A pain treatment observational study using cannabidiol feed supplement in horses.

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Abstract

Joint swelling and pain effect horses health, performance, and temperament. Numerous studies confirm the safety and effacy of cannabidiol (CBD) to reduce inflammation and pain without adverse side effects in humans. CBD products are making their way into use to treat horse pain, mainly by individual animal owners. A proprietary 16-component, phytocannabinoid rich (PCR), CBD-based, dry powder feed additive was specifically formulated to treat horse pain. A fourteen-day, three group, ten horse preliminary study was conducted to assess: pain reduction, improved mobility, behavioral response, and changes in core temperature, appetite, urine coloration and manure output. Ten horses were selected, those exhibiting pain (n=8) and those not (n=2). Horses were then randomized into three groups; Group 1 (n=6) demonstrated pain, exhibited joint swelling and were treated, Group 2 (n=2) did not demonstrate pain, yet exibited limited joint inflammation and were treated, while Group 3 (n=2) demonstrated pain, exhibited join swelling, and were not treated (conrol group). Daily data collected by measurements and video included; temperature, joint stiffness, joint heat, visual inflammation, appetite, attitude, urine color, and manure output. All Group 1 horses exhibited reduced pain and increased flexibility favorable responses beginning on or around day-7, and were either flexibile or completely flexible without pain by day-10. All Group 2 horses, with no presenting original pain, exhibited reduced joint swelling and improved behavior. All Group 3 horses remained with chronic joint stiffness and pain. An unexpected beneficial response in one test horse was eradication of cresty neck mass, 60-pound weight loss, ceased loss of hair, and recuperated coat sheen. This limited study demonstrated total effectivity in pain reduction, improved mobility, and behavioral response, while also improving appetite, urine coloration and manure output, with no change in animal core temperatures.

Keywords: Cannabidiol, Pain, Behaviour, Inflammation, Joint Swelling, Horse

1. Background

Joint swelling and pain effect thousands of horses health, performance, and temperament. Numerous studies confirm the safety and effacy of cannabidiol (CBD) to reduce inflammation and pain without adverse side-effects in humans. Certain CBD products, available in tinctures, pellets, and balms, are currently used in limited settings to treat horse pain by individual animal owners. Clinical results are often anecdotal and not commonly available.

A phytocannabinoid rich (PCR) feed supplement was specifically formulated to reduce inflammation and treat horse joint pain that contains CBD, the active pharmaceutical ingredient (API). The powder mixture was designed as a single daily dose to be added atop the daily feed. The company that developed the feed supplement has extensive

experience in human and small pet PCR research and development, manufacturing, and sales. As this feed additive is a new and novel product and application, it was decided that a limited duration, observational clinical study should be conducted to examine safety and efficacy.

A regional horse farm located in Ocala, Florida boarding all ten study animals was selected, appropriate approvals were obtained from the owners. Data for this 14-day study was collected daily based on observation of primary and secondary end points. The study was to terminate for all subjects if there were any indications of adverse effects (e.g., increase temperatures, joint stiffness, etc.). The purpose of the study was to provide objective data based on subjective observational results for the safety and effectiveness of a PCR feed additive product intended to reduce inflammation and pain in active horses.

2. Materials and Methods

This study examined the safety and efficacy of new, first-pass metabolism, powder PCR based feed additive designed for pain reduction in horses, that also improved mobility and related behaviors. A fourteen-day, three group, ten horse observational study was conducted to assess specific pain related responses.

2.1 Feed Additive Product. A PCR feed supplement was specifically formulated to reduce inflammation and treat horse joint pain containing CBD plus an additional fifteen components added to enhance CBD's biphasic, synergistic effects. The amount and dose of CBD was determined based on an equivalent human to horse mg/kg basis, considering surface area ratios. The additional product components were selected for their known anti-inflammatory properties. A filler component was added to the product to insure adequate volume. Product was filled into single-dose, sealed mylar pouches totalling 25 grams each. All horse received one packet per day, 14 packets per horse, 140 total packets. The study subject packets contained the CBD treatment, while the control subject packets contained only filler. Feed packets were identical in appearance, packaging and labelling. Product was manufactured in Baltimore, MD and shipped directly to the study site in Ocala, FL.

