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Production and characterization of hypromellose phthalate nanoparticles containing levofloxacin for ophthalmic applications

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Although eyedrops are nowadays the most used administration form of ophthalmic drugs, they present several problems: they imply repeated applications, lead to significant drug losses, and may cause undesirable side effects, as a result of the rapid drug absorption into the blood stream. Several attempts have been made to develop new drug delivery systems, which increase the residence time of the drugs in the eye and improve its bioavailability. Therapeutic soft contact lenses (SCLs) seem to constitute a promising alternative due to the prolonged contact with the eye. Although drug soaked contact lenses have demonstrated to be more efficient than eyedrops, they still present limitations: maximum drug load is limited and diffusion is the only resistance to drug transport across the gel, which may lead to short release times. Designing an effective system for the treatment of ocular diseases is a challenging task, to which nanotechnologies may give a valuable contribution. The incorporation of drug-loaded nanostructures in the SCLs materials may help to control the drug release rates and to maintain drug therapeutic levels for longer periods of time.

The main objective of this work is to produce hypromellose phthalate (HPP 50) nanoparticles (NPs) containing levofloxacin (LOF) to incorporate in hydrogels for SCLs. LOF is an antibiotic which offers a broad spectrum against ocular infections and is used both in prophylaxis and treatment [1]. The NPs were produced using a supercritical atomization process developed by the research team - Supercritical Enhanced Atomization (SEA) [2] and were engineered in order to improve the release rate of LOF. Different working pressures, LOF concentrations and polymer+antibiotic starting solution concentrations were tested. The morphology and size of the obtained particles were analysed by scanning electron microscopy (SEM) (Figure 1). The release profiles of the drug were determined using a standard dissolution tester. The quantification of the drug in the supernatant was done by high performance liquid chromatography (HPLC). The particles which presented the best release rate were SEA 15 (Figure 2), containing 10% w/w of LOF and produced at 20 MPa with a concentration of polymer+antibiotic of 5 mg/mL. These particles were further characterized by dynamic light scattering (DLS) (Figure 3), which confirmed the wide size dispersion of the particles, and by zeta potential measurements, which gave a slightly negative potential, -10 mV.

Future work may involve both the optimization of the experimental conditions to decrease the size dispersion of the particles and their eventual coating with polyelectrolytes in order to extend the drug release time.

References

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2. Rodrigues M.A. *et al*., Journal of Supercritical Fluids, 48:253–260, 2009.

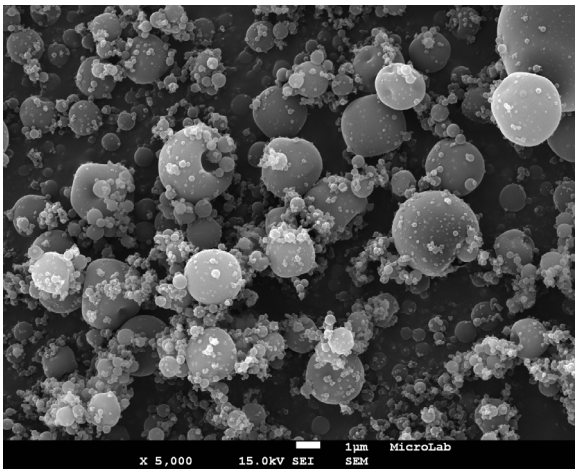

Fig. 1 - SEM image of the particles SEA15.

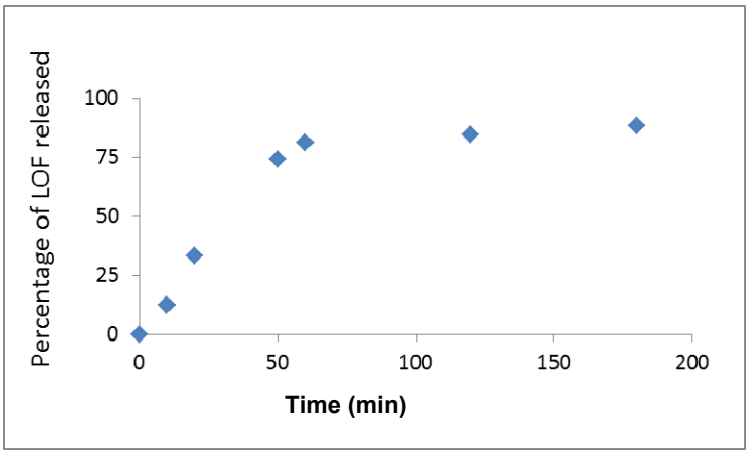

Fig. 2 - Drug release profile of LOF from particles SEA 15.

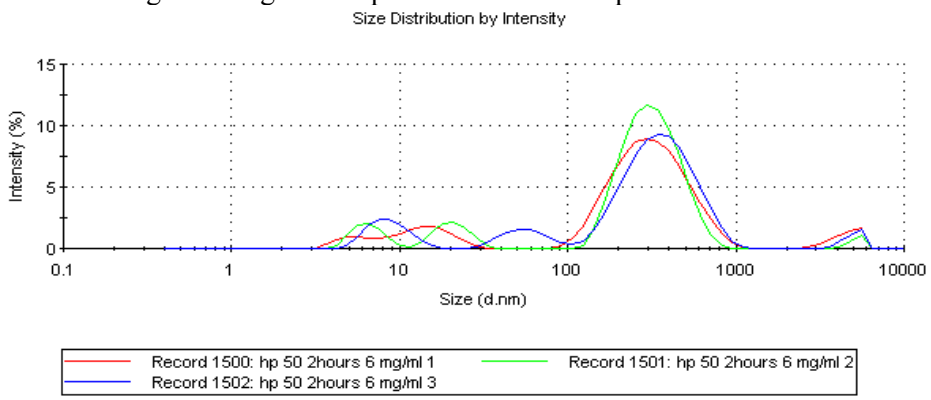

Fig. 3 - Dynamic light scattering graph showing the size distribution of the particles SEA15.

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