

Deposition of Triglyceride on Soft Contact Lenses from Lipid-Containing Artificial Tears

Atiporn Thuangtong, M.D.*, Daroonporn Lertpongparkpoom, M.D.*, Chatchawan Srisawat, M.D., Ph.D.***, Sarawut Junnu, B.Sc.**,
Busadee Pratumnvinit, M.D.***

*Department of Ophthalmology, **Department of Biochemistry, ***Department of Clinical Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

Objective: To determine the amount of triglyceride deposition from a lipid-containing artificial tear eye drop (Endura®) on three different types of contact lenses after one day and one month of simulated use.

Methods: Simulated use of artificial tears was performed in vitro on three different types of contact lenses, including: high water content (HW), low water content (LW), and silicone hydrogel (SI) contact lenses. To simulate one day of use, contact lenses were incubated in artificial tear solution for 16 hours. To simulate a one month of use, they underwent repeated cycles of 16-hour incubation in artificial tear solution, lens cleaning, and 8-hour storage in a multipurpose solution daily for 30 days. Triglyceride deposited was extracted and determined.

Results: After one day of simulated use, amount of deposited triglyceride was significantly different among 3 types of contact lenses with the highest deposition in SI followed by LW and HW contact lenses; the corresponding values (mean \pm SD) were 3.79 ± 0.35 , 0.84 ± 0.27 , and 0.26 ± 0.17 $\mu\text{g}/\text{lens}$, respectively. Only between SI and HW was it found to be statistically different. After one month of simulated use, deposition on SI lenses was slightly increased (6.56 ± 1.10 $\mu\text{g}/\text{lens}$) with that on LW and HW lenses remaining low (0.10 ± 0.12 and 0.55 ± 0.34 $\mu\text{g}/\text{lens}$, respectively).

Conclusion: Triglyceride from lipid-containing artificial tears can absorb into contact lenses, particularly those made of silicone hydrogel, most notably after long periods of use. However, levels of triglyceride deposition are relatively low, when compared to lipid deposition from normal tear films during regular use.

Keywords: Lipid-containing artificial tear, lipid deposition, soft contact lens

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INTRODUCTION

Soft contact lenses are increasingly used, both for visual correction and cosmetic enhancement. To relieve dry eye symptoms and improve eye comfort, artificial tear eye drops are frequently used by contact lens wearers.

Only preservative-free artificial tear eye drops are recommended for soft contact lens wearers due to the chemical and physical properties of soft contact lenses. Soft contact lenses can absorb surrounding substances, such as protein and lipid that are dissolved in natural tear films. Other absorbable substances include environmental substances and eye drop preservatives, which may induce immunological and/or pathological reactions producing unfavorable effects on the wearer, such as decreased vision, discomfort, intolerance, giant papillary conjunctivitis, keratitis,

Corresponding author: Atiporn Thuangtong

E-mail: atipornpam@yahoo.com

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TABLE 1. Composition of Endura[®] per Nebule (0.4 mL).

Ingredients	Amount
Active ingredients	
Polysorbate 80	4.0 mg
Glycerol	4.0 mg
Inactive ingredients	
Castor oil*	5.0 mg
Pemulen TR-2 (also known as Carbomer 1342)	0.2 mg
Mannitol	8.0 mg
Sodium hydroxide	To adjust pH
Purified water	q.s.** to 0.4 mL

*Castor oil is a triglyceride that is composed of many free fatty acids: 89.5% ricinoleic acid, 4.2% linoleic acid, 3% oleic acid, 1% stearic acid, 1% palmitic acid, 0.7% dihydroxystearic acid, 0.3% linolenic acid, and 0.3% eicosanoic acid²⁴

**quantity sufficient; ml = milliliters; mg = milligram

and corneal ulcer.¹⁻³ Some new preservative-free artificial tear eye drops contain not only water and electrolytes, but also lipid in the form of oils. One of these new artificial tear eye drops is Endura[®] (Allergan plc, Dublin, Ireland). Its formulation consists of 1.25% weight per volume (w/v) castor oil (Table 1), which helps reconstruct preexisting tear lipid films, as well as create thicker and more stable tear lipid films in dry eye patients.⁴ As such, Endura[®] has lipid content that differs from conventional artificial tear formulations. The use of a high-lipid artificial tear formulation like Endura[®] raises lipid deposition-related concerns for contact lens wearers. The objective of this study was to investigate the amount of the lipid deposition effects of Endura[®] on soft contact lenses.

