

DOSING AND MEDICAL MARIJUANA

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Marijuana Med Today



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Medical Cannabis Today- Finding Your Dose

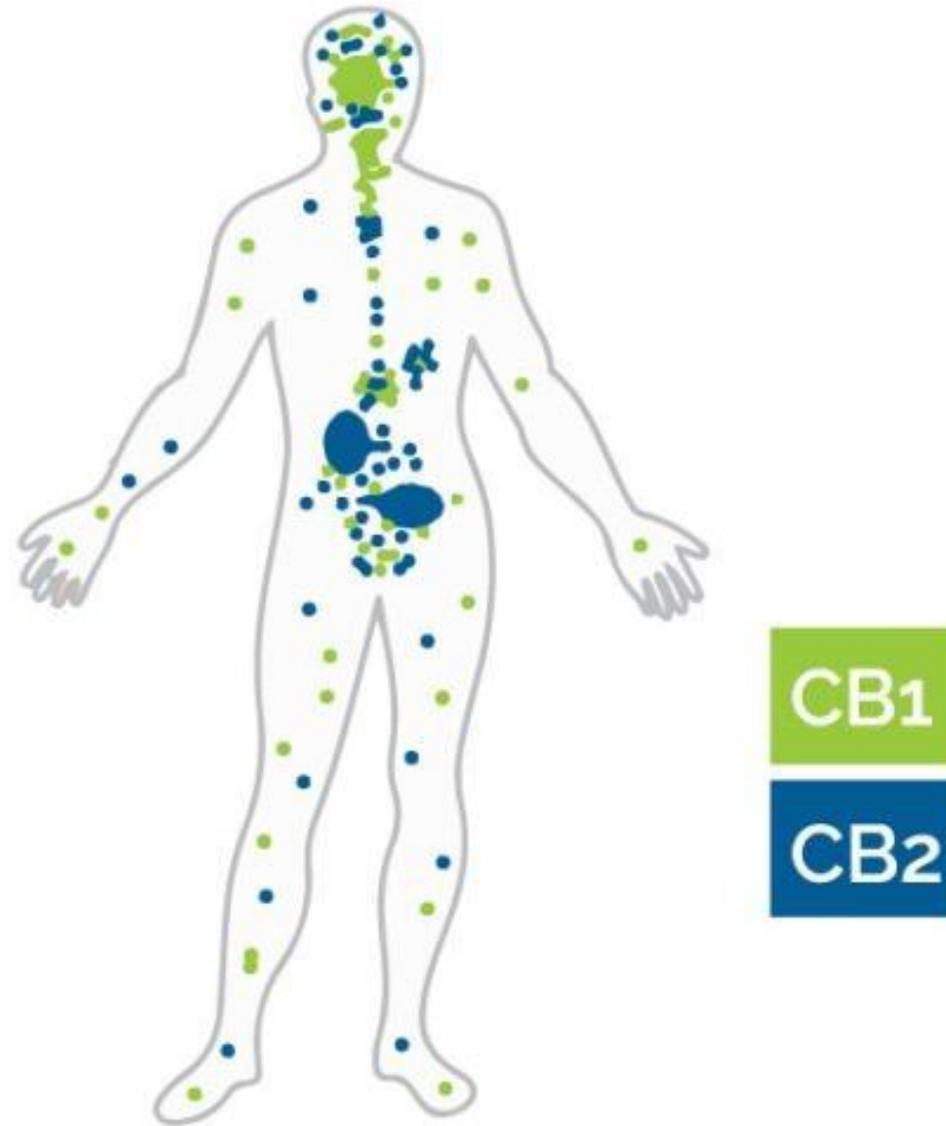
Cameron Vance PharmD, CIO

Medical Marijuana Treatment Clinics of Florida

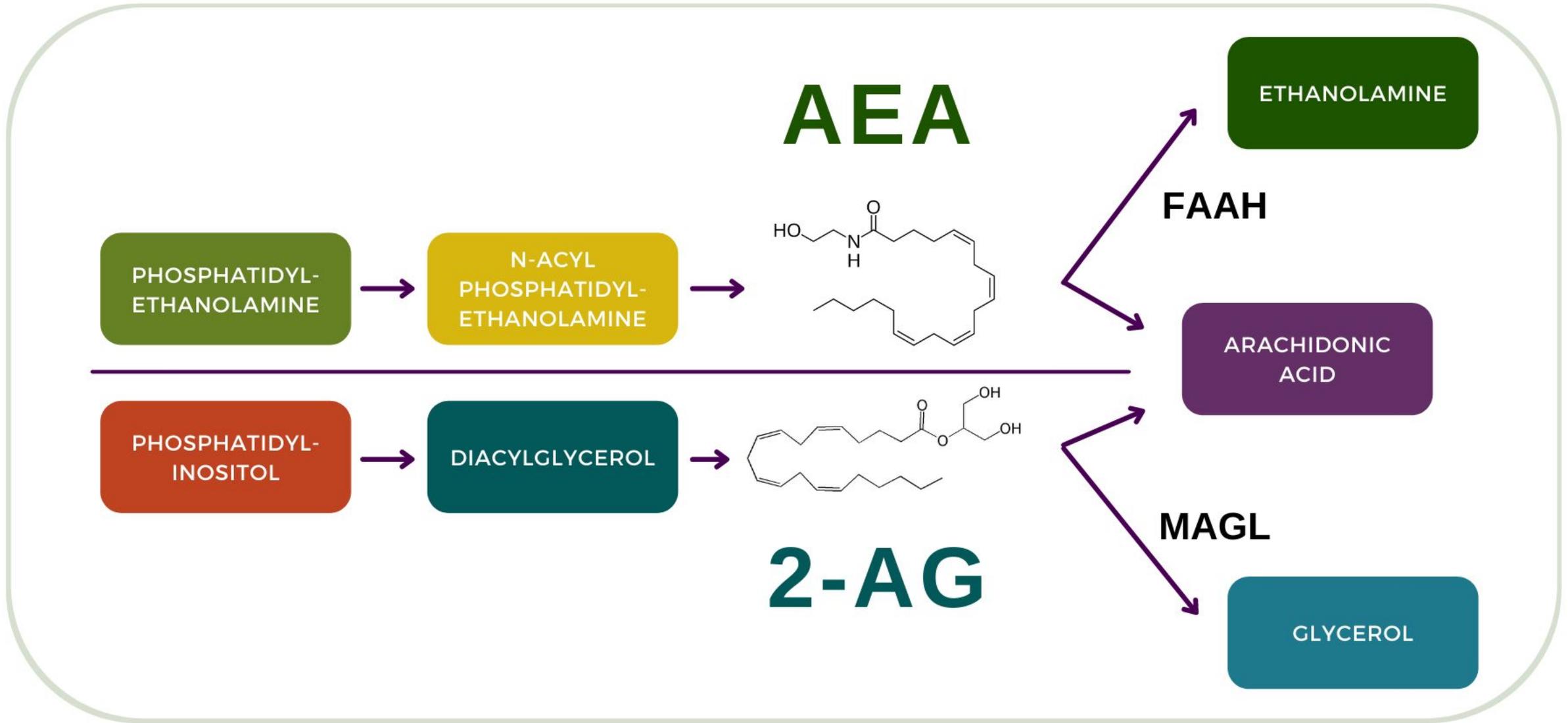
The Endocannabinoid System



Receptors & The Cannabis Plant



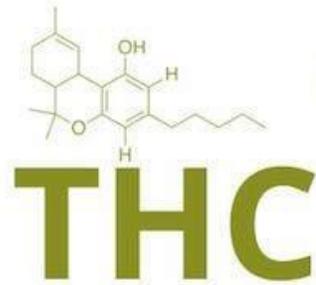
Endocannabinoids



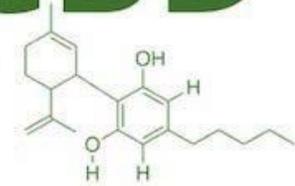
WHAT IS MEDICAL CANNABIS / MARIJUANA?

THC – Tetrahydrocannabinol

Psychoactive cannabis chemical



