ข้อมูลทางการแพทย์ของ กัญชา และ กระท่อม

ผศ. นพ. สหภูมิ ศรีสุมะ

ศูนย์พิษวิทยารามาธิบดี

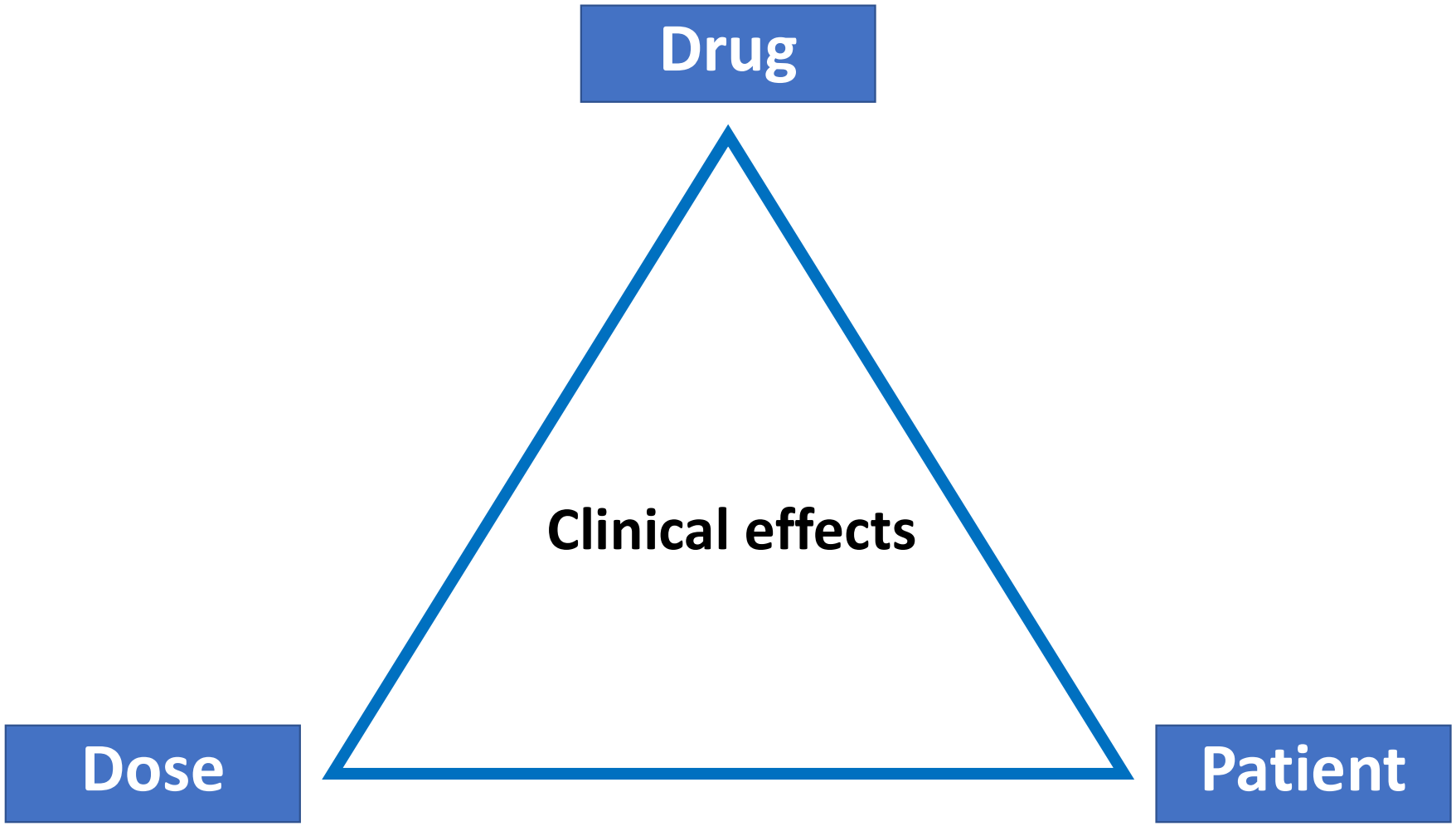
ภาควิชาอายุรศาสตร์

คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี

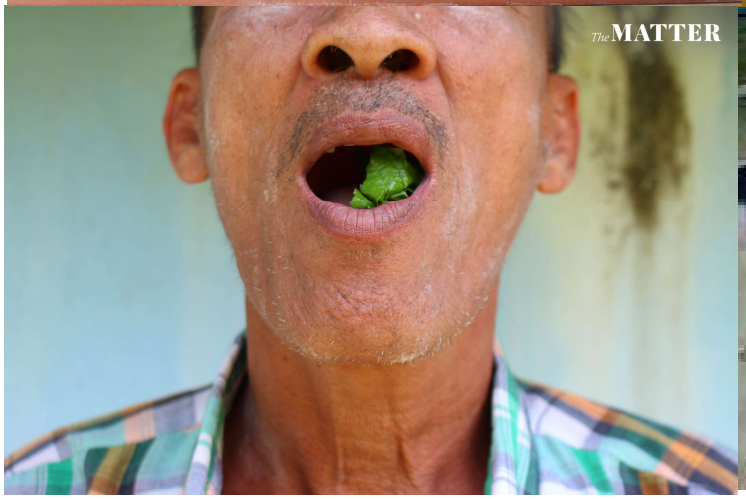
Sola dosis facit venenum

"Only the dose makes the poison"

