USAARL Report No. 97-24

An Apparent pH-Induced Effect on Extended Wear Hydrogel Lens Water Content (Reprint)

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July 1997

U.S. Army Aeromedical Research Laboratory
Fort Rucker, Alabama 36362-0577

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Released for publication:

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Unclassified

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION Unclassified	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION / AVAILABILITY OF REPORT Approved for public release, distribution unlimited
2b. DECLASSIFICATION / DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S) USAARL Report No. 97- 24	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION U.S. Army Aeromedical Research Laboratory 6b. OFFICE SYMBOL *(If applicable)* MCMR-UAC	7a. NAME OF MONITORING ORGANIZATION U.S. Army Medical Research and Materiel Command
6c. ADDRESS *(City, State, and ZIP Code)* P.O. Box 620577 Fort Rucker, AL 36362-0577	7b. ADDRESS *(City, State, and ZIP Code)* Fort Detrick Frederick, MD 21702-5012
8a. NAME OF FUNDING / SPONSORING ORGANIZATION 8b. OFFICE SYMBOL *(If applicable)*	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c. ADDRESS *(City, State, and ZIP Code)*	10. SOURCE OF FUNDING NUMBERS

PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.
0602787A	3M162787A879	PE	164

11. TITLE *(Include Security Classification)*
(U)An Apparent pH-Induced Effect on Extended Wear Hydrogel Lens Water Content (Reprint)

12. PERSONAL AUTHOR(S)
Morris R. Lattimore, Jr.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT *(Year, Month, Day)*	15. PAGE COUNT
Final	FROM TO	1997 July	10

16. SUPPLEMENTAL NOTATION
Optometry and Vision Science, Vol. 73, No. 11, pp 689-694

17. COSATI CODES

FIELD	GROUP	SUB-GROUP
20	06	

18. SUBJECT TERMS *(Continue on reverse if necessary and identify by block number)*
Tearfilm pH, hydrogel contact lenses, extended wear, and water content.

19. ABSTRACT *(Continue on reverse if necessary and identify by block number)*
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20. DISTRIBUTION / AVAILABILITY OF ABSTRACT ☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS	21. ABSTRACT SECURITY CLASSIFICATION Unclassified
22a. NAME OF RESPONSIBLE INDIVIDUAL Chief, Science Support Center	22b. TELEPHONE *(Include Area Code)* (334) 255-6907 22c. OFFICE SYMBOL MCMR-UAX-SS

DD Form 1473, JUN 86 *Previous editions are obsolete.*

SECURITY CLASSIFICATION OF THIS PAGE
Unclassified

19. Abstract (Continued)

under the same conditions ($p < 0.001$ by ANOVA). Correlation of these two nonlinear functions yielded a negatively sloped linear regression ($r = 0.99$ and 0.97) for each material. The slopes of the resultant linear functions were significantly different ($p < 0.01$) by t-test; the higher water content material exhibited a greater sensitivity to pH. The routine labeling of pH-induced water content changes by hydrogel lens manufacturers would provide an objective model for clinical lens behavior, and assist in lens type and parameter selection when fitting extended-wear soft lenses. Additionally, as other lens materials are characterized, it may be possible to model the "ideal" hydrogel material in terms of apparent pH-dependent or -independent behavior.

