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By Josh Sosnow, DVM (<https://www.companioncbd.com/author/josh/>) 11 Nov (<https://www.companioncbd.com>)

## ATTENUATION OF EARLY PHASE INFLAMMATION BY CBD PREVENTS PAIN AND NERVE DAMAGE IN RAT OA MODEL

*Holly T. Philpott*

*Melissa O'Brien*

*Jason J. McDougall*

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### Abstract

Osteoarthritis (OA) is a multifactorial joint disease, which includes joint degeneration, intermittent inflammation, and peripheral neuropathy. Cannabidiol (CBD) is a noneuphoria producing constituent of cannabis that has the potential to relieve pain. The aim of this study was to determine whether CBD is anti-nociceptive in OA, and whether inhibition of inflammation by CBD could prevent the development of OA pain and joint neuropathy. Osteoarthritis was induced in male Wistar rats (150-175 g) by intra-articular injection of sodium monoiodoacetate (MIA; 3 mg). On day 14 (end-stage OA), joint afferent mechanosensitivity was assessed using in vivo electrophysiology, whereas pain behaviour was measured by von Frey hair algometry and dynamic incapacitance. To investigate acute joint inflammation, blood flow and leukocyte trafficking were measured on day 1 after MIA. Joint nerve myelination was calculated by G-ratio analysis. The therapeutic and prophylactic effects of peripheral CBD (100-300 µg) were assessed. In end-stage OA, CBD dose-dependently decreased joint afferent firing rate, and increased withdrawal threshold and weight bearing ( $P < 0.0001$ ;  $n = 8$ ). Acute, transient joint inflammation was reduced by local CBD treatment ( $P < 0.0001$ ;  $n = 6$ ). Prophylactic administration of CBD prevented the development of MIA-induced joint pain at later time points ( $P < 0.0001$ ;  $n = 8$ ), and was also found to be neuroprotective ( $P < 0.05$ ;  $n = 6-8$ ). The data presented here indicate that

local administration of CBD blocked OA pain. Prophylactic CBD treatment prevented the later development of pain and nerve damage in these OA joints. These findings suggest that CBD may be a safe, useful therapeutic for treating OA joint neuropathic pain.

Josh Sosnow, DVM

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