Results Are In!

The Positive Behavioral Impact of a CBD-containing Nutraceutical Formulation on Privately-Owned Dogs

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SUMMARY

A broad-spectrum, CBD-nutraceutical blend, contained in a soft chew “dosage-form treat” was evaluated for its impact on behavioral considerations in client-owned dogs. A numerically scaled 20-item questionnaire was applied to 98 dogs recruited nationally. Participants completed the questionnaire before and after 14 days of administration of soft chews dosed by weight. Questionnaire results were analyzed for significant differences in subject behavior following the 14-day course of treatment. Significant differences showing improvement in the pre-treatment versus post-treatment scores were determined in questions regarding anxiety levels, destructive behavior, fear at the veterinarian office or groomers, hyperactivity and fear of meeting other dogs, fear of loud noises, thunderstorms, and car rides, as well as restlessness during the day or at night. Behaviors such as excessive scratching, issues with food or appetite, and separation anxiety were also evaluated. In each behavior evaluated, that behavior improved over the 14-day treatment period. Behaviors such as playfulness and calmness also increased after the 14-day treatment period, although without the same degree of statistical significance as the negative behaviors.

INTRODUCTION

Behavior problems in dogs account for the highest percentage of pet relinquishments to animal shelters. Many of those dogs relinquished are not able to be sufficiently rehabilitated to be readopted and are then subsequently euthanized (11). Cannabidiol (CBD) has anecdotally been reported to have a positive effect on behavior in the dog, but the single study published evaluating CBD compared to trazadone as an anxiolytic concluded that CBD was ineffective.(6)

The hypothesis of this open-label, questionnaire-based study is that a zero-THC, broad-spectrum, proprietary CBD extract blended with three nutraceuticals and one herb – all studied and known for their “calming” qualities – administered at a relatively low dosage based on weight, can improve canine behavior following only two weeks of daily administration.

The 20-item questionnaire was formulated to determine the impact of this proprietary formula on dog behaviors such as generalized anxiety, arousal with barking at doorbell ringing, separation anxiety characterized by nervous behavior or destructiveness, fear of car rides, fear of loud noises, fireworks or thunderstorms, nervousness at vet/groomer, disturbed sleep, hyperactivity, depressiveness, appetite and selectivity and caution toward food, scratching, fear/aggression of other dogs, and restlessness at night.

Paired-samples t-tests were used to determine whether there were significant differences between the pre- and post-treatment survey scores from the 98 canine participants. Results were tabulated and summarized through tables and charts.

METHODS

Animals

Dogs owned by private individuals were recruited through a website-based company[1] providing a guide to local pet services in four major metropolitan centers: Chicago, Denver, Minneapolis-St Paul, and Seattle. Forty-eight thousand dog owners in this company's database were contacted by email. Interested individuals were then sent a qualifying survey to determine eligibility to participate in this study. Exclusion criteria included age less than one year or taking prescription medication. Over-the-counter (OTC) medication use was allowed, except for products containing CBD. Survey participants were instructed to discontinue any CBD supplements for two weeks prior to completing the pre-evaluation survey to allow for a washout of the effects of prior CBD administration before initiating the two-week treatment phase of this study.

Test Material

The proprietary[2] formulation of these soft chews contains a THC-reduced, broad-spectrum CBD-dominant extract of hemp flowers (*Cannabis sativa* L.), blended into a soft-chew matrix with tryptophan, choline chloride, phosphatidylcholine, and German chamomile (*Matricaria chamomilla*) extract.

