Use of Kratom as an Alternative Pain Treatment

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Disclosure Information

Use of Kratom as an Alternative Pain Treatment

March 31, 2022 – 14:00

Stephanie T. Weiss, MD PhD

I have no conflicts of interest to disclose.





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Learning Objectives

- Describe the non-medically supervised use of kratom by patients as an unregulated and mostly legal alternative method of self-treatment for pain
- Analyze the preclinical and clinical literature evidence regarding the use of kratom to treat pain
- Identify the role of the internet and social networks as information sources for patients to learn about kratom



What Is Kratom?

- Tropical tree that is indigenous to SE Asia (Thailand, Malaysia)
- Like coca or khat, kratom leaves are chewed or prepared as a powder or juice
 - Low dose (1-5 g): stimulant effects used to reduce fatigue in laborers
 - Moderate dose (5-15 g): opioid effects
 - High dose (> 15 g): severe opioid effects including stupor





Warner, ML et al. (2016), Int. J. Legal Med.; 130: 127-138.

Kratom Use in SE Asia

Traditional uses Laborers (stimulant activity)

Pain and other ailments

Additional uses

- Self-treat opioid and stimulant withdrawal
- Recreational use

"4 x 100" Cocktail

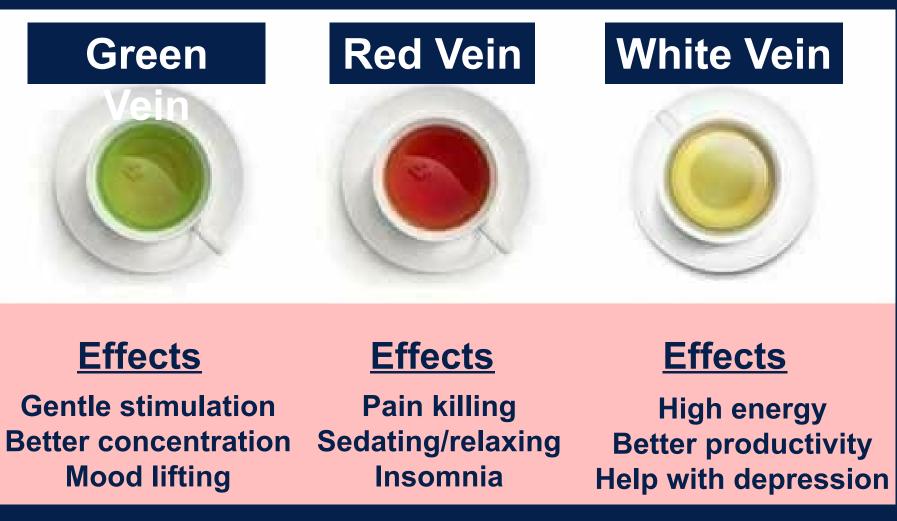


https://www.cbc.ca/fifth/blog/more-on-4-x-100



#ASAMAnnual2022 Singh, D., Narayanan, S. and Vicknasingam, B. (2016). Brain Research Bulletin; 126: 41-46.

Kratom Use in the West

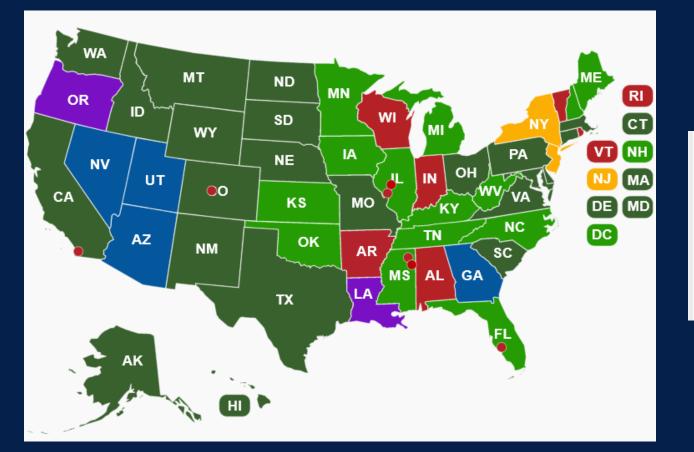




http://borrabnudfilms.blogspot.com/2018/07/

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Kratom Legality in the United States



- ✓Green: Kratom is legal and no restrictions
- V Light Green : Legislation in these states have failed or been amended
- * Orange: There is pending legislation on Kratom in these states
- Red: banned states schedule 1 for Kratom
- Purple: Study involving Kratom
- Red Dot: banned city for Kratom
- Blue: States that have adopted the Kratom Consumer Protection Act Bill



