

Surpassing NSAIDs side-effects with Lipid Nanoparticles

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The inflammatory process is the innate immune response for the presence of pathogens, toxic molecules, tissue injuries or any other harmful conditions. The inflammation process is characterized for redness, pain, swelling, heat and disturbance of function and comprises inducers, sensors, mediators and effectors components from cellular and humoral origin. Macrophages are one of the most important cells in the inflammatory process. Macrophages actively phagocytose particles with sizes superior to 200 nm and express folate receptor making them of great interest for passive and active targeting strategies. Non-Steroidal Anti-Inflammatory Drugs, like oxaprozin, are one of the most used drugs prescribed for these conditions, however these drugs have adverse side effects, namely at the level of the gastric mucosa, that must be avoided and pharmacokinetic properties that need to be improved and for these purpose many delivery systems arise. Lipid Nanoparticles allow an effective drug packaging and targeted delivery, improving drug's pharmacokinetics and pharmacodynamics properties and avoiding some of their side effects. In this work, two formulations containing oxaprozin were developed: nanostructured lipid carriers with and without folate functionalization obtained by the addition of a synthesised DSPE-PEG₂₀₀₀-FA conjugate. These formulations revealed high stability, low polydispersity and mean diameters that allowed macrophages passive targeting along with high encapsulation and loading capacity. The formulations avoided the oxaprozin release in simulated gastric fluid promoting its release on simulated intestinal fluid, physiologic and inflammatory medium, remaining only a small amount entrapped on the lipid carrier matrix. MTT and LDH assays revealed that the formulations only seemed to present cytotoxicity in Caco-2 cells, for oxaprozin concentrations superior to 100 µM and permeability studies in the same cell line shown that oxaprozin encapsulation on the lipid nanoparticles did not interfere with oxaprozin permeability.