



UNDERSTANDING THE **ENDOCANNABINOID SYSTEM (ECS)**



GENESTRA
BRANDS®

CBD: MECHANISM OF ACTION

CBD has multiple molecular targets that extend beyond the classical cannabinoid receptors. By inhibiting fatty acid amide hydrolase (FAAH), the enzyme that degrades anandamide, CBD activates cannabinoid receptors indirectly.

Fatty Acid Amide Hydrolase

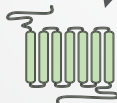
inhibition
 $IC_{50} \sim 10-20\mu M$

FAAH

↑Anandamide



CB₁, CB₂
receptor
activation



5HT_{1A}
Serotonin receptor
activation
 $EC_{50} = 0.007\mu M$



TRPV1
Vanilloid receptor
activation/
desensitization
 $EC_{50} < 5\mu M$



GPR55
receptor inhibition
 $IC_{50} < 0.5\mu M$



PPAR_γ
activation
 $EC_{50} = 5\mu M$

Adenosine
reuptake inhibition
 $IC_{50} < 5\mu M$

CBD

Legend

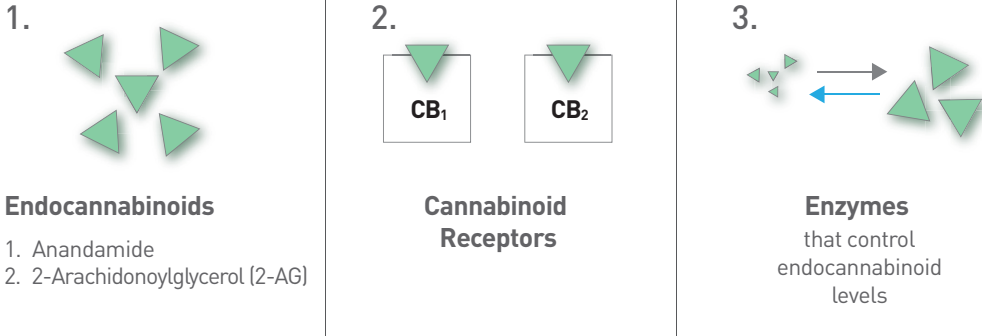
- Low-affinity interaction supported by limited/inconclusive data
- Low-to moderate-affinity interaction supported by satisfactory data
- Potent interaction supported by satisfactory data

COMPOUND: Cannabidiol (CBD)

CBD is one of approximately 100 phytocannabinoids that are naturally occurring in hemp plants. Cannabinoids refer to molecules found in the cannabis plant that interact with cannabinoid receptors. Common cannabinoids include D9-THC, THCV, CBD, CBDV, CBG and CBC.

KEY FACTS: Understanding the ECS

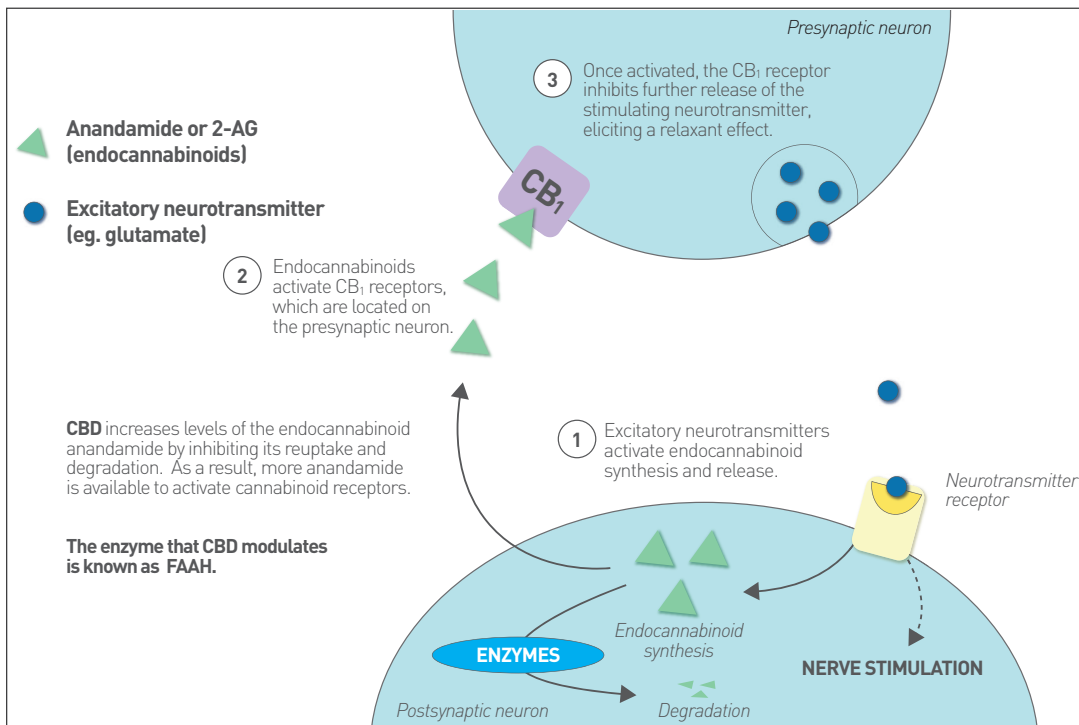
- Plays vital neurological and immunomodulatory roles that can affect overall health
- Comprised of specialized eicosanoids, known as endocannabinoids, that the body makes from lipid precursors



