

Pilocarpine dispensation for the soft hydrophilic contact lens

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The instillation of drops containing pilocarpine for the treatment of glaucoma has certain local disadvantages. If the action of the drug depends upon its concentration in the aqueous, there are likely to be large fluctuations between administrations of the drops. It is even likely that from time to time no pilocarpine will be present. To obviate this, a high concentration of pilocarpine can be used or the length of time between administrations reduced. If the concentration of pilocarpine in the aqueous depended upon a simple flow by diffusion over the cornea, the ideal method of ensuring a constant pilocarpine concentration in the anterior chamber (AC) would be to effect a constant flow of solution on to the cornea. This is made possible by the use of a constant flow capillary tube from a tank, which is to be the subject of a subsequent paper. The alternative is to place in contact with the superficial ocular tissues a dispenser containing a high concentration of pilocarpine in water solution. This is diffused at a relatively constant rate, depending upon the physical and chemical properties of the dispenser and the rate and quantity of tear flow. There are thus likely to be variations between one patient and another depending upon the amount of reflex lacrimal fluid flow and environmental factors, such as temperature and air velocity. The eye tissue may also fix some part of the pilocarpine and thus act as a depot dispenser to the AC. The dispenser when in the eye can only be clinically evaluated, but it is essential to discover how such a contact dispenser will function under standard pharmacological conditions.

Historically long-term dispensing of drugs has been achieved in the eye by combining them with vehicles of low water content, such as fats and waxes. The use of gelatin preceded the present use of polymers.

The use of hydrophilic polymers able to absorb between 40 and 85 per cent weight of water is discussed in this paper. A Czech ophthalmologist

first described the use of hydrophilic lenses to disperse pilocarpine in 1964 (Sedláček, 1965). The most recent reports are those of Hillman (1974), Roger (1975), and Podos, Becker, Asseff, and Hartstein (1972). Hillman (1974) reported rapid control of acute congestive attacks and Roger (1975) of chronic simple glaucoma, the tension falling to very low levels in some instances. The proposed dispenser takes the form of a thin contact lens or membrane usually 13.5 to 15.0 mm in area and between 0.20 and 0.45 mm thick. It is of interest to note that hydrophilic polymer was used as a vehicle for penicillin eye drops as early as 1946 in the form of 'Carbowax' (Ruben and Hanson, 1946).

Laboratory method

Discs of contact lens material were dried in a desiccator to constant weight and then hydrated by soaking for 3 hours in normal saline. They were then transferred to 4 per cent pilocarpine hydrochloride solution and soaked for a further 3 hours. This period was chosen because previous studies had shown that most lenses are close to saturation after this exposure.

The charged discs were removed from the solution, any surface moisture was gently wiped away, and then they were immersed in 5 ml aliquots of distilled water, which was agitated and maintained at 37°C in a water bath. At set intervals, the discs were removed, the surface moisture was dried off and they were immersed again in a fresh 5 ml of distilled water.

The process was continued until it was no longer possible to detect the presence of pilocarpine hydrochloride in the distilled water samples.

Each of the samples was acidified with 1 ml 0.1 N HCl and the amount of drug determined by measurement of the absorbance at 216 nm using a Pye-Unicam SP1800 recording spectrophotometer. The pilocarpine hydrochloride content of each sample was found by reference to a standard curve obtained from known concentrations of the drug in distilled water that had been similarly acidified.

Spectra were recorded in all cases. It was then immediately apparent that the absorbance was due to pilocarpine and not to the presence of some other substance leaching from the lens and absorbing or filtering

light at a similar wavelength. This was found to be the case in some of the later samples obtained from the Sauflon lenses. Here, what appeared to be an antioxidant caused interference that made it difficult to obtain accurate determination of low pilocarpine concentrations. Attempts were made to form pilocarpine complexes from these samples so that determinations could be made at a higher wavelength. This proved impossible with the very small amounts of pilocarpine believed to be present.

Three samples of each of the lens materials were used, and the results averaged. Surprisingly close results were obtained from each sample. The results shown in the Table were calculated to obtain the amount of pilocarpine released from the weight of lens material of each type that would be required to produce a lens of equivalent strength.

