PRODUCTION AND CHARACTERIZATION OF LIPID NANOPARTICLES FOR THE TRATMENT OF NEURODEGENERATIVE PATHOLOGIES

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Purpose

Neurological inflammation is a common characteristics of many disorders, such as Alzheimer, Parkinson and multiple sclerosis. The present study describes the production and characterization of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC), appropriately functionalized, as drug delivery systems for three different model compounds effective against neuroinflammation, namely URB597 (URB), Dimethylfumarate (DMF) and Progesterone (PRG).

Methods

SLN and NLC dispersed in a 2.5% w/v poloxamer 407 solution were produced by a water in oil (W/O) method and then characterized. Morphology and dimensional distribution have been investigated by cryogenic transmission electron microscopy (cryo-TEM) and sedimentation field flow fractionation (SdFFF), respectively. Moreover, X-ray was performed.

The percentage of drug incorporation was determined by disintegration and ultrafiltration method. This evaluation has been used for stability studies of the formulations after 30, 60 and 90 days from preparation. Drug release modalities were *in vitro* investigated using equilibrium dialysis.

Results

Morphological analysis as found by cryo-TEM showed that SLN and NLC have a flat ovoid structure, although in the case of NLC structure is more rounded than SLN. The dimensional analyses as found by SdFFF showed that the size distribution of SLN is more homogeneous than that of NLC.

The presence of drugs does not alter the macroscopic appearance of the suspension and does not lead to the formation of aggregates. Moreover, recovery of all drugs in nanoparticles is higher than 50% as compared to the initial amount of molecule. In particular, the recovery of DMF and PRG in SLN and NLC is higher than 90%.

The drug encapsulation was found quantitative (94,64% w/w÷99,95% w/w) for lipophilic drugs (i.e. URB and PRG), while DMF is lower (66,90% w/w) being partially solubilized in the aqueous dispersing phase.

The X-ray diffraction showed that the addition of drug to nanoparticle does not change the internal structure of SLN nor NLC.

Drug release studies demonstrated that the slower kinetics was obtained in the case of URB, confirming that the better release is related with the lipophilicity of the molecules.

The stability of URB, PRG, DMF incorporated into SLN was evaluated over 90 days and it was found that SLN are able to better maintain the stability of the more lipophilic drugs URB and PRG instead DMF.

Conclusions

This study confirms that the incorporation of active substances in different types of lipid nanoparticles is possible and the gradual release kinetics and stability of the incorporated active molecules is strictly dependent on their lipophilicity.