HEALCON 2020

The Future of Nutrition: the Interaction among the Microbiome & the Endocannabinoid System

Laura Lagano, MS, RDN, CDN
Holistic Cannabis Practitioner
Laura Lagano Wellness
Co-Founder & Education Director,
Holistic Cannabis Academy

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Disclosures

Laura Lagano, MS, RDN, CDN, IFM (Certification-Ready)

Owner
- Laura Lagano Wellness

Co-Founder & Education Director
- Holistic Cannabis Academy

Author
- The CBD Oil Miracle, St. Martin's Press, 2019

Contributing Writer
- Kitchen Toke Magazine
- The Fresh Toast
- Holistic Primary Care

Medical Advisory Boards
- Patients Out of Time
- Eleven Eleven Wellness

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Learning Outcomes

Participants will be able to:

- Explain the endocannabinoid system (ECS)and its role in cell biology
- Define three cannabinoids and their roles
- Categorize various cannabis delivery systems
- Recognize the complex interaction among the microbiome and the endocannabinoid system

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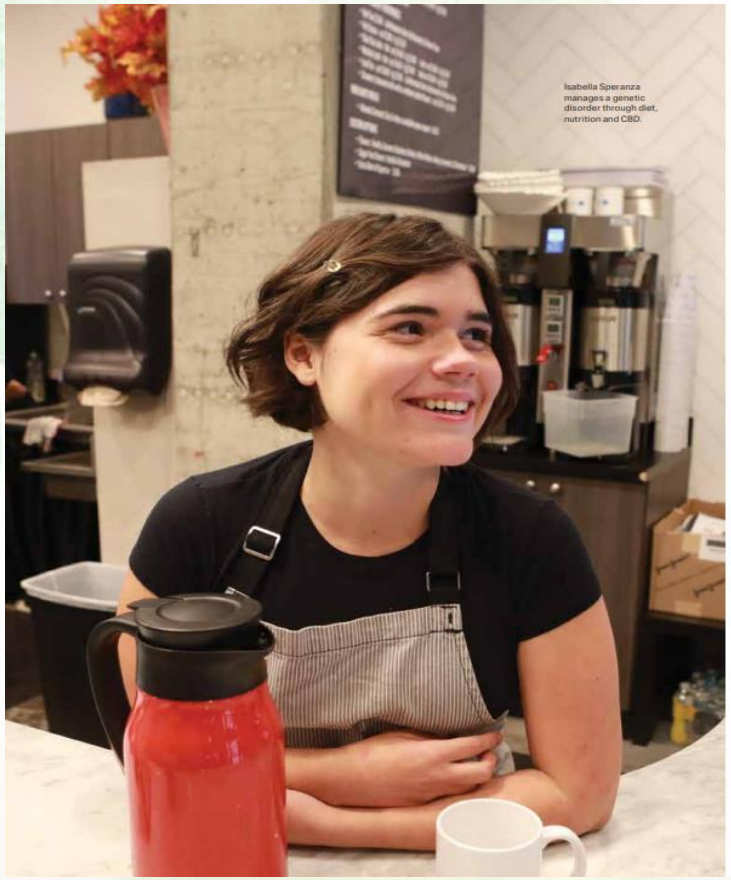
My Journey to Cannabis



[ME & MY BUD]

MOTHER'S BIG HELPERS

HOW DIETARY CHANGES, FISH OIL + CANNABIS DEFIED THE DOCTORS

By Laura Lagano
Photography by Bill Weinpahl
Illustration by Daniel Warren Johnson

If you had told me when I was in college that I'd be teaching patients and practitioners about using cannabis, I would have replied, "Are you high?" I also never would have imagined that I'd give my child cannabis to help her manage anxiety, improve focus and quell gut issues.

But here I was, a registered dietitian nutritionist, who was delivered a child with special needs. My daughter Isabella Speranza, whose name means beautiful hope, has a chromosomal duplication, one of the most common genetic disorders associated with autism.

We can sometimes express or suppress genetics by making certain lifestyle choices. Many of these choices have to do with food and nutrition, which I've explored on this journey known as motherhood. The journey has been scary, unpredictable, and exhausting at times. But most of all it has been enlightening.

As a baby, Isabella was not meeting developmental milestones, and was given the vague diagnosis of low tone, which is actually code for: We don't know what's happening. At 9 months old, she had a 10-minute grand mal seizure. I refused medication for her, standing firm until two days after her second birthday. That's when she had a seizure that lasted 50 minutes. By age 4, Isabella was on a cocktail of medications, which featured an anti-epileptic and other drugs with side effects. She was completely unhinged, running around like a wild child, a child whose behavior was so extreme that we could not leave the house at times.

Laura Lagano is an integrative cannabis nutritionist, educator, consultant and founder of the Holistic Cannabis Academy in New York. Discover more at **lauralagano.com.**

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Clarification Question

Are marijuana and hemp the same plant?

True

False

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Maijuana Plant

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Hemp Plant

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Cannabis Plant

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A Case of Mistaken Identity

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Cannabis Plant

Marijuana contains over 0.3% THC

Hemp contains less than 0.3% THC

Cannabis & Hemp & CBD — Oh My!

- Marijuana & hemp are both cannabis!
- Designation based of percentage of THC
- THC & CBD are among 100+ cannabinoids
- Terpenes—volatile molecules present in plants
- Hemp-derived *CBD—caveat emptor*
- THCA & CBDA—acids, prior to heating
- Decarboxylation

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Cannabis Characteristics

- Lipophilic = binds to fat
- Hydrophobic = repels waters
- Body fat impacts absorption
- Start low, go slow
- Cannabinoid release from adipose
    - Vigorous exercise
    - Rapid weight loss

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Cannabis Delivery Systems

- Smoking: raw plant flower, immediate impact
- Vaporizing: raw plant flower or extracts (more controlled dosage)
- Edibles: extracts in foods, slow absorption
- Extracts: oil bases, highly concentrated, sublingual, mid-range absorption
- Tinctures: alcohol-based
- Sprays: oil bases, epithelial tissue
- Topicals: lotions, balms, salves, oils
- Suppositories, epithelial tissue
- Fibers
- Powders
- Sublingual strips

Lagano, L. (2019). *The CBD Oil Miracle*. New York: St. Martin's Press.

Format Follows Function

- Format depends on individual patient
- 90/90 rule for inhaled meds: 90% peak plasma drops in 90 minutes
- Oils & Tinctures: 15-20 minute onset lasting 2-4 hours
- Patch: up to 8 hours of relief

Lagano, L. (2019). *The CBD Oil Miracle*. New York: St. Martin's Press.

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Cannabis as Medicine

Review > Clin Pharmacol Ther, 97 (6), 575-86 Jun 2015

Cannabis in Cancer Care

D I Abrams [1], M Guzman [2]
Affiliations + expand
PMID: 25777363 DOI: 10.1002/cpt.108

Abstract

Cannabis has been used in medicine for thousands of years prior to
substance status. Cannabinoids, the active components of Cannabis
endogenous cannabinoids (endocannabinoids), activating specific c
CB1 found predominantly in the central nervous system and CB2 fou
involved with immune function. Delta-9-tetrahydrocannabinol, the
plant, has been available as a prescription medication approved for
chemotherapy-induced nausea and vomiting and anorexia associate
syndrome. Cannabinoids may be of benefit in the treatment of canc
synergistic with opioid analgesics. Cannabinoids have been shown t
HIV-related peripheral neuropathy, suggesting that they may be wo
other neuropathic symptoms. Cannabinoids have a favorable drug safety profile, but their medical use
is predominantly limited by their psychoactive effects and their limited bioavailability.

"Cannabis has been used in medicine for thousands of years prior to achieving its current illicit substance status. Cannabinoids, the active components of Cannabis sativa, mimic the effects of the endogenous cannabinoids (endocannabinoids), activating specific cannabinoid receptors, particularly CB1 found predominantly in the central nervous system and CB2 found predominantly in cells involved with immune function."

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A Brief History as a Healing Tool

- Cannabis as medicine for thousands of years
- Only illegal in US for about 80 years
- US Pharmacopeia listing
- Ancestors used mother nature's medicines, also known as plants, to heal

From 1850 to 1936, cannabis was used as the primary medicine for more than 100 separate illnesses and/or diseases in the U.S.

Bearman, D. (2015). *Drugs Are Not the Devil's Tools.* Santa Barbara: Blue Point Books.

