IVa25-014

Development of mucoadhesive PVA/CMC based hydrogel for intravesical chemotherapy

Lima, C.S.A.(1); Varca, J.O.(2); Ferrari, A.(1); Nogueira, K.M.(1); Varca, G.H.C.(2); Lugão, A.B.(2);
Universidade de São Paulo(1); IPEN/CNEN-SP(2); USP(3); Universidade de São Paulo(4); Instituto de Pesquisas Energéticas e Nucleares(5); Instituto de Pesquisas Energéticas e Nucleares(6);

Bladder cancer (BC) is one of the main diseases that attack the urinary tract and is globally responsible for 165,000 deaths per year. Bladder tumor may be classified as non-muscle invasive (superficial) or muscle invasive. About 70% of patients present the superficial bladder cancer which is treated by transurethral resection for tumor removal followed by intravesical chemo or immunotherapy. The main challenge reported in the instillation of chemotherapy is the limited drug residence time in the bladder as a consequence of urine levels that leads to fast drug removal from the bladder.1 Hydrogels are chemically or physically crosslinked polymer systems that form three-dimensional networks with high water absorption capacity. Carboxymethylcellulose (CMC) is one of the major soluble derivatives of cellulose widely applied in the medical and pharmaceutical fields due to its biocompatibility, nontoxicity, biodegradability and film forming ability.2 Polyvinyl Alcohol (PVA) is a synthetic polymer with wide pharmaceutical and biomedical applications as it is non-toxic, non-carcinogenic, bioadhesive and easy to process.3 In this work, we developed a mucoadhesive hydrogel from a CMC and PVA polymer blend for chemotherapeutic loading and suitable rheological properties for intravesical instillation, especially designed for treating superficial BC with increased residence time of chemotherapeutic agent. Three formulations (C1, C2 and C3) at different CMC concentrations were prepared - 1%, 2% and 3% (w/v), respectively. PVA concentration corresponded to 1% (w/v) for all formulations. The polymers were separately solubilized in Milli-Q water and then mixed prior to the addition of 20% (v/v) glycerin to increase the mucoadhesiveness of the material. The hydrogels were characterized according to their organoleptic and rheological properties to evaluate the behavior of the material under tension and temperature. Accelerated stability tests of the pharmaceutical form were also performed. Comparatively, formulations with glycerin presented improved mucoadhesiveness, and formulations with 1 and 2% of CMC presented more adequate rheological behavior for the proposed application. In conclusions, the systems presented adequate properties for the delivery of chemotherapeutic agents for optimized BC treatments. 1.KOLAWOLE, O. M. et al. Advances in intravesical drug delivery systems to treat bladder cancer. International Journal of Pharmaceutics, v. 532, n. 1, p. 105-117, 2017. 2.AKBARI, Z.Z et al. pH sensitive bionanocomposite hydrogel beads based on caborboxymethyl cellulose/ZnO nanoparticle as drug carrier. International Journal of Biological Macromolecules, v. 72, P. 640-648, 2015. 3.MARSI, C.et al. Influence of processing parameters on the macroscopic mechanical behavior of PVA hydrogels. Materials Science and Engineering C, v. 75, p.769-776, 2017