



Welcome to Medical Cannabis Education Day

Hosted by the
Hawai'i State Department of Health
Office of Medical Cannabis Control and Regulation

Disclaimer: The information provided in this webinar is for educational and informational purposes only and is provided as part of OMCCR's public education mandate. It is intended to keep qualifying medical cannabis patients informed about the safe and responsible use of medical cannabis. You should consult a medical doctor to address any health concerns specific to you. While we strive to ensure accurate and up-to-date content, the information may not reflect the most current legal standards or scientific research. The views expressed in this webinar do not necessarily reflect the opinions or policies of the State of Hawaii or the Department of Health.



December 7, 2024



Cannabis Medicine

From A Pharmacist's Perspective

By: Codi Peterson, PharmD, MS

Brought to you by

**Hawaii's Office of Medical Cannabis
Control and Regulation**

Learning Questions

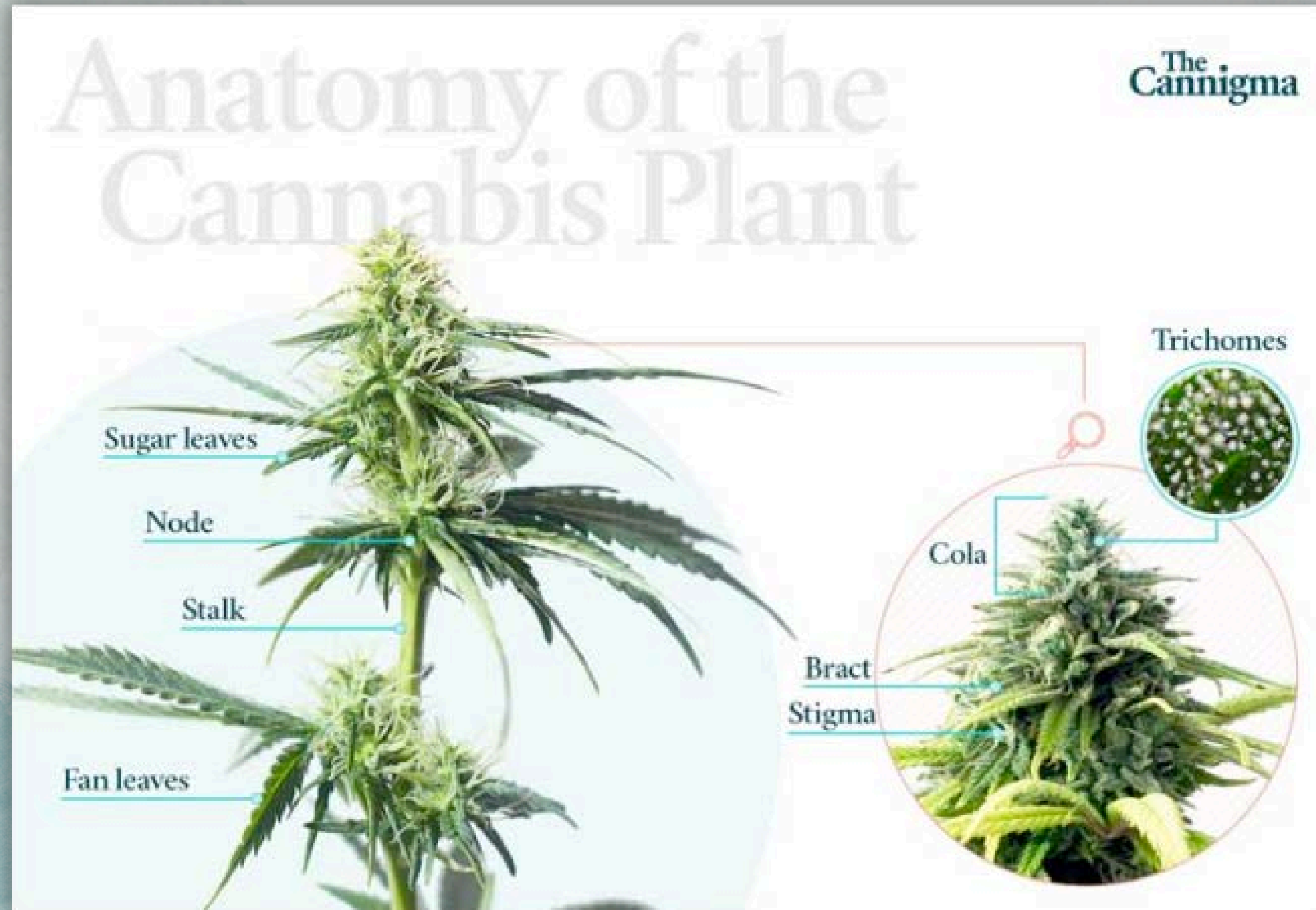
What components of cannabis influence the body and brain?

How can we maximize the benefits of cannabis while minimizing side effects?

How does cannabis interact with prescription medications, and how can these interactions be managed?



What is Cannabis?



What's In Cannabis?

Cannabinoids - Pharmacologic effects

Terpenes - Flavor, & Effects?

Flavonoids - Colors

Sterols - Antioxidants (roots)

Chemistry of cannabis

The
Cannigma

27K studies

have been published about cannabis since 2010.

150+ cannabinoids

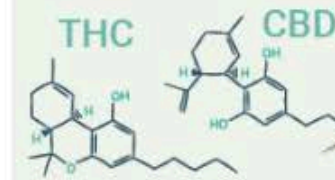
have been isolated from the cannabis plant to date

8 primary terpenes

have been identified in the cannabis plant

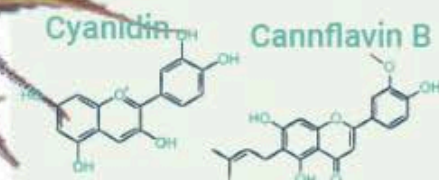
Cannabinoids

Produced in the trichomes, cannabinoids are the main reason cannabis can treat so many conditions. At least 150 of these amazing molecules have been identified so far - THC and CBD are the most prominent.



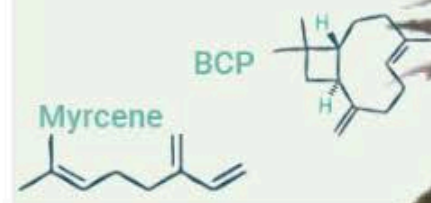
Flavonoids

Contrary to what the name might suggest, flavonoids give cannabis plants (and most plants) their unique colors. These molecules are mostly produced in the leaves, and include anthocyanins, cannflavins, luteolin, and kaempferol.



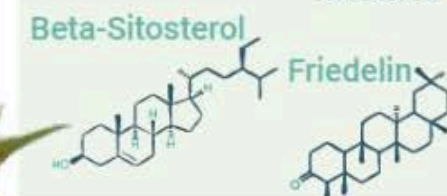
Terpenes

Also produced in the trichomes, terpenes are the "essential oils" of the cannabis plant. The 8 primary cannabis terpenes are myrcene, limonene, humulene, linalool, beta-caryophyllene, ocimene, pinene and terpinolene.



Sterols & Triterpenoids

Cannabis roots have been used as medicine dating back to ancient times, to treat ailments including arthritis, fever, and inflammation. These molecules are produced in the bark and roots, and include friedelin, epifriedelanol, and sitosterol.



References:

Jin, D., Dai, K., Xie, Z. et al. Secondary Metabolites Profiled in Cannabis Inflorescences, Leaves, Stem Barks, and Roots for Medicinal Purposes. *Sci Rep* 10, 3309 (2020). <https://doi.org/10.1038/s41598-020-60172-6>

Ryz NR, Remillard DJ, Russo EB. Cannabis Roots: A Traditional Therapy with Future Potential for Treating Inflammation and Pain. *Cannabis Cannabinoid Res.* 2017;2(1):210-216. Published 2017 Aug 1. doi:10.1089/can.2017.0028

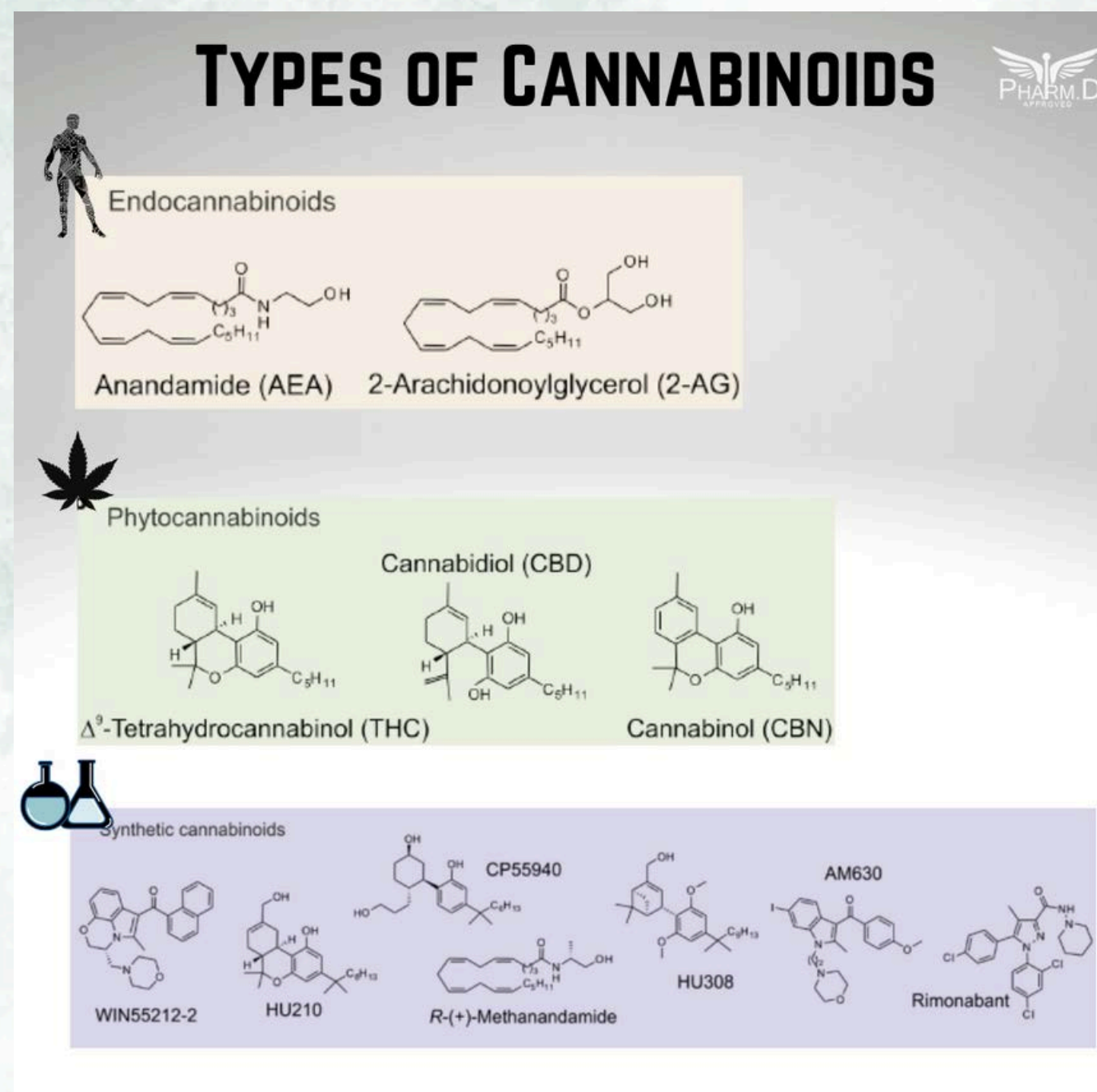
Lowe H, Steele B, Bryant J, Toyang N, Ngwa W. Non-Cannabinoid Metabolites of Cannabis sativa L. with Therapeutic Potential. *Plants (Basel).* 2021;10(2):400. Published 2021 Feb 20. doi:10.3390/plants10020400

