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The effect on the five FDA soft contact lens material types of prolonged exposure to phospholipid-based eye drops

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Abstract. – OBJECTIVE: The aim of this study was to assess the effects of regular phospholipid tear supplement application on five soft contact lens materials (FDA Types I-V).

MATERIALS AND METHODS: **Twenty unworn lenses of each lens type were assessed and given an identification number. An initial set of measurements was made on each lens before being immersed in the phospholipid tear supplement solution for one hour. After one hour, the lens was removed, gently rinsed in saline, and the measurements were repeated. This process was repeated for each lens, of each type. Each lens parameter was assessed in the sequence: Refractive Index (% H_2O), Dioptric Power (BVP), Lens Diameter (OD), and Lens Curvature (BCOR).**

RESULTS: **All measurements of % H_2O, BVP, OD and BCOR did not differ between baseline and after lenses being immersed in the phospholipid tear supplement solution for one hour [all soft contact lens materials (FDA Types I-V) $p > 0.05$]. However, in the type IV lenses, a statistically significant change in the % H_2O was found. Only a 1% reduction was observed, and, in the investigator's opinion, the significance of these results is due more to a statistical anomaly produced by having very repeatable measurements showing very little variation.**

CONCLUSIONS: **The phospholipid tear supplement solution did not adversely change the physical parameters of unworn soft contact lenses, of the five FDA Types, to the extent that would be considered clinically significant.**

Key Words:
Soft contact lens, Phospholipid tear supplement, Lens parameter.

Introduction

The complications of contact lens wear, particularly dry eye symptoms, are thought to be associated with the mechanical barrier created by the lens rather than the duration of wear or lens material[1-3]. Almost half (44%) of soft contact lens wearers use the one-month disposable types[4]. However, nearly 50% of all contact lens wearers, including dailies, complain of dry eye symptoms that can be severe enough for more than one-fifth of those who started using any soft contact lenses to stop wearing them[1-3]. This high rate of intolerance has mostly stayed the same, despite the utilization of enhanced oxygen-permeable materials made of a combination of siloxane monomers and hydrogel material[5,6]. This combination is thought to cause less irritation to the eye and better morphological adaptability with the ocular refractive surfaces for short and medium periods of wear[6]. However, according to the Tear Film and Ocular Surface Society (TFOS) workshop[6], this improvement in contact lens material has not prevented millions of contact lens wearers from abandoning their contact lenses permanently or for some time (up to two years or longer). Refractive disorders are generally associated with higher rates of dry eye symptoms, but dry eye disease (DED) remains five times higher in those who wear contact lenses *vs.* those who wear spectacles only[4]. The contact lens splits the tear film into an aqueous-lipid layer in front of the lens and an aqueous-mucin layer behind the lens[4,7].

Further, the siloxane monomers render the soft contact lens more hydrophobic[6,8]. Without the mucin layer in the part of the tear film in front of the lens, this layer becomes less adherent to the hydrophobic lens surface and more prone to evaporation[7]. Moreover, contact lens wearers can blink less frequently than normal, distorting tear film spread and increasing evaporation of the part of the tear film in front of the lens and permeation and evaporation (pervaporation) of the aqueous behind the lens[7-9].

This problem becomes more apparent in patients with dry eye[5,6]. The only solution for those patients may be tear supplements or rewetting drops while wearing contact lenses[7,10,11]. Conventionally, most of these rewetting agents are water or non-lipid based. However, some reports[12,13] have

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shown that patients who have used lipid-based eye drops (especially those with MGD) have reported a higher rate of symptom relief and restoration of their tear film's lipid layer. Many of these reports[14,15] assessed the advantages of lipid-based supplements on contact lens wearers as a rewetting agent and treatment for dry eye while wearing contact lenses. One of the possible limitations may be the incompatibility of the tear supplement preparations and their interference with the contact lens refractive function. The latter can be caused by changes in the composition of the contact lenses or their morphological properties[16,17]. This was once theoretically thought to be more likely the case with lipid-based tear supplements, especially with some concerns of deposits accumulation in the lens material. However, the new investigations[14] continue to report this not being the case.

