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KEY POINTS

- ▶ The endocannabinoid system is an increasingly researched target of action that appears to be involved in target system homeostasis.
- ▶ Clinicians should be knowledgeable of the potential differences among *Cannabis sativa* products.
- ▶ Available research suggests there is great potential variation in product quality and pharmacokinetics between brands.

Hemp Oil & Cannabidiol: What Clinicians Should Know

Clinicians are likely seeing owners of pets that are receiving cannabidiol (CBD) supplements; thus, it is important for clinicians to be knowledgeable of hemp-based CBD products and how they work. CBD is increasing in popularity and is being used as an adjunct or alternative treatment option for a wide range of conditions in pets. This growing interest may be due to recent legal changes or an increasing understanding of CBD. Increasing marijuana use may have also contributed to this interest.

Definitions

Cannabis sativa is a plant that has been used for both medicinal and recreational purposes for centuries. Industrial hemp is the legal term for any strain of *Cannabis sativa* with <0.3% of Δ -9-tetrahydrocannabinol (THC), and marijuana is a strain of *Cannabis sativa* with greater THC content.¹

Cannabis sativa has chemical compounds known as phytocannabinoids and other phytochemicals (eg, terpenes, flavonoids). There are >100 different phytocannabinoids that have been identified and may be present in the different strains of *Cannabis sativa*.² The amount and type of phytocannabinoids present can be influenced by many factors, such as strain and growing location.³ Two well-known and researched phytocannabinoids are CBD and THC. These phytocannabinoids work in the endocannabinoid system (ECS) of the body, a newly discovered body system.⁴

The Endocannabinoid System

The ECS is a broad-spectrum system that acts as a modulator or regulator for many different body systems. It is also involved, to some degree, in most basic bodily functions. The overall guiding purpose of the ECS is to maintain a stable state (ie, homeostasis) in each system it is involved in.⁵

Endogenous compounds bind to ECS receptors throughout the body. Several ECS receptors have been identified, but CB1 and CB2 are the most well-known. CB1 and



CB2 are G protein-coupled receptors found in the cytoplasm of cells. CB1 receptors are most commonly found in the CNS, whereas CB2 receptors are primarily associated with immune cells, but both can be found throughout the body. The body synthesizes endocannabinoids, with the 2 best characterized endocannabinoids being anandamide (AEA) and 2-arachidonoylglycerol (2-AG). AEA and 2-AG, both endogenous endocannabinoids, are capable of acting as agonists or antagonists on their corresponding receptors. Phytocannabinoids that are not endogenous but plant-based (eg, CBD, THC) appear to alter the ECS system similarly to AEA and 2-AG either by directly binding to the cannabinoid receptors or through

a host of other receptors that regulate body responses (eg, appetite, behavior, inflammation).^{6,7}

Hemp Oil Variants

There are 3 main classifications of hemp oil in the market: isolate, broad-spectrum hemp, and full-spectrum hemp. An isolate is usually described as a product that isolates and contains a single phytocannabinoid, typically CBD. Broad-spectrum hemp oils are a group of extracted isolates like phytocannabinoids, terpenes, and/or flavonoids that are blended together with a carrier oil. Full-spectrum hemp oils contain all of the phytocannabinoid, terpenes, and/or flavonoids that are present in the plant. The “entourage effect” occurs when all of these components are able to work with each other to potentially provide additional or greater benefits than the phytocannabinoids and terpenes could provide individually.²

Hemp Oil Research

There are few published studies that have researched the safety, efficacy, and pharmacokinetics of hemp oil in dogs. Ongoing efficacy studies are evaluating hemp oil for possible use for other indications. Because not all hemp oil products are equal, selecting a product from a company with a known history of excellent quality control and assurance is crucial. In a recent study of commercial veterinary hemp products, only 23% (3/13) of hemp oil extracts met the levels stated on the label; the remaining 77%

(10/13) either made no label claim or contained less than what was stated on the label.⁸

Additional studies of the pharmacokinetics in both dogs and cats are also being performed at major veterinary universities. Auburn University has been conducting some initial pharmacokinetic research on Chroniquin, a full-spectrum hemp oil product.⁹ This initial pharmacokinetic research on Chroniquin was compared with the published pharmacokinetic data on other veterinary hemp oil products; Chroniquin was shown to provide a longer CBD half-life and higher serum concentrations of CBD 24 hours postadministration as compared with published data on other products, despite some of those products having administration rates up to 5 times higher than that of Chroniquin (2 mg/kg).^{10,11}

Conclusion

As the use of hemp oil products increases and more CBD-rich research is published, veterinary healthcare providers should become aware and knowledgeable of CBD products, as well as the laws and regulations regarding the legality of recommending CBD products in their area of practice. Clinicians should also be able to relay to pet owners the importance of selecting a safe, quality product from a trusted company for their pets. ■

References

1. United States Senate Committee on Agriculture, Nutrition, & Forestry. 2018 farm bill. United States Senate Committee on Agriculture, Nutrition, & Forestry website. <https://www.agriculture.senate.gov/2018-farm-bill>. Accessed January 10, 2020.
2. Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Br J Pharmacol*. 2011;163(7):1344-1364.
3. Andre CM, Hausman JF, Guerriero G. *Cannabis sativa*: the plant of the thousand and one molecules. *Front Plant Sci*. 2016;7:19.
4. Battista N, Di Tommaso M, Bari M, Maccarrone M. The endocannabinoid system: an overview. *Front Behav Neurosci*. 2012;6:9.
5. Grant I, Cahn BR. Cannabis and endocannabinoid modulators: therapeutic promises and challenges. *Clin Neurosci Res*. 2005;5(2-4):185-199.
6. Maccarrone M, Bab I, Biró T, et al. Endocannabinoid signaling at the periphery: 50 years after THC. *Trends Pharmacol Sci*. 2015;36(5):277-296.
7. Di Marzo V, Piscitelli F. The endocannabinoid system and its modulation by phytocannabinoids. *Neurotherapeutics*. 2015;12(4):692-698.
8. Nie B, Henion J, Wakshlag J. Analysis of veterinary hemp-based oils for product integrity by LC/MS. *Cannabis Sci & Tech*. 2019;2(3).
9. Boothe DM, Warner CG, Gillette R, et al. The disposition of cannabidiol (CBD) in dogs after single dose oral administration. Auburn, Alabama: The Society of Phi Zeta at Auburn University; 2019.
10. Bartner LR, McGrath S, Rao S, Hyatt LK, Wittenburg LA. Pharmacokinetics of cannabidiol administered by 3 delivery methods at 2 different dosages to healthy dogs. *Can J Vet Res*. 2018;82(3):178-183.
11. Gamble LJ, Boesch JM, Frye CW, et al. Pharmacokinetics, safety, and clinical efficacy of cannabidiol treatment in osteoarthritic dogs. *Front Vet Sci*. 2018;5:165.

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