Per Chew Active Ingredients:	
Tryptophan	50 mg
Choline chloride	50 mg
Phosphatidylcholine	25 mg
German Chamomile	15 mg
Broad Spectrum Hemp Extract	3 mg

Recommended administration of these chews by weight	
< 25 pounds	½ chew twice daily
25-50 pounds	**1** chew twice daily
> 50 pounds	**2** chews twice daily

Study dosing was based on numerous anecdotal private communications with this author[3] from veterinarians and pet owners regarding their observations that behavior-based responses to CBD were judged effective in the lower dosing ranges averaging approximately 0.25 mg/kg BID (twice daily) of CBD. A higher dosage of 2 mg/kg BID has been found to be effective for the discomfort associated with osteoarthritis in the dog in two peer-reviewed published studies.(2)(5)

[1] Sidewalk Dog Media Group; www.SideWalkDog.com
[2] Okoa "Hush Puppy" Calming Chews; www.OkoaPet.com
[3] RJ Silver DVM, MS

The authors predicted that the inclusion of supportive nutraceuticals and herbs previously shown to promote calming nutraceutical neurotransmitter production (such as tryptophan, choline, and phosphatidylcholine) would have a strong synergistic effect with cannabidiol to orchestrate behavioral effects on participants in the study.

SURVEY

A 20-question survey detailing dog owner perceptions of their pet's behavior and mood was administered to dogs owners. The survey was constructed with a visual 0-10 sliding scale for the participants to record their answers to the questions based on their observations and impressions. Choosing "0" indicated no improvement, and choosing "10" denoted a lot of improvement. Criteria for selection included: 1) a desire to participate in the study, 2) their dog was not receiving any prescription medication for any reason, and 3) their dog was not currently on a CBD product. Of 102 dogs initially recruited, 98 dogs met the criteria for inclusion in this study.

The pre-survey was conducted in January 2021 before the canine participants were administered the dog chews. Following two weeks of twice-daily administration of the chews (0.25 mg/kg CBD), participants were instructed to complete the survey a second time to evaluate the efficacy of the treats in having an impact on the dog's behavior and mood.

The resulting data was analyzed using a paired t-test to determine if the change in survey scores from before administration to after two weeks of administration was found to be statistically significant.

DATA ANALYSIS

A two-way frequency table was generated to compare the weight and age of dog subjects included in the analysis. For each of the 20 behavioral questions involving a numerical scale answer, a paired-sample t-test was conducted as a repeated-measures design to compare the pre-treatment and post-treatment survey results.

As part of the paired-sample t-test, paired sample statistics were generated for each pre-treatment and post-treatment question. Significance (p-values) was recorded from a two-tailed test. Statistical analyses were performed using SPSS Software.[4]

[4] SPSS Software; version 27.0 (IBM Corp., Armonk, NY, USA)

RESULTS

Table 1 shows the proportion of dog subjects analyzed in the observational survey by weight and age. Of the 98 subjects included, the largest proportion of dogs were between 2-5 years and 25-50 lbs. The fewest number of dogs were 0-2 years compared to every other age category, and only seven dogs were over 75 lbs.

TABLE 1: TWO-WAY FREQUENCY TABLE OF SUBJECT WEIGHT AND AGE.

	< 15lbs	15-25lbs	25-50lbs	50-75lbs	> 75lbs	Total
0-2 years	0	0	0	4	0	4
2-5 years	3	8	18	9	4	42
5-8 years	5	3	10	6	1	25
8-10 years	4	3	4	3	2	16
> 10 years	1	2	2	6	0	11
Total	13	16	34	28	7	98

Table 2 contains the pre- and post-treatment means, standard deviations, t-test values, and p-values indicating which values were significantly different when comparing the pre-treatment survey mean scores to the post-treatment survey mean scores. P-values greater than 0.05 did not meet the threshold for significance, and have been marked in red.

TABLE 2: SURVEY PRE-TREATMENT AND POST-TREATMENT AVERAGE SCORES.