2.2 Animal's Selected. Appropriate approvals were obtained for the ten (10) study horses that included; male (5), female (5), aged 6 to 27 (average=13). The breeds included Andalusian (3), Friesian (4), Quarter Horse (1), Rocky Mountain (2). The animal weights ranged from 900 to 1,100 pounds. All horses exhibited either joint stiffness, swelling, plus visible pain (n=8), or no visible pain but with inflammation and behavior issues (n=2).

Study Horse Demographic Data

	Breed	Gender	Age	Weight	Pain
Group 1	Friesian	M	11	1100	Yes
	Andalusian	M	14	1000	Yes
	Friesian	F	12	1100	Yes
	Andalusian	M	10	1000	Yes
	Andalusian	F	6	1000	Yes
	Friesian	F	12	1100	Yes
Group 2	Friesian	F	8	1100	No
	Quarter Horse	M	27	975	No
Group 3	Rocky Mnt	F	17	900	Yes
	Rocky Mnt	M	15	900	Yes

Of the eight with visible pain, two were selected at random to serve as control subjects. The remaining horses were treated and observed.

Number of Study Horses by Group

	Pain	No Pain	TOTAL
Treated	Gp1 (n=6)	Gp2 (n=2)	8
Untreated	Gp3 (n=2)	N/A	2

2.3 Dosing and Administration. A powder feed additive was chosen as the route of administration for commercial purposes. It is believed that a single dosed, dry-powder additive placed atop the daily feed that requires no mixing is the easiest, most effective means of dosing and administration. To date, the product used in this study is the only one of its kind.

2.4 Assessing Data. Certain data were measured (i.e., temperature, swelling reduction), while others were observational (i.e., joint stiffness, appetite, attitude, urine color, and manure output). To quantify the observed data, the authors applied a numeric scale to each subjective measurement.

2.4.1 Temperature. Taken daily, rectally, measured in degrees Fahrenheit. Temperature ranges for each horse, average temperatures for all horses, and the total deviation were compiled.

2.4.2 Joint Stiffness. Graded on 10-point basis using the following definitions. Complete flexibility (10) meant completely flexible joints, no visible pain, and no horse withdrawal. Flexible (8) meant flexibility without stiffness but moderate pain and some withdrawal. Stiffness (6) meant no movement, considerable pain, horse moved away. Very stiff (4) meant visible pain, joint hot to the touch, and the horse lifting foot/leg to

avoid pain. Extreme stiffness (2) meant visible pain, joint hot to the touch, and the horse laying down to avoid pain.

2.4.3 Joint Swelling. Inflamed and swollen joints were measured, the daily increase or decrease recorded. Due to the different animal sizes, a numeric value was given to correlate with the increase or decrease. These values ranged from "Increased" (8) to "Present" (6) to "Reduced" (4) to "None" (2).

2.4.4 Behavioral Responses. These were subjectively classified into three groups by the handlers who know the animals behaviors: "Hot Horse" (2), "Bad Horse" (4), and "Good Horse" (2).

2.4.5 Urine Color. As an easy visual indication for hydration, the urine color was noted daily. A numeric value of 4 was given for clear urine, while a numeric value of 2 was given for any yellow coloration.

