Cholesterol Penetration into Daily Disposable Contact Lenses Using a Novel *In Vitro* Eye-Blink Model

H. Walther, C. Phan, L.N. Subbaraman, L.W. Jones

Centre for Contact Lens Research, School of Optometry and Vision Science, University of Waterloo, Waterloo, ON, Canada

Introduction

- Daily disposable (DD) lens materials continue to show an increase in use for practitioners and patients and provide lens wearers with a decreased proportion of complications, improved comfort and visual acuity, and lower quantities of lens deposits. [1-8]
- Lipid uptake on silicone hydrogel (SH) DDs is far less than on their daily wear material counterparts. [9, 10]
- However, current *in vitro* methods/models to evaluate tear film (TF) deposition on various contact lens (CL) materials do not simulate physiological eye conditions, such as tear flow or blink motion. [9, 11-15]
- Several unique *in vitro* eye models have been developed to include tear flow or tear replenishment, [16,17] intermittent air exposure, [18] or *in vivo* fouling, [19] generating results differing from those obtained with the static vial model.

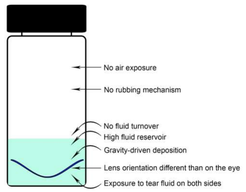

Figure 1. Drawbacks of using a simple vial model to evaluate contact lenses

Purpose

- To determine differences in lipid uptake penetration, comparing a traditional static incubation method with a novel *in vitro* eye model.

Materials & Methods

- Three silicone hydrogel (SH) and four conventional hydrogel (CH) DD were tested:
  - ❖ Delefilcon A (Dailies Total1®; Alcon)
  - ❖ Somofilcon A (clariti® 1day; CooperVision)
  - ❖ Narafilcon A (1-Day Acuvue® TruEye®; Johnson & Johnson)
  - ❖ Etafilcon A (1-Day Acuvue® Moist®; Johnson & Johnson)
  - ❖ Ocufilcon B (Biomedics® 1day, CooperVision)
  - ❖ Nesofilcon A (Biotrue® ONEday; Bausch + Lomb)
  - ❖ Nelfilcon A (Dailies® AquaComfort Plus®, Alcon)
- CLs were incubated for 4 hours (h) and 12 h in an artificial tear solution (ATS) containing a variety of proteins and lipids (mucin, albumin, lysozyme, triolein, cholesterol ester, cholesteryl oleate, phosphatidylcholine, oleic acid methyl ester).
- In addition, a small amount of cholesterol, labeled with 7-nitrobenz-2-oxa-1,3-diazol-4-yl (NBD) fluorophore, was added to the ATS.
- Contact lenses (n=3) were incubated at room temperature (21°C), employing two different methods:
  - ❖ in a vial containing 3.5 mL of ATS on a orbital shaker, and
  - ❖ using our novel *in vitro* eye-blink model (OcuFlow), which consist of a "corneal/scleral eye piece" and a "eyelid piece" that are attached to two individual actuators, which enable us to simulate a blinking motion. Furthermore, through a microfluidic pump, we simulated a physiological tear flow of 1.3µL/min.

Materials & Methods cont'd

- After incubation, the central and peripheral 5 mm of each CL were punched out and mounted on a microscope slide.
- Subsequently, the penetration of NBD-cholesterol within the lens materials was determined by laser scanning confocal microscopy (LCMS) with argon laser at 488 nm.
- CLs were optically sectioned at 0.5 µm intervals (z stack).
- The fluorescence intensity profile of each CL sample was calculated with ImageJ software, using the "Plot Z axis profile" module.
- Curves of relative intensity of fluorescence (RIF) were plotted using Graphpad Prism

Results

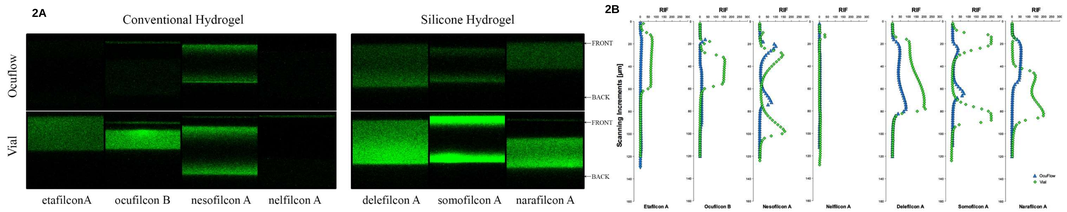

Figure 2. *A) Composite representative confocal image illustrating the lipid distribution in the central section of various CLs after 4 h incubation with NBD-cholesterol in the vial as compared to the eye model; B) Relative intensity of fluorescence (RIF) across the thickness of the CL samples in the vial as compared to the eye model*

