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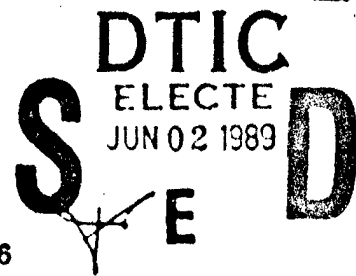
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**SOFT CONTACT LENSES:
SINK OR BARRIER
TO CHEMICAL WARFARE AGENTS?**

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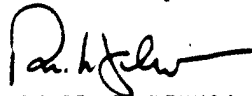
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The voluntary informed consent of the subjects used in this research was obtained in accordance with AFR 169-3.

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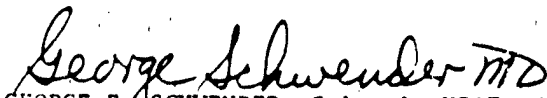
This report has been reviewed and is approved for publication.



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19 ABSTRACT (Continue on reverse if necessary and identify by block number) Contact lens wear by United States military personnel in a chemical warfare environment is a controversial issue. Several studies in industrial settings have suggested that contact lenses may safeguard the cornea from chemical and mechanical trauma. The purpose of this experiment was to see if a soft contact lens would act as a barrier to a chemical agent and protect the cornea, perform as a sink and spread the dosage of the chemical agent out over time, or both. Eight subjects were fitted with soft contact lenses (butilcon A, 45% water content). Subjects wore the left lens only for the study, while the right eye was used for a control. Both eyes were challenged with small volumes (5, 10, and 20 µl) of a 0.2% physostigmine aqueous solution which was chosen to simulate the live agent diisopropyl fluorophosphate (DFP). Pupil size was monitored over an 8-h period using a modified photoelectric keratometer. The results indicate that a soft contact lens does act as a barrier to chemical agents for the first hour following exposure, but then acts as a sink, spreading out the dosage over time.			
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TABLE OF CONTENTS

	<u>Page</u>
INTRODUCTION	1
METHODS.	2
RESULTS.	3
DISCUSSION	6
REFERENCES	7

List of Figures

Fig.
No.

1. The mean pupil diameters for the contact lens-wearing eye and the control eye after exposure to 5 μ l of 0.5% aqueous solution of physostigmine	4
2. The mean pupil diameters for the contact lens-wearing eye and the control eye after exposure to 10 μ l of 0.5% aqueous solution of physostigmine.	5
3. The mean pupil diameters for the contact lens-wearing eye and the control eye after exposure to 20 μ l of 0.5% aqueous solution of physostigmine.	6

List of Tables

Table
No.

1. Sample sizes	2
2. Iris Pigmentation Data	3
3. Pupil Size Data Over Time (Drug volume = 5 μ l)	9
4. Pupil Size Data Over Time (Drug volume = 10 μ l).	10
5. Pupil Size Data Over Time (Drug volume = 20 μ l).	11
6. Comparison of Differences in Pupil Size (Drug volume = 5 μ l)	12
7. Comparison of Differences in Pupil Size (Drug volume = 10 μ l).	13
8. Comparison of Differences in Pupil Size (Drug volume = 20 μ l).	14



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SOFT CONTACT LENSES: SINK OR BARRIER TO CHEMICAL WARFARE AGENTS?

INTRODUCTION

Contact lens wear by United States military personnel in a chemical warfare environment is a controversial issue. Technical Order 14P4-9-31 has been amended (Oct 87) to preclude the wear of contact lenses by ground crew wearing the M-17 and/or MCU-2/P chemical warfare defense masks because of unsuitable field conditions (1). If contact lenses are made available to aircrew, the question of the appropriateness of wearing contact lenses with aircrew chemical defense ensembles in a chemical warfare environment must be answered. Will a contact lens offer any temporary or permanent protection to the corneas of aircrew in a chemical warfare environment?

