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## INTRODUCTION

- Acute and chronic ultraviolet (UV) exposure can lead to various ophthalmic pathologies.
- The type and extent of damage from UV radiant energy is associated with the wavelength, duration, intensity, and size of the exposure.
- Spheroidal degeneration, UV keratitis, pinguecula and pterygium.<sup>1</sup>
- Crystalline lens opacification/cataract.
- Most common cause of visual impairment.<sup>2, 3</sup>
- Cataract extraction is one of the most common surgical procedures.<sup>3, 4</sup>
- Estimates of the increase in UV-associated cataract in the next 20 years are staggering given the current rates of ozone depletion.<sup>5</sup>
- Even slowing the progression of cataracts, could dramatically impact the reduction in morbidity associated with cataracts in addition to costs to society
- Class I (filter at least 90% UVA and 99% UVB) UV-absorbing silicone hydrogel polymers have been introduced, providing the highest level of UV protection.
- A hydrogel contact lens is in intimate contact with the ocular surface, therefore potentially protecting the surface it covers in addition to the internal structures of the eye that are vulnerable to UV induced damage.
- It is hypothesized that use of Class I ultraviolet (UV)-absorbing hydrogel polymers will prevent deleterious changes associated with UV exposure in the cornea, aqueous humor, and crystalline lens.

## METHODS

### Design and In Vivo UVR Exposure

- Approved by Institutional Animal Care and Use Committee (IACUC); conducted according to ARVO Statement for Use of Animals
- Prospective, non-masked study with 12 adult pigmented rabbits (2.5-3.0 kg).
- Minimal number needed to show differences in the observed outcomes.
- Treatment groups were as follows (n = 4 per treatment group):
- 1) Senofilcon A lenses (Acuvue Oasys, absorbs 100% of UV-B and 96% of UV-A).
- 2) Lotrafilcon A lenses (Focus Night and Day, minimal UV absorption).
- 3) No contact lens (but exposed to UV radiation).

The contralateral eye of each rabbit was patched without contact lenses.

- Rabbits received UV-B (1.667 J/cm2) and UV-A (0.245 J/cm2) exposures daily for 5 days.
- Allowed to recover from for 2 days.
- On day 8, rabbits were euthanized.
- Eyes were enucleated, dissected, and stored within 30 minutes of death.

### Outcomes

### Zymography (Corneal MMP-2 and MMP-9)

- SDS-PAGE gelatin zymography was performed as previously described.
- Digested bands compared with active-recombinant human MMP-2 and MMP-9 standards (Oncogene; San Diego, CA) included as positive controls and protein molecular weight markers (BioRad) run in tandem.
- Analyzed by Kodak ImageStation 4000MM (Carestream Molecular Imaging; Rochester, NY) for densitometry readings of digested bands.

### **Caspase-3 ELISA (Corneal and Lenticular Apoptosis)**

- Determined with caspase-3 colourimetric assay kit (R&D Systems; Minneapolis, MN).
- Read on the Infinite M200 (Tecan; Durham, NC) microplate reader at 405 nm.

### **TUNEL (Corneal and Lenticular Apoptosis)**

- Performed on paraffin-embedded tissue slides with Apoptosis Detection System (Promega; Madison, WI).
- (cornea or lens) and two non-consecutive slides were counted.

### Nuclear magnetic resonance (NMR) (Aqueous Ascorbic Acid **Concentration**)

- 500 uL of aqueous humor aspirated from each eye and dissolved in 2,2,3,3-d4 (TSP) in deuterium oxide (D2O).
- (Bruker DRX800; Biospin GmbH, Rheinstetten, Germany).

### Statistical Analysis

- Analyses focused on three main hypotheses.
- benefit)
- blocking contact lens provides benefit).
- difference in the outcomes).

# Uv-Blocking Silicone Hydrogels Prevent Uv-Induced Damage to the Anterior Segment

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a 500 µL solution of 0.25 mM sodium-3'-trimethylsilypropionate-

• High resolution NMR spectra were recorded on a NMR spectrometer

1) Exposed senofilcon A eyes vs. corresponding eyes with patch (same 4 rabbits) using Wilcoxon signed rank test (hypothesis: no difference between the two eyes if the UV-blocking CL provides

2) Exposed senofilcon A eyes vs. exposed lotrafilcon A eyes (4) different rabbits) using the Wilcoxon rank sum test (hypothesis: there should be a difference between the two eyes if the UV-

3) Exposed eyes wearing lotrafilcon A vs. exposed eyes wearing no contact lenses (again, four different rabbits in each group) using the Wilcoxon rank sum test (hypothesis: there should be no

### Aqueous Humor Changes





were noted in either caspase-3 activity or TUNEL positive cells.

Figure 3. Aqueous humor ascorbate levels following UV exposure. A statistically significant (p = 0.03) decrease in aqueous humor ascorbate was observed in the exposed lotrafilcon A wearing group compared to the exposed senofilcon A wearing group. There were no significant differences in ascorbate when the lotrafilcon A wearing group was compared to the non-lens wearing group or when the senofilcon A group was compared to the unexposed patched control eyes.



