

BIOCOMPATIBILITY OF CONTACT LENS CARE SYSTEMS USED WITH SILICONE HYDROGEL LENSES.

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Introduction

Silicone hydrogel lenses are firmly established and a high percentage dispensed are used for daily wear^{1,2}. Various surface technologies are used with silicone hydrogel (SiH) lenses to ensure surface wetting and these broadly fall into two categories; those with hydrophilic continuous or non-continuous surfaces (lotrafilcon vs. balafilcon), and those that release polymers (galyfilcon and senofilcon). At the same time, lens care technology has evolved from incorporating specialized surfactants to satisfy requirements for no-rub regimens, to adding moisture retaining components for better lens wearability. As the lens and lens care technologies meet, it might be expected that corneal exposure to these increasingly complex systems may result in differences in physiological response such as corneal staining³ and there are such reports in the literature^{3,4}. In vitro testing has also found a range of cellular response with the polyquad-based products showing greater cytotoxicity than PHMB-based products⁵. However, little correlation has been found with comfort, and patients are generally asymptomatic^{6,9}. Presented here is an update of a series of controlled clinical trials started in 2003¹⁰ comparing the clinical performance of two lens care systems (one for each eye) on subjects fit with various SiH lenses. The protocols have largely remained the same through the series.

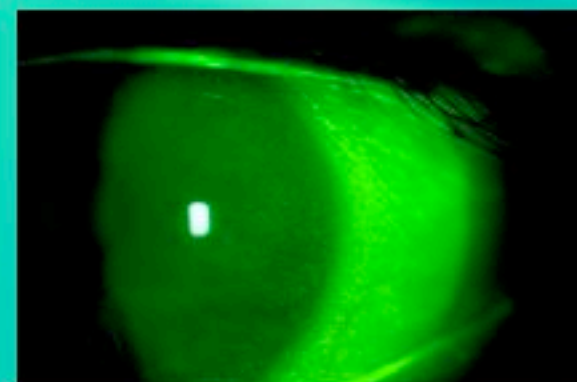
Methods and Materials

Study Design: All studies were 1-month, randomised, single-masked (investigator), contralateral design. **Subjects:** For inclusion in the study, subjects were required to have no clinically significant slit-lamp findings (i.e. >Grade 2) and no difference in slit-lamp findings >Grade 1 between the two eyes. **Care Systems:** The formulations of the lens care products used in the studies are shown in Table 1. Care systems were used according to the manufacturers' instructions approved in the UK, without a 'rub and rinse' step. Subjects used the manufacturer's approved lens case for each solution with one side of the case rendered unusable to aid compliance. No saline rinse or rewetting drops were used for the duration of the study. **Procedure:** Clinical variables determined at baseline, 2-weeks and 1-month included slit-lamp findings, aspects of lens comfort, visual acuity at high and low contrast, vision quality and lens fit, non-invasive break-up time and pre-lens tear film quality. After fitting according to the manufacturer's fitting guide, a new pair of lenses was dispensed at the start of the study and these were not replaced except in the case of loss or damage. At each follow-up visit, investigators asked subjects about their overall preference between the two care systems. At the end of the study, subjects also completed a questionnaire comparing the systems and indicating which performed better for a range of features. **Corneal staining** was graded by investigators using a 0-4 scale with 0.5 increments using a Wratten #12 filter and blue light. If staining was present, an objective measurement of the surface area of the corneal staining in mm² from a captured image (video initially and digital still images in later studies) with subsequent analysis by 'Image Tool' software. This system has been shown to be an effective objective method of evaluating different corneal staining responses¹². When corneal staining ≥Grade 1 was punctate, symmetrical and extending to three or more peripheral quadrants of the cornea, it was generally regarded as solution related.

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TABLE 1 LENS CARE SOLUTION FORMULATIONS

	A0Sept Plus	Pure Aqua	Complete	ReNu MoistureLoc	Opti-Free Express
Disinfectant:	Hydrogen peroxide 1%	PHMB 0.0001%	PHMB 0.0001%	PHMB 0.0001%	Acidic dihydrochloride 0.0045%
Surfactants:	Pluronic F124	Pluronic F127	Polyoxamer 25F	Polyoxamer 1.0%	Potassium Terephthalate 1.04
Lubricant/Comfort agent:	N/A	Sorbitol, Disaccharides	Hydroxypropyl methylcellulose, Polyethylene glycol	N/A	Polyoxamer 110T, Polyquaternium-10
Buffers:	Sodium phosphate, Disodium phosphate	Sodium phosphate, Tris(hydroxymethyl)aminomethane	Tris(hydroxymethyl)aminomethane	Sorbitol, Boric acid	Boric acid, Sodium citrate
Chelating agent:	Phosphoric acid	EDTA 0.02%	EDTA	EDTA 0.1%	Hydrazine 0.05%
Other:	Sodium chloride	N/A	Sodium chloride, Polyoxamer chloride, Phosphate	Sodium chloride	Sodium chloride, Boric acid
Case:	A0Sept case with Platinum-coated lid	CIBA Vision Multiflex and Multiflex Advanced lens case	A.M.O soft lens case	Seauich & Lomb soft lens case	Seauich & Lomb soft lens case



