

Mood Booster or Mood Buster: What's Up with Medical Marijuana?

UZMA ZAKIR, RPH
DIRECTOR OF OUTREACH
CANNABIS EDUCATION COORDINATOR
ACREAGE HOLDINGS CONNECTICUT REGION

1

Learning Objectives



RECOGNIZE

Recognize how the endocannabinoid system functions in human disease



DESCRIBE

Describe how to select the right products and dosages and prevent drug interactions



DIFFERENTIATE

Differentiate between recreational and medicinal laws and products



IDENTIFY

Identify the various initiatives

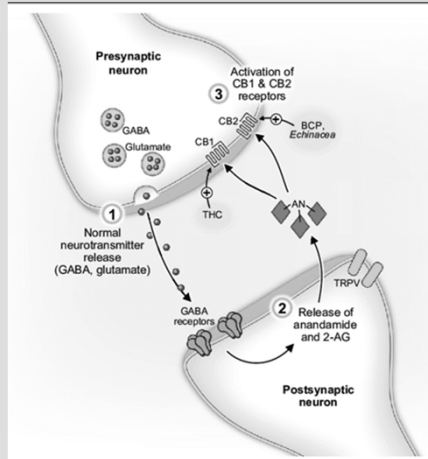
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About Me



“All financial interests with ineligible companies (if noted) have been mitigated”

