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The cannabinoid CB_2 receptor-selective phytocannabinoid beta-caryophyllene exerts analgesic effects in mouse models of inflammatory and neuropathic pain.

Klauke AL[1], Racz I[2], Pradier B[1], Markert A[1], Zimmer AM[1], Gertsch J[3], Zimmer A[1].

Author information

Abstract

The widespread plant volatile beta-caryophyllene (BCP) was recently identified as a natural selective agonist of the peripherally expressed cannabinoid receptor 2 (CB_2). It is found in relatively high concentrations in many spices and food plants. A number of studies have shown that CB_2 is critically involved in the modulation of inflammatory and neuropathic pain responses. In this study, we have investigated the analgesic effects of BCP in animal models of inflammatory and neuropathic pain. We demonstrate that orally administered BCP reduced inflammatory (late phase) pain responses in the formalin test in a CB_2 receptor-dependent manner, while it had no effect on acute (early phase) responses. In a neuropathic pain model the chronic oral administration of BCP attenuated thermal hyperalgesia and mechanical allodynia, and reduced spinal neuroinflammation. Importantly, we found no signs of tolerance to the anti-hyperalgesic effects of BCP after prolonged treatment. Oral BCP was more effective than the subcutaneously injected synthetic CB_2 agonist JWH-133. Thus, the natural plant product BCP may be highly effective in the treatment of long lasting, debilitating pain states. Our results have important implications for the role of dietary factors in the development and modulation of chronic pain conditions.

KEYWORDS: Beta-caryophyllene; CB(2); Dietary cannabinoid; Inflammatory pain; Neuropathic pain

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