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Nanostructured lipid carriers loaded with cannabidiol: A novel antibiofilm approach

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ABSTRACT

Introduction: Staphylococcus aureus and Staphylococcus epidermidis are major contributors to skin dysbiosis and infections, e.g., folliculitis and intravascular catheter infections, forming biofilms that enhance their resistance to antibiotics and immune responses. Given that antibiotic resistance is a serious challenge, new solutions are constantly being explored. The endocannabinoid system is essential for maintaining skin homeostasis, regulating inflammation, and promoting skin regeneration. Cannabidiol has been shown to have antimicrobial properties and therapeutic effects on some pathophysiological skin conditions, e.g., chronic and uremic pruritus, by modulating the endocannabinoid system. However, cannabidiol has properties that limit its bioavailability when applied to the skin. Although it has an adequate molecular weight, its high logP value limits permeation into the skin's deeper layers. To address these limitations and improve cannabidiol stability, it is proposed that it will be loaded in nanostructured lipid carriers. Since biofilms make infections more difficult to treat, studying nanostructured lipid carriers-cannabidiol's effects on these bacterial communities could provide insight into alternative or complementary therapeutic strategies.
Objective: By assessing nanostructured lipid carriers-cannabidiol's ability to target these biofilms, researchers aim to explore its potential role in improving treatments for skin infections.
Methodology: Six nanostructured lipid carriers' formulations (three nanostructured lipid carriers- and three nanostructured lipid carriers+), with and without cannabidiol, were prepared using a modified melt emulsification method followed by ultrasonication, stored at 4ºC, and physicochemical properties were measured over eight weeks.
Results: With no significant change in zeta potential (−29.91 to −29.93 mV; P = 0.9999), nanostructured lipid carriers-cannabidiol showed the highest stability. Although a statistically significant reduction in particle size was observed (224.14 to 213.24 nm; P < 0.0001), stability was not affected, with a low polydispersity index (0.2076±0.0133) indicating a homogenous particle distribution. Fourier Transform Infrared Spectroscopy spectra reveal the characteristic bands of cannabidiol, confirming cannabidiol's encapsulation efficiency (%) higher than 99%. After 48 hours, treatment with nanostructured lipid carriers-cannabidiol resulted in a significant reduction in bacterial biofilm viability, with a decrease of approximately 2.5 and 1.5 log Colony Forming Unit/mL in S. aureus and S. epidermidis, respectively.

Discussion: Encapsulation of cannabidiol within lipid-based carriers appears to be a key factor in enabling its activity against biofilm-forming bacteria. The observed antimicrobial effects likely result from improved retention at the infection site, facilitating interaction with the biofilm matrix. Moreover, the absence of significant activity in the placebo formulations underscores the importance of the active compound. This delivery strategy may offer a means to overcome common limitations associated with topical cannabidiol, particularly in terms of solubility and penetration, providing a focused and potentially more effective alternative in the context of skin infections involving biofilms.

Conclusions: The results demonstrate the potential of nanostructured lipid carriers' to improve cannabidiol's biofilm delivery and penetration. In conclusion, cannabidiol-loaded negatively charged nanostructured lipid carriers may be a promising strategy as anti-biofilm treatment..

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