**Figure 4.** Apoptosis in the rabbit crystalline lens following UV exposure. (A) A statistically significant (p = 0.03) increase in caspase-3 activity was observed in the exposed lotrafilcon A wearing group compared to the exposed senofilcon A wearing group. No significant differences were found in caspase-3 activity when the lotrafilcon A wearing group was compared to the non-lens wearing control group. (B) There were no significant differences between any of the treatment groups when the total number of TUNEL positive cells were counted. When the senofilcon A group was compared to the unexposed patched control eyes, no significant differences were noted in either caspase-3 activity or TUNEL positive

were found in either caspase-3 activity or TUNEL positive cells when the lotrafilcon A wearing group was compared to the non-lens wearing control group. When the senofilcon A group was compared to the unexposed patched control eyes, no significant differences

### Crystalline Lens Changes

## DISCUSSION

### **Corneal Findings**

- UV-B radiation makes up small percentage of the solar spectrum but produces most of the damage to mammalian cells.<sup>7-9</sup>
- UV-B has been shown to induce the production of matrix metalloproteinases (MMP) by the corneal epithelium and stroma in dogs and humans.<sup>10, 11</sup>
- There was significant induction of both MMP-2 and -9 in both the lotrafilcon A group and non-lens wearing control group compared to the senofilcon A group.
- There was no difference in MMP-2 or MMP-9 expression in the senofilcon A test eyes compared with the unexposed (patched) eyes.
- This data supports the hypothesis that blocking UV exposure can decrease protease expression in the cornea.
- There was induction of cell death due to UV exposure (TUNEL-positive cells and caspase-3 activity) in the non-contact lens control group and the lotrafilcon A group following irradiation.
- The use of senofilcon A contact lenses significantly decreased apoptosis in the cornea.

### Aqueous Humor

- Composition of aqueous humor is suggested to play a protective role in the pathogenesis of cataract, acting as a filter against both UV-A and UV-B radiation.<sup>12</sup>
- Filtering effect is mainly related to its high ascorbic acid concentration, operating as an antioxidant.<sup>13-16</sup>
- Aqueous humor from cataract patients has shown decreased ascorbic acid compared to normal patients.<sup>17</sup>

## CONCLUSIONS

- These data support our hypothesis that UV-blocking contact lenses show similar protective findings in the cornea and crystalline lens as compared with non-UV absorbing contact lenses and exposed eyes.
- This is supported by data from previous studies that have demonstrated that UV-absorbing contact lenses can minimize UV-induced ocular damage.<sup>26-32</sup>

## REFERENCES

- Bergmanson JP, Soderberg PG. The significance of ultraviole UV-blocking contact lenses. Ophthalmic Physiol Opt 1995;1
- Resnikoff S. Pascolini, D., Etya'ale, D., Kocur, I., Pararajaseç impairment in the year 2002. Bulletin of the World Health (
- . Baltussen R, Sylla, M., Mariotti, S. P. Cost-effectiveness ar World Health Organization 2004;82:338-345.
- Ellwein LB, Urato, C. J. Use of eve care and associated ch Ophthalmology 2002;120:804-811.
- 5. Javitt JC, Taylor, H.R. Cataract and latitude. Documenta O 6. Sobrin L, Liu, Z., Monroy, D.C., Solomon, A., Selzer, M.G., I tear fluid and corneal epithelial culture supernatant. Investi
- 7. Young A. Acute effects of UVR and human eyes and skin. Pr 8. Adhami VM, Syed, D.N., Khan, N., Afag, F. Phytochemicals
- Photochemistry and Photobiology 2008;84:489-500. Friedlaender MH. Ultraviolet radiation and the eye. 45 vol. I
- 10. Chandler HL, Kusewitt, D.F., Colitz, C.M.H. Modulation of m Veterinary Ophthalmology 2008;11:135-144. 1. Kozák I, Klisenbauer, D., Juhás, T. UV-B induced productic
- 2003;52:229-234. 12. de Berardinis E, Tieri, O., Polzella, A., Iugio, N. The chemica
- conditions. Experimental Eye Research 1965;4:179-186. 13. Gribbestad IS, Midelfart, A. High-resolution 1H NMR spectro
- and Experimental Ophthalmology 1994;232:494-498. 14. Rose RC, Richer, S.P., Bode, A.M. Ocular oxidants and antiox
- and Medicine 1998;217:397-407.
- 15. Ringvold A. Aqueous humour and ultraviolet radiation. Acta 16. Ringvold A. The significance of ascorbate in the aqueous hu
- 1996:62:261-264.





- The lotrafilcon A and non-lens wearing eyes showed decreases in ascorbic acid following UV exposure.
- The senofilcon A wearing eyes showed no significant changes in ascorbic acid levels (compared with the patched eyes).
- Supports the hypothesis that contact lenses with UV-absorbing polymers are able to prevent reduction in aqueous humor antioxidant levels, thus potentially protecting the crystalline lens from cataractous changes.

