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Antihyperalgesic effect of a Cannabis sativa extract in a rat model of neuropathic pain: mechanisms involved.

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Abstract

This study aimed to give a rationale for the employment of phytocannabinoid formulations to treat neuropathic pain. It was found that a controlled cannabis extract, containing multiple cannabinoids, in a defined ratio, and other non-cannabinoid fractions (terpenes and flavonoids) provided better antinociceptive efficacy than the single cannabinoid given alone, when tested in a rat model of neuropathic pain. The results also demonstrated that such an antihyperalgesic effect did not involve the cannabinoid CB1 and CB2 receptors, whereas it was mediated by vanilloid receptors TRPV1. The non-psychoactive compound, cannabidiol, is the only component present at a high level in the extract able to bind to this receptor: thus cannabidiol was the drug responsible for the antinociceptive behaviour observed. In addition, the results showed that after chronic oral treatment with cannabis extract the hepatic total content of cytochrome P450 was strongly inhibited as well as the intestinal P-glycoprotein activity. It is suggested that the inhibition of hepatic metabolism determined an increased bioavailability of cannabidiol resulting in a greater effect. However, in the light of the well known antioxidant and antiinflammatory properties of terpenes and flavonoids which could significantly contribute to the therapeutic effects, it cannot be excluded that the synergism observed might be achieved also in the absence of the cytochrome P450 inhibition.

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