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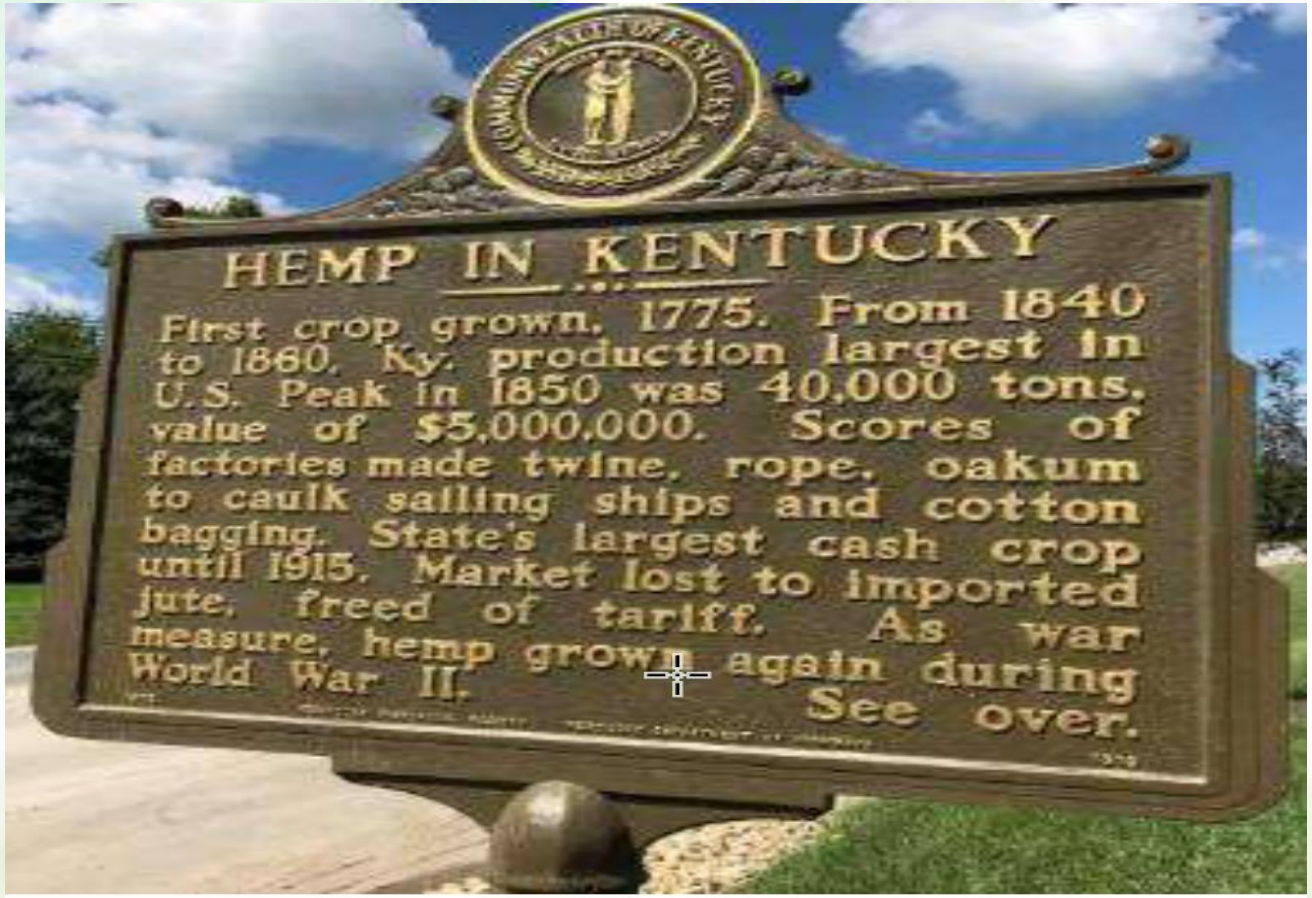
Cannabis (Hemp) as a US Crop



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Sanja Gupta Does a 180!

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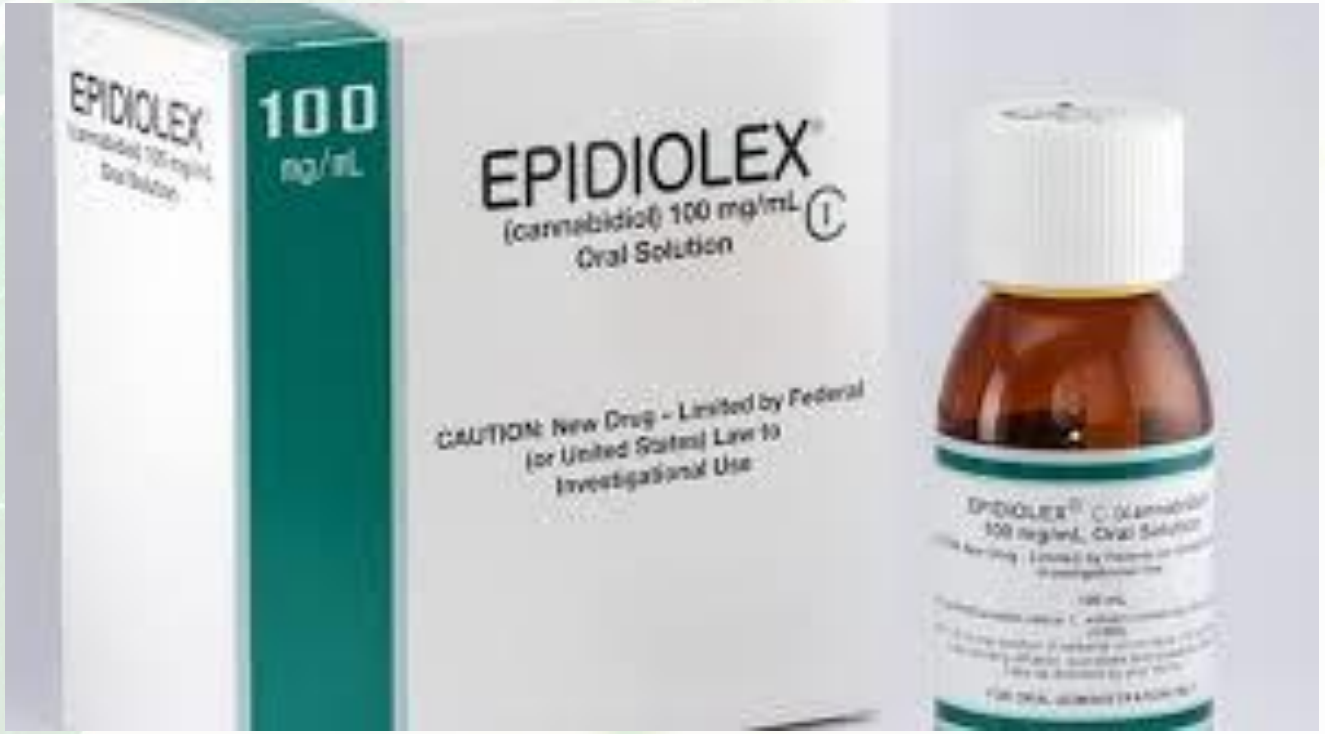
Cannabis as a Prescription



https://www.epilepsybehavior.com/article/S1525-5050(18)30191-4/pdf

Cannabis Is Not Just for Seizures!

CBD is a potent anti-inflammatory.

Inflammation underlies the vast majority of **CHRONIC DISEASE.**

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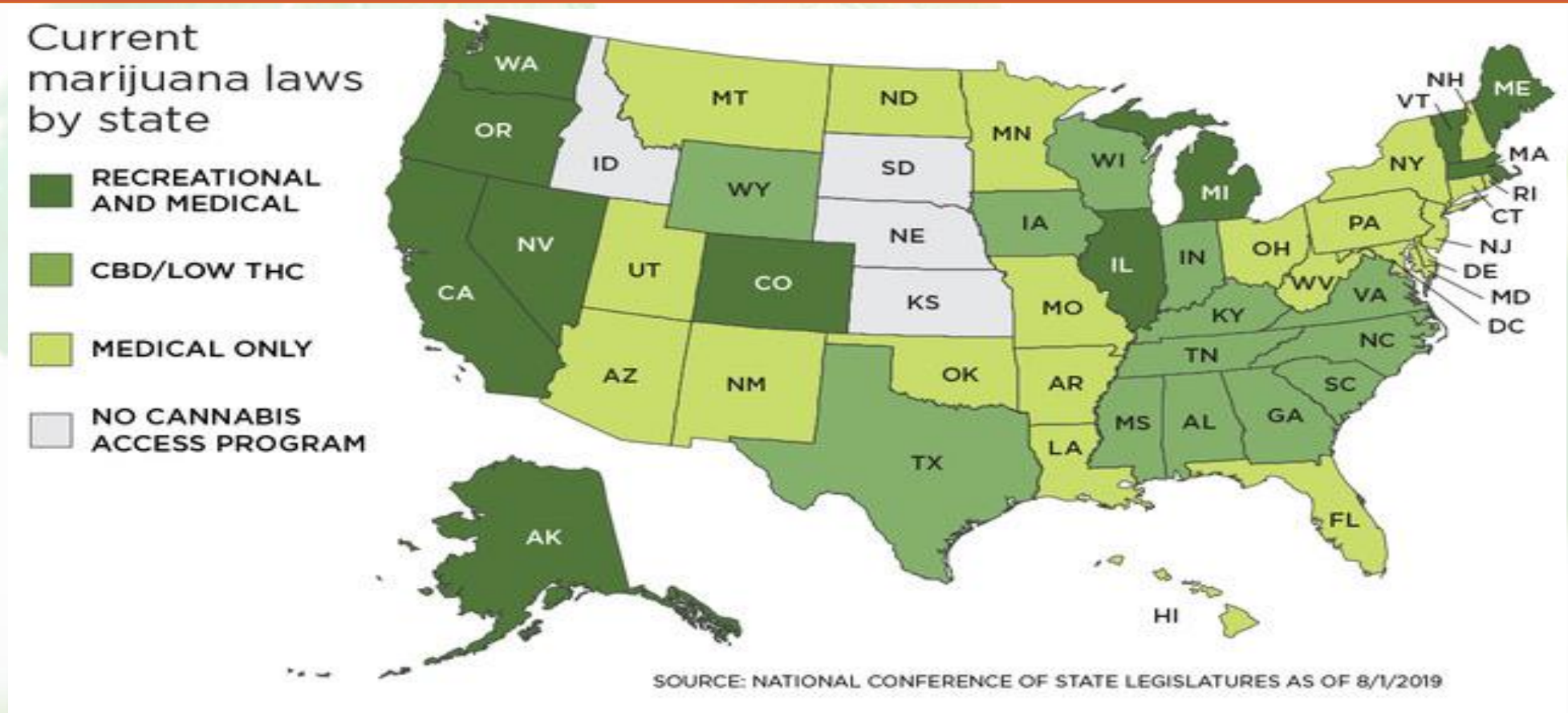
State Cannabis & CBD Programs



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DEA Schedule 1 Listing

- Controlled Substances Act
- Listed as a schedule 1 drug with heroin, cocaine, MDMA, LSD
- Contradicts states with medical marijuana regulations

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US Patent #6630507

http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PALL&p=1&u=%2Fnetahtml%2FPTO%2Fsrchnum.htm&r=1&f=G&l=50&s1=6630507.PN.&OS=PN/6630507&RS=PN/6630507