The current study considers the possible effects of prolonged exposure to a phospholipid-based eye drop on the five soft contact lens materials (FDA Types I-V). Four separate lens parameters were measured before and after exposure to phospholipid-based eye drops. These included lens curvature (BOZR), overall lens diameter (OD), lens central thickness, lens power (BVP) and refractive index (RI) as a measure of water content (% H_2O).

The hypothesis is that the phospholipid-based eye drop formulation should not cause morphological changes to any contact lens type. Thus, allowing contact lens wearers to be able to use this formulation while having their lenses on.

Materials and Methods

Twenty unworn lenses of each lens type were assessed and given an identification number. An initial set of measurements was made of each lens before being immersed in the phospholipid-based eye drop formulation for one hour. This period corresponds to the rapid kinetics of the lens-drug systems (uptake/release) reported in previous drug delivery studies[15,18] of the contact lens *in vitro* and is reasonable to study the effect of phospholipid-based eye drop formulation contact lens with *in vivo* use. After one hour, the lens was removed and gently rinsed in saline (NaCl), and the measurements were repeated. This process was repeated for each lens of each type. Each lens parameter was assessed in the following sequence: RI (% H_2O), BVP, OD, BOZR, and lens central thickness.

Contact lenses included in this study:

Five types of contact lenses were used in this study according to the FDA group classifications of soft contact lens materials:

Type I: < 50% water content, non-ionic: BOZR: 8.70 mm, OD: 14.00 mm, BVP: -3.00 DS Softlens® 38, Bausch & Lomb (Polymacon A | 1, 38% water).

Type II: > 50% water content, non-ionic: BOZR: 8.60 mm, OD: 14.20 mm, BVP: -3.00 DS Softlens® daily disposable, Bausch & Lomb (Hilafilcon B || 2, 59% water).

Type III: < 50% water content, ionic: BOZR: 8.60 mm, OD: 14.00 mm, BVP: -3.00 DS Purvision 2HD, Bausch & Lomb [Balafilcon A (Silicon Hydrogel), 36% water].

Type IV: > 50% water content, ionic: BOZR: 8.60 mm, OD: 14.20 mm, BVP: -3.00 DS Biomedics® 1-Day Extra, Coopervision (Ocufilcon D IV 1, 55% water).

Type V: Enhanced oxygen porous materials (e.g., Silicon Hydrogel SiH): BOZR: 8.40 mm, OD: 14.20 mm, BVP: -3.00 DS Coopervision [fanfiction (Silicon Hydrogel), 55% water].

Note: There were no hydrogel soft contact lenses under type III available. However, there are several SiH materials available that fit this type. Regarding type V, another SiH was chosen to represent this contact lens material.

Lens Refractive Index

The water content of a soft contact lens can be estimated indirectly by measuring the refractive index. As the water content increases, the refractive index decreases, and there is a high correlation between these two variables in the range between 30% and 70% water content. The refractive index under specific conditions and for a given wavelength is the sine of the angle of incidence divided by the sine of the angle of reflection. The angle at which total internal reflection occurs can be easily measured using a hand-held Abbé Refractometer - the Atago CL-1 Soft Lens Refractometer[19]. The hydrated lens is blotted dry and, using a glass daylight plate, planted onto the fixed prism of the refractometer. The instrument is then directed toward an external light source, and a border between dark and light fields is observed. The water content is then read directly from the eyepiece scale.

Before each series of measurements, the instrument is calibrated using a saturated sodium chloride solution. One drop of this solution is placed on the fixed prism, and the scale is observed. A correctly calibrated instrument will give a scale reading of 21% H_2O.

Lens Power

The lens's back vertex dioptric power can be determined using a focimeter (Figure 1)[20]. The focimeter's theory of operation is based upon Newton's relationship, which links the distance between the object and the first principal focus and the distance between the image and the second principal focus with the back vertex power of the lens. For this measurement, the lens is removed from its storage solution, and any excess solution is removed before being placed on the focimeter. Immediate measurement is made as soon as the lens is taken out of the solution, while studies have shown that accurate measurement can be made with up to four minutes' exposure to air. However, to avoid any risk of influencing the other measurements, lens power is the second parameter assessed after refractive index measurement and before lens curvature and diameter. Since these last two measurements are made with the lens immersed, any possible dehydration is reversed.

The focimeter is calibrated, before use, by pre-setting the scale to zero dioptric power and adjusting the eyepiece lens to bring the ring target into focus. This standardizes the instrument for the observer.