Defining "Cannabinoid"

Molecules that interact directly or indirectly with cannabinoid receptors, often modulating neurotransmitter signaling

OR

Molecules that share certain chemical structure similarities to THC or CBD



Made inside of bodies (all animals)

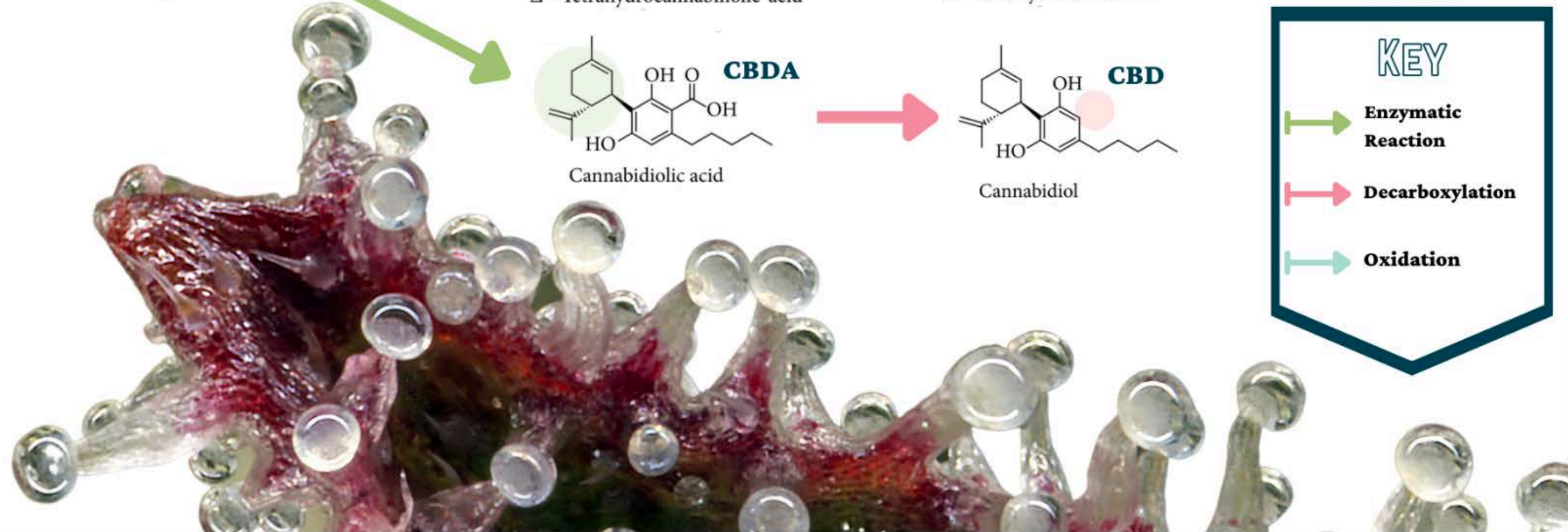
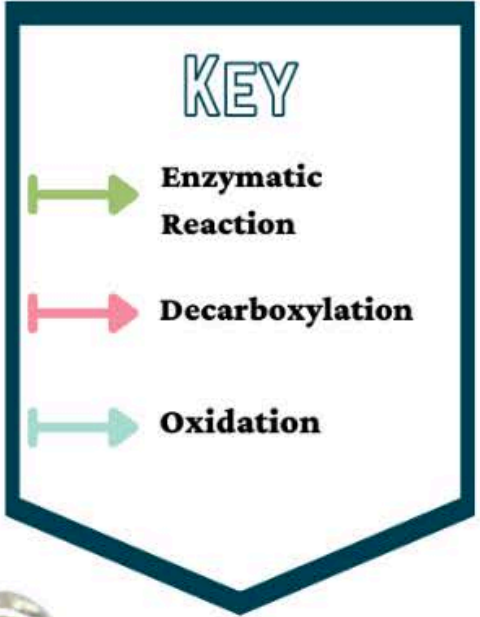
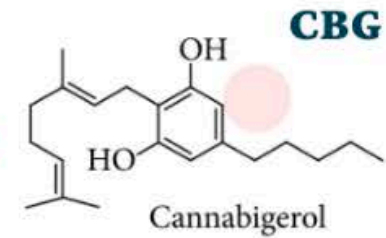
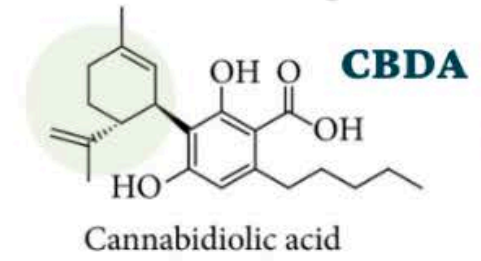
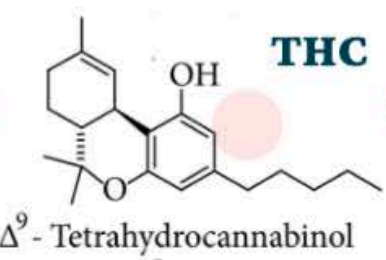
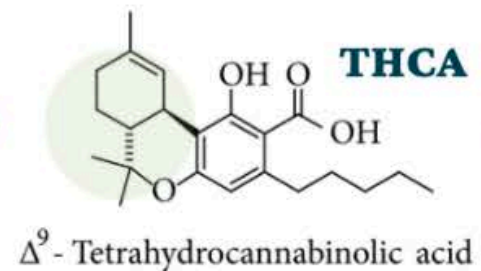
Made inside of plants and fungi (beyond cannabis, too!)

Designed and produced by man; not naturally occurring in nature

Cannabinoids in Cannabis

Cannabinoid transformation

The Cannigma



Cannabinoids

- THC (Tetrahydrocannabinol): Primary psychotropic compound
 - Stereotypical “high” and side effects (dry mouth, dry eyes, hunger, memory changes, etc)
- CBD (Cannabidiol): Psychoactive (but not psychotropic); may alter THC effects (evidence unclear); anti-inflammatory
- CBG: rising in popularity; may help combat anxiety (alpha-2 activity)
- THCV: “short tailed” cousin of THC; may act oppositely (to some extent)

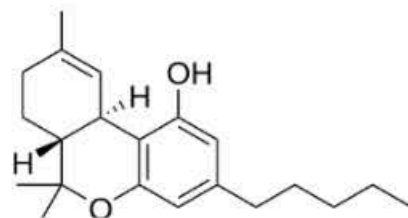


Cannabinoids

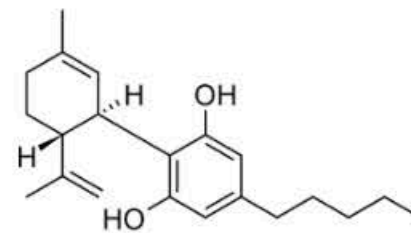


FDA APPROVED CANNABINOIDS

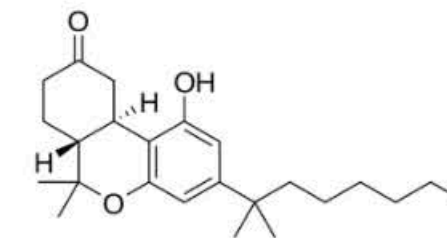
Dronabinol
(Synthetically Derived THC)



Epidiolex
(Plant Derived CBD)



