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Involvement of peripheral cannabinoid and opioid receptors in β-caryophyllene-induced antinociception

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Abstract

β-caryophyllene (BCP) is a common constitute of the essential oils of numerous spice, food plants and major component in Cannabis. The present study investigated the contribution of peripheral cannabinoid (CB) and opioid systems in the antinociception produced by intraplantar (i.pl.) injection of BCP. The interaction between peripheral BCP and morphine was also examined.

The antinociceptive effect of i.pl. BCP was assayed by the capsaicin tests in mice. Antagonists for CB and opioid receptors, and antisera against β-endorphin were injected peripherally prior to i.pl. injection of BCP. Morphine in combination with BCP was injected subcutaneously or intrathecally.

The i.pl. injection of BCP dose-dependently attenuated capsaicin-induced nociceptive response. The antinociceptive effect produced by BCP was prevented by pretreatment with AM630, a selective CB2 receptor antagonist, but not by AM251, a selective CB1 receptor antagonist. Pretreatment with naloxone, an opioid receptor antagonist, and β-funaltrexamine, a selective μ-opioid receptor antagonist, reversed the antinociceptive effect of BCP. Pretreatment with naloxone methiodide, a peripherally acting antagonist for opioid receptors and antisera against β-endorphin, resulted in a significant antagonizing effect on BCP-induced antinociception. Morphine-induced antinociception was increased by a low dose of BCP. The increased effect of morphine in combination with BCP was antagonized significantly by pretreatment with naloxone.

The present results demonstrate that antinociception produced by i.pl. BCP is mediated by activation of CB2 receptors, which stimulates the local release from keratinocytes of the endogenous opioid β-endorphin. The combined injection of morphine and BCP may be an alternative in treating chemogenic pain.

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