DEVELOPMENT OF AN ELUTING-SUPRAMOLECULAR ASSEMBLED CONTACT LENS-LIKE DEVICE FOR THE TOPICAL BIOGENIC TREATMENT OF CATARACTS

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A dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, in fulfillment of the requirements for the degree of Master of Pharmacy

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DECLARATION

I, Zikhona Hayiyana, declare that this dissertation is my own work. It is being submitted for the degree of Master of Pharmacy in the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg. It has not submitted before for any degree or examination at this or any other University.

..................................................

Signed at ........on this.... day of November 2016
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Above all, to God is the Glory, now and forever more, Amen.
I would like to dedicate this work to my siblings. I hope that it will remind you that we truly can achieve all things and no mountain is too high for us to climb. Keep pushing. All things are possible to those who believe. Let us therefore continue to climb to higher dimensions.
1. Review Paper

2. Research Papers
   b. A nanosponge-modified stimuli sensitive sol-gel system for ocular drug delivery: For submission to an ISI-accredited international journal (Journal of Inclusion Phenomena and Macrocyclic Chemistry).
1. **Podium**

2. **Poster**
I hereby confirm that the study entitled: ‘In vivo assessment of topical ocular drug delivery systems in rabbits’, received approval from the Animal Ethics Screening Committee of the University of the Witwatersrand. Ethics clearance number: 2014/66/C (See Appendix C1).
A Provisional Patent will be submitted to the South African Provisional Patents Association.
This project tackles two main issues: poor ophthalmic drug bioavailability and treatment alternatives for cataract. A synergistic approach of developing a bi-composite drug delivery system with components possessing the capacity to improve drug solubility, drug stability, residence time, amount of drug available at the membrane surface and membrane permeability was developed through the application of highly potent nanosponges and an in situ gelling system.

The newly synthesized bi-composite system was assessed for toxicity using the Epioocular Tissue Model™ and was found to be non-toxic with a Draize score of 18.15. It was then assessed for potential to deliver bioactives in vivo using 2-2.5kg New Zealand White Rabbits. Two main administration routes were tested; the topical and intravitreal route. Assays for detection of the bioactives from the aqueous humor, lens and vitreous humor were performed and quantitative analysis was performed using Ultra Performance Chromatography (UPLC). The bioactive levels reached up to 80% saturation in some ocular tissue sites. The next step involved a second in vivo study where cataract was induced on 4-5 weeks New Zealand White pups using diquat dibromide. Following confirmation of cataract development by slit lamp illumination, the bi-composite drug delivery system was used as a carrier for a bioactive combination (acetyl-carnosine and nicotinamide). A single intravitreal injection of the bioactive bi-composite system was able to dissolve early stage cataract within minutes of administration and was able to delay onset and progression of cataract in the preventative group of the study. Although this positive effect was observed, the cataract returned in 24-48 hours, which lead to the hypothesis that continuous use or multiple administrations of the system may derail cataract onset and progression. Although signs of cataract development were observed in the preventative group, some structures such as the cornea still remained clear for prolonged periods of time (14 days) as compared to the group that was only administered the cataract-inducing agent.

An alternative drug delivery approach that was assessed was the use of a contact lens-like device. The short-comings experienced such as the inability to obtain the correct shape and surface properties without the proper instrumentation, and inability to assess important properties such oxygen permeability in the absence of the instrumentation lead to its exclusion during the in vivo studies to prevent causing unnecessary harm and discomfort to animals.
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