CBD and Immune System Effects

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Introduction

CBD and its benefits have been touted for several years now. In the human field there are many more studies done but since there is growing interest in the use of CBD for animals, the research in veterinary medicine is starting to finally catch up.

CBD is known to act as an anti-inflammatory and immunomodulant agent, and the effects of CBD on immune responses can involve both innate (immediate) or adaptive (over time) responses (Atalay, Jaroka-Karpowicz & Skrzydlewska, 2019). In my own practice I discuss its advantages for anxiety, seizures, arthritis, and anti-tumor effects. Being that there are so many products on the market for both human and animal, my first discussion is on quality and safety.

Quality and Safety

Quality is considered by how the CBD is grown, processed, and formulated. Safety is considered by testing for heavy metals, pesticides and the multiple compounds found in a product. I personally look for organically grown plants, grown in controlled environments that have

reproducible genetics. The current most efficient and cleanest extraction process is supercritical CO2. It requires qualified personnel to run the equipment but is environmentally safe and manufacturers are left with full-spectrum CBD oil. Unfortunately, many small local producers use solvent extraction such as butane or hexane which end up with lower quality and contaminated oil. I advise my clients to always ask their local store if the product comes with a COA (Certificate of analysis). This is the documentation that shows the product has been tested for heavy metals and pesticides. Hemp is an amazing plant, and it has been shown to pull heavy metals from the soil up to five feet below the root growth. The hemp plant itself is also quite pest resistant but it is much easier for farmers to harvest when they don't need to separate the plant from weeds. Therefore, many hemp farms are sprayed with pesticides to decrease the extra work. If a producer is concentrating the CBD compounds, they will also be concentrating the heavy metals and pesticides. That is not good!

Clinical Use for Immune Support

I have been using CBD in my practice for over eight years now and have based the majority of my indications for use centered around human studies. Due to CBD's high safety profiles in humans and animals I felt comfortable recommending it for my patients. I've used it in conjunction with clinic treatments such as acupuncture, herbal, and ozone therapy as well as allopathic treatments such as anti-seizure and osteoarthritis medications and anti-anxiety and anti-cancer protocols.

A recent study on the effects of CBD on Canine inflammatory Response using LPS (lipopolysaccharides) stimulated whole blood showed a reliable model supporting its positive effects on both inflammatory

and anti-inflammatory responses (Gugliandolo et al., 2021). It feels validating to read that this recent canine study shows CBD's ability to stimulate anti-inflammatory cells and suppress inflammatory markers. The LPS in this study is used as an inflammatory stimulus to induce a reliable inflammatory response in the blood samples.

Effect of CBD on IL-6 and TNF-α Response in LPS Stimulated Whole Blood

Cytokines are the driving factors for inflammation and immune response. Two of the major pro-inflammatory mediators, IL-6 and TNF-α (Tumor Necrosis Factor), were used in this study. IL-6 overproduction is associated with a spectrum of age-related conditions including cardiovascular disease, osteoporosis, arthritis, type 2 diabetes, certain cancers, periodontal disease, frailty, and functional decline (Kiecolt-Glaser et al., 2003). TNF-α is involved in pathological processes such as chronic inflammation, autoimmunity such as asthma and, in apparent contradiction to its name, malignant disease (Balkwill, 2006). Being that both of these cytokines have enormous

effect with aging, my recommendation for CBD use in my geriatric and chronic disease patients has become part of my 'aging seniors' protocol.

In the study, the ELISA test showed when stimulated with LPS in the presence of CBD (at 50 and 100 µg/ml) a significant reduction in cytokine secretion. There was also a dose dependent effect of CBD; when compared to CBD 50 µg/ml, the dose of CBD 100 µg/ml produced a greater inhibitory effect on IL-6 and TNF-α release in whole blood supernatant (Gugliandolo et al., 2021). These results really add to the recommendations to my clients with adding CBD to chronic disease protocols.

Currently, I'm treating a FS 12-year-old terrier with a history of asthma and anxiety. Her owner has tried oral steroids with multiple negative side effects and inhalant steroids with administration failures (dog will not tolerate the inhaler over her nose.) I started her on daily CBD and within one month her asthma breathing episodes reduced to one to two a week from several a day. Her anxiety also reduced appreciably. Per the owner the dog would pace in circles in the kitchen, and it completely resolved within three weeks. Could it be the asthma improvement effected the anxiety… possible, but the dog is much happier, and the owner is quite thrilled with both outcomes.

