



What is the Endocannabinoid System?

First discovered in 1992, the endocannabinoid system (ECS) is a very important part of the human body responsible for many vital functions. It is also present in all vertebrates and many invertebrates. In general, it is responsible for maintaining physiologic balance and specifically plays a role in the moderation of pain and inflammation, reducing anxiety, maintaining, and protecting brain function and bone health, inducing, and maintaining sleep, and fighting infection.

There are three important components of the ECS: chemicals called endocannabinoids, the receptors with which they bind (like a lock and key), and enzymes that break down the endocannabinoids shortly after they are produced. The two main endocannabinoids are called Anandamide and 2-AG. They bind to two types of receptors, CB1 and CB2. CB1 receptors are found throughout the brain and nervous system and CB2 receptors are found on immune cells, in bone, and in many human organs including the GI tract, heart, liver, lungs, and spleen.

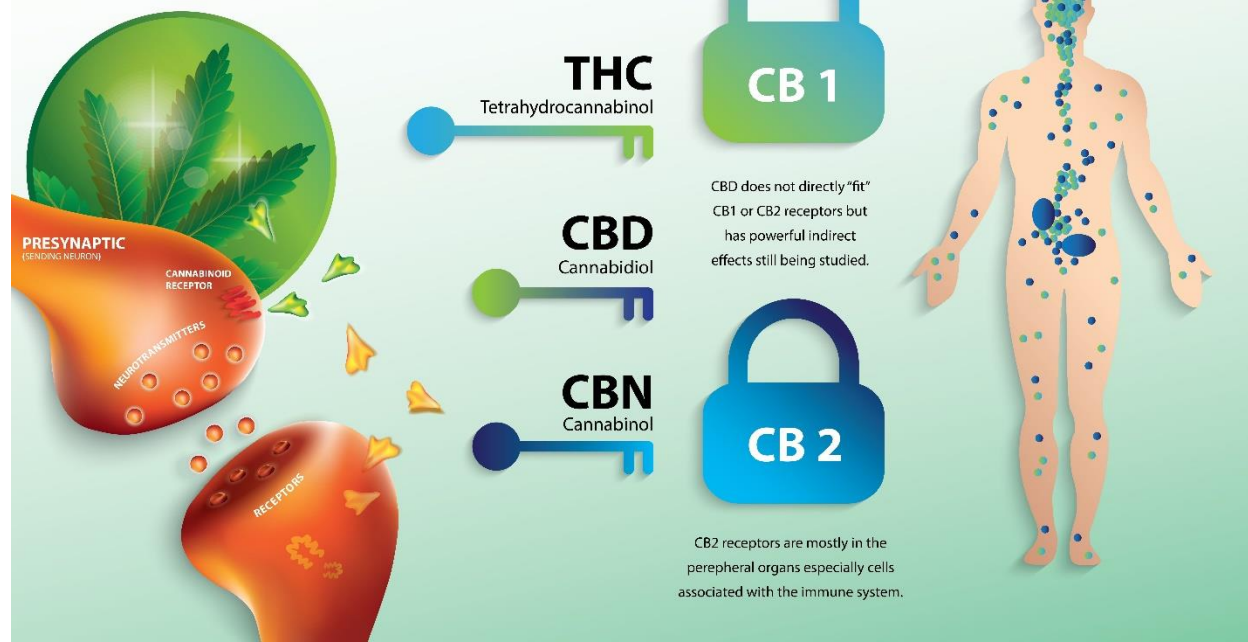
Chemicals from the cannabis plant (Phyto cannabinoids) work by interacting directly or indirectly with the CB1 and CB2 receptors in the human body. For example, the intoxicating chemical in the cannabis plant (THC) causes its effects by binding directly to the CB1 receptors in the brain, but by binding these receptors in the brain and nervous system, it also moderates pain processing as well the subjective experience of pain in the brain. CBD, on the other hand, interacts indirectly with CB1 and CB2 receptors by blocking the enzyme (FAAH) which breaks down the endocannabinoid Anandamide. This raises the Anandamide levels in the brain and body, allowing more binding to these receptors which help to moderate pain and inflammation, reduce anxiety, and induce and maintain sleep. By binding these receptors, Phyto cannabinoids also appear to indirectly affect levels of other brain chemicals including serotonin, dopamine, and glutamate.

Recent research has suggested that anxiety may be caused, at least in part, by a deficiency of Anandamide in an area of the brain called the amygdala^{1,2} and that fibromyalgia and long Covid may be mediated in part by a systemic deficiency of endocannabinoids^{3,4}.

Another chemical that interacts with the ECS and can have positive effects in the human body is called Palmitoylethanolamide (PEA). This chemical is also naturally produced in the human body, often in response to pain or inflammation. PEA works in a similar way to CBD by inhibiting the breakdown of Anandamide by blocking the FAAH enzyme. Unlike the Phyto cannabinoids such as THC, CBD, CBN, CGB, and CBC, it does not come from the cannabis plant. Rather it comes from several dietary sources including soy, egg yolks, and peanuts. It is considered a dietary supplement and can be obtained from several reputable companies on the internet. PEA is a good option for those who want or need to avoid intoxication, federal government employees or contractors with a security clearance, those who are drug tested at work, and individuals who take medications that can interact with Phyto cannabinoids.

The Human Endocannabinoid System

CBD, CBN and THC fit like a lock and key into existing human receptors. These receptors are part of the endocannabinoid system which impact physiological processes affecting pain modulation, memory, and appetite plus anti-inflammatory effects and other immune system responses. The endocannabinoid system comprises two types of receptors, CB1 and CB2, which serve distinct functions in human health and well-being.



Although our understanding of the ECS is still evolving, it is clear to scientists that it plays a fundamental role in maintaining human health and that medical cannabis seems to exert its positive effects by interacting directly or indirectly with the ECS.

¹Amygdala FAAH and anandamide: mediating protection and recovery from stress. Ozge Gunduz-Cinar, Matthew N. Hill, Bruce S. McEwen, and Andrew Holmes. *Trends in Pharmacological Sciences* November 2013, Vol. 34, No. 11

²Corticotropin-Releasing Hormone Drives Anandamide Hydrolysis in the Amygdala to Promote Anxiety. J. Megan Gray, Haley A Vecchiarelli, Maria Mrena, et al. *Journal of Neuroscience* 4 March 2015, 35(9) 3879-3892.

³Clinical Endocannabinoid Deficiency Reconsidered: Current Research Supports the Theory in Migraine, Fibromyalgia, Irritable Bowel, and Other Treatment-Resistant Syndromes. Russo, E. *Cannabis and Cannabinoid Research*. 2016. Jul 1:1 (1): 154-165.

⁴The Immunopathology of COVID-19 and the Cannabis Paradigm. Nicole Poland, Antonia Pechkovsky, Miran Aswad, et al. *Front. Immunol.*, 12 February 2021. Volume 12-2021.