Amount of lipid deposition from Endura[®] was evaluated on three different types of contact lenses, including: high water content, low water content, and silicone hydrogel contact lenses. Lipid deposition evaluation was based on one day and one month of simulated use. Because triglyceride is the predominant lipid contained in castor oil, triglyceride deposition on contact lenses was specifically quantified and evaluated. The results of this investigation may be useful in establishing guidelines and recommendations regarding the use of oil-based artificial tears for contact lens wearers, particularly those who could benefit from this type of artificial tear formulation.

MATERIALS AND METHODS

Materials

The contact lenses used in this study varied in water content and materials and were divided into 3 groups, as follows: high water content hydrogel contact lenses (HW), low water content hydrogel contact lenses (LW), and silicone hydrogel contact lenses (SI). Details relating to the contact lenses used in this study are shown in Table 2.

Endura[®] (Allergan plc, Dublin, Ireland) was the lipid-containing artificial tear eye drop evaluated in this study. The daily cleaner solution used was Sensitive Eyes[®] Daily Cleaner (Bausch & Lomb, Rochester, NY, USA). The multipurpose solution used was Maxim[®] C&C Color & Clean Contact Lens Cleaning Solution (Maxim Inter Corporation Co., Ltd, Rajthevi, Bangkok, Thailand).

Simulated Use of Endura[®] on Soft Contact Lenses

One day and one month of simulated use of Endura[®] artificial tears was performed on three different types of contact lenses (HW, LW, and SI hydrogel contact lenses). To simulate one day of use, five contact lenses from each of the 3 lens types were placed into a 24-well culture plate and 13 drops of Endura[®] (approximately 330 μ L) were added to completely immerse the lenses.

TABLE 2. Types of Soft Contact Lenses Used in This Study.

Type	Lens material	Brand (Manufacturer)	Water content (%)
High water content hydrogel lenses	Omafilcon A	Ultraflex XC (CooperVision, Inc., Pleasanton, CA, USA)	69
Low water content hydrogel lenses	Polymacron	Maxim Clear [®] (Maxim, Rajthevi, Bangkok, Thailand)	42
Silicone hydrogel lenses	Latrafilcon B	O2 Optix [®] (Ciba Vision [®] , Duluth, GA, USA)	33

The amount of Endura[®] used was based upon the approximate use of one drop per hour, from 8 AM to 8 PM. The lenses were then incubated at 37°C for 16 hours. Lenses were then transferred to a 15 ml conical tube containing 10 ml of normal saline solution. The tube was inverted gently a couple of times to remove any residual artificial tear coating on the surface of the lenses. This washing step was performed three times.

To simulate one month of use, five contact lenses from each of the 3 lens types were completely immersed in Endura[®] and incubated at 37°C for 16 hours, as described in the preceding paragraph. At the end of incubation, each lens was cleaned with 2-3 drops of daily cleaner solution and a process of rubbing the lens in the palm of the hand for 30 seconds and then rinsing it with a multipurpose solution was followed before storing the lens in multipurpose solution for 8 hours. This procedure was repeated at the same time each day for 30 days. On day 30, the lenses were washed 3 times in normal saline solution in a process exactly similar to the process described at the end of the one day simulation in the preceding paragraph.

Extraction of Triglyceride from Contact Lenses

After washing with normal saline solution, contact lens was removed from the conical tube using a pair of forceps and gently shaken to remove as much of the normal saline solution as possible. It was then put into a 1.5 ml microcentrifuge tube. Five hundred microliters of methanol/chloroform (1:1) solvent was added to each tube and incubated for one hour at room temperature with gentle shaking on a shaker. The solvent was then transferred to another 1.5 ml microcentrifuge tube and evaporated using a centrifugal vacuum

concentrator to complete dryness (approximately 1.5 hours). Each tube was then resuspended with 20 µl of phosphate buffered saline solution by vortex mixing for 30-60 seconds.