1040-5488/96/7311-0689$03.00/0
Optometry and Vision Science

Vol. 73, No. 11, pp. 689–694

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ABSTRACT

Numerous studies have examined the separate issues of precorneal tearfilm pH and hydrogel lens water content. None have examined the two issues in an associated, clinical fashion. Earlier research by this author has shown that stabilized hydrogel lens anterior surface pH correlates with established values for the precorneal tearfilm pH. This technique was therefore paired with two different methods of hydrogel lens water content assessment to determine if there was a predictable tear pH-related effect on soft lens hydration. Sixty-five volunteer subjects were fitted with either 38% (polymacon) or 58% (etafilcon A) water content hydrogel lenses on an extended-wear basis. The *in situ* hydrogel lens anterior surface pH was measured with a flat-surfaced, self-referenced pH electrode 5 min after initial fitting, and on subsequent extended wear follow-up examinations. On each follow-up, associated lens water content was determined by gravimetric and/or refractive analysis, yielding a total of 517 paired data points over a 33 month period. While the anterior lens surface pH increased in a nonlinear fashion with immediate duration of extended lens wear [$p < 0.001$ analysis of variance (ANOVA) by number of days extended lens wear], the water content decreased in a nonlinear fashion under the same conditions ($p < 0.001$ by ANOVA). Correlation of these two nonlinear functions yielded a negatively sloped linear regression ($r = 0.99$ and 0.97) for each material. The slopes of the resultant linear functions were significantly different ($p < 0.01$) by t-test; the higher water content material exhibited a greater sensitivity to pH. The routine labeling of pH-induced water content changes by hydrogel lens manufacturers would provide an objective model for clinical lens behavior, and assist in lens type and parameter selection when fitting extended-wear soft lenses. Additionally, as other lens materials are characterized, it may be possible to model the "ideal" hydrogel material in terms of apparent pH-dependent or -independent behavior.

Key Words: tearfilm pH, hydrogel contact lenses, extended wear, water content

Received October 30, 1995; revision received May 10, 1996.
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INTRODUCTION

Anterior Lens-Surface pH

The anterior corneal surface is associated closely with an overlying canopy of moisture known as the precorneal tearfilm. Traditionally, clinicians have been concerned with how certain characteristics of the tears can influence corneal integrity; tearfilm formation problems[1] and tear osmolarity issues[2] represent two examples of purported tearfilm influence upon the cornea. However, the tearfilm can be susceptible to influence by the cornea, as evidenced by the presence of both glycolytic and tricarboxylic acid cycle enzymes within the tear layer. The source of these enzymes has been shown not to be the lacrimal gland, but rather the underlying corneal tissue.[3] Therefore, tear chemistry is affected directly by the cornea. Consequently, clinicians should be reminded that although anatomically distinct, the cornea and its tearfilm are functionally interactive.

Attempts at quantifying the normal tear pH value have yielded varying results (Table 1). Although one cause of variation appears to be due to instrumentation differences, the primary cause of variation appears to be the location or source of the tear sample. Efforts at documenting the pH of the precorneal tearfilm (i.e., that canopy of mucin, aqueous, and oil directly anterior to the cornea) have obtained a mean value range of 7.45 to 7.83. Because measurements of precorneal tearfilm pH under the extended open-eye condition have been shown to match that predicted by carbon dioxide equilibration calculations,[6] it is likely these values are very close to the true precorneal tearfilm pH.

Initial hydrogel lens research indicated these contact lenses may provide a barrier to carbon dioxide efflux from the cornea, although at the time this was considered to be insignificant in terms of corneal physiology.[12] Nonetheless, recent measurements of tear carbon dioxide accumulation under hydrogel lenses, paired with the detection of a decrease in both subcontact lens and stromal pH after contact lens wear, indicate yet another functional link between the precorneal tearfilm and corneal physiology.[10, 13–15] The purpose of this portion of the study was to docu-

TABLE 1. Recent tear pH studies.

Author(s)	Location	Instrument	No.	Mean ± SEM
Carney and Hill[4]	Meniscus	Microelectrode	16	7.45 ± 0.16
Abelson et al.[5]	Inferior	Microcombination	44	7.00 ± 0.20
Fischer and Wiederholt[6]	Limbus (1 o'clock)	Micro-pH electrode	4	7.60 ± 0.09
	Limbus (5 o'clock)	Micro-pH electrode	4	7.50 ± 0.08
Coles and Jaros[7]	Lateral fornix	Direct contact microelectrode	133	7.11 ± 0.13
Norn[8]	Inferior fornix	Microglass electrode	41	6.93 ± 0.24
Andres et al.[9]	Precorneal	Micro-pH electrode	71	7.51 ± 0.18
Chen and Maurice[10]	Precorneal	Fluorescent probe	6	7.83 ± 0.10
Lattimore[11]	Precorneal	Self-referenced pH electrode	28	7.43 ± 0.06

ment anterior lens surface pH over the course of 7 days extended lens wear for two hydrogel lens types.