Q#	Corresponding Survey Question	Pre-Treatment (Mean ± SD)	Post-Treatment (Mean ± SD)	t	df	p-value
1	My dog is anxious during a thunderstorm.	5.265 ± 3.735	3.439± 3.318	6.159	97	P<.0001
2	My dog is upset by loud noises.	6.510 ± 3.054	4.224 ± 2.768	9.520	97	P<.0001
3	My dog barks intensely when someone comes to the door or rings the doorbell.	7.163 ± 3.267	5.265 ± 3.158	6.844	97	P<.0001
4	My dog is nervous when I get ready to leave the house.	5.643 ± 3.547	3.439 ± 3.153	8.365	97	P<.0001
5	My dog is destructive when left alone.	2.786 ± 2.919	1.153 ± 1.885	5.988	97	P<.0001
6	My dog panics when riding in a car.	3.980 ± 3.443	2.378 ± 2.856	7.367	97	P<.0001
7	My dog is nervous when visiting the vet or getting groomed.	6.112 ± 3.287	4.061 ± 3.268	7.040	97	P<.0001
8	My dog does not sleep well.	2.459 ± 2.718	1.010 ± 1.489	5.316	97	P<.0001
9	My dog is hyperactive.	3.457 ± 2.986	1.897 ± 2.177	5.874	97	P<.0001
10	My dog is depressed.	2.469 ± 2.710	1.245 ± 1.675	5.312	97	P<.0001
11	My dog is happy.	7.449 ± 2.006	7.776 ± 2.023	-1.454	97	P= 0.149
12	My dog is mostly calm	4.847 ± 2.476	5.388 ± 2.547	-1.987	97	P= 0.050
13	My dog is playful	6.163 ± 2.720	6.673 ± 2.436	-2.112	97	P= 0.037
14	My dog always seems hungry.	5.367 ± 3.444	4.133 ± 3.409	4.236	97	P<.0001
15	My dog is a picky eater.	3.204 ± 3.364	1.867 ± 2.794	5.144	97	P<.0001
16	My dog is anxious.	6.786 ± 2.796	4.837 ± 2.746	7.702	97	P<.0001
17	My dog frequently scratches his/her skin.	3.990 ± 3.430	2.367 ± 2.726	5.494	97	P<.0001
18	My dog is afraid when meeting other dogs.	4.265 ± 3.267	2.469 ± 2.488	6.837	97	P<.0001
19	My dog is aggressive when meeting other dogs.	4.071 ± 3.420	2.286 ± 2.573	6.192	97	P<.0001
20	My dog wakes me up in the middle of the night.	3.031 ± 3.075	1.224 ± 1.831	6.064	97	P<.0001

Survey results showed that participants reported a decrease in a particular dog behavior for 17 of the 20 questions analyzed after two weeks of administration of the CBD-Nutraceutical chews, compared to before taking the chews (Table 2). These 17 behaviors were associated with anxiety, fear, appetite, itching, sleep patterns, reactions to other dogs/people, and situational reactions to the vet/groomer and riding in a car. A matched pairs t-test found these 17 decreases from pre- treatment to post-treatment to be very significant (df = 97, p<.0001).

The remaining three questions – namely questions 11-13, which pertained to mood or state of mind – showed that participants reported an improvement (increase) in those states of mind (Calm, Happy, Playful). A matched pairs t-test found Question 12 and 13 to be significant (p = 0.05 and p = 0.037, at an α= 0.05). The increase in question 11 was not found to be significant, t(97) = -1.454, p = 0.149.