CBD

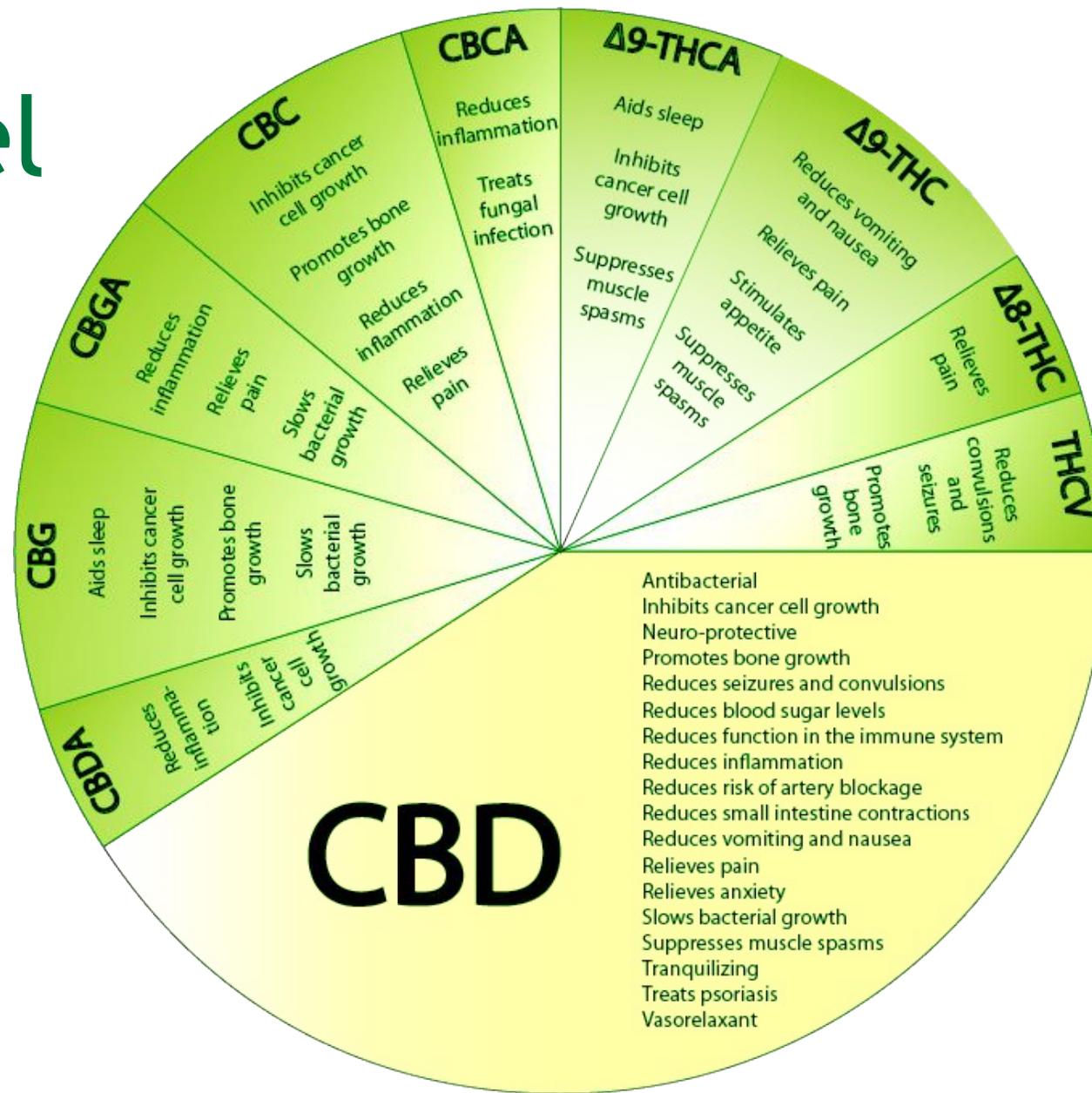


CBD – Cannabidiol

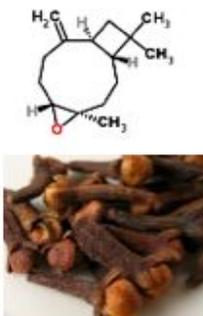
Non-Psychoactive cannabis chemical

– Also found in Hemp

CBD Wheel



Terpenes



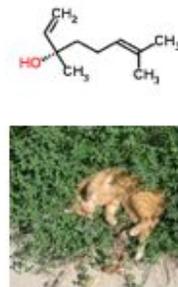
Caryophyllene Oxide

- antifungal in onychomycosis
- decreases platelet aggregation



Limonene

- antidepressant
- antifungal
- antimicrobial
- antispasmodic
- anxiolytic
- gastroprotective
- immunostimulant



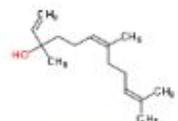
Linalool

- analgesia
- anticonvulsant
- antiepileptic
- antineoplastic
- antipsychotic
- anxiolytic
- sedative



