Pharmacokinetics of Intraocular Drug Delivery by Periocular Injections Using Ocular Fluorophotometry

Deepa Gbate, William Brooks, Bernard E. McCarey, and Henry F. Edelhauser

PURPOSE. To evaluate the pharmacokinetics of the periocular injections: posterior subtenon (PST), retrobulbar (RB), and subconjunctival (SC) injection.

METHODS. Two sodium fluorescein (NaF) concentrations, 2.5 mg in 0.1 ml (NaF1) and 2.5 mg in 0.5 ml (NaF2) were injected into live rabbits by the PST (NaF1 n = 4, NaF2 n = 3), RB (NaF1 n = 10), SC (NaF1 n = 6), and intravenous (IV, NaF1 n = 6) routes and into euthanatized rabbits by the RB (NaF1 n = 8) route. NaF concentrations in the choroid/retina, vitreous, and anterior segment were measured by ocular fluorophotometry. The NaF level in the contralateral choroid/retina was used as a measure of the systemic drug levels.

RESULTS. The maximum NaF concentrations (nanograms per milliliter) in the choroid/retina after PST, RB, SC, and IV were 757 ± 549 at 2 hours, 906 ± 1014 at 1 hour, 320 ± 462 at 2 hours, and 865 ± 363 at 5 to 10 minutes, respectively. The PST had the highest and most prolonged vitreous NaF1 concentration (maximum: 270 ± 226 ng/ml at 3.5 hours). The contralateral peak choroid/retina NaF levels after the RB, SC, and IV injections were 7, 4, and 21 times greater than after the PST injection. The SC injection had the highest anterior segment NaF concentration (5364 ± 2840 ng/ml at 2 hours). PST with NaF2 resulted in intraocular NaF levels higher than with NaF1.

CONCLUSIONS. NaF reaches the choroid/retina by transscleral diffusion from the periocular depot. The orbital and conjunctival vasculature and lymphatics have a larger role in NaF clearance than does the choroid. NaF diffuses into the vitreous from the choroid and the anterior segment; the periocular depot location determines the predominant diffusion pathway. The duration of high NaF levels in the choroid/retina or the anterior segment determines vitreous NaF levels. PST is the best periocular route for vitreous NaF delivery with minimal systemic levels. Increasing the volume of NaF PST depot enhances transscleral drug delivery. (Invest Ophthalmol Vis Sci. 2007;48:2230–2237) DOI:10.1167/iovs.06-0954

The advent of new therapies for posterior segment disorders has led to an increased interest in drug delivery. An ideal drug delivery technique should be minimally invasive and eliminate reliance on patient compliance, with a drug depot that delivers a steady posterior segment drug concentration over extended periods. However, as of now, the posterior segment can be treated by one of three routes: by the intravenous (IV) or oral route, which has low bioavailability and high systemic side effects; by the intravitreal route, which has excellent bioavailability, but is the most invasive with the highest ocular complication rates; or by the periocular route.

Periocular injections can be administered via the posterior subtenon (PST), retrobulbar (RB), subconjunctival (SC), and peribulbar routes. A depot of drug injected periocularly can reach the posterior segment in three ways: transsclerally, hematomagenously, or via the anterior segment. The major barriers to the drug's reaching the vitreous are the ocular barriers consisting of the Tenon's capsule, sclera,1 choroid, pigment epithelium, retina, and clearance by the choroidal vasculature2 and by the orbital and conjunctival vasculature and lymphatics.3,4 Theoretically, the PST injection should be closer to the sclera and farther from the orbital vasculature than should the RB injection. Thus, a greater amount of the drug should reach the vitreous transsclerally after PST injection than after a RB injection, and a RB depot should have higher systemic absorption than a PST depot. This difference is not distinct clinically, and trials have reported equal efficacy for posterior segment inflammation after both PST and RB steroids.5,6

Wijten et al.7–9 found that the SC injection of 2.5 mg of dexamethasone diphosphate resulted in an estimated vitreous dexamethasone concentration (peak at 3 hours) that was three times higher than a 5-mg peribulbar injection (peak at 6–7 hours) and 12 times higher than a 7.5 mg oral dose and that the systemic absorption after both the peribulbar and SC injections were similar to an oral dose. They hypothesized that after a peribulbar and SC injection, the drug reached the vitreous through both the hematogenous and the transscleral route. In addition, in an SC injection, the transcorneal (via leakage through the puncture wound in the conjunctiva into the tear film) route was also important. The same group found that subretinal fluid concentrations of dexamethasone in patients with retinal detachments were higher with SC than peribulbar injections or oral administration.10

