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# The Use of Cannabidiol-Rich Hemp Oil Extract to Treat Canine Osteoarthritis-Related Pain: A Pilot Study

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### Abbreviations

ADLs	Activities of daily living
CBD	Cannabidiol
NSAIDs	Nonsteroidal anti-inflammatory drugs
OA	Osteoarthritis
THC	Tetrahydrocannabinol

### Abstract

The objective of this 90-day pilot clinical trial was to assess the impact of a full-spectrum product containing hemp extract and hemp seed oil on dogs with chronic maladaptive pain. A total of 37 dogs diagnosed with chronic maladaptive pain primarily as a result of osteoarthritis were enrolled in the study. The dogs were given an initial physical examination that included systematic pain palpation, mapping of pain patterns, informal gait analysis, metabolic profile, and owner interview. The same palpations and mappings were performed during each biweekly assessment to identify trends, chart progress, and inform dose adjustments. The metabolic parameters were repeated at the end of the study. Of the 32 dogs that completed the study, 30 dogs demonstrated improved pain support. Of the 23 dogs in the study that were taking gabapentin at the

time of enrollment, 10 dogs were able to discontinue the gabapentin, and an additional 11 dogs were able to have their daily dose reduced with the addition of the cannabidiol (CBD) oil. *Conclusion:* The addition of a hemp-derived CBD oil appears to positively affect dogs with chronic maladaptive pain by decreasing their pain, thereby improving their mobility and quality of life. The reduction in gabapentin dose may be the result of changes in analgesia and/or sedation with the addition of the hemp oil extract.

### Introduction

Laws in the United States surrounding cannabis have undergone tremendous changes over the last several years. In 2018, the US government enacted the Agriculture Improvement Act of 2018, which removed hemp from Schedule I of the federal Controlled Substances Act. Hemp

is a form of *Cannabis sativa* L with low levels (<0.3%) of tetrahydrocannabinol (THC). The federal act authorized the states to seek approval from the USDA to have primary regulatory authority over hemp production within the state by preparing and submitting a state plan of regulation to the secretary of the USDA (1). Subsequently, the state of Colorado (the location of the current study) passed a bill in May 2019 stating that “Colorado leads the nation in public policy supporting the hemp industry and is poised to continue that leadership with the passage of the federal ‘Agricultural [*sic*] Improvement Act of 2018’” (2).

Due to the myriad of laws concerning cannabis and only recent changes in the legal status of hemp, there is little empirical research regarding the veterinary use of cannabis products (3). Yet many pet owners are increasingly willing to try cannabis products to help their pets with a wide array of medical and behavioral issues (4, 5). Some of the benefits of cannabis products reported by pet owners include improved mobility in animals with osteoarthritis (OA) as well as reduced anxiety, pain, and occurrence of epileptic seizures (5, 6). When pet owners were asked to compare cannabis products to other forms of medication or therapy, the majority (93%) reported that cannabis products work better than other treatments (only 7% felt that cannabis does not work as well) (6). When asked about side effects, these pet owners most frequently reported sedation and overactive appetite.

Despite the interest by pet owners, however, the lack of scientific studies has made veterinarians reluctant to initiate cannabis-related conversations with their clients. In addition, state laws legalizing medicinal and/or recreational forms of cannabis do not apply to animals. The laws surrounding the use of cannabis products, including hemp products, in veterinary medicine are complex and evolving. One study found that 85% of veterinarians rarely or never initiate conversations about cannabis (3). Similarly, very few advise (73% either never or rarely), recommend (83% either never or rarely), or prescribe (91% either never or rarely) cannabis products, with a lack of knowledge being the most common reason (3). With the changing laws, however, clinical trials are now permitted. This paper outlines one such study.

