

## Team THC verse CBD

There is no doubt that cannabis is effective in treating pain. The most common recommendation for medical cannabis is for the treatment of chronic pain. The International Association for the Study of Pain describes pain as<sup>1</sup> "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".<sup>[1]</sup> Pain is different when it is acute, as opposed to chronic pain. Chronic pain is often associated with maladaptation in the central nervous system that can facilitate the worsening of pain. Pain is generally characterized as nociceptive or neuropathic. These highly variable presentations of pain make the endocannabinoid system an opportune target to treat pain.

To choose THC or cannabidiol in isolation does not take into account the different routes of administration and the entourage effect when administered as broad-spectrum verses as a single component. Studies have shown that broad-spectrum administration of cannabis responds in a linear dose-response curve and a bell-shaped curve when delivered as an isolated compound.<sup>2</sup> The role of cannabinoids in pain is supported by the preclinical observation of significant tissue overlap of CB1 and CB2 receptors in the parts of the nervous system that processes painful stimuli. These include the periaqueductal gray, raphe nuclei, and central-

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<sup>1</sup> ["International Association for the Study of Pain: Pain Definitions". Archived from the original on 13 January 2015. Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage](#) Derived from Bonica JJ (June 1979). "The need of a taxonomy". *Pain*. **6** (3): 247–8

<sup>2</sup> Gallily R, Yekhtin Z, Hanus L. Overcoming the Bell-Shaped Dose-Response of Cannabidiol by using Cannabis extract enriched in Cannabidiol. *Pharmacology & Pharmacy*,. 2015; 6:75-85.

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The role of cannabinoids in pain is supported by the preclinical observation of significant tissue overlap of CB1 and CB2 receptors in the parts of the nervous system that processes painful stimuli. These include the periaqueductal gray, raphe nuclei, and central-medial thalamic nuclei. These are the same locations that have significant mu receptor concentrations.<sup>3</sup> These interactions between mu receptors and cannabinoid receptors are the subject of much research.

Given that THC is the psychoactive component of the cannabis plant, one would think that THC would have effects on the central nervous system aspect in pain processing. A double-blinded study of several types of neuropathic pain indeed showed that in a dose-response curve, THC alone did significantly reduce pain.<sup>4</sup> Cannabidiol likewise is useful in the treatment of pain based on several studies. CBD appears to be particularly effective when the pain has an inflammatory component. CBD upregulates superoxide dismutase to decrease oxidative stress and inflammation, thereby reducing damage on dopaminergic neurons<sup>5</sup>. CBD has demonstrated

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<sup>3</sup> Bushlin, I et al. (2010) Cannabinoid-opioid interactions during neuropathic pain and analgesia. *Curr. Drug Targets*. 11:462-473

<sup>4</sup> Wilsey, B., Marcotte, T., Deutsch, R., Gouaux, B. and others. (2012). Low-Dose Vaporized Cannabis Significantly Improves Neuropathic Pain. *J.Pain*. 14: 136-148.

<sup>5</sup> Lastres-Becker I et al. Cannabinoids provide neuroprotection against 6-hydroxydopamine toxicity in vivo and in vitro: Relevance to Parkinson's disease. *Neurobiology of Disease*. 2005; 19 (1-2): 96-107

neuroprotective antioxidative and anti-inflammatory benefits for Parkinson's patients.<sup>6</sup> CBD is shown to inhibit tumor necrosis factor-alpha (TNF- $\alpha$ ) and other inflammatory mediators in a rodent model of acute pain. Enhancement of adenosine signaling by CBD through inhibition of adenosine uptake has been associated with decreased inflammation in preclinical models.<sup>7</sup>

Even though CBD supposedly has no demonstrable psychoactive component, it is anxiolytic, and this may have beneficial effects especially in chronic pain conditions. Single-photon emission computed tomography (SPECT) brain imaging studies showed that in contrast to placebo, CBD decreased regional cerebral blood flow in the limbic and paralimbic cortical areas, regions implicated in the pathophysiology of anxiety (658).

It appears that CBD may have the most utility when it comes to treating pain, but the dosing and role of THC is not entirely understood.

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<sup>6</sup> Lastres-Becker I et al. Cannabinoids provide neuroprotection against 6-hydroxydopamine toxicity in vivo and in vitro: Relevance to Parkinson's disease. *Neurobiology of Disease*. 2005; 19 (1-2): 96-107

<sup>7</sup> Carrier EJ et al. Inhibition of an equilibrative nucleoside transporter by cannabidiol: a mechanism of cannabinoid immunosuppression. *Proceedings of the National Academy of Sciences of the United States of America*. 2006; 103 (20): 7895-7900.