UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

Design and characterisation of an intraocular nanobubble drug delivery system

Kealeboga Mokolobate

Supervisor:
Professor Viness Pillay
University of the Witwatersrand, Department of Pharmacy and Pharmacology
Johannesburg, South Africa **Co-supervisors:**
Professor Yahya E. Choonara
University of the Witwatersrand, Department of Pharmacy and Pharmacology
Johannesburg,South Africa **and**
Associate Professor Lisa C. du Toit
University of the Witwatersrand, Department of Pharmacy and Pharmacology,
Johannesburg, South Africa

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Abstract

The posterior segment of the eye poses many challenges in terms of drug delivery. Procedures such as intraocular injections are invasive, are associated with low compliance, and may yield health hazards such as cataracts. This study aimed to design a layer-by-layer-originated lipopolymeric intraocular nanoparticulate system, administered in the cul-de-sac of the eye, for the treatment of uveitis. The main aim is for the formulation to have theranostic capability: the ability to treat the disease, and also visually track the movement of the nanoparticulate systems through ultrasound the use of Vevo®2100 high resolution ultrasound imaging system. These nanoparticulate systems were produced by dissolving the lipids (cholesterol and soybean oil), buffer pH 7.4 and drug in chloroform. This emulsion was sonicated and the organic solvent was removed. The emulsion was then freeze-thawed. Following that, a layer of chitosan was added to the nanoparticles, allowed to deposit, and finally, a layer of polyethene glycol was added and allowed to deposit. Zetasizing was used conducted to ensure stable particles within the nanometre range (below 200nm). Drug release studies were conducted on the formulations and images through atomic force microscopy highlighted nanoparticles with a thick shell due to the reinforced layering, effectively entrapping the drug. This study illustrated how the variables (time of sonication, number of freeze-thaw cycles and amount of polymer [soybean oil]) affected the formulation and enabled determination of an optimised formulation. The chemical stability of the formulations was examined by Fourier Transform Infrared(FTIR) and X-Ray Crystallography. Differential Scanning Calorimetry and Thermogravimetric Analysis assessed the formulation's reaction to heat, and thus stability. Rheological studies assisted in elucidating rheological behaviour and likely behaviour in the eye. This formulation (once incorporated into a suspension) will circumvent the need for invasive procedures regarding infections in the posterior segment of the eye in treating uveitis.