Capsules  
 ★★★★★ 253 Rating(s)  
 Starting at: **\$15.45**



White Vein Borneo Kratom Capsules  
 ★★★★★ 93 Rating(s)  
 Starting at: **\$15.45**



Maeng Da Thai Kratom Capsules (OG Red Vein)  
 ★★★★★ 192 Rating(s)  
 Starting at: **\$21.45**



# Kratom = Herbal Extract

## Mitrogyna Speciosa



# Kratom = *Mitragyna Speciosa*

- Kratom: from a tropical evergreen tree or shrub related to the coffee plant
- Native to Southeast Asia, Thailand, Malaysia, and Papua New Guinea
- Used by indigenous population historically as a stimulant to enhance stamina and reduce fatigue
- Also used in traditional medicine for a variety of conditions including pain, diarrhea, cough, Opioid W/D, Depression, Anxiety

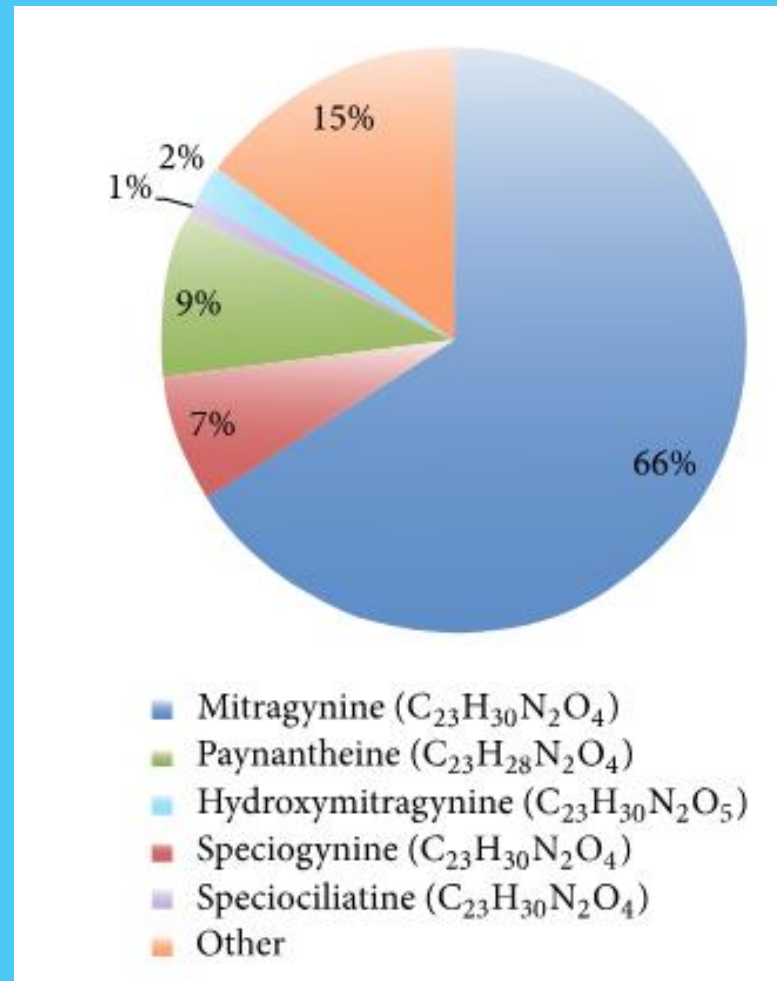
# Kratom—Local Names

- Ketum
- Biak
- Thom
- Mambog
- Kakuam
- Krathom
- Thang

Of the 25 most abundant compounds in kratom, 22 are known to bind  $\mu$ -opioid receptors and to effectively act as opioid agonists.



