The Immunomodulating Effects of Delta-9 Tetrahydrocannabinol (THC) and Cannabidiol (CBD) In the Context of Infection

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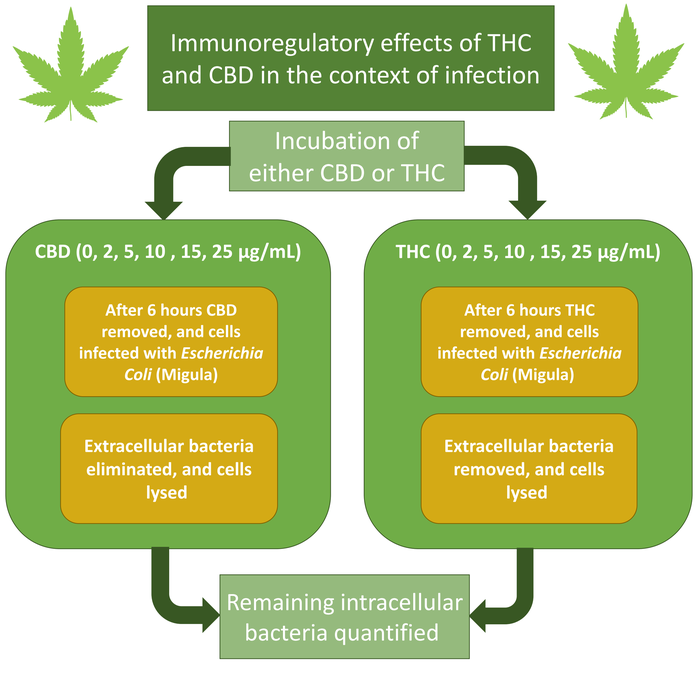
Introduction

The therapeutic potential of cannabinoid-based medicines has led many U.S. states and countries to authorize their clinical use. Delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD), the biologically active compounds of cannabis, possess a wide range of immune regulatory properties. Macrophages are specialized immune cells that express endocannabinoid receptors which can affect inflammatory phenotypes and phagocytosis. Developing broad awareness of cannabis has led to regulatory findings of various aspects of physiological, behavioral, and metabolic function; however, the effects on immunological regulation in the context of infection is less well understood. The purpose of the current study was to test the immunoregulatory effects of various THC and CBD doses in the context of infection. Secondary, THC and CBD temporal and tissue-specific cytotoxic effects were evaluated.

Hypothesis

CBD and THC will have different effects on immunoregulatory activities of macrophages, specifically phagocytosis, in an agonist or antagonist manner. Additionally, the effects of CBD and THC on cytotoxicity and cytokine release will correlate with macrophage functionality.

Materials and Methods



Results

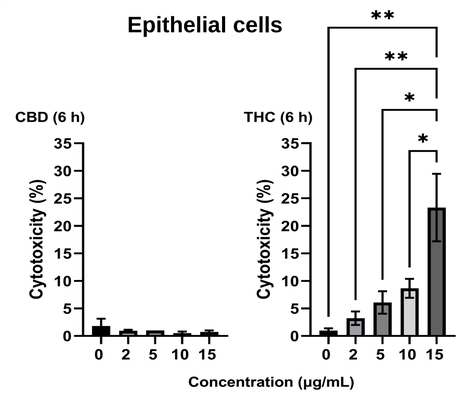


Figure 1: Cytotoxicity. Epithelial cells were treated CBD (left) or THC (right) for 6-hours. Supernatant was collected and LDH quantified. P = ≤ 0.05; ** (≤ 0.01).

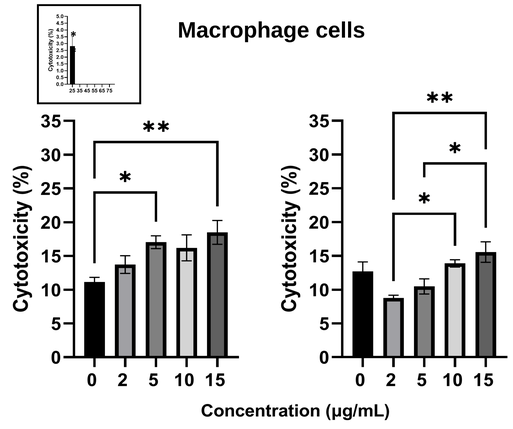


Figure 2: Cytotoxicity. Macrophage cells were treated with CBD (left) or THC (right) for 6-hours. Supernatant was collected and LDH quantified. P = ≤ 0.05; ** (≤ 0.01).

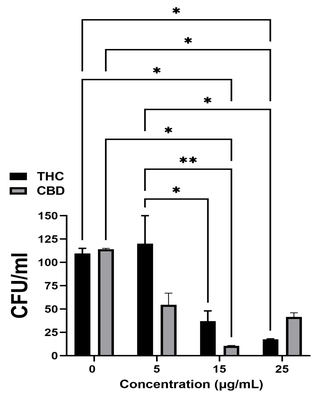


Figure 3: Live infection. Macrophage cells were treated with CBD or THC for 6-hours; treatment was removed, and cells infected (MOI 1:1) for 2 hours. Extracellular bacteria eliminated, cells lysed, and intracellular bacteria quantified. P = ≤ 0.05; ** (≤ 0.01).

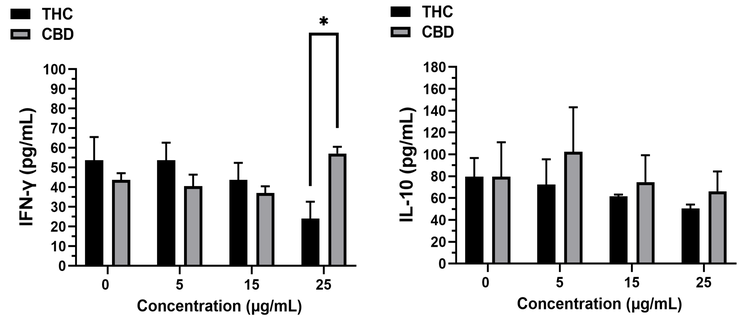


Figure 4: Cytokine analysis. Macrophage cells were treated with CBD or THC for 6-hours; cells infected (MOI 1:1) for 2 hours. Supernatant collected and analyzed by ELISA. P = ≤ 0.05.

Significant Findings & Conclusion

THC cytotoxicity against epithelial cells increases in a dose-dependent manner.

After a 6-hour exposure, THC is approximately 4-fold more cytotoxic to epithelial cells compared to CBD at 15 µg/mL.

CBD cytotoxicity against macrophage cells increases at lower doses (2 - 15 µg/mL) and decreases at higher doses (≥ 25 µg/mL)

After a 6-hour exposure, CBD is approximately 2-fold more cytotoxic to macrophage cells compared to THC at 15 µg/mL.

After a 6-hour exposure, CBD is approximately 3-fold less cytotoxic to macrophage cells compared to THC at 25 µg/mL.

INF-γ secretion is decreased in a dose dependent manner when cells are incubated with THC

In low doses CBD creates a decrease in cell function and cytokine release, however at high doses CBD increases cell function, and improves cytokine release

Future Directions

Testing different CBD and THC ratios in the context of infection.

Studying the endocannabinoid system and other cell types.

Test additional endocannabinoid receptor and intracellular cascade responses.