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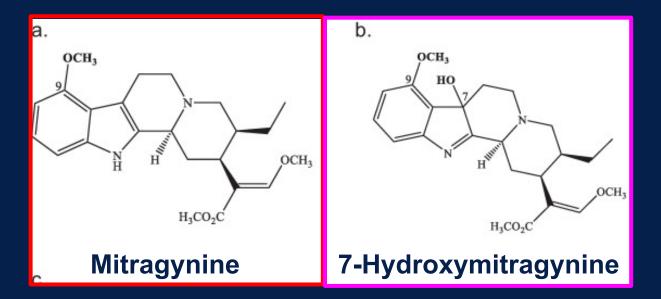
http://speciosa.org/home/kratom-legality-map/

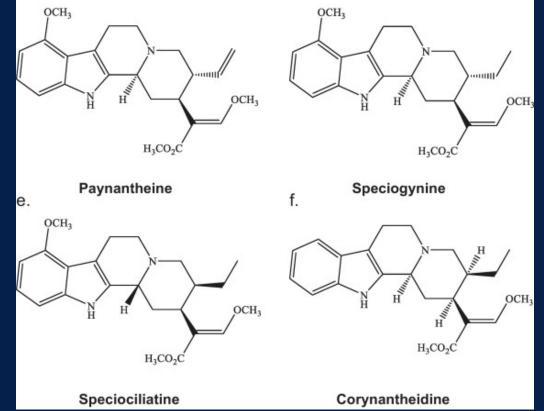
Kratom Use Surveys

Reference	# Respondents Taking Kratom for Pain	Demographics	Type of Pain
Grundman n (2017)	68% (4811/7060 respondents)	57% male, 89% white Solicited online (AKA)	Not specified
Coe (2019)	48% (1451/3024 respondents)	54% male, 93% white Solicited online (AKA)	Spine/back pain (n=596) Fibromyalgia (n=165) Injury-related (n=138) Osteoarthritis (n=95)
Garcia- Romeu (2020)	69% (1924/2798 respondents)	61% female, 90% white Solicited online (multiple sites including AKA website)	Back pain (72%) Muscle pain (63%) Neck pain (55%) Joint pain (54%) Arthritis (44%)

Kratom Alkaloids

>40 kratom alkaloids have been identified



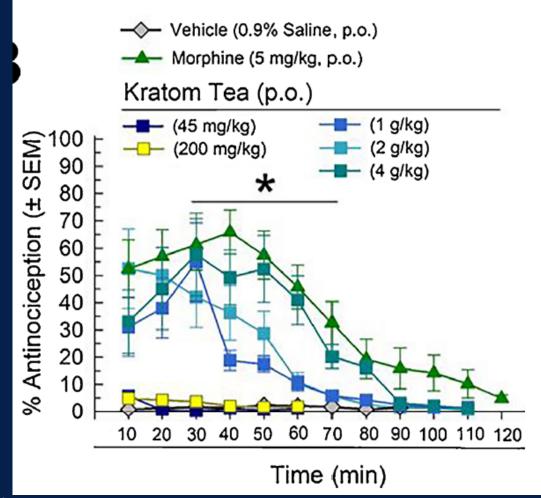


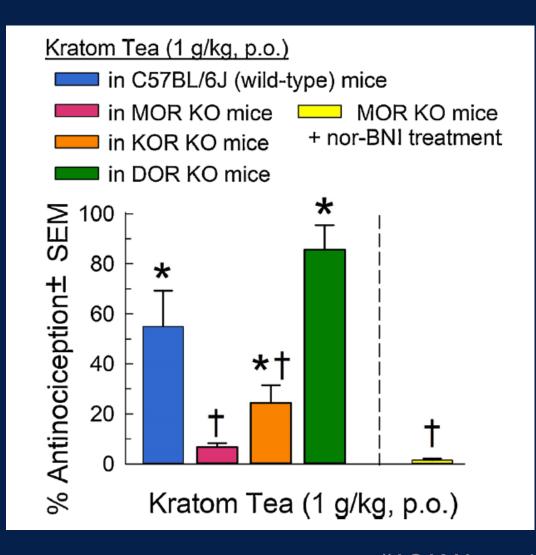


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Hassan, Z. et al. (2013), Neuroscience & Biobehavioral Reviews, 37(2): 138-151.

