


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


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## 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



**IDENTIFY**  
Identify the components of the ECS and the various initiatives

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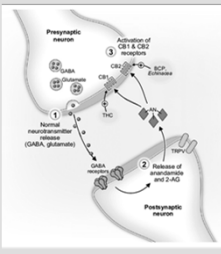
## About Me



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

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## 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

VanDuisen, Harrison & Bauer, Ghent & Masch, K. (2019). Clinicians' Guide to Cannabis-Based Therapies. *Mayo Clinic Proceedings*, 94, 10, 1016-1020. doi:10.1016/j.mayocp.2019.07.002

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## The Endocannabinoid System: upregulated in disease



**CB1**  
CB1 Receptor's target

- Motor activity
- Learning
- Neuroprotection
- Neuroinflammation
- Short-term memory
- Pain perception
- Immune cells

**CB2**  
CB2 Receptor's main locality: from CB2 and endocannabinoid system of the body

- Eye
- Adipose
- Immune system
- Reproductive system
- Endocrine system
- Stomach
- CB2 Receptor's system
- Heart

Image from: "What is the Endocannabinoid System?" by Andrew Harrison, 2017. Retrieved from <https://www.hempandcannabis.com/what-is-the-endocannabinoid-system/>

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## Cannabinoids: A Family of Molecules

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**Endogenous Ligands:** endocannabinoids

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**Synthetic cannabinoids:** cannabinoid-mimetic compounds

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

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## 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, P., and George Kunos. "Modulating the endocannabinoid system in human health and disease—successes and failures." *The FEBS Journal* 280.9 (2013): 1918-1945.

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## 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

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## 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

DOI: 10.1002/ajim.13888

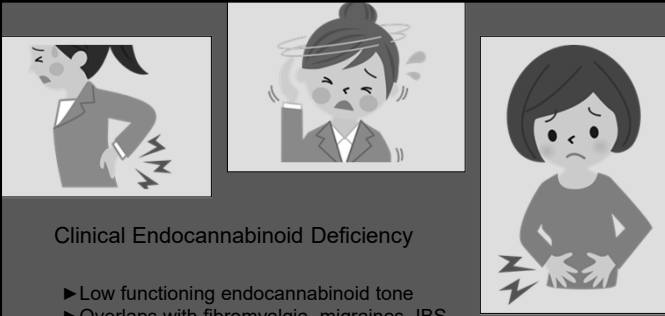
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## Stress: ECBs have an essential role in maintaining our emotional homeostasis

- 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

Hil, 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): 10006-10015.

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## Clinical Endocannabinoid Deficiency

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

DOI: 10.1002/ajim.13888

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## ULCERATIVE COLITIS AND CROHN'S DISEASE

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### Formulation: Inhaled

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### Formulation: Tablets/Capsules/Edibles

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### Formulation: Topicals

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## RECREATIONAL VS. MEDICAL MARIJUANA PRODUCTS

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### Testing and Labeling

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

### Stigma

### Laws

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### 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

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## 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

Houdelet, Helien, 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.

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

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

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## question

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

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

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DISCUSSION/QUESTIONS

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THANK  
YOU!

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