NAPROXEN-CHITOSAN-TRIPOLYPHOSPHATE NANOPARTICLES DISPERSED IN THERMOREVERSIBLE HYDROGELS FOR INTRA-ARTICULAR DELIVERY

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Introduction and objective: Naproxen (NPX) is a non-steroidal anti-inflammatory drug used for the treatment of inflammatory disorders. For prolonging the duration of action and to reduce the side effects, drug-delivery systems have been developed. We aimed to prepare, to characterize and to evaluate the in vitro release of NPX from chitosan-tripolyphosphate nanoparticles (CHI-NANO) dispersed in poloxamer-based (PL) thermoreversible hydrogels for intra-articular delivery.

Materials and Methods: NPX (0.5 or 1.0 mg/mL) was encapsulated in CHI-NANO composed of chitosan (0.1 wt%) and tripolyphosphate (0.1 wt%). CHI-NANO were dispersed in PL 407 (18 and 20 wt%) or PL 407:403 (18:2 wt%) micellar hydrogels. Formulations were characterized by Light Scattering (173° angle) for hydrodynamic diameter, polydispersion index (PDI) and zeta potential measurements. NPX encapsulation efficiency (EE) was also determined in CHI-NANO. For sol-gel transition temperature (Tgel) studies, Differential Scanning Calorimetry (DSC) was used. In vitro release assays were performed, using vertical diffusion Franz-cell (1.72 cm² permeation area at 37°C), across artificial membranes (cellulose acetate, 1000 MWCO).

Results and Conclusion: NPX-CHI-NANO presented hydrodynamic diameter of 182.7 ± 3.9 nm, PDI 0.36 ± 0.01, zeta potential 8.96 ± 1.3 mV. The EE was 99.4%. However, PL micelles presented hydrodynamic diameter (at 37°C) from 23.1 ± 3.1 to 30.9 ± 1.4 nm in the presence of NPX (PDI= 0.167 ± 0.01). PL407-PL403 hydrogels increased NPX aqueous solubility (from 0.016 to 6.1 mg/mL. Tgel values changed according to the PL type, concentration and NPX incorporation (34-30 °C). The NPX in vitro release followed the Higuchi model (R²= 0.9604) with release constants of 34.5 ± 5.4 and 14.4 ± 4.0 %/h. These results pointed out CHI-NANO/PL hydrogels as possible new strategies for future NPX intra-articular delivery.

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Key Words: nanoparticles, poloxamer, naproxen