

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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Table of Contents Biodegradable Polymers As Drug Delivery Systems

1. Understanding the eBook Biodegradable Polymers As Drug Delivery Systems
 - The Rise of Digital Reading Biodegradable Polymers As Drug Delivery Systems
 - Advantages of eBooks Over Traditional Books
2. Identifying Biodegradable Polymers As Drug Delivery Systems
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Biodegradable Polymers As Drug Delivery Systems
 - User-Friendly Interface
4. Exploring eBook Recommendations from Biodegradable Polymers As Drug Delivery Systems
 - Personalized Recommendations
 - Biodegradable Polymers As Drug Delivery Systems User Reviews and Ratings
 - Biodegradable Polymers As Drug Delivery Systems and Bestseller Lists
5. Accessing Biodegradable Polymers As Drug Delivery Systems Free and Paid eBooks
 - Biodegradable Polymers As Drug Delivery Systems Public Domain eBooks
 - Biodegradable Polymers As Drug Delivery Systems eBook Subscription Services
 - Biodegradable Polymers As Drug Delivery Systems Budget-Friendly Options
6. Navigating Biodegradable Polymers As Drug Delivery Systems eBook Formats
 - ePub, PDF, MOBI, and More
 - Biodegradable Polymers As Drug Delivery Systems Compatibility with Devices
 - Biodegradable Polymers As Drug Delivery Systems Enhanced eBook Features
7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Biodegradable Polymers As Drug Delivery Systems
 - Highlighting and Note-Taking Biodegradable Polymers As Drug Delivery Systems
 - Interactive Elements Biodegradable Polymers As Drug Delivery Systems
8. Staying Engaged with Biodegradable Polymers As Drug Delivery Systems

- Joining Online Reading Communities
- Participating in Virtual Book Clubs
- Following Authors and Publishers Biodegradable Polymers As Drug Delivery Systems
- 9. Balancing eBooks and Physical Books Biodegradable Polymers As Drug Delivery Systems
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Biodegradable Polymers As Drug Delivery Systems
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Biodegradable Polymers As Drug Delivery Systems
 - Setting Reading Goals Biodegradable Polymers As Drug Delivery Systems
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Biodegradable Polymers As Drug Delivery Systems
 - Fact-Checking eBook Content of Biodegradable Polymers As Drug Delivery Systems
 - Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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