

How Biodegradable Polymers Can be Effective Drug Delivery Systems for Cannabinoids? Prospectives and Challenges

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Abstract: Cannabinoids are compounds found in and derived from the *Cannabis* plants that have become increasingly recognised as significant modulating factors of physiological mechanisms and inflammatory reactions of the organisms, thus inevitably affecting maintenance of homeostasis. Medical *Cannabis* popularity has surged since its legal regulation growing around the world. Numerous promising discoveries bring more data on cannabinoids' pharmacological characteristics and therapeutic applications. Given the current surge in interest in the medical use of cannabinoids, there is an urgent need for an effective method of their administration. Surpassing low bioavailability, low water solubility, and instability became an important milestone in the advancement of cannabinoids in pharmaceutical applications. The numerous uses of cannabinoids in clinical practice remain restricted by limited administration alternatives, but there is hope when biodegradable polymers are taken into account. The primary objective of this review is to highlight the wide range of indications for which cannabinoids may be used, as well as the polymeric carriers that enhance their effectiveness. The current review described a wide range of therapeutic applications of cannabinoids, including pain management, neurological and sleep disorders, anxiety, and cancer treatment. The use of these compounds was further examined in the area of dermatology and cosmetology. Finally, with the use of biodegradable polymer-based drug delivery systems (DDSs), it was demonstrated that cannabinoids can be delivered specifically to the intended site while also improving the drug's physicochemical properties, emphasizing their utility. Nevertheless, additional clinical trials on novel cannabinoids' formulations are required, as their full spectrum therapeutical potential is yet to be unravelled.

Keywords: cannabinoids, drug delivery systems, cannabidiol, tetrahydrocannabinol, biodegradable polymers, nanomedicine

Introduction

Cannabinoids are obtained from plants belonging to the genus *Cannabis*, *Cannabaceae* family. *Cannabis*, particularly *Cannabis sativa*, has been known for its therapeutic and psychotomimetic applications for over 6000 years. Every *Cannabis sativa* plant produces active compounds, but the levels and proportions of these compounds vary among different varieties. These variations cannot be attributed solely to genetic makeup, as environmental factors such as climate and growing conditions may also influence them. Therefore, it is more accurate to refer to these variables as chemical varieties or chemovars, instead of strains.¹ The main active components present in *Cannabis sativa* comprise Δ^9 -tetrahydrocannabinol ((6aR,10aR)-6,6,9-trimethyl-3-pentyl-6a,7,8,10a-tetrahydrobenzo[c]chromen-1-ol) (THC) and cannabidiol (2-[(1R,6R)-3-methyl-6-prop-1-en-2-ylcyclohex-2-en-1-yl]-5-pentylbenzene-1,3-diol) (CBD).²

The mechanism of action of cannabinoids is dependent on their interaction with two cannabinoid receptors known as CB1 and CB2, which are found throughout the central and peripheral nervous systems. They are present in axons, dendrites, and cell bodies, and they influence neuronal, glial, and microglial activity.³ When these receptors are activated, they inhibit adenylyl cyclase production causing hyperpolarization of neurons, which stops the transmission of electric

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