Clinical results

Only those patients with glaucoma who were being treated by miotics and who also required contact lenses were selected for the trial. Thus the number included was small, especially as many patients who were offered this treatment were not prepared to wear contact lenses. They were classified into two clinical groups:

- (1) Glaucoma—Narrow and wide angles with myopia and hypermetropia
- (2) Glaucoma—Aphakics
—Aphakics with bullous keratopathy.

In both groups the primary indication for contact lens wear was not the treatment of glaucoma.

The methods of using pilocarpine were:

- Presoaked lens (using 2 or 4 per cent pilocarpine without preservatives)
- Saline soaked lens with administration of 2 per cent pilocarpine, three to four times daily with the lens *in situ*.

The full clinical analysis of several patients will be reported at a later date. But, as examples, the two following typical case histories of chronic simple glaucoma with hypermetropia and myopia will be of interest:

Case 1, a 53-year-old single woman with chronic simple, wide-angle glaucoma.

The visual acuity in both eyes was 6/6 with -4 D sph., -1 D cyl., axis 90° . In July 1971 the intraocular pressure was 26 mm Hg in the right eye and 29 mm Hg in the left, or with the Schiötz applanation tonometer 29 right and 30 left.

In this patient the periods of high tension seen in the course of 20 months (Fig. 1) fall into two parts. First she had 10 months on drops alone and then readings were taken within 2 days of applying hydrophilic contact lens pilocarpine dispensation.

Phasing over 48 hr a few days before contact lens treatment and with drops showed right eye 18 to 24 and left eye 22 to 32 mm Hg. After hydrophilic pilocarpine regime the maximum and minimum over a period of 10 months was right eye 7 to 14, left eye 7 to 15 mm Hg. This sudden drop to hypotension soon after starting treatment was also noted by Roger (1975).

Case 2, a 59-year-old married woman, with chronic simple glaucoma had narrow but open angles.

The visual acuity in each eye was 6/6 pt with $+3$ D sph.,

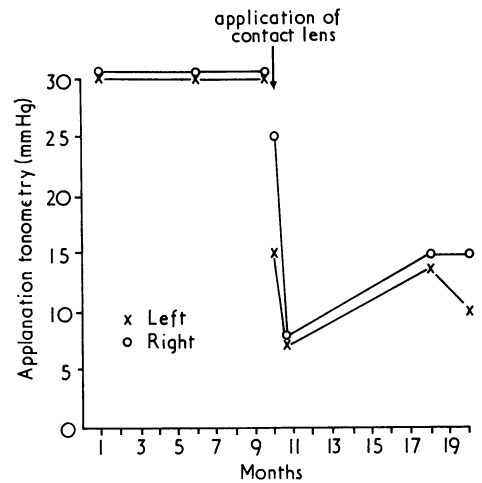


FIG. 1 Intraocular pressure in Case 1 in period of 20 months. Contact lens pilocarpine dispenser applied in 10th month

$+0.5$ D cyl., axis 90° (right) and $+4.5$ D sph., $+0.5$ D cyl., axis 90° (left). The visual fields were full. In January 1972 the ocular tension was 20 mm Hg in each eye, or by Schiötz applanation tonometry 22 mm Hg in the right eye and 25 mm Hg in the left. The facility of aqueous outflow P_o/C was 80 in each eye.

Before hydrophilic pilocarpine dispensation she was treated by pilocarpine 2 per cent four times a day. All tensions averaged 25 mm Hg in each eye over a 6-month period before treatment with lenses.

This patient is of interest because the material used was a high water content plastic with rapid release properties and also because a few periods without contact lens wear showed significant rises in tension on the old drop regime (Fig. 2).