Lens Curvature, Lens Central Thickness and Lens Diameter

These three parameters can be assessed using the same instrument - the JCF Optimec Lens Analyser (Figure 2)[21]. This instrument uses a front projection system. For lens curvature and central thickness, the lens is placed in an immersion chamber, convex surface upwards, on an 8.50 mm diameter cylinder, and centered. The lens profile is then viewed on a built-in screen at X15 magnification. A probe is manually advanced until contact is confirmed by the observer, detecting a just noticeable edge lift. The same amount lowers the probe, and the back optic radius and central lens thickness is read directly in millimeters. For lens diameter, the lens is transferred to a second immersion bath, and its transverse section is projected against a millimeter scale engraved on one edge of the immersion bath. The JCF Optimec Lens Analyser is self-calibrating, and no adjustment is required.

Figure 1. The focimeter used in the current study to measure a lens's back vertex dioptric power.

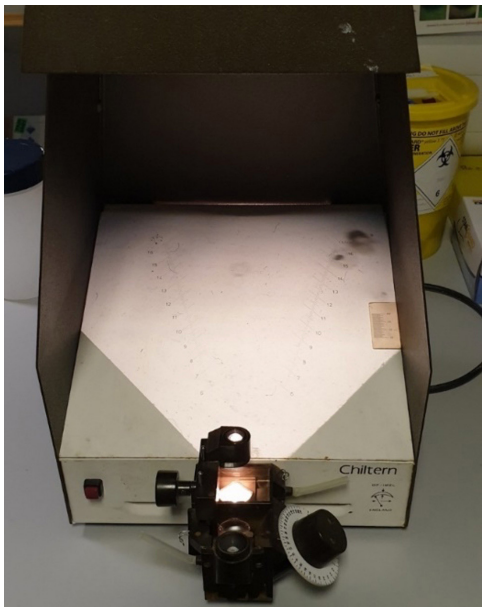

Figure 2. JCF Optimec Lens Analyser, used in this study to assess lenses' curvature, diameter, and central thickness.

Statistical Analysis

Data were entered and analyzed using SPSS released 2017 (SPSS Statistics for Windows, Version 25.0. IBM Corp., Armonk, NY, USA). A two-tailed *p*-value lower than 0.05 was considered significant for all comparisons. The data sets were checked for normality (Shapiro-Wilk test) before statistical analysis. All data sets reject the null hypothesis. Statistical analysis was performed on the data using the Wilcoxon (non-parametric) test to consider the differences between pre-and post-immersion in phospholipid-based eye drop formulation.

Results

The changes were measured for each of the five types of lenses, respectively, for lens refractive index as a measure for water content, lens refractive power, lens curvature, lens diameter, and lens central thickness.

All the measurements for types I, III, IV and V showed no statistically significant differences between pre-immersion and post-immersion measurements for all lens parameters (p-value > 0.05).

In type II, the water content showed statistically significant reductions (p-value = 0.034) based on repetitive measures (Table I). However, all other parameters for type II did not show any significant change (p-value > 0.05), as with other lens types.

Discussion

Developing an adequate artificial tear solution that is both physiologically relevant and stable is critical in developing an *in vitro* model to examine the dynamics of tear film interactions on a contact lens surface.

The most recent tear film model comprises a glycocalyx layer surrounding the corneal epithelium, an outer non-polar lipid layer, an inner polar lipid layer with intercalated proteins, an aqueous phase with various proteins, and mucins that form gels[22,23].

The idea of administering medications, especially through a hydrogel (contact lens), was first proposed in the 1960s[24]. Developing contact lenses as an eye drug delivery system has been and continues to be fraught with difficulties[25-29]. Controlled drug release must be maintained for the proper amount of time while also ensuring satisfactory optical clarity, patient comfort during extended wear, and biocompatibility. These are the current concerns. Several strategies were used to load the target drug into a lens delivery device. The following section addresses several major ways for developing a contact lens-based drug delivery system, including lenses soaked in a drug solution, molecularly imprinted polymeric hydrogels, drug-polymer films integrated with contact lenses, and contact lenses loaded with liposomes[30].