Animal Data: MOR and KOR Agonism





#ASAMAnnual2022 Wilson, L.L., et al. (2020) *Drug and Alcohol Dependence*, *216:* 1-9.



Earlier Rodent Studies of Antinociception

Reference	Kratom Form	Type of Pain	Mechanism
Macko (1972)	PO, SQ, intraperitoneal mitragynine	Acute (tail flick, hot plate and paw inflammation	Not solely a MOR agonist
		assays)	
Matsumoto	Intraperitoneal and	Acute (tail pinch and hot	MOR agonist
(1996a)	intraventricular mitragynine	plate assays)	
Matsumoto (1996b)	Intraventricular and intrathecal mitragynine	Acute (tail pinch and hot plate assays)	5-HT ₂ and α ₂ agonist
Thongpradichote (1998)	Intraventricular mitragynine	Acute (tail pinch and hot plate assays)	Mostly MOR, DOR agonism
Raja Aziddin (2005)	Intraperitoneal kratom alkaloid extracts	Acute (carrageenan-induced paw edema assay)	Likely multifactorial
Matsumoto (2005)	SQ 7-hydroxymitragynine	Acute (tail flick assay)	MOR, some KOR agonism
Matsumoto	SQ 7-hydroxymitragynine	Acute (tail flick and hot plate	MOR agonism,

Recent Rodent Studies of Antinociception

Reference	Kratom Form	Type of Pain	Mechanism
Sabetghada m (2010)	PO organic/aqueous	Acute (tail flick and hot plate assays)	MOR agonist (both extracts)
	kratom extracts		
Shamima	Intraperitoneal	Acute (hot plate assay)	DOR agonist, some KOR and
(2012)	mitragynine		MOR activity, not a CB1 agonist
Hiranita	Intraperitoneal	Acute (hot plate assay)	No reversal with naltrexone
(2019)	mitragynine		
Foss	Intraperitoneal	Acute (oxaliplatin-	Primarily α_2 , some MOR and α_1
(2020)	mitragynine	induced neuropathic allodynia)	agonism
Obeng (2020)	IV mitragynine	Acute (hot plate assay)	MOR partial agonist, α ₁ antagonist/partial agonist
Wilson (2020)	PO lyophilized kratom tea	Acute (warm water tail withdrawal assay)	MOR agonist
Leon (2021)	IV mitragynine	Acute (hot plate assav)	No antinociception but weak 5-

Case Report: Kratom for Acute Pain

 29 y/o male w/ PMH ulcerative colitis and primary sclerosing cholangitis who contracted COVID19

Clinical Course

Sx: fever, malaise, weakness, body aches, muscle pain

• Pt took APAP x 4 days w/out relief, then tried kratom

Regimen: 2.75 g TID x 3 days (total 9 doses)

No withdrawal noted after stopping this short-term use



#ASAMAnnual2022 Metastasio, A. *et al.* (2020) *Frontiers in* psychiatry; 11: 1-

Case Report: Kratom for Chronic Pain

◆26 y/o male w/ chronic heel pain after fracture

Clinical Course

Initially took 4 g kratom/day (divided QID)

- Developed tolerance over 3 months => 30 g/day
- After 3 yrs, pt sought help d/t inability to abstain



#ASAMAnnual2022 Müller, E., Hillemacher, T. and Müller, C.P. (2020) *Heliyon*, 6(7): e04507.

"The Effect of Mitragynine on Man"

illumination. The subject's hand was warmed by placing it in water at 40° C. and wiped dry. He was asked to hold the resistance wire with firm pressure; and the electric current was passed through the wire. The time the subject could hold the resistance wire after the current was passed was registered by a stop-watch. Great care was exercised that the subject held the wire as firmly after the drug as before it, and did not relax the hold during the experiment. The results are tabulated in Table II.

 Table II. Shows the effect of mitragynine acetate on heat tolerance (time in minutes and seconds).

	Before the drug		After the drug			
	Right hand	Left hand	Right hand	Left hand		
С.	18''	14''	2' 15''	1' 17''		
с.	47''	15″	1' 37''	32''		
г.	27''	16''	1' 22''	43″		
А.	31″	15''	20''	11″		
s.	12''	7″	32''	13″		
к.	19.4"	14″	33''	25''		

It will be seen from the table that with the exception of A. all the subjects could hold the wire for a much longer time after the drug.