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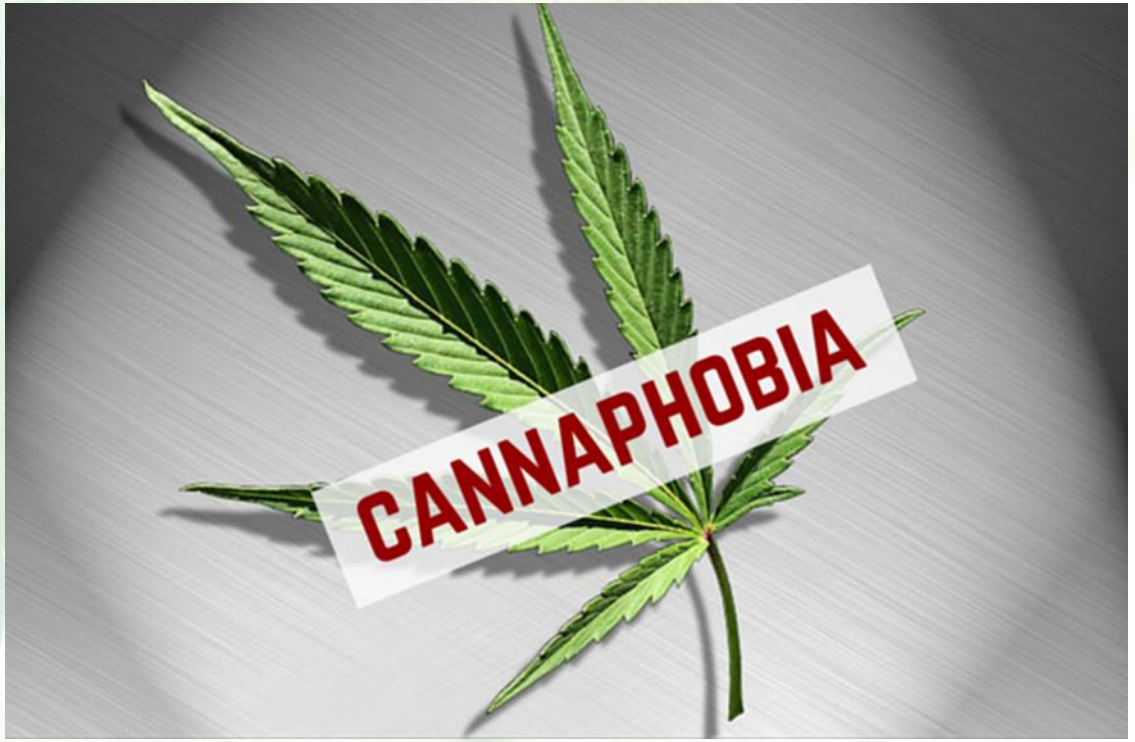
Confusion about the Model

Fear of Cannabis Persists!



Lagano, L. (2019). *The CBD Oil Miracle.* New York: St. Martin's Press.

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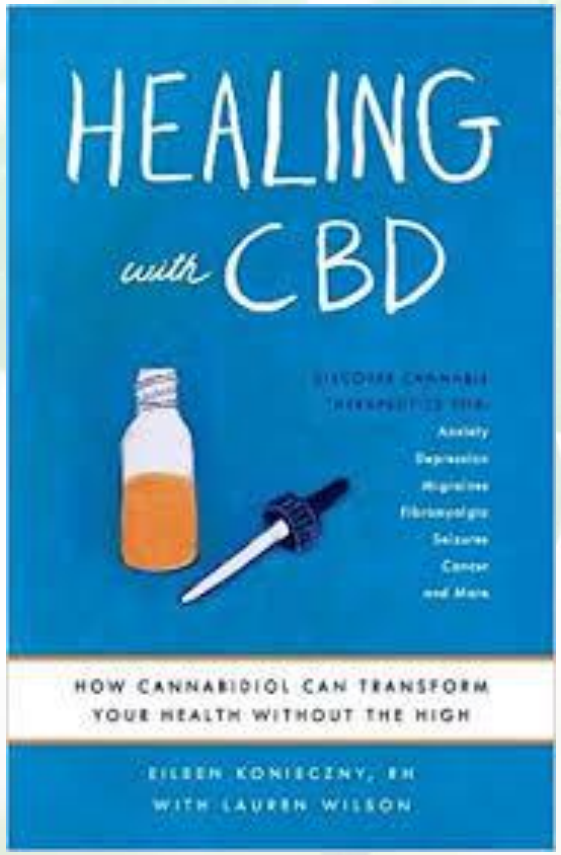
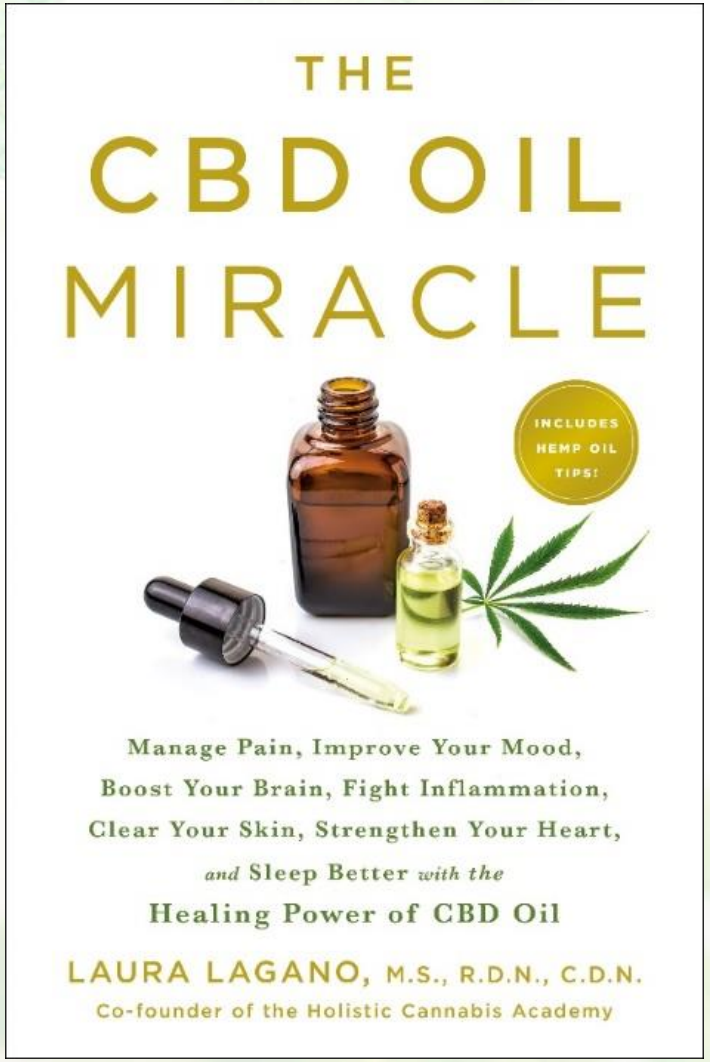
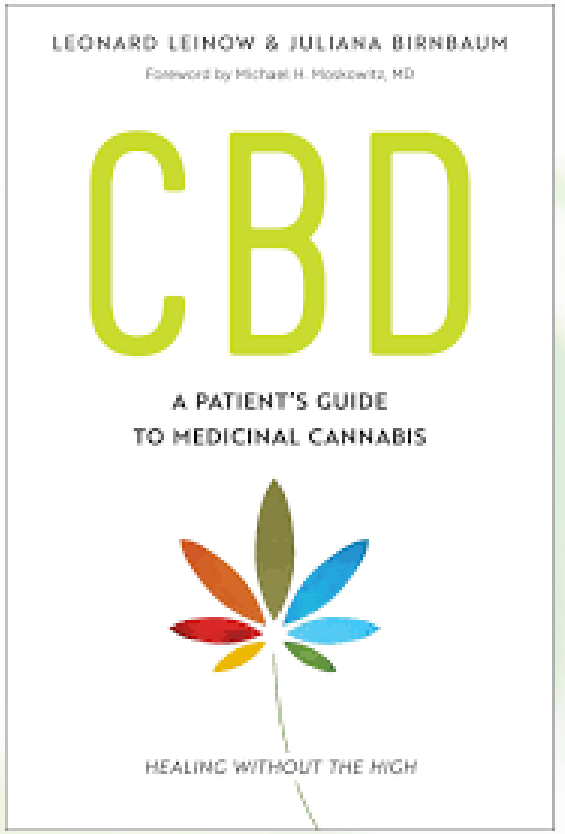
The CBD Explosion!







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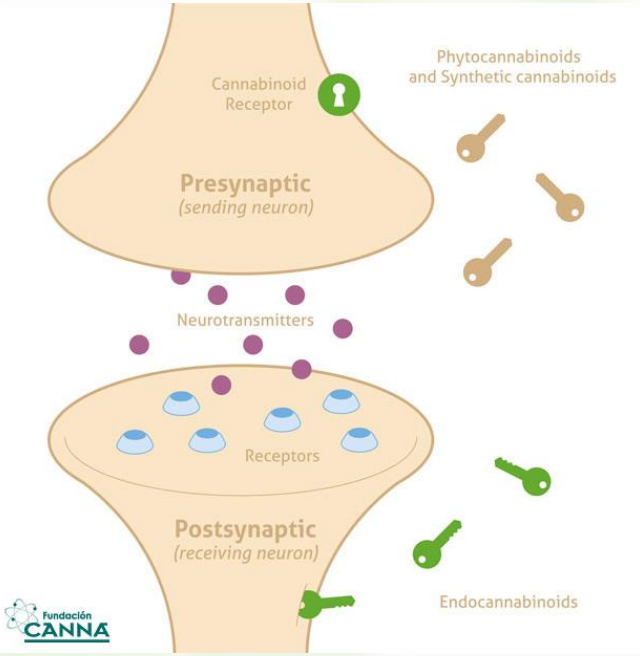
Why Does Cannabis Work? ECS!