Many multifunctional contact lens care products comprise an antibacterial agent, surfactant, and buffer system. The lipid removal performance

Table I. Lens refractive index as a measure of water content (H_2O%), lens power (BVP), lens curvature (BCOR), overall lens diameter (OD) and central lens thickness (CT) were assessed for twenty unworn lenses of the FDA Type II before and after prolonged exposure to phospholipid-based eye drop formulation.

Lens refractive index		Lens refractive		Lens curvature power		Lens diameter		Lens central thickness	
Before	After	Before	After	Before	After	Before	After	Before	After
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1
59	58	-3	-3	8.2	8.2	14	14	0.1	0.1
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1
59	58	-3	-3	8.3	8.2	14	14	0.1	0.1
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1
59	59	-3	-3	8.2	8.1	14	14	0.1	0.1
58	57	-3	-3	8.2	8.2	14	14	0.1	0.1
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1
59	57	-3	-3	8.3	8.3	14	14	0.1	0.1
59	59	-3	-3	8.1	8.1	14	14	0.1	0.1
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1
58	58	-3	-3	8.2	8.1	14	14	0.1	0.1
58	58	-3	-3	8.2	8.2	14	14	0.1	0.1
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1
59	58	-3	-3	8.2	8.2	14	14	0.1	0.1
59	59	-3	-3	8.2	8.2	14	14	0.1	0.1

of three commercially available lens care solutions was investigated. The results revealed no significant differences in the total concentration of either polar or non-polar lipid deposits. Eye drops are the most frequent means of medication delivery to the eye, accounting for over 90% of all ophthalmic formulations[31-33]. While eye drops are easy to administer, the low bioavailability of less than 5% is a significant disadvantage.

Bontempo and Rapp[34-37] conducted experiments in the mid to late 1990s to investigate lipid deposition and the influence of lipid and protein interactions on standard hydrogel and rigid gas permeable (RGP) contact lens formation. According to their findings, FDA group III contact lens materials deposit the least lipid, while group II lenses, which are high water non-ionic lenses, deposit the most[34]. This discovery prompted them to devise the "pull/push" paradigm to explain lipid deposition[34,38]. According to their theory, the "pull" symbolizes the contact lens polymer material drawing the lipids into the matrix and away from the aqueous ATS. At the same time, the "push" reflects the lens's water content urging the lipid to go into the matrix[34,38].

No statistically significant correlations of lens refractive index as a measure of water content (% H_2O), lens power (BVP), lens curvature (BCOR), overall lens diameter (OD) and central lens thickness (CT) were assessed for twenty unworn lenses of the FDA Type I before and after prolonged exposure to phospholipid-based eye drop formulation in this study.

The composition of phospholipids found in tears and on contact lenses was examined, as well as the impact of contact lens material and lens cleaning solutions on the concentration of total and specific phospholipids and cholesterol that may be measured. Although earlier research[39-41] has established the profile of proteins in tears, little has been done to identify phospholipids in tears, and the profile of non-polar lipids is still a matter of debate.

Balafilcon A contact lenses are FDA group III contact lenses with low water content and an ionic polymer. In contrast, Senofilcon A is an FDA (Food and Drug Administration, USA) group I material with low water content and a non-ionic polymer. Various studies[42-44] have demonstrated that non-ionic polymer-containing contact lenses deposit more lipids, whereas ionic contact lenses deposit more protein but less lipid. Pain and infection are just two of the many contact lens-related problems linked to the deposition of tear film components onto contact lenses[45,46]. The creation of better contact lenses or lens care products that focus on removing these compounds may be made possible by a thorough understanding of the precise molecules that are deposited.

Conclusions

The study found no significant alterations in type I, III, IV, and V lens parameters. A statistically significant change in the water content was found in the type II lenses. However, only a 1-2% reduction was observed. This small reduction showed statistical significance due to a statistical anomaly produced by having repeatable measurements but cannot carry interpretable clinical significance.

In conclusion, we found that the physical parameters determining morphology and formulation of unworn soft contact lenses of the five FDA Types were not altered, to the extent that would be considered clinically significant, after exposure to phospholipid-based eye drop formulation by mode of *in vitro* immersion, which surpasses the eye wearing conditions.

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Conflict of Interest
The author declares he has no conflict of interest.

Informed Consent
Not applicable.

Ethics Approval
Not applicable.

Authors' Contributions
Conceptualization, statistical analysis and Manuscript write up and review were done by Saleh Alshammeri.