### Crystalline Lens

- The crystalline lens absorbs nearly all UV light to which it is exposed
- Primary target of UV-B are the lens epithelial cells (LEC), resulting in unstable free radicals causing molecular changes.<sup>18-20</sup>
- Changes can include degradation or modification of lens proteins (increased protein cross-linking), increased DNA damage, and changes in cell survival.<sup>18, 21</sup>
- LEC apoptosis is an initiating factor in cataract formation.<sup>22, 23</sup>
- Dysregulation of LEC apoptosis is associated with opacification of the rat lens and can be stimulated by UV-B radiation.<sup>22-25</sup>
- There was increased caspase-3 activity in the lotrafilcon A group and the non-lens control group following UV exposure.
- There was a significant decrease in caspase-3 activity in the senofilcon A group compared to the lotrafilcon A group.
- The LEC were protected from apoptosis in the senofilcon A group

et radiation for eye diseases. A review with comments on the efficacy of 5:83-91.	18.	Beebe DC. The Lens. In: Kaufman PL AA, ed. Adler's Physiology of the Eye. 10 ed. St. Louis: Mosby; 2003:117.
jaram, R., Pokharel, G. P., Mariotti, S. P. Global data on visual	19.	Maisel H. The Ocular Lens: Structure, Function, and Pathology. 1 ed. New York: Marcel Dekker; 1985.
rganization 2004;82:844-851. alvsis of cataract surgery: a global and regional analysis. Bulletin of the	20.	Klein BE, Klein, R., Linton, K.L., Magli, Y.L., Neider, M.W. Assessment of cataracts from photographs in the Beaver Dam Eye Study. Ophthalmology 1990;97:1428-1433.
rges among the Medicare population: 1991-1998 Archives of	21.	Long AC, Colitz, C.M.H., Bomser, J.A. Apoptotic and necrotic mechanisms of stress-induced human lens epithelial cell death. Experimental Biology and Medicine 2004;229:1072-1080.
nthalmologica 1994-1995-88-307-325	22.	Li WC, Kuszak, J.R., Dunn, K., Wang, R.R., Ma, W., Wang, G.M., Spector, A., Leib, M., Cotliar, A.M., Weiss M., et al. Lens epithelial cell apoptosis appears to be a common cellular basis for noncongenital cataract
keshwar B.L. Pflugfelder S.C. Regulation of MMP-9 activity in human		development in humans and animals. Journal of Cell Biology 1995;130:169-181.
gative Ophthalmology and Vision Science 2000;41:1703-1709.	23.	Li WC, Spector, A. Lens epithelial cell apoptosis is an early event in the development of UVB-induced cataract. Free Radical Biology and Medicine 1996;20:301-311.
For prevention of solar ultraviolet radiation-induced damages.	24.	Wride MA. Cellular and molecular features of lens differentiation: a review of recent advances. Differentiation 1996;61:77-93.
Philadelphia: Lippincott Williams & Wilkins: 2005	25.	Spector A. Oxidative stress-induced cataract: mechanism of action. FASEB Journal 1995;9:1173-1182.
atrix metalloproteinases by ultraviolet radiation in the canine cornea.	26.	Walsh JE, Bergmanson, J.P., Saldana, G. Jr., Gaume, A. Can UV radiation-blocking soft contact lenses attenuate UV radiation to safe levels during summer months in the southern United States? Eye and
of MMP-2 and MMP-9 in human corneal cells. Physiological Research		Contact Lens 2003;29:S174-179.
Learna sitistication of the human acuse us human in normal and nothelegical	27.	Bergmanson JP, Pitts, D.G., Chu, L.W. The efficacy of a UV-blocking soft contact lens in protecting cornea against UV radiation. Acta Ophthalmologica 1987;65:279-286.
r composition of the numan aqueous numour in normal and pathological	28.	Bergmanson JP, Pitts, D.G., Chu, L.W. Protection from harmful UV radiation by contact lenses. Journal of the American Optometric Association 1988:59:178-182
oscopy of aqueous humour from rabbits. Graefes Archive for Clinical	29.	Dumbleton KA, Cullen, A.P., Doughty, M.J. Protection from acute exposure to ultraviolet radiation by
kidant protection. Proceedings of the Society for Experimental Biology	20	Culler AD Dumbleter, K.A., Chev. D.D. Centert lenses and eaute expressive to ultraviolet rediction
Anthalmologica 1080.58.60.82	30.	Optometry and Vision Science 1989;66:407-411.
mour protection against UV-A and UV-B. Experimental Eye Research	31.	Ahmedbhai N, Cullen, A.P. The influence of contact lens wear on the corneal response to ultraviolet radiation. Ophthalmic and Physiological Optics 1988;8:183-189

17. Rose RC, Bode, A.M. Ocular ascorbate transport and metabolism. Comparative Biochemistry and Physiology. A 1991;100:273-285.

- 32. Bergbauer KL, Kuck, J.F.R., Su, K.C., Yu, N. Use of a UV-blocking contact lens in evaluation of UV-induced
- damage to the guinea pig lens. International Contact Lens Clinic 1991;18:182-186.