Many pet owners and veterinarians working with animals suffering from OA-related pain desire an alternative to traditional medications (nonsteroidal anti-inflammatory drugs

[NSAIDs], gabapentin, etc). NSAIDs, as well as other drugs such as gabapentin, are sometimes inadequate in relieving OA-related pain and come with potential side effects, especially for geriatric patients (7). The facts that the endocannabinoid receptor system is involved with pain modulation and cannabis has antihyperalgesic and anti-inflammatory properties have made cannabidiol (CBD) an attractive option to explore for the reduction of canine pain (8, 9). CBD is a component of cannabis, which is derived from the hemp plant and is low in psychoactive THC. One clinical trial conducted with dogs suffering from OA found that CBD oil increased the canine subjects’ comfort and activity levels and decreased their pain without side effects (7). This study emphasized, however, that different strains of cannabis contain different amounts of cannabinoids, including CBD, making the results difficult to generalize (7). For this reason, the current study was undertaken to continue the exploration of cannabis products’ effects on dogs suffering from OA-related pain. This pilot study had 4 objectives: (1) to determine if this particular hemp-derived CBD product could positively influence pain relief and overall function in dogs experiencing chronic maladaptive pain from OA; (2) to determine if it would be well tolerated and accepted by the enrolled dogs; (3) to observe any potential effects on the doses of pain-related medications already in place for the dogs; and (4) to identify an appropriate dosing range to facilitate improved pain management in dogs suffering from chronic maladaptive pain.

## Materials and Methods

A total of 37 dogs were enrolled in this 90-day pilot study. All of the enrollees suffered from chronic maladaptive pain, primarily as a result of OA. All but 5 of the dogs were patients of a specialty clinic in animal pain management in Colorado prior to participating in the study. Of the 37 enrolled dogs, 32 dogs completed and had their final assessment at 90 days, and 5 dogs did not complete the study due to their medical conditions or their owners’ life/schedule changes. Specifically, changes in 1 owner’s schedule precluded her ability to participate in the reassessment appointments; 1 dog was diagnosed with a bleeding splenic tumor and was euthanized; 1 dog developed an iris mass and the ophthalmologist recommended withdrawal from the study; 1 dog was diagnosed with an osteosarcoma and was withdrawn; and 1 dog’s pre-existing liver and kidney disease progressed, and she was therefore withdrawn from the study.

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To minimize the potential for inconsistencies among multiple observers, all enrollments and assessments were conducted at the same hospital by the same veterinarian (RD). Independent observations from the owners played an important role in how these patients were managed, providing feedback on the efficacy of increasing the hemp oil extract and decreasing the gabapentin dose. Descriptive statistics and paired *t* tests were conducted in SPSS (IBM SPSS version 25) for changes in pain, ALKP, and ALT. Statistical significance was set at  $P < .05$ .

Eligible canine subjects and their owners met the following criteria: dogs with chronic pain from OA for at least 3 months in duration; owners who desired trying a CBD product to manage their dogs' pain; owners who could commit to a 90-day study with dogs' medical assessments every 2 weeks; owners who were willing to keep an informal journal of their dogs' activities of daily living (ADLs) using the Cincinnati Orthopedic Disability Index (see **Appendix 1** p. 44) as a guide during the duration of the study to better understand the impact of the CBD product; and owners who agreed not to use any medications or supplements during the 90-day course of the study unless approved by the veterinarian performing the assessments.

The owners of the enrolled dogs consented to have the data generated during the study anonymously aggregated for evaluation, statistical analysis, and publication at a future date. Likewise, they consented to a review of their dogs' complete medical records to ensure that all inclusion criteria were met. This study was classified as exempt by the institutional review board at Colorado State University.

Several specific pain-directed medications and therapies were excluded during the 90-day study. With the limited study population and in order to create as consistent a "baseline" as possible, the use of NSAIDs was restricted from all participants. The intention was to have NSAIDs available only as a "rescue" therapy for individuals whose pain could not be relieved with the CBD product under investigation. In addition, none of the patients enrolled in the study were taking tramadol or amantadine at the commencement of the study, and to minimize extraneous variables, the addition of tramadol or amantadine during the course of the study was disallowed. Finally,

to limit some of the inherent variability in a study of this nature, study participants were limited to a single physical medicine modality. Because several participants were receiving medical acupuncture for neurologic support (rather than for pain management) at the time of enrollment, the decision was made to not withdraw acupuncture support from their treatment protocols in order to avoid compromising these patients.

Specific pain-directed medications that were permitted during the 90-day study included gabapentin and polysulfated glycosaminoglycan (a). Most of the dogs enrolled in this study were under the care of a veterinary pain management expert and were already taking gabapentin as part of a multimodal pain management strategy. Taking into consideration the phenomenon of rebound pain in response to an abrupt withdrawal of gabapentin, it was determined that dogs already taking gabapentin would be able to continue their dosing, but any new prescriptions of gabapentin were disallowed during the course of the study.

