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Abstract Title: Solid Lipid Nanoparticles Topically Administered in Rabbits as New Drug Delivery System: A Preliminary Study of Safety and Bioavailability

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Abstract Body: Purpose: Solid lipid nanoparticles (SLN) are new carriers able to incorporate and deliver hydrophobic and hydrophilic drugs. Aim of this work was to evaluate the ocular toxicity and bioavailability of Unloaded-SLN and fluorescent SLN (Fluo-SLN) and to study the bioavailability and pharmacokinetics of Triamcinolone Acetonide-loaded SLN (TA-SLN) in rabbits.

Methods: The different types of SLN were prepared by a warm o/w microemulsion method. Ocular toxicity (assessed by clinical examination, electroretinography, light and electron microscopy) and fluorescence distribution were evaluated 30 minutes, 2, 4 and 24 hours after topical administration of 50 microliter of Unloaded- and Fluo-SLN in 24 eyes.

50 microliter of TA-SLN (2,1 mg/ml) were topically administered in 15 eyes and drug levels in the cornea, aqueous humor, lens, vitreous, retina and choroid were determined at 30 minutes, 1, 2, 4 and 24 hours.

Results: SLN dispersion was perfectly tolerated: there was no evidence of toxic effects based on the clinical examinations. Electroretinography evaluations showed no functional alterations. SLN caused no histopathological or ultrastructural damage to the retina or other ocular tissues. Fluorescence analysis revealed a dotted positivity on cornea surface and a diffuse positivity in retina tissues. Topical administration of TA-SLN resulted in detectable drug levels in the retina and in all the analyzed tissues. Mean concentration  $\pm$  SEM in different tissues at different times are reported in Figure 1.

Conclusions: Topically administered SLN are safe and sustain retinal drug delivery. These results add further support to the potential use of these nanoparticles as drug carriers to topically treat retinal diseases.

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