

Research Findings Relating to Cannabidiol (CBD) and its Influence on Immune Function

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Our innate endocannabinoid system has been shown to act as a balancing mechanism for many body systems, including our immune system. Research is showing how plant based phytocannabinoids, such as cannabidiol (CBD) hold a unique potential to gently influence our body through the effects that they exert upon our endocannabinoid system.

Much of the research about natural cannabinoids and the influence they could have on cell mediated immunity focus on THC, the most abundant psychoactive compound found in *Cannabis*. THC has a high affinity for CB1 and CB2 receptors within the body. CB1 receptors are mostly found on neurons and CB2 receptors are located on immune cells. The second most abundant phytocannabinoid belonging to the *Cannabis* genus is the non-psychoactive CBD. Interestingly, the reason that CBD does not hold the same psychoactive effect as THC is because it “has a very weak affinity towards the CB1 and CB2” receptors in the body and therefore lack “CB1-mediated psychoactivity” (Kozela et al., 2016, p. 2). Recently, CBD has been gaining much interest as a potent immunomodulatory compound.

Research shows that CBD holds immune suppressive potential – this is particularly important when looking at the myriad of autoimmune diseases that fill scientific journals and medical textbooks. Autoimmune disease is driven by autoreactive memory T cells that receive a false message from antigen-presenting cells (APC) to target own cells. This self-attack can lead to tissue degeneration and eventual autoimmune disease. Studies show that CBD has prompted anti-inflammatory effects and ameliorated symptoms in animal models of (1) T cell mediated collagen-induced arthritis, (2) autoimmune diabetes, (3) autoimmune hepatitis, (4) autoimmune encephalitis, and (5) multiple sclerosis; an autoimmune disease “initiated by autoreactive T cells targeting myelin sheaths” (Kozela et al., 2016, p. 4). Although there are studies and clinical trials investigating how CBD can be used for immune-

related diseases, the exact mechanisms through which CBD acts on these antigen-specific memory T cells are not well explained, warranting further research (Dhital, Stokes, Park, Seo, & Kaplan, 2017).

A recent study published in 2016 sought to answer the question of how CBD acts to ameliorate clinical symptoms in those afflicted with autoimmune disease. The scientists wanted to better understand the gene networks mediating the regulatory effects of CBD in autoimmune T cells. Through microarray-based gene expression profiling, a technology that measures the expression of genes, the researchers described the “gene networks and intracellular pathways involved in CBD-induced suppression” of activated memory T cells (Kozela et al., 2016, para. 2). Research findings showed that CBD treatment exerts immunoregulatory effects through suppressing a large number of proinflammatory genes in activated memory T cells. Additionally, CBD was found to increase the number of interferons that are known to have an anti-proliferative effect on activated memory T cells. Certain transcripts including transcription factors, cytokines and chemokines were maintained at high levels in the presence of CBD, indicating that “CBD may promote the exhaustion of memory T cells” (Kozela et al., 2016, para. 3). Interestingly, the researchers stated that the addition of CBD caused an increase in the transcription of oxidative stress modulators that are known to hold potent anti-inflammatory benefits (Kozela et al., 2016). This study is important as it helps to better explain the mechanisms at a genetic and cellular level through which CBD acts on immune function.

A recent *in vitro* study using mouse splenocytes sought to determine how CBD acts on Interleukin-2 (IL-2) and transforming growth factor beta-1 (TGFB1) in response to low-level immunological stimuli. IL-2 is a cytokine that stimulates the growth and replication of disease-fighting immune cells. IL-2 plays an essential role in immune response as it works to stimulate the production of B lymphocytes (B cells) and T lymphocytes (T cells). IL-2 acts to prevent autoimmune disease by promoting the differentiation of a type of immature T cell into regulatory T cells, which in turn suppress other T cells that would otherwise be set to attack normal healthy cells in the body. TGFB1 is a protein that is found throughout the body and it regulates cell proliferation, differentiation and growth. TGFB1 is integral to wound healing, inflammatory processes and the prevention of tumor growth. In this preclinical study, the researchers found that “CBD [enhanced] IL-2 production in response to low-level T cell stimulation” (Dhital, Stokes, Park, Seo, & Kaplan, 2017, p. 25). IL-2 and

TGFB1 were detected intracellularly within 1 day suggesting that CBD stimulated the appropriate cytokine environment necessary for Treg development. Tregs are regulatory T cells and are responsible for modulation of the immune system, maintaining tolerance to self-antigens and the prevention of autoimmune disease (Dhital, et al. 2017).

Another preclinical study that was published in 2012 investigated the molecular mechanisms through which cannabinoids modulate T cell responses. Researchers found that under conditions of high stimulation, CBD suppressed cytokine production and under conditions of low stimulation, CBD enhanced cytokine production. Cytokines refer to any number of substances, for example interferon, interleukin and growth factors, all of which are secreted by cells of the immune system and work to trigger inflammation and respond to infection. In detail, the authors describe that CBD was found to have a dichotomous effect, either to suppress or enhance Interleukin-2 (IL-2) production in the mouse model under optimal or suboptimal stimulation, respectively. These research findings suggest that cannabinoids can impose differential effects dependent upon the specific immune stimuli. This result was consistent with previous studies that show how cannabinoids can act to suppress or enhance immune function, specific to disease process and body requirements (Chen et al., 2012). Overactive immune responses as seen with conditions such as multiple sclerosis, rheumatoid arthritis, lupus and even common allergies could show benefit from an immunosuppressive agent, such as CBD. In line with this reasoning, this preliminary research shows how CBD could also act to strengthen immune function, thereby showing potential advantages for those with compromised immunity.

The documented immunosuppressive potential of CBD is particularly exciting for people who experience chronic pain and inflammation related to an autoimmune process because as immune function is dampened, inflammation and pain are reduced. The consensus within the studies reviewed is that CBD has the potential to alter immune function. The exact mechanisms of how CBD exerts its effect on the immune system is not completely understood and more research is needed to fully shine a light on the complex subject of CBD and immunity.

References:

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