Hydrogel Lens Water Content

Soft lens water content, after initial placement on the surface of the eye, has been shown to change during wear.[16–21] The relatively low volume of aqueous component (1 μl) within the precorneal tearfilm[22] could intuitively be blamed for this dehydration process. Clinically, hydrogel lenses appear to "tighten" over the first day of wear. Because the major proportion of hydration change in the above studies occurred within the first several hours, it was assumed, but not documented, that water content stabilization developed by the end of 1 day of continuous lens wear. Additionally, only one means of water content determination was used, without concurrent method cross-comparison. Therefore, the intention of this portion of the overall research protocol was two-fold: to compare two methods of water content determination, and to describe the dehydration course over 7 days of wear for both lens types used.

Definitively, material sciences have already shown a pH change in hydrogel solution *in vitro* to influence material water content directly.[23] A correlative clinical model of this reported laboratory relation has not been documented. The purpose of the combined study, then, was to evaluate the fluid exchange interactions between hydrogel lenses and the precorneal tearfilm with the intent of modeling the apparent pH-water content relation in two distinct types of hydrogel lenses.

MATERIALS AND METHODS

Sixty-five myopic subjects, wearing corrections that varied from −0.50 to −3.50 D, were followed on a quarterly basis for approximately 1 year. Subjects were on a 1 week wearing cycle, after which time the lenses were removed, disposed of, and replaced after at least 1 night of lens-free sleep.

Tear Film pH

A self-referenced pH electrode, designed for pH recording from semisolid materials, was used to assess the *in situ* anterior contact lens surface pH response to extended- or continuous-wear of 38% and 58% water content hydrogel lenses worn on a disposable basis. The recorded pH reading was the peak value of a transient response. Upon initial probe application, the measured pH value was within 0.2 of the final or peak value. However, a gradual drift in the alkaline direction led to stabilization of the reading, presumably due to temperature changes at the probe surface. If the probe was kept in contact with the lens beyond the stabilization period, a gradual shift in the acidic direction was noted. This has been attributed to carbon dioxide accumulation under the probe (I. Fatt, personal communication).

Use of this pH electrode methodology assumes the anterior contact lens surface pH measurement accurately represents both the prelens tearfilm pH and the pH of the anterior water component of the hydrogel contact lens. However, it is entirely possible these two entities could have slightly different pH values secondary to a CO_2 accumulation gradient under the contact lens. Control or manipulation of ambient temperature and humidity were not attempted secondary to the conclusion of Brennan et al.[24] that those factors have little value in the prediction of water content of hydrogel lenses under normal wearing conditions.

The pH electrode was calibrated with a 7.00 and a 10.00 pH standard solution at 35°C and disinfected by alcohol swab and surface drying between each assessment. Baseline measurements were recorded from the contact lens in its storage packet immediately after opening, 5 min after initial lens application onto the volunteer subject's eye, 24 h after initial lens application, 7 days after initial lens application, and on subsequent quarterly follow-up examinations. Each measurement for any one individual was taken at the same time of day in order to minimize error from individual diurnal variations. However, pH assessments across individuals occurred at varying times of day, thereby masking any group diurnal effect. All data gathering was accomplished at the U.S. Army Aeromedical Research Laboratory, Fort Rucker, AL.

Lens Water Content

The gravimetric determination of water content was obtained by way of an analytical scale enclosed in a controlled environmental chamber kept at 35°C. The change in lens weight from the fresh, wet state to the completely dehydrated state was used to calculate the beginning water content once reference standards were established. All 38% water content lenses were measured by this method. One-half of the 58% lenses were measured via this methodology by using 1 lens from each subject.

The refractive method used a commercially purchased Abbe refractometer with a fixed measurement scale (based on one specific index of refraction). The refractive scale ranged from 35 to 75% water. The 38% lenses could not be measured with this method because they tended to drift just below a 35% water content with even a small amount of wearing time. The other half of the 58% lenses were assessed by this refractive method, using 1 lens from each subject. In this manner a correlation between the 2 methods could be established for the 58% water content lenses.

RESULTS

Tearfilm pH

Fig. 1 provides a graphical representation of the data for both lens types; lens brand or material differences were not statistically significant ($p = 0.43$). The contact lenses in solution were at or very near a neutral pH of 7.00 (38% lenses = 7.05; 58% lenses = 7.00). Within the first 5 min of contact lens wear, the pH reading started to rise into the alkaline region (7.23); this increase in pH continued over the course of the first 2 days of wear to asymptote near the established precorneal tearfilm norm (7.45). Statistical analysis (ANOVA) of pH by duration of extended wear was significant ($p < 0.001$).

