Minimal Cholesterol Extraction and Maintenance of Pre-lens Tear Film Stability Associated with an EOBO-Containing Lens and Lens Care Regimen

Christopher Lievens[1], Sebastian Marx[2], Wolfgang Sickenberger[2], Stefan Schwarz[3], Amanda Shows[4], Jessie Lemp[4]

[1]Southern College of Optometry, Memphis, TN, USA; [2]JENVIS Research, Ernst Abbe University Jena, Jena, Germany; [3]Private Practice, Hildesheim, Germany; [4]Alcon, Fort Worth, TX, USA

Introduction

- This study focused on evaluation of cholesterol deposition onto contact lenses (CLs) and the wettability of CLs.
- Cholesterol is the most abundant lipid component of tears deposited onto contact lenses (CLs),[1,2] and can negatively impact CL comfort and visual performance.[3] Overall, significantly higher amounts of cholesterol are deposited onto silicone hydrogel lenses than onto conventional hydrogel lens materials.[4]
- One aim in the development of silicone hydrogel contact lenses was to enhance the wettability of the CL surface: the ability of fluid to spread and the tear film to be maintained over the surface.[5] Silicone hydrogel CLs made of lotrafilcon B are manufactured with hydrophilic surface technology and have been shown to resist lipid deposition and to maintain good surface wettability through 30 days of wear.[2]
- The addition of the substantive wetting agent polyoxyethylene-polyoxybutylene (EOBO®) to the packaging solution of spherical lotrafilcon B lenses has been shown to result in longer retention of moisture on the lens surface on the first day of wear.[6,7]
- EOBO is also used in two lens care solution products, one containing hydrogen peroxide (H_2O_2) CLEAR CARE® PLUS with HydraGlyde® Moisture Matrix (CCP) and in OPTI-FREE® PureMoist® multi-purpose disinfecting solution (OFPM) to provide longer lasting lens surface wettability, further reducing lipid deposition.[8,9]

Objective

- To determine the total cholesterol extracted from lotrafilcon B lenses and pre-lens tear film stability (PLTF) of lotrafilcon B lenses packaged in blister solution containing the EOBO wetting agent (lotrafilcon B +EOBO) cared for with lens care solutions formulated with EOBO (H_2O_2+EOBO [CCP] or MPS+EOBO [OFPM]) after 30 days of wear.

Methods

Subjects

- Subjects were current, full-time (habitual) wearers of four other reusable silicone hydrogel contact lenses: comfilcon A, samfilcon A, senofilcon C monthly replacement, or senofilcon A two-week replacement lenses and were currently using an MPS not containing EOBO.

Study Design

Overall

- This was a multicenter, prospective, randomized, observer-masked, controlled, parallel group study conducted at eight sites: five in the USA, two in Germany, and one in Canada.
- The study protocol was approved by the institutional review board/ethics committee of each site, was conducted in accordance with the principles of the Declaration of Helsinki, and and all subjects provided written informed consent.
- The trial was registered at clinical trials.gov as NCT03026257.
- At their initial visit, subjects were randomized 1:1 to either lotrafilcon B lenses packed in solution containing EOBO (AIR OPTIX® with HydraGlyde®, Alcon Laboratories, Fort Worth, TX, USA) or to their habitual silicone hydrogel contact lenses.
- Subjects randomized to lotrafilcon B CLs were further randomized 1:1 to either of two solutions containing EOBO: CLEAR CARE PLUS® (CCP) with HydraGlyde Moisture Matrix, which contains H_2O_2, or OPTI-FREE PureMoist® (OFPM)+EOBO MPS. This analysis was restricted to subjects who were fitted on Day 1 with lotrafilcon B+EOBO (AIR OPTIX plus HydraGlyde) CLs and randomized 1:1 to care for their lenses with one of two lens care solutions containing EOBO, either CCP or OFPM.
- After 30 + 3 days of wear, right contact lenses were collected from all subjects, lenses frozen at -20 °C or below and sent to the laboratory for analysis.