3

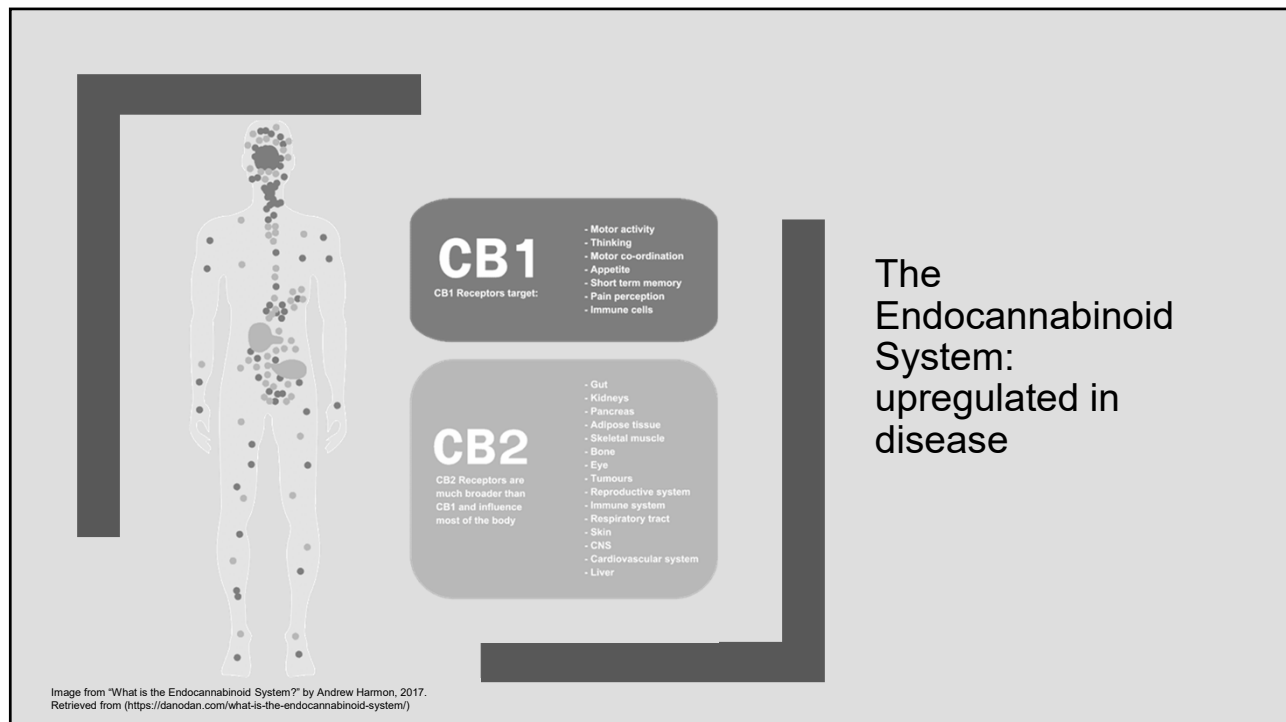


VanDolah, Harrison & Bauer, Brent & Mauck, K.. (2019). Clinicians' Guide to Cannabidiol and Hemp Oils. Mayo Clinic Proceedings. 94. 10.1016/j.mayocp.2019.01.003.

Intro to Endocannabinoid System (ECS)

- Components
 - *Ligands: Anandamide and 2AG*
 - *G-Protein Coupled Receptors: CB1 and CB2*
 - *Enzymes: FAAH, MAGL*
- Purpose
 - *Homeostasis*
- Functions
 - *Regulates response to pain*
 - *Stimulates hunger*
 - *Plays a part in the brain's "reward pathway"*
 - *Regulates mood and emotion*
 - *Reduces anxiety and depression*
 - *Regulates hormones, sperm, and eggs in the human reproductive system*
 - *Involved in cell regulation, cell signaling and tumor surveillance*

4



5

Cannabinoids: A Family of Molecules

Endogenous Ligands: endocannabinoids

Synthetic cannabinoids: cannabinoid-mimetic compounds

Phyto-cannabinoids: bio-active components of the cannabis plant

6

THE ENDOCANNABINOID SYSTEM IN DISEASE

- Deviations from homeostasis, such as injury, inflammation, or acute change, will usually result in the elevation of at least one ecb in the involved tissue and the upregulation of cannabinoid receptors
- This is in attempt to reestablish normal levels and activate pathways to help protect cells from death
- Inflammation & stress

Pacher, Pál, and George Kunos. "Modulating the endocannabinoid system in human health and disease—successes and failures." *The FEBS journal* 280.9 (2013): 1918-1943.

7

Questions!

- **1. Which of the following has been shown to occur in PTSD?**
 - A. release in THC
 - B. release in CBD
 - C. Upregulation of cannabinoid receptors
 - D. Inactivation of cyclooxygenase

8

Inflammation: Anandamide is released by activated immune cells in response to injury to induce chemotaxis

- Decrease in INF-a and INF-b
- Decrease serum levels of TNF
- Suppress levels of cyclooxygenase
- Increase in production of anti-inflammatory mediators

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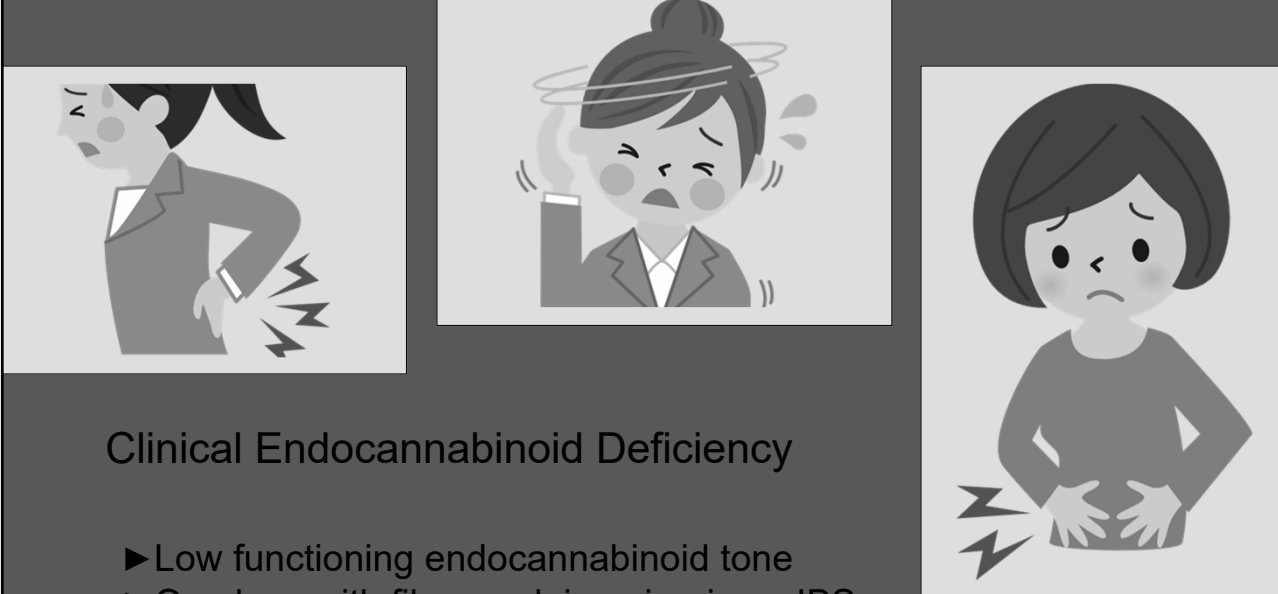
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Stress: ECBs have an essential role in maintaining our emotional homeostasis