Data Availability
The data will be available with the corresponding author and can be made available after email requisition.

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References

1) Schein OD, Tielsch JM, Muñoz B, Bandeen-Roche K, West S. Relation between signs and symptoms of dry eye in older people: A population-based perspective. Ophthalmology 1997; 104: 1395-1401.
2) Efron N, Morgan PB, Helland M, Itoi M, Jones D, Nichols JJ, van der Worp E, Woods CA. Daily disposable contact lens prescribing around the world. Cont Lens Anterior Eye 2010; 33: 225-227.
3) Chalmers RL, Begley CG, Edrington T, Caffery B, Nelson D, Snyder C, Simpson T. The agreement between self-assessment and clinician assessment of dry eye severity. Cornea 2005; 24: 804-810.
4) Nichols JJ, Mitchell GL, Nichols KK, Chalmers R, Begley C. The performance of the contact lens dry eye questionnaire as a screening survey for contact lens-related dry eye. Cornea 2002; 21: 469-475.
5) Kunzler J. Silicone-based hydrogels for contact lens application. CL Spectrum 1999; 14: 9-11.
6) Nicolson PC, Vogt J. Soft contact lens polymers: An evolution. Biomaterials 2001; 22: 3273-3283.
7) Nichols JJ, Sinnott LT. Tear film, contact lens, and patient-related factors associated with contact lens–related dry eye. Invest Ophthalmol Vis Sci 2006; 47: 1319-1328.
8) Holden BA, Sweeney DF, Seger RG. Thin high water content lenses cause epithelial erosions. Clin Exp Optom 1986; 69: 103-107.
9) Orsborn GN, Zantos SG. Corneal desiccation staining with thin high water content contact lenses. CLAO 1988; 14: 81-85.
10) Young G, Veys J, Pritchard N, Coleman S. A multi-center study of lapsed contact lens wearers. Ophthalmic Physiol Opt 2002; 22: 516-527.
11) Pritchard N, Fonn D, Brazeau D. Discontinuation of contact lens wear: A survey. ICLC 1999; 26: 157-162.
12) Lee SY, Tong L. Lipid-containing lubricants for dry eye: A systematic review. Optom Vis Sci 2012; 89: 1654-1661.
13) Rieger G. Lipid-containing eye drops A step closer to natural tears. Ophthalmologica 1990; 201: 206-212.
14) Jones L, Downie LE, Korb D, Benitez-Del-Castillo JM, Dana R, Deng SX, Dong PN, Geerling G, Hida RY, Liu Y, Seo KY, Tauber J, Wakamatsu TH, Xu J, Wolffsohn JS, Craig JP. TFOS DEWS II Management and Therapy Report. Ocul Surf 2017; 15: 575-628.
15) Lesher GA, Gunderson GG. Continuous drug delivery through the use of disposable contact lenses. Optom Vis Sci 1993; 70: 1012-1018.
16) Churaev N, Sobolev V. Wetting of low-energy surfaces. Adv Colloid Interface Sci 2007; 134: 15-23.
17) Menzies KL, Jones L. The impact of contact angle on the biocompatibility of biomaterials. Optom Vis Sci 2010; 87: 387-399.
18) Karlgard C, Wong N, Jones L, Moresoli C. In vitro uptake and release studies of ocular pharmaceutical agents by silicon-containing and p-HEMA hydrogel contact lens materials. Int J Pharm 2003; 257: 141-151.
19) Efron N, Brennan NA, Bruce AS, Duldig DI, Russo NJ. Dehydration of hydrogel lenses under normal wearing conditions. CLAO 1987; 13: 152-156.
20) Pearson RM, Evans BJ. A comparison of in-air and in-saline focimeter measurement of the back vertex power of spherical soft contact lenses. Ophthalmic Physiol Opt 2012; 32: 508-517.
21) Coldrick BJ, Richards C, Sugden K, Wolffsohn JS, Drew TE. Developments in contact lens measurement: A comparative study of industry-standard geometric inspection and optical coherence tomography. Cont Lens Ant Eye 2016; 39: 270-276.
22) Green-Church KB, Butovich I, Willcox M, Borchman D, Paulsen F, Barabino S, Glasgow BJ. The International workshop on meibomian gland dysfunction: report of the subcommittee on tear film lipids and lipid-protein interactions in health and disease. Invest Ophthalmol Vis Sci 2011; 52: 1979-1993.
23) Butovich IA, Millar TJ, Ham BM. Understanding and analyzing meibomian lipids--a review. Curr Eye Res 2008; 33: 405-420.
24) Witcherle O, Lim D. Hydrophilic gels for biological use. Nature 1960; 185: 117-118.
25) Peterson RC, Wolffsohn JS, Nick J, Winterton L, Lally J. Clinical performance of daily disposable soft contact lenses using sustained release technology. Cont Lens Anterior Eye 2006; 29: 127-134.
26) Schrader S, Wedel T, Moll R, Geerling G. Combination of serum eye drops with hydrogels bandage contact lenses in treating persistent epithelial defects. Graefes Arch Clin Exp Ophthalmol 2006; 244: 1345-1349.
27) Gulsen D, Chauhan A. Ophthalmic drug delivery through contact lenses. Invest Ophthalmol Vis Sci 2004; v45: 2342-2347.
28) Peng CC, Kim J, Chauhan A. Extended delivery of hydrophilic drugs from silicone-hydrogel contact lenses containing vitamin E diffusion barriers. Biomaterials 2010; 31: 4032-4047.
29) Jung HJ, Chauhan A. Temperature sensitive contact lenses for triggered ophthalmic drug delivery. Biomaterials 2012; 33: 2289-2300.
30) Kompella UB, Kadam RS, Lee VH. Recent advances in ophthalmic drug delivery. Ther Deliv 2010; 1: 435-456.
31) Creech JL, Chauhan A, Radke CJ. Dispersive mixing in the posterior tear film under a soft contact lens. I&EC Res 1999; 40: 3015-3026.
32) Mc Namara NA, Polse KA, Brand RD, Graham AD, Chan JS, Mc Kenney CD. Tear mixing under a soft contact lens: Effects of lens diameter. Am J Ophthal 1999; 127: 659-665.