Cholesterol Extraction

- A subset of lenses were thawed and lipids were extracted using a two-step chloroform:methanol (1:1) method.[9]
- Free cholesterol and cholesterol ester (total cholesterol) concentrations obtained from each contact lens/lens care group were measured using a fluorometric enzymatic assay.[1,2]

PLTF Stability

- The tear film was assessed by measuring noninvasive keratography break-up time (NIKBUT) using the Keratograph 5 (Oculus, Germany) without lenses at baseline.
- Subjects were then classified as having marginal (≥6 and <12 seconds) or optimal (≥12 seconds) NIKBUT, and randomization was stratified by NIKBUT category (marginal or optimal).
- NIKBUT videos over the right lens were taken 5 minutes after insertion on Day 1 and after wearing lenses for 8 hours on Days 1 and 30.
- Percent area of distortion (PAD) at each timepoint was determined at 15 seconds.

Statistical Analysis

- Descriptive statistics (means, standard deviations [SDs], 95% confidence intervals [CIs]) and geometric coefficients of variations were calculated for the total cholesterol extraction data.
- Descriptive statistics (means, standard deviations [SDs], and 95% confidence intervals [CIs]) were calculated for the PLTF data for each measure at each timepoint.

Results

Subject Characteristics

- Characteristics of subjects is presented in **Table 1**.
- Most of the subjects were female and white.
- Subgroups were generally balanced with respect to age, sex, and race.

Table 1. Demographic characteristics

	Cholesterol Extraction		PLTF Stability	
	lotrafilcon B*/ CCP** (n=23)	lotrafilcon B*/ OFPM** (n=25)	lotrafilcon B*/ CCP** (n=60)	lotrafilcon B*/ OFPM** (n=64)
Age, yr (mean ± SD)	26.5±5.4	27.8±5.9	27.7 ± 7.0	27.8 ± 6.0
Sex, female, n (%)	18 (78.3)	21 (84.0)	39 (65.0)	49 (76.6)
Race, n (%)				
White	16 (69.6)	20 (80.0)	45 (75.0)	52 (81.3)
African-American	1 (4.3)	2 (8.0)	5 (8.3)	3 (4.7)
Asian	6 (26.1)	3 (12.0)	9 (15.0)	8 (12.5)
Other/Multiracial	0 (0.0)	0 (0.0)	1 (1.7)	1 (1.6)

*Lotrafilcon B lenses packaged in blister solution containing the wetting agent EOBO **Clear Care Plus (CCP) and OPTI-FREE PureMoist (OFPM) lens care solutions formulated with EOBO (HydraGlyde); SD, standard deviation.

Cholesterol Extraction Analysis

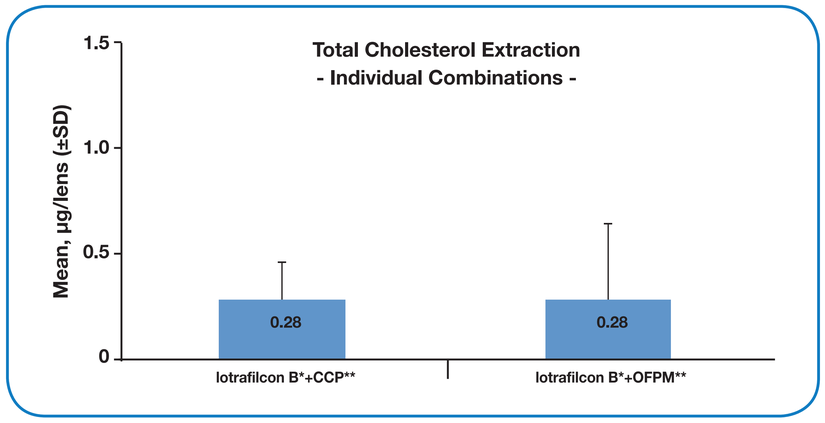
- The mean ± SD amount of total cholesterol extracted from lotrafilcon B CLs maintained with the EOBO-containing solutions CCP and OFPM was 0.28 ± 0.18 µg/lens and 0.28 ± 0.48 µg/lens, respectively (**Table 2; Figure 1**).
- There was no significant difference between the amount of cholesterol extracted from lotrafilcon B+ EOBO lenses maintained with the EOBO-containing solutions CCP and OFPM