Paracelsus


Drug
Clinical effects
Dose
Patient

Types of uses



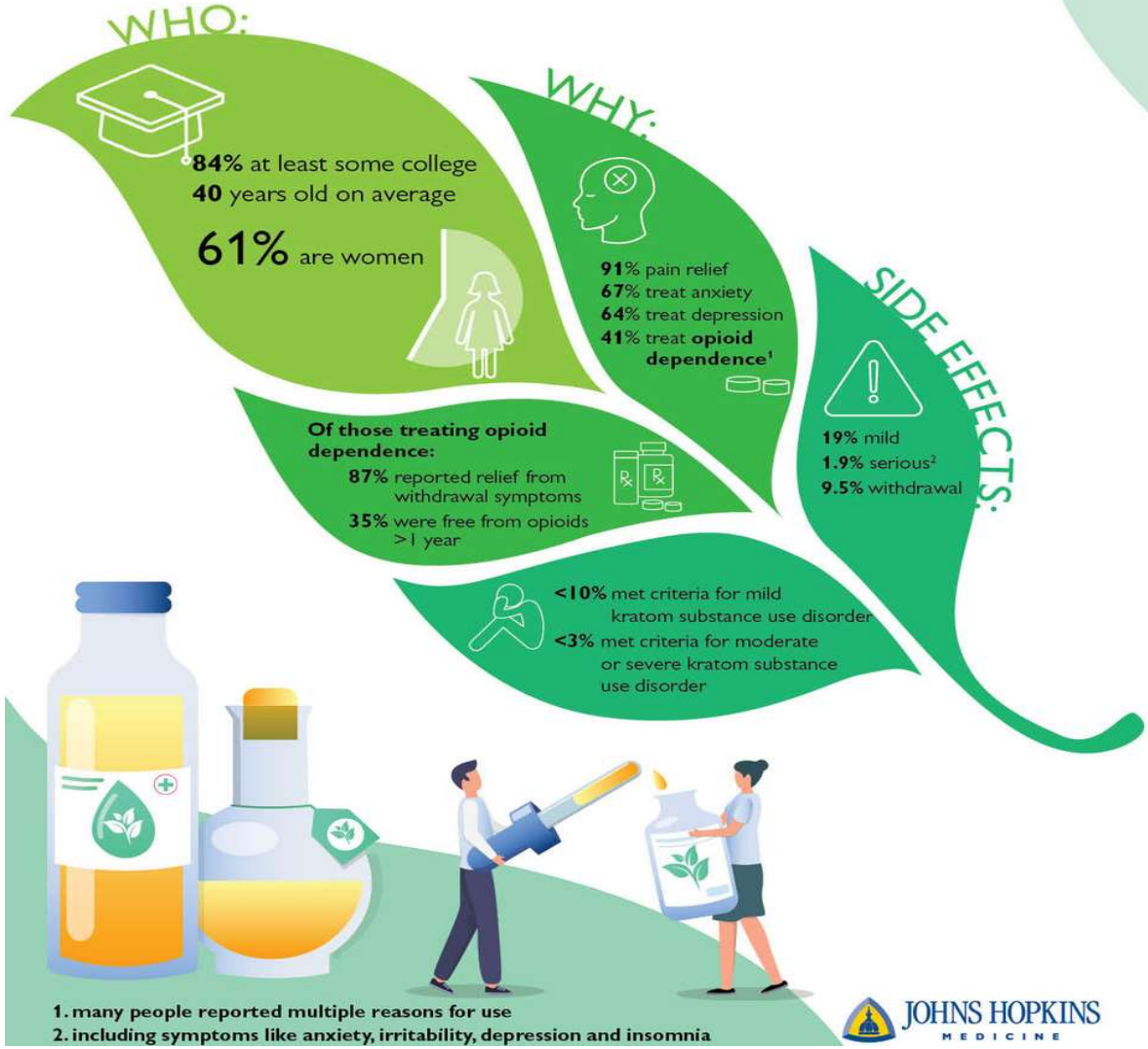
สภาองค์กรชุมชนจับมือ ป.ป.ส.นำร่อง ‘พืชกระท่อม’ ใช้ประโยชน์ทางการแพทย์-สร้างเศรษฐกิจชุมชน

สยามรัฐ
อัพเดต 12 ก.ย 2563 เวลา 10.52 น. • เผยแพร่ 12 ก.ย 2563 เวลา 10.52 น. • สยามรัฐออนไลน์

Survey of Adult Kratom Users in the U.S.