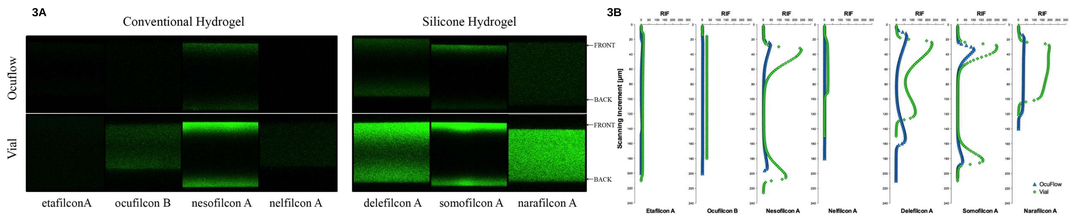

Figure 3. *A) Composite representative confocal image illustrating the lipid distribution in a peripheral section various CLs after 4 h incubation with NBD-cholesterol in the vial as compared to the eye model; B) RIF across the thickness of the CL samples in the vial as compared to the eye model*

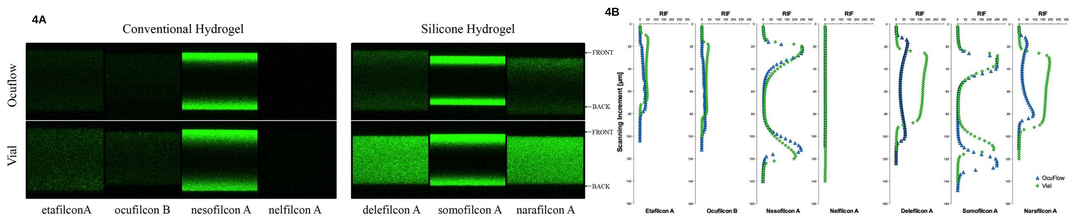

Figure 4. *A) Composite representative confocal image illustrating the lipid distribution in the central section of various CLs after 12 h incubation with NBD-cholesterol in the vial as compared to the eye model; B) RIF across the thickness of the CL samples in the vial as compared to the eye model*

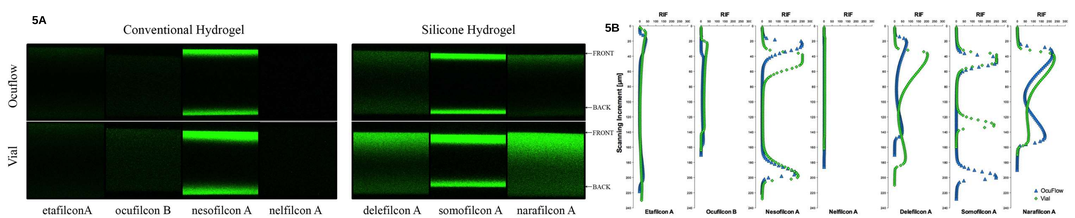

Figure 5. *A) Composite representative confocal image illustrating the lipid distribution in a peripheral section of various CLs after 12 h incubation with NBD-cholesterol in the vial as compared to the eye model; B) RIF across the thickness of the CL samples in the vial as compared to the eye model*

Results cont'd

- Penetration profiles of the TF lipid vary between the static and the eye-blink (OcuFlow) model incubation methods.
- Incubating the lenses traditionally (in a vial) showed lipid uptake throughout the lens material, starting from both sides of the contact lenses.
- However, employing our eye-model (OcuFlow), cholesterol penetration was less and can be seen starting from the front surface of the lenses.
- SHs showed higher RIF than CH lens materials, except for nesofilcon A.
- Furthermore, RIF varied between incubation methods, incubation time, lens materials, and between the centre and periphery of the lens materials, with the traditional method showing more RIF than our novel eye-model (OcuFlow).