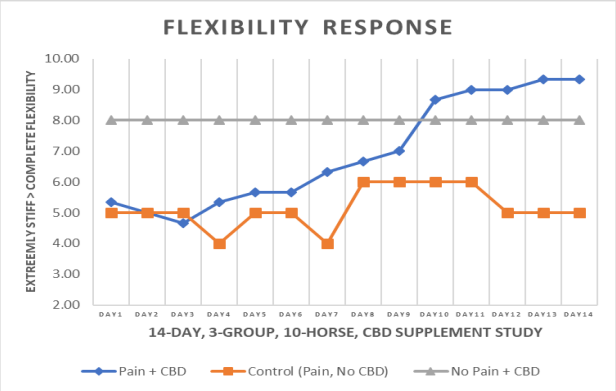
2.4.6 Appetite and Manure Output. These were given separate numeric scales but combined in the data analysis as related events. Appetite was given a numeric value of 2 if it was "good" and a 4 if it "increased." Manure output was given a numeric value of 2 if it was "normal" and a 4 if it "increased." Both the appetite and manure scores were combined to create a scoring scale from 2 (good appetite, normal manure output) to 6 (good of one measurement, increased of another) to 8 (increased both measurements). Numeric values were combined by group for graph analysis.

2.5 Data Collection and Compilation. Data was collected daily, in both written format, and video tape. It was entered in an MS Excel spreadsheet in verbiage format. For example, joint stiffness was recorded as; C-flex, Flex, Stiff, V-Stiff, or Ex-Stiff. When the data were analyzed, these were converted into numeric values, then compiled into respective groups, and plotted into various graphs and charts using MS Excel formats and functions. The video was/is used to corroborate findings and, when necessary, obtain consensus for evaluations.

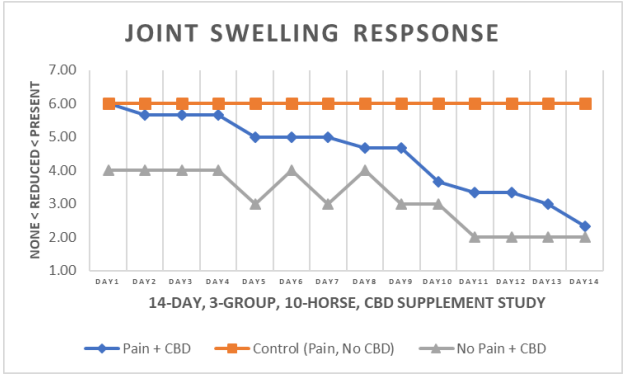
3. Results and Data Analysis

Data were compiled to examine the primary endpoints of reduced pain and increased flexibility, along with secondary endpoints of behavioral responses, appetite, and/or hydration increase/decrease, while monitoring daily core temperatures.

3.1 Flexibility Response. The Group 1 treated population exhibited an average 80% increase in flexibility (5 to 9), while the control group showed 0% change (5 to 5). The Group 1 horses were able to achieve "complete flexibility" whereas the Group 2 horses began the study "flexible" and remained the same (8 to 8). This suggests that responses are more pronounced in animals that begin treatment in pain and with greater stiffness.



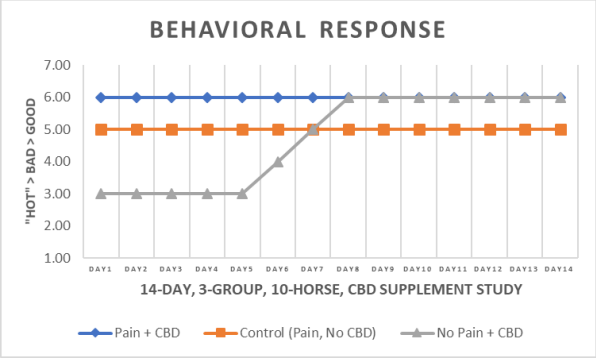
3.2 Joint Swelling Response. The Group 1 population exhibited an average 67% decrease in joint swelling (6 to 2), while the control group showed 0% change (6 to 6). The Group 2 population, although no increase in flexibility, exhibited an average 50% decrease in joint swelling (4 to 2). Both Group 1 and Group 2 horses joint swelling were reduced from visibly noticeable to "none."