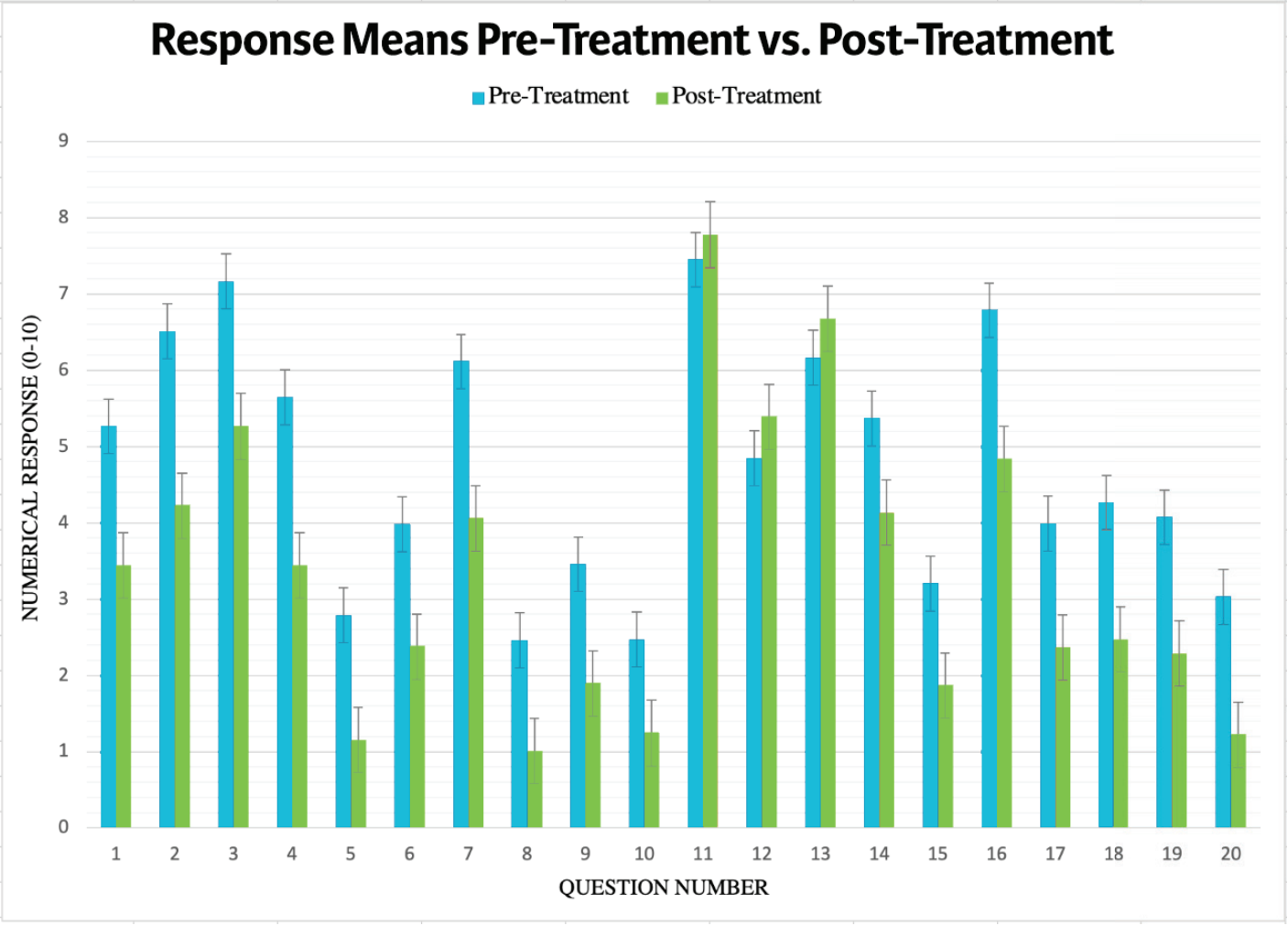

Figure 1: Response means pre-treatment vs. post-treatment. Fig. 1 shows the mean reported score of participants before taking the CBD-nutraceutical chew and the mean score after administration for two weeks for each of the 20 questions analyzed. Error bars show a 95% confidence interval around the mean.

The paired bar graph in Figure 1 illustrates the significant changes pet owners reported in their dogs' behavior before taking CBD-Nutraceutical chews (bars shown in blue) compared to after two weeks of taking the chews (bars shown in orange). All significance tests were run at a 95% confidence interval, shown with error bars around the mean. Questions where the error bars do not overlap numerically from pre-treatment to post-treatment represent reported changes that were found to be statistically significant. All of the questions dealing with problematic dog behavior (#1-10, #14-20) were found to be highly significant where every post-treatment score was less than the pre-treatment score. Two of the remaining questions (#12, #13) about the mood of the dogs were also found to be significant. However, while questions 12 and 13 were found to be significant, the differences from pre- to post-treatment were not as drastic as the questions pertaining to dog behavior. Question 11 was the only question where differences from pre- to post-treatment were not found to be significant at an α level of 0.05.

