NANOPARTICLE-LOADED CONTACT LENS: A POTENTIAL OCULAR DRUG DELIVERY SYSTEM FOR A CONTROLLED RELEASE

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Background: Treatment of ocular disorders have often relied upon topical delivery strategies, which can be associated with low drug bioavailability. While improving therapeutic bioavailability, intravitreal routes can be associated with side effects (retinal detachment). Developments in nanoscience have resulted in the study of several novel, safe, patient-friendly drug delivery systems. Additionally, the use of therapeutic contact lenses (CLs) has received considerable research focus. This project aims to develop a soft CL impregnated with drug-loaded polymer nanoparticles for controlled drug release.

Methods: Various process parameters: curing conditions, hydration/extraction processes and sterilization methods were investigated in the manufacturing of the CL. Lenses were fully characterised to establish their optical, physical and mechanical properties.
To optimise drug loading, inclusion complexes were prepared using various drug concentrations, solvent systems and complexation methods. Phase solubility studies determined the optimum stoichiometric ratio of drug and cyclodextrin. The complex was characterized by thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), Fourier-transform infrared spectroscopy (FTIR) and high performance liquid chromatography (HPLC).
Chitosan (CS) and Hyaluronic acid (HA)-coated CS nanoparticles were synthesized using an ionic gelation technique at room temperature. These particles were then loaded with naringenin (NAR), a drug chosen because of its wide range of pharmacological activity for ocular therapy. The developed NAR-loaded nanoparticles were examined by dynamic light scattering, TGA, DSC, and FTIR with drug encapsulation efficiency determined by HPLC.

Results: Soft hydrogel CLs were successfully manufactured to commercial standards on-site. These lenses exhibited >99% optical transparency, 78% water content, refractive index of 1.37332, dimension of 14.3 mm and tensile strength of 0.64 ± 0.05 MPa.
Phase solubility studies (25 °C) demonstrated that the optimum drug:cyclodextrin molar ratio was 1:3. Freeze-drying of a tert-butyl alcohol:water co-solvent system was determined to be the best preparation method after characterizing the complexes by TGA, DSC and FTIR, with a resulting complexation efficiency of 98.7% ± 0.8%. A significant (>6000-fold) increase in hydrophobic drug aqueous solubility was obtained.
Non-drug and NAR-loaded CS NPs were successfully developed and characterised, with a particle size of 360 ± 9.9 nm and 333.3 ± 26.6 nm, a zeta potential of +38.6 ± 2.1 mV and +22.0 ± 4.3 mV, and a polydispersity index of 0.0671 ± 0.0362 and 0.0777 ± 0.0580, respectively. NAR encapsulation efficiency in CS NPs was measured to be 13.0 ± 1.9%. HA-coated CS NPs (366.3 ± 27.7 nm, -28.6 ± 1.1 mV and 0.1212 ± 0.0216) were also formulated and shown to enhance the stability of CS NPs at pH 6.8-7.4.

Conclusions: The results from this study demonstrated that NAR-loaded NPs for ocular drug delivery (ODD) were successfully prepared by ionic gelation of CS and cyclodextrin. Coating the NP with HA improves NP stability and targeted delivery, as well as enhancing eye comfort for CL wearers. Such nanoparticulate systems will be loaded into the developed SCL of commercial quality. This model can act as a novel ODD system to provide a more sustained, less invasive and controlled delivery of a drug or supplement to the eye.