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Grewal, K.S. (1932) British Journal of Medical Psychology, 12(1): 41-58.

"The Effect of Mitragynine on Man"

(2) The effect of powdered leaves on the heat tolerance test.

The technique is described on p. 46. The subject was given powdered leaves instead of the salt of the alkaloid mitragynine. The results of the experiment are given in Table VIII.

	Time befor	e the drug	Time after the drug			
	Right hand	Left hand	Right hand	Left hand		
	3' 49''	3' 12''	11' 42''	15' 10''		
	4' 27''	2' 37''	5' 5''	3' 47''		
	6' 46''	4' 13''	6' 5''	4' 0''		
	5' 7''	2' 37''	4' 50''	$2^{\prime} 28^{\prime\prime}$		
I	1' 49''	1' 17''	4' 7''	2'23''		
	3′ 46′′ .	5' 13''	5' 40''	4' 32''		
•	3' 47''	2' 24'' .	3′ 35′′	2' 43''		
•	4' 47''	2' 37''	4' 24''	3'5''		

Table VIII. Shows the effect of Mitragyne leaves on heat tolerance test.

The table shows that all subjects but C. showed very slight change in heat tolerance after taking the powdered leaves.



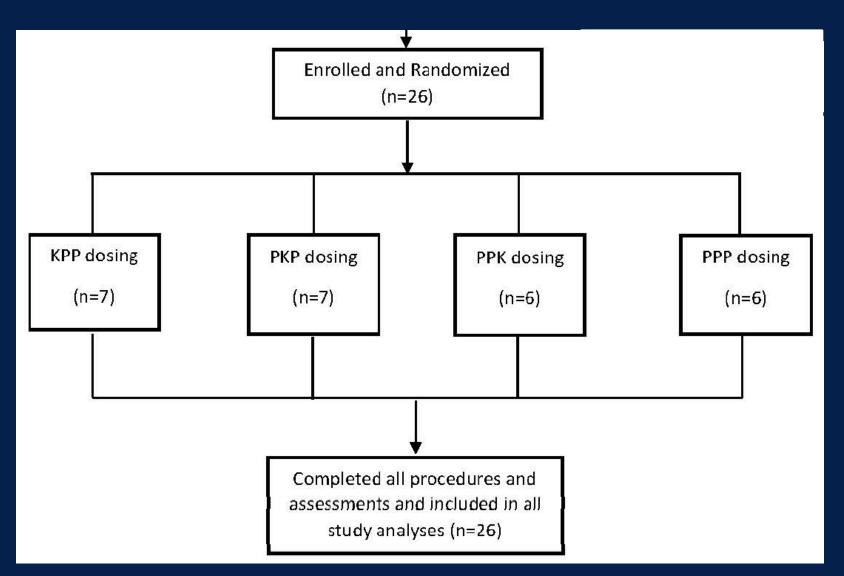
C. C. L. F. F. S. K.

K.

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Grewal, K.S. (1932) British Journal of Medical Psychology, 12(1): 41-58.

"Kratom and Pain Tolerance" RCT





https://souseikaiglobal.com/ cold_pressor_test.php

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Vicknasingam, B. et al. (2020) The Yale Journal of Biology and Medicine, 93(2): 229.