Conclusions

- The results of this study provide new insight and a novel *in vitro* approach on the penetration of tear film components on/into contact lenses.
- Furthermore, we can show that the traditional methods used for *in vitro* lens incubation expose the materials to amounts of ATS that exceed physiological limits, which can lead to overestimating lipid deposition.
- This novel eye-blink platform (OcuFlow) is able to better simulate on-eye conditions than previous models and will help to further our knowledge about the interactions between CLs and TF components, *in vitro.*

References

1. Jones L, Jones D, Langley C, Houlford M. Subjective responses of 100 consecutive patients to daily disposables. Optician. 1996;211(5336):28-32.
2. Solomon OD, Freeman MI, Boshnick EL, Cannon WM, Dubow BW, Kame RT, et al. A 3-year prospective study of the clinical performance of daily disposable contact lenses compared with frequent replacement and conventional daily wear contact lenses. CLAO J. 1996;22(4):250-7.
3. Hayes VY, Schnider CM, Veys J. An evaluation of 1-day disposable contact lens wear in a population of allergy sufferers. Cont Lens Anterior Eye. 2003;26(2):85-93.
4. Dumbleton K, Woods C, Jones L, Fonn D, Sarwer DB. Patient and practitioner compliance with silicone hydrogel and daily disposable lens replacement in the United States. Eye Contact Lens. 2009;35(4):164-71.
5. Fahmy M, Long B, Giles T, Wang CH. Comfort-enhanced daily disposable contact lens reduces symptoms among weekly/monthly wear patients. Eye Contact Lens. 2010;36(4):215-9.
6. Wolffsohn JS, Emberlin JC. Role of contact lenses in relieving ocular allergy. Cont Lens Anterior Eye. 2011;34(4):169-72.
7. Chalmers RL, Keay L, McNally J, Kern J. Multicenter case-control study of the role of lens materials and care products on the development of corneal infiltrates. Optom Vis Sci. 2012;89(3):316-25.
8. Diec J, Papas E, Naduvilath T, Xu P, Holden BA, Lazon de la Jara P. Combined effect of comfort and adverse events on contact lens performance. Optom Vis Sci. 2013;90(7):674-81.
9. Walther H, Lorentz H, Heynen M, Kay L, Jones LW. Factors that influence in vitro cholesterol deposition on contact lenses. Optom Vis Sci. 2013;90(10):1057-65.
10. Walther H, Subbaraman L, Jones LW. In Vitro Cholesterol Deposition on Daily Disposable Contact Lens Materials. OptomVisSci. 2015;accepted for publication(OVS15089).
11. Bontempo AR, Rapp J. Protein-lipid interaction on the surface of a hydrophilic contact lens in vitro. Curr Eye Res. 1997;16(8):776-81.
12. Carney FP, Nash WL, Sentell KB. The adsorption of major tear film lipids in vitro to various silicone hydrogels over time. Invest Ophthalmol Vis Sci. 2008;49(1):120-4.
13. Iwata M, Ohno S, Kawai T, Ichijima H, Cavanagh HD. In vitro evaluation of lipids adsorbed on silicone hydrogel contact lenses using a new gas chromatography/mass spectrometry analytical method. Eye Contact Lens. 2008;34(5):272-80.
14. Zhao Z, Carnt NA, Aliwarga Y, Wei X, Naduvilath T, Garrett Q, et al. Care regimen and lens material influence on silicone hydrogel contact lens deposition. Optom Vis Sci. 2009;86(3):251-9.
15. Lorentz H, Heynen M, Trieu D, Hagedorn SJ, Jones L. The impact of tear film components on in vitro lipid uptake. Optom Vis Sci. 2012;89(6):856-67.
16. Tieppo A, Pate KM, Byrne ME. In vitro controlled release of an anti-inflammatory from daily disposable therapeutic contact lenses under physiological ocular tear flow. Eur J Pharm Biopharm. 2012;81(1):170-7.
17. Mohammadi S, Postnikoff C, Wright AM, Gorbet M. Design and development of an in vitro tear replenishment system. Ann Biomed Eng. 2014;42(9):1923-31.
18. Lorentz H, Heynen M, Khan W, Trieu D, Jones L. The impact of intermittent air exposure on lipid deposition. Optom Vis Sci. 2012;89(11):1574-81.
19. Peng CC, Fajardo NP, Razunguzwa T, Radke CJ. In Vitro Spoilation of Silicone-Hydrogel Soft Contact Lenses in a Model-Blink Cell. Optom Vis Sci. 2015;92(7):768-80.

Acknowledgements

E-mail correspondence: hendrik.walther@uwaterloo.ca