Medical Cannabis and Cannabinoids

Med Cannabis Cannabinoids 2022;5:36–60
DOI: 10.1159/000522395

Published online: March 10, 2022

6th International Medical Cannabis Conference (CannX 2022) Tel Aviv, Israel, March 14–15, 2022

Abstracts

Scientific Committee

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INHIBITION OF HEPATOCELLULAR CARCINOMA GROWTH AND LIVER FIBROSIS BY NANOMOLAR CANABINOID CONCENTRATIONS

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Background and Aim: Cannabinoids bind to the CB1 and CB2 receptors regulating the function of multiple organs and tissues of the body. Interestingly, cannabinoids also bind to the Gi protein associated A3 adenosine receptor (A3AR), up-regulated in inflammatory and tumor cells. Can-Fite research shows that A3AR agonists can knock down inflammation and cancer via the specific induction of apoptosis in these cells. The goal of the current study was to investigate the anti-growth effect of cannabinoids towards hepatocellular carcinoma and fibrotic in the liver and the molecular mechanism involved. **Methods:** Hep-3b hepatocellular carcinoma cells and LX-2 stellate cells were cultured for 48 hours in the presence and absence of 10 nM CBD-rich THC3/CBD15 (T3/C15) and the A3AR antagonist MRS1523. ^{3}[H]-thymidine proliferation assay, and Western blot analyses were performed. **Results:** CBD-rich T3/C15 significantly inhibited Hep-3b and LX-2 cell proliferation (56%± 5.5 ; $p < 0.05$ and 37.4%± 4.0 ; $p < 0.05$, respectively). This response was neutralized by the A3AR antagonist MRS1523. Growth regulatory proteins down-stream to A3AR activation, including p-Akt, NF- kappa B, GSK-3β and β-catenin were all down-regulated. **Conclusion:** Our findings highlight the ability of CBD-rich T3/C15 in nanomolar concentrations to inhibit the growth of hepatocellular carcinoma and liver stellate cells via A3AR activation and de-regulation of the Wnt/β-catenin pathway. The findings open a novel therapeutic opportunity in liver cancer and fibrosis with minute CBD concentrations and low content of psychotropic THC fraction.

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