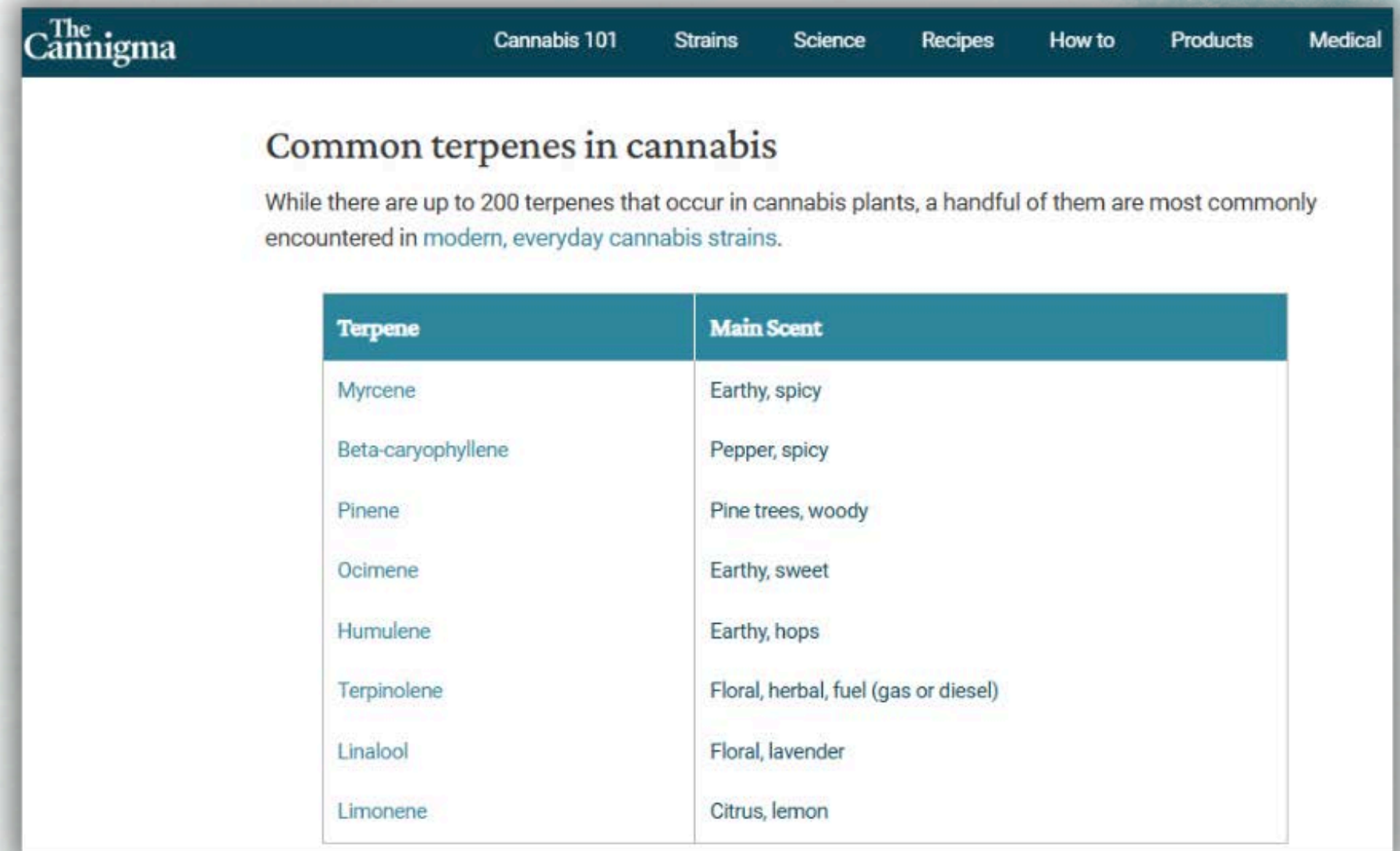
Nabilone (Cesamet)
(Synthetic Cannabinoid)



Clearly cannabinoids are medicine, yet herbal cannabis remains a schedule I substance

Terpenes (aka terpenoids)

- The “essential oil” of plants
 - Aromatic compounds found in cannabis that contribute to its scent and (potentially) to therapeutic effects.
 - Primary, but not sole contributor to scent (also acetates, aldehydes, esters, canna-sulfurs, and more)

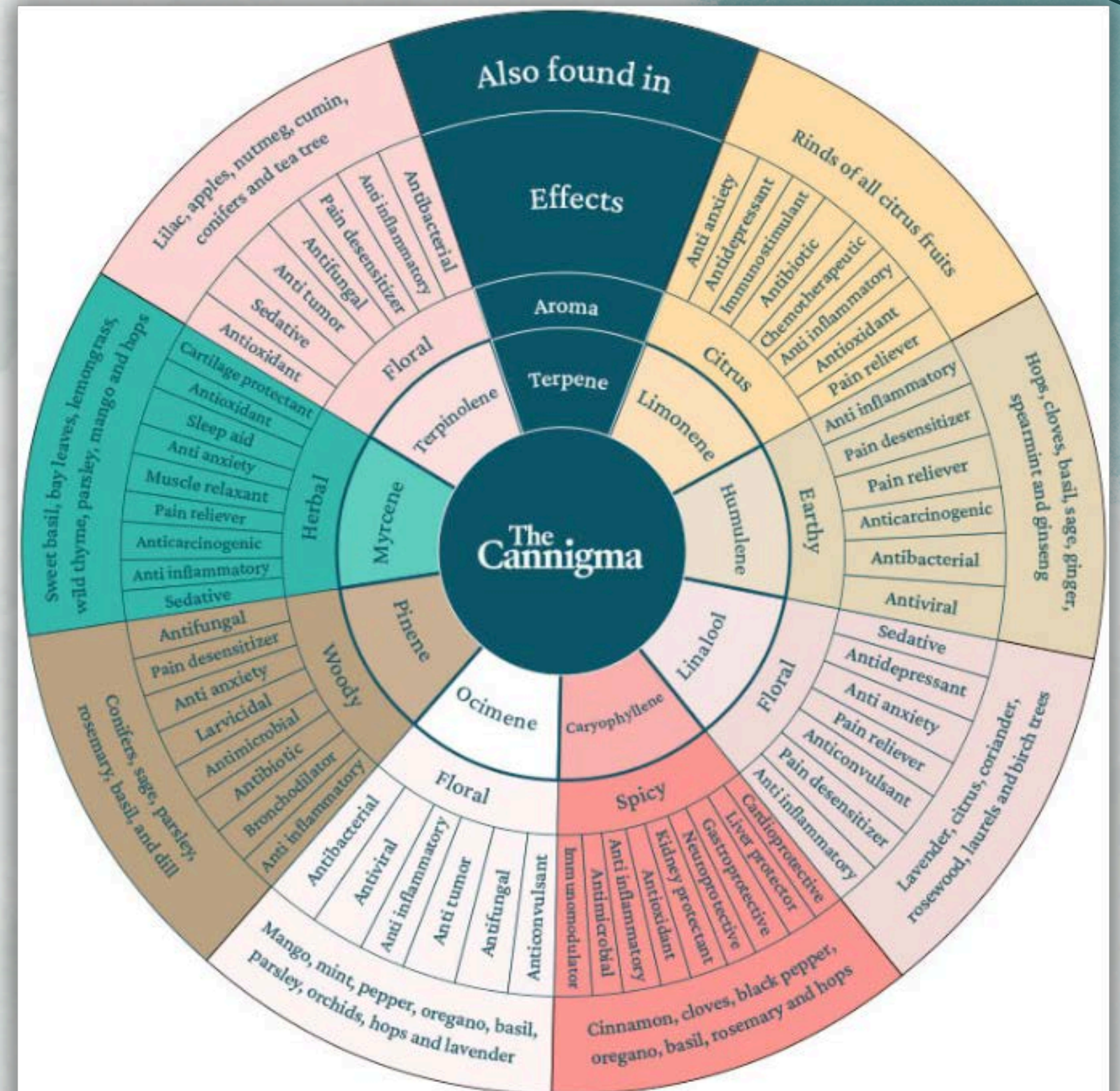


The screenshot shows a webpage from 'The Cannigma' with a dark teal header containing navigation links: Cannabis 101, Strains, Science, Recipes, How to, Products, and Medical. The main heading is 'Common terpenes in cannabis'. Below the heading is a paragraph: 'While there are up to 200 terpenes that occur in cannabis plants, a handful of them are most commonly encountered in modern, everyday cannabis strains.' A table follows with two columns: 'Terpene' and 'Main Scent'.

Terpene	Main Scent
Myrcene	Earthy, spicy
Beta-caryophyllene	Pepper, spicy
Pinene	Pine trees, woody
Ocimene	Earthy, sweet
Humulene	Earthy, hops
Terpinolene	Floral, herbal, fuel (gas or diesel)
Linalool	Floral, lavender
Limonene	Citrus, lemon

Terpenes (aka terpenoids)

- Terpene content of cannabis product highly variable
 - Product form (flower vs extract vs edible)
 - Age and Storage
 - Cultivation
 - Indoor vs outdoor
 - Latitude and Microclimate
 - Soil difference
 - Stressors
- 200 different terpenoids have been found
 - Usually dominant or Co-Dominant (1 or 2 major terpenes)



References:

* *Medicinal Properties of Cannabinoids, Terpenes, and Flavonoids in Cannabis, and Benefits in Migraine, Headache, and Pain*, Eric P Baron

* *Cannabis Pharmacology: The Usual Suspects and a Few Promising Leads*, Ethan B Russo, Jahan Marcu

The Entourage Effect

The Entourage Effect

The
Cannigma

History



1998:
Shimon Ben Shabbat notices:
Potential synergy in body-molecules that interact with the ECS

1999:
Raphael Mechoulam and Shimon Ben Shabbat suggest:
This synergy "may play a role in the widely held (but not experimentally based) view that in some cases plants are better drugs..."

2001:
Elizabeth Williamson presents:
The synergistic benefits of cannabis vs isolated THC

2011:
Ethan Russo writes:
Taming THC, which suggests cannabinoid and terpene synergy in cannabis

Criticism

There's some criticism about the enhancing effect aspects of the theory, suggesting there's not enough evidence to support it. But this seems to be mostly related to lack of research. For now, the jury is still out.

References:

*From *gan-zi-gun-nu to anandamide and 2-arachidonoylglycerol: the ongoing story of cannabis*, Raphael Mechoulam, Shimon Ben-Shabat, 1998.

**Synergy and other interactions in phytomedicines*, Elizabeth Williamson, 2001.

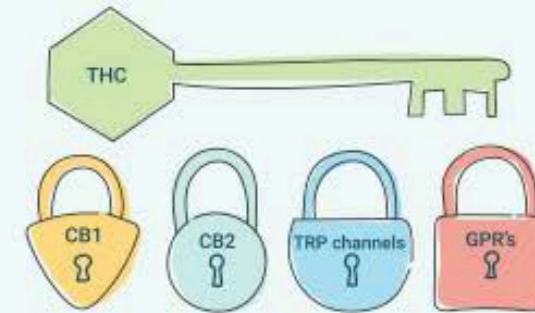
**Synergy research: Approaching a new generation of phytopharmaceuticals*, Hildebert J. Wagner, Gudrun S. Ulrich-Merzenich, 2009.

**Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects*, Ethan Budd Russo, 2011.

Mechanisms

1. Multi-target enhancing effects

Molecules can bind to several receptors thereby enhancing effects (e.g. THC binds to CB1 & CB2 receptors, and also interacts with select GPRs & TRP channels).