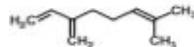
β -Myrcene

- analgesic
- anti-inflammatory
- antipsychotic
- antispasmodic
- hypnotic
- muscle relaxant
- sedative



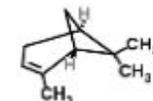
Nerolidol

- antimicrobial
- sedative



Phytol

- aids in lowering cholesterol
- increases GABA via SSADH inhibition



α -Pinene

- Acetylcholinesterase inhibitor
- anti-inflammatory
- gastroprotective



The Cannabis Plant



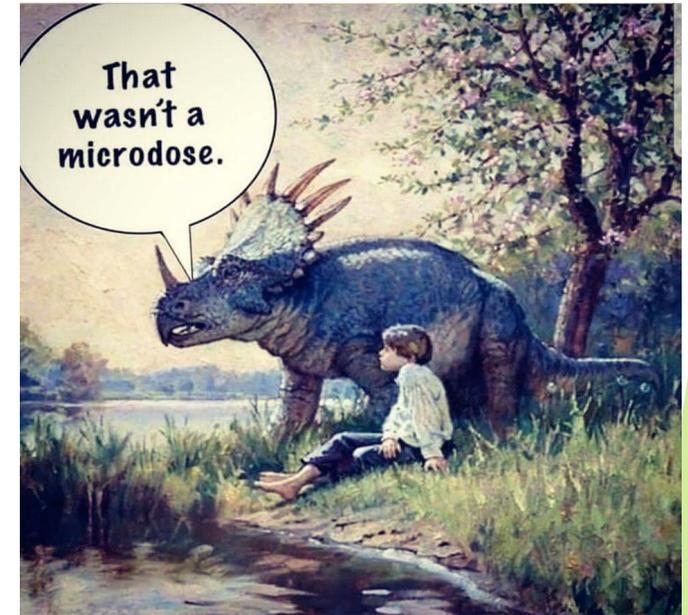
Dosing Concepts

BB Gun or Shotgun? (i.e. Less is More)

Medical Marijuana – The Goal is Relief with minimal side-effects (intoxication).

This is called **Microdosing**

Definition: the action or practice of taking or administering very small amounts of a drug in order to test or benefit from its physiological action while minimizing undesirable side effects.



Dosing Challenges

Individual Variation – Cannabis is Unusual

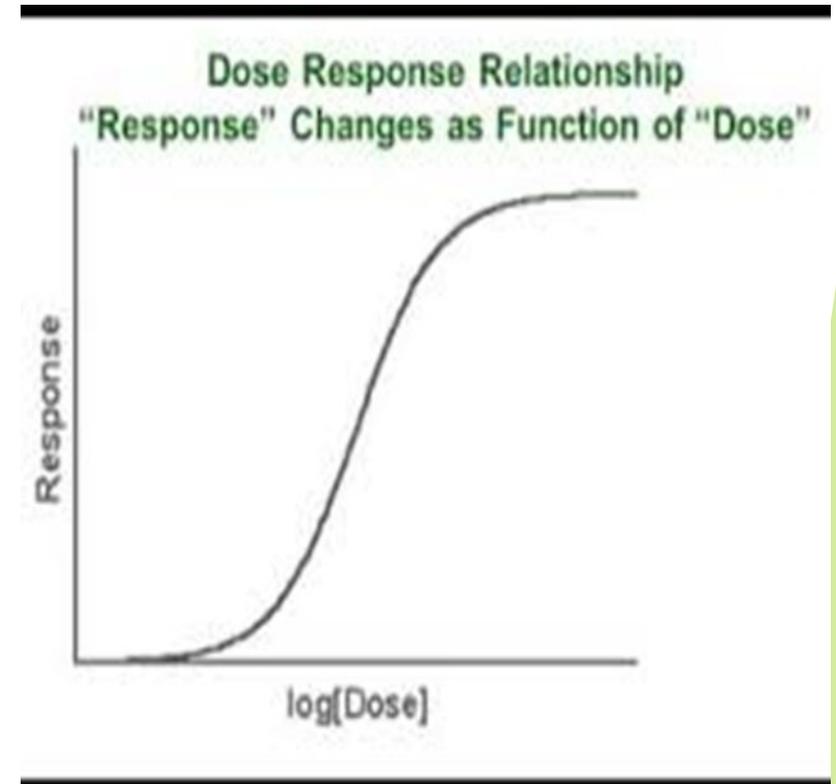
- Some patients effectively use tiny amounts of cannabis, while others use incredibly high doses.
- Some adult patients achieve therapeutic effects at 1 mg of total cannabinoids daily, while others consume over 2,000 mg daily without adverse effects.
- While a 2000-fold dosing range is unusual for a medication, researchers have failed to kill monkeys at doses even 300 times higher[i]