- Cannabinoid receptors (locks)
  - CB1 (*CNS*, adipose, heart, lungs, *GI tract*, muscles, joints, skin)
  - CB2 (*immune*, bone, spleen)
- Cannabinoids (keys)
  - Endocannabinoids (Anandamide + 2-AG)
  - Phytocannabinoids (CBD, THC, etc.)
- Enzymes
  - Synthesizing enzymes
  - Degrading enzymes



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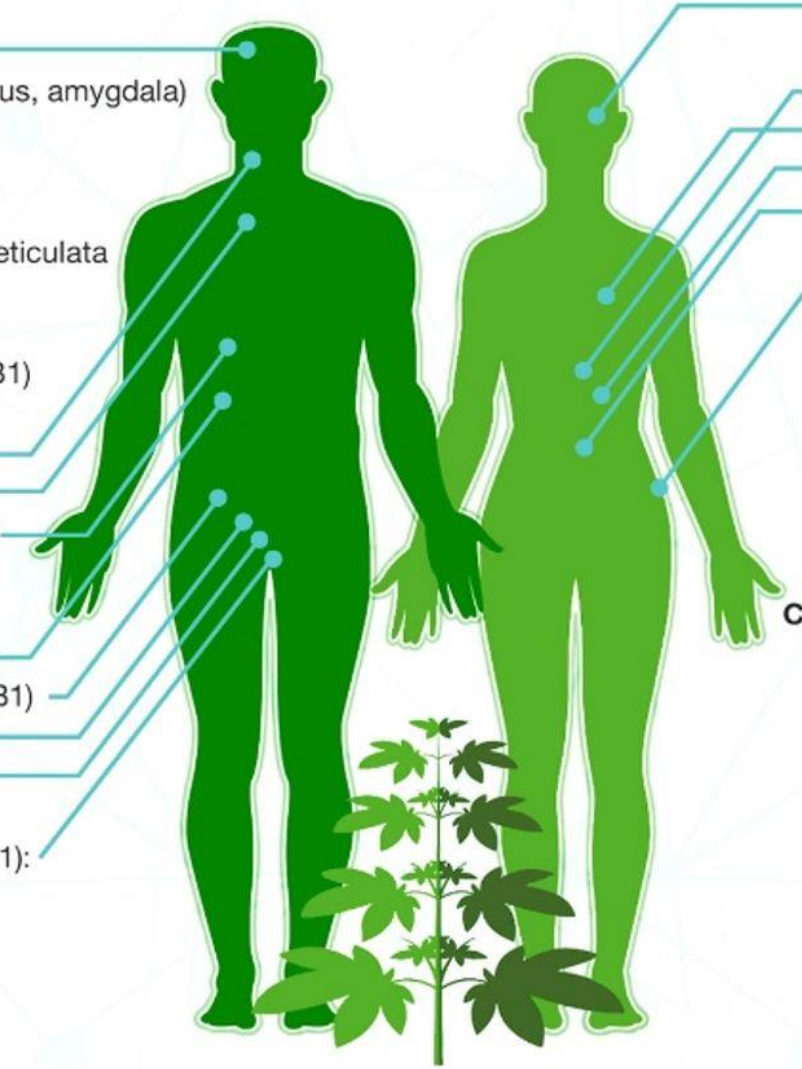
CB1 RECEPTORS ARE LOCATED IN CELLS OF THE:

Brain/CNS/Spinal cord (CB1)
Cortical regions (CB1):
(neocortex, pyriform cortex, hippocampus, amygdala)
Cerebellum (CB1)
Brainstem (CB1)
Basal ganglia (CB1):
globus pallidus, substantia nigra pars, reticulata
Olfactory bulb (CB1)
Thalamus (CB1)
Hypothalamus (endocrine-brain link CB1)
Pituitary (CB1)
Thyroid (endocrine gland (CB1))
Upper Airways (of mammals CB1)
Liver (CB1): kupffer cells (macrophage immune cells), hepatocytes (liver cell), hepatic stellate cells (fat storage cell)
Adrenals (endocrine gland CB1)
Ovaries (gonads and endcrine gland CB1)
Uterus (myometrium CB1)
Prostate (CB1): epithelial and smooth muscle cells
Testes (gonads and endocrine gland CB1): leydig cells ; sperm cells



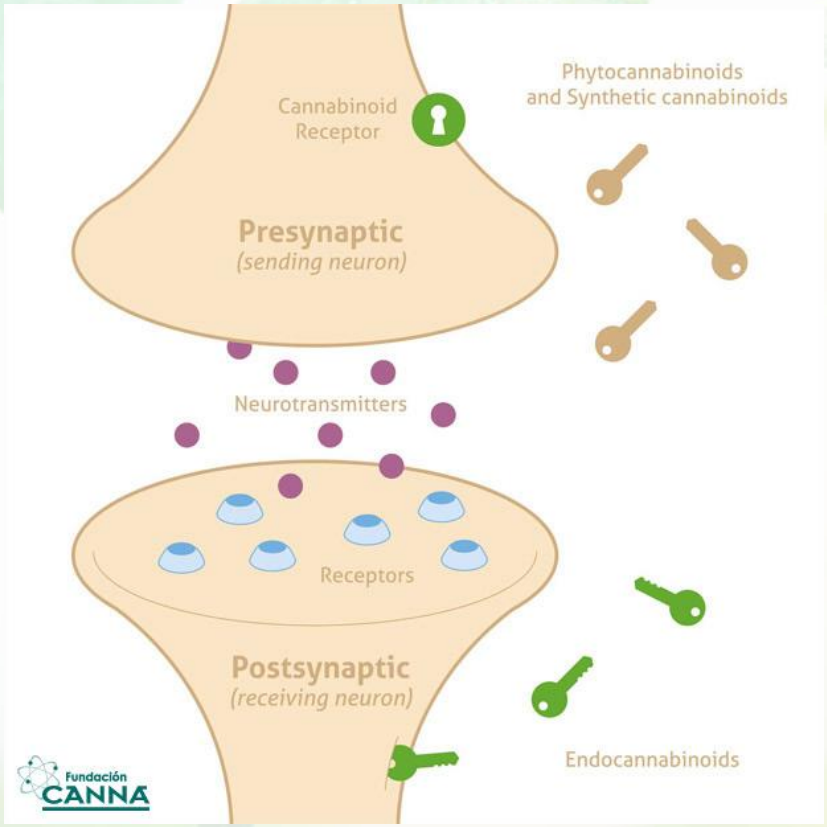
CB1 AND CB2 RECEPTORS ARE LOCATED IN CELLS OF THE:

Eye (CB1 and CB2)
retinal pigment epithelial/RPE cells
Stomach (CB1 and CB2):
Heart (CB1 and CB2)
Pancreas (CB1 and CB2)
Digestive tract (CB1 and CB2)
Bone (CB1 and CB2)

Non-CB1 and non-CB2 are located in cells of the:
Blood vessels: epithelial cells of arterial blood vessels (non-CB1 and non-CB2)

CB2 receptors are located in cells of the:
Lymphatic and Immune system
Spleen (CB2)
Thymus (CB2)
Tonsis (CB2)
Blood (CB2) lymphocytes
Non-Immune cell CB2 receptors are found in the Skin keratinocytes

Lock & Key Receptor System



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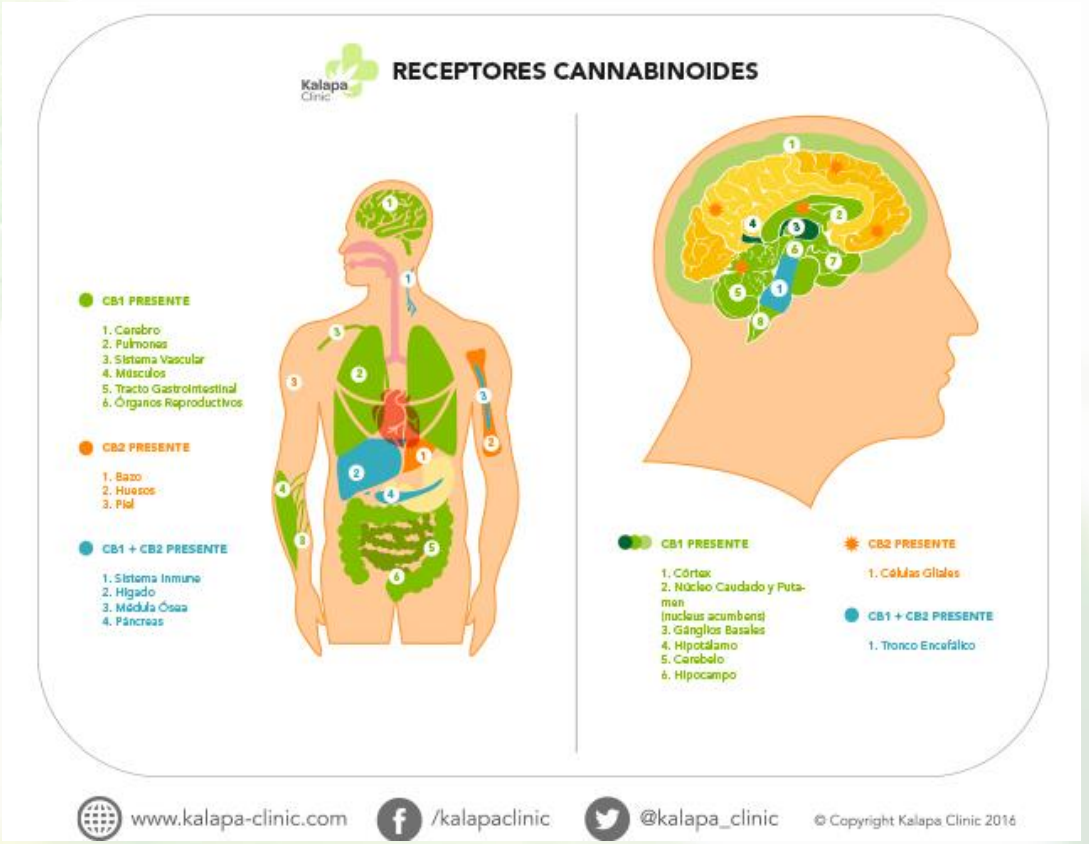
Endocannabinoid System Functions

- Brain development
- Coordination & movement
- Learning & memory
- Appetite
- Pain
- Nausea & vomiting
- Sleep
- Stress & anxiety
- Mood
- Immune function
- Neuroplasticity
- Eating behavior