Provides Insight Into Potential for Harm or Abuse

2,798 kratom users



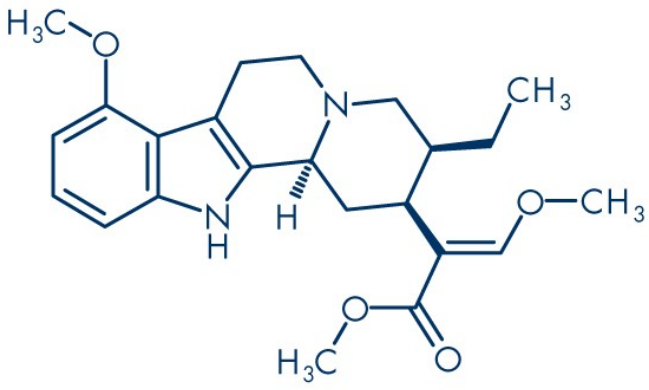
1. many people reported multiple reasons for use
2. including symptoms like anxiety, irritability, depression and insomnia

JOHNS HOPKINS MEDICINE

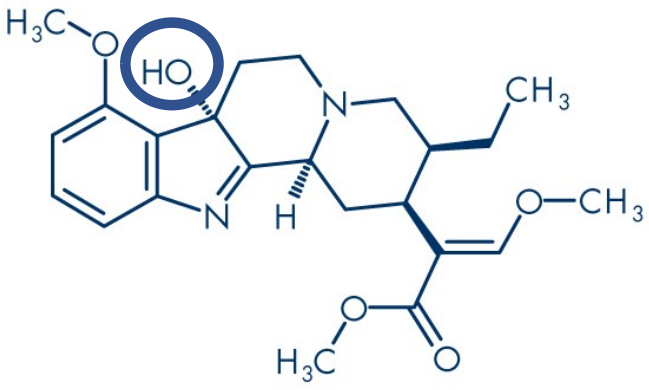
Kratom *(Mitragyna speciosa)*

- More than 25 bioactive alkaloids have been identified
- Active compounds act on monoaminergic and opioid receptors

Mitragynine (upto 66%)



7-Hydroxymitragynine (upto 2%)



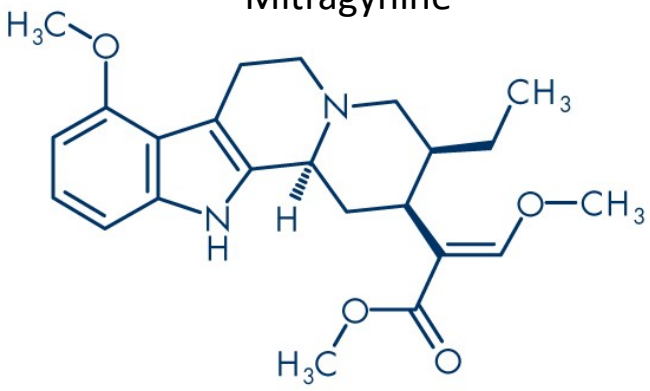
https://www.emcdda.europa.eu/publications/drug-profiles/kratom_en

Kratom *(Mitragyna speciosa)*

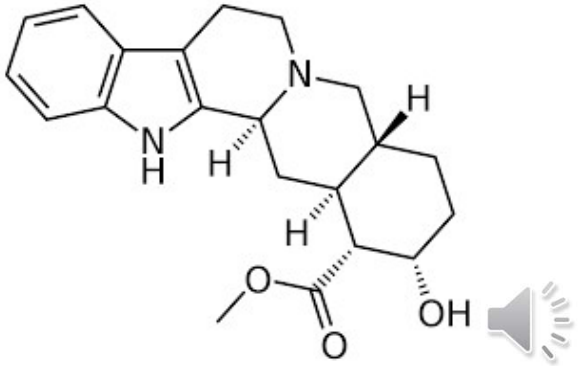
- **Low dose → Stimulant effects**
  Mitragynine's structure is resemble with Yohimbine (presynaptic α-2 antagonist)
  ↑ catecholamine release

- **High dose → Opioid effects**
  Mu and Delta opioid agonist
  7-hydroxymitragynine potency is 13 times higher than morphine

Mitragynine



Yohimbine



Kratom *(Mitragyna speciosa)*

- Onset 5-10 min after mastication
- Duration of effect is varied about 1-7 hours (depend on dose)

- In workers or farmers reports
  - ↑ work capacity
  - Alertness
  - Sociability
  - ↓ appetite

Journal of Pharmacology and Experimental Therapeutics November 1932
Barceloux DG. Medical Toxicology of Drug Abuse: Synthesized Chemicals and Psychoactive Plants
https://www.emcdda.europa.eu/publications/drug-profiles/kratom_en

Kratom intoxication

- CNS: agitated, drowsy, confused, hallucination, **seizure**, tremor
- CVS: tachycardia, hypertension, **bradycardia, hypotension**
- Others: nausea, abdominal pain, diaphoresis, **electrolyte abnormality**, **muscle rigidity, dystonia**, **respiratory depression**

The American Journal of Drug and Alcohol Abuse, 2020
Clinical Toxicology, 2019
Clinical Toxicology, 2013

Table 3. Common clinical effects of kratom abuse exposures reported to National Poison Data System and Ramathibodi Poison Center, both single and multiple substance exposures, during 2010 to 2017.