The initial *in situ* pH reading of 7.23, taken just 5 min after lens application, suggests that a fluid exchange between the anterior tearfilm and the contact lens occurs very quickly. Yet, the pH does not stabilize until 2 days of extended wear. The initial data (days 0 and 1) are presumably less alkaline compared to precorneal tearfilm norms (7.45) due to the starting lens storage solution pH being a nominally neutral pH of 7.0; if the lenses were packaged in a storage solution of a slightly more alkaline nature near 7.45, this pattern of pH adjustment might not be exhibited.

The fact that both types of lenses chosen for use in the protocol were packaged in neutral, or near neutral, solutions may be significant. It is possible that hydrogel stability and physical performance parameters are optimum near a pH of 7. Therefore, lenses may be packaged at that pH in order to maximize shelf life or performance characteristics. If that is the case, and if the inference of decreased stability and decreased physical performance at pHs other than neutral is also correct, then future material research should perhaps be centered on finding polymers possessing optimal qualities at or near the precorneal tearfilm pH of 7.45.

Lens Water Content

A logarithmic water content decline occurred over the time period tested by both measurement systems for the etafilcon lenses (Fig. 2). An independent ANOVA for water content factored by number of days wear was highly significant ($p < 0.001$). There was an apparent stabilization that developed by day 4 extending through day 7. This is contrary to suggestions in the literature of a 24 h hydration stabilization; these data demonstrate long-term dehydration occurring over the first 3 to 4 days of wear. Additionally, the two methods of water content determination agreed remarkably well, correlating with each other at a Pearson coefficient of 0.96.

Gravimetric data on etafilcon lenses were initially being gathered in the summer of 1990. A number of subjects seen at Fort Rucker were deployed to Saudi Arabia on Operation Desert Shield. In order to meet the requirements of the research protocol, the subjects were given a quarterly follow-up examination in Saudi Arabia in November 1990. As a part of the examination,

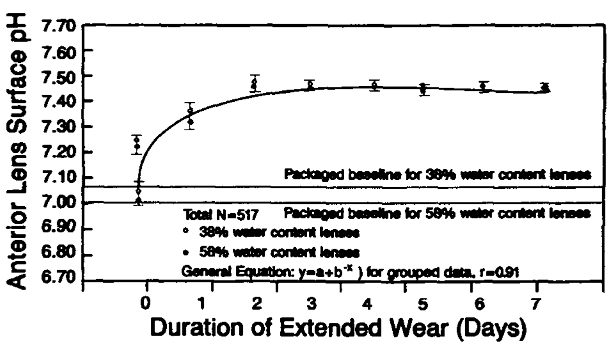

Figure 1. Influence of wearing time on hydrogel lens anterior surface pH. Both types of hydrogel lenses exhibit the same logarithmic pattern of long-term pH change with extended wear.

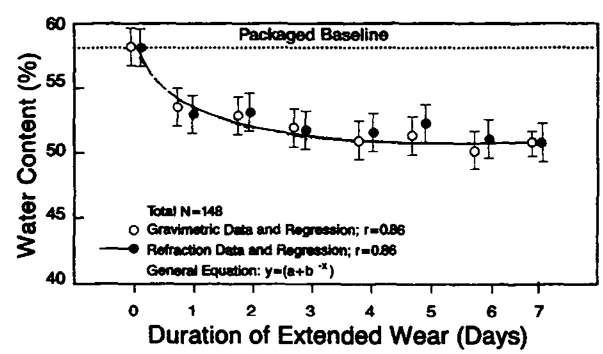

Figure 2. Influence of wearing time on hydrogel lens water content. Both measurement methods establish a statistically similar water content decrease for the etafilcon material with extended wear.

water content data were obtained using the refractive method (Fig. 3). After 6 to 11 weeks in Saudi Arabia, the subjects exhibited the same pattern of lens hydration, as a function of duration of lens wear, as they did at Fort Rucker. Data obtained were for 1, 2, 6, and 7 days of wear. In and around Saudi Arabia, it seemed that soft lens wearers fell into two groups: those who maintained their habitual wearing schedule of 6 or 7 days with no subjective problems, and those who decreased their wearing time to 2 or 3 days of wear because of changes in comfort or clarity. Neither group exhibited a lens water content different from their Fort Rucker baseline. The assumption that soft lenses are subject to excessive dehydration in the desert may be incorrect. However, the altered wearing behavior may be indicative of some other unknown factor(s). Although there may have been excessive dehydration on initial deployment, by 6 to 11 weeks of acclimitization, some sort of adaptation could have occurred which functioned to return contact lens hydration levels to the previously established physiological norm.