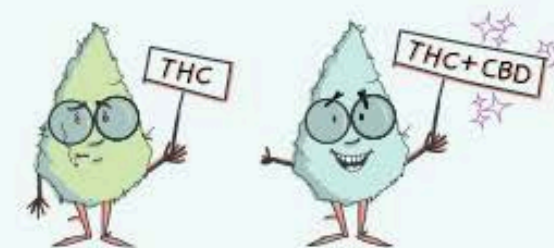
2. Molecular movement enhancing effects

Molecules which are inactive by themselves may enhance the effects of active molecules by altering their movement through the body (e.g. Cannabinoids absorption through the lungs could be improved by the presence bronchodilating terpenes such as limonene or pinene).



3. Modulating adverse effects

Molecules can interact to neutralize or reduce side effects (e.g. CBD can modulate the adverse effects of THC).



“The whole is greater than the sum of its parts.”

- Aristotle

Indica

vs.

Sativa

What's the difference?

Sativa & Indica: What's the deal?

The
Cannigma

Indica

Shorter stature
Broad leaves
Shorter flowering cycles



Sativa

Tall stature
Narrow leaves
Longer flowering cycles



Indica

vs.

Sativa

What's the difference?



Myth

Botanical heritage predict a cultivar's effects:

Sativa = uplifting **Indica** = sedating



Fact

A combination of factors influence the effect of a given strain:

- Cannabinoids
- Terpenes
- Your body, age and tolerance
- Dose
- Delivery method



“When you have someone labeling something as 70% sativa, 70% indica, it's 100% subjective. It's done by somebody smoking it and deciding that they are getting either an indica or a sativa effect from it.”

- Cannabis cultivator Kyle Kushman

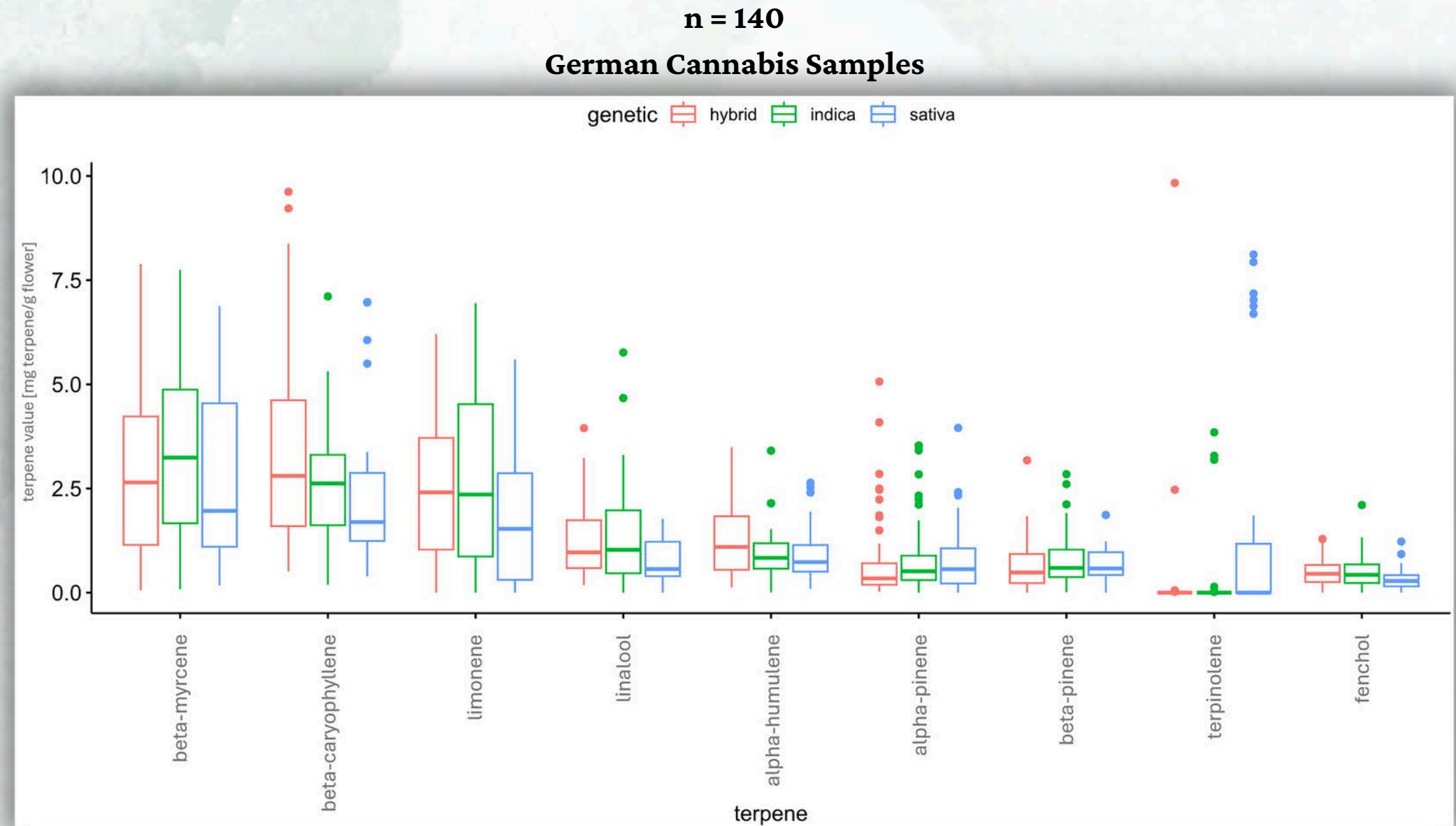
Indica

vs.

Sativa

- Terpene content similar across Indica, Sativa Hybrid
- Cannabinoids too, generally

SO WHAT DO INDICA AND SATIVA MEAN IN TODAY'S CANNABIS MARKET?



Indica

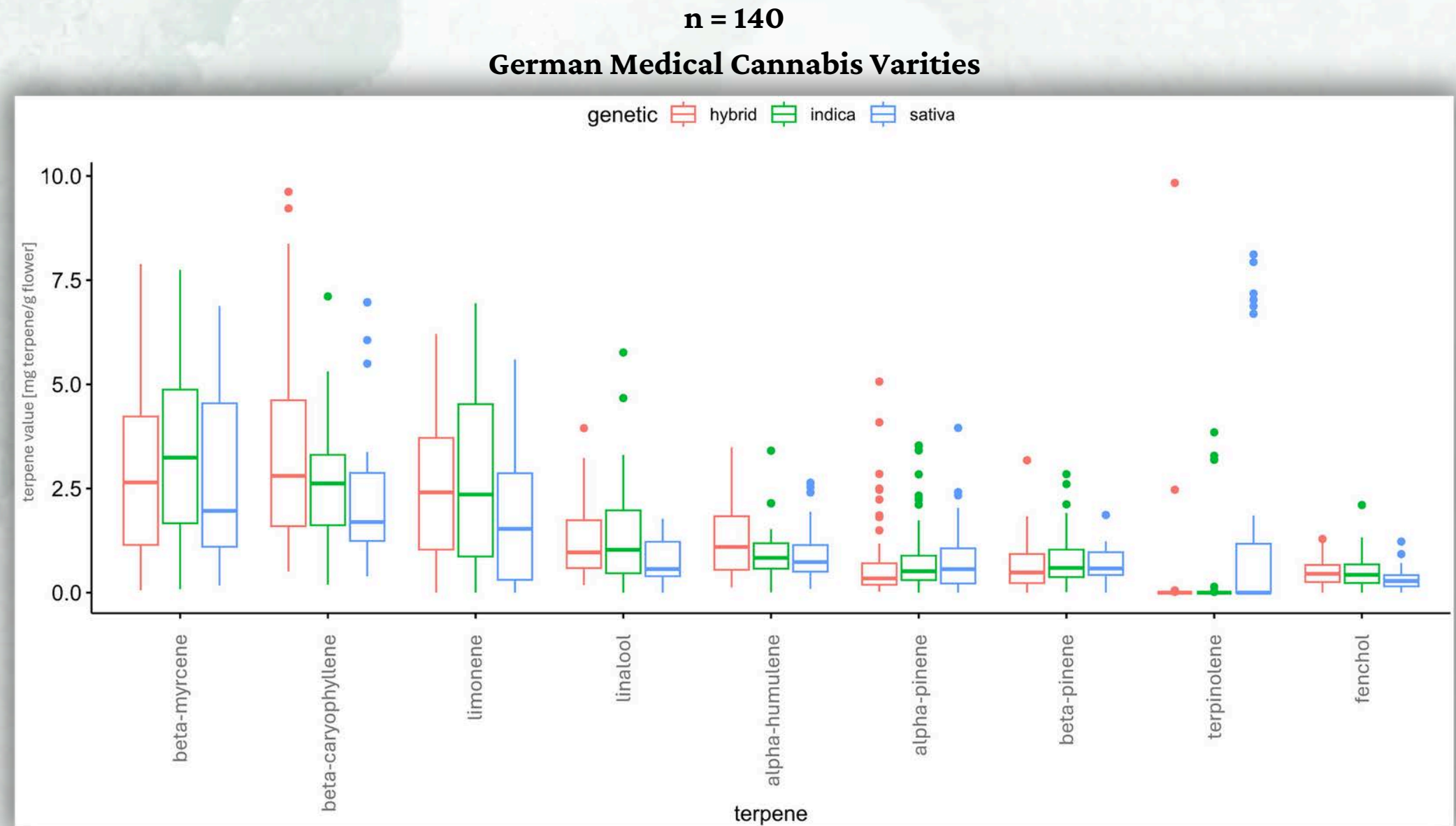
vs.

Sativa

- Terpene content similar across Indica, Sativa Hybrid
- Cannabinoids too, generally

SO WHAT DO INDICA AND SATIVA MEAN IN TODAY'S CANNABIS MARKET?

NOT MUCH



Herwig N, Utgenannt S, Nickl F, Möbius P, Nowak L, Schulz O, Fischer M. Classification of Cannabis Strains Based on their Chemical Fingerprint-A Broad Analysis of Chemovars in the German Market. Cannabis Cannabinoid Res. 2024 Aug 13. doi: 10.1089/can.2024.0127. Epub ahead of print. PMID: 39137353.