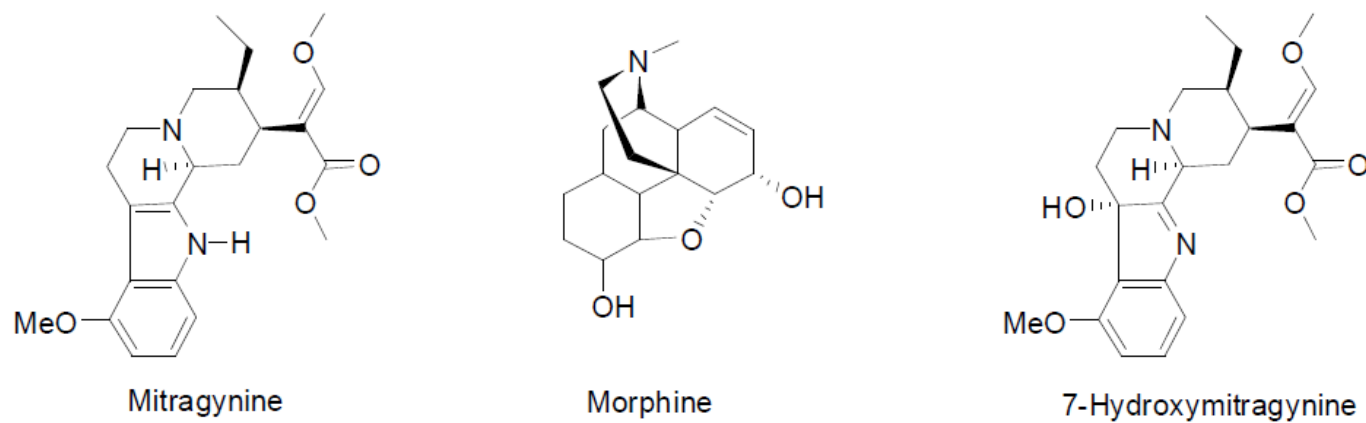
An estimate of Thai kratom extract composition. The phytochemicals isolated from various parts of the tree include overall 40 structurally related alkaloids as well as several flavonoids, terpenoid saponins, polyphenols, and various glycosides





# Kratom--Pharmacology

- Low Dose: 1-5g: Stimulant resembling caffeine/cocaine: ?MOA
- High Dose: 5-15g: Opioid Like Effects
- $\mu$  and  $\delta$  Opioid (?k) Receptor Agonist/?Partial
- 7-OH Mitragynine 13 and 46 > Potent: Morphine:Mitrgynine
- $\alpha$ 2 Adrenergic Agonist, Descending Pathway-NE, 5HT
- Animal self administration
- Analgesic and Sedation Effect Reversed by Naloxone
- Onset of action: 30 minutes:  $\frac{1}{2}$  life ~4 hrs
- Mitragynine inhibits CYP 3A4, 2D6, 2C9, 1A2
- ? Hepatic Cholestasis—dose dependent



