

Effects of cannabis extract on murine neuropathic pain model

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Introduction: Neuropathic pain is observed in patients with cancer, leprosy, AIDS, diabetes and after surgery, representing a major health problem worldwide^[1]. According to folk medicine and anecdotal reports, cannabis use reduces pain. Many studies show that certain cannabinoids may have efficacy in treating chronic pain^[2]. The aim of this study is to determine the effects of cannabis extracts in a mouse model of neuropathic pain (sciatic nerve cuffing).

Methods: All procedures were performed under approved UBC animal care committee protocol. 48 female CD-1 mice (25-30g) were anesthetized with isoflurane and neuropathic pain was induced by surgical implantation of a polyethylene cuff around the main branch of the sciatic nerve^[3]. Extracts were prepared from cannabis and dosing was based on cannabidiol (CBD) content as analyzed using high pressure liquid chromatography. Mechanical allodynia was tested using the von Frey assay, which utilized series of filaments ranging from 0.008-2.0g. Mechanical allodynia was assessed before surgery, and then 2 weeks after surgical implantation of the polyethylene cuff once before treatment (baseline) and 5 min after treatment with vehicle (ethanol:Alkamuls-620:saline = 1:1:18), 4, 8, 12, 16 or 32 mg/kg i.v. of cannabis extract (N=8 per group). Data were analyzed by one-way ANOVA followed by Tukey post-hoc analysis.

Results: A significant difference was observed between baseline values of the hind paw ipsilateral to the ligation and the contralateral paw ($P<0.0001$). Treatment with cannabis extract significantly increased withdrawal threshold of the ipsilateral paw compared to baseline values and treatment with vehicle, with a measured ED₅₀ of 11 mg/kg (95% CI, NE-12.7). There were no significant differences on the ipsilateral paw between baseline, vehicle and cannabis extract treatment at 4 and 8 mg/kg. With 12 mg/kg extract, results indicated significant differences between pre-treatment and post-treatment threshold values ($P<0.0001$). Cannabis extract treatment at 16 and 32 mg/kg significantly increased ipsilateral withdrawal threshold to the cut-off value (2g) compared to baseline values for pre-treatment, as well as post-treatment with vehicle ($P<0.0001$).

Conclusions: Chronic pain was induced by cuffing the sciatic nerve in mice. Cannabis extract dose-dependently increased the withdrawal threshold of the hind paw ipsilateral to the cuff, compared to vehicle and baseline, suggesting utility of cannabis extract as a therapy for neuropathic pain.

Reference:

1. Muthuraman A et al.(2011). *Food and Chemical Toxicology* **49**:2557–2563
2. Pascual D et al. (2005). *Pain* **118**:23-34
3. Yalcin I et al.(2014). *J Visualized Experiments*:1-7