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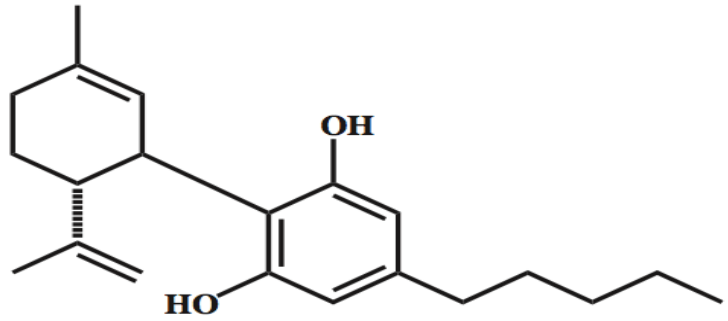
Endocannabinoid: Anandamide

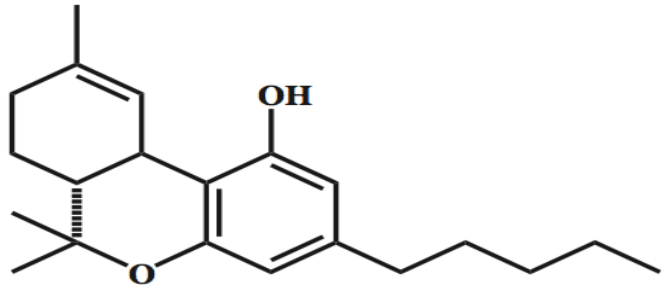
- Derived from ananda = Sanskrit for bliss
- Chronic anti-depressant/anti-psychotic meds elevate anandamide production
- Receptors eventually get desensitized to
- Deep breathing + meditation help maintain bliss levels

आनन्द

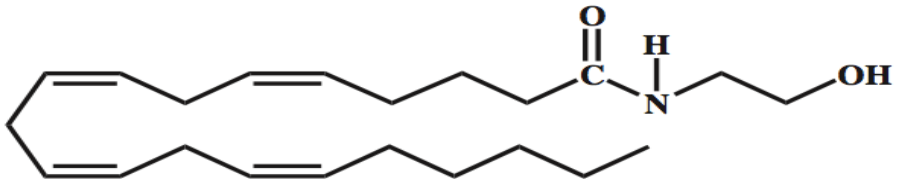
Cannabinoid Chemical Structures



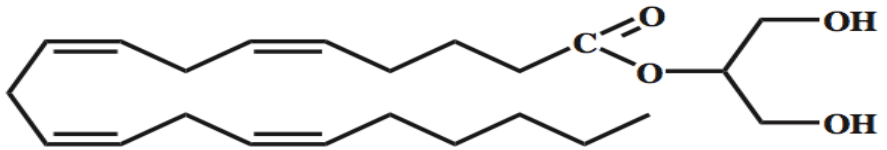
Cannabidiol (CBD)



Δ^9-tetrahydrocannabinol (Δ^9-THC)



Arachidonoyl ethanolamide (anandamide)



2-arachidonoyl glycerol (2-AG)

Cannabis Is a Plant!

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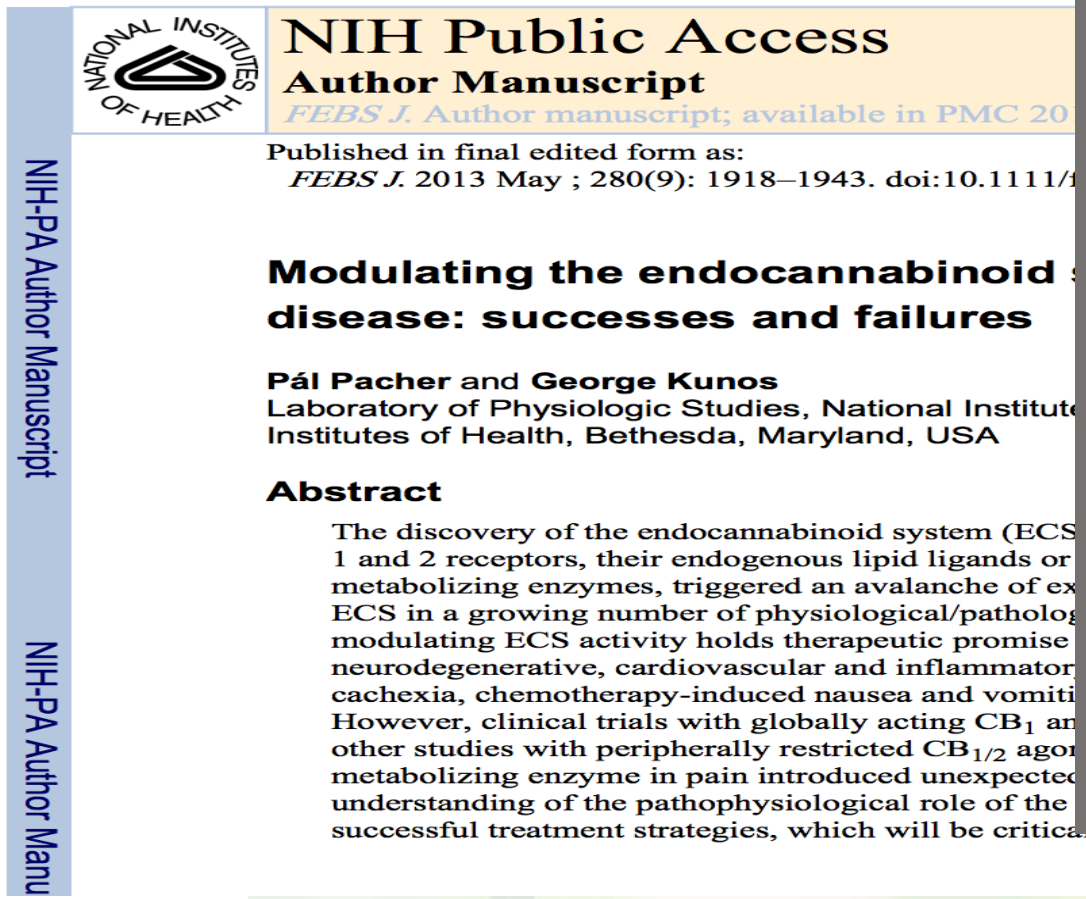
Why Modulate the ECS?



NIH Public Access
Author Manuscript
FEBS J. Author manuscript; available in PMC 20

Published in final edited form as:
FEBS J. 2013 May ; 280(9): 1918–1943. doi:10.1111/

Modulating the endocannabinoid
disease: successes and failures

Pál Pacher and **George Kunos**
Laboratory of Physiologic Studies, National Institute
Institutes of Health, Bethesda, Maryland, USA

Abstract

The discovery of the endocannabinoid system (ECS
1 and 2 receptors, their endogenous lipid ligands or
metabolizing enzymes, triggered an avalanche of ex
ECS in a growing number of physiological/patholog
modulating ECS activity holds therapeutic promise
neurodegenerative, cardiovascular and inflammator
cachexia, chemotherapy-induced nausea and vomiti
However, clinical trials with globally acting CB_1 an
other studies with peripherally restricted $CB_{1/2}$ agon
metabolizing enzyme in pain introduced unexpected
understanding of the pathophysiological role of the
successful treatment strategies, which will be critica

"Modulating ECS activity may have therapeutic potential in almost all diseases affecting humans, including obesity/metabolic syndrome, diabetes and diabetic complications, neurodegenerative, inflammatory, cardiovascular, liver, gastrointestinal, skin diseases, pain, psychiatric disorders, cachexia, cancer, chemotherapy-induced nausea and vomiting, among many others."

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Actions of Phytocannabinoids

Neurotherapeutics. 2015 Oct; 12(4): 692–698.
Published online 2015 Aug 14. doi: 10.1007/s13311-015-0374-6
PMCID: PMC4604172
PMID: 26271952

The Endocannabinoid System and its Modulation by Phytocannabinoids

Vincenzo Di Marzo and Fabiana Piscitelli

Associated Data

Supplementary Materials

Abstract

Go to:

The endocannabinoid system is currently defined as the ensemble of the two 7-transmembrane-domain and G protein-coupled receptors for Δ^9-tetrahydrocannabinol (but not for most other plant cannabinoids or phytocannabinoids)—cannabinoid receptor type-1 (CB_1R) and cannabinoid receptor type-2 (CB_2R); their two most studied endogenous ligands, the "endocannabinoids" *N*-arachidonoylethanolamine (anandamide) and 2-arachidonoylglycerol (2-AG); and the enzymes responsible for endocannabinoid metabolism. However, anandamide and 2-AG, and also the phytocannabinoids, have more molecular targets than just CB_1R and CB_2R. Furthermore, the endocannabinoids, like most other lipid mediators, have more than just one set of biosynthetic and degrading pathways and enzymes, which they often share with "endocannabinoid-like" mediators that may or may not interact with the same proteins as Δ^9-tetrahydrocannabinol and other phytocannabinoids. In some cases, these degrading pathways and enzymes lead to molecules that are not inactive and instead interact with other receptors. Finally, some of the metabolic enzymes may also participate in the chemical modification of molecules that have very little to do with endocannabinoid and cannabinoid targets. Here, we review the whole world of ligands, receptors, and enzymes, a true "endocannabinoidome", discovered after the cloning of CB_1R and CB_2R and the identification of anandamide and 2-AG, and its interactions with phytocannabinoids.

- Relax
- Eat
- Sleep
- Forget
- Protect

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Dr. Russo's Endocannabinoid Tone

Published online 2016 Jul 1. doi: 10.1089/can.2016.0009 PMID: 28861491

Clinical Endocannabinoid Deficiency Reconsidered: Current Research Supports the Theory in Migraine, Fibromyalgia, Irritable Bowel, and Other Treatment-Resistant Syndromes

"...[the] hypothesis is that all humans have an underlying endocannabinoid tone that is a reflection of levels of the endocannabinoids, anandamide (arachidonylethanolamide), and 2-arachidonoylglycerol, their production, metabolism, and the relative abundance and state of cannabinoid receptors. Its theory is that in certain conditions, whether congenital or acquired, endocannabinoid tone becomes deficient and productive of pathophysiological syndromes."