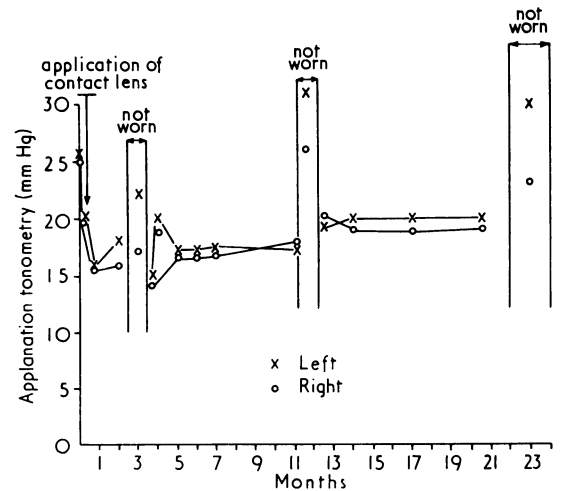


FIG. 2 Intraocular pressure in Case 2 in period of 24 months after application of contact lens pilocarpine dispenser, showing three intervals when lens was not worn

Table Results with three types of lens material

Lens material			A		B		C	
Initial dry weight (g)			0.04		0.0238		0.0137	
Weight when soaked in pilocarpine 4 per cent for 3 hrs (g)			0.626		0.0761		0.0552	
Weight of pilocarpine absorbed (g)			0.0226		0.0523		0.0415	
Theoretical pilocarpine content (mg)			0.904		2.092		1.66	
Pilocarpine release	Soaking time (hrs)	Total (hrs)	μg	per cent	μg	per cent	μg	per cent
	$\frac{1}{2}$	$\frac{1}{2}$	732	61.82	2081	90.47	1666	95.19
	1	1 $\frac{1}{2}$	251	21.20	179	7.78	65.5	3.74
	2	3 $\frac{1}{2}$	130	10.98	28.6	1.24	17	0.99
	4	7 $\frac{1}{2}$	51	4.21	10.2	0.44	1.5	0.03
	8	15 $\frac{1}{2}$	16.6	1.4	2.1	0.09	nil	
	16	31 $\frac{1}{2}$	3.4	0.29	nil		nil	
	32	62 $\frac{1}{2}$	nil		nil		nil	
Total release (mg)			1.184 100		2.30 100		1.75 100	

Conclusions

The three materials tested were different polymers and from the results shown in the Table the percentage 'water' content was (water/water + dry mass \times 100).

- (1) A 36 per cent
- B 68.5 per cent
- C 75 per cent

The manufacturers' figures for these three materials are

- (2) A (PolyHEMA) 42 per cent
- B (Sauflon, CLM) 70 per cent
- C (Sauflon, CLM) 85 per cent

The discrepancy between the manufacturers' advertised percentages and those found by analysis is common for hydrophilic plastics used in contact lens manufacture.

Of significance is the reading taken after 30 min when the PolyHEMA has released 61.82 per cent and the highest water content material (85 per cent) has released 95.19 per cent of the pilocarpine (Fig. 3).

Total release for PolyHEMA is at 16 hours' soaking time or a total of 31 $\frac{1}{2}$ hours' testing time, whilst for 85 per cent Sauflon the figures are 4 and 7 $\frac{1}{2}$ hours, the true amount of pilocarpine released being slightly greater than that calculated theoretically, but in each case of the same order.

It is not practicable to equate the percentage of pilocarpine released *in vivo* and the concentration available in the tears, either pre-lens or pre-corneal, as there are too many variables. For example, the rate of release will depend upon the amount of water lost from the lens by evaporation and temperature. The rate of tear flow or water flow into the lens from

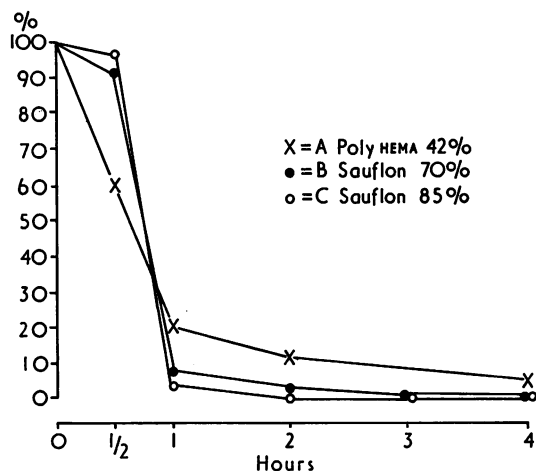


FIG. 3 Pilocarpine release (per cent) from lenses made of three different substances in a period of 4 hrs

the cornea is unknown and will vary not only periodically but for each patient individually.

