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# Cannabinoids in the management of difficult to treat pain.

Russo EB[1].

Author information

## Abstract

This article reviews recent research on cannabinoid analgesia via the endocannabinoid system and non-receptor mechanisms, as well as randomized clinical trials employing cannabinoids in pain treatment. Tetrahydrocannabinol (THC, Marinol((R))) and nabilone (Cesamet((R))) are currently approved in the United States and other countries, but not for pain indications. Other synthetic cannabinoids, such as ajulemic acid, are in development. Crude herbal cannabis remains illegal in most jurisdictions but is also under investigation. Sativex((R)), a cannabis derived oromucosal spray containing equal proportions of THC (partial CB(1) receptor agonist ) and cannabidiol (CBD, a non-euphoriant, anti-inflammatory analgesic with CB(1) receptor antagonist and endocannabinoid modulating effects) was approved in Canada in 2005 for treatment of central neuropathic pain in multiple sclerosis, and in 2007 for intractable cancer pain. Numerous randomized clinical trials have demonstrated safety and efficacy for Sativex in central and peripheral neuropathic pain, rheumatoid arthritis and cancer pain. An Investigational New Drug application to conduct advanced clinical trials for cancer pain was approved by the US FDA in January 2006. Cannabinoid analgesics have generally been well tolerated in clinical trials with acceptable adverse event profiles. Their adjunctive addition to the pharmacological armamentarium for treatment of pain shows great promise.

**KEYWORDS:** analgesia; cannabidiol; cannabinoids; multiple sclerosis; pain management; tetrahydrocannabinol

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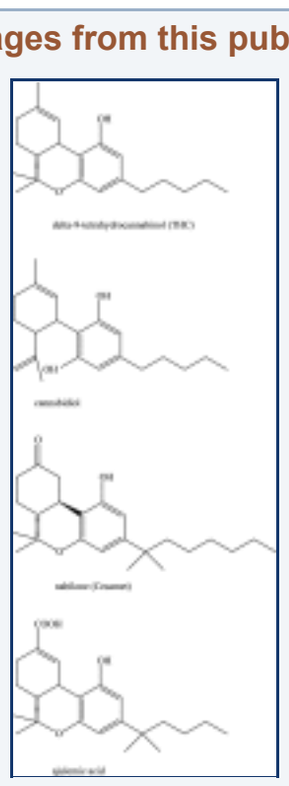

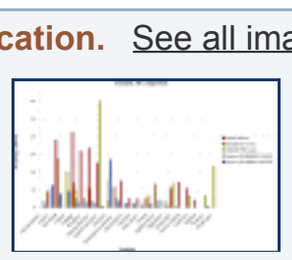

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