Results

- Significant differences in Investigator graded staining were seen at 1 month except between AQUA and ReNu MoistureLoc on PureVision and O2Optix lenses (Figure 1)
- Objective image analysis found significant differences between all lens/solution combinations (Figures 2 & 3 – note log scale on figure 3)
- Subjective rating were not significantly different except between AQUA vs. ReNu MoistureLoc on PureVision lenses and between AQUA vs. Optifree Express on O2Optix (Figure 4)
- The pattern of the differences between Investigator evaluated staining and objective analysis was generally similar.
- The pattern of the differences between staining and subjective ratings was generally dissimilar.
- Significant differences in corneal staining were noted with each of the contralateral comparisons. PHMB-based products performed differently from each other, some were better and some were worse compared to POLYQUAT-based products, and all were lens dependent. For instance, Aqua showed less staining than ReNu MoistureLoc with O2Optix lenses, however, this was reversed with Pure Vision lenses.
- The prevalence of SRS ranged from 0% (A0Sept + N&D) to 79% (ReNu Multiplus + N&D). (Figure 5)
- Using the criterion of SRS ≤20%, approximately half of the lens-solution combinations proved acceptable.



Discussion

These studies have demonstrated differences in corneal staining response between multipurpose solutions and a peroxide-based system when used with SiH lenses in daily wear. Corneal staining was shown to be significantly better with A0Sept Plus peroxide-based system than any of the other solutions and there were significant differences between PHMB based multipurpose solutions. These findings suggest that PHMB may not be the only ingredient of MPS implicated in corneal staining and that other constituents are involved. Among the SiH lens materials, substantially more staining was associated with the Purevision lens and this may be related to the non-continuous nature of its coating. Subjects were largely asymptomatic - as has been previously noted - however since SRS may be indicative of a reduced barrier function of the epithelium it would be desirable to have the least amount of SRS as possible, especially in the hours immediately after lens handling/insertion. Fluorometric studies would be a suitable method to demonstrate the presence of reduced barrier function but so far have not been conclusive^{11,12}, sensitive toxicology methods⁸ have found differences in toxicity between lens care products and studies have shown differences in uptake and release of preservatives between the various combinations of lens materials and solutions¹³. Eyecare practitioners should be mindful of the fact that staining peaks a few hours after lens insertion and then gradually diminishes during the day¹⁴. Solution Related Staining has a distinctive appearance and pattern-based identification is probably more relevant than multi-dimensional grading scales.

Conclusion

Clinical testing is required in order to confirm the biocompatibility of a given SiH lens and care system combination. Generalisations about the biocompatibility of lens care preservatives and SiH lenses can not be made since the response varies between lens-solution combinations and, therefore, wider clinical testing is required than has previously been the case.

TABLE 2A FOCUS NIGHT & DAY LENSES

Investigator	No. of eyes	BASELINE		2 WEEKS		1 MONTH	
		Optifree Express	A0Sept Plus	Optifree Express	A0Sept Plus	Optifree Express	A0Sept Plus
Extent (0-4 grade)	25	25	25	25	25	25	25
Mean (SD)		0.4 (0.6)	0.4 (0.6)	0.8 (0.6)	0.4 (0.4)	0.7 (0.5)	0.3 (0.3)
Proportion > Grade 1		4%	8%	4%	0%	7%	0%
Objective Image Analysis	Total area in mm²	8.72 (0.4)	9.20 (0.1)	10.8 (0.1)	10.2 (0.4)	8.27 (0.6)	8.85 (0.7)
Mean (SD)		5.5 (0.1)	6.3 (0.1)	6.8 (0.1)	6.3 (0.1)	5.3 (0.1)	5.8 (0.1)
Subjective	End of Day Comfort (0-100 mm)	N/A	N/A	8.7 (0.6)	8.8 (0.6)	8.7 (0.6)	8.9 (0.4)