- The ECS is a signaling system in the brain that is active even in the early stages of brain development by controlling neurotransmitter release
- ECB signalling activates and terminates the HPA axis in acute and repeated stress
- ECB signalling is also recruited by stress and glucocorticoid hormones to modulate cognitive and emotional processes

Hill, Matthew N., et al. "Recruitment of prefrontal cortical endocannabinoid signaling by glucocorticoids contributes to termination of the stress response." *Journal of Neuroscience* 31.29 (2011): 10506-10515.

10



Clinical Endocannabinoid Deficiency


- ▶ Low functioning endocannabinoid tone
- ▶ Overlaps with fibromyalgia, migraines, IBS and even PTSD

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BQD>?B?LT B?VKALJ B?KALBQDQ>QT BQD?BQ-QQBLKQKQKPI BRL"KALQBLZ/BQDXX " \$MOZa Z"NaZ"XXX P 0 , " P" \X\Y\ \t

11

ULCERATIVE COLITIS AND CROHN'S DISEASE

12

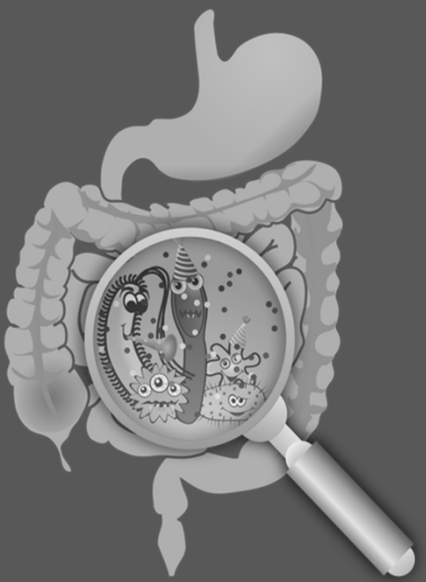


Captain Marvel

- ▶ CC: *“worst GI virus ever that just never went away, I would look into the bowl and thought my insides were coming out”*
 - ▶ *experiencing bloody and mucus filled diarrhea*
- ▶ HPI: 65 yo F diagnosed with Crohn's Disease at 40 years of age
- ▶ Prior treatments: oral corticosteroids
- ▶ Flare-ups and hospitalization occurred every 5-7 years for 20 years
- ▶ Diagnostics: colonoscopy
- ▶ CM was consulted as a medical marijuana patient

yamaorce.deviantart.com

13



ECS in the Gut

- *“my gut always hurts!”*
- The role of anandamide:
 - *downregulates IL-2 transcription and secretion*
 - *reduces TNF- α and IFN- γ production*
 - *induces lymphocyte apoptosis*
 - *inhibits neutrophil recruitment at the site of inflammation*
- CB1 receptors located on colonic epithelium, smooth muscle, and the myenteric plexus
- CB1 receptor-related mechanisms modify the colonic transit time

