

The use of cannabinoids in colitis: a systematic review and meta analysis

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Introduction: The clinical use of cannabinoid drugs for the treatment of intestinal inflammation is anticipated secondary to preclinical experiments demonstrating their efficacy in reducing inflammation, in addition to the licenced use of cannabinoids drugs for epilepsy and multiple sclerosis.

Methods: We systematically reviewed existing publications on the use of cannabinoid drugs in intestinal inflammation in order to assess the existing literature. We collated controlled studies examining similar outcomes for meta-analysis.

Results: From a search of 2008 papers we identified 54 publications examining the effect of cannabinoid agents on experimental colitis in mice, rats and human tissue, and one clinical study examining the effect of THC in Crohn's disease. 24 cannabinoid agents were assessed across 108 experiments assessing 34 endpoints. 71 experiments favoured cannabinoids over vehicle, 33 were neutral and 4 negative. Macroscopic disease activity scores (DAS) and myeloperoxidase activity (MPO) were widely assessed throughout publications and therefore meta-analysed using random effects models. 27 publications investigated the effects of 23 cannabinoid drugs on MPO throughout 46 individual experiments (n= 781). Cannabinoid drugs reduced MPO in comparison with vehicle; SMD -1.26, 95% CI -1.26 to -0.98, $P < 0.00001$. Cannabidiol was the most studied drug across all publications (23 experiments), and was significantly favoured over vehicle; -1.03, -1.40 to -0.66, $P < 0.00001$. Cannabigerol caused the largest reduction in MPO compared to vehicle; -6.20, -9.90 to -2.50, $P < 0.01$. All cannabinoid drugs had a significantly positive effect on MPO. 33 publications examined the effects of 26 cannabinoid drugs on DAS across 48 experiments (n= 1056). Cannabinoid drugs reduced DAS in comparison with vehicle; -1.34, -1.58 to -1.10, $P < 0.00001$. Cannabidiol was the most studied drug (19 experiments); favouring cannabidiol over vehicle; -0.68, -1.10 to -0.26, $P < 0.0001$. The synthetic cannabinoid AM2141 caused the largest reduction in DAS; -3.11, -5.01 to -1.22, $p = 0.001$. All cannabinoid drugs used had a positive effect on DAS over vehicle. We found no evidence of reporting bias in MPO or DAI reporting, median study quality was 5/10 (against mSTAIR score). No significant difference was found between the prophylactic and therapeutic use of cannabinoid drugs.

Conclusions: There is abundant pre-clinical literature demonstrating the anti-inflammatory effects of cannabinoid drugs in inflammation of the intestinal tract. Preclinical literature favours the study of cannabidiol over other agents. Two initial small clinical studies have demonstrated the safe use of phytocannabinoids, though are inhibited by small patient numbers. Larger randomised controlled trials are now warranted to test cannabinoid efficacy.