

# The Endocannabinoid System, Cannabinoids, and Pain

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**Perry G. Fine, M.D.<sup>1\*</sup> and Mark J. Rosenfeld, M.S., Ph.D.<sup>2</sup>**

<sup>1</sup>Professor of Anesthesiology, Pain Research and Management Centers, Department of Anesthesiology, School of Medicine, University of Utah, Salt Lake City, Utah, USA; and <sup>2</sup>Chief Executive Officer, ISA Scientific, Draper, Utah, USA

## ABSTRACT

The endocannabinoid system is involved in a host of homeostatic and physiologic functions, including modulation of pain and inflammation. The specific roles of currently identified endocannabinoids that act as ligands at endogenous cannabinoid receptors within the central nervous system (primarily but not exclusively CB1 receptors) and in the periphery (primarily but not exclusively CB2 receptors) are only partially elucidated, but they do exert an influence on nociception. Exogenous plant-based cannabinoids (phytocannabinoids) and chemically related compounds, like the terpenes, commonly found in many foods, have been found to exert significant analgesic effects in various chronic pain conditions. Currently, the use of  $\Delta^9$ -tetrahydrocannabinol is limited by its psychoactive effects and predominant delivery route (smoking), as well as regulatory or legal constraints. However, other phytocannabinoids in combination, especially cannabidiol and  $\beta$ -caryophyllene, delivered by the oral route appear to be promising candidates for the treatment of chronic pain due to their high safety and low adverse effects profiles. This review will provide the reader with the foundational basic and clinical science linking the endocannabinoid system and the phytocannabinoids with their potentially therapeutic role in the management of chronic pain.