Triglyceride Determination

Triglyceride content of each sample was analyzed in duplicate using a Serum Triglyceride Determination Kit (Zen-Bio, Inc., Research Triangle Park, NC, USA). Stepwise glycerol and triglyceride determination procedures were performed according to manufacturer's instructions, as follows. Forty microliters of reconstituted reagent A was dispensed into each well of a NUNC[®] 384-well plate (Thermo Fisher Scientific, Inc., Lafayette, CO, USA). Five microliters of resuspended sample or glycerol standard was then added into the corresponding wells and incubated for 15 minutes at room temperature. To determine glycerol content, absorbance of reactions was measured at 540 nm using a Synergy[™] HT Multi-Mode Microplate Reader (Bio-Tek Instruments, Inc., Winooski, VT, USA). For triglyceride quantification, 10 µL of reconstituted reagent B was added into each of the same wells and the reaction was further incubated for 15 minutes at room temperature before measuring absorbance at 540 nm.

Statistical Analysis

Data were processed and analyzed using PASW statistics v. 18.0 (SPSS, Inc., Chicago, IL, USA). Normality test by Shapiro-Wilk showed *p*-value ranged from 0.226 to 0.928. Continuous variables were presented as mean and standard deviation or median and range. ANOVA was used to compare amount of triglyceride among groups, followed by Bonferroni for pairwise

TABLE 3. Amount of triglyceride on contact lenses after one day and one month of simulated use.

Contact lenses	Triglyceride ($\mu\text{g}/\text{lens}$)		<i>p</i> -value **
	Mean \pm SD		
	One time 16 hours incubation	1 month incubated contact lenses	
Omafilcon A (high water content contact lenses)	0.26 \pm 0.17	0.55 \pm 0.34	0.131
Polymacron (low water content contact lenses)	0.84 \pm 0.27	0.10 \pm 0.12	0.001
Lotrafilcon B (silicone hydrogel contact lenses)	3.79 \pm 0.35	6.56 \pm 1.10	0.001
<i>p</i> -value*	<0.001	<0.001	

*ANOVA, **Independent t-test

comparison. Independent t-test was used to test difference in changes between one day and one month. All tests of significance were two tailed, with a *p*-value<0.05 considered to be statistically significant.

RESULTS

To simulate a one day of use, each of the contact lenses was incubated with artificial tear solution for 16 hours. The highest triglyceride deposition was found on SI lenses (3.79 \pm 0.35 $\mu\text{g}/\text{lens}$; mean \pm SD.), followed by LW lenses (0.84 \pm 0.27 $\mu\text{g}/\text{lens}$), and HW lenses (0.26 \pm 0.17 $\mu\text{g}/\text{lens}$), as shown in Table 3. Significant differences in triglyceride deposition were found among the three contact lenses (*p* < 0.001).

To simulate one month of use, contact lenses were incubated in artificial tear solution for 16 hours, followed by lens cleaning and 8 hours storage in multipurpose solution. This process was repeated daily for 30 days. After one month of simulated use, no contact lenses in this study exhibited any abnormal appearance, as compared to new lenses. For one month of simulated use, triglyceride deposition was still highest on the SI lenses (6.56 \pm 1.10 $\mu\text{g}/\text{lens}$). Triglyceride deposition on HW and LW lenses remained below 1 $\mu\text{g}/\text{lens}$ (0.55 \pm 0.34 and 0.10 \pm 0.12 $\mu\text{g}/\text{lens}$, respectively). Only triglyceride deposition between SI and the other contact lenses was found to be statistically significantly different (*p* < 0.001).

When comparing triglyceride deposition between short-term (one day) and long-term (one month) use, it was found that deposited triglyceride on SI contact lenses was significantly increased after one month of simulated use, as compared to one day of use (*p*=0.001). Triglyceride deposition on HW contact lenses after one month of use was not significantly higher than after one day of use (*p*=0.131).

DISCUSSION

Normally, the lipid layer is the outermost layer of tear film. It accounts for about 1% to 1.5% of the total thickness of tear film.⁵⁻⁸ Most of the lipids contained within the lipid layer are secreted from meibomian glands. Many types of lipids are found in human meibum, such as wax esters, sterol esters, triglycerides, and free fatty acids.⁹⁻¹³ Meibomian gland secretions are composed of triglyceride at about 4% of its lipid composition.⁸

Many substances from tear fluid can deposit on soft contact lenses after insertion. These deposits can result in contact lens spoilage that may lead to clinical complications, such as lens discomfort, decreased vision, intolerance, inflammation, and bacterial adhesion. Excessive lipid deposition on soft contact lenses can cause detrimental effects to lenses, as well as to wearers. Several factors can influence extent of lipid deposition, including contact lens material and amount of lipid in tears.

