PL 10 - Functional Granules Containing Didanosine-Loaded Chitosan Microspheres

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A process was developed for the production of functional granules containing chitosan microspheres, loaded with the drug didanosine (ddl), which is used in Acquired Immunodeficiency Syndrome (AIDS) therapy. The global process was designed to maintain the active form of the drug didanosine, which is sensitive to acidic pH conditions, and to obtain a final product with modified release, better mucoadhesiveness and intestinal permeation compared to the conventional formulation. In the first stage, didanosine-loaded chitosan microspheres were prepared by ionotropic gelation with sodium tripoliphosphate (TPP) as the crosslinking agent and magnesium hydroxide to ensure the stability of ddl. The incorporation was previously optimized using Response Surface Methodology and the maximum ddl loading in microspheres of 1433 mg of ddl/g of chitosan was obtained with 2.00% (w/v) chitosan and 10.00% TPP. The average diameter of microspheres was about 11.42 micrometer and ddl was gradually released during a 2 h period in a simulated enteric fluid. In the second stage, the extrusion-spheronization process was used for preparing granules. Microspheres were gently dried (35-40 Celsius degrees) to get a wet mass with moisture content of 75 %. Extra chitosan as excipient was added to the wet mass before extrusion and spheronization. The granules were characterized according to the in vitro mucoadhesiveness through the adsorption isotherm of mucin, and their ex vivo intestinal permeation, determined using the everted gut sac technique (Barthe et al., Fundamental & Clinical Pharmacology, 13, 154-168, 1999). Concerning the adsorption isotherm, the Langmuir model fitted very well to the experimental data. The results showed that the granules with extra chitosan as excipient presented greater affinity for the mucin as well as promoting an increase of 18 % in the ddI absorption through the duodenal segment compared with commercial free drug. The granules containing the chitosan microspheres showed a slower release of ddI compared to the commercial gastroresistent granules. These results demonstrate the feasibility to production of granules containing chitosan microspheres and their potentiality for AIDS therapy in terms of efficiency and comfort of the patients compared to the conventional formulations.