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Development and characterization of a novel polymeric nanomicellar formulation (size 10-15 nm) for intermediate and posterior uveitis

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Purpose: To develop Dexamethasone (DEX) loaded polymeric nanomicelles in size range of 10-15 nm for the treatment ofintermediate and posterior uveitis.

Methods: A low molecular weight diblockco-polymers (mPEG750-PCL1200) was synthesized by ring opening polymerization usingmPEG as macroinitiator and stannous octoate as catalyst. Polymer was characterized by H1 NMR, IR spectroscopy, gelpermeation chromatography, critical micelle concentration (CMC), and cytotoxicity studies in conjunctival and retinal cell lines. DEX-loaded nanomicelles were prepared by modified film hydration method. In order to achieve an optimizedformulation containing 1 mg/mL DEX, a 2 factors-3 level response surface methodology was generated using SAS 9.02. Theindependent factors were polymer amount (X1) and DEX amount (X2). Solubility of DEX in micelle solution was taken asresponse variable (Y). The optimized formulation was characterized for solubility of DEX, micelle size and PDI, and TEM analysis. The formulation was also subjected to *in vitro* drug release, *in vitro* transport across conjunctival cell line and *exvivo* transport across excised rabbit sclera.

Results: The diblock copolymer was successfully synthesized and characterized for structure by H1-NMR and IR spectroscopies. The Mw, Mn and PDI were 1972 Da, 1627 Da and 1.21, respectively. The CMC was 3.87 µg/mL. The model for predicting the DEX solubility was found to be significant and was validated by check point analysis. The optimized nanomicelles exhibited mean size in range of 10-13nm with unimodel size distribution and low polydispersity. The optimized formulations exhibiteda 2 fold increase in DEX permeability across the conjunctival cell line as compared to DEX suspension. The permeability of DEX across the excised rabbit sclera with the nanomicelles was 2.65E-06 cm/sec, which was 2.2 fold higher compared to DEX in suspension.

Conclusion: The design of experiment was successfully utilized for predicting the DEX solubility in micellar formulation. Higherpermeability of DEX was observed across both conjunctiva and sclera with nanomicellar formulation. This nanoformulation might have potential to deliver drugs to the posterior segment by noninvasive route.

Biography

Chandramouli Natarajan completed his Bachelors in Microbiology from Bharathidasan University, India and Masters in Biotechnology from Sri Ramachandra University, India. He is currently pursuing his Ph.D. from University of Missouri Kansas City, in Dr. Mitra's lab with focus on drug delivery of cancer therapeutics. Prior to my admission to Ph.D. program at UMKC, he was offered a fellowship by the Government of India on a project to characterise compounds from plants against the malarial parasite, Plasmodium falciparum. Other than his interest in cancer therapeutics and parasitology, he is also interested in drug delivery for treatment of inflammation in the eye.

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