Formulation Aspects and Potential Therapeutic Applications of Cannabidiol-Loaded Nano-formulations

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Introduction

Nano-delivery systems help in improving the stability of phytocompounds, enhance their absorption, protect them from early enzymatic deprivation or metabolism within the body, and extend their circulation time, thus limiting the various adverse effects (*Assadpour et al., 2023*).

Cannabidiol (CBD) is a non-psychoactive cannabinoid isolated from *Cannabis sativa* L. and the modified nanocarriers improve the solubility and permeability and assist in the sustained delivery of CBD to the targeted diseased sites, thus improving the bioavailability. and that has not been shown to have any intoxicating effects.

According to the Biopharmaceutics Classification System (BCS), pharmacologically active CBD intended for oral use is classified as Class II, due to its very low water solubility and high lipophilicity (12.6 mg/L, logP 6.3, pKa 9.29). CBD has a very poor oral bioavailability in plasma and tissues (around 6% and 1%, respectively) due to its high lipophilicity, sensitivity to light, and major breakdown in the duodenum (*Barbara et al., 2021*).

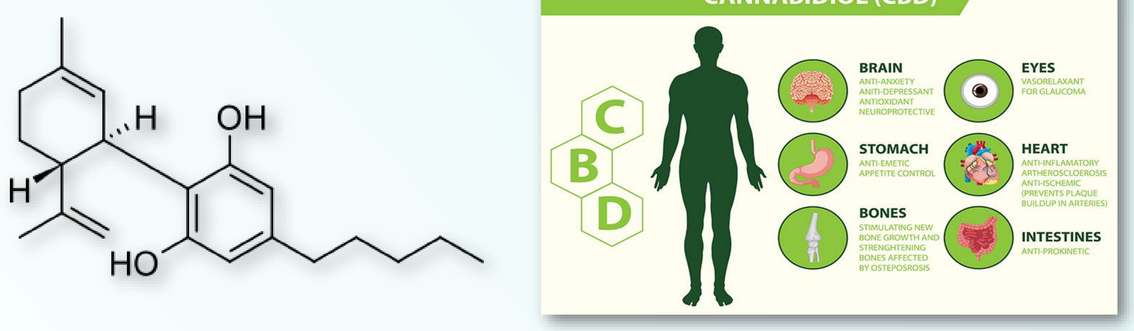

Figure 1. Chemical Structure of Cannabidiol and Its Therapeutic Effects.

Methodology

For the purposes of our research, we used literature research of several original and review articles indexed in the databases: PubMed, SCOPUS and Web of Science.
For the complete literature search in the indicated databases, we used the following keywords: nanocarriers AND cannabidiol; nano-formulations AND cannabinoids; niosomes AND cannabidiol; liposomes AND cannabidiol; cannabidiol formulations AND therapeutics.

Results & Discussion

Nanoemulsions

Taskar et al. (2019) observed that modified CBD-loaded nanoemulsions made by conjugating analogs of amino acids and dicarboxylic acids, CBD–divalinate–dihemisuccinate and CBD–divalinate, respectively, increased the bioavailability and permeability of CBD. Particle size, surface charge, emulsifying agent type, pH, and other manufacturing parameters are important for the efficient delivery of CBD via nanoemulsions.

In a different study, castor oil-based nanoemulsions were created to distribute hydrophobic medications (such as fenofibrate or CBD) more efficiently while enhancing their stability and bioavailability. To increase the solubility and oral bioavailability of CBD, CBD-loaded nanoemulsions made of ethanol, Tween-20, CBD oil, and vitamin E acetate were created. When given as CBD-loaded nanoemulsions (50 mg/kg), the results of pharmacokinetic tests conducted on a rat model demonstrated enhanced oral bioavailability of CBD (*Taskar et al., 2019*).

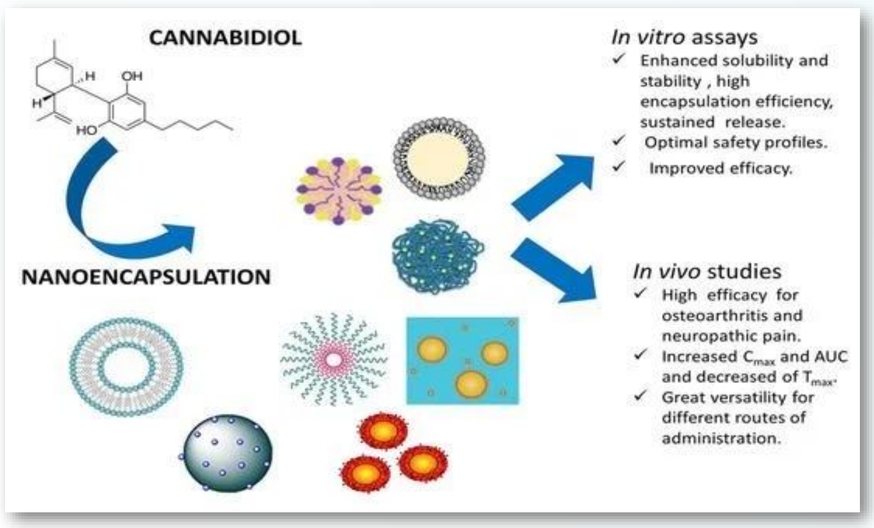

Figure 2. Promising Nanocarriers to Enhance Solubility and Bioavailability of Cannabidiol for a Plethora of Therapeutic Opportunities (Grifoni et al., 2022).