TABLE 3 PURE VISION LENSES

Investigator	No. of eyes	BASELINE		2 WEEKS		1 MONTH	
		ReNu MoistureLoc	Pure Aqua	ReNu MoistureLoc	Pure Aqua	ReNu MoistureLoc	Pure Aqua
Extent (0-4 grade)	25	25	25	25	25	25	
Mean (SD)		0.7 (0.6)	0.7 (0.6)	1.3 (0.5)	1.4 (0.6)	1.5 (0.6)	
Proportion > Grade 1		15%	24%	38%	35%	37%	
Objective Image Analysis	Total area in mm²	9.59 (0.6)	9.48 (0.6)	12.0 (0.6)	12.0 (0.6)	12.8 (0.7)	
Mean (SD)		115.4 (20.6)	117.1 (19.6)	162.7 (21.6)	162.9 (21.6)	169.0 (20.6)	
Subjective	End of Day Comfort (0-100 mm)	N/A	N/A	8.1 (0.6)	7.9 (0.6)	8.0 (0.6)	

TABLE 2B FOCUS NIGHT & DAY LENSES

Investigator	No. of eyes	BASELINE		2 WEEKS		1 MONTH	
		Optifree Express	Pure Aqua	Optifree Express	Pure Aqua	Optifree Express	Pure Aqua
Extent (0-4 grade)	25	25	25	25	25	25	
Mean (SD)		0.3 (0.1)	0.4 (0.1)	0.3 (0.1)	0.4 (0.1)	0.3 (0.1)	
Proportion > Grade 1		0%	0%	0%	0%	0%	
Objective Image Analysis	Total area in mm²	0.03 (0.0)	0.03 (0.0)	0.03 (0.0)	0.03 (0.0)	0.04 (0.0)	
Mean (SD)		12.4 (2.1)	12.1 (2.1)	12.3 (2.1)	12.1 (2.1)	12.4 (2.1)	
Subjective	End of Day Comfort (0-100 mm)	N/A	N/A	8.1 (0.6)	8.2 (0.6)	8.4 (0.6)	

TABLE 4A O2OPTIX LENSES

Investigator	No. of eyes	BASELINE		2 WEEKS		1 MONTH	
		ReNu MoistureLoc	Pure Aqua	ReNu MoistureLoc	Pure Aqua	ReNu MoistureLoc	Pure Aqua
Extent (0-4 grade)	25	25	25	25	25	25	
Mean (SD)		0.4 (0.6)	0.4 (0.6)	0.4 (0.6)	0.4 (0.6)	0.4 (0.6)	
Proportion > Grade 1		0%	0%	0%	0%	0%	
Objective Image Analysis	Total area in mm²	0.03 (0.0)	0.03 (0.0)	0.03 (0.0)	0.03 (0.0)	0.03 (0.0)	
Mean (SD)		12.4 (2.1)	12.1 (2.1)	12.3 (2.1)	12.1 (2.1)	12.4 (2.1)	
Subjective	End of Day Comfort (0-100 mm)	N/A	N/A	8.1 (0.6)	8.2 (0.6)	8.4 (0.6)	

TABLE 4B O2OPTIX LENSES

Investigator	No. of eyes	BASELINE		2 WEEKS		1 MONTH	
		Complete MoisturePlus	Pure Aqua	Complete MoisturePlus	Pure Aqua	Complete MoisturePlus	Pure Aqua
Extent (0-4 grade)	25	25	25	25	25	25	
Mean (SD)		0.7 (0.6)	0.7 (0.6)	0.8 (0.6)	0.8 (0.6)	0.8 (0.6)	
Proportion > Grade 1		16%	12%	16%	17%	16%	
Objective Image Analysis	Total area in mm²	9.27 (0.6)	9.27 (0.6)	9.27 (0.6)	9.27 (0.6)	9.27 (0.6)	
Mean (SD)		121 (20)	121 (20)	121 (20)	121 (20)	121 (20)	
Subjective	End of Day Comfort (0-100 mm)	N/A	N/A	7.9 (0.6)	7.9 (0.6)	7.9 (0.6)	

TABLE 4C O2OPTIX LENSES

Investigator	No. of eyes	BASELINE		2 WEEKS		1 MONTH	
		Complete MoisturePlus	Pure Aqua	Complete MoisturePlus	Pure Aqua	Complete MoisturePlus	Pure Aqua
Extent (0-4 grade)	25	25	25	25	25	25	
Mean (SD)		0.7 (0.6)	0.7 (0.6)	0.7 (0.6)	0.7 (0.6)	0.7 (0.6)	
Proportion > Grade 1		16%	12%	16%	17%	16%	
Objective Image Analysis	Total area in mm²	9.27 (0.6)	9.27 (0.6)	9.27 (0.6)	9.27 (0.6)	9.27 (0.6)	
Mean (SD)		121 (20)	121 (20)	121 (20)	121 (20)	121 (20)	
Subjective	End of Day Comfort (0-100 mm)	N/A	N/A	7.9 (0.6)	7.9 (0.6)	7.9 (0.6)	

N/A: Assessable indicates significant differences by paired analysis. * P < 0.05, ** P < 0.01, *** P < 0.001

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