Several recent studies in industrial settings have indicated that hydrogels (soft) and polymethylmethacrylate (hard) contact lenses may safeguard the cornea, in some instances, from chemical and mechanical trauma. Nilsson et al. (2,3) suggested that both hard and soft lenses had a protective effect, albeit small, against mechanical foreign body injury, although hard lenses are prone to subcontact lens foreign bodies. Kergstorff and Black (4) reviewed over 10 incidences involving contact lens wearers (primarily hard lenses) exposed to physical trauma and chemical irritants. In many cases, the contact lenses were thought to have prevented or minimized serious injury to the eye.

Nilsson and Anderson (5) also examined soft contact lens wear, in conjunction with chemical fumes and splashes, using the rabbit model. Even though lens uptake of the chemicals extended the exposure time to the cornea, the authors concluded that the eyes suffered less from the lower chemical concentration in the lenses than from a direct exposure. Guthrie and Seitz (6) demonstrated that even a hard lens, at times, can act as a barrier to chemical irritants. Kok-van Aalphen et al. (7) subjected a number of Dutch special police to CS (o-chlorobenzylidene malonitrile) tear gas. The subjects wearing soft contact lenses were not only able to see clearly after leaving the chamber, but also had normal corneal examinations, while the nonwearers were more disoriented and had corneal epithelial damage.

Soft contact lenses are being studied by many researchers as a means of altering drug delivery to the eye (8,9,10). Hull et al. (11) used a 45% hydrophilic lens to determine whether it created a barrier effect in the corneal penetration of prednisolone in rabbits. In their experiment, the lens did act as an impediment for the first 2 h. The control eye (without a contact lens) had prednisolone concentrations in the cornea and aqueous four to six times higher than the soft contact lens-wearing eye. Praus and Krejci (12) demonstrated that the elution of ophthalmic drugs from hydrophilic contact lenses dependent upon each drug's molecular weight. The low-molecular-weight drugs are released faster from the lens than the high-molecular-weight drugs.

The purpose of this experiment was to determine if a soft contact lens would act as a barrier to a chemical agent and protect the cornea, perform as a sink and spread the dosage of the chemical agent out over time, or both. T

assess the effect of a chemical agent, a drug was needed that would mimic the actions of a live agent. Eserine (physostigmine) was selected since it has a similar mode of action as the live agent diisopropyl fluorophosphate (DFP). Both drugs are anticholinesterases (anti-CHE), although eserine is a reversible anti-CHE with a duration of miosis that recedes over a 24- to 72-h period, while DFP is relatively irreversible, inducing prolonged miosis that may last for several days (13).

METHODS

Eight subjects, from whom informed consent had been obtained, participated in the study. Each subject was fitted with soft contact lenses (bucfilcon A, 45% water content) and allowed to fully adapt to them. A lens was worn only in the left eye (O.S.) for the study, and the non-lens-wearing right eye (O.D.) was used as the control. All of the analyses assumed that the results were dependent only on the contact lens and not on the side (right or left) in which the lens was placed.

A 0.5% physostigmine aqueous solution was used to simulate the chemical warfare agent DFP. The scenario was a limited exposure to an agent that becomes dissolved in the tear film of the eye. Therefore, small volumes (5, 10, and 20 μ l) of the simulant were used so as not to exceed the maximum tear volume of the eye. Mishima et al. (14) reported that the human eye can hold up to 30 μ l of lacrimal fluid, if the subject does not blink. Each eye in each subject was challenged with the simulant and monitored for an 8-h period. The drug was instilled into the lower cul-de-sac with a micropipette. The first eye to be challenged was chosen at random, while the second eye received the drug after a 10-min interval. Subjects who were exposed to the 5- μ l volume were also exposed to the 10- μ l volume, and those exposed to the 10- μ l volume were exposed to the 20- μ l volume. Thus only 3 subjects were exposed to all 3 volumes of solution. Table 1 displays the number of subjects for each volume and dose sequence combination.