DISCUSSION:

This survey-based study with 98 canine subjects examined the effects of a proprietary CBD-nutraceutical blend on 20 dog behaviors. The results demonstrated with a great deal of statistical significance that adverse behaviors as well as positive moods can be enhanced in 19 of the 20 behaviors and moods surveyed with a low-dosage administration of these dog chews.

Though the results of this study have many positive implications, the study also has its own limitations. Due to the observational nature of this study, results cannot be compared to a placebo product. Additionally, all results rely on pet owner observations of behavioral changes which allows for potential bias in the evaluation of the pet owner responses. However, the fact that a large sample group (n=98) was used and still resulted in high statistical significance does provide assurance that these results reflect the actual effect of the test material.

A recent study assessed dog owners' perceptions regarding the use of psychoactive compounds such as CBD. This study concluded that pet owners were most comfortable using CBD and other psychoactive compounds for the treatment of their dogs' behavior problems if the pet owners had their own positive personal experience with these types of medications.(12) This effect on the owners based on their own subjective experience indicates the potential for a placebo effect in this current study. For pet owners, the placebo effect in this questionnaire-based study would be due to their hope that their dogs are benefiting as they did with their own use of psychoactive medication. As a result, this placebo effect may have had an influence on the pet owners' answers.

At this point in time, this is only the second published study examining the relationship between CBD, nutraceuticals, and dog behavior. Future studies of this nature should include a placebo group to further reduce the potential for bias in the results.

Both the negative and positive dog behavior traits were measured to have much higher statistical differences than the single mood question of "happiness." For mood and attitude, such as happiness, differences in pre- and post-treatment were much more difficult to observe due to the subjectiveness of this parameter. "Playfulness" and to a lesser extent "calmness" are both associated with physical activity that could be more objectively noted

and thus more likely to result in an observed difference following the administration of the test material.

It is important to note that some questions on the survey ask for changes of easily observable behavior, while other questions regard behaviors that can only be subjectively reported. To some extent the data reflect this difference between subjectively observed mood such as happiness and the more objectively observed positive behaviors of calmness and playfulness. It is likely that higher statistical significance on certain survey questions was due in part to pet owners' improved ability to observe certain pet behaviors over others. To address this limitation of the study, the authors suggest that future studies be conducted using only questions that focus on objectively observable behavior traits.

CBD has been recognized for the role it can play in managing anxiety, which is due to its effect on the endocannabinoid system that is present in all mammals. The endocannabinoid system is the biological target for plant cannabinoids such as CBD. The cannabis in the test material is a broad-spectrum hemp extract, meaning that it has no detectable THC and contains Cannabidiol (CBD) and other plant cannabinoids such as Cannabichromene (CBC), Cannabigerol (CBG), Cannabidivarin (CBDV), and Cannabinol (CBN). The hemp extract also contains cannabis plant terpenes such a linalool, which produces the calming effect of lavender essential oils. Terpenes, like cannabinoids, cross the blood-brain barrier and thus can exert an effect on behavior. The synergy among all of these constituents in the cannabis plant is termed the "Entourage" effect, which simply means that together they are more potent than any one individually. This effect has been borne out by research.(9)

The endocannabinoid system is a target for the pharmaceutical development of anxiolytic medications due to its role in modulating the connections between nerve cells (synaptic plasticity) and in inhibiting neuronal involvement in the anxiety response. CBD helps to maintain therapeutic blood levels of the body's naturally occurring endocannabinoids – N-arachidonoylethanolamine, (anandamide) and 2-arachidonoylglycerol (2-AG) – by reducing their inactivation. CBD has also been shown to signal the 5HT1a receptors, which are considered an important source of its anti-anxiety effects.(11)

