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A new approach for development of nanostructured lipid carriers for topical drug delivery

Nanostructured lipid carriers (NLC) are the second generation of lipid nanoparticles, that were created to overcome some problems of solid lipid nanoparticles (SLN) [1]. NLCs are composed by a mixture of solid and liquid lipid, usually in a ratio up to 70:30 [2]. The addition of a liquid lipid in the formulation promotes changes in the structure of the nanoparticle, leading to higher drug loading than SLN [3]. There are several techniques to produce NLC, but most of them use heating in the process making it undesirable to encapsulate thermolabile drugs [4]. The aim of this work was to produce NLC without heating by a modified solvent-evaporation double emulsion technique.

NLCs were produced using a modified solvent evaporation method [5], by placing the liquid lipid in the organic phase. It was performed an experimental design to evaluate the capacity of several lipids, surfactants and its combinations to obtain particles in the nanosized range with low polydispersity (PdI), good colloidal stability and high association efficiency (AE) of the drug. After production, it was evaluated the diameter, PdI, zeta potencial and association efficiency of the model drug, lidocaine hydrochloride.

The nanoparticles diameter may be affected by many factors, but the most important parameters include the amount of lipid, type of lipid and surfactant concentration [3]. The criteria used to choose the best formulation was to have the lower diameter, good zeta potencial, formulation homogeneity and higher drug association efficiency. Considering all these parameters, the best formulation was Tween 80® 2% (w/v) + Precirol® ATO 5 and Oleic Acid (Figure 1). The polidispersity index ranged between 0,18 and 0,84 and AE of the formulation was higher than 70%.

The developed protocol allowed to produce NLC with good physico-chemical properties and without the need of heating, and with high association efficiency of the drug. It is foreseen the application of this encapsulation protocol to load thermolabile drugs, such as therapeutic proteins.

Figures

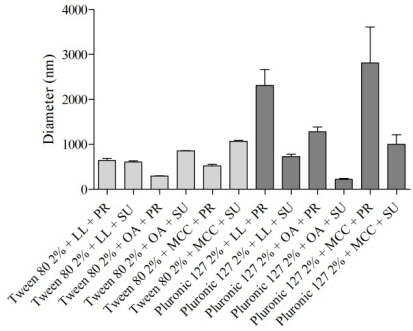

Figure 1: Particle size characterization of NLC formulations. LL: Labrafac Lipophile WL 1349; OA: Oleic Acid; MCC: Maisine CC; PR: Precirol ATO 5; SU: Suppocire DM Pallets

References

[1] Muller, R.H., M. Radtke, and S.A. Wissing, *Adv Drug Deliv Rev*, 2002. 54,131.
[2] Beloqui, A., et al., Nanomedicine, 2016, 12, 143.
[3] Pathak, K., L. Keshri, and M. Shah, Crit Rev Ther Drug Carrier Syst, 2011, 28, 357.
[4] Parhi, R. and P. Suresh, Curr Drug Discov Technol, 2012, 9, 2.
[5] Fonte, P., et al., Biomacromolecules, 2014, 15, 3753.