Chitosan-coated BSA nanoparticles for oral delivery

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Despite years of research, chronic pathologies, like cancer and chronic inflammatory diseases, are still in need of therapeutic approaches that allow easy administration, high compliance of the patient to the treatment and few or minor side effects. Engineered medicines, like surface-decorated nanoformulations, have the potential to accomplish all these important goals. However, oral administration of these formulations is a challenge due to the need to overcome the gastric harsh environment and be absorbed in the intestinal tract, reaching the blood flow as a whole functionalized particle.

This work aims to face this challenge using chitosan and/or poloxamer 407 as mucoadhesive and mucopenetrant polymers that will coat bovine serum albumin (BSA) nanospheres. Mucoadhesion increases the contact time of the particles with the intestinal epithelium, while mucopenetrance allows the progression of the particles through the intestinal mucosa, promoting their approach to the epithelial cells.

The nanospheres were produced by an emulsification method and then coated by incubation with polymers solution. The formulations were characterized by their size, zeta potential, morphology, and coating deposition in order to optimise the concentrations of the polymers.

Then, the nanoformulations were subjected to stability tests in simulated digestive fluids. The results obtained are promising since they showed diffusion of the coating polymers of the protein nanospheres to receptors fluids, liberating the protein nanospheres to be permeated throughout the intestinal mucosa. We detected differential profiles in terms of the size of the spheres coated with only one or with the two polymers and also in the amount of BSA that is released to the fluids, as measurement of spheres degradation. However, further improvements are being implemented in the analytic protocols.

Elemental biological tests were also performed. The formulations showed to be non-toxic to Caco-2 cells in the tested concentrations and preliminary results of *ex vivo* experiments with pig intestine showed the permeation of some material. However, it is necessary to develop new approaches to clarify these findings.

In conclusion, we believe that the use of chitosan and poloxamer 407 as coating polymers of nanospheres can mean a significant advance in the field of oral delivery and targeted-therapy and could have a high impact in the pharmaceutical industry.