

## Cannabidiol as a potential anti-epileptic dietary supplement in dogs with suspected epilepsy: three case reports

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### Summary

Epilepsy is the most common chronic neurological disorder in dogs and the almost lifelong administration of anti-epileptic drugs (AEDs) is recognized as the most successful treatment in veterinary medicine. Current pharmacological therapies for epilepsy have shown undesirable side effects. The dietary use of cannabidiol (CBD) in humans has shown therapeutic potential for the treatment of epileptic seizures. We administered CBD for 8 weeks to three dogs with epileptic seizures; decrease in the seizure interval was observed in two dogs, while one dog showed no improvement. Regarding the owners' impressions, one reported considerable symptom improvement, one that the symptoms improved, and one that the symptoms remained unchanged.

**Keywords:** keyword 1, cannabidiol; keyword 2, dog; keyword 3, epilepsy

## Introduction

Epilepsy is the most common chronic neurological disorder in dogs (Heske et al, 2013), and the almost lifelong administration of anti-epileptic drugs (AEDs) is recognized as the most successful treatment in veterinary medicine (De Risio et al, 2015). However, many potential adverse effects of AEDs, including polyphagia, sedation, restlessness, and polydipsia, have been reported (Charalambous et al., 2016). To achieve effective seizure control without reducing the quality of life of dogs with epilepsy, new treatment strategies are needed (Martlé et al, 2014). In humans, the dietary use of cannabidiol (CBD) is reported to reduce seizure frequency and duration (Devinsky et al, 2016); the serum levels of commonly used AEDs also increase with increasing CBD dose (Gaston et al, 2017). CBD, a phytocannabinoid compound derived from the cannabis plant, has been gaining attention as a potential anticonvulsant without the psychoactive effects seen with tetrahydrocannabinol (Gaston et al, 2017); however, these beneficial therapeutic effects have not yet been explored in dogs with epilepsy. Therefore, we conducted an open-label CBD study in three dogs with epileptic seizures to investigate the efficacy, tolerability, and safety of CBD.

## Case Description

Clinical and therapeutic history of Dog 1: The dog was a 3-year 2-month-old, 33-kg castrated male Labrador Retriever raised with 5 other dogs. The owner first noted episodes of seizure-like behavior when the dog was about 6 months old. During these episodes, the dog lay shivering on the floor with his head up; these bouts generally lasted several minutes. The dog had not received any AEDs. He had experienced 6 episodes this year, with an interval of approximately 30 days.

Clinical and therapeutic history of Dog 2: The dog was a 11-year 2-month-old, 4-kg castrated male Papillon raised with 3 other dogs. The owner first noted episodes of epilepsy when the dog was 3-years, 11 months old. Zonisamide (Consave, DS Pharma Animal Health Co., Ltd., Japan) 15 mg/kg, an AED, was administered twice daily for the last three years. The attacks were spaced about 2-3 months apart. During the CBD treatment period, the dog received only zonisamide 15 mg/kg twice daily. He also had urinary incontinence and salivation (foaming) as a result of the attacks.

Clinical and therapeutic history of Dog 3: The dog was a 10-year 2-month-old, 2-kg male Chihuahua raised alone by a family containing children. The owner first noted episodes of epilepsy when the dog was 3 years old. During these episodes, the dog lay on the floor shivering and salivating. He had experienced 2 episodes this year, and the intervals were irregular.

*Table 1. Cases in the study*

Case	Age years	Sex	Body weightkg	Breed	CBD trade name	Dosage (mg/kg/day)	AED
Dog1	2	M	33	Labrador Retriever	Hemp oil 1700	0.51	none
Dog 2	10	M	4	Papillon	Hemp oil 1000 (for first 5 weeks)	1.25	zonisamide
					Hemp oil 330 (for remaining 3 weeks)	1.24	zonisamide
Dog 3	9	M	2	Chihuahua	Hemp oil 1000	5.00	none

*Table 2. Seizure interval. Seizure dates during the administration period are boldface.*

Case	CBD administration period	Seizure date	Seizure interval (days)	Owners' impressions
Dog 1	2018/6/26 - 2018/8/21	2018/6/14		improved
		<b>2018/8/8</b>	55	
		<b>2018/8/11</b>	3	
		2018/8/26	15	
		2018/9/3	8	
Dog 2	2018/6/18 - 2018/8/14	2018/4/22		unchanged
		<b>2018/6/26</b>	65	
		<b>2018/6/27</b>	1	
		<b>2018/6/28</b>	1	
		<b>2018/6/29</b>	1	
		<b>2018/8/10</b>	42	
		<b>2018/8/11</b>	1	
		<b>2018/8/12</b>	1	
Dog 3	2018/6/11 - 2018/8/10	2018/5/5		considerably improved
		2018/5/8	3	
		<b>2018/7/11</b>	64	

## Treatment

Each dog received a plant-derived formulation of natural CBD-containing full-spectrum hemp extract, Pet Releaf Hemp Oil (Peat Releaf LTD, U.S.A.), in organic coconut oil. CBD was administered in two divided doses (12 hourly) on an empty stomach. The efficacy, tolerability, and safety of CBD were assessed every 2 weeks for 8 weeks.

Outcomes of CBD treatment and owner perception (Dog 1): The male Labrador Retriever received CBD at 0.51 mg/kg/day. The dog had 2 epileptic attacks during the 8-week treatment course. After withdrawal of CBD, an epileptic attack occurred within 5 days. The owner reported that the dog slept longer and barked less in the daytime, even when other dogs were excited, during the first 2 weeks than in the preceding weeks. Overall, the owner felt that the dog showed improvement.

Outcomes of CBD treatment and owner perception (Dog 2): The male Papillon received CBD at 1.24-1.25 mg/kg/day. The dog had 8 epileptic attacks during the 8-week treatment course. During the first 2 weeks, the owner reported that the dog ate more willingly. It was also noted that the dogs settled down and slept longer during the day. Overall, the owner's impression was unchanged.

Outcomes of CBD treatment and owner perception (Dog 3): The male Chihuahua received CBD at 5.00 mg/kg/day. The dog had only 1 attack during the 8-week treatment course. The owner felt that seizure-like behavior during the attacks had decreased slightly with treatment. The owner also reported that the dog showed less aggression toward familiar people, such as the owner's children.

This study was approved by the Committee for Institutional Animal Care and Use of Yamazaki University of Animal Health Technology (Permission number: 20180630-002) and carried out according to the guidelines of the committee.

## Discussion

In this study, the seizure frequency improved considerably and owners reported a positive impression. In humans, the mental factors implicated in epileptic seizures have been successfully treated with behavioral interventions (Martinovic, 2001). Mental stress, such as anxiety, can influence seizure episodes. Blessing et al. reported that CBD has considerable potential for treatment of multiple anxiety disorders in patients with epilepsy

(Blessing et al., 2015). This anxiolytic effect may attenuate the symptoms of epilepsy in dogs as well as humans. Further research is needed for better understanding the neurobiological mechanisms of CBD treatment. This study has several limitations. First, the number of dogs was small and the owners may not be representative of all epileptic dog owners. Dogs with more severe epilepsy phenotypes may be administered AEDs. To investigate the potential interactions of CBD with AEDs, further research is needed.

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