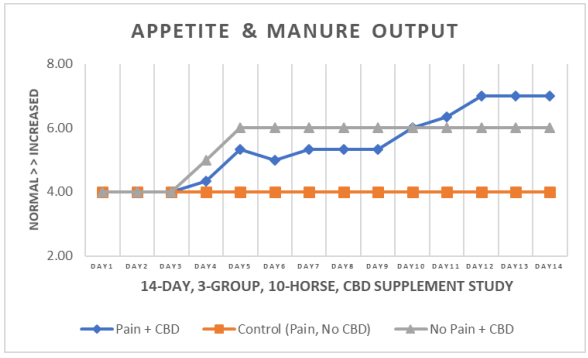
3.3 Temperature Results. This study presumed normal equine rectal temperatures of 98^0 - 101^0 F. The protocol precluded febrile horses (>103^0 F) from inclusion. It also mandated should any individual rectal temperature exceeded 106^0 F the study be suspended. Temperatures ranged from 98.2F to 101.2F, averaged 99.4F for all horses.

There was a high to low total deviation of 1.72F. The PCR feed additive had little to no effect on the study animal's core temperatures.

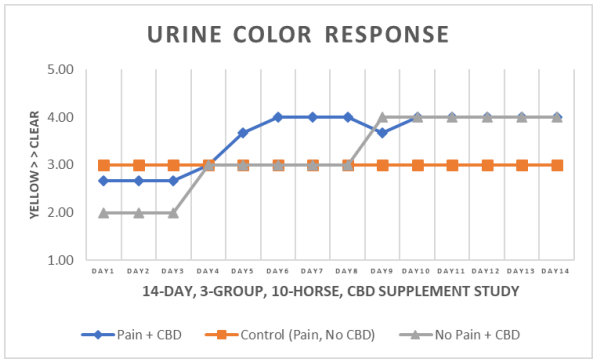
3.4 Behavioral Response. Of interest was the behavioral response in study animals that exhibited pain versus those that did not. While not intended as a product claim, the Group 2 horses, not initially exhibiting pain, attained and held a favorable behavioral response. One subject, initially labelled "hot," on or about day-6 was upgraded to "bad" then on or about day-8 upgraded to "good." The good behavior continued for the study duration.



3.5 Appetite and Manure Output. An inclusion criterion for all test subjects was "normal appetite, and bowel movements" as a caution against including horses with potential ulcerative stomachs. The Group 1 population exhibited an average 75% increase in appetite and manure output (4 to 7), while the control group showed 0% change (4 to 4). The Group 1 horses were able to achieve both "increased appetite" and "increased manure output" whereas the Group 2 horses achieved an increased appetite but not an increase in manure output.



3.6 Hydration. As a visual indication of adequate hydration, urine color was monitored. The Group 1 population exhibited an average 43% increase in hydration (2.8 to 4), while the control group exhibited 0% change (3 to 3). The Group 2 population exhibited the most significant change, a 100% increase (2 to 4). Both Group 1 and Group 2 horses exhibited improved hydration during the course of the study.



3.7 Additional Findings. Two unexpected beneficial responses occurred. Stringhalt was initially present, diminished until absent at day 10 as swelling in one horse went from very stiff to complete flexibility. In another horse there was total eradication of a cresty neck mass, in addition to a 60-pound weight loss, cessation of hair loss and a recovered coat sheen. These anecdotal data may indicate an improved thyroid condition. The authors make no curative claims whatsoever and include these findings solely for the purpose of disclosure.

3.8 Feed Supplement Taste. Horses consumed the feed supplement without issue. However, on days 4, and 7 two horses "ate around" the supplement: both in Group 1. Handlers added a small amount of water, the dissipated in the feed, the horses proceeded to eat the mixture. The manufacturer was notified, they intend to make minor additive changes to enhance the supplement flavor.

4. Conclusions

The data indicate a 100% favorable therapeutic response in a limited, 10-horse study to a newly developed CBD feed additive for relief of inflammation, joint stiffness and pain-related behaviors without evidence of any adverse or side-effects. In addition, in one horse, an unexpected beneficial thyroid-type response occurred. Feed additive is more easily administered than oral products. Based on these results the following follow-up studies are planned. 1) For humanitarian purposes, both Group 1 and Group 2 horses will remain on supplement indefinitely, and monitored collecting the same data over the next 30-days. 2) The Group 3 control subjects will be administred the feed supplement along with twenty new test subjects that will be randomized in the same way as this study. Pending outcome of the follow-up study, commercialization of this product is anticipated.