Dosing Challenges

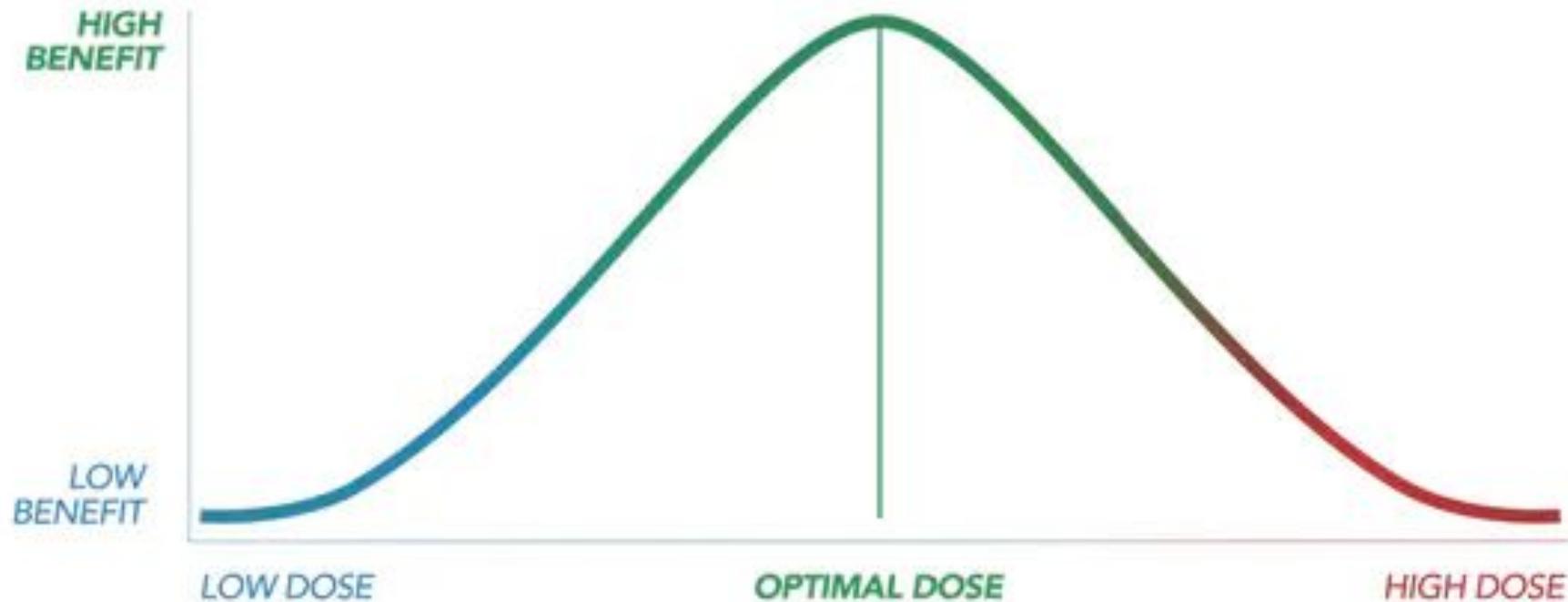
Multiphasic dose-response relationships

- Cannabis exhibits an unusual relationship between the dose and the expected response.
- For most medications, a higher dose will result in a stronger therapeutic effect and a higher likelihood of adverse effects; this is described as a monophasic dose-response relationship.
- Cannabis simply does not follow this pattern.



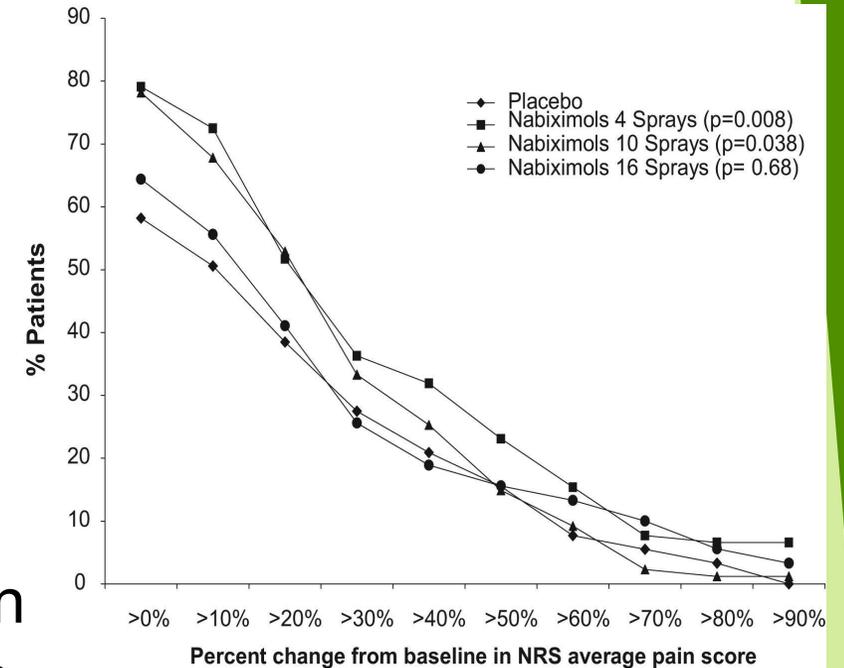
Are Higher Doses More Effective?

Ultra-high doses are more expensive and produce more unwanted side effects. Most patients do much better at the lowest effective dose (microdosing).



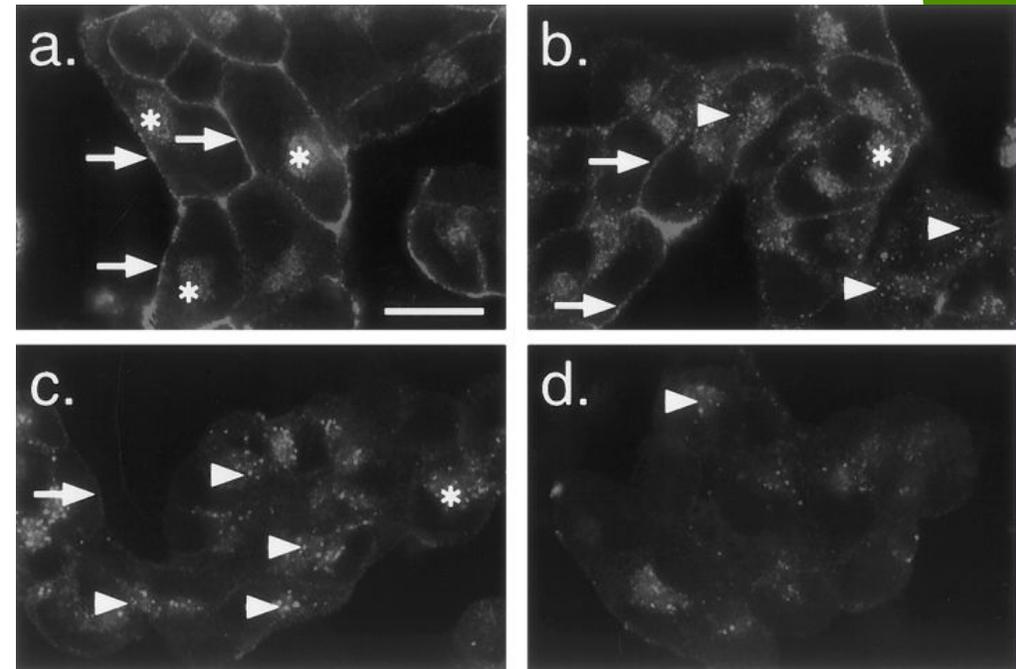
Are Higher Doses More Effective?

- For many cannabis users, this means that less is more.
- In a study of 263 opioid-treated cancer patients with poorly controlled pain, the group receiving 21 mg of combined THC and CBD each day experienced significant improvements in pain levels, more so than the group that received 52 mg/d.
- The group that received 83 mg daily reduced their pain no better than placebo, but experienced more adverse effects.[ii]



How is this possible?

- The endocannabinoid system is a sensitive, highly-tuned physiologic infrastructure designed to maintain balance at a cellular level.
- When the cannabinoid receptors become overstimulated by high doses of cannabis, the cells pull the receptors inside, where they are either recycled or degraded. [iii]
- As cannabinoid receptor levels diminish the effects of cannabis will diminish as well, even (or especially) in the face of dose escalation.
- This is known as “tolerance-building,” something that many regular cannabis users have experienced.