	Number of cases; n (%)					
Clinical Effect	NPDS exposure (760 cases)	RPC exposure (168 cases)	Total exposure (928 cases)	Adjusted odds ratio*	95% CI	*P* value
Tachycardia	232 (30.5)	50 (29.8)	282 (30.4)	0.81	0.55–1.19	NS
Agitated/irritable	217 (28.6)	26 (15.5)	243 (26.2)	0.42	0.27–0.67	<0.01
Drowsiness/lethargy	175 (23.0)	21 (12.5)	196 (21.1)	0.39	0.24–0.65	<0.01
Confusion	136 (17.9)	14 (8.3)	150 (16.2)	0.34	0.19–0.62	<0.01
Hypertension	95 (12.5)	20 (11.9)	115 (12.4)	0.78	0.45–1.32	NS
Vomiting	90 (11.8)	20 (11.9)	110 (11.9)	1.13	0.66–1.94	NS
Seizure (single)	65 (8.6)	26 (15.5)	91 (9.8)	2.03	1.21–3.44	<0.01
Nausea	75 (9.9)	14 (8.3)	89 (9.6)	1.03	0.55–1.92	NS
Hallucinations/ delusions	63 (8.3)	5 (3.0)	68 (7.3)	0.28	0.11–0.73	0.01
Coma	56 (7.4)	3 (1.8)	59 (6.4)	0.18	0.06–0.61	0.01
Tremor	53 (7.0)	5 (3.0)	58 (6.3)	0.48	0.18–1.24	NS
Diaphoresis	43 (5.7)	12 (7.1)	55 (5.9)	0.88	0.44–1.76	NS
Respiratory depression	51 (6.7)	0 (0)	51 (5.5)	cannot be calculated**		
Electrolyte abnormality	26 (3.4)	21 (12.5)	47 (5.1)	3.88	2.02–7.49	<0.01
Muscle rigidity	7 (0.9)	32 (19.1)	39 (4.2)	21.77	8.96–52.89	<0.01
Dystonia	5 (0.7)	16 (9.5)	21 (2.3)	15.07	4.85–46.82	<0.01

NPDS: National Poison Data System. RPC: Ramathibodi Poison Center. *Odds ratio more than 1 indicates a greater proportion of occurrences in RPC group. Adjusted for age, gender, single or multiple substance exposure.

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Table 5. Deaths and critical care unit admission associated with kratom abuse exposures reported to National Poison Data System and Ramathibodi Poison Center during 2010 to 2017.

	NPDS exposure (760 cases)			RPC exposure (168 cases)			
Medical outcome	Single substance exposure (476 cases)	Multiple substance exposure (284 cases)	Total (760 cases)	Single substance exposure (59 cases)	Multiple substance exposure (109 cases)	Total (168 cases)	Total (928 cases)
Death	1 (0.2)	3 (1.1)	4 (0.5)	0	2 (1.8)	2 (1.2)	6 (0.7)
Survival after Intensive care unit admission	64 (13.4)	81 (28.5)	145 (19.1)	0	1 (0.9)	1 (0.6)	146 (15.7)

NPDS: National Poison Data System and RPC: Ramathibodi Poison Center

Table 6. Multivariate analysis of factors associated with deaths or intensive care admission in kratom abuse exposures reported to National Poison Data System and Ramathibodi Poison Center.

Factors	Odds ratio	*P* value	95% Confident interval
Cases reported by NPDS (United States)	18.82	<0.01	5.85–60.56
Multiple-substance exposure	2.79	<0.01	1.92–4.04

Multivariate analysis included age, gender, countries, and number of substances ingested.

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J Med Toxicol. 2016 Dec;12(4):341-349. doi: 10.1007/s13181-016-0588-y. Epub 2016 Oct 17.

Suspected Adulteration of Commercial Kratom Products with 7-Hydroxymitragynine

Table 2 Concentration of mitragynine and 7-hydroxymitragynine in naturally occurring Kratom leaf and marketed Kratom supplements

Brand name	Concentration	
	Mitragynine	7-Hydroxymitragynine
Natural Kratom leaf [30]	23.8 μg/mg (range 23.6–24.0)	124.0 ng/mg (114.0–134.0)
Phoria^{tm} Borneo white vein	18.3 μg/mg	593.2 ng/mg
Phoria^{tm} red	18.5 μg/mg	410.8 ng/mg
Phoria^{tm} green	11.7 μg/mg	378 ng/mg
Phoria^{tm} Borneo red vein	14.9 μg/mg	346.2 ng/mg
Phoria^{tm} maeng da kava	10.9 μg/mg	300.8 ng/mg
Phoria^{tm} maeng da blue lotus	9.7 μg/mg	146.7 ng/mg
Phoria^{tm} Borneo green vein	17.5 μg/mg	146.7 ng/mg
Phoria^{tm} regular	19.0 μg/mg	93.0 ng/mg
Kratom shot (liquid formulation)	190.7 ng/μL	2.51 ng/μL
Green vein extra strength (liquid formulation)	396.4 ng/μL	1.96 ng/μL

J Med Toxicol. 2016 Dec;12(4):341-349. doi: 10.1007/s13181-016-0588-y. Epub 2016 Oct 17.