TABLE 1. SAMPLE SIZES

Drop sequence	Drug volume (μ l)		
	5	10	20
O.D./O.S.	2	3	3
O.S./O.D.	1	2	5
Totals	3	5	8

Before placing a drop in either eye, a Polaroid photograph was taken of each eye with a photoelectric keratometer (PEK). The PEK was modified by occluding the central and mid-diameter rings. Only the peripheral rings

provided illumination, thus enabling an unobstructed view of the pupil. After instillation, photographs were taken at one-half hour and then at hourly intervals for the duration of the experiment. The absolute pupil size (in millimeters) for each subject was derived by comparison of the post-instillation photographs with a PEK photograph taken of the subject in which his eyes are closed and a millimeter (mm) scale is in front of the closed eye. Although we were concerned with relative pupil size differences, the subjects remained under constant illumination in our night vision laboratory throughout the experiment.

Data concerning the effect of the drug on individual iris pigmentation was also collected. Table 2 displays the iris color of each subject for each drug volume combination.

TABLE 2. IRIS PIGMENTATION DATA

Iris color	Drug volume (μ l)		
	5	10	20
Light (blue or green)	3	4	5
Dark (brown)	0	1	2
Not classified (dark green)	0	0	1

RESULTS

Tables 3, 4, and 5 illustrate the pupil size statistics at each time interval (hour) and for each drug volume. For the purpose of analysis, a difference (DIFF) was measured between the pupil size of the control eye (O.D.) and the pupil size of the contact lens-wearing eye (O.S.). A negative DIFF indicated that the control eye responded more to the physostigmine, while a positive DIFF indicated that the eye with the contact lens reacted more to the drug.

Analyses were performed to ascertain whether the drop sequence had any influential effect on the DIFF. Using the first three time intervals only (0.5, 1, 2 h), a repeated measures analysis of variance (ANOVA) was performed for the 20- μ l volume category. No significant difference was detected due to drop sequence. However, due to the small sample size, the power of detecting a significant difference was also small.

Because increased pigment in the iris generally prolongs the onset of the drug action (15), an analysis was also done to determine whether iris pigmentation had an effect on the experiment. Examining only the 20- μ l trials, a repeated measures ANOVA indicated that no statistically significant difference in pupil size change was due to iris pigmentation. Again, the power of the test was limited by the sample size.

The disparity in pupil size (DIFF) was examined using a two-way ANOVA for each drug volume separately, with SUBJECTS and HOUR as the sources of variation.

The effect due to HOURS was found to be statistically significant for each volume ($p < 0.05$), which indicated that the pupils of the two eyes did not react to the drug in the same manner across the time intervals. The results are as follows:

Volume	Hour (p-value)
5 μ l	.006
10 μ l	<.001
20 μ l	<.001

Additionally, two-sided t-tests were performed at each time interval and for all 3 drug volumes. The DIFF at each time interval was tested against no pupil size difference (0), and the results are shown in Tables 6, 7, and 8. All 3 drug volumes demonstrated the same statistically significant differences in pupil size between the control eye and the contact lens-wearing eye at the tested time intervals (see Figs. 1, 2, 3).