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THE ECS IN THE CNS

The two major endocannabinoids — **anandamide** and **2-AG** — activate two different cannabinoid receptors: **CB₁** and **CB₂**. The **CB₁ receptor** is primarily expressed on neurons in the **brain and nervous systems**; a main function is to inhibit excitatory neurotransmission.



THE ECS IN THE PERIPHERY

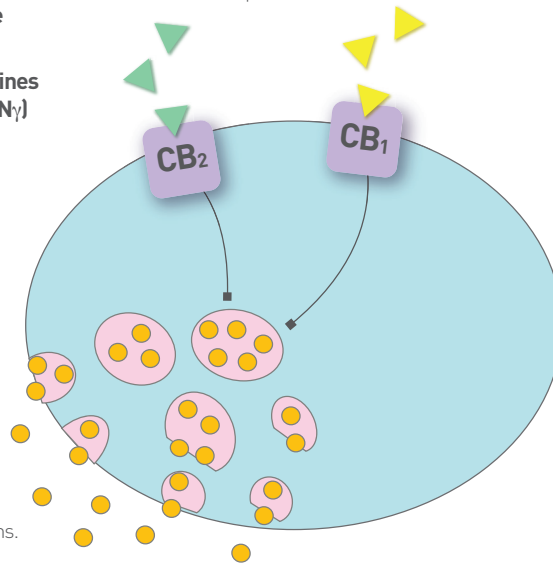
The **CB₂ receptor** is located primarily in the gut, immune system and periphery, where it **modulates the immune response** and downregulates the production of cytokines, such as IL-6, IL-1 β , TNF α , IFN β , and IFN γ . The levels of anandamide and 2-AG are tightly controlled by the balance of synthesis and degradation.

-  **Anandamide or 2-AG (endocannabinoids)**
-  **Beta-caryophyllene**
-  **Inflammatory cytokines (e.g. TNF- α , IL-6, IFN γ)**

