Assessment of *in vitro* Contact Lens Material Biocompatibility at the Ocular Surface

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Introduction:

Over 125 million people wear contact lenses worldwide, of which approximately 90% wear water-containing, soft (hydrogel) lenses [1]. Following removal from the eye, contact lenses must be placed in a contact lens solution for disinfection and to remove tear film deposits. Clinical and retrospective studies have shown that different combinations of contact lens and lens care products may be more biocompatible than others. Assessing biocompatibility or the impact of lens and solution combination on corneal epithelial cells is a complex and controversial issue as *in vivo* and *in vitro* measures of compatibility are significantly different. In an effort to gain a better understanding of lens-solution interactions, a novel, 3D curved, *in vitro* stratified multilayer of the human corneal epithelium was recently developed in our laboratory. Due to its curvature and stratification, it is a much closer mimic of the lens interactions with the human corneal epithelium and may be more physiologically relevant than a monolayer, currently the most widely used *in vitro* model.

As hydrogel materials, contact lenses are recognized to uptake and release components of solution [2,3], and as such may be considered as drug delivery devices on the cornea. The power of the lens has been shown to be related to oxygen transmissibility and lens thickness [4,5]. Effects of blinking and tear replenishment have also been purported to affect material interaction at the cornea [6]. All of these parameters combined may affect the uptake and release of chemicals from contact lenses and thus the outcome of *in vitro* tests.

Benzalkonium chloride (BAK) is a common preservative used in ophthalmic solutions and has previously been demonstrated to be cytotoxic *in vitro*. Our current study uses the curved, stratified model of the human corneal epithelium to investigate changes in biocompatibility as a result of exposure to BAK released from commercially available lens materials in both a static and dynamic system.

Materials and Methods:

30 mm cellulose inserts were permanently deformed into a curve by a die with the dimension and curvature of an average human cornea. SV40-immortalized HCEC were cultured on the curved inserts in a keratinocyte serum-free medium supplemented with growth factors. On day 7, cells were differentiated into a stratified multilayer.

For this study, commercially available conventional hydrogel lenses omafilcon A and etafilcon A and silicone hydrogel lens balafilcon A were used. Powers of lenses varied from -

0.50D to -6.00D which had thicknesses on the order of 0.1mm. Contact lenses were soaked for 24 hours in a solution of Moisture Eyes (Bausch and Lomb) which contains BAK at a concentration of 0.01% w/v. The lenses were then placed on the stratified multilayers in a static system for periods of 2, 6, and 24 hours and were compared to controls of lenses soaked in phosphate buffered saline. Cells were also exposed to the dynamic Tear Replensihment System [6] for two hours in order to determine the effects of spraying and regular fluid exchange on the corneal cell multilayer. After the incubation period, viability of cells in the constructed multilayer was assessed using the metabolic assay thiazoyl blue tetrazolium bromide (MTT). Viability results are reported as percentage relative to control cells: cells incubated in a static environment without a contact lens.

Results and Discussion:

Formazan staining as a result of MTT on the cellulose inserts indicated proper growth and stratification of the multilayers. Compared to cells grown in the absence of a lens, there was no difference in viability for any of the PBS-soaked lenses. Exposing the multilayers to the Tear Replenishment System did not result in any significant difference in viability (96 ± 14% vs control) suggesting that the "spraying" did not affect cells.

In the static model, reduced viability was observed with the two conventional hydrogels (etafilcon A and omafilcon A) when compared to the silicone hydrogel, suggesting a higher BAK release. This is in agreement with previous work where higher release of latanoprost has been observed with omafilcon A [7]. As expected, as the lens incubation time increased, the viabilities were reduced for lenses containing BAK. At two hours, the level of viability for BAK soaked lenses was around 80% but by 24 hours this was reduced to a viability of roughly 20-30%. The highest reduction in viability was observed with the -3.00D omafilcon A, suggesting a higher BAK release. For a power of -3.00D, the thickness of the lens is the smallest and our results would agree with Ali et al. who have previously shown that drug release (by mass) is proportional to the inverse of the square of thickness [8]. Spraying of the BAK-soaked lenses on the corneal models resulted in a change in biocompatibility in etafilcon A and omafilcon A lenses. Etafilcon A lenses showed a lower viability with tear replenishment whereas omafilcon A showed a higher viability with tear replenishment.

Conclusion:

This novel curved-stratified in vitro human corneal model was able to detect differences in release of BAK, as evidenced by changes in viability, from varying thicknesses of commercially available contact lenses. Spraying the multilayers also showed a marked difference in the release from lenses. Differences were also observed in multilayers that were incubated with BAK-soaked contact lenses in the TRS. Our results indicate that physical parameters such as lens thickness and tear replenishment may play a role in lens-solution

interaction and further highlights the complexity of developing *in vitro* models of biocompatibility.

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