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<AT>*In vitro, ex vivo* and *in vivo* characterization of PLGA nanoparticles loading pranoprofen for ocular administration

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<ABS-Head><ABS-HEAD>Graphical abstract

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<ABS-HEAD>Abstract

<ABS-P>Pranoprofen (PF) is a NSAID considered as a safe anti-inflammatory treatment for strabismus and/or cataract surgery. The drug has been formulated in poly (lactic/glycolic) acid (PLGA) nanoparticles (PF-F1NPs with cPF 1.5 mg/ml, PF-F2NPs with cPF 1 mg/ml) produced by solvent displacement technique and tested the *in vitro* cytotoxicity, *ex vivo* corneal permeation, *in vivo* ocular tolerance and *in vivo* anti-inflammatory efficacy of PF-F1NPs, PF-F2NPs, in comparison to eye drops conventional dosage form (Oftalar®, PF 1 mg/mL) and free drug solution (PF dissolved in PBS, 1.5 mg/mL). The mean particle size of both formulations was around 350 nm, with polydispersity index below 0.1, and a net negative charge of –7.41 mV and –8.5 mV for PF-F1NPs and PF-F2NPs, respectively. **Y-79 human retinoblastoma cell line was used to evaluate the cytotoxicity of PF-F1NPs and PF-F2NPs, which were compared to blank NPs and free drug solution (PF dissolved in PBS, 1.5 mg/mL). Concentrations up to 75 µg/mL exhibited no toxicity to Y-79 cells, whereas at 150 µg/mL a decrease of about 80% on the cell viability was observed after exposing the cells to PF-F1NPs. When treating the Y-79 cells with concentrations of PF-F2NPs between 1 µg/mL to 100 µg/mL, the cell viability was similar to control values after 24h and 48h of exposure**. An *ex vivo* corneal permeation study was carried out **in** New Zealand rabbits. **A very similar profile has been observed for the permeation of PF through the cornea when administered as eye drops and as free drug solution, which was kept much lower in comparison to PF-NPs formulations**. The permeated amount of PF from the PF-