**Fig. (6).** Comparison of mitragynine, morphine, and 7-hydroxymitragynine.

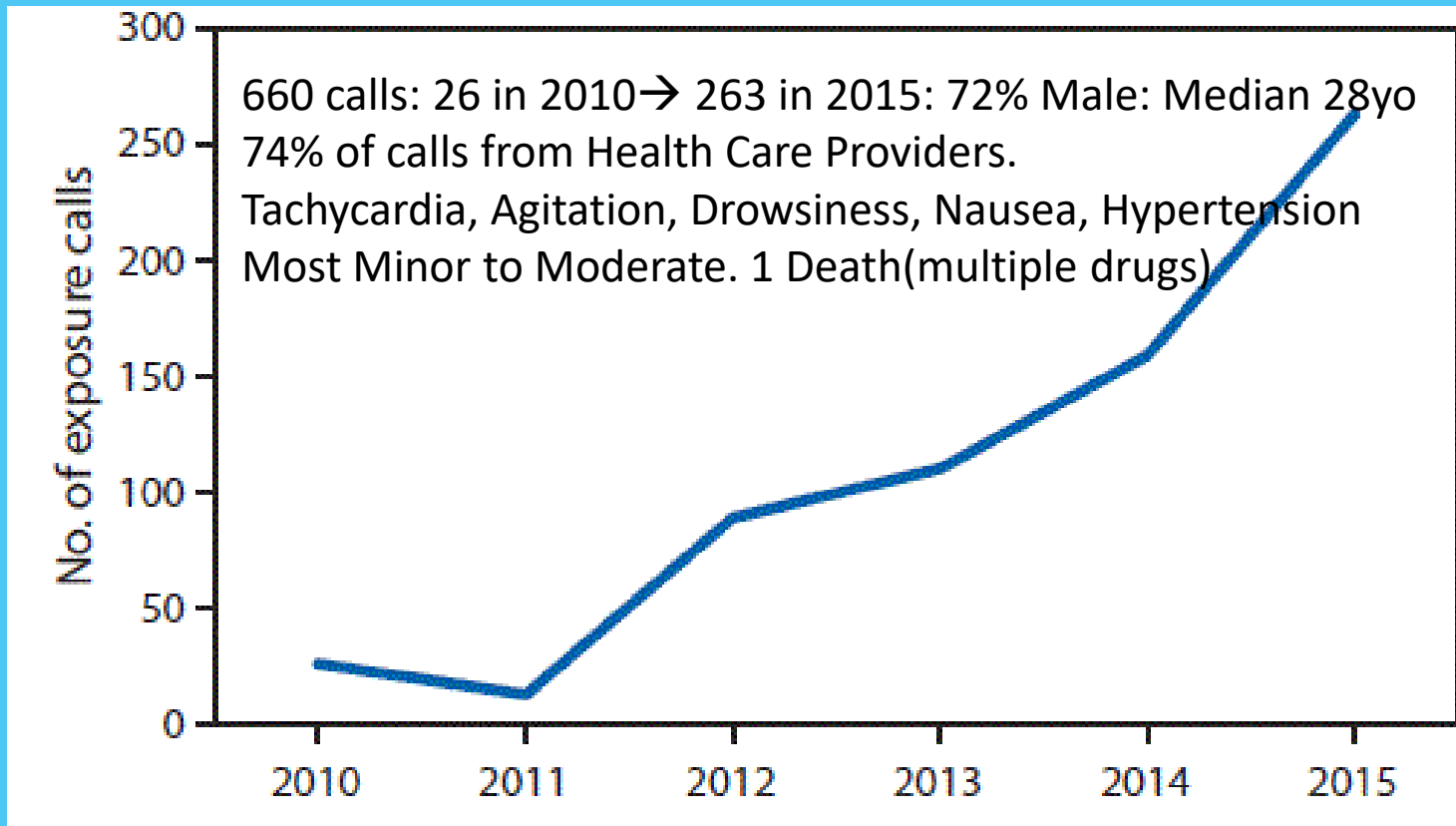
# Kratom--Formulations

- Leaves—chew, brew tea
  - Powder— capsules(po), smoke,
  - Bitter Taste—Honey Added
- 

