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POLY-EPSILON-CAPROLACTONE/CHITOSAN NANOPARTICLES: PHYSICOCHEMICAL CHARACTERIZATION, BLOOD COMPATIBILITY AND POTENTIAL APPLICATION AS ACTIVE VECTORIZATION SYSTEM

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Introduction: Of critical importance for systemically administered nanoparticles (NP) is their compatibility with blood and blood cells. There are different studies using nanoparticles mainly to transport drugs, genes or in diagnostic imaging. These studies are focused on different biological applications[1,2]. However, complete characterization of the particles under the physiological conditions is still lacking[2]. Surface modifications that inhibit capture by the immune system or complexation with ligands are able to decrease the interaction of nanoparticles with proteins present in biological fluids. Moreover, the functionalization with carbohydrates, peptides and antibodies can direct these nanostructures to specific sites in the body[1,3]. This goal is challenging, but highly interesting as a means of reducing adverse effects, increasing drug half-life and promoting physical and chemical stability of various compounds[1,4].
Objective: The aim of this study is to develop and characterize PCL nanocapsules coated with chitosan as a model for antibody binding in an active vetorization system. Beisdes, this study was focused in to assess the hemocompatibility of the proposed system.
Materials and Methods: Nanoparticles made of PCL were prepared by interfacial deposition of pre-formed polymers (NC PCL). After that, these nanoparticles were coated with chitosan (NC PCL-CS). The size and size distribution of particles were evaluated by laser difraction, dynamic light scaterring (DLS) and nanoparticle tracking analysis (NTA). The values of surface charge (zeta potential) before and after coating with chitosan were determined by electrophoretic mobility. Hemocompatibility studies using two differents concentrations of NC PCL and NC PCL-CS (2 and 10% w/v) in human blood was carried out by evaluation of hemolisys, platelet function, membrane integrity, and blood coagulation.
Results and Discussion: We can verify that the nanocapsules maintained their nanometric size even after coating with chitosan. Size mean values were 119 ± 1.71 and 133 ± 1.12 nm for NC PCL and NC PCL-CS respectively. Both nanoparticle suspensions showed a monodisperse distribution in all measurement particle size tecchniques used, which is of great importance for parenteral systems[4]. The polydispersity index (PDI) were lower than 0.17. The NC PCL suspension showed negative zeta potencial (-15.1 mV), while the NC PCL-CS suspension presented a positive value (+ 9.3 mV). The evaluation of the extrinsic coagulation pathway (prothrombin time - PT) showed that NC PCL and NC PCL-CS in both concentrations used did not significantly change the plasma clotting time, keeping the prothrombin activity higher than 70%, as recommended. The intrinsic pathway (activated partial thromboplastin time - aTTP) presented higher activation in 10% (w/v) nanocapsules concentration in plasma, but keep within the reference limits. For the same concentration of NC PCL and NC PCL-CS in the blood, we observed significant hemolysis after 8 h evaluation, differently from that observed in the concentrations of 2% (< 4% of the hemolyis). Besides, there was no presence of platelet aggregates in a blood smear containing NC PCL or NC PCL-CS (2 and 10% w/v) was analyzed under optical microscope.
Conclusions: The particle distribution of NC PCL and NC PCL-CS systems were in nanometrical range. The NC PCL-CS system is promising to be functionalized with antibodies. Besides the hemocompatibility studies showed that NC PCL and NC PCL-CS had an acceptable degree of hemocompatibility and therefore they can be considered suitable for intravenous administration.

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