Combining CBD and THC

- In a study of 177 patients with cancer pain, one group received an oral spray of THC, while another group received an oral spray of combined THC and CBD at an approximate 1:1 ratio.
- Both groups were allowed to gradually increase their dose until they experienced satisfactory relief.
- The THC group ended up using an average of 27 mg daily, while the CBD+THC group used close to 60 total mg daily, but the CBD+THC group had a superior reduction in pain. [iv]

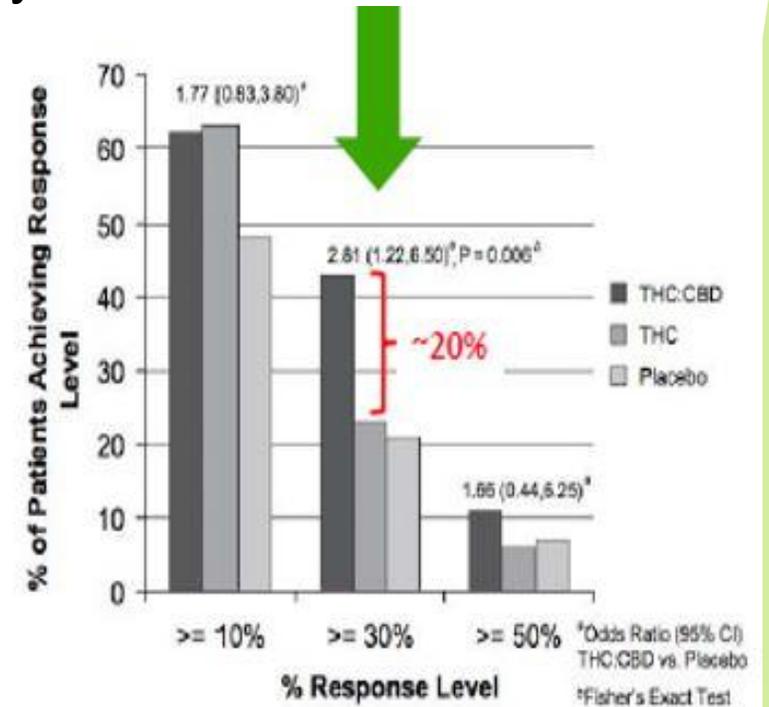


Fig. 3. Pain 0–10 Numerical Rating Scale scores: responder analysis (ITT analysis). ^aOdds ratio (95% CI) THC:CBD vs. placebo; ^bFisher's exact test.

Dosing Suggestions

How much should I take?

What about formulations? Strains?

Factors that influence dosing

- Method of Administration
- Safety, Tolerability, Efficacy
- Potency
- Isolate vs. Whole Plant Extract
- Tolerance / “ECS Tone”

Symptom relief



Impairment

STANDARD DOSING FORMS

- Sublingual Drops/Tinctures
- Inhalation Vape Pens
- Capsules
- Topicals
- Sprays
- Edibles
- Flower
- Crumble & Shatter
- Suppositories



MEDICAL MARIJUANA ROUTES OF ADMINISTRATION



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SUBLINGUAL DROPS/ TINCTURES



When taking cannabis via liquid drops under your tongue, components are absorbed via the digestive system or blood vessels in the mouth.

TIME BEFORE ONSET OF EFFECT
15-20 minutes

DURATION OF EFFECT
4-6 hours

EDIBLES



Gummies, hard candies, brownies, and cookies are common forms for edibles.

Patients should pay special attention to dosage for a desired effect.

TIME BEFORE ONSET OF EFFECT
15-40 minutes

DURATION OF EFFECT
4-6 hours

CAPSULES



The content of oral capsules enters the bloodstream after digestion.

This method is especially beginner-friendly because of the pre-portioned doses.

TIME BEFORE ONSET OF EFFECT
30 min - 2 hr

DURATION OF EFFECT
30 min - 5-8 hr

TOPICALS



A topical medication is applied directly to the skin at the site where the effect is needed.

This form is useful for its quick relief and ability to focus effect on a specific area.

TIME BEFORE ONSET OF EFFECT
almost immediately

DURATION OF EFFECT
1-2 hours

INHALATION (VAPING)

Vaporization delivers inhaled cannabis into the lungs via water molecules, avoiding absorption of potentially harmful material produced by combustion.



TIME BEFORE ONSET OF EFFECT
almost immediately

DURATION OF EFFECT
2-6 hours

TRANSDERMAL PATCHES



A patch is applied directly to skin so that a controlled release of medication is delivered through skin into the bloodstream. This allows for a long-lasting effect.

TIME BEFORE ONSET OF EFFECT
10 minutes - 1 hour

DURATION OF EFFECT
8-72 hours

FLOWER (SMOKABLE)

Dry flower, also called bud, can be ignited or vaporized and the smoke is inhaled into the lungs.



This product requires a state form

TIME BEFORE ONSET OF EFFECT
almost immediately

DURATION OF EFFECT
2-6 hours

SPRAY



This form of medical marijuana is absorbed via blood vessels in the mucous membranes in the mouth.

Sprays are beginner-friendly with simple doses

TIME BEFORE ONSET OF EFFECT
almost immediately

DURATION OF EFFECT
2-4 hours

SUPPOSITORIES

A suppository lets the patient administer medication rectally or vaginally so that it is absorbed near the site where the effect is needed, such as the pelvis, legs, spine, and stomach.



TIME BEFORE ONSET OF EFFECT
varies significantly by individual product; see packaging

DURATION OF EFFECT
varies significantly by individual product; see packaging

What are routes of administration?

Also called administration forms, these are the various ways that medical marijuana patients ingest medication. For the best effects, speak to your medical marijuana doctor and dispensary staff about your tolerance and familiarity.

Start low, go slow

Experts recommend starting with a low dosage and making note of how it affects your condition, then increasing your dose after several sessions to determine whether the effect is noticeably increased. The goal is to find the minimum dose that produces the maximum effect for your needs.

Pay attention to packaging

When using any medical marijuana product, read dosing information carefully before administration. This can help you with details such as the placement of a patch, the best time to take your medication, and how to adjust dosing for the ideal effect.

