AVOIDING KETOPROFEN PLASTICIZATION DURING MICROPARTICLES MANUFACTURING: THE CASE OF CYCLODEXTRINS

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Purpose
To prepare a ketoprofen-β-cyclodextrin (K-βCD) inclusion complex in order to hinder the plasticizing effect of ketoprofen (K) on poly(lactic-co-glycolic) acid microparticles (PLGA MPs).
Methods
K-βCD inclusion complex was prepared using the kneading method and a molar ratio K:βCD of 1:2. K in the inclusion complex was determined using ultraviolet-visible (UV-VIS) spectrophotometry. The inclusion complex was also characterized by Fourier transform-infrared spectroscopy (FT-IR) and X-ray powder diffraction analysis.
PLGA MPs were prepared using the solvent diffusion-evaporation method. K-βCD inclusion complex was dispersed in the polymer solution successively injected in a hydroxypropyl methylcellulose aqueous solution (2.5% w/v) maintained under stirring at 4°C. This emulsion (solid/oil/water) was heated to allow the complete solvent evaporation and the formation of MPs. Different type of PLGA MPs were prepared changing the amount of K-βCD and dichloromethane, and the amount and type of PLGA. MPs were characterized in terms of morphology using scanning electron microscopy (SEM) and particle size. PLGA glass transition temperature (Tg) was determined using differential scanning calorimetry (DSC) and the encapsulation efficiency (EE) by UV-VIS spectrophotometry.
Results
The formation of the inclusion complex was confirmed by X-ray and FT-IR analyses while UV-VIS analysis showed that only ~15% of K was not included in the CDs. Using large amount of dichloromethane it was possible to obtained spherical MPs characterized by different diameters. In fact, using 3.3 g of dichloromethane instead of 4.4 g, the average MP size increased of about 20 μm. The EE was always higher than 60%. DSC analysis showed that K loaded MP had a Tg of 20°C while the Tg values of K-βCD loaded PLGA MPs were comparable to that of raw PLGA Tg (~41°C).
Conclusions
K-βCD inclusion complex allowed to hinder the plasticizing effect of K on PLGA MPs during their preparation. In fact, the interaction between K and βCD did not allow K to interact with PLGA causing plasticization by lubricant effect.