"Kratom and Pain Tolerance" RCT

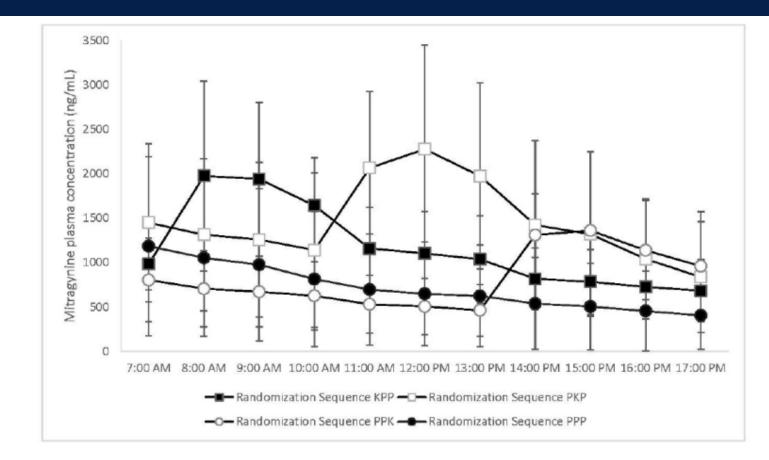
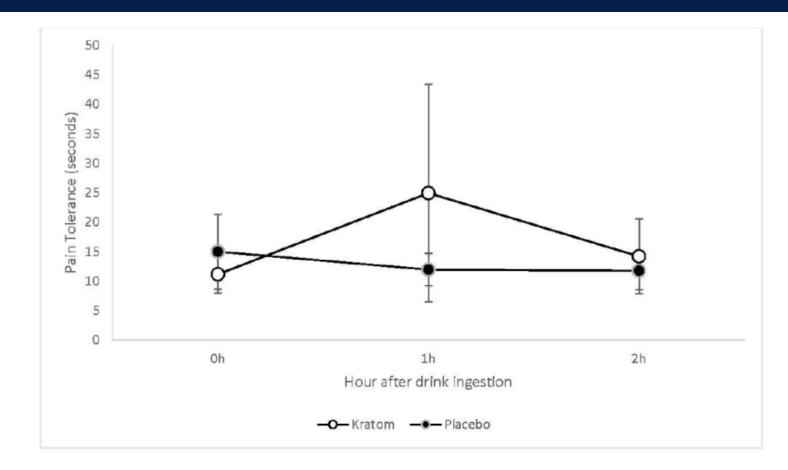


Figure 2. Hourly means of mitragynine plasma concentrations for each of the four study randomization groups. The error bars represent 95% confidence intervals.

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Vicknasingam, B. et al. (2020) The Yale Journal of Biology and Medicine, 93(2): 229.

"Kratom and Pain Tolerance" RCT



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Figure 3. The means of pain tolerance, in seconds, immediately before the drink consumption and at 1 and 2 hours after consumption for kratom and placebo drinks. The error bars represent 95% confidence intervals.

Vicknasingam, B. et al. (2020) The Yale Journal of Biology and Medicine, 93(2): 229.

Erowid: www.erowid.org

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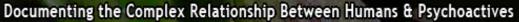


















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Vaults of Erowid



Psychoactive Plants and Drugs

ALCOHOL	ALPRAZOLAM	AYAHUASCA	CACTI	CAFFEINE	SANNADA	
COCAINE	DMT	DXM	GHB	KETAMINE	KRATOM	X
LSD	MDMA (MOLLY)	MDPV	METH	MXE	MUSHROOMS	
PEYOTE	SALVIA D.	ZOLPIDEM	25I-NBOMe	2C-B	MORE	

OPIATE CLASS	FENTANYL	MORPHINE	OXYMORPHONE	OXYCODONE
TRAMADOL	HEROIN	BUPRENORPHINE	OPIUM	POPPIES
NALOXONE	CODEINE	HYDROCODONE	METHADONE	HYDROMORPHONE

Common Psychoactives	~	Go	Chemicals	~	Go	Plants	~	Go
		6.		_	6.			6.
Smart Drugs	~	GO	Pharmaceuticals	~	GO	Herbs	~	GO



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https://www.erowid.org/psychoactives/psychoactives.shtml

Vaults of Erowid

Kratom

BOTANICAL CLASSIFICATION

Family : Rubiaciae Genus : Mitragyna Species : speciosa

COMMON NAMES

Kratom; Ketum; Kakuam; Ithang; Thom; Mambog

EFFECTS CLASSIFICATION

Stimulant; Depressant; Intoxicant

DESCRIPTION



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Mitragyna speciosa is a leafy tree that grows from 3-20 meters tall. Its leaves contain 7-Hydroxymitragynine and mitragynine. The leaves are chewed as an opiate substitute and stimulant in Thailand and South-East Asia, primarily among the working class. It has a relatively long history of human use.





https://www.erowid.org/plants/kratom/kratom.shtml

Erowid Experiences

For Chronic Pain Kratom by <u>Hartrench</u>

Citation: Hartrench. "For Chronic Pain: An Experience with Kratom (exp99200)". Erowid.org. Aug 19, 2015. erowid.org/exp/99200

DOSE: 1/4 cup oral Kratom (ground / crushed)

BODY WEIGHT: 145 lb

I became interested in Kratom while looking for new ways to help manage my chronic low back pain. purchased crushed leaf and spent a few days allergy testing before I took a large quantity for the drug effect. I made a paste and rubbed some on the skin on my inner forearm near my elbow. after 24 hours with no reaction I made a weak tea with the leaves, about 1 tsp in a cup of boiling water, I drank the liquid only, it was very bitter. I felt no effect. After 48 hours I had no digestive issues or allergic symptoms. I decided to take a dose for drug effects the following day.

