DEFINITIONS

Ligand chemical/molecule that fits into a receptor and activates or deactivate it.

Agonist A ligand molecule (chemical) that activates a receptor.

Antagonist A ligand molecule that deactivates a receptor.

Analgesic Pain reliever (i.e. acetaminophen, ibuprofen, morphine, THC)

Anxiogenic Anxiety increasing effects

Anxiolytic Anxiety reducing effects

Biphasic when something shows distinct effects in two different stages. i.e. small amount of something being beneficial versus a large amount of it being detrimental or vice versa.

Inhalation Dosing Smoking and/or vaping. The vaporized cannabinoids are absorbed directly through the lungs into the bloodstream.

Sublingual Dosing Holding a chemical or solution under the tongue. The chemical passes through the thin "oromucosal skin" directly into the bloodstream. Typically, a portion ends up travelling to the stomach as an oral dose as well.

Titration Slowly increasing dose to reach desired effect.

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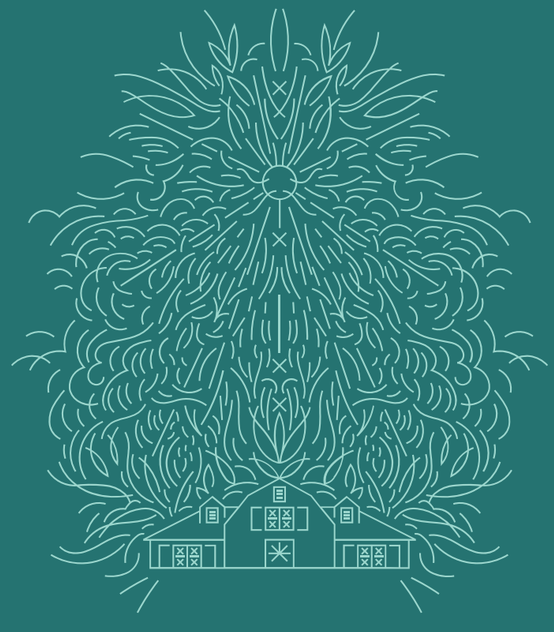

A medical cannabis primer

Cannabis has been used medically for thousands of years. It has the potential to treat many ailments, from chronic pain and inflammation to anxiety and stress. By acquiring a deeper knowledge of the elements of the plant and how the chemicals interact with the body's signaling systems, symptoms can be targeted to optimal effect. Coupling quality product with an in-depth education will guide patients to make informed decisions about their own treatment.

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ENDOCANNABINOID SYSTEM

The endocannabinoid system regulates natural signaling processes through its receptors and their corresponding ligands, which are molecules that fit into a receptor and activate or deactivate it. Most animals have an endocannabinoid system, which likely evolved as an adaptive and protective check on uncontrolled mental and physical states. This regulatory system acts as a molecular “shock absorber” on natural signaling as well as a “brake” on reactive processes and is expressed throughout the nervous, immune, digestive, and metabolic systems as well as in the skin.

Cannabinoid receptors are activated by ligands (endocannabinoids produced by the body) as well as plant derived molecules (phytocannabinoids) and some chemically derived synthetics.

The Cannabinoid Receptor Type 1 (CB1) is highly expressed throughout the peripheral and central nervous systems and in the digestive tract. Its natural ligands include Anandamide and 2-AG. The CB1 receptor’s primary responsibility is to act as a negative feedback messenger (retrograde signaling) to achieve signaling balance – re-calibrate to reach homeostasis. The CB1 receptor can control signaling throughout the list of central nervous system processes, including pain sensing, control of memory, motor function, energy use, and storage and has far reaching effects through interaction with other will defined neurological systems (serotonin, opioid, dopamine, glutamate, and GABA). THC is a potent partial agonist (activator) of the CB1 receptor. As a “partial agonist”, THC doesn’t activate the receptor to the full extent that Anandamide and 2-AG do.

The Cannabinoid Receptor Type 2 (CB2) is highly expressed in the immune system, lymphocytes, macrophages, and microglial cells. Macrophages (and microglia in the brain) act as the body’s sentinels (amoeba-like white blood cells) searching for bad news. In response to an invader or an injury, these sentinels send-off inflammatory signals: chemical messengers called cytokines and chemokines that alert the body of an emergency. These immune inflammatory signals result in increased immune cell response to the site of injury, including additional fluid, cells, and cleanup crew processes. All of this added “volume” is what we refer to as inflammation. The CB2 receptor’s natural biological job is to shut off the initial “alarm” response as well as regulate the cleanup. 2-AG is the natural ligand for CB2 with which THC acts as a partial agonist.