Clinical Endocannabinoid Deficiency

Neuro Endocrinol Lett, 29 (2), 192-200 Apr 2008

Clinical Endocannabinoid Deficiency (CECD): Can This Concept Explain Therapeutic Benefits of Cannabis in Migraine, Fibromyalgia, Irritable Bowel Syndrome and Other Treatment-Resistant Conditions?

Ethan B Russo [1]
Affiliations + expand
PMID: 18404144

Abstract

Objectives: This study examines the concept of clinical endocannabinoid deficiency (CECD), and t
prospect that it could underlie the pathophysiology of migraine, fibromyalgia, irritable bowel syndrome, and other functional conditions alleviated by clinical cannabis.

"Anandamide (AEA) potentiates 5-HT1A and inhibits 5-HT2A receptors supporting therapeutic efficacy in acute and preventive migraine treatment. Cannabinoids also demonstrate dopamine-blocking and anti-inflammatory effects."

Eating Perceptions about Cannabis

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Cannabinoid Eating Experience

Exploring the munchies: An online survey of users' experiences of cannabis effects on appetite and the development of a Cannabinoid Eating Experience Questionnaire

Carl A Roberts, Gerry Jager, Paul Christiansen, more...

Show all authors

First Published July 26, 2019 | Research Article | Find in PubMed | Check for updates

https://doi.org/10.1177/0269881119862526

Article information

Altmetric 12

Abstract

Background:

Cannabis intoxication is commonly reported to increase appetite and enhance appreciation of food (the 'munchies'). These effects are attributed to activation of the endocannabinoid system. However, the psychological changes that underlie these phenomena are under-researched. We report here the results of an extensive online survey of cannabis users with an exploratory Cannabinoid Eating Experience Questionnaire (CEEQ).

Method:

Frequent cannabis users completed a 46-item questionnaire about their eating behaviour under the influence of cannabis. An English-speaking sample (*n*=591) provided data for the initial exploratory validation of the scale. A second Dutch-language survey (*n*=163) was used for confirmatory factor analysis. Test-retest reliability was based on a third English-speaking sample (*n*=40) who completed the revised, 28-item CEEQ twice across 2 weeks.

"Our data confirm that cannabis principally influences the motivational factors that lead to the initiation of eating and the hedonic factors implicated in maintaining eating."

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Obesity & Cannabis Use

Obesity and Cannabis Use: Results From 2 Representative National Surveys FREE

Yann Le Strat ✉, Bernard Le Foll

American Journal of Epidemiology, Volume 174, Issue 8, 15 October 2011, Pages 929–933, https://doi.org/10.1093/aje/kwr200

Published: 24 August 2011 **Article history** ▾

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Abstract

The role of cannabis and endocannabinoids in appetite regulation has been extensively studied, but the association of cannabis use with weight in the general population is not known. The authors used data from 2 representative epidemiologic studies of US adults aged 18 years or older, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; 2001–2002) and the National Comorbidity Survey–Replication (NCS-R; 2001–2003), to estimate the prevalence of obesity as a function of cannabis use. The adjusted

"This cross-sectional analysis indicated that despite the evidence that cannabis use stimulates appetite in clinical trials and laboratory studies, cannabis users are actually less likely to be obese than nonusers in the general population."

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Eating Disorders & Hyperphagia

- ECS signaling in the gut may drive overeating of the SAD diet, leading to elevated levels of endocannabinoids promoting continued consumption of sugary, fatty processed foods
- PWS plus other genetic aberrations on chromosome 15
- ECS appears to be involved in ED via ECS signaling

The EC Olfactory Systems

The endocannabinoid system controls food intake via olfactory processes

Edgar Soria-Gómez, Luigi Bellocchio, [...] Giovanni Marsicano

Nature Neuroscience **17**, 407–415(2014) | Cite this article

867 Accesses | 115 Citations | 590 Altmetric | Metrics

"Hunger arouses sensory perception, eventually leading to an increase in food intake,...cannabinoid type-1 (CB_1) receptors promote food intake in fasted mice by increasing odor detection. CB_1 receptors were abundantly expressed on axon terminals of centrifugal cortical glutamatergic neurons that project to inhibitory granule cells of the main olfactory bulb (MOB)."

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The ECS, Microbiome & Obesity

Mol Syst Biol. 2010; 6: 392.
Published online 2010 Jul 27. doi: 10.1038/msb.2010.46
PMCID: PMC2925525
PMID: 20664638

The endocannabinoid system links gut microbiota to adipogenesis

Giulio G Muccioli,[a,1,2] Damien Naslain,[1,3] Fredrik Bäckhed,[4] Christopher S Reigstad,[4] Didier M Lambert,[1,5] Nathalie M Delzenne,[1,3] and Patrice D Cani[b,1,3]

Abstract

Go to:

Obesity is characterised by altered gut microbiota, low-grade inflammation and increased endocannabinoid (eCB) system tone; however, a clear connection between gut microbiota and eCB signalling has yet to be confirmed. Here, we report that gut microbiota modulate the intestinal eCB system tone, which in turn regulates gut permeability and plasma lipopolysaccharide (LPS) levels. The impact of the increased plasma LPS levels and eCB system tone found in obesity on adipose tissue metabolism (e.g. differentiation and lipogenesis) remains unknown. By interfering with the eCB system using CB_1 agonist and antagonist in lean and obese mouse models, we found that the eCB system controls gut permeability and adipogenesis. We also show that LPS acts as a master switch to control adipose tissue metabolism both *in vivo* and *ex vivo* by blocking cannabinoid-driven adipogenesis. These data indicate that gut microbiota determine adipose tissue physiology through LPS-eCB system regulatory loops and may have critical functions in adipose tissue plasticity during obesity.

LAURA LAGANO WELLNESS

H·E·A·L CON

“Ancient Human Microbiomes”

ELSEVIER

Journal of Human Evolution
Volume 79, February 2015, Pages 125-136

Ancient human microbiomes

Christina Warinner [a], Camilla Speller [b], Matthew J. Collins [b], Cecil M. Lewis Jr. [a]

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https://doi.org/10.1016/j.jhevol.2014.10.016

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Abstract

Very recently, we discovered a vast new microbial self: the human microbiome. Our native microbiota interface with our biology and culture to influence our health, behavior, and quality of life, and yet we know very little about their origin, evolution, or ecology. With the advent of industrialization, globalization, and modern sanitation, it is intuitive that we have changed our relationship with microbes, but we have little information about the ancestral state of our microbiome, and we therefore lack a foundation for characterizing this change. High-throughput sequencing has opened up new opportunities in the field of paleomicrobiology, allowing us to investigate the evolution of the complex microbial ecologies that inhabit our bodies. By focusing on recent coprolite and dental calculus research, we explore how emerging research on ancient human microbiomes is changing the way we think about ancient disease and how archaeological studies can contribute to a medical understanding of health and nutrition today.

- “There can be no doubt that modern behavior and dietary changes are altering the microbial ecology of humans. While some of these changes could be beneficial, others are disruptive and may be a driving force behind the rapidly increasing rates of chronic inflammatory diseases in developed countries. Common medical interventions, such as antibiotic therapy, have dramatically reduced infectious disease burdens worldwide. However, rather than being targeted strikes against harmful bacteria alone, such therapies can also act as weapons of mass microbial disruption.”

H·E·A·L CON

Start with the Gut

- The ancient plant *Cannabis sativa* has been used for digestive disorders and vomiting for millennia
- Long before the receptors were discovered, cannabinoids were recommended to influence the motility of the gastrointestinal tract

The Human Microbiome Organ

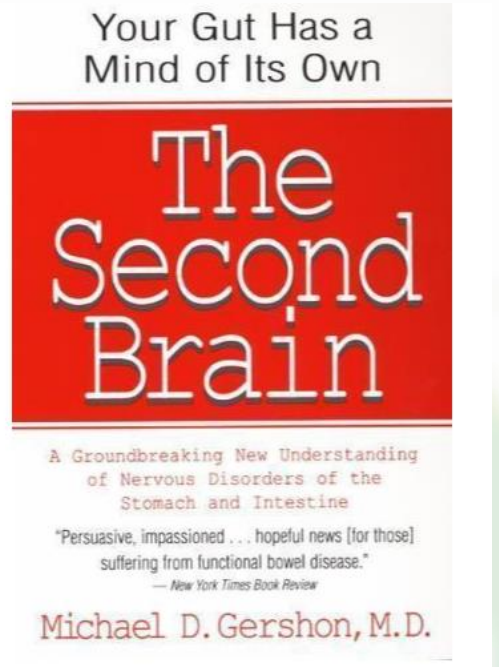
- Collection of microorganisms throughout the body
- 100 trillion microbes—bacteria, viruses, fungi, yeast & protozoa
- 1,000+ different species of bacteria
- Found in the nose, mouth, gut, genitals, lungs & skin
- More complex than the human genome of 23K genes
- Dynamic, continually changing in response to numerous factors

Microbiota Dynamic Diversity

- Genetics
- Antibiotic exposure
- Breastfeeding
- Birth delivery mode—vaginal or C-section
- Infection
- Food & nutrition
- Stress
- Additional environmental factors
- Age

The Human Microbiome & You

- 99% of microbiota are beneficial
- Significant impact on *gut, immune, brain health*—*the* Bermuda triangle of integrative & functional nutrition
- 85% of neurotransmitters are produced in the gut
- Digestion, metabolism, vitamin synthesis, protection from pathogens
- Immune system dysfunction allows the microbiome to malfunction
- Health conditions associated with microbiome imbalance—autism, IBD, Crohn's, food & environmental allergies & sensitivities, obesity