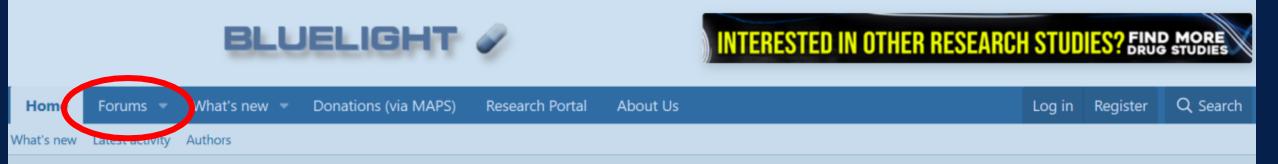
I soaked 1/4 cup of leaf in boiling water and left it overnight in the refrigerator. The next afternoon I was home alone and I mixed the leaf and the tea with frozen blueberries and vanilla yogurt in a smoothy blender. I ended up adding extra honey to cover the bitter taste. After drinking the whole smoothy I started organizing my schoolwork and checking my email. Normally I can only sit for about 30 minutes before my pain is distracting and about 45 minutes before the pain is so bad I have to stand up and move around. That day I sat at the computer, focused and productive for over an hour before looking at the clock again. This was shocking to me. I was feeling very good, in very little pain, able to focus, productive and feeling just a little bit fearless. I hadn't felt this free of the chronic pain in many years.



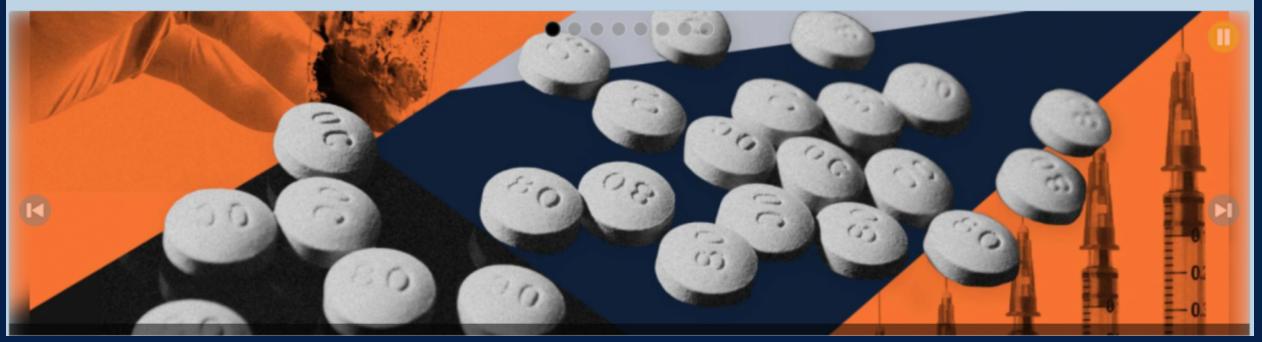
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https://www.erowid.org/experiences/exp.php?ID=99200

