Formation of dexamethasone-loaded nanoparticle dispersions from nano-emulsions as inhaled anti-inflammatory drug delivery systems

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Abstract

Polymeric nanoparticle dispersions are interesting colloidal systems for a large range of biomedical applications. Nano-emulsions are useful templates to prepare nanoparticle dispersions [1]. For this purpose, biocompatible and biodegradable polymers, such as poly(lactic-co-glycolic acid) (PLGA), approved for human use, are required. The addition of drugs may render the nanoparticle dispersions valuable drug delivery systems. In this context, glucocorticosteroids, such as dexamethasone (DXM), are the most used anti-inflammatory drugs against airway and bronchiolar inflammation produced in some pulmonary diseases such as asthma [2]. The administration of glucocorticosteroid-loaded nanoparticle dispersions by the pulmonary route is promising for the treatment of several pulmonary and systemic diseases. Nanoparticles can provide a local, sustained and controlled release of the drug, penetration into tissues, protection of drugs from metabolism and degradation and decreased drug toxicity [3]. The main objectives of this study were: 1) the formulation and characterization of O/W polymeric DXM-loaded nano-emulsions; 2) the preparation and characterization of suitable nanoparticle dispersions for inhalatory administration using the nano-emulsions as templates; and 3) the study of the encapsulation and release properties of DXM-loaded nanoparticle dispersions. Polymeric O/W nano-emulsions have been obtained in the water / non-ionic ethoxylated surfactant / [4wt% PLGA + 0.18wt% DXM in ethyl acetate] system by the phase inversion composition (PIC) method at 25ºC. Nano-emulsions were obtained at oil to surfactant (O/S) ratios between 45/55 and 75/25 and water contents above 70wt%. For this study, nano-emulsions with a water content of 90 wt% were chosen. The droplet size of the nano-emulsions as a function of the O/S ratio was determined by cross-correlation light scattering. It has been found that droplet sizes were below 200 nm and varied only slightly with the O/S ratio. The visual examination of the nano-emulsions at 25ºC revealed no macroscopic changes for at least 25 days. Accelerated stability tests, performed by light backscattering disclosed that the main destabilization mechanism is sedimentation, which was detected by this technique after at least 18 hours. Nanoparticle dispersions were prepared from the nano-emulsions by solvent evaporation. As observed by transmission electron microscopy (TEM), nanoparticles showed spherical shapes, with smooth, sometimes cracked surface (Figure 1). Nanoparticle size, as determined by TEM image analysis, was below 150 nm, smaller than the template nano-emulsion. This nanoparticle size is suitable for inhalatory administration [4,5]. The DXM encapsulation efficiency was above 74wt% and decreased at increasing O/S ratios. The release of DXM from the nanoparticle dispersions to a receptor solution was studied and compared to a DXM aqueous solution. It was found that the release of DXM from nanoparticle dispersions is slower than from the solution. The release curves were fitted to a Fickian diffusion model. The diffusion coefficients of DXM from nanoparticle dispersions are about one order of magnitude lower than from an aqueous solution and depended on the O/S ratio. Encapsulation efficiency decrease at higher O/S ratios (70/30), allowing for a faster release of the DXM. These results confirm that, these nanoparticle dispersions could be suitable candidates for the sustained release of DXM to the lungs.

References

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Figures

Figure 1: TEM micrograph of a negatively stained PLGA nanoparticles showing the characteristic spherical shape and cracked surface.