Studies from animal shelters confirm that the majority of pet relinquishments that result in euthanasia are of dogs (or cats) with intractable behavior problems. It is possible that by helping to reduce anxiety-based negative pet behaviors, fewer animals might need to be euthanized at animal shelters.(10)

Currently there is a single published study in dogs that were research-bred, looking at the ability of CBD to be an anxiolytic, as compared to trazadone. This research compared the effects of CBD to the effects of trazadone but did not find any statistically significant value to the use of CBD to reduce anxiety and fear-based behaviors secondary to loud noises such as fireworks or gunshots. There were some design issues with this study, including the use of research Beagles versus client-owned dogs, that may have affected its ability to measure an anxiolytic value for CBD.(6)

In a study in laboratory animals, where the experimental models for anxiety are more controlled than the questionnaire approach in this current study, the anxiety-creating (anxiogenic) or anxiety-extinguishing (anxiolytic) effects of Δ^9-THC, CBDA, and CBD were evaluated using the light-dark emergence test in rats. THC was found to be anxiogenic, whereas both CBD and CBDA exhibited anxiolytic effects.(8)

The accessory nutraceuticals in this proprietary formulation also have a history and scientific evidence to support their role in modulating anxiety and reducing stress. Sunflower lecithin, which contains ~42% phosphatidylcholine, was found in a published double-blind, placebo-controlled study in humans to be non-toxic and effective in the treatment of mania in 5 out of 6 patients studied. Mania isn't anxiety, but it is an abnormal mental state. (3) In a second study, choline levels in a population of middle-aged and elderly men were found to be inversely related to anxiety, thus supporting the role that choline plays in reducing stress.(4) Choline and phosphatidylcholine are precursors for the neurotransmitter acetylcholine and provide structural and functional support for the nervous system, supporting healthy memory, hearing, and muscle tone.

The amino acid tryptophan is the direct precursor in the manufacture of serotonin in the brain and is included in this formula to ensure adequate production of this relaxing neurotransmitter. Tryptophan blood levels are directly associated with serotonin blood levels, since tryptophan is its precursor. Tryptophan is associated with anti-depressant activity and has also been found to decrease aggression.(13) In dogs, an association between serotonin levels and aggressive behavior has been studied, although the direct numerical relationship between serotonin levels and aggression has not been proven.(7)

German chamomile, on the other hand, has a centuries-old reputation for calming colic in infants and supporting a calm and settled state of mind. Several fractions of molecules found in the German chamomile plant have been found to bind to benzodiazepine receptors, thus producing a mild effect like the drug valium (benzodiazepine). GABA (gamma amino butyric acid – a calming neurotransmitter) has been detected in micromolar amounts in this herb, thus reinforcing its calming effect.(1)

Working together, these synergistic supplements augment each other's effect to produce a more substantial relaxation and a calm state of mind, as has been clearly indicated by the results of this study.

CONCLUSION

This study shows that two weeks of continued twice-daily, low-dosage administration of this proprietary CBD-nutraceutical blend of branded chews has the potential to decrease the negative dog behaviors characterized in the questionnaire, and to have a benefit in positive traits such as calmness and playfulness.

This questionnaire-based study of the impact of a CBD-nutraceutical blend on a number of aspects of dog behavior demonstrates that the anecdotal reports from veterinarians and dog owners about the beneficial effects of CBD on their pets have scientific merit.

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FINANCIAL DISCLOSURE

Robert J. Silver DVM, MS is the Veterinary Science Officer for **Okoa Pet** Products (www.OKOAPET.com) , who manufacture and distribute this calming treat.

Zipporah R. Abraham Paiss was paid by **Okoa Pet** Health to statistically analyze the results of this questionnaire-based study.

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