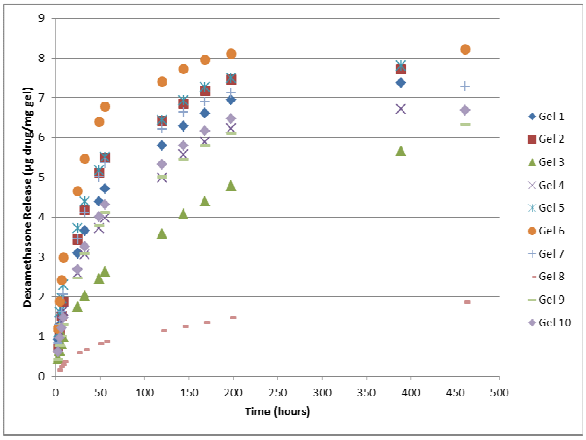
Evaluating the Relationship Between Transparent Ocular Hydrogel Chemistry and Dexamethasone Delivery Parameters

G. Guidi,[1] M. Whinton,[1] M. Brook,[1] T. Hughes,[2] H. Sheardown. [1]
1.Department of Chemical Engineering, McMaster University, Hamilton, Canada
2.CSIRO Materials Science and Engineering, Melbourne,

Statement of Purpose: Topical delivery of ophthalmic formulations through the use of eye drops remains the primary means of treatment for various ocular diseases. However, there exist significant drawbacks with delivering drugs using eye drops, specifically the short residence time, resulting in low levels of bioavailability [1,2]. Contact lens based drug delivery systems represent a promising alternative to address these issues by providing a means of controlled delivery of ophthalmic therapeutics. Various studies have evaluated both commercial and developmental hydrogel systems [3]. However, there exist limited literature related to understanding the fundamental relationships between lens hydrogel chemistry, drug loading and release kinetics. This study aims to show how underlying chemistry has a direct impact on drug partitioning and release parameters and evaluates the influence of different hydrophilic and hydrophobic monomer functionality on a multitude of lens properties.

Methods: A range of hydrogel materials were synthesized to model both conventional and silicone commercial lenses through bulk free radical polymerization. Materials were created using combinations of the hydrophilic monomers, dimethylacrylamide (DMA), hydroxyethyl methacrylate (HEMA) and the hydrophobic silicone monomers, polydimethylsiloxane methacrylate (MA-PDMS), (methacryloxyhydroxypropoxypropyl)methylbis(trimethyl siloxy)silane (TRIS-OH) and Silmer ACR-A008 from Siltech Corp. using ethylene glycol dimethacrylate (EGDMA) as a crosslinker and Irgacure 184 as the photoinitiator. These materials were extracted using a 50:50 mixture of isopropyl alcohol in water for 24 hours; extraction was confirmed by UV spectroscopy. Materials were then loaded with dexamethasone by soaking in a 1mg/mL solution in 50:50 methanol-water for 48 hours. The amount of drug loaded was quantified by measuring the concentration change in the uptake solution and partition coefficients were calculated. Materials were then dried for 3 days to remove any residual solvent and subsequently used for release in 1.5mL of PBS at 37°C. The dynamic release was then measured at 240nm by sampling at regular intervals while infinite sink conditions were maintained throughout. Additional properties such as equilibrium water content, contact angles, light transmittance and optical haze were measured.

Results: The release curves demonstrate significant differences in the rate and durations of release from the range of different hydrogel materials. It is evident that the nature and ratios of both hydrophilic and hydrophobic monomers directly impact the drug partitioning, release rate and drug release amount. In all hydrogels a consistent trend of short burst release followed by a longer period of prolonged slow release was observed. After 2 weeks, total drug release across all the materials ranged from approximately 1.8-8.2 µg dexamethasone/mg dry gel. HEMA based materials repeatedly demonstrated slower more controlled release than comparable DMA based hydrogels. The inclusion of MA-PDMS reduced the release rate of dexamethasone. Furthermore, the inclusion of a polymerizable silicone surfactant monomer increased the silicone content while simultaneously increasing the release rate and surface wettability. All materials except one showed light transmittance and scattering properties that would be suitable for contact lens applications. Equilibrium water content of these materials ranged from 10%-35% and appears to be the major property that governs release rate.



Conclusions: Studies of contact lens drug delivery often evaluate commercial branded lenses for their drug delivery properties. However, without a detailed understanding of the chemical composition of these lenses it is difficult to relate the quantifiable changes in release kinetics to the differences in the chemistry of the lens types. This study bridges that gap to fundamentally understand how the hydrogel monomer formulation can affect the drug uptake and release properties from such materials in the context of a hydrophobic drug. These results help to establish correlations between monomer polarity, respective contribution to overall polymer composition and the release parameters. It is possible in the future that through modification of polymer chemistry, specifically designed hydrogel systems can be exploited to generate a therapeutic release that would be useful in extended wear contact lens applications.

References: [1] Peng C et al. Biomaterials. (2010). 41: 4032-4047. [2] Rosa dos Santos J et al. Biomaterials. (2009). 30: 1348-1355. [3] Boone A et al. Eye and Contact Lens. (2009). 35: 260-267.