Effect of CBD on IL-10 in LPS Stimulated whole blood

The role of IL-10 was interesting as its levels were not altered with CBD. What was observed was the TNF-α to IL-10 ratio shifted in the inflammatory phenotype. The results showed a significant increase in TNF-α to IL-10 ratio induced by LPS, while the CBD produced a significant decrease in the TNF-α to IL-10 ratio in a dose dependent manner (Gugliandolo et al., 2021). So, it appears that CBD does not increase IL-10 but improves its ability to reduce TNF-α inflammatory effects on the body.

I must say this information really supports the effects I see in my clinic. Even with my patients on a product that I don't have the production and testing information, there have been a plethora of improvements in their mobility, skin, and gastrointestinal issues. A 15-year-old FS grey tabby was referred to me with chronic miliary dermatitis and had been on a low dose of steroids for several years. On the steroids the formally sweet tabby was grumpy, and the rest of her hair coat had become thin and dull. The owner requested alternative options for the chronic steroid treatment. Her diet was changed to a home prepared diet, and she was started on CBD once daily. Within one month her gentle disposition returned and hair coat greatly improved in texture and color. She was slowly and successfully tapered off the steroid regimen.

Effect of CBD on Nf-κB and COX-2 Induction in LPS Stimulated Whole Blood

The last evaluation of the effectiveness of CBD on inflammatory pathways was through the evaluation of Nf-κB and COX-2 expression levels. Nf-κB activation has significant effects on the regulation of inflammatory response and in the regulation of many pro-inflammatory cytokines,

including TNF-α and IL-6. There was a significant increase in Nf-κB expression in the LPS group. Predictably there was a reduction in Nf-κB expression for the groups incubated with LPS and

CBD (50 μg/ml and 100 μg/ml) compared to the LPS-only group. Since COX-2 is known to be upregulated during inflammation, its mRNA and protein levels were also evaluated. COX-2 plays a fundamental role in the inflammatory cascade, and thus in acute and chronic inflammation. Additionally, it was observed for COX-2, significant increased levels of both mRNA and protein for the LPS group, while the treatment with CBD (50 μg/ml and 100 μg/ml) showed significantly lower COX-2 mRNA and expression compared to the LPS only group.

Over the past year I worked with a MN 13-year-old Doodle patient that had a hind toe removed due to a mast cell tumor diagnosis. Mast cells were then found in the dogs' spleen and liver. The owner came to me for my clinic's treatment protocol for cancer with ozone and microbiome transfer. The dog was on a short course of chemotherapy but did very poorly and the owner preferred a better quality of life for the dog if he could also still be treated for cancer. As I started his weekly treatments, I also added several supportive supplements. One of them being CBD to primarily treat his arthritis and increasing 'senior moments' at night. I felt NSAIDs were not an option due to the dog's liver cancer diagnosis. The CBD benefited his mobility and alleviated most of his evening nervousness. One of the surprising things I noticed was that his white blood cell count which had been quite low following his previous chemotherapy treatments was now normal and stable.

Conclusion

As we all know, chronic stress suppresses the immune system and being able to keep stress in check and not let it 'wind up' makes for happier pets and owners. Addressing anxiety is important to maintain wellbeing and a robust immune system in our patients. CBD is one of the first treatments I use to regulate anxiety behaviors in my patients. Unlike endogenous cannabinoids, which work on the CB1 receptor, CBD supplementation leads to direct activation of the 5-HT1A serotonin receptor (Crippa et al., 2011). CBD stress-relieving properties are also related to its ability to modulate cerebral blood flow in brain regions involved in anxiety including the amygdala, hippocampus, hypothalamus, and cingulate cortex (Soares & Campos, 2017).

As a first line treatment that has multiple benefits, it seems apparent and appropriate to me to use CBD in protocols for many diseases and issues. The more we learn about its effects on the immune system, CBD will hopefully become a standard protocol for veterinarians and physicians alike. I am disappointed in the lack of research and studies on CBD in veterinary medicine. It appears that its inopportune association with marijuana, saturation of the market with poor quality products and lack of material regulation has kept it out of the laboratories for significant and critical study. These would include well-controlled studies considering differences with administration routes, dose, and pharmacokinetics. The one major thing that everyone seems to appreciate is that it has a high safety profile. Personally, that gives me confidence to use it as a therapy for diseases for which other available treatments have not been effective.

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