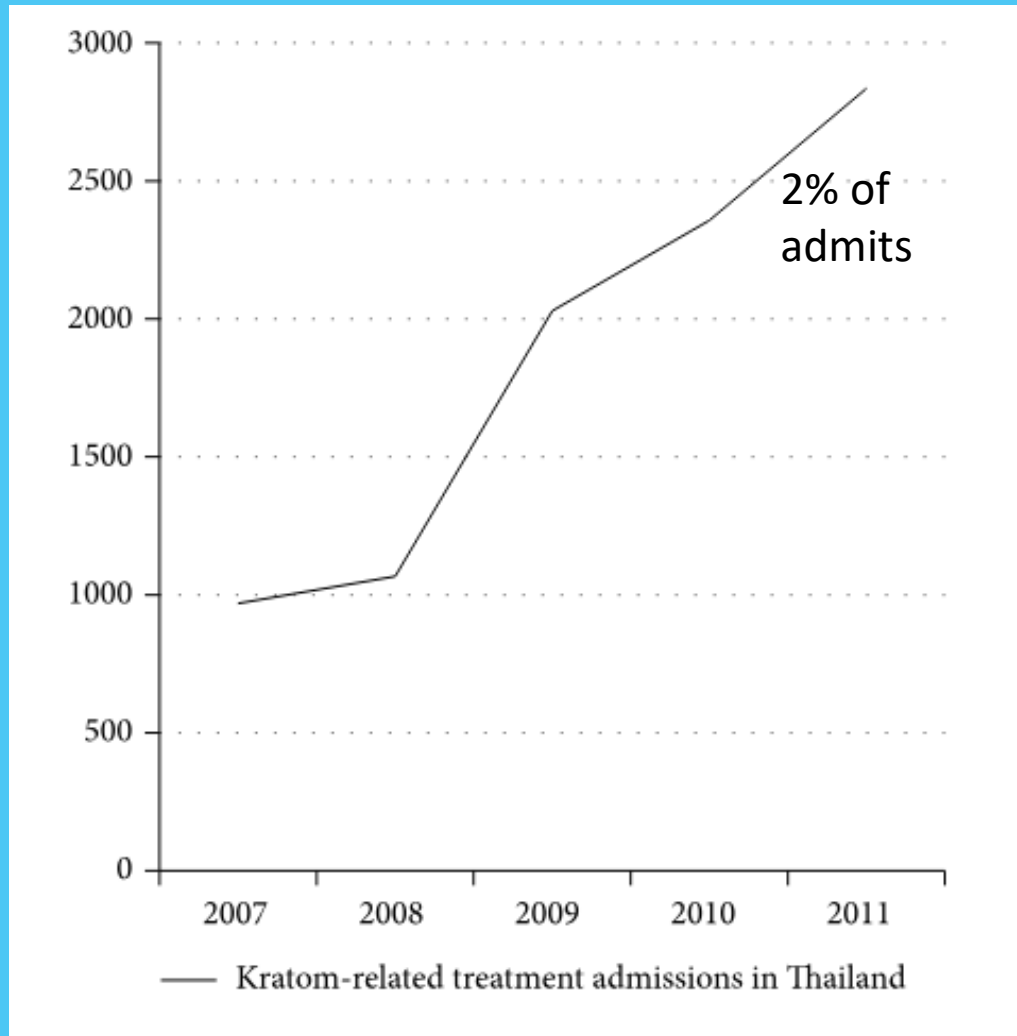
Krypton—Mitragynine+O-desmethyltramadol--  
Sweden→Fatal ODs

4 X 100—Kratom Tea+Coca-Cola+Codeine Cough  
Syrup+Ice Cubes Alcohol Mimicking Effect for Young  
Muslims

# Number of reported exposure calls to poison centers related to Kratom use, by year — National Poison Data System, United States and Puerto Rico, January 2010–December 2015

