

A guide to the endocannabinoid system

Learn about medicinal cannabis and how it interacts with the endocannabinoid system (ECS) in pets. Discover the components of the ECS, the potential therapeutic benefits of CBD, and the fascinating mechanisms of action behind this natural plant molecule.

If you have started prescribing or even looking into cannabinoids as a potential treatment option for your pet patients, you'll know there are many new concepts and terminology to understand when you start prescribing medicinal cannabis.

In Australia veterinarians can prescribe medicinal cannabis that meets Schedule 4 requirements, meaning it must contain 98% or more cannabidiol (CBD) and less than 2% other cannabinoids. While there are over 140 phytocannabinoids (exogenous plant cannabinoids), in the cannabis plant, we are most familiar with two: CBD and tetrahydrocannabinol (THC).

THC is the most abundant part of the cannabis plant and it is responsible for its psychoactive effects. CBD on the other hand, is the non-psychoactive, non-addictive part of the cannabis plant and the second most abundant, with a range of potential therapeutic effects.

CBD interacts with multiple metabolic pathways in the body, which helps explain the broad application this natural plant molecule can have. It's not just phytocannabinoids that offer therapeutic effect, the plant's terpenes and flavonoids do too. When multiple parts of the plant are used together this can offer a synergistic benefit, called the entourage effect.

One of the fascinating aspects of starting to use CBD is learning about its promiscuity in interacting with many different receptor types. CBD molecules interact with the receptors of the endocannabinoid system, but there are many other targets for CBD and receptor types that it interacts with. Many of us are learning about the endocannabinoid system for the first time – we were not taught about it at vet school, and doctors are not taught about it in medical school either, yet the endocannabinoid system has been identified in humans, animals and plants (although not in insects) and research is uncovering that this system plays an important role in health and homeostasis.²

So what is the endocannabinoid system?

The endocannabinoid system (ECS) is a complex, widely distributed regulatory system that provides essential mechanisms for maintaining the biologic balance and feedback throughout the body.³ Discovered in the early 1990s¹ through scientific studies of how molecules in the cannabis plant interact with receptors in human bodies, the system was named after the cannabis plant.

The ECS is made up of 3 components:

1. Cannabinoid receptors
2. Endocannabinoids
3. Enzymes

1. Cannabinoid receptors

Two main receptor types have been identified. Broadly, CB1 receptors are found throughout the nervous system and CB2 receptors are found throughout the immune system, though both receptor types are found throughout the body. Interestingly, CB2 receptors may increase up to 100-fold in inflamed or injured tissue, compared to normal, healthy tissue.

2. Endocannabinoids

After the discovery of exogenous plant cannabinoids, scientists isolated endogenous cannabinoids, or endocannabinoids, naturally produced by the body. These endocannabinoids are made on demand from lipid precursors in cell membranes. The two main endocannabinoids that have been identified are anandamide (AEA) and 2- arachidonoglycerol (2-AG) which interact with the orthosteric or active site of the cannabinoid receptors, based on a key and lock analogy.

3. Enzymes

Various enzymes are required for the activation, transportation, and degradation of endocannabinoids.

In a simplified explanation of how components of the ECS interact; endocannabinoids are produced on demand, particularly in times of stress, injury, or disease. They bind to cannabinoid receptors present throughout the body in an attempt to regulate cell-signaling and bring back balance and homeostasis.

While humans have been cultivating cannabis for use in ancient medicine practices for more than 5000 years, we are only just beginning to fully understand these mechanisms of action. Discovering the ECS and how plant molecules interact with this system but also how cannabinoids interact with opioid, dopamine and serotonin receptors is fascinating. It is not dissimilar to the history of penicillin where almost four decades passed between the discovery of its antibiotic

properties by Alexander Fleming in 1928 and the final elucidation of its mechanisms in 1965.⁴ The evolution of research on this topic means that curious-minded clinicians can continue to learn about the endocannabinoid system and medicinal cannabis and pet patients today can access many potential therapeutic benefits that this plant has to offer.

References:

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