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Phoria^{tm} regular	19.0 μg/mg		93.0 ng/mg	
Kratom shot (liquid formulation)	**190.7 mcg/mL**	190.7 ng/μL	**2,510 ng/mL**	2.51 ng/μL
Green vein extra strength (liquid formulation)	**396.4 mcg/mL**	396.4 ng/μL	**1,960 ng/mL**	1.96 ng/μL

Management of acute intoxication

- Symptomatic & supportive treatment
  - Airway & breathing: Intubation in cases with coma or apnea
  - Tachycardia: IV fluids, observe, EKG
  - Benzodiazepine for agitation and seizure

- **Naloxone for cases with reparatory depression**

- **Benzodiazepine for dystonic reaction**
  (if there is no other co-ingestion may use benztropine or diphenhydramine)

Kratom withdrawal

- Withdrawal symptoms:
  - Persist 2-4 days: myalgia, muscle twitching, fatigue, abdominal pain, watery eyes, runny nose
  - May persist 2-4wk: insomnia, anxiety, and depressed mood

- Management:
  - Pain control
  - Benzodiazepine for insomnia
  - ? Opioid replacement; buprenorphine
  - ? Clonidine, Gabapentin

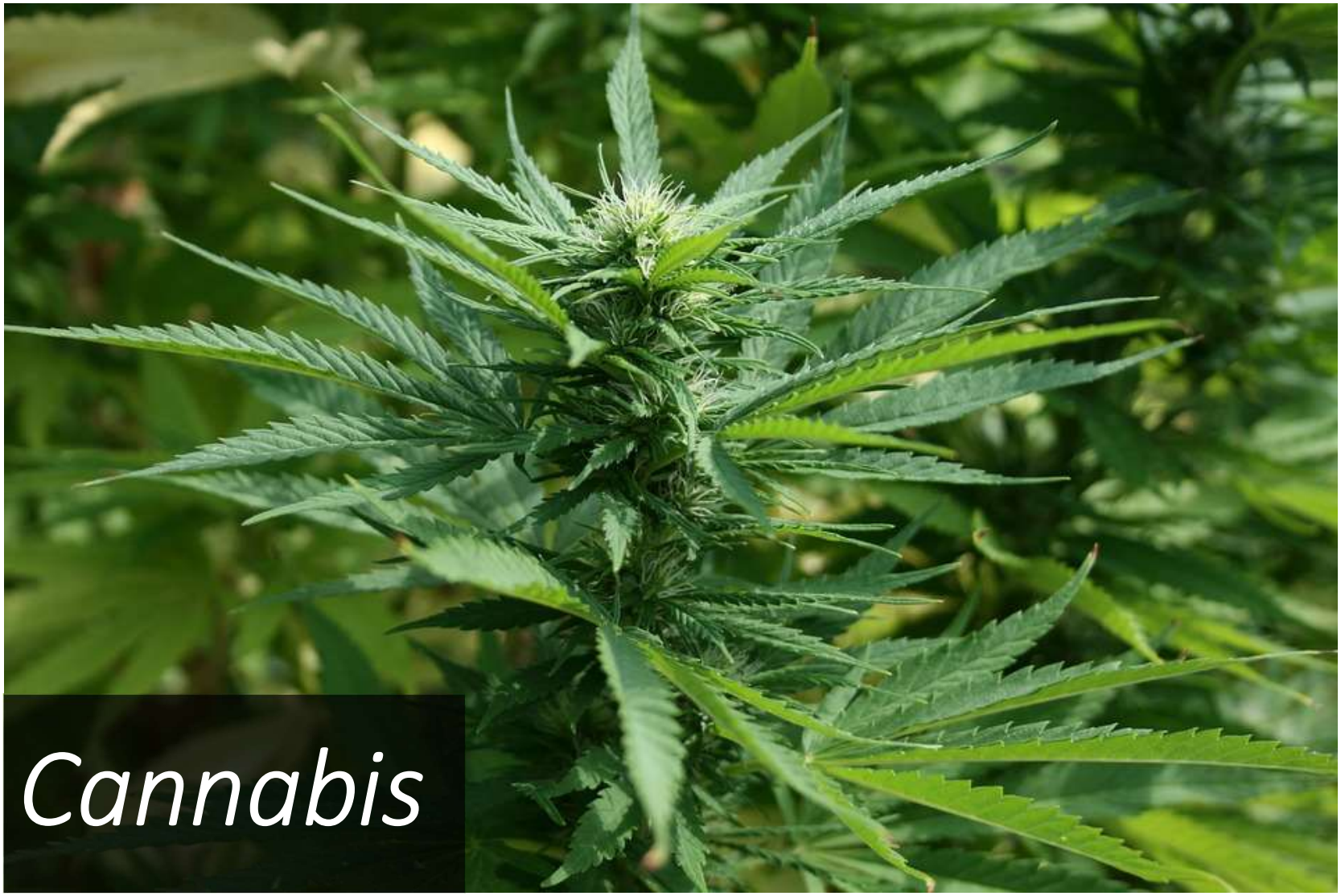
Journal of Psychoactive Drugs, 2019
Journal of Psychoactive Drugs, 2018
Clinical Toxicology, 2013

Beware of co-abuse substance

- Methamphetamine
- Antihistamine
- Codeine
- Dextromethorphan
- Tramadol
- Antipsychotics