Specific pain-directed therapies that could possibly be permitted during the 90-day study pending approval included medical acupuncture, therapeutic laser, and nutraceuticals. These therapies were evaluated on a case-by-case basis. Although these therapies can alter the degree of pain and may have affected the results, the intent of the study was to determine the role of the hemp oil extract as an adjunct in the management of chronic pain. In this group of patients, chronic pain was managed using a multimodal approach, and the authors were interested in determining the role of the hemp oil extract in the presence of other therapeutic modalities.

The initial assessment of the dogs enrolled in this study included a full physical examination and informal gait analysis. The physical examination consisted of a systematic pain palpation and mapping of pain patterns. The same palpation and mapping were performed during each biweekly assessment to identify trends, chart progress, and inform dose adjustments. A metabolic profile, including a CBC, serum chemistry profile, and a screening thyroid profile, to evaluate organ system function and to provide a baseline for future comparison were performed on each enrollee. These same metabolic parameters were repeated at the end of the study. The informal gait analysis consisted

of observing the dog, with the owner as the handler, at a slow walk, a fast walk, and a trot. The dogs were in an inside hallway approximately 40 feet in length, moving first away from and then toward the observer (RD). Lameness was noted as to limb and severity. In addition to identifying lameness, the purpose was to gain insight into each patient's ability and willingness to move at various speeds and to note any changes over the course of the study. No force plate or film analysis was conducted. Informal assessment of the dogs' ease and willingness to move was one aspect of evaluating their quality of life. Initial assessment also included a detailed interview with each dog owner to discuss the dog's ADLs and quality of life as well as the owner's desired outcome goals for the dog.

At the initial evaluation and enrollment, qualified dogs received a CBD oil product at a dose of 0.25 mg/kg delivered on food QD for 3 days and then morning and night (approximately every 12 hours). The product given was a certified organic, cold-pressed hemp seed oil infused with 1,000 mg of full-spectrum hemp extract derived from organically grown hemp plants, cultivated in Colorado. Full-spectrum extract includes cannabinoids (such as cannabidiolic acid, CBD, cannabigerol, cannabichromene), flavonoids, terpenes, and other constituents within the cannabis plant (see Cannabinoid Profile in **Appendix 2** p. 45).

Pain assessments of each participant were conducted every 2 weeks during the 90-day study and consisted of a systematic pain palpation and pain pattern mapping, informal gait analysis, and review with each dog's owner of the previous week's ADLs and owner observations as recorded in the owner's log. The CBD dose was adjusted as needed in response to the new assessment. CBD dose escalations of 0.5 to 0.75 mg/kg approximately every 12 hours were prescribed at each reassessment until the patient's pain score on palpation was 0 to 1 on a scale of 10. Each modified dose of the CBD product within that dose escalation range reflected a volume that was easy for the owner to measure. The primary goal was to achieve acceptable comfort without inducing sedation. Although sedation is a known potential side effect of CBD ingestion, the sedation may be occurring as a result of low levels of THC in the formula, not the CBD (10).

Each patient's overall pain severity was scored using a 0 to 10 scale, with 10 representing the worst possible pain. This overall pain score alongside the pain map was used to guide CBD oil dose adjustments. The pain map recorded anatomic locations that were reactive to systematic palpation. This pain palpation technique has been described in detail (11). In addition, for the dogs taking gabapentin for chronic maladaptive pain at the time of study enrollment, once their comfort level was stable following CBD dose escalations, gabapentin dose reductions were attempted. Gabapentin dosing varied from 10 to 40 mg/kg delivered every 8 to 12 hours, depending on the needs of the individual patient to achieve adequate pain relief without inducing sedation. At times, deescalating the gabapentin dose changed the dosing interval from every 8 hours to every 12 hours or from every 12 hours to every 8 hours, depending on the total dose per day, ease of achieving the required dose based on currently available strengths of gabapentin, and ease of dosing with respect to the owners' schedules. The gabapentin dose was reduced by 20% to 40% of the total daily dose based on the reduction amount that would provide the easiest dose delivery (for instance, reducing a dog's dose from 1,200 to 900 mg per day, which would reduce the daily dose by 300 mg). The new dose was maintained until the next assessment. If a dose reduction was too great (defined as increased pain noted in the following pain reassessment), the dose would be increased to the previous level. These dose reductions were a way to assess the ability of the CBD oil to reduce the required dose of gabapentin to support the dog's comfort level.