Choose the form for your needs

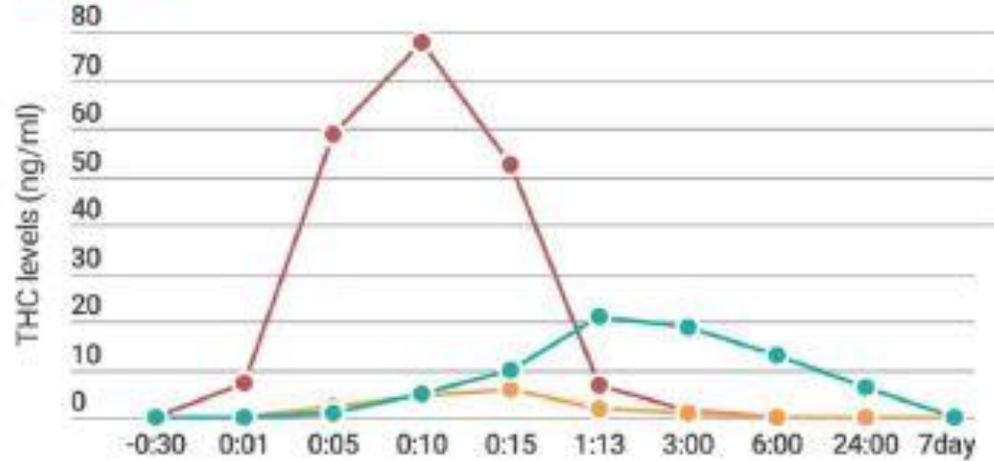
We often default to the familiar when it comes to medications, because it feels most safe. We encourage you to take the time to determine which form will best suit your individual condition.

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Inhalation versus Ingestion

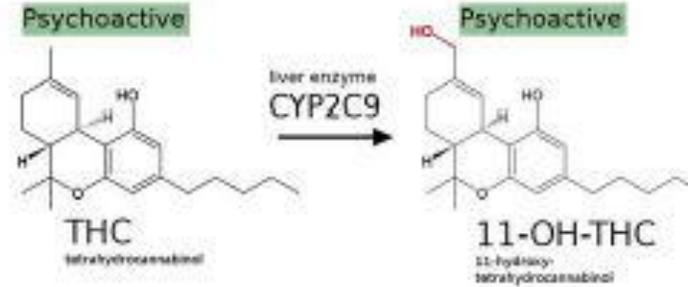


Average concentration of **delta-9-THC** and its metabolites after **INHALATION** of 15.8 mg (= one joint) of THC. Measured from half an hour before inhalation until 7 days after.

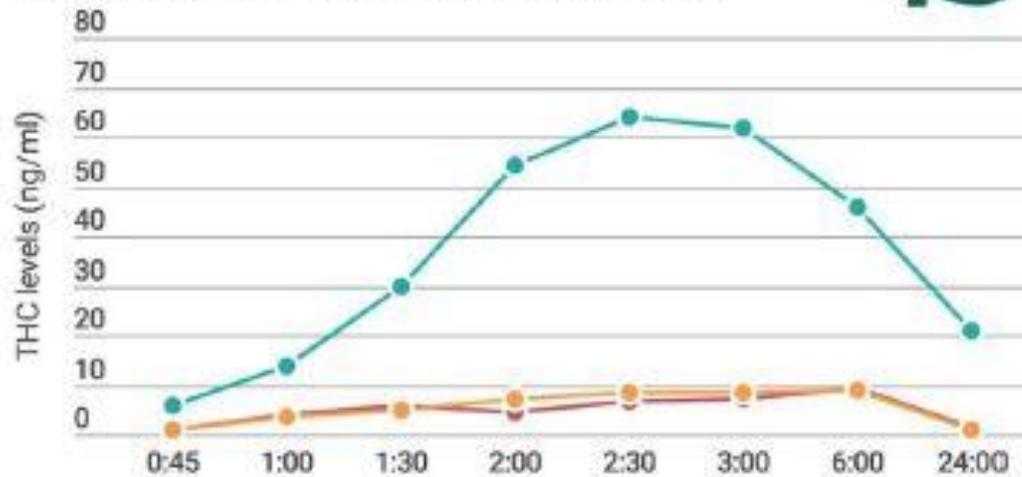


- Inhalation**
- Delta-9-THC
 - 11-OH-THC
 - 11-COOH-THC

Source: SeplenSoup Blog; Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet.* 2003;42(4):327-60. Review. PubMed PMID: 12648025.; Lindgren JE, Ohlsson A, Agurell S, et al. Clinical effects and plasma levels of delta 9-tetrahydrocannabinol (delta 9-THC) in heavy and light users of cannabis. *Psychopharmacology [Berl.]*. 1981;74(3):208-12.



Average concentration of **delta-9-THC** and its metabolites after **INGESTION** of 20 mg (= one chocolate cookie) of THC. Measured from 45 minutes until 24 hours after consumption.

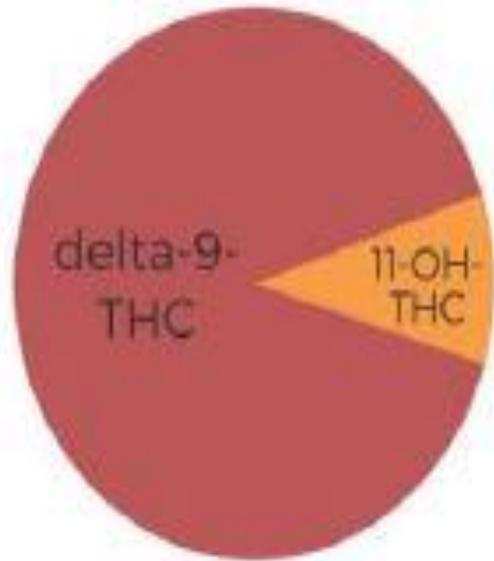


[4]



Route of Administration Matters

WHEN INHALED



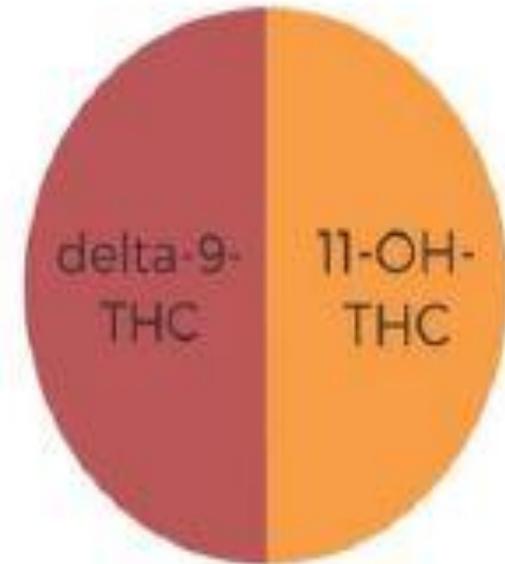
PROPORTION matters

11-OH-THC passes the brain barrier more easily than **delta-9-THC**.