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Works Cited

1. **Ocean State Equine Associates.** Equine Metabolic Syndrome. [Online] 2019. http://www.oceanstateequine.com/client-education/equine-metabolic-syndrome/.

2. *Cresty Neck Prevalence, Risk Factors Evaluated*. **Janicki, Kristen.** s.l. : The Horse, 2015.

3. **Gupta, Ramesh C.** *Method for treating pain and inflammation associated with arthritis using chromium-three cation in combination with phyllanthus emblica and shilajit. US20140356466A1* USA, 2014.

4. *Understanding pain: the enigma of pain and suffering.* **Shenker, Nicholas and Blake, David R.** s.l. : Clin Med JRCPL, 2002, Vol. 2, pp. 574–7.

5. *Opioid-Sparing Pain Therapy in Animals: Working Task Force.* **Muir, W, et al.** San Diego : The American College of Veterinary Anesthesia and Analgesia, 2018. 5th International Veterinary Pain Short Course.

6. **Denapoli, Cynthia.** *Method of reducing stress and anxiety in equines. 10220061* USA.

7. *Development of the Horse Grimace Scale (HGS) as a Pain Assessment Tool in Horses Undergoing Routine Castration.* **Dalla-Costa, E, et al.** s.l. : Plos One, 2014.

8. **Animal Pain.** Unidimensional Scales. *Animal Pain.* [Online] 2012. http://animalpain.com.br/en-us/escalas-unidimensionais.php.

9. *Systematic pain assessment in horses.* **de Grauw, Janny C and van Loon, Johannes P.** s.l. : The Veterinary Journal, 2015, Vol. 209.

10. *Objective pain assessment in horses (2014–2018).* **van Loon, J and Van Dierendonck, MC.** s.l. : The Veterinary Journal, December 2018, Vol. 242, pp. 1-7.

11. *Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis.* **Hammell, D, et al.** 6, s.l. : Eur J Pain, 2016, Vol. 20, pp. 936–948.

12. *Measurement of articular cartilage stiffness of the femoropatellar, tarsocrural, and metatarsophalangeal joints in horses and comparison with biochemical data.* **Garcia-Seco, E, et al.** s.l. : Vet Surg., Nov-Dec 2005, Vol. 34, pp. 571-8.

13. *Thyroid hormones are important for growth, maturation of organ systems, and regulation of metabolism.* **Breuhaus, Babette.** Oct 2011, dvm360.

14. **Ramey, David.** Your Horse's Thyroid Gland. *David Ramey DVM.* [Online] February 15, 2017. https://www.doctorramey.com/horses-thyroid-gland/.

15. **Wag Labs.** Secondary Hyperthyroidism in Horses. *Wag*. [Online] 2019.

16. *Parameters of Thyroid Function in Serum of 16 Selected Vertebrate Species: A Study of PBI, Serum T4, Free T4, and the Pattern of T4 and T3 Binding to Serum Proteins.* **Refetoff, S, Robin, N and Fang, V.** 4, s.l. : Endocrinology, 1970, Vol. 86, pp. 793–805.

17. *Thyroid-Stimulating Hormone in Adult Euthyroid and Hypothyroid Horses.* **Breuhaus, Babetta.** s.l. : J Vet Intern Med, 2002, Vol. 16, pp. 109–115.

18. **Gaynor, J and Muir, W.** Alternative Drugs and Novel Therapies Used to Treat Pain. *Handbook of Veterinary Pain Management.* s.l. : Elsevier.

19. *Measurement of articular cartilage stiffness of the femoropatellar, tarsocrural, and metatarsophalangeal joints in horses and comparison with biochemical data.* **Garcia-Seco, E, et al.** 6, s.l. : Vet Surg. , 2005, Vol. 34, pp. 571-8.