Approved Conditions Hawaii Medical Cannabis



1. Amyotrophic Lateral Sclerosis
2. Cancer
3. Glaucoma
4. Lupus
5. Epilepsy
6. Multiple Sclerosis
7. Rheumatoid Arthritis
8. HIV positive
9. Acquired immune deficiency syndrome (AIDS)
10. Post-traumatic stress disorder (PTSD)



OR any chronic or debilitating disease or medical condition, or its associated treatment, is eligible if it results in one or more of the following: **cachexia or wasting syndrome, severe pain, severe nausea, seizures (including those characteristic of epilepsy), or severe and persistent muscle spasms (including those characteristic of multiple sclerosis or Crohn's disease).**



What we know

Conditions cannabis can help with

(Conclusive or substantial evidence)

Pain

Chronic pain; fibromyalgia; cancer

Cesamet (Nabilone), Dronabinol
or even smoked cannabis

Cachexia

AIDS wasting or cancer

Appetite stimulant

Marinol (THC)

N/V

Chemo induced

Cannabinoid Hyperemesis?

Marinol (THC
(Syndros)

Epilepsy (certain types)

Dravet, Lennox-Gastaut, TSC

Good data - RCTs

FDA approved

Epidiolex (CBD)

Spasticity (Multiple Sclerosis)

Not FDA-approved,
but approved in 18 countries

Sativex (THC:CBD)

What we don't know

Inconclusive evidence (no RCTs, limited human data)

Alzheimer's

Inflammatory Bowel
Disease

Parkinson's

Obesity
(metabolic syndrome)

Huntington's Disease

Hepatitis C

Depression

Cancer

Insomnia (sleep)

Diabetes

Ischemia
(anoxic injury)

Heart Failure

Anxiety



"Mental Health"

By: Rachelle Beaudry



The ECS is everywhere

...

Is shared by all vertebrae on earth

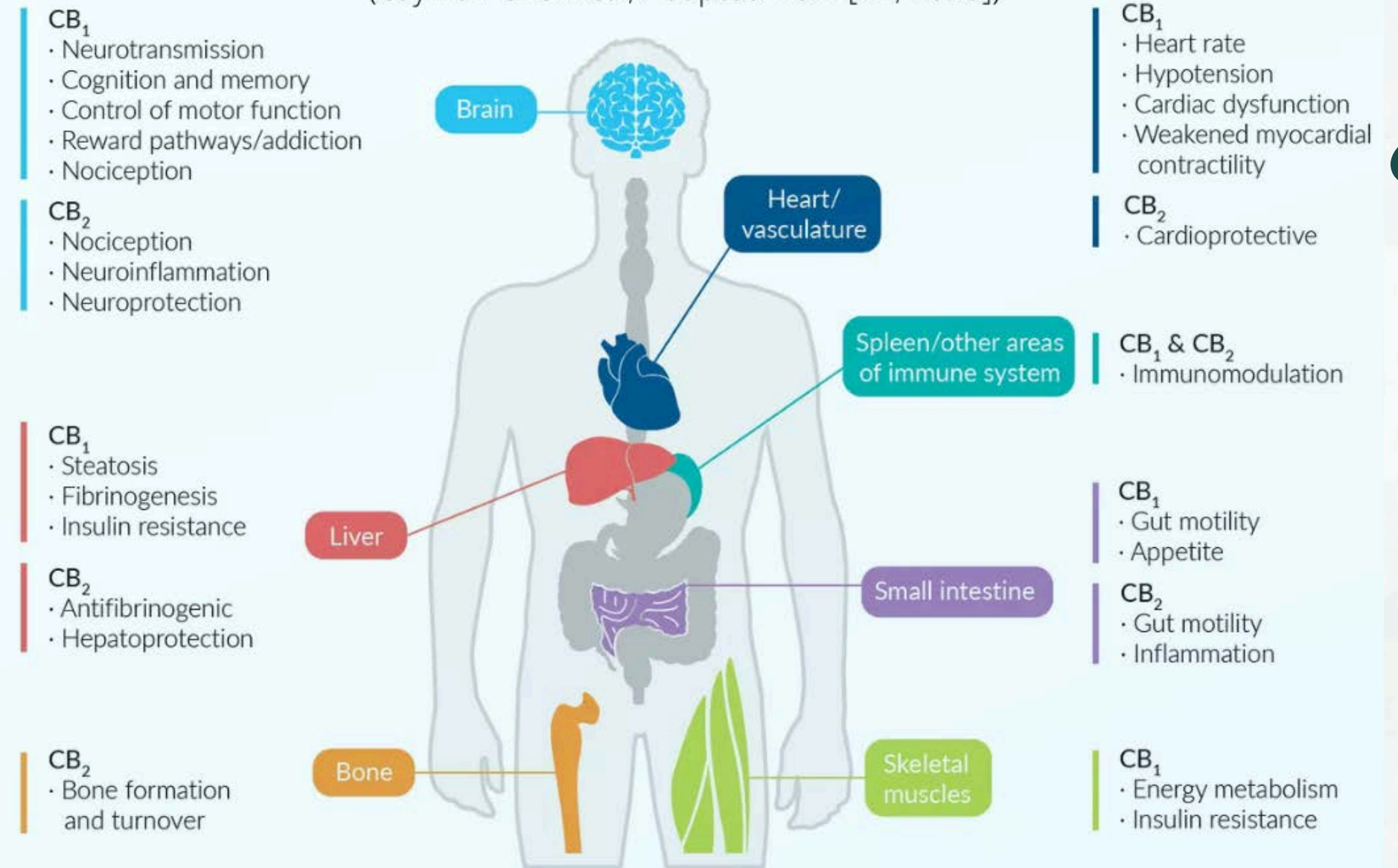
...

Regulates countless functions

HUMAN ENDOCANNABINOID SYSTEM

The actions of ECS are different in each organ system

(Cayman Chemical; Adapted from [An, 2020])



Cannabinoids treat a range of conditions because the ECS performs broad homeostatic functions

Choosing a route of admin

- Patient needs can vary highly
- Onset and duration are most common concerns
- Can use dose layering (oral and inhalation or SL)

Table 2 Differences between inhaled and oral cannabinoid administration

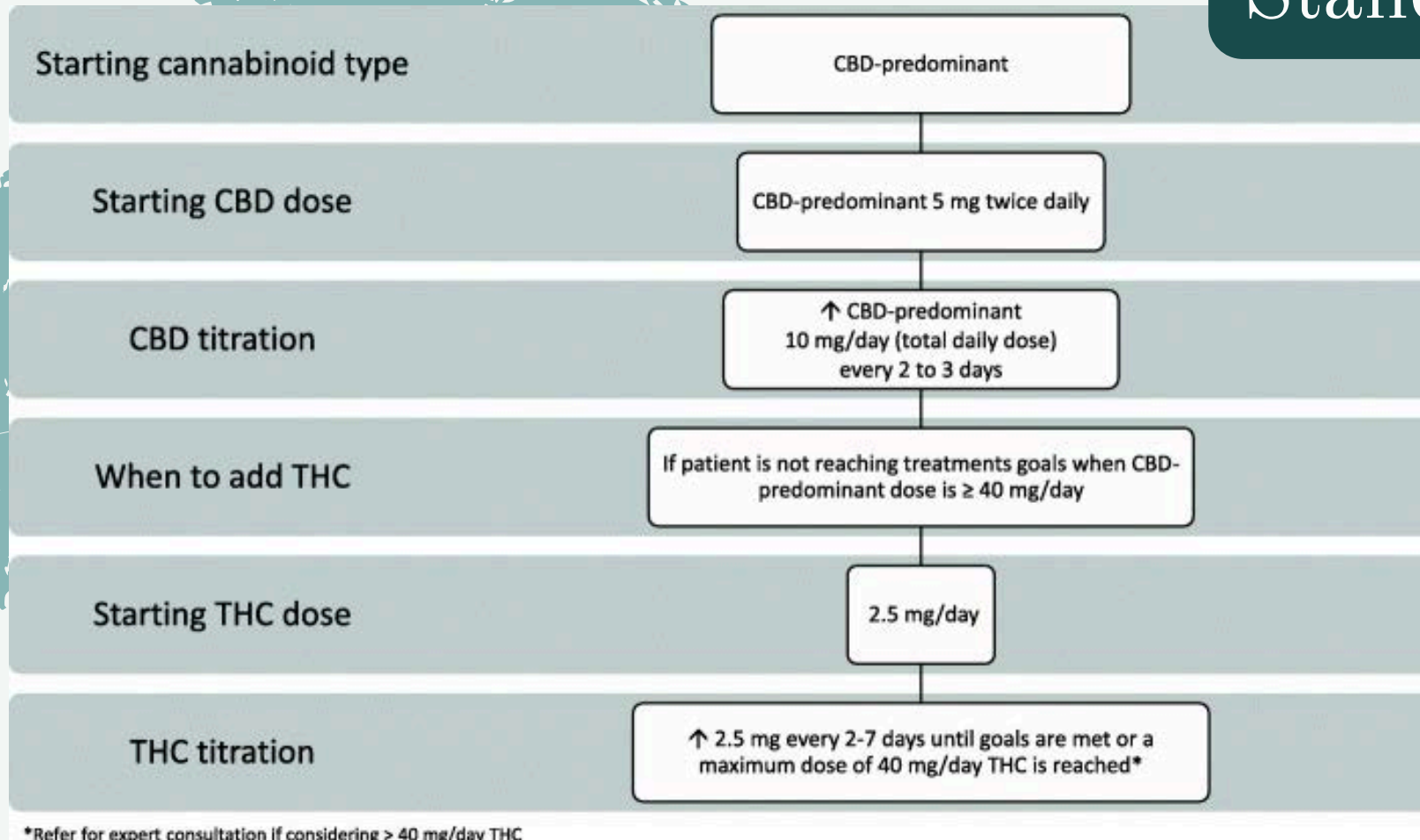
Characteristics	Inhaled	Oral
THC and CBD concentrations in available products sold in Canada	THC: <1–30%; CBD: <1–20%	THC: <1–30 mg/mL (maximum concentration); CBD: <1–25 mg/mL or more (no maximum concentration)
Titration characteristics	Quick titration	Lengthier titration
Ease of dosing	More challenging with higher potency strains	More precise with standardized preparations (oils, tinctures)
Average bioavailability of THC	10–25%	10% (variable 6–20%)
Active metabolites	$\Delta 9$ -THC > 11-OH-THC	$\Delta 9$ -THC < 11-OH-THC
Psychoactivity	THC-mediated	THC-mediated*
First onset of effects	3–10 minutes	60–90 minutes
Peak concentration	2–10 minutes	1–3 hours
Peak psychoactive effects: euphoria, depersonalization, sensory perceptions	15 minutes	3 hours
Peak cognitive effects: short-term memory, attention, concentration	15 minutes	5 hours
Duration of effects	2–4 hours	8–12 hours or more
Dosing frequency	5–6/day	1–3/day

*, 11-OH THC may be more psychoactive than $\Delta 9$ THC. THC, tetrahydrocannabinol; CBD, cannabidiol.