## Results

A total of 32 dogs completed the study, with only 2 dogs deemed by their owners and supported by the veterinary assessments to have achieved no measurable improvement in pain with the addition of the CBD oil. The final CBD dose used in the 2 "non-responders" was 2 mg/kg every 12 hours. These dogs' overall mobility and comfort did not change during the course of the 90-day study, with their overall pain scores remaining at 1/10. It is unclear why they seemed to show no changes with the addition of the CBD product. The 30 remaining dogs represent a variety of breeds with an average weight of 23.2 kg (range: 5–50 kg) and average age of 10.9 years (range: 2–16.6 years) (**Table 1**). All 30 dogs demonstrated improved pain

**Table 1. Patient Characteristics of Dogs With Chronic Pain Enrolled in CBD Trial**

Patient #	Breed	Age (years)	Sex	Weight (kg)
<b>Existing patients</b>				
1	Border collie	8.9	FS	25
2	German shepherd	8.2	FS	31
3	Rhodesian Ridgeback	11.9	FS	38.6
4	Rhodesian Ridgeback	2	FI	38
5	Labrador retriever	12.8	MN	34
6	Labrador retriever	12.8	FS	25
7	Maltese	13.3	FS	5
8	Labrador retriever	13.5	MN	40
9	American pit bull terrier	10.3	MN	28.5
10	Australian shepherd	13.3	MN	10.4
11	French bulldog	5.75	MN	13.6
12	Bichon frise/cocker spaniel	14	FS	9
13	Scottish terrier	16.6	MN	11.8
14	German shepherd	12.9	MN	43.2
15	Shepherd/chow	12.1	FS	21
16	Great Dane	9	FS	50
17	King Charles spaniel	8.1	FI	8
18	Beagle	13.25	MN	10.2
19	King Charles spaniel	8.8	MN	10
20	American pit bull terrier	6.3	FS	27.3
21	Australian shepherd	11.4	FS	27.6
22	Peke-a-poo	15.5	MN	8.2
23	Beagle	9.8	FS	10.5
24	Labrador retriever	8.4	MN	41
25	Border collie X	13.7	FS	27
26	Dachshund (standard)	10.2	FS	5.5
<b>New patients</b>				
27	Shiba Inu mix	14.25	FS	11
28	Pit bull	5.25	FS	27
29	Australian shepherd	13.25	FS	26
30	Labrador retriever	11.6	FS	33
Patients were either existing or new patients to the clinic for the treatment of chronic pain.				
<b>Abbreviations:</b> FI, intact female; FS, spayed female; MN, neutered male.				

support, with their pain scale score decreasing from an average of  $3.2 \pm 2.2$  (mean  $\pm$  standard deviation) to  $0.97 \pm 0.81$ , or an average change of  $-2.23 \pm 2.3$  (Table 2). Of the patients, 7 patients had no change in their overall pain scores, starting and ending the study with pain scores of 1. These 7 dogs started the study with gabapentin as a part of their pain management protocols, and their gabapentin doses were reduced and comfort was retained. Of the 23 dogs that were taking gabapentin at the time of enrollment, 10 dogs were able to discontinue taking gabapentin after the addition of the CBD oil to their pain management protocols. Of the 13 dogs in the study that were taking gabapentin when they were enrolled and were unable to discontinue gabapentin by the end of the study, 11 dogs were able to have their daily dose of gabapentin reduced with the addition of the CBD oil; 5 enrolled dogs received no gabapentin during the course of the study.

Of the 30 dogs deemed to benefit from the addition of CBD oil to treat their chronic maladaptive pain, all ended the study with an overall pain score ranging from 0/10 to 2/10 (Table 2). Of these 30 dogs, 6 dogs experienced an improvement in their overall pain scores of 5 or better: 2 dogs' scores reduced from 8/10 to 1/10; 2 dogs' scores reduced from 7/10 to 1/10; 1 dog's score reduced from 6/10 to 1/10; and 1 dog's score reduced from 5/10 to 0/10.