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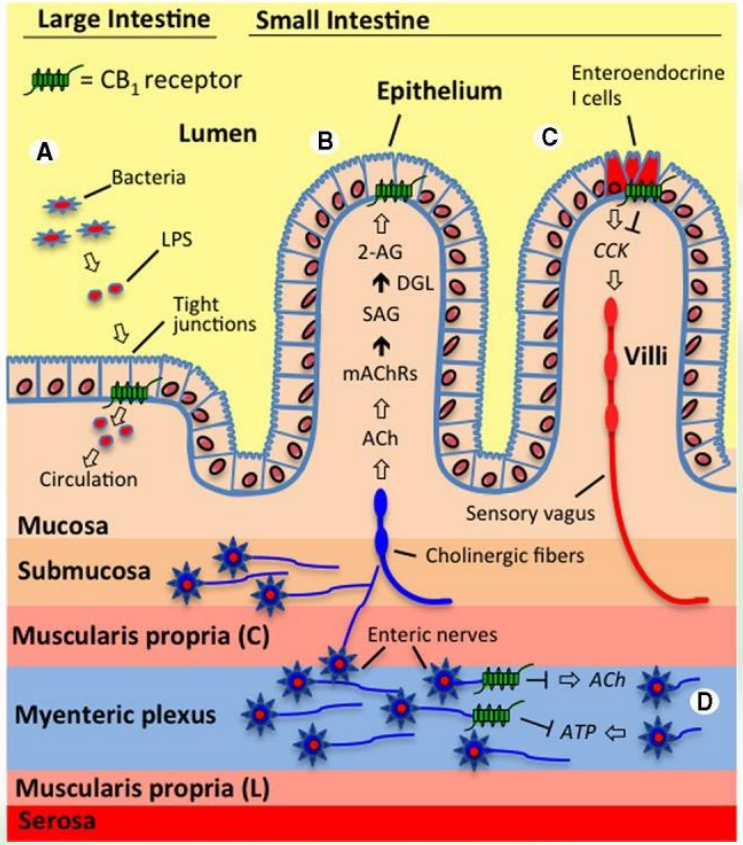
The Role of the Microbiome

- Modulates the central nervous system
- Regulates sleep
- Involved in immune health & function
- Directs digestion & metabolism
- Regulate appetite & weight
- Synthesizes some vitamins
- Metabolizes complex foods
- Modulates energy recovery
- Controls the gut barrier
- Synthesizes essential amino acids
- Produces short chain fatty acids

EC & GI Systems

- CB1 receptors present in the GI tract
- ECS regulates:
  - Intestinal inflammation
  - Gastrointestinal motility
  - Intestinal permeability
  - Visceral sensitivity



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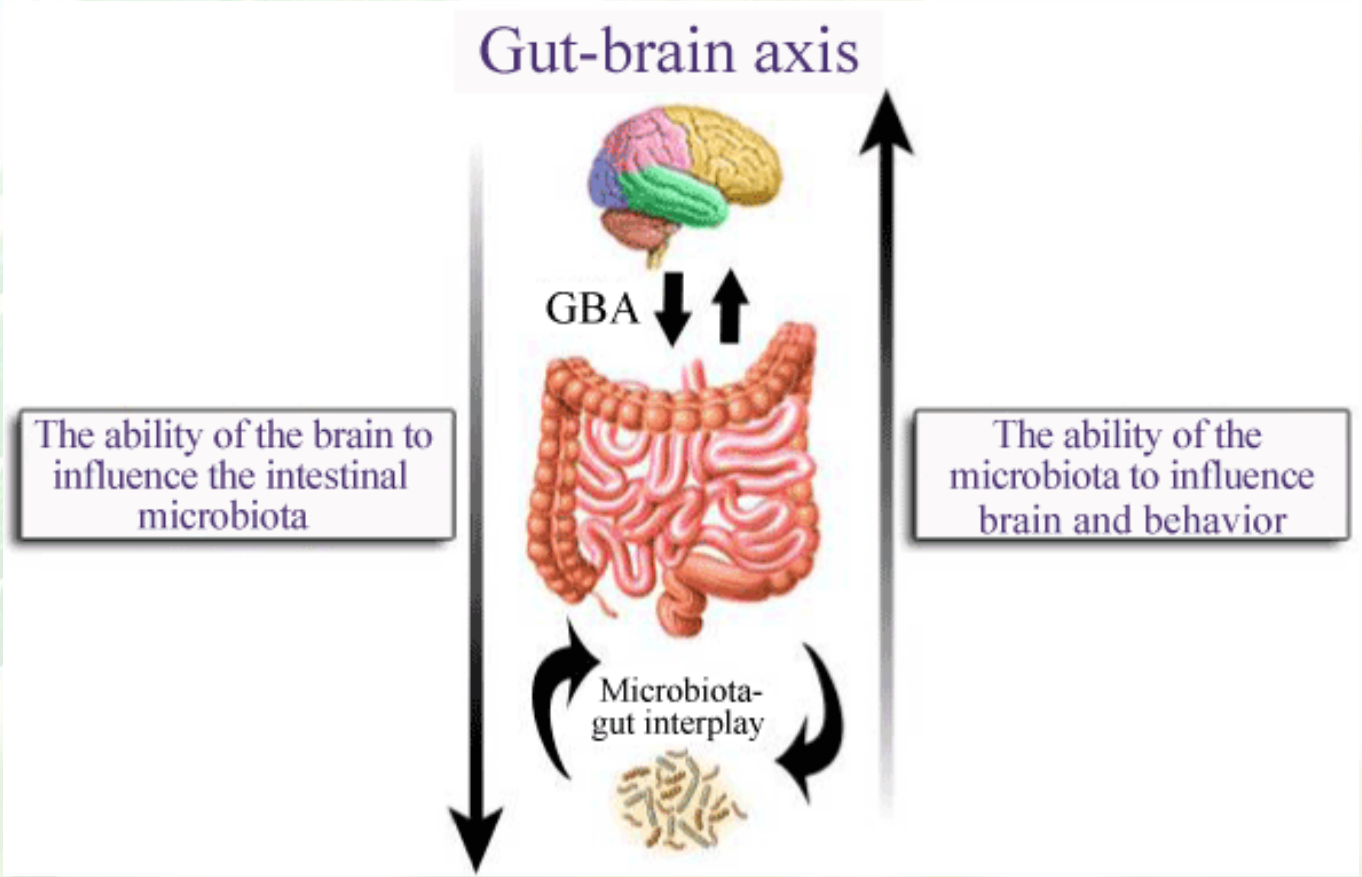
Gut-Brain Axis



Gut-Brain Axis

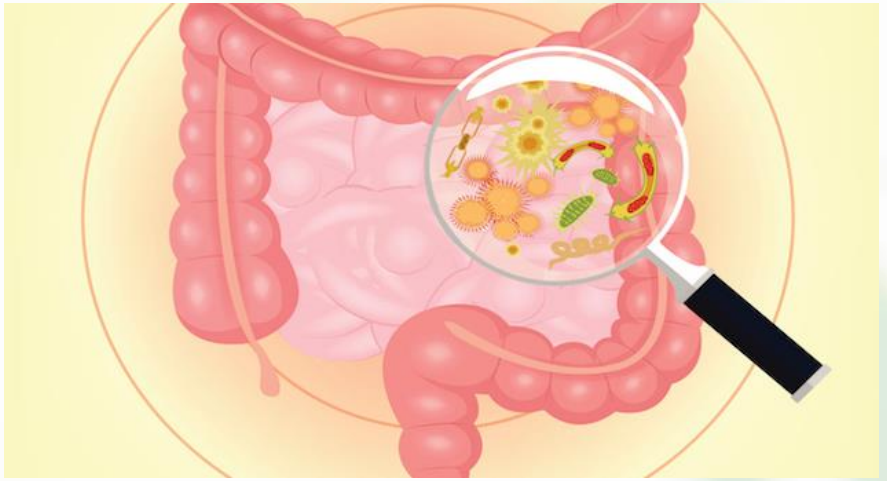
- Bidirectional communication between CNS & GI system
- Superhighway of biochemical signaling: neuro-endocrino-immunological connection
- Gut influences: mood, stress, anxiety, behavior, neurotransmitter signaling
- Brain influences: motility, secretion, nutrient delivery, microbial balance

Gut-Brain Axis Communication

- Vagus nerve
- Gut hormone signaling
- Immune system signaling
- Tryptophan metabolism
- Microbial metabolites (short chain fatty acids)
- Endocannabinoid system

Intestinal Gut Barrier Function

- Interactions between the microbiome & the ECS, acting as a gatekeeper
- Improves adipose tissue metabolism, blood sugar regulation, energy balance, inflammatory response & overall health
- *Akkermasia muciniphila* bacterium protective against obesity, metabolic syndrome & diabetes
- Decreases inflammatory markers & inflammatory endotoxemia by improving the intestinal mucosa barrier



ECS & the Gut & FAAH

- The microbiome can influence the CB1 receptor & the enzymes that breakdown endocannabinoids, such as FAAH (fatty acid amide hydrolase)
- Elevated levels of anandamide associated with ulcerative colitis, diverticulitis & celiac disease
- Change how receptors are expressed, altering endcocannabinoid levels

Intestinal Inflammation

Gut. 2006 Oct; 55(10): 1373–1376.
doi: 10.1136/gut.2005.090472
PMCID: PMC1856409
PMID: 16966693

Endocannabinoid overactivity and intestinal inflammation

V Di Marzo and A A Izzo

Abstract

Go to:

Cannabinoid receptors of type 1 and 2 (CB_1 and CB_2), endogenous ligands that activate them (endocannabinoids), and mechanisms for endocannabinoid biosynthesis and inactivation have been identified in the gastrointestinal system. Activation of CB_1 receptors by endocannabinoids produces relaxation of the lower oesophageal sphincter and inhibition of gastric acid secretion, intestinal motility, and fluid stimulated secretion. However, stimulation of cannabinoid receptors impacts on gastrointestinal functions in several other ways. Recent data indicate that the endocannabinoid system in the small intestine and colon becomes over stimulated during inflammation in both animal models and human inflammatory disorders. The pathological significance of this "endocannabinoid overactivity" and its possible exploitation for therapeutic purposes are discussed here.

"These findings indicate that: (1) endocannabinoids and CB_1 receptors are upregulated during intestinal inflammation [and] (2) enhanced endocannabinoid tone, by acting at least in part through CB_1 receptors, affords protection against both epithelial damage and increased motility occurring during intestinal inflammation."

