The Human Endocannabinoid System
Meets the Inflammatory Cytokine Cascade

The Endocannabinoid System (ECS) started revealing itself to researchers in the 1940s and by the late '60s the basic structure and functionality had been laid out. Today we know the ECS is a comprehensive system of biochemical modulators that maintain homeostasis in all body systems including the central and peripheral nervous systems, all organ systems, somatic tissues, and all metabolic biochemical systems, including the immune system.

This homeostatic matrix is not a recent evolutionary twist just for humans; we find the Endocannabinoid System in every chordate creature for the last 500 million years. It is a fully mature biochemical technology that has maintained health and metabolic balance for most of the history of life itself.

The two major interactive systems within the ECS are (1) the cannabinoid receptors that we find on all cell surfaces and neurological junctions and (2) the endocannabinoids that fit the receptors to trigger various metabolic processes. Looking at a cannabinoid receptor distribution map we see that CB1 receptors, that are most sensitive to anandamide, are found in the brain, spinal nerves, and peripheral nerves. CB2 receptors preferred by 2-arachidonoylglycerol (2-AG) are found largely in the immune system, primarily the spleen. A mix of CB1 and CB2 receptors are found throughout the rest of the body including the skeletal system. And yes, 2-AG or CBD will grow new trabecular bone.[1] It is also useful to note that both anandamide and 2-AG can activate either CB1 or CB2 receptors.

The nature of the endocannabinoids are functionally much like neurotransmitters, but structurally are eicosanoids in the family of signaling sphingolipids. These signaling cannabinoids keep track of metabolic systems all over the body. This information is shared with the nervous system and the immune system so that any imbalance is attended to. If the body is in chronic disease or emotional stress, the immune system can fall behind and lose control of compromised systems. It is here that phytocannabinoids can pitch in to support the stressed body in a return to health. The cannabis plant provides analogues of the body's primary signaling cannabinoids. Tetrahydrocannabinol (THC) is mimetic to anandamide, and cannabidiol (CBD) is mimetic to 2-AG, and has the same affinity to CB1 and CB2 receptors; providing the body with additional support for the immune and endocannabinoid systems.

Phytocannabinoids supercharge the body's own Endocannabinoid System by amping up the response to demand from the immune signaling system in two modes of intervention: one, of course, is in bonding with the cannabinoid receptors; the other is in regulation of innumerable physiological processes, such as cannabinoid's powerful neuroprotective and anti-inflammatory actions, quite apart from the receptor system. It is interesting to note here that the phytocannabinoids and related endocannabinoids are functionally similar, but structurally different. As noted above, anandamide and 2-AG are eicosanoids while THC and CBD are tricyclic terpenes.

Let us look more closely at the two primary therapeutic cannabinoids, THC and CBD. The National Institutes of Health tell us that THC is the best known because of its signature psychotropic effect. This government report shows THC to be effective as an anti-cancer treatment, an appetite stimulant, analgesic, antiemetic, anxiolytic, and sedative.[2]

CBD (cannabidiol) is a metabolic sibling of THC, in that they are alike in many ways but are also different in important properties. First we see that CBD has no psychotropic effects and there are few CB2 receptors in the brain and peripheral nerves. There appears to be a broader therapeutic profile associated with CBD, which is listed here:[3]

anxiolytic	anticancer
antipsychotic	antidiabetic
antiepileptic	antisporiatic
neuroprotective	intestinal anti-prokinetic
vasorelaxant	analgesic
antispasmodic	bone-stimulant
anti-ishcemic	anti-inflammatory
antiproliferative	immunosupressive
antiemetic	antibacterial

One of the most important health benefits of cannabinoids is their anti-inflammatory property. In this, they are strong modulators of the inflammatory cytokine cascade. Numerous disease states arise out of chronic inflammation; such as, depression, dementias including Alzheimer's, cancer, arthritis and other autoimmune disorders, viral infection, HIV, brain injury, etc.

Inflammatory cytokines can be activated by oxidative stress and disease states. Cannabinoids, being immunomodulators interrupt the cytokine inflammatory cascade so that local inflammation does not result in tissue pathology. Thus we are spared morbid or terminal illnesses.[4]

If our own endocannabinoid system can maintain metabolic homeostasis and even cure serious disease, why are we plagued by illness? We know that the body produces only small amounts of anandamide and 2-AG; enough to maintain the body but not enough to overcome chronic stress, illness, injury, or malnutrition. Cannabis is the only plant we know of that produces phytocannabinoids that mimic our own endocannabinoids. One of the great benefits of this mimetic medicine is that cannabinoids are essentially natural to our biology and do no harm to our tissues and systems.

It is well known that most diseases of aging are inflammatory in origin, thus making cannabis the best anti-aging supplement we could take to avoid arthritis, dementia, hypertension, diabetes, osteoporosis, and cancer. This is our key to good health and long life.

Since it is such an important attribute, as well as being independent of the cannabinoid receptor system, let's look a little deeper into the ability of cannabinoids to inhibit the inflammatory cytokine cascade. Inflammation is good for us, a little here, a little there; it brings T-cells and macrophages to infection sites. This is good. However, chronic inflammation can cause serious illness and death. How do phytocannabinoids rescue us from dreaded infirmities? When the call comes in to the immune system to send troops, the first thing to happen is that the immune system signals glial cells to produce cytokines. Once this cat is out of the bag, the process can go one of two ways.

A) Killer cells clean up the infection and all is well.
B) Cytokines can stimulate more cytokine production and cause many more cytokine receptors to awaken. Unchecked, this becomes a cytokine storm showing symptoms of swelling, redness, fatigue, and nausea; even death.

Phytocannabinoids have the ability to suppress this inflammatory cytokine cascade by inhibiting glial cell production of the cytokines interferon or interleukin. Here we see the seeds of chronic inflammation dissolved by the modulation process of cannabinoids bringing homeostasis to systems out of balance. This is a good example of how cannabinoids normalize biological processes all throughout the body and allows us to keep that glow of well-being through a long and happy lifetime.

~Dennis Hill

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