≠


SELECTED KRATOM
SUPER K
EXTRA STRONG
K
SHOT
0.5 fl.oz (15ml)
MIT
45
MIT
45
KRATOM
EXTRACT
O.P.M.S.
Optimized Plant Mediated Solutions
LIQUID KRATOM


Cannabis


Cannabis


Cannabis
Trichrome

Marijuana

THC vs CBD

THC (tetrahydrocannabinol)

- เมาเคลิ้ม
- โรคจิต ประสาทหลอน
- ใช้แก้อาเจียน
- ใช้ลดปวด/คลายกล้ามเนื้อ
- มีการดื้อต่อสารทำให้ต้องเพิ่มขนาดที่ใช้และเสพติดได้

CBD (cannabidiol)

- ต้านฤทธิ์เมาประสาทหลอน
- ทำให้สงบลดอาการวุ่นวาย
- ใช้ลดปวดได้บ้าง
- กำลังศึกษาในอีกหลายโรค
- กระตุ้นอาการคลื่นไส้ อาเจียน
- ไม่มีฤทธิ์เสพติด

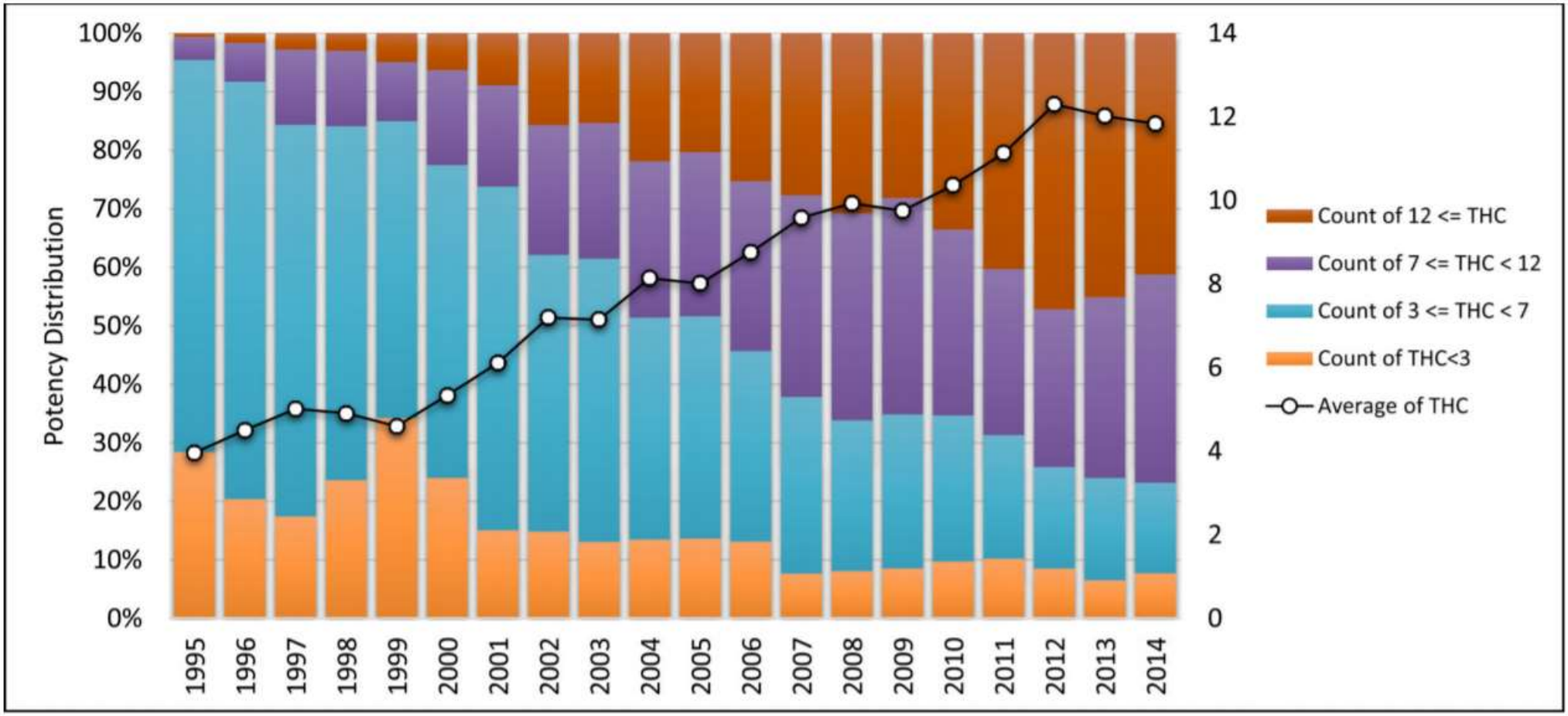


Figure 4.
THC potency distribution of cannabis samples from DEA specimens and average THC by year, 1995 – 2014.