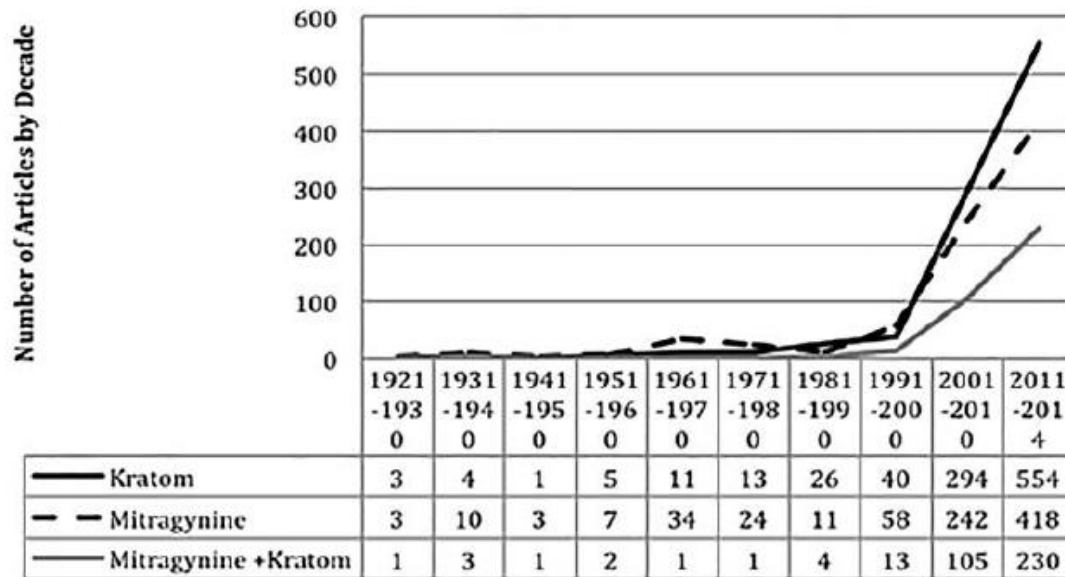


# Kratom: Thailand Treatment Admissions



BioMed Research  
International  
Volume 2015,  
Article ID 968786,  
11 pages

### Number of Scholarly Publications about Kratom & Mitragynine by Decade



**FIGURE 2** Numbers of scholarly publications about Kratom 1920–2014. This graph illustrates the number of scholarly articles published about Kratom each decade dating back to 1920. The number of articles published from 2010 to 2014 demonstrates a significant increase in research and scientific interest in Kratom.

# Kratom: Adverse Effects

**Table 1:** Report of adverse/toxicological effects of kratom.

Short time use effects	Nausea, constipation, sleep problems, temporary <a href="#">erectile dysfunction</a> , itching, or sweating
Long time use effects	Anorexia, dry mouth, problems in diuresis, darker skin, and hair loss
Withdrawal <a href="#">symptoms</a>	Hostility, aggression, aching of muscles and bones, jerky movements of the limbs, anorexia <a href="#">and weight loss</a> , and insomnia
Infrequent effects	Seizures (individuals using high doses of kratom, either alone or combined with other drugs), intrahepatic cholestasis, psychotic symptoms, Adult Respiratory Distress Syndrome, and hypothyroidism
Fatalities	<a href="#">Kratom</a> mixed with other substances: O-desmethyltramadol; propylhexedrine; over-the-counter cold medications and benzodiazepines; venlafaxine, diphenhydramine, and mirtazapine; zopiclone, <a href="#">citalopram</a> , and lamotrigine

# Kratom—Chronic Use

- Anorexia, Weight Loss, Constipation, Dark Pigmentation of the Face(↑Melanocyte Stim)
- Deaths: Generally in combination with alcohol, other opioids, benzos, others
- Typical, but Milder, Opioid Physical Dependence, Tolerance, and Withdrawal Syndrome
- Secondary Hypogonadism



# Kratom-Regulations

- Controlled Substance in Thailand and Malaysia
- DEA 2016: Consider Schedule I: Opposed by FDA and Congress-- +therapeutic effects      DEA  
Blinked: Legal under Federal Law
- DEA: “Drug and Chemical of Concern”
- Schedule I in these States: AL, WI, TN, IN
- Primarily Used to Self Manage Chronic Pain, Opioid Withdrawal, Opioid Analgesic “Holidays”

