A Laboratory Model to Determine the Uptake and Release of Olopatadine by Soft Contact Lenses

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Introduction

Topical ophthalmic solutions can be absorbed by soft contact lenses if the lenses are worn when the drops are instilled. This absorption has been shown to vary depending upon the nature of the lens material and the ingredients of the ophthalmic solution (1). The absorption of active ingredients has been used to enhance and prolong delivery of drugs to the eye (2, 3). In other cases, the absorption was found to be small with no side effects (4).

Olopatadine is a dual action human conjunctival mast cell stabilizer and antihistaminic anti-allergic drug available in a topical drop formulation for ocular use. Patients with contact lenses are instructed to remove their lenses, instill Patanol® (olopatadine hydrochloride 0.1% ophthalmic solution) and replace the lenses 10 minutes later. Recently, it has been shown that removing soft contact lenses for 5 minutes is sufficient to prevent absorption of clinically significant amounts of an active ingredient (5).

Off-label dosing with lenses in place is known to occur frequently. In this study, a simple laboratory model was used to exaggerate the exposure of soft contact lenses to Patanol® and then to measure the uptake and subsequent release of olopatadine after washing with saline solution. Acuvue® (etafilcon A) lenses (Johnson & Johnson) were used as a representative FDA Group 4 lens. This group of lenses is known to have the highest affinity for ingredients in contact lens care products, and can accumulate up to 1000 µg of protein during use (6–8). Because of this, Acuvue® lenses were also collected after 14 days of human wear to repeat the measurements of uptake and release of olopatadine. HPLC was used to determine levels of olopatadine with a detection limit of 0.025 µg. Contact lenses were supported on a glass marble during dosing and rinsing.

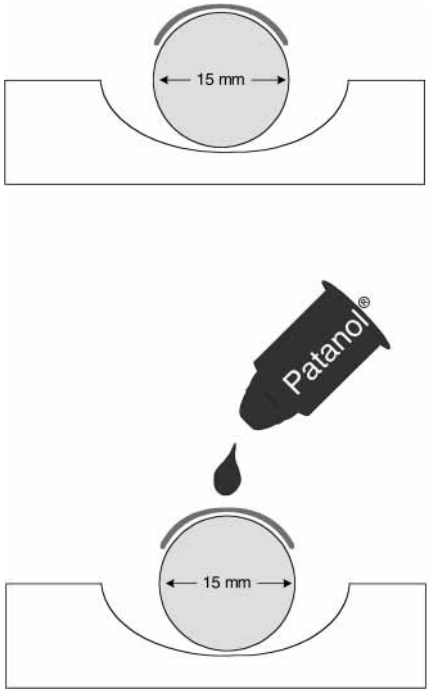

Fig. 1.

Like many ophthalmic drugs, Patanol® is preserved with benzalkonium chloride (BAC) (0.01%). Using the same model, the uptake and release of the preservative also were determined.

Materials and Methods

The soft contact lenses used were Acuvue® (etafilcon A), BC 8.4, DIA 14.0, power –2.00. These are FDA Group 4 lenses manufactured by Johnson & Johnson. Human-worn Acuvue® lenses were

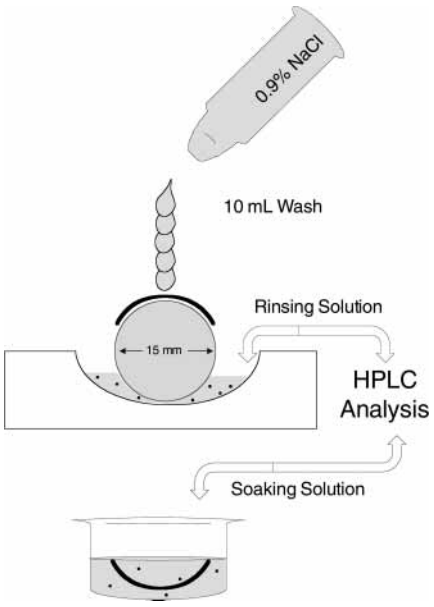

Fig. 2.

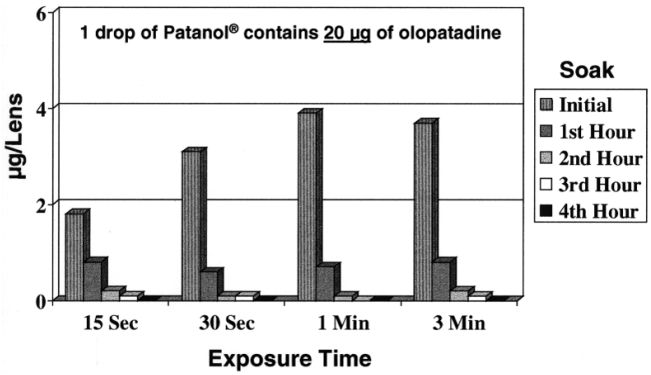

Fig. 3. Uptake of Olopatadine by New Soft Contact Lenses.