14

Treatment



- Initiated a full plant extract oil formulated with the Remedy strain, a cross between Cannatonic and Afghan Skunk, called the Sunrise oral syringe by CuraleafCT to be taken QAM, THC indica blend edible QHS, and patient would vape THC in the evenings
- CM saw improvement in symptoms in 4 weeks and in 6 months and colonoscopy results no evidence of active disease

15

question

- 2. What is the role of anandamide in the human GI tract?
- A. increases TNF- α production
 - B. enhances neutrophil recruitment
 - C. downregulates IL-2 transcription and secretion
 - D. increases INF- γ production

16

Drug Selection



- " Detailed patient intake
 - " *i.e., lifestyle, current medication regimen, past medical history*
- " Assess cannabis hesitance and tolerance
- " Understand patient goals
- " Tailor drug delivery system needs to individual patient comfort
- " Cost
- " Drug Interactions
 - " *CYP3A enzymes*
 - " *CYP2C9*
 - " *CYP2C19*
 - " *CYP2D6*
- " Clinical relevance

17

Formulation: Sublingual

HH Red C137 T7 Syringe 12663

Concentrate

Testing Date:	
9/8/2021	
Packaging Date:	Expiration Date:
9/8/2021	9/8/2022
Equivalency:	Batch #:
0.57 g	210818C-BL
NDC #:	Quantity:
12663	1.0 mL

Contains Sesame Seed Oil / Intended for ingestion only
 137.00mg CBD / 6.53mg THC per unit
 14.70% CBD / 0.70% THC per unit
 Cannabinoids (mg/unit): d9THC-A: ~0.10mg,
 THC: 6.53mg, CBD-A: ~0.10mg, CBD: 137.00mg,
 CBG-A: ~0.10mg, CBG: ~0.10mg, CBN:
 ~0.10mg, CBC: ~0.10mg.

Microbiological, mycotoxins, heavy metals,
 chemical residue: **ALL PASS**

34 Hopmeadow Street, Westogue, CT 06089 |

18

Formulation: Inhaled

Directions: Remove rubber stopper from bottom of cartridge, screw on battery. Do not over tighten. Store upright in a cool, dark place.

88.25% // 431.25 MG THC TOTAL PER UNIT //

CANNABINOIDS: THC A: ~4%, THC: 88.25%, CBD A: ~1%, CBD: 0.26%, CBG A: ~1%, CBG: 0.40%, CBN: 0.55%, CBC: 0.42% //

TERPENE: A-PINENE: 0.61%, CAMPHENE: 0.04%, B-PINENE: 0.40%, B-MYRCENE: 2.70%, LIMONENE: 0.51%, B-CARYOPHYLLENE: 0.65%, A-HUMULENE: 0.10%, TRANS-NEPHTHOL: 0.10%, GUAIOL: 0.11%, A-BISABOLOL: 0.20% //

TESTING DATE: 8/12/2021 // PACKAGING DATE: 8/12/2021 //

EXPIRATION DATE: 8/12/2022 // EQUIVALENCY: 1.74 G //

BATCH#: 210803L-CT // NDC#: 12605 // QUANTITY: 0.50 G //

INGREDIENTS: CANNABIS OIL AND CANNABIS LIVE RESIN //

MANUFACTURED BY CURALEAF // 34 HOPMADDO STREET, WEATGATE, CT 06099

curaleaf

Microbiological, Mycotoxins, Heavy Metals and Chemical Residue: ALL PASS

Leave the planet better than how you found it. Please recycle.

