CYTOTOXICITY EVALUATION OF FREE IMMUNOSUPPRESSIVE AGENT (RD-07) AND COATED IN NANOPARTICLES OF ε-POLYCAPROLACTONE

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RD-07 is a potent immunosupressant agent, which is a macromolecule containing a large lactone ring, has been show several pharmacological applications. However, this compound has undesirable effects such as renal and liver toxicity. Biodegradable polymers have been extensively used for development of drug delivery system. Nanoparticle drug delivery systems have emerged as one of the most promising strategy to achieve modified release of many drugs improving efficacy and reducing toxicity. Hamster Chinese fibroblast (V79) and primary rat hepatocyte cultures were used for toxicity evaluation of free RD-07 and ε-polycaprolactone (PCL) nanoparticles containing RD-07 (prepared by spray dryer process-90% yield/loading 50%). Different biomarkers were used for relative toxicity assessment: MTT dye reduction, neutral red uptake (NRU) and nucleic acid content. Prior to *in vitro* experiments, the systems were characterised by means of their physic-chemical properties including size (250-650 nm) and morphology by scanning electronic microscopy. The cytotoxic effects of RD-07 incorporated in PCL were lower compared to the free FK506 evaluated by those viability assays (IC50 of 3 µM for the free form and no cytotoxic effects until 60 µM on the cells treated with RD-07 coated in nanoparticles). Unloaded PCL had no cytotoxic effects on V79 and hepatocyte cells. On the basis of these results, we suggested that RD-07 coated in nanoparticles present a lower cytotoxicity effect on V79 cells and hepatocytes than the free RD-07. In conclusion, our results indicate a potential beneficial application of encapsulated RD-07 since it was verified a toxicity reduction *in vitro*.

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