Bluelight: https://bluelight.org/xf/



Bluelight.org



Bluelight Forums

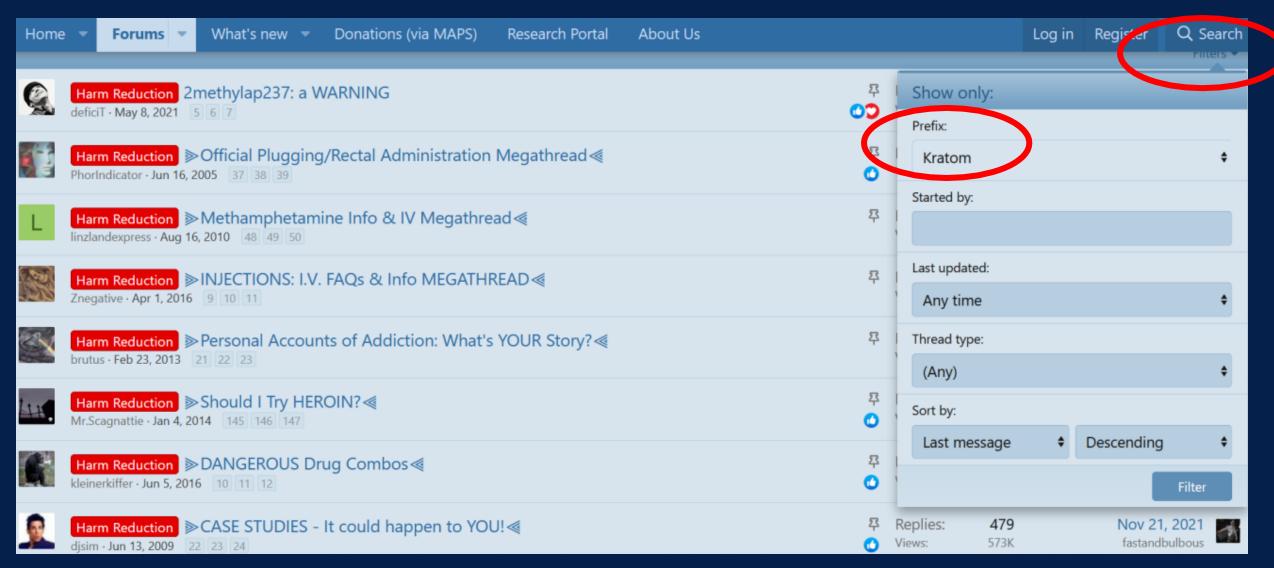
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MDMA & Empathogenic Drugs MDMA, MDA and other empathogenic drugs	Threads 13.4K	Messages 284.1K	What is wrong with the MDMA avai Today at 11:20 AM · unodelacosa	Guests online: Total visitors:	301 339
Pillreports.net - Testing Q&A and Discussion	Threads	Messages	Is this fake oxy?	Totals may include hidden vi	sitors.
Cannabis Discussion	5.4K	39.1K Messages	Yesterday at 8:27 AM · Opi_Kid_Rock	Share this page	
Intelligent discussion of cannabis related topics	8.6K	186.5K	S Today at 3:36 PM · SmokinBuddha	† ♥ ☞ ₽ ⊠ &	t
Sports & Image Enhancing Drugs Bodybuilding, sports and image-enhancing drugs and supplements	Threads 2.6K	Messages 44.1K	does it make sense to take roids as Yesterday at 5:11 AM · hardtack		
Advanced discussion of psychedelics and dissociatives	Threads 20.1K	Messages 546.9K	Miscellaneous Amanita pantherina. 52 minutes ago · Kaleida		
Other Drugs In-depth HR focused discussion about all other drugs	Threads 48.7K	Messages 698.6K	Opioids Questions about injecting Today at 2:06 PM · Just a little pinpricl		



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https://bluelight.org/xf/forums/

Bluelight Forums: Use the Filter



https://bluelight.org/xf/forums/other-drugs.58/

Bluelight Forums: Kratom Threads

Home	Forums What's new Donations (via MAPS) Research Portal About Us			Log in Register	Q Search
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Prefix	Kratom ×				Filters 🔻
	Kratom Please post any negative side effects from kratom usage. 6am-64-14m · Wednesday at 8:20 PM 2	Repli		Yesterday at 10: 6am-	44 PM 64-14m
	Kratom Vitamin content? Anonymous Dissident · Tuesday at 4:59 AM 2	Repli	es: 20 176	Yesterday at 2: Ja	39 PM ackARoe
	Kratom Kratom for low-dose Suboxone user? magickmarck · Jan 30, 2022	Repli Views:	es: 5 85	Friday at 3:	07 PM Xorkoth
	Kratom The mystery of Kratom dosage for optimal results, why no reports of positivity from more? xbandit07x · Sep 22, 2020 3 4 5	Repli Views:			8, 2022 BWG707
	Kratom Various binding affinities of mu antagonists in kratom polarthedog · Jan 21, 2022	Repli Views:			2, 2022 grogesic
М	Kratom Kratom for days off heroin? menidiatis · Oct 19, 2021 2 3	Repli	es: 59 982		1, 2022 vocet21
NA	Kratom Supplementing with Kratom to reduce heroin dosage?	Repli	es: 6	Dec 18	3, 2021 M