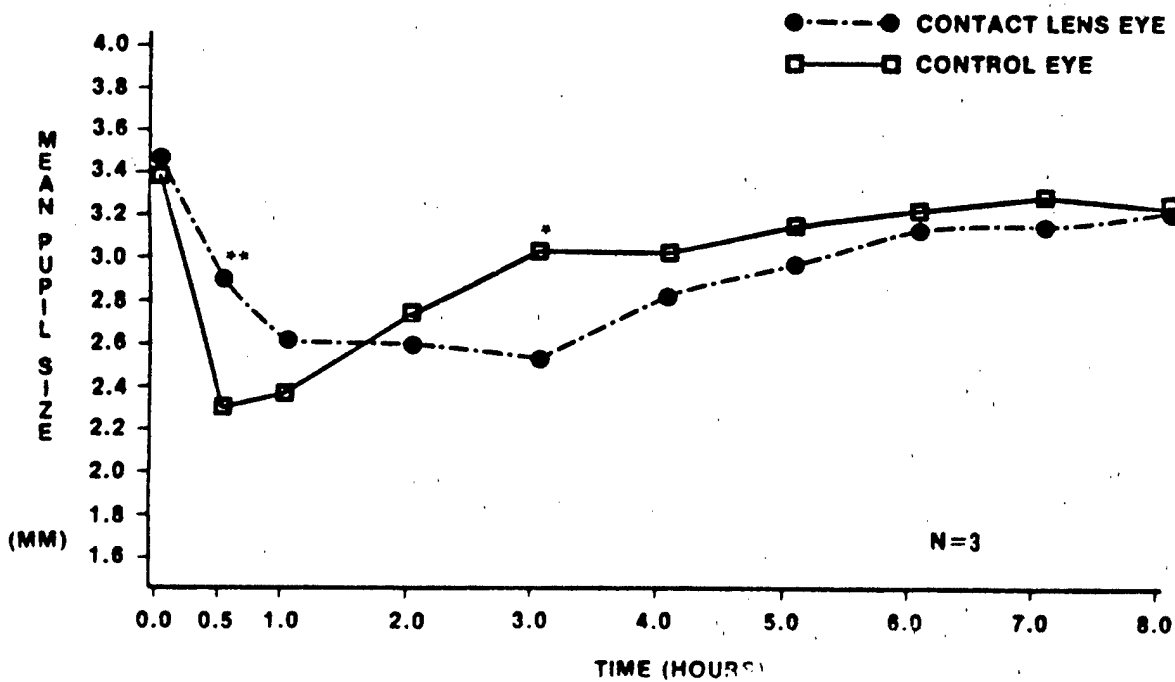


Figure 1. The mean pupil diameters for the contact lens-wearing eye and the control eye after exposure to 5 μ l of 0.5% aqueous solution of physostigmine. * indicates a significant difference between groups ($p < 0.05$). ** denotes a highly significant difference ($p < 0.001$)

Before the 0.5% physostigmine aqueous solution was administered (HOUR = 0), no significant difference was detected in pupil size ($p > .05$). One-half hour after drug instillation, for each drug volume, the pupil of the control eye was smaller than the contact lens-wearing eye, creating a statistically significant negative DIFF ($p < .005$). After one hour, the DIFF had returned to a nonstatistically significant value ($p > .05$). By the third hour, the pupil of the contact lens-wearing eye was smaller than the control eye, resulting in a statistically significant positive DIFF ($p < .005$) for each drug volume.

