

## Abstract

A new delivery system based on drug cyclodextrin (Cd) complexation and loading into nanostructured lipid carriers (NLC) has been developed to improve ketoprofen therapeutic efficacy. The proposed strategy exploits both the solubilizing and stabilizing properties of Cds and the prolonged release, high tolerability and percutaneous absorption enhancer properties of NLC. Two different polymeric Cds, i.e.  $\beta$ -Cd-epichlorohydrin polymer (EPI- $\beta$ Cd) and carboxymethylated- $\beta$ -Cd-epichlorohydrin polymer (EPI-CM $\beta$ Cd) were tested and two different techniques to obtain solid ketoprofen-polymeric Cd complexes (i.e. co-grinding and co-lyophilization) were compared, to investigate the influence of the preparation method on the physicochemical properties of the end product. EPI- $\beta$ Cd was more effective than EPI-CM $\beta$ Cd in enhancing the solubility and dissolution properties of ketoprofen. Co-grinding in dry conditions was the best preparation technique of solid drug-Cd systems, allowing obtainment of homogeneous amorphous particles of nanometric range. NLC consisting in a mixture of Compritol® 888 ATO (glyceryl behenate) and Labrafac Lipophile were obtained by ultrasonication. Both empty and loaded NLC were suitably characterized for particle size, pH, entrapment efficiency and drug release behavior. The best (drug-Cd)-loaded NLC system, formulated into a xanthan hydrogel, exhibited drug permeation properties clearly better than those of the plain drug suspension or the plain drug-loaded NLC, in virtue of the simultaneous exploitation of the solubilizing effect of cyclodextrin and the penetration enhancer properties of NLC.