Many reports¹⁴⁻¹⁶ have shown that silicone hydrogel contact lenses absorb lipids at a higher rate than conventional hydrogel contact lenses. Rapp and colleagues¹⁷⁻¹⁸ found that lipid type and lipid deposit amounts vary according to contact lens composition material. Tear film lipid deposit profiles have been studied, with deposition findings varying according to method of evaluation and measurement. Bowers and colleagues¹⁹ found that white substance film on contact lenses had lipid components that were mainly cholesterol and cholesterol ester. Rapp and colleagues¹⁷⁻¹⁸ analyzed lipid deposition on worn hydrophobic lenses and found that deposits were composed of wax esters, fatty sterols, fatty alcohols, free fatty acids, and diglycerides; whereas, cholesterol, cholesterol esters, and triglycerides were not detectable. Maziarz, *et al*,²⁰ analyzed the amount of lipids from tear film which deposited on silicone hydrogel contact lenses from subjects after 30 days of wear and found that cholesterol was the most commonly deposited lipid (deposition range: 1.50-37.0 µg/lens). According to a report by Hatou, *et al*,²¹ the level of total lipid deposition on silicone hydrogel contact lenses after 2 weeks of wear was approximately 30-40 µg/lens.

Endura[®] has distinctive properties, as compared to other artificial tears, that provide the benefit of creating thicker and more stable tear film from its lipid (triglyceride) composition. Endura[®] can increase lipid film thickness in normal persons and can temporarily correct irregular tear film or modified lipid film in persons with severe aqueous tear deficiency (ATD). This type of lipid-enhanced artificial tear formulation tends to relieve symptoms in older people with Meibomian gland dysfunction, severe ATD dry eye, and/or surface dye staining.⁴ Because Endura[®] is preservative-free, contact lens wearers that have dry eye symptoms or that have Meibomian gland dysfunction may use this to relieve their symptoms. However, concerns relating to Endura[®] center on potential for lipid deposition on lenses as a result of high triglyceride content.

In the present study, we analyzed the amount of triglyceride deposition on 3 different types of contact lenses from the use of Endura[®]. Using the maximum recommended daily amount

of Endura[®], silicone hydrogel contact lenses had higher levels of triglyceride deposits than the other 2 types of hydrogel contact lenses. We then evaluated triglyceride deposits on contact lenses from 1 month (30 days) simulated use of Endura[®]. Our study protocol simulated the normal use of contact lenses, specifically: incubating the lens with Endura[®] for 16 hours, followed by cleaning with a multipurpose solution and daily cleaner, and then storing the lens in multipurpose solution for 8 hours. Triglyceride deposit concentrations were highest on silicone hydrogel contact lenses; ~10 to 60-fold higher than concentrations found on the other two types of contact lenses.

According to our review of the literature, there are no previous reports regarding deposition of lipids from an artificial tear solution on contact lenses. As a result, we compared our deposit findings with previously reported rates of lipid deposit from tear film. Despite using the maximum daily recommended amount of Endura[®], amounts of triglyceride deposition from Endura[®] on all 3 types of contact lenses studied were much lower than normal tear lipid deposition on contact lenses, according to the studies by Maziarz, *et al*,²⁰ and Hatou, *et al*,²¹ (cholesterol deposition 1.5-3.7 µg/lens and total lipid deposition 30-40 µg/lens, respectively). We assumed that lipid deposition from the maximum recommended daily amount of Endura[®] would not exceed the amount of lipid deposition from natural tear film lipids in normal human subjects. There are many methods for managing complications associated with contact lens deposition, including replacement of contact lenses every month²² and using multipurpose solution with rubbing step.²³ These methods significantly reduce lipid deposition on contact lenses. However, we found that for silicone hydrogel contact lenses, lipid deposition increased even when contact lenses were cleaned with multipurpose solution and daily cleaner with the rubbing step. Although lipid deposition increased with long-term use of Endura[®] and daily cleaning and rubbing, the increased amount of lipid deposit was still lower than lipid deposition from normal human tear film lipids.

In summary, we found lipid deposition to be highest in silicone hydrogel contact lenses,

similar to previous reports.¹⁴⁻¹⁶ We tested short (1 day) and long-term (30 days) duration of use and found that triglyceride deposition increased with longer period of use by ~70% in SI lenses, but remained low (<1 µg/lens) in HW and LW lenses. Endura[®] may be safe for contact lens wearers to use, particularly those with indications. Limitations of this study include small sample size and in vitro study. Further studies are needed to correlate symptoms and clinically significant signs from these deposits.

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