Gastrointestinal Motility

J Cell Mol Med. 2018 Feb; 22(2): 706–715. PMCID: PMC5783846
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Endocannabinoid-related compounds in gastrointestinal diseases

Marcella Pesce, [1,2] Alessandra D'Alessandro, [1] Osvaldo Borrelli, [2] Stefano Gigli, [3] Luisa Seguella, [3] Rosario Cuomo, [1] Giuseppe Esposito, [3] and Giovanni Sarnelli [1]

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Abstract

Go to:

The endocannabinoid system (ECS) is an endogenous signalling pathway involved in the control of several gastrointestinal (GI) functions at both peripheral and central levels. In recent years, it has become apparent that the ECS is pivotal in the regulation of GI motility, secretion and sensitivity, but endocannabinoids (ECs) are also involved in the regulation of intestinal inflammation and mucosal barrier permeability, suggesting their role in the pathophysiology of both functional and organic GI disorders. Genetic studies in patients with irritable bowel syndrome (IBS) or inflammatory bowel disease have indeed shown significant associations with polymorphisms or mutation in genes encoding for cannabinoid receptor or enzyme responsible for their catabolism, respectively. Furthermore, ongoing clinical trials are testing EC agonists/antagonists in the achievement of symptomatic relief from a number of GI symptoms. Despite this evidence, there is a lack of supportive RCTs and relevant data in human beings, and hence, the possible therapeutic application of these compounds is raising ethical, political and economic concerns. More recently, the identification of several EC-like compounds able to modulate ECS function without the typical central side effects of cannabino-mimetics has paved the way for emerging peripherally acting drugs. This review summarizes the possible mechanisms linking the ECS to GI disorders and describes the most recent advances in the manipulation of the ECS in the treatment of GI diseases.

"Recent evidence suggests that along with the inhibition of acetylcholine release, the effects of the ECS on GI motility are likely to be related to the inhibition of all the components of the peristaltic reflex."

LAURA LAGANO WELLNESS

H·E·A·L CON

Intestinal Permeability

The gastrointestinal tract – a central organ of cannabinoid signaling in health and disease

Carina Hasenoehrl,[1] Ulrike Taschler,[1] Martin Storr,[2] and Rudolf Schicho[1]

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The publisher's final edited version of this article is available at Neurogastroenterol Motil

See other articles in PMC that cite the published article.

Background and Purpose

Go to:

In ancient medicine, extracts of the marijuana plant *Cannabis sativa* were used against diseases of the gastrointestinal (GI) tract. Today, our knowledge of the ingredients of the *Cannabis* plant has remarkably advanced enabling us to use a variety of herbal and synthetic cannabinoid compounds to study the endocannabinoid system (ECS), a physiologic entity that controls tissue homeostasis with the help of endogenously produced cannabinoids and their receptors. After many anecdotal reports suggested beneficial effects of *Cannabis* in GI disorders, it was not surprising to discover that the GI tract accommodates and expresses all the components of the ECS. Cannabinoid receptors and their endogenous ligands, the endocannabinoids, participate in the regulation of GI motility, secretion, and the maintenance of the epithelial barrier integrity. In addition, other receptors, such as the transient receptor potential cation channel subfamily V member 1 (TRPV1), the peroxisome proliferator-activated receptor alpha (PPARα) and the G-protein coupled receptor 55 (GPR55), are important participants in the actions of cannabinoids in the gut and critically determine the course of bowel inflammation and colon cancer. The following review summarizes important and recent findings on the role of cannabinoid receptors and their ligands in the GI tract with emphasis on GI disorders, such as irritable bowel syndrome, inflammatory bowel disease and colon cancer.

"Endocannabinoids are involved in the regulation of energy metabolism and food intake and communicate in this respect with the microorganisms of the gut. The epithelial lining expresses CB receptors and they are most likely involved in these mechanisms. 2-AG and PEA cause an increase in epithelial barrier function ("gate keeper") while anandamide is thought to be a "gate opener." Thus, the intestinal ECS may have an important role in the control of microbial products entering the bloodstream and in the development of metabolic diseases."

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Visceral Sensitivity

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"The antinociceptive effects of CB1 are probably intimately connected to a reciprocal down-regulation of TRPV1 receptors, while CB2 is likely able to counteract the sensitizing effects of inflammatory mediators, such as bradykinin, on peripheral endings of visceral afferents."

Changing the Microbiome & ECS

- Food is the ultimate health modulator
- Relationship between the GI system & the brain
- 85% of neurotransmitters produced in the gut
- Brain & gut speak the same language with ECS as a modulatory force
- Food choices & nutrition modulate the microbiome & the ECS

4 Rs Gut Restoration

Integrative & functional nutrition edit: *Always Start with the Gut!*

1. *Remove* factors contributing to gut issues (toxins, irritants, allergens)
2. *Replace* digestive enzymes & stomach acid
3. *Reinoculate* with good bacteria to reestablish a healthy microflora
4. *Repair* the gut lining with healing nutrients

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#5 Restore ECS health

Feeding the Microbiome

- Prebiotics
- Probiotics
- Nondigestible carbohydrates (fiber)
- Restorative fats (olive oil, avocado, coconut, nuts, seeds)
- Stay hydrated!
- Limit added sugars, processed foods, alcohol

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Reinoculate: Prebiotics

- Prebiotics: oligosaccharides that feed prebiotics
  - Artichokes, garlic, onions, dandelion greens, jicama, raw garlic, onions, leeks, asparagus, Jerusalem artichokes, bananas, seaweed
  - Inulin fiber
  - Prebiotic supplement

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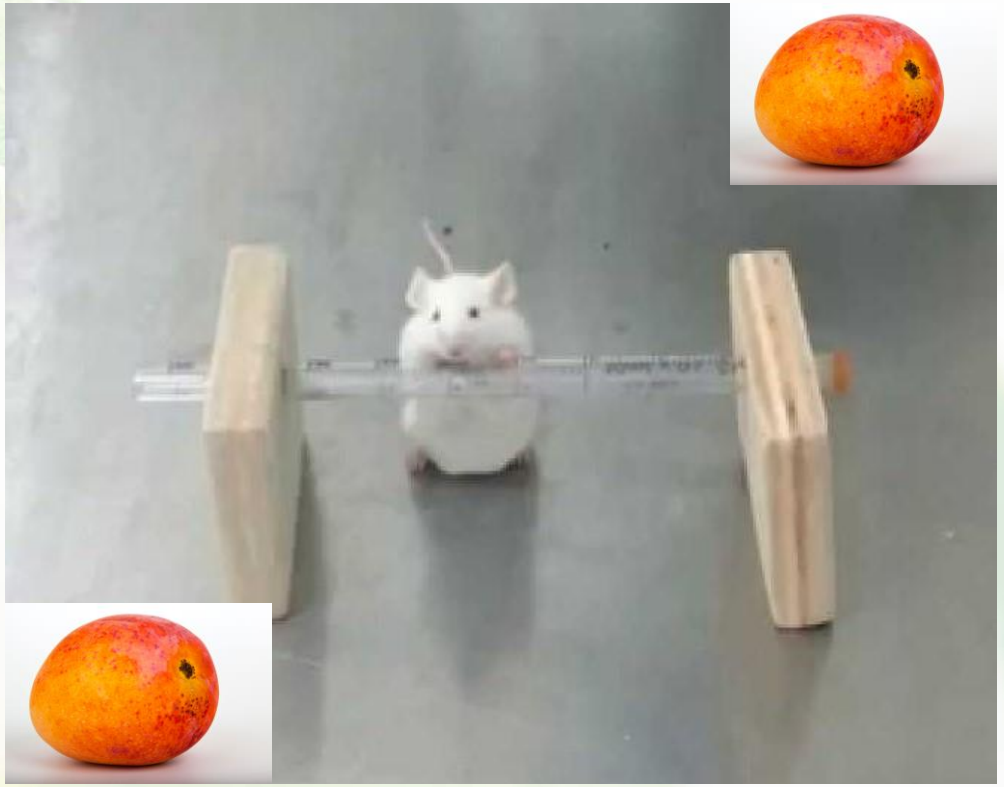
Reinoculate: Probiotics

- Probiotics
  - Lactofermented foods: kombucha, yogurt, kimchi, sauerkraut & fermented vegetables, miso
  - Probiotic supplement

Mango, the Microbiota & Cannabis

- Mango supplementation may prevent the loss of beneficial gut bacteria
- Mango supplementation regulated gut bacteria in favor of *Bifidobacteria* & *Akkermansia* & enhanced SCFA production
- Myrcene can synergistically enhance the sedative effects of THC



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Why Should You Care?

- The ECS is the basis of cell biology
- Medical marijuana is legal in 33 states + DC
- Healthcare paradigm is shifting—driven by demand
- CBD is available everywhere—*caveat emptor*
- Cannabis integrates with various holistic modalities including mind-body medicine and nutrition
- Ancient plant medicine works!

Ancient Plant Medicine Works!

- ADHD
- Alzheimer's Disease
- Anxiety
- Autism Spectrum Disorder
- Cancer
- Depression
- Eating Disorders
- Epilepsy
- Fertility
- Fibromyalgia
- Gut Issues
- Inflammation
- Insomnia
- Menopause
- Migraine
- Multiple Sclerosis
- Osteoporosis
- Pain
- PMS
- PTSD
- Skin Disorders
- Stress
- Weight Management

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Integrating Cannabis Holistically










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Practitioners vs. Dispensary Staff

Cannabis and Cannabinoid Research
Volume 1.1, 2016
DOI: 10.1089/can.2016.0024

Cannabis and Cannabinoid Research
Mary Ann Liebert, Inc. publishers

ORIGINAL RESEARCH Open Access

Training and Practices of Cannabis Dispensary Staff

Nancy A. Haug,[1,2,*] Dustin Kieschnick,[1] James E. Sottile,[3] Kimberly A. Babson,[4] Ryan Vandrey,[5] and Marcel O. Bonn-Miller[4,6–8]

"...some are recommending cannabis that has either not been shown effective for, or could exacerbate, a patient's condition. Findings underscore the importance of consistent, evidence-based, training of dispensary staff who provide specific recommendations for patient medical conditions.

How Can You Get Educated?

Online learning platform about integrating cannabis holistically into personalized lifestyle medicine

holisticcanna.com
Use promo code: NANP

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Laura & the grandfather of cannabis research,
Raphael Mechoulam

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