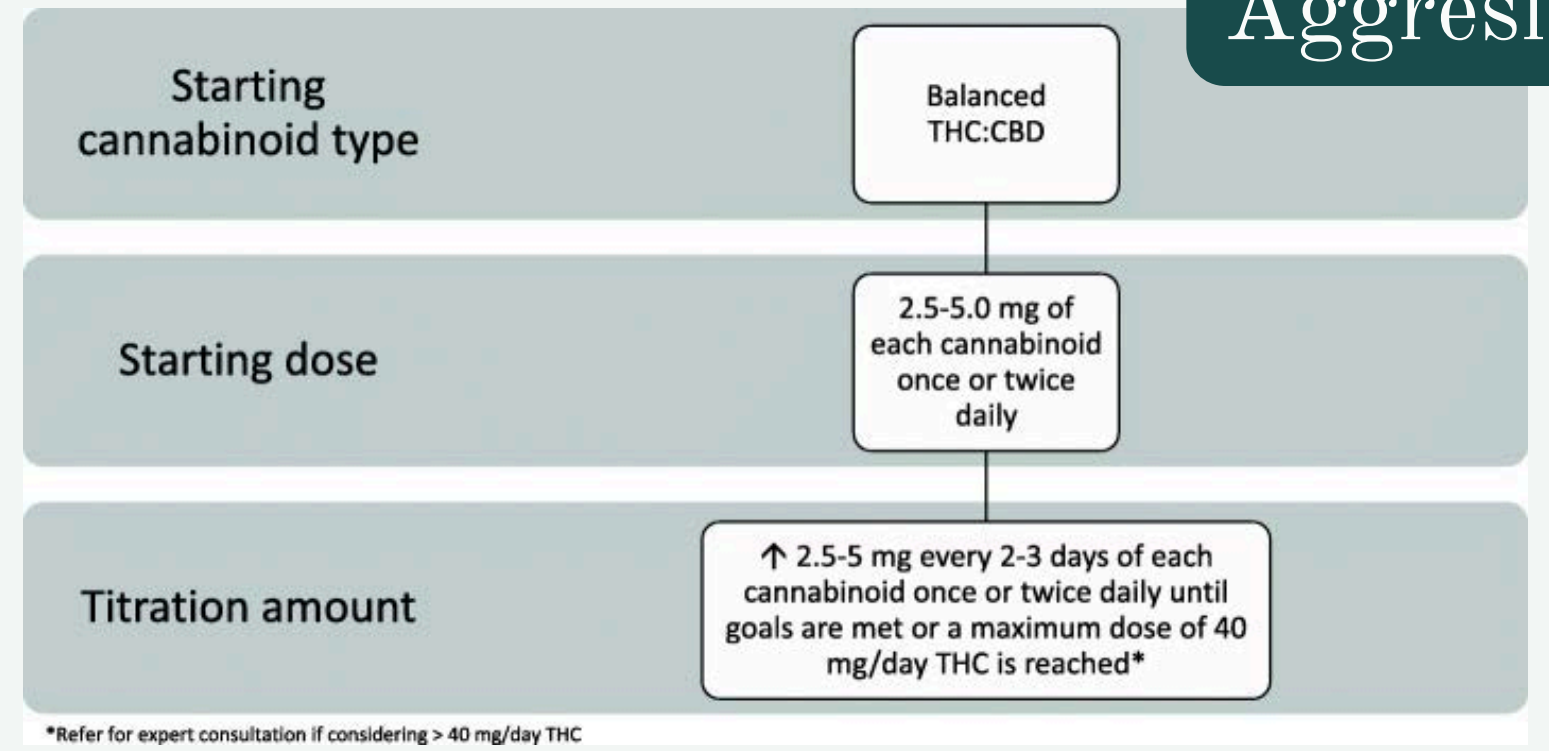
Cyr C, Arboleda MF, Aggarwal SK, Balneaves LG, Daenineck P, Néron A, Prosk E, Vigano A. Cannabis in palliative care: current challenges and practical recommendations. *Ann Palliat Med* 2018;7(4):463-477. doi: 10.21037/apm.2018.06.04

Approaching dosing (pain)