Sapphire T86% LR 12605
88.25% THC

High Terpene Extract Oil Cartridge

88%
0.50g

Sapphire T86% LR 12605

19

Formulation: Tablets/Capsules/Edibles

ACTIVE INGREDIENTS Per Pill THC: 10.00mg THCA: 0.19mg CBD: <0.01mg CBDA: <0.01mg CBG: 0.05mg CBGA: <0.01mg CBN: 0.19mg CBC: <0.01mg THCV: 0.05mg CBDV: <0.01mg	 THERAPLANT Indol T10 12973 INDICA 10 Capsules EQUIVALENCY: 0.42g - 0.01oz	Package ID: 12973 Batch: IPJL21-005 Package Date: 11/05/2021 Expiration Date: 11/04/2022 Tested On: 11/04/2021 Cannabinoids: 104.81mg 10.48mg Per Pill ADDITIVES Coconut Oil LAB TESTED FOR Microbiology Pass Mycotoxins Pass Heavy Metals Pass Pesticides Pass WARNINGS May be habit forming. Do not use when operating vehicle/vessel/machine. Do not use if pregnant or breastfeeding. Contains coconut. Store upright in a cool, dry place. THERAPLANT, LLC 856 ECHO LAKE RD. WATERTOWN, CT 06795
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20

Formulation: Topicals

Type Indica
Total THC 110mg
Total CBD 110mg
NDC# 12597
LOT# L0045
Gram Equivalent 0.44g
Date Tested 09/15/2021
Expiration Date 09/15/2022
Terpenes: β -pinene - 0.03, p-cymene - 0.02, (-)-isopulegol - 0.01, trans-nerolidol - 0.01, guaiol - 0.01, α -bisabolol - 0.01
TOTAL TERPENES: 0.09%
THC: 0.11% **CBD: 0.11%**
THCA: 0.00% **CBDA: 0.00%**

mend
1:1 I Cooling Body Balm 12597
100g / 3.5oz
 Manufactured by Connecticut
 Pharmaceutical Solutions, Rocky Hill, CT
 860.740.4340 • ctpharma.com



Directions: Apply topically on the affected area.
 MICROBIOLOGICAL, MYCOTOXINS, HEAVY METALS, CHEMICAL RESIDUE: ALL PASS
Ingredients: Water, Ethanol, Menthol, Glycerine, Butylene Glycol, Polysorbate 20, Peppermint Oil, Spearmint Leaf Oil, Rosemary Leaf Oil, Eucalyptus Leaf Oil, Carbomer, Sodium Polyacrylate, Dimethicone, Cyclopentasiloxane, Trideceth-6, Triethanolamine, PEG-PPG 18-18 Dimethicone, Phenoxyethanol, Caprylyl Glycol, Ethylhexylglycerin, Hexylene Glycol, Marijuana extract.

21

RECREATIONAL VS. MEDICAL MARIJUANA PRODUCTS

22



Testing and Labeling

- mycotoxins, mold, heavy metal residue, pesticides
- cannabinoid content
- terpene content
- mg/percentages

Stigma Laws

23

questions

■ 3. Which of the following is not a factor when determining appropriate medicinal marijuana products for a patient?

- A. Patient's cannabis experience
- B. Gender
- C. Medications
- D. Patient goals

4. What is an example of how medicinal marijuana and recreational marijuana differ?

- A. They come from two different plants
- B. Testing & Labeling
- C. Medicinal Marijuana only has CBD
- D. Recreational Marijuana only has THC

24

RX Cannabinoids



- Current
 - ... *plant derived Cannabidiol - **Epidiolex***
 - ... *synthetic - **Sativex** (nabiximols) **Marinol** (dronabinol)*
- Investigational
 - ... ***Cara Therapeutics' Cannabinoid Compound CR701***
 - oral synthetic cannabinoid receptor agonist
 - decrease neuropathic pain and hyperalgesia
 - preclinical developmental stage
 - ... ***Zynerba Pharmaceutical's ZYN002 Product***
 - permeation enhanced synthetic CBD gel
 - 12 month trial found clinically relevant reduction in focal seizures

Heussler, Helen, et al. "A phase 1/2, open-label assessment of the safety, tolerability, and efficacy of transdermal cannabidiol (ZYN002) for the treatment of pediatric fragile X syndrome." *Journal of neurodevelopmental disorders* 11.1 (2019): 1-9.