Among these 30 dogs, the dose of CBD needed to achieve a positive effect ranged from 0.3 up to 4.12 mg/kg BID. The 2 dogs in the study requiring the highest dose of the CBD product were both Cavalier King Charles spaniels (not related to one another), and neither of these dogs experienced any changes/elevations in liver enzymes. It is unclear why some patients responded to a very small dose of the CBD product (0.3 mg/kg per dose), whereas the majority required dosing in the range of 1 to 2 mg/kg per dose. This wide dosing range suggests that practitioners must approach CBD use for chronic pain in dogs with the intention of following these patients carefully during their initial treatment in order to fine-tune the CBD dose to meet the needs of the individual. As an analogy, it is a well-known phenomenon in human pain management that individuals can have very different requirements of opioids to control pain. Further studies of CBD use in dogs for chronic pain may facilitate a better understanding of variable needs among individuals. The majority,

**Table 2. Starting and Ending Numeric Rating Score, CBD Dose, and Gabapentin Doses in a Clinical Trial of Dogs Receiving CBD for the Treatment of Chronic Pain**

	Pre	Post	Change
Numeric Rating Score*	3.2 ± 2.2	0.97 ± 0.81	-2.23 ± 2.3
CBD dose (mg/kg)	0.31 ± 0.04	1.67 ± 0.09	1.36 ± 0.88
Gabapentin dose (mg/day)**	1,846 ± 1,756	710 ± 1,112	-1,263 ± 1,314

\*NRS ( $t = 5.35, df = 29, P < .001$ ); \*\*Gabapentin ( $t = 5.12, df = 29, P = .001$ ).

Data are presented as mean ± standard deviation.

Abbreviations: *df*, degrees of freedom; NRS, Numeric Rating Scale.

or 19, of these dogs ended the study with a dose ranging between 1.2 and 2 mg/kg BID.

Among the study’s dogs taking gabapentin that experienced a dose reduction (but not a withdrawal of gabapentin), the final doses varied from 20% to 60% of the original dose. The dogs taking gabapentin at the time of enrollment had been taking gabapentin for a time that ranged from 3 months to 10 years.

The only clinically meaningful change in blood parameters obtained was an increase in ALKP (Table 3). Interestingly, there was a slight decrease in ALT between the beginning and end of the study, but it was not statistically significant (Table 4).

During the course of the study, the dog owners shared their subjective impressions of their dogs’ responses to the CBD oil. These impressions included observations of increased energy and stamina for daily activities. Quotes from clients include: “She’s more like a puppy”; “He is acting like a much younger dog”; and “I haven’t seen him play like this

for a long time.” Additionally, several of the dog owners reported noticing that their dogs were more attentive, animated, and mentally engaged after starting the CBD oil. During the study, gabapentin was decreased ( $n = 11$ ) or eliminated ( $n = 10$ ) for 21 dogs. Many of these dog owners reported that their dogs subsequently slept less, which translated into more interaction time with the family. Our results could not differentiate the reason for less sleep in these patients: a reduction in gabapentin-induced sedation, improved analgesia from the hemp oil extract, or both. Overall feedback from 94% of the owners ( $n = 30$ ) indicated they felt their dogs’ quality of life had improved after starting the CBD product.

## Discussion

Increasing interest in hemp-derived CBD products for pain relief in dogs, coupled with minimal research demonstrating safety and efficacy to date, prompted this pilot study to examine the potential role of a CBD oil as a strategy for managing chronic maladaptive pain in dogs with OA. Of the 32 dogs that completed the study, 30 dogs demonstrated benefits from the addition of this hemp-derived

**Table 3. Changes in Liver Enzymes (ALKP) in Dogs With Chronic Pain Receiving CBD in a 90- Day Trial**

Starting ALKP (U/L)	Ending ALKP (U/L)	Change in ALKP (U/L)*
133.3 ± 118	264 ± 233.2	130.8 ± 135

\*ALKP ( $t = -5.22, df = 28, P = .001$ ).

Biochemistry values were obtained before beginning the clinical trial and at 90 days.

Abbreviation: *df*, degrees of freedom.