33) Saettone M. Progress and problems in ophthalmic drug delivery. Pharmatechnology 2002; 3: 1-6.

34) Bontempo AR, Rapp J. Lipid deposits on hydrophilic and rigid gas permeable contact lenses. CLAO J 1994; 20: 242-245.

35) Bontempo AR, Rapp J. Protein-lipid interaction on the surface of a rigid gas permeable contact lens in vitro. Curr Eye Res 1997; 16: 1258-1262.

36) Bontempo AR, Rapp J. Protein-lipid interaction on the surface of a hydrophilic contact lens in vitro. Curr Eye Res 1997; 16: 776-781.

37) Bontempo AR, Rapp J. Protein and lipid deposition onto hydrophilic contact lenses in vivo. CLAO J 2001; 27: 75-80.

38) Franklin V, Tighe B. Hydrogel lens spoilation - deposit formation and the role of lipids. Optician 1991; 202: 19-26.

39) Wollensak G, Mur E, Mayr A, Baier G, Gottinger W, Stoffler G. Effective methods for investigating human tear film proteins and lipids. Graefes Arch Clin Exp Ophthalmol 1990; 228: 78-82.

40) Fullard RJ, Snyder C. Protein levels in nonstimulated and stimulated tears of normal human subjects. Invest Ophthalmol Vis Sci 1990; 31: 1119-1126.

41) McGill JI, Liakos GM, Goulding N, Seal DV. Normal tear protein profiles and age-related changes. Br J Ophthalmol 1984; 68: 316-320.

42) Gachon AM, Richard J, Dastugue B. Human tears: Normal protein pattern and individual protein determination in adults. Curr Eye Res 1982; 2: 301-308.

43) McCulley JP, Shine WE. A compositional-based model for the tear film lipid layer. Trans Am Ophthalmol Soc 1997; 95: 79-93.

44) Bron AJ, Tiffany JM, Gouveia SM, Yokoi N, Voon L W. Functional aspects of the tear film lipid layer. Exp Eye Res 2004; 78: 347-360.

45) Fonn D. Targeting contact lens induced dryness and discomfort: What properties will make lenses more comfortable. Optom Vis Sci 2007; 84: 279-285.

46) Willcox MDP, Holden BA. Contact lens-related corneal infections. Biosci Rep 2001; 21: 445-461.