Urits, Ivan, et al. "An update of current cannabis-based pharmaceuticals in pain medicine." *Pain and therapy* 8.1 (2019): 41-51.

Pacher, Pál, and George Kunos. "Modulating the endocannabinoid system in human health and disease—successes and failures." *The FEBS journal* 280.9 (2013): 1918-1943.

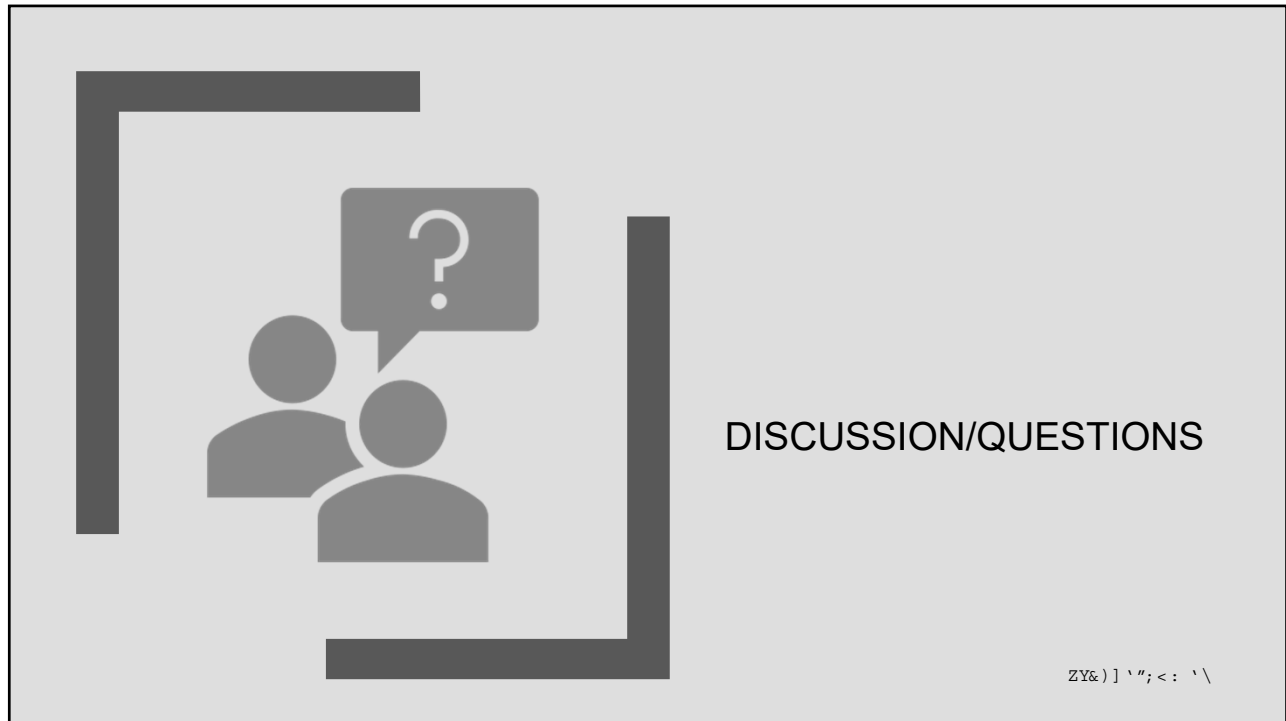
25

question

5. What is the route of administration for Zynerba Pharmaceutical's ZYN002 Product?

- A. Inhalant
- B. Topical
- C. Oral
- D. Rectal

26



27



28