https://bluelight.org/xf/forums/other-drugs.58/?prefix_id=217

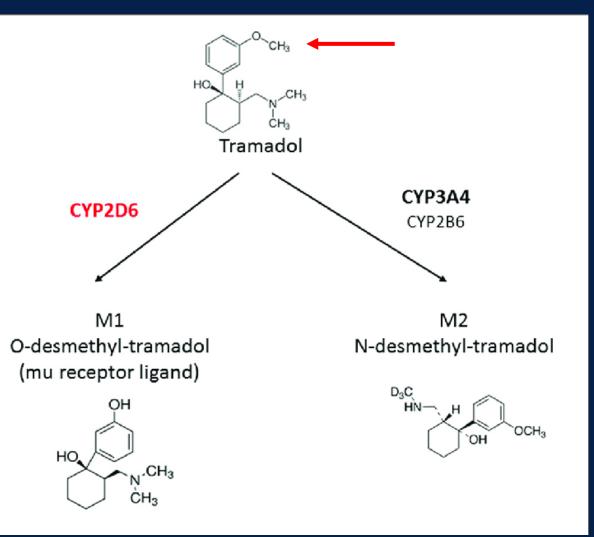
Bluelight Forums: Kratom Thread

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Gam-64-14m Bluelight Crew Joined: Mar 18, 2018 Messages: 9,390 Location: Onda Cona	Dec 27, 2021 Went to doc for non narc pain meds and he tried celebrex. for chronic old people pain. Iol it doesnt do a fuckin thing this is not a 1 1/2 g of kratom every 4-5 hrs not only keeps my pain at bay rather reliably it gives me a bit of a mood boost. i may ask for something else from doc but after ~3 yrs replacing opiods with kratom i doubt ill go back to narc. just has taken too it away). fuck, a half a gram does great if that is all i have. 1/2 g is where i started when i came off opiods and it worked for me for a uear of and i still do. i have been as high as 4g but i get more from it at lower doses and appreciate it more. 1 1/2 to 2 g a few times a day to catxh a buzz; just not that kinda thing for me. if i wanna buzz i get one from a different source. best wishes and hopes of finding what works best for you peace Nurse Ratched	o much fro or so. i use	om me (or ra ed it for mai	ntenence
	Dec 27, 2021			~ #32
Negentropic	sewerslide.666mg said: ① Nice, always good to get fresh brands, I use to get mine from benni I believe			0
Bluelight Crew Joined: May 27, 2020 Messages: 13,442	I'm telling you bro, order some from NJOY you can find it online			

https://bluelight.org/xf/threads/post-your-experience-with-kratom-please.913905/page-2

Adulteration of Kratom: A Case Study

- Krypton = mixture of kratom + O-desmethyltramadol, the active metabolite of tramadol
 - O-desmethyltramadol is twice as potent as tramadol
- Case series of nine deaths from Sweden from krypton
 - All had evidence of opioid overdose, including 8 with pulmonary edema
 - No parent drug (tramadol) and no other metabolites found





Kronstrand, R. *et al.* (2011) J. Anal. Tox.; 35: 242-247. Rodieux, F., *et al.* (2018) *Frontiers in Pharmacology; 9:* 148.

Kratom for Pain

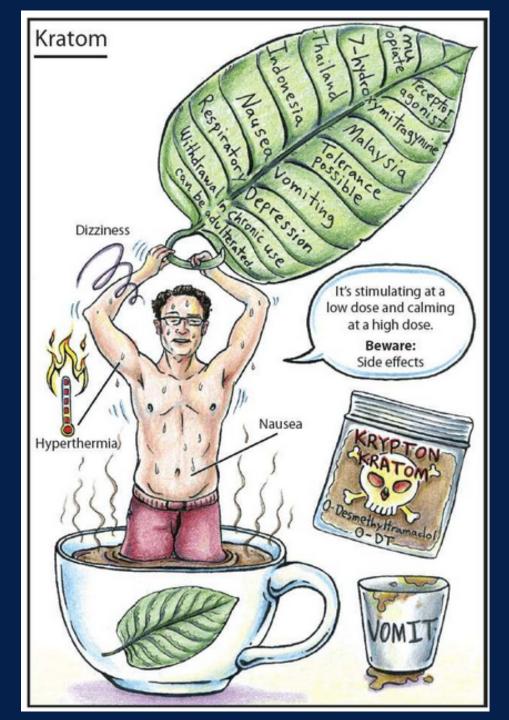
 Kratom is mostly legal and readily available over the internet/in local stores but is NOT FDA-approved

It has multiple effects

- Stimulant + opioid
- Receptor effects (μ-opioid, δ-opioid, 5-HT, α-adrenergic)
- Anti-inflammatory effects

Most data is preclinical and based on pure mitragynine, not kratom

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