11-OH-THC is 3 to 7 times more potent than **delta-9-THC** in activating receptors in the brain.

WHEN INGESTED

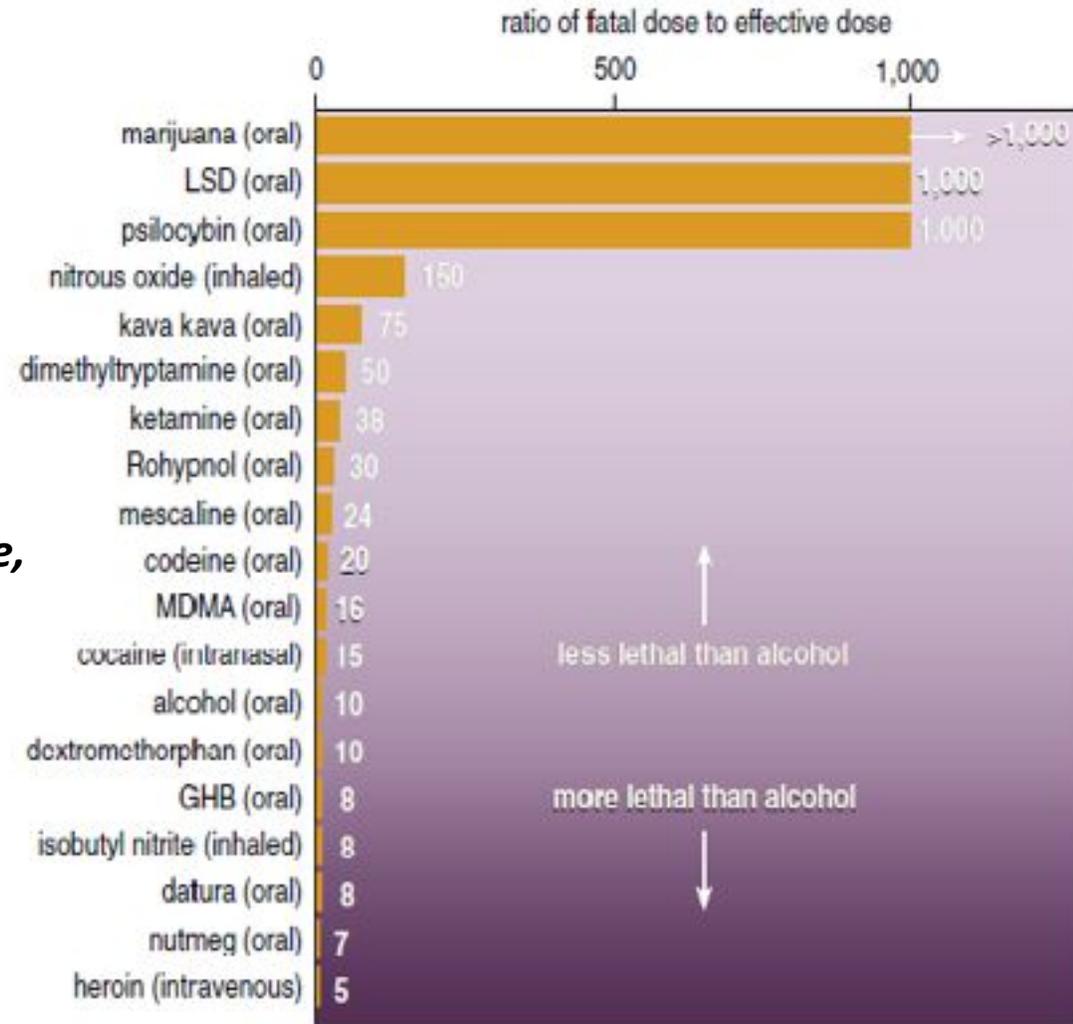


World Health Organization

PUBLICATION: “The Health and Social Effects of Non-medical Use Cannabis”, 2016

“There are no reports of fatal overdoses in the epidemiological literature”

Ranking psychoactive substances by their ratios of lethal dose to effective dose gives a general picture of how likely each is to precipitate an acute fatal reaction. **By this measure, many illicit drugs are considerably safer than alcohol.**



Options for achieving CBD and THC balance

- THC products can ONLY be purchased with a Florida Medical Marijuana Card approved by a physician and purchased from a Florida licensed dispensary.
- CBD products are available without a medical marijuana card, and can be purchased at a lower cost outside of a dispensary.
- MMTC physicians generally recommend full spectrum CBD products to maximize the entourage effect

Doctor-Recommended CBD Products

- Full Spectrum CBD products contain a wide variety of cannabinoids other than THC
- This allows maximum engagement of the endocannabinoid system
- Full spectrum CBD is available at \$0.06 - \$0.08 per mg as opposed to \$0.12 - \$0.20 per mg at Florida dispensaries.
- MMTC offers full spectrum CBD in clinic and online at:



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Potential Adverse Effects

Affecting more than 1 in 10 people

- Feeling dizzy or tired.

Affecting less than 1 in 10 people

- Eating more or less than usual
- Changed sense of taste or a dry mouth, mouth ulcers, burning
- Constipation, diarrhea, or nausea
- Feeling abnormal or drunk.
- Loss of balance or falling over
- Red eyes, blurred vision
- Dizziness
- Anxiety



Safety Profile

RESEARCH

Adverse effects of medical cannabinoids: a systematic review

Tongtong Wang MSc, Jean-Paul Collet PhD MD, Stan Shapiro PhD, Mark A. Ware MBBS MSc

∞ See related article page 1685

ABSTRACT

Cannabis (*Cannabis sativa*) is widely used as a recreational drug, with an estimated worldwide annual prevalence (defined as use at least once per year) of 160

A systematic review of 31 studies (23 randomized controlled trials and 8 observational studies) found that 96.6% of adverse effects were “not serious”.

events and to facilitate future cannabis research initiatives. We critically evaluated the quality of published studies with a view to identifying ways to improve future studies.

