



The Endocannabinoid System, Phytocannabinoids, Terpenes, and Drug Interactions

Endocannabinoid System:

Cannabinoid neurotransmitters and corresponding receptors.

- Endocannabinoids
- Endocannabinoid receptors

The Function of the Endocannabinoid System:

To maintain homeostasis in the body.

- Endocannabinoids are released by cells as needed and quickly degraded.
- Retrograde signaling of the nervous system acts as dampening mechanism on the nervous system.

Cannabinoids: Fat-based neurotransmitters that signal cannabinoid receptors.

Endocannabinoids: Endogenous/human cannabinoids.

Phytocannabinoids: Plant cannabinoids.

Cannabis species has abundant cannabinoids, including CBD and $\Delta 9$ -THC.

- THC can bind to Endocannabinoid receptors.
- CBD does not bind to Endocannabinoid receptors.
- Other cannabinoids include CBG, CBN, CBC, $\Delta 8$ -THC

Cannabinoid receptors

1. CB1 receptors: primarily found in the brain and nervous system.
2. CB2 receptors: primarily found in the immune system.

CB1 and CB2 receptors are found in numerous tissues including:

- | | |
|---------------------------------|--------------------------|
| • Testes/Uterus | • Spleen |
| • Adipose (fat) tissue | • Heart |
| • Connective tissue | • Gastrointestinal cells |
| • Endocrine and exocrine glands | • Liver |

Lifestyle Factors to support the Endocannabinoid system:

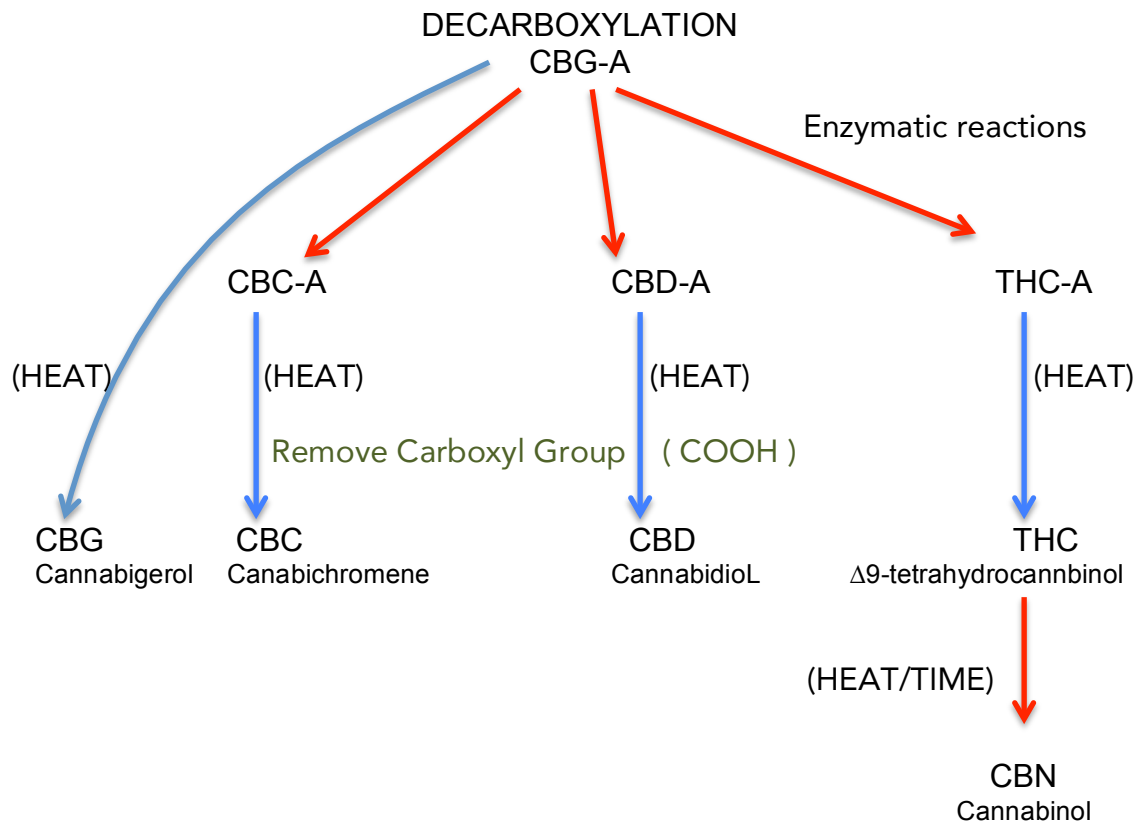
- Moderate to high intensity exercise
- Pre/Probiotics
- Healthy socialization/play enhances
- Electro acupuncture skin
- Physical manipulation

Lifestyle factors that damage the Endocannabinoid system.