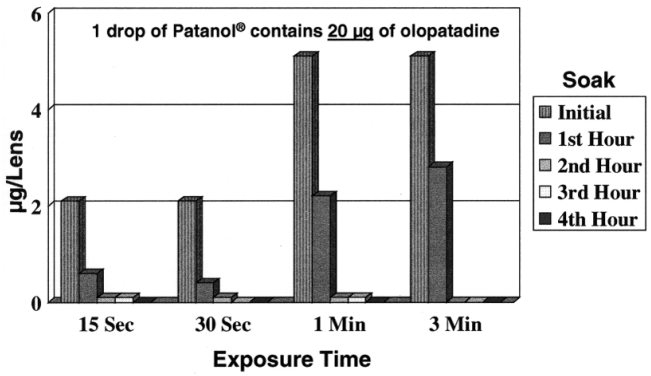

Fig. 4. Uptake of Olopatadine by Human-Worn Lenses.

collected after 14 days wear. Patanol® (olopatadine hydrochloride 0.1% ophthalmic solution) is manufactured by Alcon Laboratories, Inc.

The in vitro model of drug uptake and release was carried out as follows: A glass marble was placed in one side of a flat polypropylene screw-cap contact lens case. An Acuvue® lens was placed on the top of the marble, followed by the application of one drop of Patanol® (Fig. 1). After various times (15 sec, 30 sec, 1 min, and 3 min), the lens was rinsed with phosphate buffered saline solution (10 ml). The lens was then placed in 0.9% sodium chloride solution (2 ml) for one hour. This soaking of the lens was repeated with fresh solutions for a 2nd, 3rd, and 4th hour. Finally, the lens was placed in methanol at 60°C for 1 hour to extract any remaining olopatadine. Each of the rinsing, soaking and extraction solutions was analyzed for olopatadine by HPLC (Fig. 2).

Similarly, the uptake and release of benzalkonium chloride was determined. In this case, after dosing and rinsing, lenses were soaked in 0.9% sodium chloride solution overnight, and any remaining BAC was extracted with trimethylammonium chloride solution.

A Hitachi HPLC system was used with a Waters Spherisorb® S5 CN RP analytical column and acetonitrile/phosphate buffer (45:55) as the eluent. The detection limit was 0.025 µg for both olopatadine and benzalkonium chloride.

Table 1. Uptake of BAC by New Soft Contact Lenses. Micrograms of BAC/lens. 1 drop of Patanol® contains 2 µg of BAC

Exposure Time	Soak Time	New Lens
15 sec	Initial	0.16
15 sec	Overnight	0.15
1 min	Initial	0.58
1 min	Overnight	0.45
3 min	Initial	1.31
3 min	Overnight	1.20

Results

The uptake and release results of olopatadine are shown for new lenses (Fig. 3) and for human-worn lenses (Fig. 4). The number of lenses used for each determination was either 3 or 6, and the standard deviation of the results is approximately ±0.5 µg.

The uptake and release results of benzalkonium chloride are shown in Table 1.

Discussion

Human-worn Acuvue® lenses absorbed 5 µg (25% of available) olopatadine following an exaggerated exposure of 1 or 3 minutes to Patanol®. The amount of olopatadine in the lenses was reduced to less than detectable levels (<0.025 µg) after 3 or 4 one-hour saline soaks. New Acuvue® lenses exhibited similar olopatadine uptake and release, although the uptake appears to be slightly less (4 µg, 20% of available) after the exaggerated 1- and 3-minute exposures. New Acuvue® lenses absorbed 0.16 µg (8% of available) BAC after a 15-sec exposure, and 1.3 µg (65% of available) after an exaggerated exposure of 3 min. The BAC was slightly reduced after soaking in saline solution.

Significance

The results of the exaggerated laboratory model suggest that, if a patient applies Patanol® while wearing a soft contact lens, a portion (up to 5 µg, 25%) of the available olopatadine will be taken up by the lens, and will be washed out within 4 hours of wear. This suggests that under the recommended dosing conditions (every 6–8 hours) contained in the Patanol® labeling, drug accumulation in contact lenses will not occur.

The results also confirm that benzalkonium chloride can be taken up by lenses and that it is removed more slowly than active drug.

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