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Cyclosporine A-loaded solid lipid nanoparticles versus nanostructured lipid carriers for dermal applications

Cyclosporine A (CsA) is a well-known immunosuppressive agent that gained considerable importance in transplant medicine due to its selective and reversible inhibition of T-lymphocytes. While CsA has been widely used to prevent graft rejection in patients undergoing organ transplant it was also used to treat several systemic and local autoimmune disorders [1]. However, CsA presents some biopharmaceutical inconveniences. These include: low aqueous solubility and low permeability due to its rigid structure and high molecular weight (1203 Da), an extensive presystemic metabolism in the gut wall and liver, and P-glycoprotein efflux in the enterocytes [2]. These poor biopharmaceutical properties hamper the development of appropriate CsA delivery systems. One of the most promising strategies developed to improve drug delivery is nanotechnology. Within this field, lipid nanoparticles (LN) have attracted attention for the topical delivery of poorly soluble compounds thanks to their multiple advantages.

The aim of this study was to develop, optimize and evaluate the potential of lipid nanoparticles (LNs) as a topical delivery system for targeted and prolonged release of (CsA) via hot ultrasonication technique using Lipocire DM as solid lipid and pluronic as a surfactant for SLN, and oleic acid as liquid lipid for the NLC loaded with CsA. Lipid nanoparticles were characterized according to their surface morphology by scan electron microscopy (cryo-SEM); particle size parameters, the average diameter size, polydispersity index (PDI) and zeta potential (ZP) using dynamic light scattering (DLS); degree of crystallinity and lipid modification (polymorphism) using a differential scanning calorimetry (DSC). Moreover CsA was quantified by spectrophotometry to determine the Drug Loading (DL) and Encapsulation efficiency (EE). Then the stability of the developed LNs formulation was evaluated for 3 months with respect to particle size, ZP, PDI and drug content.

The *in vitro* CsA release studies were conducted in two different environments: physiological (pH 7.4, 37 ± 0.5 °C), and topical (pH 5.5, 32 ± 0.5 °C). CsA *in vitro* release was measured by UV-Visible spectroscopy and the release pattern of different batches was evaluated for Zero order, Higuchi, First order, Krosmeyer-Peppas and Hixson-Crowell kinetics. Finaly the permeability studies using cell culture preparations were also studied to evaluate the potential effect of the nanodelivery systems on enhancing skin absorption of (CsA). Toxicity and biocompatibility of the nanoparticles was also evaluated via MTT cell viability assay.

References

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