- Stress
- Excess alcohol consumption

Phytocannabinoids

- **Phytocannabinoids** help support the Endocannabinoid system.
- **Entourage Effect:** Using the entire plant including all cannabinoids and terpenes (see below) can have a greater effect than isolated cannabinoids.
- **Raw vs. Heated/Dried.** The raw plant produces numerous cannabinoids with a carboxyl group (COOH). Decarboxylation occurs when heat is applied, or when the plant is dried over a period of time. Heat and drying releases the carboxyl group and carbon dioxide. The carboxylated form is designated with an “A” following the name.



Examples of Beneficial Cannabinoid Effects

Δ -9-tetrahydrocannabinol (Δ 9 THC): psycho-active

- Reduces nausea/vomiting
- Pain relief
- Stimulates appetite
- Suppresses muscle spasms

Δ 9 THC-A: NOT psycho-active

- Sleep aid
- Inhibits cancer growth
- Suppresses muscle spasms

Cannabidiol (CBD): NOT psycho-active

- Blocks THC from binding to receptors, reducing the psycho activity of THC.
- Lots of functions: pain relief, anti anxiety, inhibits cancer growth

CBD-A

- Anti-inflammatory, anti-cancer.

Δ 8 THC: Pain reliever.

Δ 9—tetrahydrocannabivarin (THCV): Reduces convulsions/seizures, appetite suppressant, promotes bone growth.

Cannabigerol (CBG) : Anti-inflammatory , anti cancer, slows bacterial growth.

CBG-A: Anti-inflammatory, pain reliever, slows bacterial growth.

Canabichromene (CBC) – Inhibits cancer growth, promotes bone growth, anti-inflammatory, pain reliever.

CBC-A: Reduces inflammation, inhibits fungal growth.

Cannabinol (CBN): Pain reliever, anti- inflammatory, sleep aid.

TERPENES

Aromatic organic hydrocarbons found in the essential oil of the flowers and are often fragrant. When combined with cannabinoids, terpenes provided a synergistic effect known as the Entourage Effect.

- **Myrcene.** Sedative, anti-inflammatory, anti mutagenic, muscle relaxant, pain relief, may help reduce peptic ulcer disease. Increases saturation of CB1 recmptor (causes a greater psychoactive effect)
- **Limonene.** Improved mood, energizing, anti-inflammatory, anti fungal
- **Pinene:** bronchodilator, antiseptic, anti-inflammatory, improves energy, may be anti-cancer.
- **Caryophyllene:** Effects CB2 receptors. pain reliever, anti inflammatory, anti-septic, anti depressant. May protect kidneys from chemotherapy damage.
- **Linolool:** reduces stress, sedative, relieve seizure symptoms, anti inflammatory. May protect against lung inflammation when smoking cannabis. May protect against Alzheimer's when acting as an anti-inflammatory agent.
- **Terpinolene:** increases anti-oxidant cellular potential, anti-microbial, anti cancer (glial, leukemia), insecticide.
- **Humulene:** anti-bacterial, anti-pain, anti-inflammatory, anti-cancer, appetite suppressant.

CANNABIS-DRUG INTERACTIONS.

Please discuss all medications and cannabis use when speaking with your doctors.

THC may be affected by the detoxification enzyme including P450 2C9, 2C19, and 3A4.

Here is a list you can share with your physician regarding cannabis-drug interactions.

Inhibitors of these enzymes **increase** the pharmacological effect and duration of THC. When taking the following medications, a lower dose of THC may be needed.

- Macrolides (except arthromycin), oral contraceptives, paroxetine, fluoxetine, some proton pump inhibitors, HIV antiretrovirals, calcium channel blockers, , antifungals, cannabidiol (CBD)

Inducers of these enzymes **decrease** the pharmaceutical effect and duration of THC. When taking the following medications, a higher dose of THC may be needed.

- Carbamazepine, rifampin, phenytoin, ritonavir, St. John's wort, phenobarbital

THC induces the P450 enzyme 1A2. This property may cause a decrease in pharmacological effect of:

- Theophylline, clozapine, chlorpromazine

CBD inhibits the P450 enzymes 3A4 and 2D6. This property may cause an increased bioavailability and pharmacological effect of:

- Macrolide antibiotics, calcium channel blockers, antihistamines, haloperidol, sildenafil