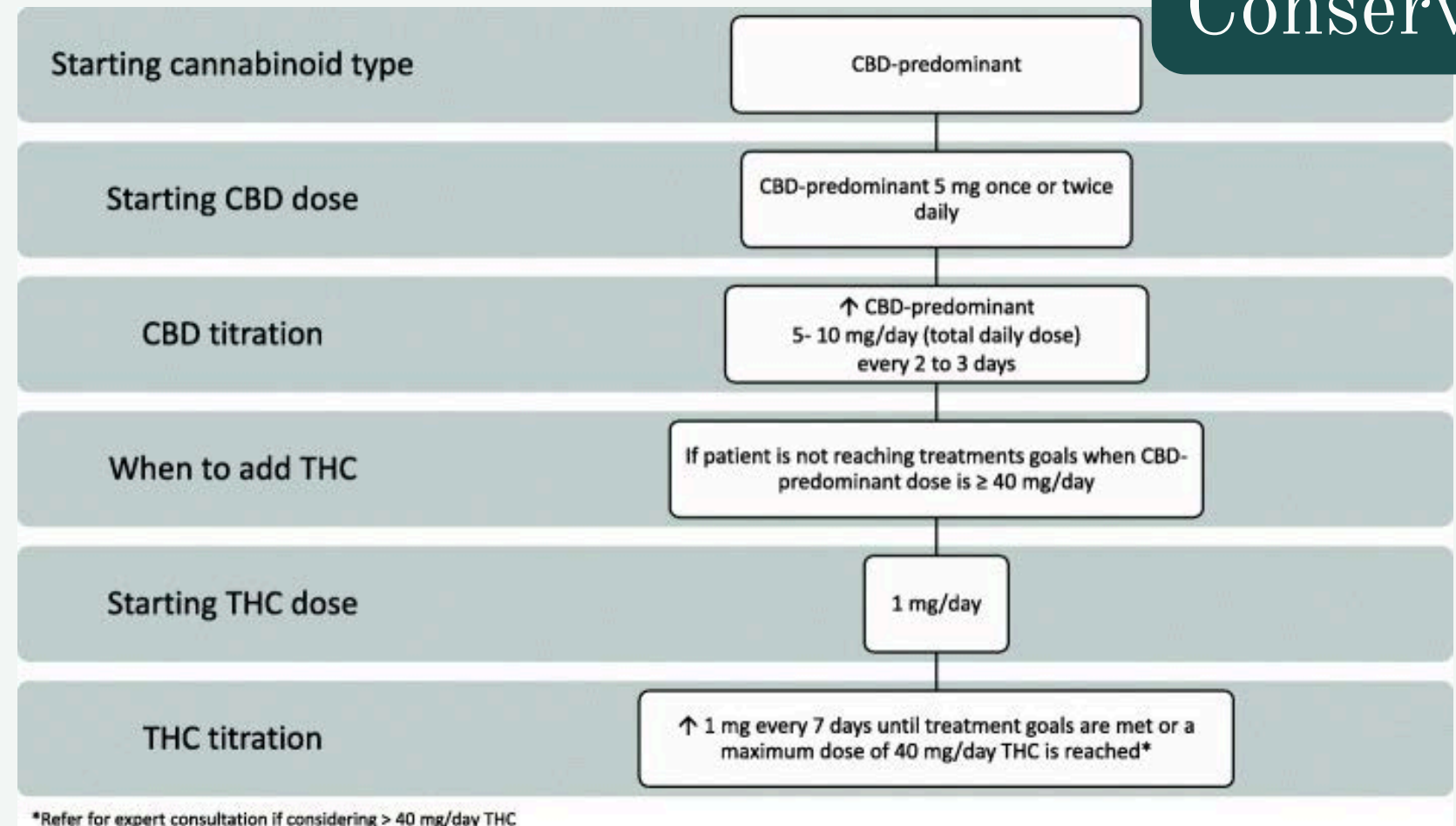
Standard



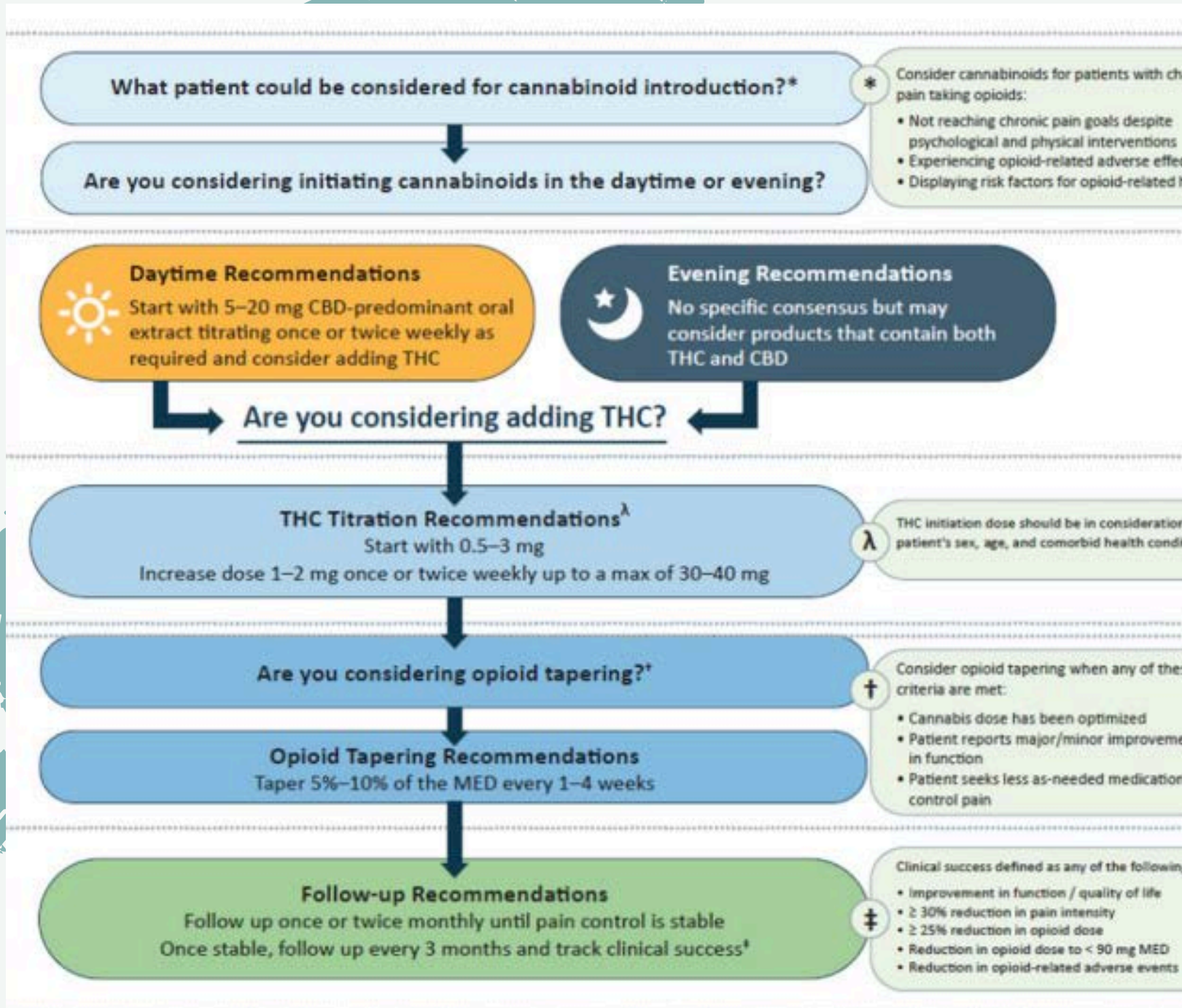
Aggressive



Conservative



Alternative approaches



Sihota A, Smith BK, Ahmed SA, et al. Consensus-based recommendations for titrating cannabinoids and tapering opioids for chronic pain control. *Int J Clin Pract.* 2021;75(8):e13871. doi:10.1111/ijcp.13871

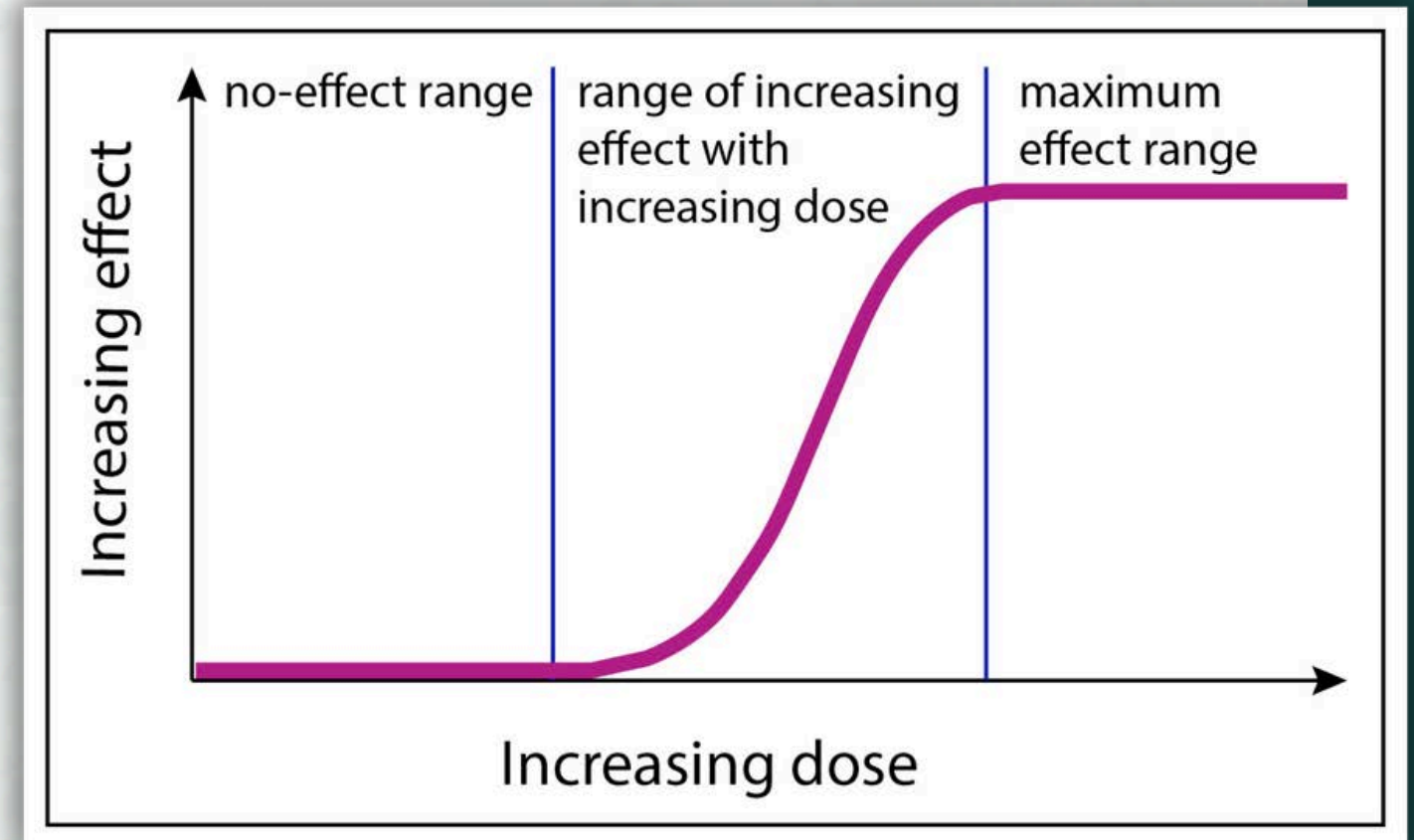
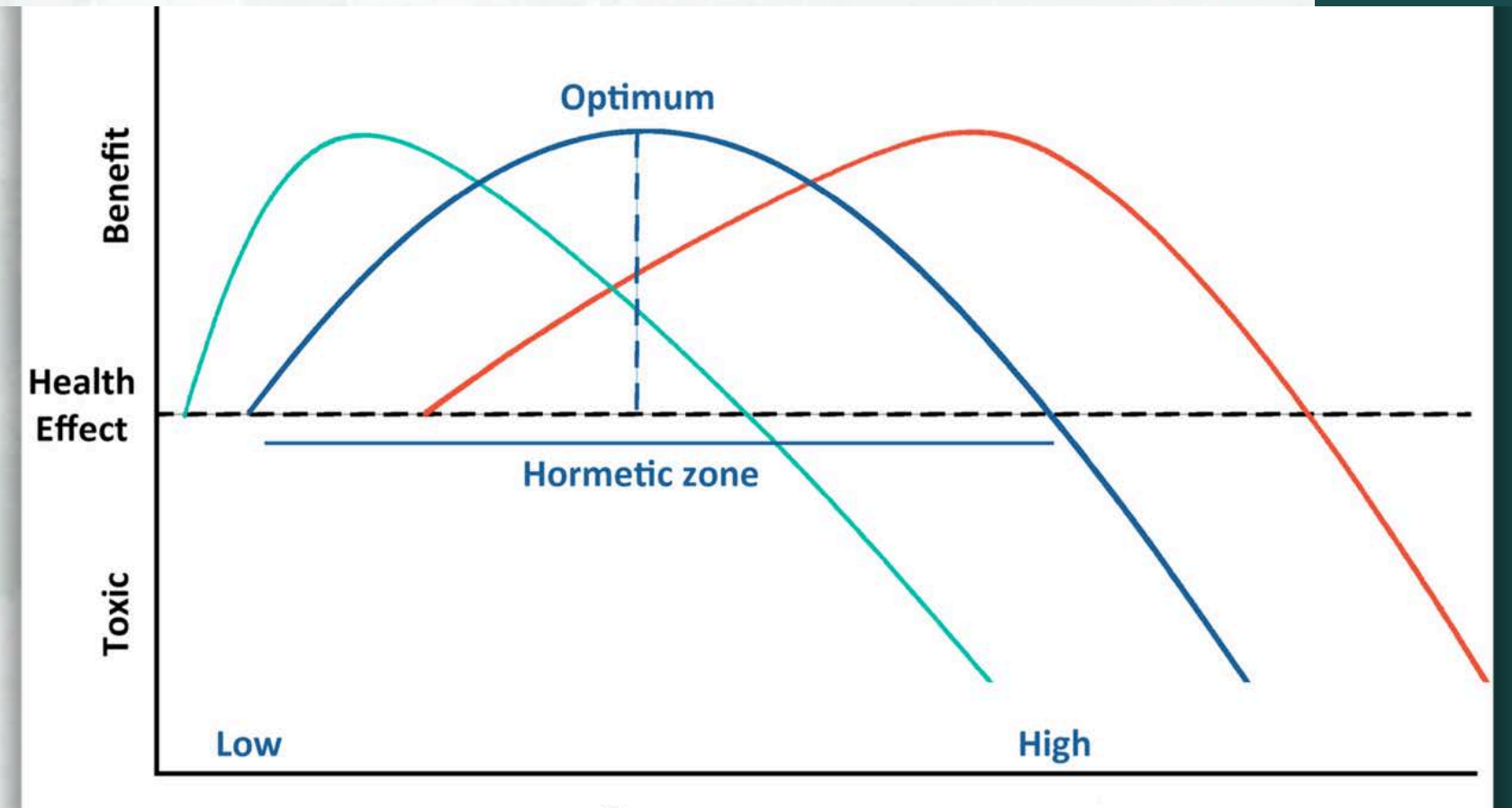
Table III: THC-Equivalent Dosing Titration.⁴

Days	Bedtime Oral Dosing Examples
1 to 2	1.25 - 2.5 mg THC equivalent at bedtime
3 to 4	If dose is tolerated, increase dose by 1.25 - 2.5 mg THC nightly
5 and beyond	Continue increasing dose by 1.25 to 2.5 mg THC nightly every two days until the desired outcome is reached, with minimal adverse effects.
Days	Daytime Oral Dosing Examples
1 to 2	2.5 mg THC-equivalent once daily
3 to 4	2.5 mg THC twice daily
5 and beyond	Increase dose as needed to 15 mg THC divided BID-TID.