Results: A total of 321 articles were eligible for evaluation. After excluding those that focused on recreational cannabis

Pharmaceuticals], which contains Δ -9-tetrahydrocannabinol and cannabidiol in an oromucosal spray); dronabinol (synthetic Δ -9-tetrahydrocannabinol, marketed as Marinol [Solvay Pharmaceuticals]); nabilone (a synthetic derivative of Δ -9-tetrahydrocannabinol, marketed as Cesamet [Valeant Pharmaceuticals International]); and the herbal form of cannabis



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TRANSDERMALS

SMOKE-FREE INHALATION



TOPICALS



EDIBLES



TINCTURES



CAPSULES



ORAL SPRAY



TRANSDERMAL GEL



72 HOUR PATCH



VAPING



METERED INHALERS



CONCENTRATES



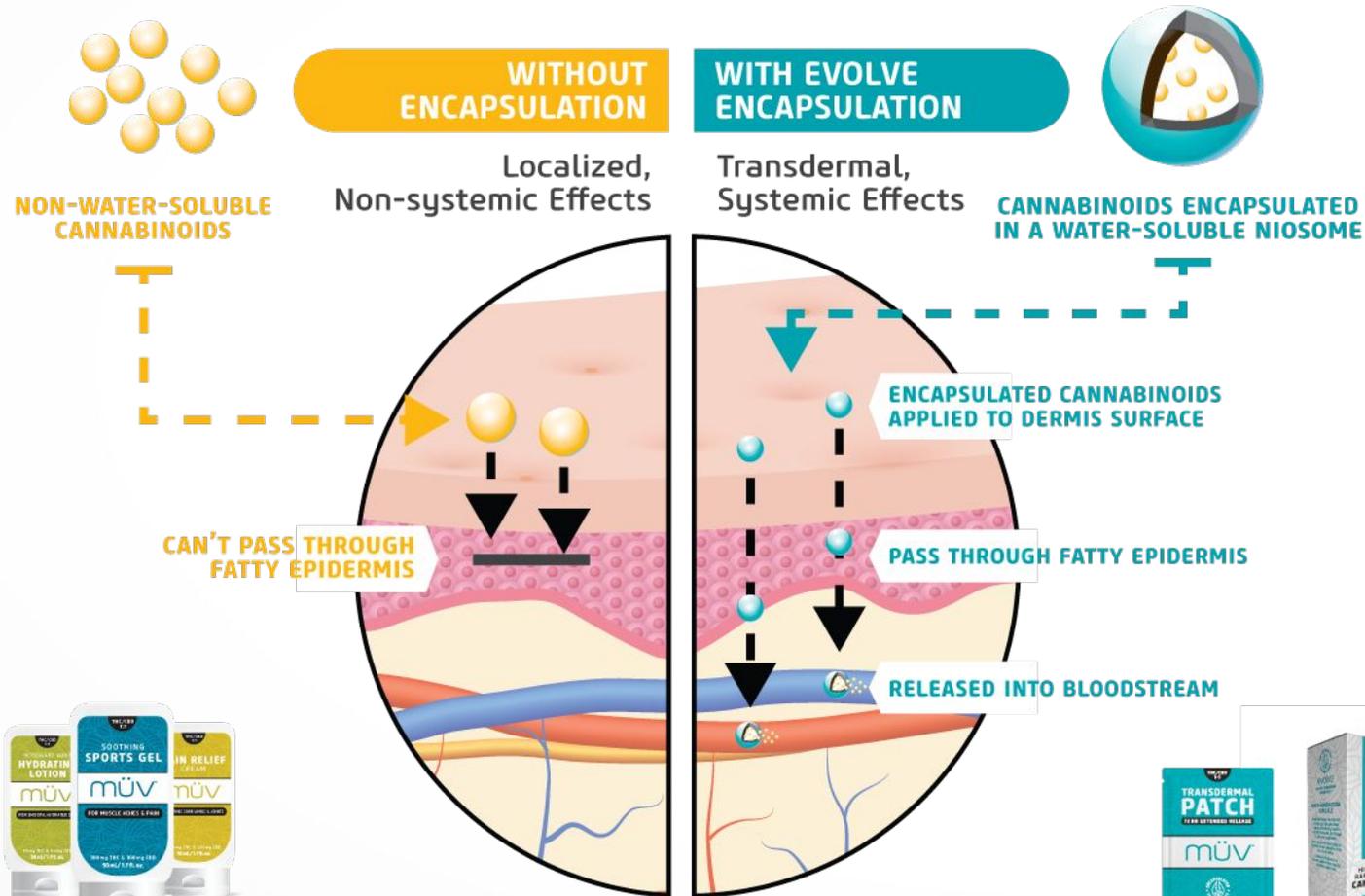
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Transdermals



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SOFT CHEWS
STRAWBERRY LEMONADE
CBD/THC 1:1
100MG CBD / 100MG THC PER PACKAGE
10MG CBD / 10MG THC PER PIECE

NET WT: 45g



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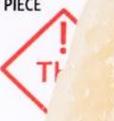
SOFT CHEWS
MANGO
sativa
100MG THC PER PACKAGE
10MG THC PER PIECE



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SOFT CHEWS
WATERMELON
hybrid
100MG THC PER PACKAGE
10MG THC PER PIECE

NET WT: 45g



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SOFT CHEWS
BLUEBERRY
indica
100MG THC PER PACKAGE
10MG THC PER PIECE

NET WT: 45g







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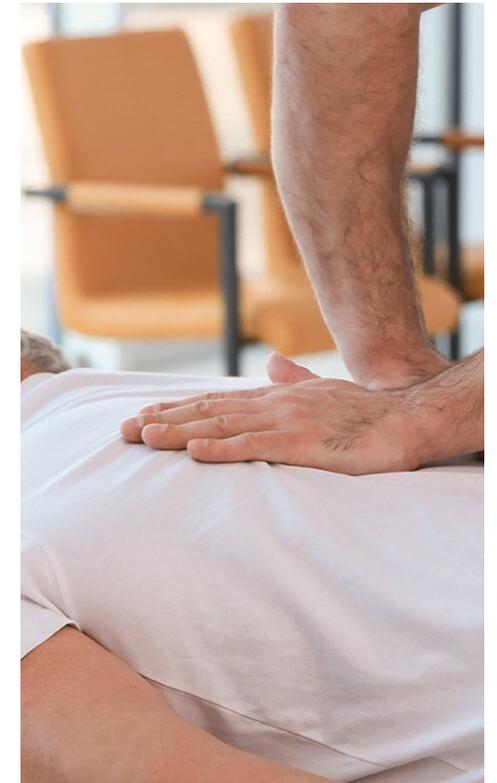
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BALANCED LIVING

A SENSE OF RESTORATION & CONTROL

- Meditation and mindfulness
- Cognitive behavioral therapy
- Yoga or stretching
- Acupressure
- Healthy diet & nutrition



GROUP DISCUSSION

References



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- [ix] Di Napoli M, et al. Prior cannabis use is associated with outcome after intracerebral hemorrhage. *Cerebrovascular Diseases*. 2016;41(5-6):248-255.



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