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Role of the cannabinoid system in pain control and therapeutic implications for the management of acute and chronic pain episodes.

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Abstract

Cannabis extracts and synthetic cannabinoids are still widely considered illegal substances. Preclinical and clinical studies have suggested that they may result useful to treat diverse diseases, including those related with acute or chronic pain. The discovery of cannabinoid receptors, their endogenous ligands, and the machinery for the synthesis, transport, and degradation of these retrograde messengers, has equipped us with neurochemical tools for novel drug design. Agonist-activated cannabinoid receptors, modulate nociceptive thresholds, inhibit release of pro-inflammatory molecules, and display synergistic effects with other systems that influence analgesia, especially the endogenous opioid system. Cannabinoid receptor agonists have shown therapeutic value against inflammatory and neuropathic pains, conditions that are often refractory to therapy. Although the psychoactive effects of these substances have limited clinical progress to study cannabinoid actions in pain mechanisms, preclinical research is progressing rapidly. For example, CB(1)mediated suppression of mast cell activation responses, CB(2)-mediated indirect stimulation of opioid receptors located in primary afferent pathways, and the discovery of inhibitors for either the transporters or the enzymes degrading endocannabinoids, are recent findings that suggest new therapeutic approaches to avoid central nervous system side effects. In this review, we will examine promising indications of cannabinoid receptor agonists to alleviate acute and chronic pain episodes. Recently, Cannabis sativa extracts, containing known doses of tetrahydrocannabinol and cannabidiol, have granted approval in Canada for the relief of neuropathic pain in multiple sclerosis. Further double-blind placebo-controlled clinical trials are needed to evaluate the potential therapeutic effectiveness of various cannabinoid agonists-based medications for controlling different types of pain.

KEYWORDS: Analgesia; cannabidiol; cannabinoid receptor; cannabis; endocannabinoid; inflammatory pain; neuropathic pain; tetrahydrocannabinol

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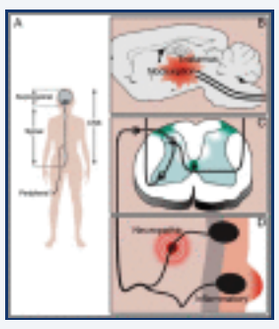

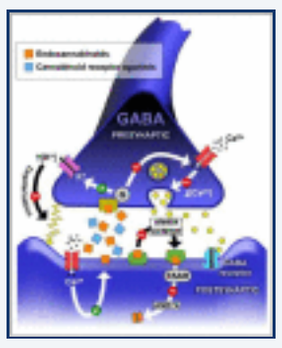

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