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Beneficial effect of the non-psychotropic plant cannabinoid cannabigerol on experimental inflammatory bowel disease

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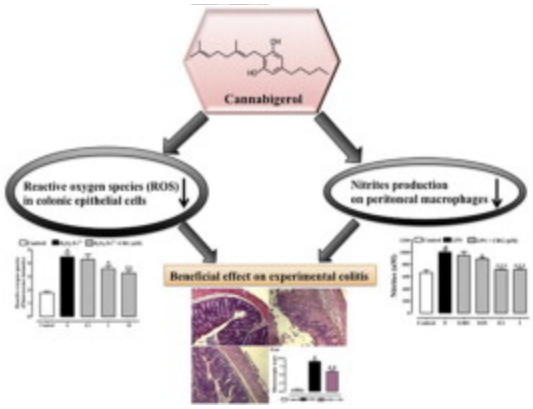
Abstract

Inflammatory bowel disease (IBD) is an incurable disease which affects millions of people in industrialized countries. Anecdotal and scientific evidence suggests that Cannabis use may have a positive impact in IBD patients. Here, we investigated the effect of cannabigerol (CBG), a non-psychotropic Cannabis-derived cannabinoid, in a murine model of colitis. Colitis was induced in mice by intracolonic administration of dinitrobenzene sulphonic acid (DNBS). Inflammation was assessed by evaluating inflammatory markers/parameters (colon weight/colon length *ratio* and myeloperoxidase activity), by histological analysis and immunohistochemistry; interleukin-1β, interleukin-10 and interferon-γ levels by ELISA, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) by western blot and RT-PCR; CuZn-superoxide dismutase (SOD) activity by a colorimetric assay. Murine macrophages and intestinal epithelial cells were used to evaluate the effect of CBG on nitric oxide production and oxidative stress, respectively. CBG reduced colon weight/colon length *ratio*, myeloperoxidase activity, and iNOS expression, increased SOD activity and normalized interleukin-1β, interleukin-10 and interferon-γ changes associated to DNBS administration. In macrophages, CBG reduced nitric oxide production and iNOS protein (but not mRNA) expression. Rimonabant (a CB_1 receptor antagonist) did not change the effect of CBG on nitric

oxide production, while SR144528 (a CB_2 receptor antagonist) further increased the inhibitory effect of CBG on nitric oxide production. In conclusion, CBG attenuated murine colitis, reduced nitric oxide production in macrophages (effect being modulated by the CB_2 receptor) and reduced ROS formation in intestinal epithelial cells. CBG could be considered for clinical experimentation in IBD patients.

Graphical abstract



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Abbreviations

CB, cannabinoid; CBD, cannabidiol; CBG, cannabigerol; CD, Crohn's disease; COX-2, cycloxygenase-2; DNBS, 2,4,6-dinitrobenzene sulphonic acid; H2DCF-DA, 2′,7′-dichlorfluorescein-diacetate; IBD, Inflammatory bowel disease; iNOS, inducible nitric oxide synthase; MPO, myeloperoxidase; ROS, reactive oxygen species; SOD, superoxide dismutase; UC, ulcerative colitis

Keywords

Cannabigerol; Phytocannabinoids; Inflammatory bowel disease; Murine colitis; Macrophages; Dinitrobenzene sulphonic acid

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