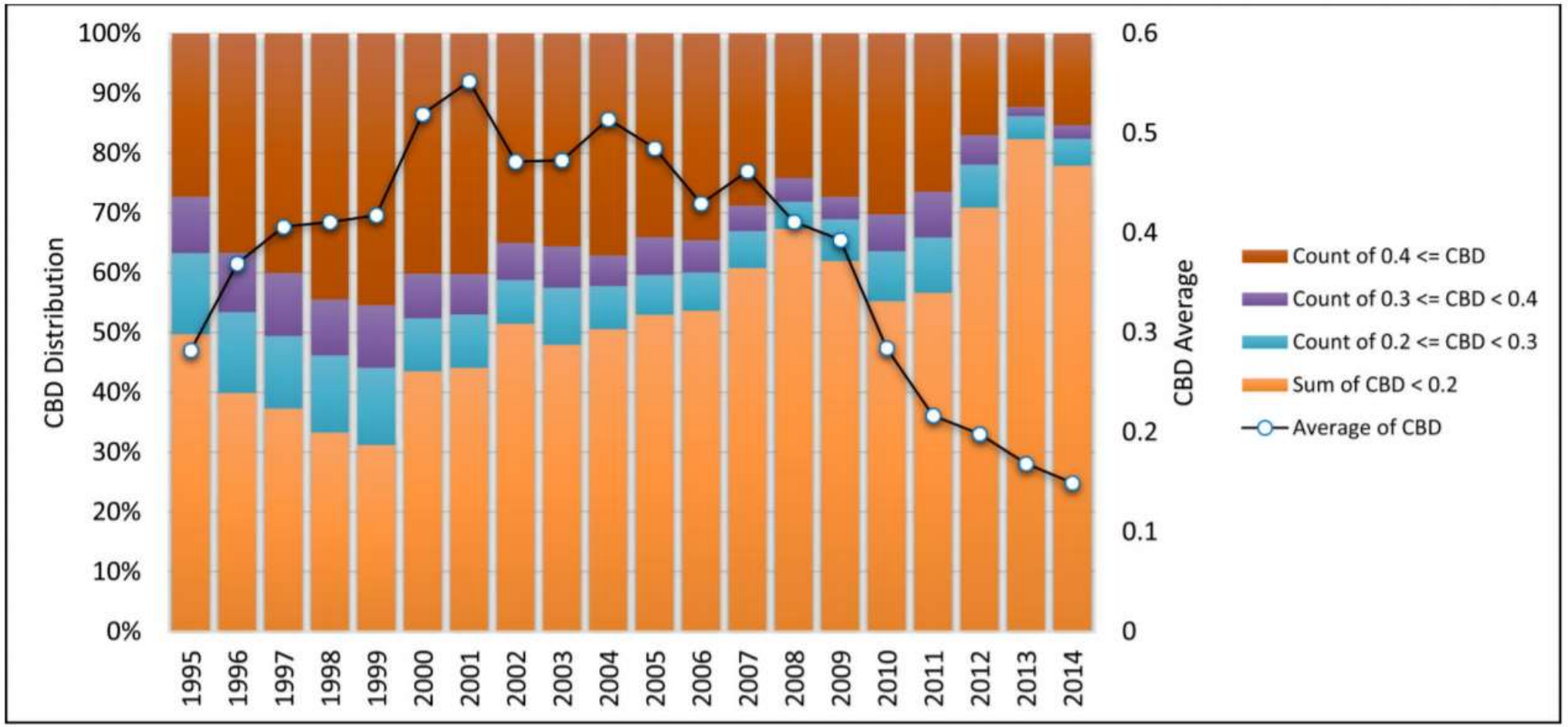


Figure 5.
CBD concentration distribution in Cannabis samples confiscated by DEA and average CBD by year, 1995 – 2014.

CBD

Medical products

- CBD
  - Epidiolex (CBD 100mg/ml)
- Synthetic THC & derivative
  - Dronabinol: THC
  - Nabilone: THC derivative
- Nabiximol spray (THC 2.7mg/CBD 2.5mg)

GPO product (release August 2019)

- CBD oil (100mg/mL, 4mg/drop)
- THC oil (13mg/ml, 0.5mg/drop)
- THC/CBD oil
  (THC27mg/CBD25mg in 1 ml, 1mg of THC and CBD/drop)

Other products






Intoxication: CNS

- Euphoria
- Panic
- Agitation
- Mood alterations
- Alterations of perception
- Loss of social inhibition
- Impairment of cognition and judgment
- CNS depression → Comatose
- Respiratory failure
- Muscle incoordination
- Myoclonic jerking
- Ataxia
- Slurred speech

Clin Toxicol (Phila). 2016;54(9):840-846
Br J Psychiatry. 2001;178:101.
Toxnet HSDB. NIH

Acute cardiovascular effects

- Tachycardia
- Arrhythmia: AF, SVT, VT, VF
- Hypertension & Hypotension
- Syncope
- Congestive heart failure
- Myocardial infarction (risk 4.8 time after acute exposures)
- Stroke

Journal of Thoracic Disease,2017; 9(7), 2079–92
Clin Pharmacol Ther. 1979 Apr; 25(4):440-6

Management of acute intoxication

- Observation in safe and calm area
  prevent self-injury and fall

- Check serum glucose and EKG

- Symptomatic & supportive treatment
  - Airway & breathing: Intubation in cases with coma or apnea
  - Tachycardia: IV fluids, observe, EKG
  - Benzodiazepine for agitation or dysphoria