**Table 4. Changes in Liver Enzymes (ALT) in Dogs With Chronic Pain Receiving CBD in a 90- Day Trial**

Starting ALT (U/L)	Ending ALT (U/L)	Change in ALT (U/L)*
93.5 ± 69.3	91 ± 60.4	-2.5 ± 43

\*ALT ( $t = .31, df = 29, P = .76$ ).

Biochemistry values were obtained before beginning the clinical trial and at 90 days.

Abbreviation: *df*, degrees of freedom.



CBD oil. Outcome benefits included decreased pain scores, improvements in mobility, and improved quality of life as defined by their owners.

A total of 23 dogs in the study were taking gabapentin as part of a multimodal pain management protocol. Of the total, 10 dogs (43.5%) were able to discontinue their reliance on gabapentin with the addition of CBD oil. Of the 13 dogs who continued to take gabapentin, 11 dogs were able to reduce the gabapentin dose necessary to retain comfort to 20% to 60% of the original dose. These results strongly suggest that a CBD product, at an appropriate therapeutic dose, may provide a gabapentin-sparing effect for dogs experiencing chronic maladaptive pain.

The dosing range for hemp-derived CBD oil suggested by this study reflects a similar range to that articulated by Gamble et al (study doses of 2 and 8 mg/kg, with anecdotal evidence suggesting efficacy as low as 0.5 mg/kg), implying that any potential variability among different hemp plant genetics may be overcome by demonstrating, via independent analysis, the presence and concentration of the active CBD molecule (7). Due to the variation in concentration from product to product of CBD content and constituents such as terpenes, cannabinoids, and flavonoids, it is essential to publish an analysis of the product being tested in order to describe that specific cultivar.

Interestingly, ALKP, but not ALT, increased significantly during the 90-day trial. In a study to investigate CBD hepatotoxicity, 8-week-old male B6C3F1 mice were gavaged with CBD in an acute and subacute toxicity model. In both models, mice developed signs of hepatotoxicity with evidence of cholestatic changes (12). The doses used in that study were significantly different from doses used

in the current study. Nevertheless, it is worthwhile to note the potential for hepatotoxicity as a result of an accidental overdose. There was no evidence of clinical hepatic disease in dogs in this study that received CBD; however, the changes in ALKP suggest the need for longer-term safety studies. The dog who was withdrawn from the study due to progressing systemic disease was determined via abdominal ultrasound to have a very advanced liver tumor that clearly predated the start of this 90-day study. His rapid decline in activity and quality of life prompted the ultrasound, which revealed the terminal neoplastic disease.

This study had several limitations. It was an open study with no placebo control group, and because a single individual assessed all patients in the absence of a control group, there was a potential for bias. In addition, the sample size was relatively small. Although the study subjects were understood to be similar in that they were all suffering from OA, OA and its resultant pain create individualized experiences among patients. In addition, the pain assessment and scoring of canine pain are subjective by nature. The investigators attempted to limit the subjectivity by having the study dogs evaluated and the owners interviewed by a single individual (RD) throughout the study. Future studies incorporating more objective assessments of pain, such as force plate analysis, are needed to quantify the amount of functional improvement associated with CBD products. Longer-term studies are needed to determine if CBD, in combination with other analgesics used to treat chronic pain, has deleterious effects on liver function.

In summary, this study provides the foundation for future research into the beneficial use of CBD products, delivered at therapeutically relevant doses, to mitigate chronic maladaptive pain in dogs with OA.

