PubMed

Format: Abstract

Full text links

ELSEVIER FULL-TEXT ARTICLE

J Control Release. 2017 Nov 28;266:1-7. doi: 10.1016/j.jconrel.2017.09.011. Epub 2017 Sep 8.

Piperine-pro-nanolipospheres as a novel oral delivery system of cannabinoids: Pharmacokinetic evaluation in healthy volunteers in comparison to buccal spray administration.

Cherniakov I[1], Izgelov D[1], Barasch D[1], Davidson E[2], Domb AJ[1], Hoffman A[3].

Author information

Abstract

Nowadays, therapeutic indications for cannabinoids, specifically Δ^9-tetrahydrocannabinol (THC) and Cannabidiol (CBD) are widening. However, the oral consumption of the molecules is very limited due to their highly lipophilic nature that leads to poor solubility at the aqueous environment. Additionally, THC and CBD are prone to extensive first pass mechanisms. These absorption obstacles render the molecules with low and variable oral bioavailability. To overcome these limitations we designed and developed the advanced pro-nanolipospheres (PNL) formulation. The PNL delivery system is comprised of a medium chain triglyceride, surfactants, a co-solvent and the unique addition of a natural absorption enhancer: piperine. Piperine was selected due to its distinctive inhibitory properties affecting both Phase I and Phase II metabolism. This constellation self emulsifies into nano particles that entrap the cannabinoids and the piperine in their core and thus improve their solubility while piperine and the other PNL excipients inhibit their intestinal metabolism. Another clear advantage of the formulation is that its composition of materials is approved for human consumption. The safe nature of the excipients enabled their direct evaluation in humans. In order to evaluate the pharmacokinetic profile of the THC-CBD-piperine-PNL formulation, a two-way crossover, single administration clinical study was conducted. The trial comprised of 9 healthy volunteers under fasted conditions. Each subject received a THC-CBD (10.8mg, 10mg respectively) piperine (20mg)-PNL filled capsule and an equivalent dose of the oromucosal spray Sativex® with a washout period in between treatments. Single oral administration of the piperine-PNL formulation resulted in a 3-fold increase in Cmax and a 1.5-fold increase in AUC for THC when compared to Sativex®. For CBD, a 4-fold increase in Cmax and a 2.2-fold increase in AUC was observed. These findings demonstrate the potential this formulation has in serving as a standardized oral cannabinoid formulation. Moreover, the concept of improving oral bioavailability described here, can pave the way for other potential lipophilic active compounds requiring enhancement of their oral bioavailability.

KEYWORDS: Bioavailability; Cannabinoids; Lipid based drug delivery; Metabolism; Piperine; SNEDDS

PMID: 28890215 DOI: 10.1016/j.jconrel.2017.09.011

[Indexed for MEDLINE]

Publication types, MeSH terms, Substances

LinkOut - more resources