Scoping Review of the Immunomodulatory Effects of Cannabidiol: Effects within T cells

B.N. Rivera, A. Svetlik[1], W.D. Klaren, D.S. Wikoff, and R. G. Henderson
1 – Texas A&M University, College Station, TX

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Abstract:

A systematic mapping study recently published on cannabidiol (CBD) safety-related literature identified immunomodulatory effects of CBD as an area warranting further investigation. Additionally, immune effects have been identified by recent literature and regulatory reviews as a data gap or potential endpoint of concern for CBD consumer use. The current scoping review was conducted as an extension of the previous systematic mapping, to provide a starting point for evaluating the available literature on this topic. Of the literature published through June2021, 108 publications were identified based on potential immunological effects following CBD administration. Titles and abstracts were screened and tagged for different attributes relating to the immune system (i.e., type of immune cells, cytokines, immunological process). The three most frequently tagged attributes were related to TNF-α (21 studies), T cells (14 studies), and experimental autoimmune encephalomyelitis (EAE) a model for multiple sclerosis (10 studies). For full text review, the effects of CBD on T cells and EAE, at a cellular and biochemical level, was further investigated. Exclusion criteria for full text review included transcriptomic or pathway-focused studies, review papers, studies using CBD/THC mixtures, or conference abstracts. This resulted in nine studies for full-text review. Within these nine studies, two different subsets were identified. In the first subset, the effects of CBD *in vivo* (0-5 mg/kg/day) or *in vitro* (0-20 µM) with or without cellular activation were investigated. Results from these studies showed differences in immunomodulation of CBD depending on experimental conditions. An increase or decrease in IL-2, T cells, and Tregs were observed based on different exposure and model parameters. Immunomodulatory effects of CBD were observed through apoptosis of T cells or through suppression of specific immune response. In the second subset, the effects of CBD on *in vivo* (0-75 mg/kg/day) or *in vitro* (0-10 µM, 0-20 µg/mL) EAE models were investigated. Results from these studies were generally consistent showing reductions in neuroinflammation from CBD exposure. CBD was shown to ameliorate the autoimmune induced effects through suppression of T cell proliferation, reduced infiltration of T cells into the CNS, and lower expression of inflammatory cytokines. Results from this subset suggests that CBD has anti-inflammatory and anti-autoimmune effects, which are primarily mediated through suppression of T cell proliferation. Overall, this scoping review identified important aspects regarding immunomodulatory effects of CBD. Particularly, differences in observed effects may be dependent on model and exposure parameters. Given that recent regulatory attention has been focused on the potential adverse effects of CBD on the immune system, the beneficial effects also observed as part of this scoping review underscore the need for further evaluation of this endpoint. Generation of additional studies, as well as systematic evaluation including study quality and reliability of available data are needed to better understand how CBD interacts with the immune system and improve the evidence base for use in hazard-based decisions.