Carr A, Ferguson M. How to Communicate with a Medical Marijuana Dispensary. *Pract Pain Manag.* 2019;19(3).

Biphasic Effects

- Biphasic response: where low and high dosages commonly induce opposing effects
- Numerous reports demonstrate the biphasic effects of $\Delta 9$ -THC and other cannabinoid agonists



Cannabis medicine is same same, but different

Patient specific

- This is not a one size fits all medication

Start low; Go slow

- Cannabis has been touted as having biphasic effects
- Different dose = different effects
- Less is often more!

Strains names won't work

- Must rely on the chemical profile of the product...not the name
- Sticking the same cultivator and variety (rather than simply following strain name) may help improve predictability of a product



Common Side Effects



Sedation

Dysphoria

Anxiety

Slowed reaction time

Increased appetite

Red eyes

Bronchitis



Dry mouth

Insomnia

Cough

Dizziness

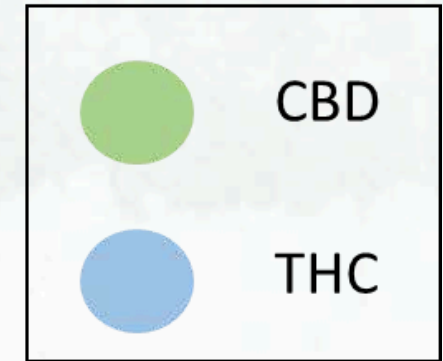
Ataxia

Drowsiness

Headache

Rare but Serious Side Effects

Rare Adverse Effects



**Orthostatic
hypotension**

**Cannabis
Hyperemesis
Syndrome
(CHS)**

**Acute
Psychosis**

Tachycardia



Elevated hepatic enzymes

Drug Interactions

What the drug
does to the body

Pharmacodynamic

"changes"

What the body
does to a drug

Pharmacokinetic

"movements"

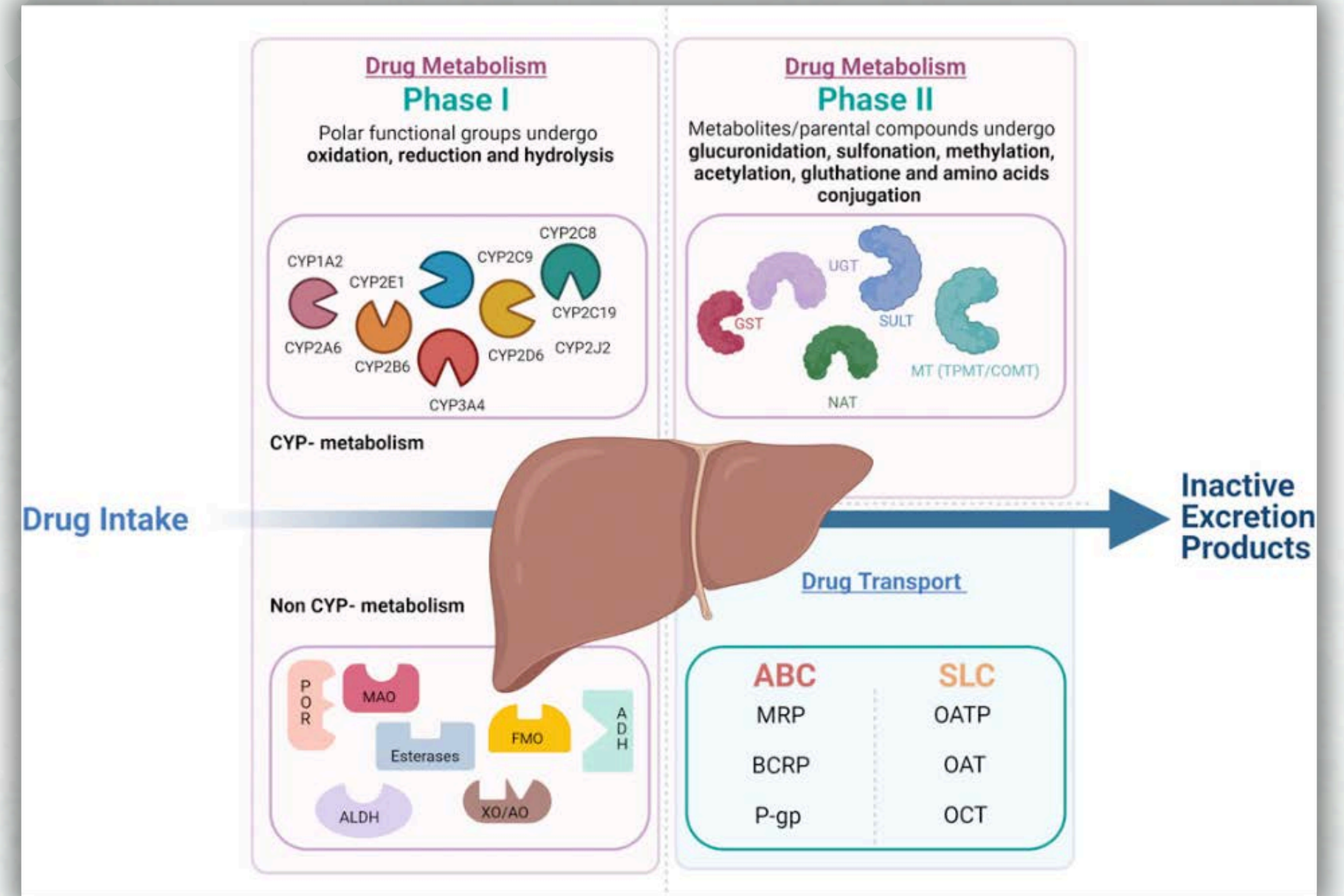
PHARMACOKINETIC Drug Interactions

- All Substances (drugs, food, poisons, herbs, etc) must be processed by the body to prepared to elimination
- CYP enzymes (Cytochrome P450) are primary enzymes involved in breaking down CANNABINOIDS
- CYP are enzymes are responsible for metabolizing the majority of pharmaceutical drugs

What does fruit have to do with it?



Potent CYP inhibition
= more (or sometimes less)
drug exposure



Citation: Abouir K, Samer CF, Gloor Y, Desmeules JA and Daali Y (2021) Reviewing Data Integrated for PBPK Model Development to Predict Metabolic Drug-Drug Interactions: Shifting Perspectives and Emerging Trends. Front. Pharmacol. 12:708299. doi: 10.3389/fphar.2021.708299

PHARMACOKINETIC Drug Interactions

Possible Cannabinoid to Drug Interactions

Cannabinoids can interact with different medicines, changing how they work in your body. This happens because cannabinoids can affect liver enzymes, especially ones in the cytochrome P450 (CYP) family, which help break down many drugs. These interactions might cause:

- Increased drug levels, making the medicine's effects (and side effects) stronger.
- Decreased drug levels, which can make the medicine less effective.

Here are some examples of how cannabinoids and medicines can interact, why it happens, and what it might do.

Key Takeaways:

- People taking medications or herbal supplements that may possibly interact with cannabinoids should consult their healthcare provider to ensure safe administration and monitor and adjust dosages if needed.
- Let your healthcare provider know prior to surgery if you use cannabis.
- There are drug interaction websites that may be utilized to check your medications and herbal supplements.

DRUG	EXAMPLE	CANNBINOID	ENZYME	EFFECT	POSSIBLE OUTCOME
Blood Thinners	Warfarin	THC/CBD	CYP2C9 CYP3A4	Increase levels of medication	Severe bleeding
Antiepileptic medications	Clobazam, Valproate	CBD	CYP2C19	Increase levels of medication	Drowsiness Enhance seizure control
Antidepressants	SSRI inhibitors like Amitriptyline	Cannabinoids	CYP2D6	Increase levels of medication	Dizziness, confusion serotonin syndrome (rare)
Antipsychotics	Haloperidol, Clozapine	Cannabinoids	CYP2D6 CYP3A4	Increase levels of medication	Drowsiness, dizziness, confusion
Opioids	Morphine, Oxycodone	Cannabinoids	CYP2D6	Increase levels of medication	Drowsiness, slowed breathing Enhance pain relief
Antifungal medications	Ketoconazole	THC	CYP3A4	Increase levels of cannabinoids	Drowsiness, dizziness, psychoactive experiences
Blood pressure medications	Beta-blockers, calcium channel blockers	Cannabinoids	CYP2D6 CYP3A4	Increase levels of medication	Changes in blood pressure, heart rate, dizziness, fainting
Sedatives and sleep medications	Benzodiazepines like Xanax	Cannabinoids	CYP3A4	Increase levels of medication	Drowsiness, dizziness, confusion
Anesthesia		Cannabinoids		Increase risk of complications	Slowed breathing, choking/blocked airway, changes in blood pressure, increased post-surgery pain

PHARMACODYNAMIC Drug Interactions

Liver Toxicity

- Concomitant drugs
- Doses used
- Liver function

CBD + valproate
may impact liver
function

Compounded CNS Effects

- Concomitant
sedative drugs

THC in combination with:

- Opioids
- Alcohol
- Benzodiazepines
- Gabapentin

Drug Interactions

<https://cann-dir.psu.edu>

CANNabinoid Drug Interaction Review



PennState
College of Medicine

Takeaways

Multi-component Medicine: Cannabinoids and terpenes drive cannabis' effects; strain names are unreliable—focus on chemical profiles.

Medical Use: Proven benefits for pain, nausea, spasticity, and epilepsy; many uses lack strong evidence.

Personalized Care: Effects vary by dose; consistency and a "start low, go slow" approach are key.

Drug Interactions: Cannabis affects drug metabolism and CNS activity; monitor for interactions carefully.



QUESTIONS?

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