Clin Toxicol (Phila). 2016;54(9):840-846
Toxnet HSDB. NIH

CMAJ Open 2018. DOI:10.9778/cmajo.20180023

Other adverse effects

- Psychosis 3.9 times
- Suicide 2.5 times
- Addiction 10% (17% in children & teens)
- Impaired learning, cognition, memory
- Decrease white matter

CMAJ Open 2018. DOI:10.9778/cmajo.20180023

Chronic cardiovascular effect

- Vasospasm
- Peripheral a. disease
- Ischemic stroke
- Reversible cerebral vasoconstriction syndrome
- Coronary spasm → MI
- Slower heart rate → heart block and syncope

Journal of Thoracic Disease,2017; 9(7), 2079–92
J Clin Pharmacol. 2002 Nov; 42(S1):58S-63S.
Brain (2007), 130, 3091-101
J Vasc Interv Neurol. 2015; 8(1): 36–38.

Cannabinoid Hyperemesis Syndrome (CHS)

CHS

- Severe nausea vomiting in chronic cannabis user (68% of cases report use > 2y, and use > 20 times/m)
- Not response well to antiemetic
- Relief by hot shower
- Recovery time weeks to months

Basic Clin Pharmacol Toxicol. 2018;122(6):660-662.
GMS German Medical Science 2017, Vol. 15, ISSN 1612-3174
J Emerg Med. 2018;54(3):354-363.

CHS

- Unknown definite mechanism
  - Down regulate CB-1 receptor
  - Change in CB-1 receptor downstream effect
  - Too much THC activate CB-1 receptor at GI tract (bowel movement, dilate splanchnic vasculature)
  - ↓TRPV-1 signaling
  - Other accumulate substance

J. Med. Toxicol. (2017) 13:71–87

CHS: complication

- Dehydration
- Electrolyte imbalance
- Esophageal rupture
- Cardiac arrhythmia
- Precipitate diabetic ketoacidosis

BMJ Open Respir Res. 2019 Feb 12;6(1):e000391. doi: 10.1136/bmjresp-2018-000391. eCollection 2019.

Pneumomediastinum in marijuana users: a retrospective review of 14 cases.

J Forensic Sci. 2019 Jan;64(1):270-274. doi: 10.1111/1556-4029.13819. Epub 2018 May 16.

Cannabinoid Hyperemesis Syndrome: Reports of Fatal Cases.

CHS: management

- Stop marijuana
- Correct dehydration and electrolyte imbalances
- Hot shower
- Capsaicin cream (0.025-0.1%)
- Benzodiazepine IV
- Antipsychotic IV

J. Med. Toxicol. 2017);13:71–87
GMS German Medical Science 2017, Vol. 15
J Emerg Med. 2018;54(3):354-363.

ข้อบ่งชี้ตามกรมการแพทย์

- ทั้งหมด 6 ข้อ โดยจะใช้ได้***เมื่อการรักษาปกติไม่ได้ผลเท่านั้น***
- ***ไม่ใช้เป็นยาเริ่มต้น***

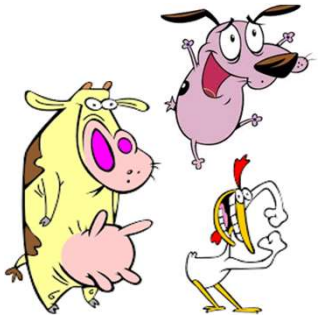
1. อาการคลื่นไส้อาเจียน จากการรับยาเคมีบำบัด
2. อาการเบื่ออาหารในผู้ป่วยเอดส์ที่น้ำหนักตัวน้อย
3. อาการปวดประสาท
4. กล้ามเนื้อหดเกร็งในผู้ป่วยโรคเอ็มเอส
5. โรคลมชักที่ดื้อยา
6. การเพิ่มคุณภาพชีวิตในผู้ป่วยที่ได้รับการดูแลแบบประคับประคอง หรือระยะสุดท้ายของชีวิต

ข้อห้ามใช้ผลิตภัณฑ์ THC ตามกรมการแพทย์

1. มีประวัติแพ้สาร
2. โรคหัวใจ โรคหลอดเลือด โรคปอด หรือมีปัจจัยเสี่ยงต่อโรคหัวใจ
3. เป็นโรคจิตมาก่อน หรือมีอาการของโรคอารมณ์แปรปรวน หรือโรควิตกกังวล
4. มีครรภ์ ให้นมบุตร สตรีผู้ไม่ได้คุมกำเนิด หรือวางแผนจะมีบุตร

- ระมัดระวังใน เด็ก ผู้สูงอายุ ผู้ป่วยโรคตับ **ผู้ติดสารเสพติด/สุรา/นิโคติน** ผู้ใช้ยาที่มีฤทธิ์ง่วงซึม

การศึกษาพัฒนายา



คนปกติ	คนปกติ	คนป่วย	คนป่วย	คนป่วย
10 คน	20-100 คน	100-300 คน	300-3000 คน	**Post-marketing**
100%	**70%**	**20%**	**4%**	

A sign of
true intelligence
is being able
to admit what
you don't know
then be able
to learn and
grow from
there.

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for
Your Attention

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