Neuropathy, Pain and β-caryophyllene

Ongoing studies show that β-caryophyllene is effective at reducing neuropathic pain in a CB2 receptor-dependent manner. Like other CB2 ligands β-caryophyllene inhibits the pathways triggered by activation of the toll-like receptor com- plex CD14/TLR4/MD2, which typically lead to the expression of pro-inflammatory cytokines (eg, IL-1 beta, IL-6; IL-8, and TNF alpha), is synergistic with opioid analgesic effects, and promotes a Th1 immune response that plays a critical role in neuroinflammation, sensitization, and pain. Therefore, the FDA approved food additive β-caryophyllene seems an attractive candidate for clinical trials targeting the CB2 receptor. Unlike many polyphenolic natural products, it is not metabolized immediately but shows a Tmax >1 hour after 1 single oral administration. Orally administered β-caryophyllene (<5 mg · kg-1) produces strong anti-inflammatory and analgesic effects in wild type mice . PMID: 25160710

BCP inhibits pathways triggered by CD14/TLR4/MD2, leading to IL-1 beta, IL-6; IL-8, and TNF alpha, is synergistic with opioid receptors and promotes a Th1 immune response a critical role in neuroinflammation, sensitization, and pain. PMID: 25160710

It is estimated that the realistic, estimated daily intake of 10 to 200 mg beta-caryophyllene from vegetable food is sufficient for significant CB2 cannabinoid receptor activation. We have demonstrated that oral administration of beta-caryophyllene reduces inflammatory responses in animal models at doses that are comparable to the nutritional intake. Beta-caryophyllene, a phytocannabinoid acting on CB2 receptors. IACM 5th Conference on cannabinoids in medicine. Cologne, Germany; 2009. Available at: http://www.cannabis-med.org/ meeting/Cologne2009/reader.pdf. Accessed March 23, 2013.

CB2R, located on immune cells (Howlett and Abood 2017; Atakan 2012) and on discrete neuronal populations, most notably within the hippocampus (Stempel et al. 2016), modulates neuropathic pain–related inflammation and behaviors (Don- vito et al. 2018). β-caryophyllene dose- and time-dependently reverse CCI-induced mechanical allodynia and thermal hyperalgesia in both male and female mice. Evaluation of the terpenes β-caryophyllene, α-terpineol, and γ-terpinene in the mouse chronic constriction injury model of neuropathic pain: possible cannabinoid receptor involvement. Psychopharmacology https://doi.org/10.1007/s00213-021-06031-2

BCP prevents nucleoside reverse transcriptase inhibitors-induced mechanical allodynia, possibly via reducing the inflammatory response, and attenuates mechanical allodynia through CB2 receptor activation. Therefore, BCP could be useful for prevention and treatment of antiretroviral-induced neuropathic pain. β-Caryophyllene, a CB2-Receptor-Selective Phytocannabinoid, Suppresses Mechanical Allodynia in a Mouse Model of Antiretroviral-Induced Neuropathic Pain. MID: 31892132

Glycemia, diabetes-related NP, and depressive-like behavior prevented/reduced by dietary BCP (10mg/kg) and correlated to Substance P and cytokines. Depression-like behavior assessed with tail suspension test was attenuated with orally chronic BCP administration. Substance P and cytokines such as interleukin-1β (IL-1β), tumor necrosis factor α (TNF-α), and interleukin-6 (IL-6). β-Caryophyllene, a Natural Sesquiterpene, Attenuates Neuropathic Pain and Depressive-Like Behavior in Experimental Diabetic Mice. PMID: 30864870

Caryophyllene, a CB2 Receptor-Selective Phytocannabinoid, Suppresses Motor Paralysis and Neuroinflammation in a Murine Model of Multiple Sclerosis. PMID: 28368293

Antiallodynic effect of β-caryophyllene on paclitaxel-induced peripheral neuropathy in mice. PMID: 28729222

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