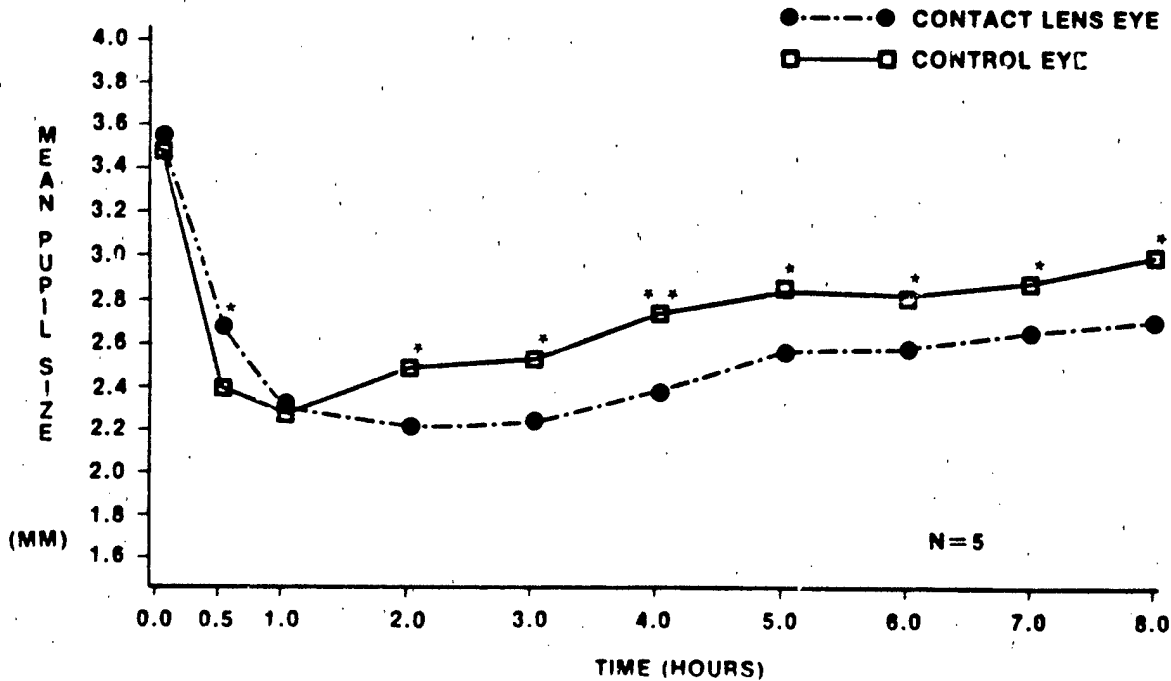


Figure 2. The mean pupil diameters for the contact lens-wearing eye and the control eye after exposure to 10 μ l of 0.5% aqueous solution of physostigmine. * indicates a significant difference between groups ($p < .05$). ** denotes a highly significant difference ($p < .001$)

For drug volumes 10 μ l and 20 μ l, the statistically significant positive DIFF remained throughout the majority of the time intervals from 4 to 8 h following drug instillation (Figs. 2, 3 and Tables 7, 8).