The TRPV1 receptor is a voltage gated ion channel expressed throughout the central and peripheral nervous system. Commonly known as the “Capsaicin Receptor”, capsaicin from hot peppers binds to these sensory receptors producing the “heat” sensation. TRPV1 is also highly expressed in the brain and spinal cord. Anandamide, which is also the natural ligand for CB1, fully activates TRPV1, which “charges” a neuron to prepare for firing and modulates its firing intensity. CBD is a natural full agonist (activator) of this receptor but does so in a way that also desensitizes the receptor.

The PPAR (Peroxisome Proliferator-Activated Receptor) is a nuclear hormone found throughout the body but is highly expressed in the digestive tract as well as the pancreas, adipose (fat) tissues and skin. As a receptor, PPAR regulates gene expression and energy metabolism. Cannabis acids (THCA, CBDA) are typically potent activators of the PPARs.

CANNABINOIDS AND MAJOR TERPENES

Cannabis is known to produce well over a hundred distinct molecules. For most purposes, cannabis’ biological effects can be explained by the action of the major cannabinoids THC and CBD, the major terpenes myrcene, ß-caryophyllene, humulene, limonene, linalool, and pinene, as well as flavonoids and components like minor terpenes (nerolidol, borneol, ocimene, etc.) Each component of the mixture produces a distinct biological effect, and when layered on top of each other, the combined effect is greater than the sum of the parts. This is the basis for what’s known as the “Entourage Effect.”

THC-A The natural acidic precursor to THC. The major cannabinoids are biologically stitched together in the cannabis plant as the acidic precursors. Heating the acidic precursors to at least 100°C (212°F) induces a chemical reaction called “decarboxylation” that produces psychoactive THC. THCA is mildly psychoactive, may decarboxylate in the body, and has some affinity for the CB1/CB2 receptors.

CBD-A The natural acidic precursor to CBD. Like THC-A, CBD-A decarboxylates into CBD.

Δ9-Tetrahydrocannabinol (THC) THC binds to and activates both CB1 and CB2 receptors. This makes THC ideal for treating both pain, which can be targeted through CB1, as well as inflammation that can be targeted through the CB2 receptor. THC is slightly better at activating CB1 than CB2 but does act as a partial agonist (activator) of both. THC also binds to and has activity in multiple other receptors, but its actions are primarily explained through CB1/CB2.

Cannabidiol (CBD) CBD interacts with the CB1/CB2 receptors, but has little binding affinity for them, much like a key that won’t turn a lock. That said, CBD impacts the endocannabinoid system in a number of important ways. CBD interrupts anandamide’s reuptake and degradation processes, which increases the active concentration of anandamide. This is an indirect way to activate the cannabinoid receptors. CBD interacts with and desensitizes the TRPV1 receptor, which can reduce the intensity of existing painful signaling. CBD also activates the serotonin system, thereby inducing the release of serotonin, which is a neurotransmitter known for promoting a sense of happiness and well-being.

Cannabinol (CBN) A thermodynamically more stable oxidation product of THC. It is significantly less potent than THC (~5x less potent) but more selective for CB2. CBN is typically found in nature in aged cannabis samples and can be induced by treating THC flower with light, heat, and oxygen.

Cannabigerol (CBG) The “mother” cannabinoid. All of the major cannabinoids begin as CBGA and are subsequently converted to THC, CBD, CBC, CBN, etc. CBG is a particularly lipophilic molecule with an interesting “balanced” structure. CBG has initially been found to be beneficial for skin issues.

ß-Caryophyllene (BCP) is a naturally occurring terpene which binds to and fully activates the CB2 receptor even in the absence of THC, making this an ideal molecule for treating inflammation. BCP is always found with humulene in natural systems.

Myrcene The most common cannabis (and hop) terpene. Myrcene is a known sedative and analgesic and acts as a barrier penetration enhancer.

Terpinolene A known sedative and barrier penetration enhancer with a very similar structure to myrcene. It is highly antioxidant.

Limonene A known muscle relaxant and anti-asthmatic. Found to be beneficial for gastric/metabolic issues.

Linalool A known anxiolytic (anti-anxiety) and sedative.

α-Pinene A known sedative (working through GABA release), anti-asthmatic bronchodilator, and antimicrobial.

Humulene Extremely similar structure to BCP and is likely a side product of BCP biosynthesis. While humulene doesn’t display any CB2 activity on its own, it is a known, powerful, systemic anti-inflammatory.