Results & Discussion

Nanoliposomes

Verrico et al. (2020) developed dipole materials like phospholipids which combined with water using a variety of mechanical (such as high-pressure homogenization, ultrasonication, and microfluidization) and non-mechanical (such as reversed-phase evaporation) techniques to create nano-sized vesicles in order to prepare nanoliposomes. To increase the bioavailability of CBD, a sunflower lecithin (phosphatidylcholine) basis was used to create a nanoliposome. About 100 nm in size, nanoliposomal CBD contained 10–20 mg/mL of CBD and shown excellent stability over three months at room temperature and in the refrigerator at pH 5–9. To increase its bioavailability for use in treating canine pain, liposomal CBD was created in a different study utilizing hydrogenated soy phosphatidylcholine with a median particle size of 5.6 μm and 50 mg/g of synthetic CBD (*Verrico et al., 2020*).

Solid Lipid Nanoparticles (SLNPs)

Hot and cold homogenization are the two techniques used to produce SLNPs on a large scale. CBD dissolves in melting lipid during heat homogenization, and high-pressure homogenization yields oil-in-water emulsions. After the lipids in the emulsion cool and recrystallize, SLNPs will develop. CBD is dissolved in melted lipid via cold homogenization, and the resulting lipid microparticles are then crushed after cooling and solidifying. SLNPs are then obtained by dispersing the lipid microparticles in a cold surfactant solution and homogenizing them at room temperature (*Balaga et al., 2022*).

Nanostructured Lipid Carriers (NLCs)

The preparation process described for SLNPs can be used to create NLCs by combining liquid and solid lipids. NLCs were created for the nasal delivery of CBD using cetylpyridinium chloride, Span 20, and stearic and oleic acids as solid and liquid lipids, respectively. Additionally, to create a CBD-NLC-gel, the CBD-NLC dispersion was mixed with the gelling polymers Pluronic F127 and Pluronic F68 (*Matarazzo et al., 2021*).

For CBD, monodisperse lipid nanocapsules (LNCs) were created as biocompatible and degradable carriers. Caprylic-capric acid triglycerides, C18E15 polyethylene glycol (15) 12-hydroxystearate, soybean lecithin with 70% phosphatidylcholine, and NaCl were used to prepare LNCs using the energetically-efficient phase inversion temperature (PIT) technique. In addition to being biocompatible and decomposable, NLCs are more stable, have higher encapsulation loads, and release more quickly than SLNs (*Verrico et al., 2020*).

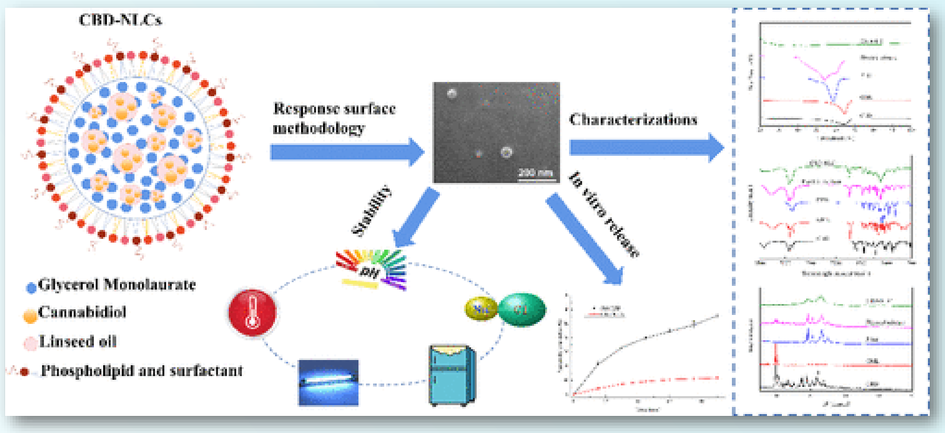

Figure 3. CBD-Loaded Nanostructured Lipid Carriers (Xie et al., 2024).

Conclusion

Although CBD and its derivatives have been found to be safe, their limited solubility and permeability raise concerns about their direct use. The use of other nanocarriers, such as polymers and lipid-based carriers, can get beyond these restrictions. By enhancing CBD's solubility and permeability across a range of biological barriers, these nanocarriers contribute to its increased bioavailability, targetability to sick areas, and minimal toxicity. Although therapeutic doses may differ between disease states, clinical trials examining the effectiveness of CBD for the treatment of pain, autoimmune diseases, mental disorders, substance use, and other ailments frequently rely on a single acute dose.
Furthermore, a number of clinical trials should be conducted to investigate the effects of many dosages given often over an extended period of time before prescribing CBD to patients.
As a result, it becomes essential to raise public knowledge of CBD usage and provide innovative delivery methods for its various applications, ranging from clinical to translational.

References

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