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## Endnote

a. Adequan®, American Regent Animal Health, Shirley, NY 11967

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## References

1. Agriculture Improvement Act of 2018, S 3042, 115th Cong (2018). <https://tinyurl.com/SB3042>.
2. Hemp Regulation Alignment With 2018 Federal Farm Bill, S 19-220, 72nd Leg, 1st Sess (CO 2019). <https://tinyurl.com/COLeg19-220>.
3. Kogan L, Schoenfeld-Tacher R, Hellyer P, Rishniw M. US veterinarians' knowledge, experience, and perception regarding the use of cannabidiol for canine medical conditions. *Front Vet Sci*. 2019;5:338.
4. Greb A, Puschner B. Cannabinoid treats as adjunctive therapy for pets: gaps in our knowledge. *Toxicol Commun*. 2018;2:10-14.
5. Hartsel JA, Boyar K, Pham A, Silver RJ, Makriyannis A. Cannabis in veterinary medicine: cannabinoid therapies for animals. In: Gupta RC, Srivastava A, Lall R, eds. *Nutraceuticals in veterinary medicine*. Switzerland: Springer International Publishing; 2019:121-155.
6. Kogan LR, Hellyer PW, Schoenfeld-Tacher R. Dog owners' use and perceptions of cannabis products. *J Am Holist Vet Med Assoc*. 2018;51:26-33.
7. 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.
8. Costa B, Giagnoni G, Franke C, Trovato AE, Colleoni M. Vanilloid TRPV1 receptor mediates the antihyperalgesic effect of the nonpsychoactive cannabinoid, cannabidiol, in a rat model of acute inflammation. *Br J Pharmacol*. 2004;143:247-250.
9. Nagarkatti P, Pandey R, Rieder SA, Hegde VL, Nagarkatti M. Cannabinoids as novel anti-inflammatory drugs. *Future Med Chem*. 2009;1:1333-1349.
10. Brutlag A, Hommerding H. Toxicology of marijuana, synthetic cannabinoids, and cannabidiol in dogs and cats. *Vet Clin North Am Small Anim Pract*. 2018;48:1087-1102.
11. Downing R. Managing chronic maladaptive pain. *NAVC Clinician's Brief*. Aug 2011:15-19.
12. Ewing LE, Skinner CM, Quick CM, et al. Hepatotoxicity of a cannabidiol-rich cannabis extract in the mouse model. *Molecules*. 2019;24:9.

# Cincinnati Orthopedic Disability Index (C.O.D.I.)

*From: Gingerich D-A, Strobel JD, Vet Ther 4:1 pp. 56-65, 2003*

**PATIENT-SPECIFIED QUESTIONNAIRE**—Please tell us what specific activities have become most troublesome to you or your dog

	(0) No Prob- lem	(1) A little	(2) Quite a bit	(3) Severe	(4) Impossi- ble
1.					
2.					
3.					
4.					
5.					

**STANDARD ORTHOPEDIC QUESTIONNAIRE**—How difficult are these activities for your dog?

	(0) No Prob- lem	(1) A little	(2) Quite a bit	(3) Severe	(4) Impossible
Walking					
Running					
Jumping					
Getting Up					
Lying Down					
Climbing Stairs					
Descending Stairs					
Posturing to urinate or defecate					

$$\text{Transformed Scale} = 100 - \frac{\text{Actual Raw Score} \times 100}{\text{Possible Raw Score}}$$

Date \_\_\_\_\_  
 CODI \_\_\_\_\_

## Appendix 2



# Cannabinoid Profile

**Customer:** HM Health  
**Customer Sample ID:** 0818A-1000  
**Laboratory Number:** 201809-0456  
**Extraction Technician:** MTO  
**Analytical Chemist:** GB  
**Density (g/mL):** 0.924

Extraction Date(s):	Analysis Date(s)
9/27/2018	9/27/2018

Cannabinoid (HPLC)		Results	
	LOD (mg/g)	Percent	mg/mL
Δ8-Tetrahydrocannabinol	<0.2		
Cannabidiolic acid (CBD-A)	<0.2		
Cannabigerolic acid (CBG-A)	<0.2		
Cannabigerol (CBG)		0.090%	0.84
Cannabidiol (CBD)		3.337%	30.83
Cannabidivarin (CBDV)	<0.2		
Cannabinol (CBN)	<0.2		
(-)-trans-Δ <sup>9</sup> -tetrahydrocannabinol (THC)		0.133%	1.23
Tetrahydrocannabivarin (THCV)	<0.2		
Cannabichromene (CBC)	<0.2		
Δ9-Tetrahydrocannabinolic acid A (THC-A)		0.122%	1.13
<b>Cannabinoids Total</b>		<b>Percent</b>	<b>mg/g</b>
<b>Max Active THC</b>		<b>0.24%</b>	<b>2.40</b>
<b>Max Active CBD</b>		<b>3.34%</b>	<b>33.37</b>
<b>T. Active Cannabinoids</b>		<b>3.56%</b>	<b>35.60</b>
<b>Total Cannabinoids</b>		<b>3.68%</b>	<b>36.82</b>
<b>Ratios</b>			
<b>13.09 :1 CBD to THC</b>		<b>0.08 :1 THC to CBD</b>	