Table 2. Total cholesterol extracted from individual combinations of contact lenses/lens care regimens

		lotrafilcon B*/CCP**	lotrafilcon B*/OFPM**
Total cholesterol extracted, µg/lens	n	23	25
	Mean ± SD	0.28 ± 0.18	0.28 ± 0.48
	Median	0.30	0.10
	(Min, Max)	(0.0, 0.8)	(0.0, 2.5)
	95% CI	(0.20, 0.36)	(0.08, 0.48)
	Geo Mean (CV%)	1.27 (13.94)	1.23 (24.77)

Geo. = Geometric; CV = Coefficient of Variation. *lotrafilcon B lenses packaged in blister solution containing the wetting agent EOBO **Clear Care Plus (CCP) and OPTI-FREE PureMoist (OFPM) lens care solutions formulated with EOBO (HydraGlyde); SD, standard deviation.

Figure 1. Total cholesterol extracted from each combination of habitual SiHy and lotrafilcon B contact lenses with solutions

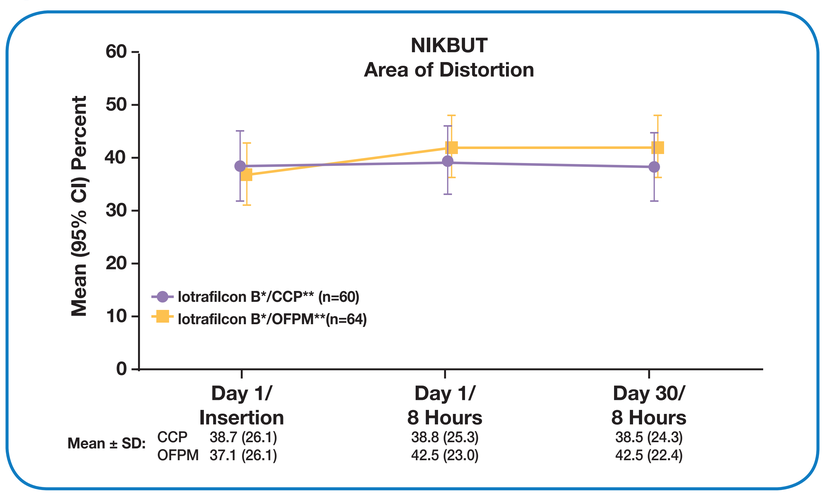


*lotrafilcon B lenses packaged in blister solution containing the wetting agent EOBO **Clear Care Plus (CCP) and OPTI-FREE PureMoist (OFPM) lens care solutions formulated with EOBO (HydraGlyde)

PLTF Stability Analysis

- PAD was similar in the CCP and OFPM groups and across timepoints (**Figure 2**).

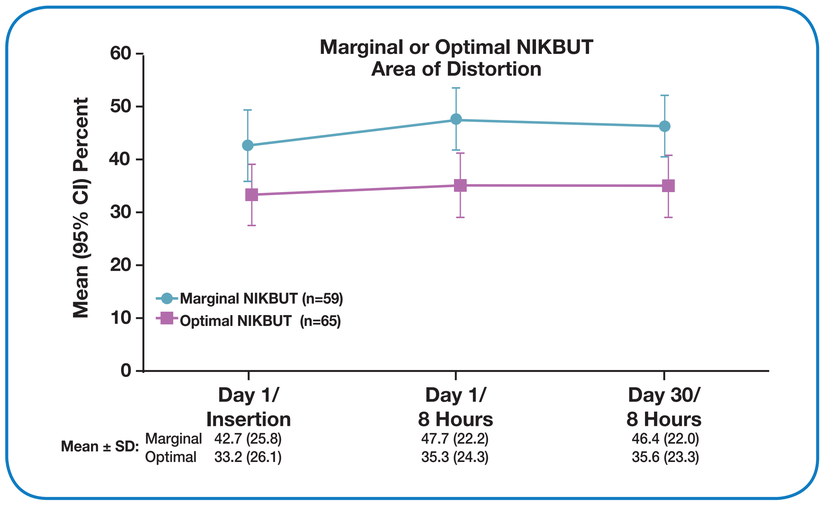
Figure 2. Area of distortion in wearers of lotrafilcon B lenses cared for with CCP or OFPM



