Development and Characterization of Indomethacin Loaded Solid Lipid Nanoparticles for Ocular Delivery
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Purpose
Indomethacin (IND) is a topical non-steroidal anti-inflammatory agent employed in the treatment of ocular inflammation. The objective of the present study is to investigate topical delivery of IND from various formulations and improve its ocular bioavailability.

Methods
IND-solid lipid nanoparticles (IND-SLN) were prepared using hot homogenization method. IND-SOL (control), IND-SLN and IND-SLN+2.5% HPβCD formulations, each containing 0.1% w/v IND, were evaluated in vitro with respect to flux across the scleral-choroid-RPE (trans-SCR) tissue (3 h). Furthermore, effect of water soluble chitosans (Mol. wt 3K, 6K, 9K) and chitosan chloride (Mol.Wt < 200 KDa) on transcorneal permeation of SLNs was determined. In the in vivo studies, IND-SOL, IND-SLNs and chitosan coated IND-SLNs were used to investigate ocular tissue concentrations 2h post topical instillation in male New Zealand white rabbits. All animal studies were conducted following IACUC approved protocols.

Results
IND content in all the formulations was found to be within 98 -103% of theoretical value. Particle size, zeta potential, polydispersity index & entrapment efficiency of IND-SLN and chitosan coated IND-SLN were observed to be 226 ± 5 nm; 265 ± 8 nm, -22 ± 0.8 mV; 27 ± 1.2 mV, 0.17;0.30,81%± 0.9% and 91.5 ± 3.2 %, respectively. Trans-SCR flux of IND-SOL, IND-SLN, IND-SLN+HPβCD was observed to be 0.08 ± 0.007,0.07 ± 0.026,0.11 ± 0.03 µg/min/cm², respectively. Transcorneal flux of SLN (control),SLN-3K,SLN-6K,SLN-9K,SLN-chitosan chloride was determined to be 0.6 ± 0.03, 0.52 ± 0.04,0.55 ± 0.03,0.46 ± 0.01,1.28 ± 0.06 µg/min/cm², respectively. IND-SLN formulations tested in vivo delivered significantly higher levels of IND to all the ocular tissues tested, including the posterior segment ocular tissues.

Conclusion
The results from these studies suggest that high levels of IND can be maintained in the ocular tissues for prolonged periods with the IND-SLN formulations. Surface modification of the IND-SLNs using chitosan chloride may further improve ocular penetration and retention at the ocular surface and thus increase bioavailability of IND. These studies are currently in progress.