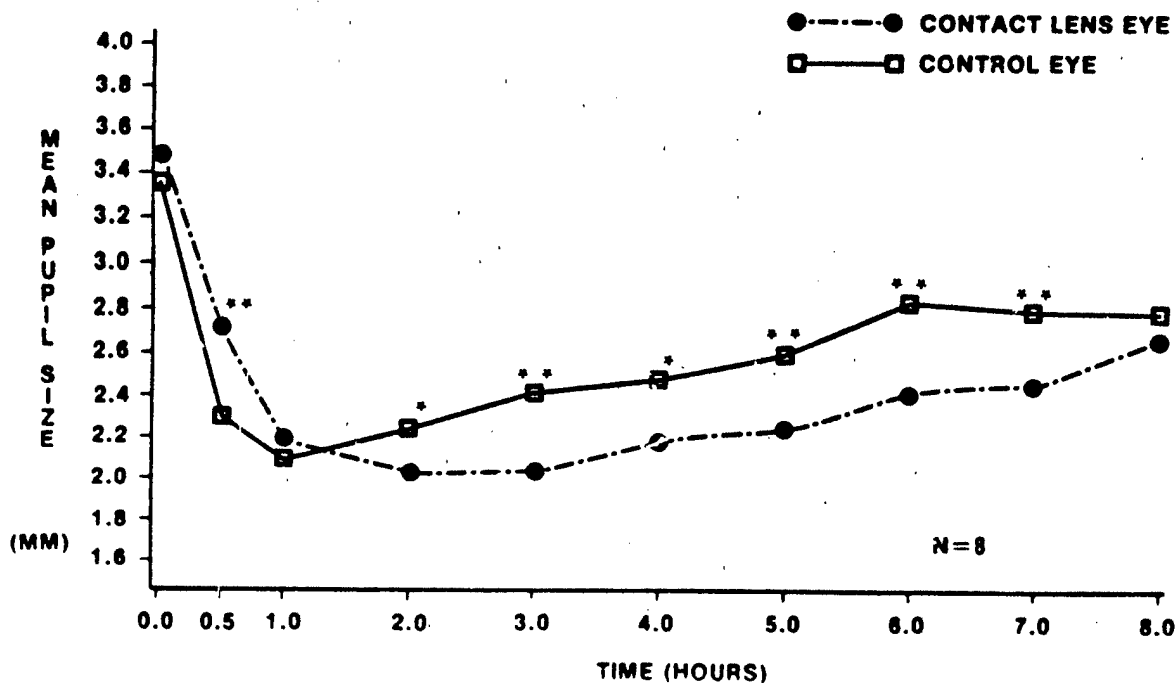


Figure 3. The mean pupil diameters for the contact lens-wearing eye and the control eye after exposure to 20 μ l of 0.5% aqueous solution of physostigmine. * indicates a significant difference between groups ($p < 0.05$). ** denotes a highly significant difference ($p < 0.001$).

DISCUSSION

Data from this experiment indicated that the bufilcon A (45% water content) contact lens did present a barrier to the corneal exposure from the chemical warfare agent simulant. However, corneal protection was limited to the first hour following chemical exposure. After the first hour, the lens offered no protection and actually performed as a sink, in that the dosage of the chemical agent remaining in the contact lens slowly leached out during the rest of the experiment.

The contact lens most likely prevented the chemical simulant from reaching the cornea by two avenues. Chemical agents must reach the cornea from beneath the edge of the lens or through the lens. The cornea is sealed off by the contact lens at the limbus. Since the sorption characteristics of the hydrophilic lens (i.e., the ability of the lens to uptake and release the chemical agent) are not clearly defined, it is somewhat difficult to predict how really effective the contact lens was as a barrier and how much of the chemical was released onto the cornea from the saturated lens matrix. Thus no quantitative determination could be made to compare the two routes of possible corneal exposure.

Soft contact lens wear may offer aircrew some temporary ocular protection in a chemical warfare environment. The dangerous and prolonged sink effect could be eliminated if the crewmember could remove the lenses after the first hour of chemical exposure. The importance of carrying a back-up pair of spectacles in potential chemical environments is further reinforced in this scenario. Although most ground crew will not be allowed to wear their contact lenses during combat, anyone who is wearing soft contact lenses and is exposed to a chemical agent during wartime should immediately don their protective masks rather than take the time to remove their contact lenses. Later, they should remove their lenses, if at all possible, within the 1-h postexposure time frame.

This study involved the use of one chemical agent and only one type of 45% water-content soft contact lens. To more accurately predict the protective abilities of soft contact lenses to vapors from chemical warfare agents, other types of soft contact lenses need to be evaluated against a variety of chemical warfare agents. An in vitro experiment to determine the elution characteristics of various soft lenses for selected chemical warfare agents should help to clarify the mechanisms and define the true protection factor of soft lenses.

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TABLE 3. PUPIL SIZE DATA OVER TIME

(Drug volume = 5 µl)

		O.D. (control eye)				O.S. (contact lens eye)			
H	N	Mean	Minimum value	Maximum value	Standard deviation	Mean	Minimum value	Maximum value	Standard deviation
0.0	3	3.40	3.0	3.8	0.400	3.47	3.0	3.8	0.416
0.5	3	2.27	1.9	2.6	0.351	2.87	2.6	3.0	0.231
1.0	3	2.33	2.1	2.6	0.252	2.57	2.1	3.0	0.451
2.0	3	2.70	2.3	3.2	0.458	2.57	2.1	2.8	0.404
3.0	3	3.00	2.6	3.6	0.529	2.50	2.1	2.8	0.361
4.0	3	3.00	2.6	3.4	0.400	2.80	2.6	3.0	0.200
5.0	3	3.13	2.6	3.8	0.611	2.93	2.8	3.2	0.231
6.0	3	3.20	2.6	3.8	0.600	3.13	2.6	3.8	0.611
7.0	3	3.27	2.6	4.0	0.702	3.13	2.6	3.8	0.611
8.0	3	3.20	2.6	3.8	0.600	3.20	2.6	3.8	0.600