Fig. 4 depicts the results of the two lens types as measured gravimetrically. The amount of water loss was greater in the higher water content lens (etafilcon). Both materials exhibited an approximate logarithmic decline in hydration level with extended wear. As for etafilcon, the change in water content for polymacon as a function of extended wearing time was significant (ANOVA, $p < 0.01$). A gross examination of Fig. 4 suggests that the relative dehydration, based on packaged baseline as the norm, may be approximately the same for both lens types.

DISCUSSION

Possible factors contributing to the long-term dehydration process include lipid and protein deposits during wear, in addition to any changes in pH. Gravimetrically, the former would serve to increase the dry material weight a greater proportion than the wet material weight, thereby skewing the measurement in the dehydrated direction. Indeed, Mirejovsky et al. demonstrated small unit protein absorption to decrease the equilibrium water content.[25]

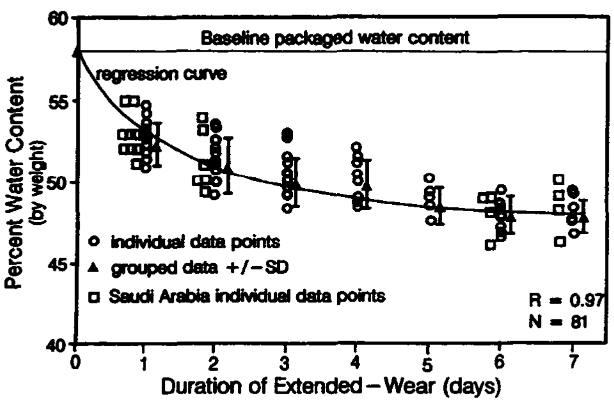

Figure 3. Hydrogel lens dehydration under extended-wear conditions. Water content data were unchanged with geographical displacement of subjects from the southern United States to east-central Saudi Arabia.

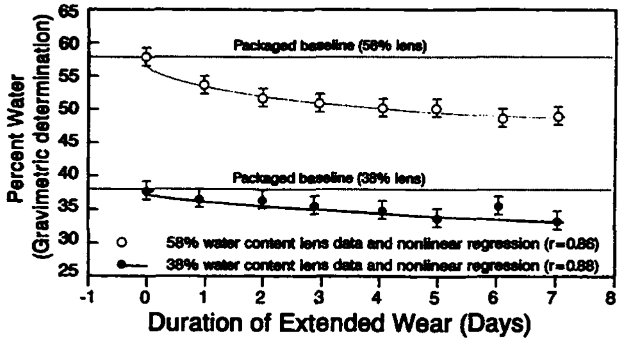

Figure 4. Hydrogel lens dehydration under extended-wear conditions. Both types of hydrogel lenses exhibited a logarithmic decrease in water content as a function of extended wear.

Possible tainting factors in the methodology could include oil contamination from fingers on lens removal, and fluid loss during the weighing and/or refractive processes. Each could serve to decrease water content, therefore the presented levels of lens hydration may slightly overestimate the amount of dehydration with wear. However, the relative relation between the two methods compared in Fig. 2 would be unaffected; the same holds for the process of long-term change. The effect of any contamination error would simply decrease the overall magnitude of the effect across the board, but not the basic characteristics of the logarithmic regression analyses.