CI, confidence interval; *lotrafilcon B lenses packaged in blister solution containing the wetting agent EOBO **Clear Care Plus (CCP) and OPTI-FREE PureMoist (OFPM) lens care solutions formulated with EOBO (HydraGlyde); SD, standard deviation.

- PAD was larger in subjects with marginal NIKBUT than in those with optimal NIKBUT at baseline. PAD remained stable across timepoints through Day 30 in the optimal NIKBUT group and increased slightly with time in the marginal NIKBUT group (**Figure 3**).

Figure 3. NIKBUT stratified by marginal and optimal in Lotrafilcon B* lenses



*lotrafilcon B lenses packaged in blister solution containing the wetting agent EOBO; CI, confidence interval; NIKBUT, noninvasive keratography break-up time; SD, standard deviation.

Conclusions

- The combination of lotrafilcon B contact lenses with packaging solution containing EOBO and the use of CCP and OFPM lens care solutions regimens containing EOBO resulted in similar low levels of extracted cholesterol and cholesterol esters.
- Both EOBO regimens were able to maintain a constant PAD from Day 1 (insertion) and Day 1 (8 hours) to Day 30 (8 hours) of CL wear, suggesting that the EOBO solutions maintain long-lasting lens surface wettability throughout the wearing period of 30 days.
- In addition, PLTF stability was similar over time in subjects who initially had optimal NIKBUT or marginal NIKBUT. Thus, the PLTF did not degrade over 30 days even among subjects who had less optimal tear film characteristics assessed at baseline.
- Low levels of cholesterol deposition observed in this study may have contributed to, or reflected, the maintenance of a stable PLTF.

References

1. Jones L, Senchyna M, Glasier MA, et al. Lysozyme and lipid deposition on silicone hydrogel contact lens materials. *Eye Contact Lens*. 2003;29(1 Suppl):S75-79; discussion S83-74, S192-194.
2. Nash WL, Gabriel MM. Ex vivo analysis of cholesterol deposition for commercially available silicone hydrogel contact lenses using a fluorometric enzymatic assay. *Eye Contact Lens*. 2014;40(5):277-282.
3. Panaser A, Tighe BJ. Function of lipids—their fate in contact lens wear: an interpretive review. *Cont Lens Anterior Eye* 2012;35:100–111.
4. 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):1057-1065.
5. Keir N, Jones L. Wettability and silicone hydrogel lenses: a review. *Eye Contact Lens.* 2013;39(1):100-108.
6. Lemp J, Muya L, Driver-Scott A, Alvord L. A comparison of two methods for assessing wetting substantivity. Global Specialty Lens Symposium; January 26-29, 2016; Las Vegas, NV.
7. Muya L, Lemp J, Kern J, Sentell KB, Lane J, Perry SS. Impact of packaging saline wetting agents on wetting substantivity and lubricity. ARVO Annual Meeting; May 1-6, 2016; Seattle, WA.
8. Huo Y, Rudy A, Wang A, Ketelson HA, Perry SS. Impact of ethylene oxide butylene oxide copolymers on the composition and friction of silicone hydrogel surfaces. Tribol Lett. 2012;45(505-513).
9. Redfern RL, Nichols JJ, Sickenberger W, al. e. Ex vivo analysis of lipid deposition with silicone hydrogel contact lenses and EOBO-based lens care solutions. ARVO Annual Meeting; April 29-May 3, 2018; Honolulu, HI.

Disclosures

This study was sponsored by Alcon Research. AS and JL are employees of Alcon. Editorial support was provided by BelMed Professional Resources, Inc. and was funded by Alcon.