2 Once activated, CB₂ receptors elicit many immunomodulating effects, which depend on the cell type and its environment.

3 CB₂ activation modifies inflammatory cytokine production, which has broad clinical implications.

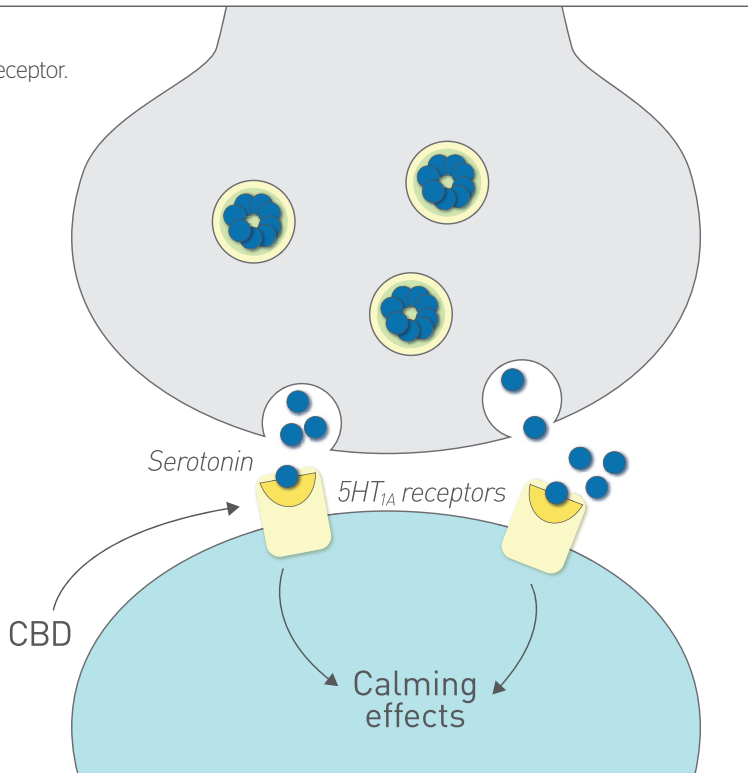
1 In cells of the immune system, GI tract, and other peripheral tissues, endocannabinoids (primarily 2-AG) activate CB₂ receptors.



While cannabidiol supports endocannabinoid signaling indirectly, **beta-caryophyllene is a direct CB₂ agonist**, potentially sharing similar immunomodulating effects as the endocannabinoids. More research is needed to explore this effect in humans.

INFLUENCE ON SEROTONIN SIGNALING

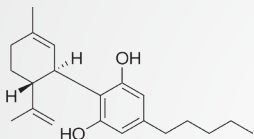
CBD facilitates neurotransmission mediated by the serotonin $5HT_{1A}$ receptor.



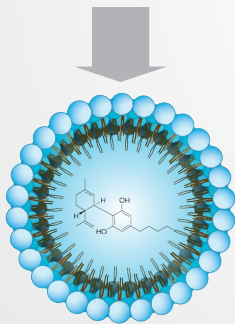
In the limbic system of the brain, activation of this receptor contributes to calming effects.

IMPORTANCE OF ENHANCED BIOAVAILABILITY

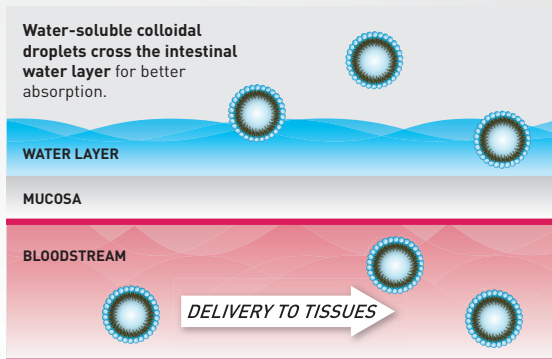
- **Colloidal delivery systems:** Water-soluble droplets allow even dispersion of CBD and terpenes in the GI tract.
- Droplets easily cross the water layer at the intestinal brush border, a major absorption obstacle for lipophilic compounds.



CBD has poor bioavailability due to its lipophilic properties.



Improving water solubility with colloidal technology greatly enhances absorption and increases plasma levels of CBD.



The intestinal brush border is coated with a water layer, which normally limits the absorption of fat-soluble compounds. Enclosing CBD and terpenes in a water-soluble droplet improves the uptake of these bioactives across the water layer, allowing better absorption.

To learn more visit [genestrabrand.com](https://www.genestrabrand.com)

4 KEY CONSIDERATIONS FOR SELECTING QUALITY CANNABIDIOL



THC-free — non-detectable and every batch tested



Solvent-free, clean CO₂ extraction



Colloidal delivery systems for enhanced bioavailability



100% US-sourced, field-grown agricultural hemp

HIGH-QUALITY CBD PRODUCTS WILL ALSO PROVIDE:

- ✓ A high-potency dosage per capsule
- ✓ Broad-spectrum support
- ✓ Ingredients FREE FROM GMOs[†]; gluten; hydrogenated fat; artificial colors, flavors and sweeteners; and magnesium stearate

[†]Visit our website for more information on our GMO policy.



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