Note:
H = HOUR
N = number

TABLE 4. PUPIL SIZE DATA OVER TIME

(Drug volume = 10 µl)

		O.D. (control eye)				O.S. (contact lens eye)			
H	N	Mean	Minimum value	Maximum value	Standard deviation	Mean	Minimum value	Maximum value	Standard deviation
0.0	5	3.52	3.2	3.8	0.228	3.56	3.2	3.8	0.261
0.5	5	2.38	1.7	3.0	0.526	2.66	2.3	3.0	0.261
1.0	5	2.26	1.7	2.8	0.439	2.28	1.9	3.0	0.427
2.0	5	2.48	2.1	2.8	0.356	2.20	1.9	2.6	0.265
3.0	5	2.52	2.1	3.0	0.342	2.22	1.9	2.3	0.179
4.0	5	2.74	2.3	3.2	0.329	2.38	2.1	2.6	0.217
5.0	5	2.84	2.6	3.4	0.329	2.54	2.8	2.8	0.261
6.0	5	2.82	2.3	3.4	0.390	2.58	2.1	2.8	0.286
7.0	5	2.88	2.6	3.4	0.303	2.66	2.3	2.8	0.219
8.0	5	3.00	2.6	3.8	0.469	2.72	2.6	2.8	0.110

Note:

H = HOUR

N = number

TABLE 5. PUPIL SIZE DATA OVER TIME

(Drug volume = 20 μ l)

		O.D. (control eye)				O.S. (contact lens eye)			
H	N	Mean	Minimum value	Maximum value	Standard deviation	Mean	Minimum value	Maximum value	Standard deviation
0.0	8	3.38	3.0	3.8	0.271	3.52	3.2	3.8	0.238
0.5	8	2.28	1.7	3.2	0.492	2.69	2.1	3.6	0.541
1.0	8	2.08	1.5	2.6	0.430	2.16	1.7	3.0	0.496
2.0	8	2.22	1.7	2.6	0.296	2.01	1.7	2.6	0.327
3.0	8	2.40	2.1	2.8	0.239	2.01	1.7	2.6	0.327
4.0	8	2.46	2.2	2.8	0.213	2.16	1.7	2.6	0.256
5.0	8	2.58	2.1	3.0	0.276	2.21	1.7	2.6	0.259
6.0	8	2.81	2.3	3.4	0.364	2.41	2.1	2.8	0.230
7.0	8	2.76	2.1	3.4	0.400	2.41	2.1	2.8	0.230
8.0	8	2.75	2.3	3.4	0.393	2.64	2.3	2.8	0.169

Note:

H = HOUR

N = number

TABLE 6. COMPARISON OF DIFFERENCES IN PUPIL SIZE (CONTROL MINUS CONTACT)

(Drug volume = 5 μ l)

HOUR	DIFF mean (mm)	t-test DIFF = 0? p-value
0	-.067	.650
.5	-.600	<.001
1	-.233	.130
2	.133	.370
3	.500	.003
4	.200	.190
5	.200	.190
6	.067	.650
7	.133	.370
8	.000	.990

TABLE 7. COMPARISON OF DIFFERENCES IN PUPIL SIZE (NAKED MINUS CONTACT)

(Drug volume = 10 μ l)

HOUR	DIFF mean (mm)	t-test DIFF = 0? p-value
0	-.04	.650
.5	-.28	.003
1	-.02	.820
2	.28	.003
3	.30	.002
4	.36	<.001
5	.30	.002
6	.24	.009
7	.22	.017
8	.28	.003

TABLE 8. COMPARISON OF DIFFERENCES IN PUPIL SIZE (CONTROL MINUS CONTACT)

(Drug volume = 20 μ l)

HOUR	DIFF mean (mm)	t-test DIFF = 0? p-value
0	-.15	.090
.5	-.41	<.001
1	-.09	.320
2	.21	.018
3	.39	<.001
4	.30	.001
5	.36	<.001
6	.40	<.001
7	.35	<.001
8	.11	.200