Correlation Analysis

Using the regression curves from Figs. 1 and 4, we can see in Fig. 5 an apparent effect of the precorneal tearfilm pH on soft lens hydration. The individual correlations for both the polymacon and etafilcon lenses were highly significant ($r = 0.97$ and 0.99, respectively) based on a linear

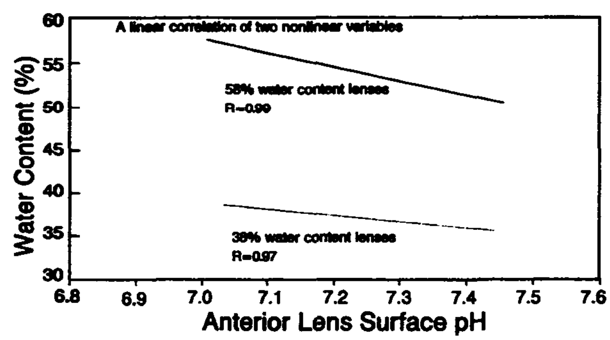

Figure 5. Influence of anterior lens surface pH on hydrogel lens water content. The significantly different slopes for the two types of lens materials are likely indicative of their differing ionic characteristics.

regression model. Clearly, hydrogel water content is directly related to the pH of the solution within which it is clinically suspended, i.e., the precorneal tearfilm. Fig. 5 also reveals etafilcon to be subject to a greater rate of relative dehydration with a steeper slope. The slopes of the two data sets are significantly different by ANOVA ($p < 0.01$). The differences in rate and degree of material dehydration *in situ* can perhaps be explained by the chemical and structural differences between the two lens types. Polymacon is a nonionic material (FDA Group 1), whereas etafilcon is ionic (FDA Group 4). The degree of molecular water attraction, and differential forces resistant to water loss, readily account for the behavior differences documented by this study.

Clinically these differences can be applied to patient management issues. Ostensibly, a patient with decreased serous tear component production would be less likely to tolerate, or be comfortable with, an ionic lens of mid- to high-water content that presents a large hydration challenge to the eye in the initial 3 to 4 days of extended wear. The low-water content, nonionic lens might provide greater comfort throughout the entire lens wearing cycle.

Additionally, if a patient's tearfilm pH were even more alkaline, then the hydration level of worn lenses would be even less than that documented here. Based on the endpoint values of the two material types, it is suggested that manufacturer data on lens water content and oxygen transmissivity should specify at what pH the data were obtained. This process would result in a direct reduction of the Dk/L, thereby yielding lower corneal oxygen levels than the clinician believes are present. Without pH information, the functional performance inferences made from such data are meaningless with no real, useful, clinical relevancy. As an adjunct to the above, if lens manufacturers provided linear behavior models similar to Fig. 5, patient care could be individually customized by the clinical measurement of precorneal tearfilm pH. Two brands of lenses, identical in all packaged parameters (power, thickness, base curve, diameter, and water content) save ionicity, would provide differing physical fits and oxygen availability on the eye, because of different *in situ* water contents.

CONCLUSIONS

The gravimetric and refractive methods of lens water content determination agree closely for the 58% water content lenses tested. The *in situ* data confirm the work of McCarey and Wilson[23] that hydrogel material water content is a function of pH, implying that functional lens parameters are in a state of flux over the first few days of extended lens wear. However, the exact pattern or degree of change is dependent upon specific lens material ionicity characteristics. It is concluded that this hydration change is a direct result of tear pH influences acting upon the hydrophilic material. Extended hydrogel lens wear is clearly a complex, dynamic process for both the lens and the cornea. A complete understanding of all lens parameters is essential for the successful practice of contact lens care. The routine labeling of pH-induced water content changes by hydrogel lens manufacturers would provide an objective model for *in situ* lens behavior, and assist clinicians in lens type and parameter selection when fitting extended wear soft lenses. Furthermore, as other lens materials are characterized, it may be possible to model the ideal hydrogel material in terms of pH-dependent or -independent behavior.

ACKNOWLEDGMENTS

1. The views of the author do not purport to reflect a position of the Department of the Army or the Department of Defense.

2. Citation of trade names does not constitute official Department of the Army endorsement or approval of the use of such commercial items.

3. Human subjects participated in the study after giving their free and informed voluntary consent. The investigator adhered to Army Regulation 70-25 and United States Army Medical Research and Development Command Regulation 70-25 on Use of Volunteers in Research.

4. The research was accomplished under the auspices of the U.S. Army Medical Research and Development Command and was conducted at the U.S. Army Aeromedical Research Laboratory.

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