# Kratom--Detection

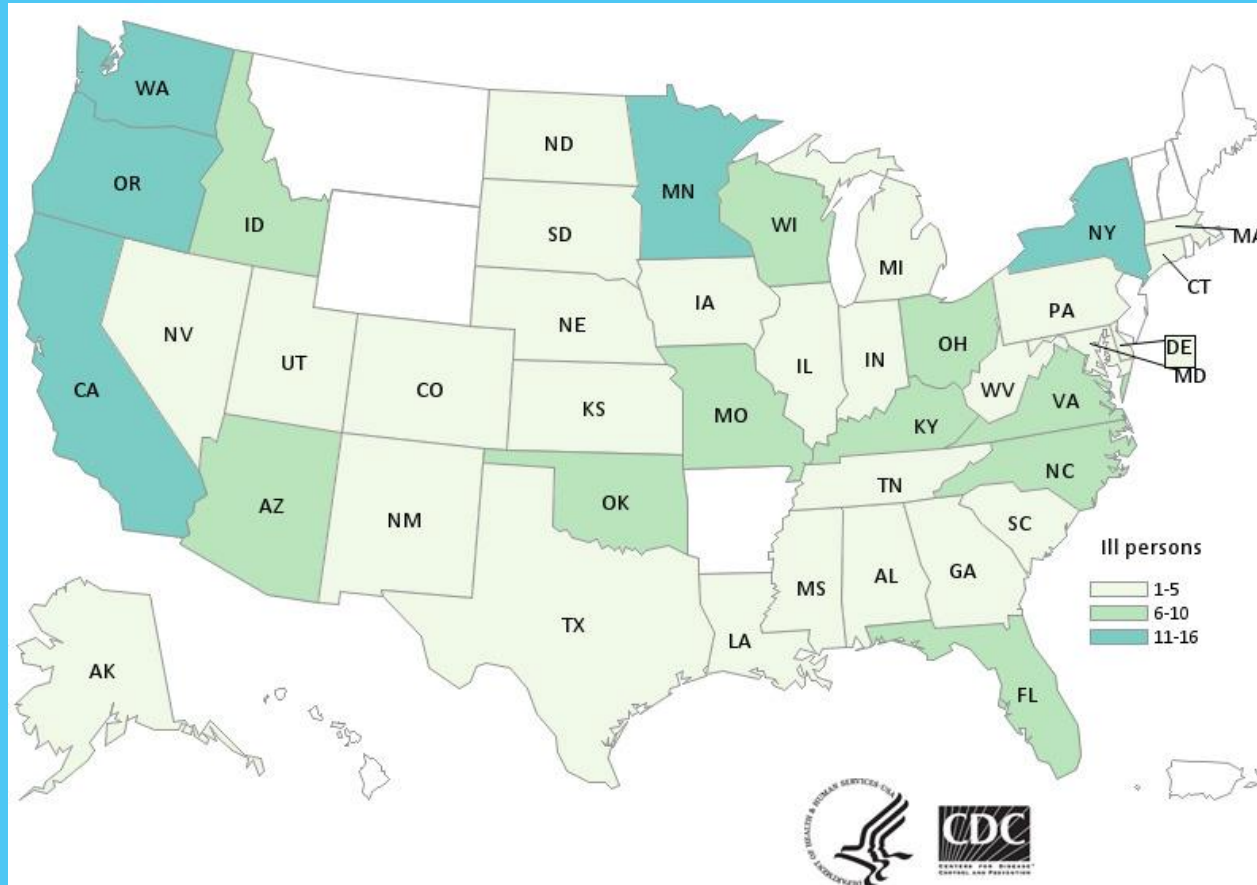
- Not Detected on Routine Screening Immunoassays
- Mitragynine and 7-OH Mitragynine detected on GC-MS testing
- May be used by Patients in Treatment for OUD
- Detected up to 6 weeks post cessation:lipophilic

# Kratom SUD--Treatment

- Buprenorphine Most Commonly Reported
- OUD Paradigm
- Maintenance or Withdrawal Management

# Multistate Outbreak of Salmonella Infections Linked to Kratom

CDC, Posted May 24, 2018



A total of 199 people infected with the outbreak strains of Salmonella were reported from 41 states. October 2017—January 2018

Thirty-eight percent of ill people were hospitalized, and no deaths were reported

FDA Statement

## **Statement by FDA Commissioner Scott Gottlieb, M.D., on risk of heavy metals, including nickel and lead, found in some kratom products**

Among the heavy metals we found were lead and nickel at levels not considered safe for human consumption. While the levels of the specific products we've tested so far are not likely to result in immediate acute heavy metal poisoning from a single use, some of these products included levels that, with chronic use, could cause some people to suffer from heavy metal poisoning.

The findings of identifying heavy metals in kratom only strengthen our public health warnings around this substance, and concern for the health and safety of Americans using it. To date, there have been no adequate and well-controlled scientific studies involving the use of kratom as a treatment for opioid use withdrawal or other diseases in humans. Nor have there been studies on how kratom, when combined with other substances, may impact the body, its dangers, potential side effects, or interactions with other drugs.

“All things are poisons, for there is nothing without poisonous qualities. It is only the **dose** which makes a thing poison.”



Philippus Aureolus Theophrastus Bombastus von Hohenheim, who published under the name **Paracelsus** was a Renaissance physician, botanist, alchemist, astrologer, and occultist. (1493—1541)