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COMPARATIVE *IN VITRO* EVALUATION OF THE TOXICOLOGICAL PROFILE OF PCL NANOPARTICLES FORMULATED WITH DIFFERENT SURFACTANTS

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INTRODUCTION: Nanotechnology encompasses various areas, being especially applied in healthcare as a matrix for drug encapsulation, dissolution, and targeted drug release. Surfactants act as stabilizers of nanoparticles (NPs) due to their amphiphilic characteristic, which allows the formation of micelles or colloids that reduce interfacial tension and increase compound solubility. However, the same physicochemical properties that influence their biological effects can trigger cytotoxic effects. Nanomaterials are in constant contact with cell membranes, so the insertion of surfactants into these structures can modify permeability and lead to cell lysis. Therefore, nanotoxicological studies are essential for the safe and effective development of NPs. **OBJECTIVE:** To compare the *in vitro* toxicological profile of polymeric NPs prepared with different aqueous phase surfactants. **MATERIALS AND METHODS:** The formulations were obtained by the nanoprecipitation method, using the polymer poly-ε-caprolactone (PCL) with the surfactants Polysorbate 80 (Tween 80), Polyvinyl Alcohol (PVA), or Poloxamer 407. After preparation, the NPs were characterized regarding average particle diameter, polydispersity index (PDI), zeta potential (ZP), and stability. The murine fibroblast cell line, 3T3, was used to evaluate the *in vitro* toxicological profile through the MTT cell viability assay. Furthermore, the biological safety and biocompatibility of the systems were estimated by the hemolysis assay to assess hemolytic potential. **RESULTS AND CONCLUSION:** The nanoparticulate systems exhibited suitable physicochemical properties and remained stable for 30 days. The NPs were found to be non-hemolytic (hemolysis < 2%) at all the tested concentration range (1 to 10% (v/v)), evidencing their biocompatibility. Cytotoxicity evaluations showed that nanoencapsulation with Tween 80 was the most cytotoxic, with cell viability of 54.07% at the highest tested concentration. In contrast, the nanoformulations with PVA and Poloxamer 407 showed viability above 80% at all concentrations, being the PVA slightly better tolerated by the cells. These results suggest that the cytotoxicity of Tween 80 is not associated with membrane disruption, as no hemolytic activity was observed in erythrocytes, indicating the involvement of an alternative mechanism.

Keywords: Surfactants; polymeric nanoparticles; *in vitro* toxicity; cell culture; nanotechnology.

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