Therefore a theoretical approximation is necessary. If the surface of the lens is *x* per cent pilocarpine, at any one instant tear film will be half that concentration. This allows that tear film is at a constant flow of zero concentration of pilocarpine and that the diffusion rate is constant. Thus, if a clinically effective concentration of pilocarpine in the AC were to be 1 per cent, the lens concentration should be 2 per cent or higher.

In the examples given, this percentage is obtainable in PolyHEMA material approximately 6 hours after soaking or 12 hours total test time. For the highest water content material it is half this.

What is perhaps of greater clinical significance is

the possibility of maintaining by this technique a tear concentration of pilocarpine in the order of 10 per cent for over 1 hour. Furthermore, the rate of diffusion when the lens is on the eye is likely to be slower, since evaporation of lens water will tend to concentrate the pilocarpine and the surface tears will contain a concentration higher than zero. The process of diffusion for surface films may not obey the same physico-chemical laws as for solutions. One would expect a slower diffusion rate. Therefore the release graphs shown must not be taken out of context. It must be inferred that for most patients with normal tear flow the rate of pilocarpine release will be much slower.

The tonography graphs (Figs 1 and 2) for the two examples of chronic glaucoma would indicate that 2 per cent solution with all-night soaking using PolyHEMA material as in Case 1 was effective. For the other example a 4 per cent solution with a higher water content material (70 per cent) was equally effective.

The use of softer and higher water content materials has problems. These materials deteriorate and break rapidly and cannot be repeatedly boiled with pilocarpine solution, so that several lenses are necessary to maintain treatment (Fig. 2).

It is recommended that patients be given the following management:

(1) *Acute congestive glaucoma*

High water content lenses (70 to 85 per cent), are presoaked for 3 hours or more, or better still, stored in a sterile state (Hillman, 1974); an average back curve of 8.50 and overall size 14.50 and thickness 0.20 is used (power approximately -4.00).

(2) *Chronic glaucoma (a) daily wear*

The contact lenses are sterilized by a pasteurization process, the container emptied and the pilocarpine added for overnight storage.

Pilocarpine solutions used for hydrophilic contact lens dispensation can be one of the following:

Minims pilocarpine (S and N) 2 or 4 per cent. This solution is free of preservatives and therefore has no complications of toxicity or irritation emanating from this source. Furthermore, pilocarpine solution has a pH at about 4.50 which, in itself, is bacteriostatic.

Pilocarpine 2 or 4 per cent with thiomersal 0.002 per cent.

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Pilocarpine 2 per cent with chlorhexidine acetate 0.002 per cent.

Higher concentrations of pilocarpine are not compatible with chlorhexidine. The above solutions avoid the use of benzalkonium chloride and chlorbutinol which at bacteriostatic concentrations could be toxic to epithelium, especially at the soft lens corneal interface where lacrimal tear flow is minimal.

(b) *Constant wear*

Two pairs of lenses should be used and whilst one pair is stored in pilocarpine solution, the other is worn and changed every 12 hours. The material should be either very thin PolyHEMA (0.1 thick) or high water content material—for example, Sauflon, Bionite.

The use of pilocarpine drops placed in the eye of a patient wearing the lenses (according to Becker) does not materially cause a selective and sustained concentration. The method of using higher water content materials may be of value.

The results are encouraging. For intensive miotic therapy the results of Hillman (1974) are significant. For the therapy of chronic glaucoma and secondary glaucoma (for example, aphakic glaucoma), where contact lenses are advised for daily or constant wear, this method of dispensation can be used.

Summary

The use of hydrophilic soft contact lenses for dispensation of pilocarpine is described. The release rate of pilocarpine from three materials of different water content was estimated and from this the surface concentrations were calculated. It is estimated that PolyHEMA can after 15 hours provide a 1 per cent surface concentration of pilocarpine, whereas higher water content materials (70 and 85 per cent) halve this, although they provide a much higher concentration in the first few hours of use. These results are based upon pre-soaking in 4 per cent pilocarpine solution.

Because contact lenses present a management problem, this method of dispensation will be used only for selected cases. Some clinical examples treated successfully over a 20 month period are discussed.

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