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Systematic Reviews and Meta-Analyses: PDF Only

# A systematic review and meta-analysis of cannabis-based medicines, cannabinoids and endocannabinoid system modulators tested for antinociceptive effects in animal models of injury-related or pathological persistent pain

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# Abstract

We report a systematic review and meta-analysis of studies which assessed the antinociceptive efficacy of cannabinoids, cannabis-based medicines, and endocannabinoid system modulators on pain-associated behavioural outcomes in animal models of pathological or injury-related persistent pain. In April 2019, we systematically searched 3 online databases and used crowd science and machine learning to identify studies for inclusion. We calculated a standardised mean difference (SMD) effect size for each comparison and performed a random effects meta-analysis. We assessed the impact of study design characteristics and reporting of mitigations to reduce the risk of bias. We meta-analysed 374 studies in which 171 interventions were assessed for antinociceptive efficacy in rodent models of pathological or injury-related pain. Most experiments were conducted in male animals (86 %). Antinociceptive efficacy was most frequently measured by attenuation of hypersensitivity to evoked limb withdrawal. Selective $CB_1$, $CB_2$, non-selective cannabinoid receptor agonists (including delta-9-tetrahydrocannabinol; THC), and PPAR-alpha agonists (predominantly palmitoylethanolamide; PEA) significantly attenuated pain-associated behaviours in a broad range of inflammatory and neuropathic pain models. Fatty acid amide hydrolase (FAAH) inhibitors, monoacylglycerol lipase (MGL) inhibitors and cannabidiol (CBD) significantly attenuated pain-associated behaviours in neuropathic pain models but yielded mixed results in inflammatory pain models. The reporting of criteria to reduce the risk of bias was low, therefore the studies have an unclear risk of bias. The value of future studies could be enhanced by improving the reporting of methodological criteria, the clinical relevance of the models and behavioural assessments. Notwithstanding, the evidence supports the hypothesis of cannabinoid-induced analgesia.



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