Lee et al.11 injected 14C labeled mannitol SC in rabbits and found that the transscleral route was the predominant pathway for drug delivery to the posterior segment with minimal contribution from the recirculation pathway and the transcorneal pathway. Lee and Robinson et al.4 evaluated the vitreous levels of triamcinolone acetonide 3 hours after PST injection in a rabbit model with a conjunctival window, to negate the effect of conjunctival vessels and lymphatics; cryotherapy to negate the effect of choroidal blood flow and euthanasia to eliminate both. Their results suggest that the conjunctival blood vessels/lymphatics are more important as barriers to transscleral drug delivery than the choroid. Studies using serial MRIs and gadolinium (Gd)-DTPA3 or Mn2+ have shown that transscleral transport is increased after euthanasia. Kim et al.5 found Gd-DTPA in lymph nodes after SC injections and suggested that the pars plana, pars plana region is the most permeable region of the sclera and that drugs reach the anterior segment transsclerally rather than transcorneally. They also implied that drugs could travel from the anterior segment through the uveoscleral pathway and diffuse into the posterior segment. Pontes De Carvalho et al.12 used ocular fluorophotometry in rabbits and found that NaF in an episcleral implant that seals it off...
from the conjunctival-orbital vasculature delivered more drug to the posterior segment that NaF injected periocularly in a viscous solvent. They concluded that leakage from the injection site into the tear film is an important route for drug delivery from a periocular depot to the posterior segment. Thus, a review of the current literature shows that the pharmacokinetics of periocular injections have not been precisely elucidated.

Traditional methods of evaluating ocular pharmacokinetics are invasive and involve either one-time sampling of the aqueous/vitreous in humans during surgery7–10 or killing animals at various time points,1 followed by enucleation, dissection, and isolation of the vitreous. Ocular fluorophotometry is a noninvasive technique that does not require anesthesia; does not disturb ocular structures; and determines the concentration of fluorescein in the conjunctival, aqueous, vitreous, and retina on a real-time basis at different time points. In albino rabbits, the technique also allows measurement of fluorescein in the contralateral choroidal circulation as an excellent real-time measure of the concentration in the systemic circulation.11

The purpose of this study was to evaluate intraocular and systemic pharmacokinetics after PST, RB, SC, and IV injections of sodium fluorescein (NaF). The effect of depot volume in the PST was studied as was the effect of blood circulation on drug clearance in a euthanasia model.

NaF was used for the pharmacokinetics study, because it is a small molecule (376 Da) that has been used traditionally to evaluate the integrity of the blood-retinal and blood-aqueous barriers. It clears rapidly, and peak fluorescence in all ocular tissues is reached within the first 5 hours.

MATERIALS AND METHODS

The experiments were performed in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Visual Research. New Zealand White rabbits, 3 to 4 kg in weight, were used in all the experiments. The rabbits were anesthetized with 6 mg/kg xylazine and 15 mg/kg ketamine intramuscularly before the periocular injections. No topical anesthesia was used before the periocular injections.

Sodium fluorescein (NaF; Fluorescite, 10% injectable; Alcon Laboratories, Fort Worth, TX) was prepared in two concentrations: 2.5 mg NaF in 0.1 mL solution (NaF1) and the same weight of drug, 2.5 mg, in 0.5 mL solution (NaF2). The study design was to vary the periocular depot volume of the drug delivery while keeping the weight of the NaF constant. The diluent was balanced salt solution (BSS; Alcon Laboratories).

Ten anesthetized rabbits received NaF1 as a RB injection. A tuberculin syringe was used with a 25-gauge, 1-in. needle. The needle was inserted into the inferotemporal aspect of the lid, toward the orbital apex. After the needle entered the muscle cone, the plunger of the syringe was withdrawn to check for blood reflux into the hub of the needle, and the solution was then injected in the muscle cone into the RB space. Eight rabbits were euthanatized with intracardiac pentobarbital (100 mg/kg). Immediately after death, they received a RB injection of NaF1. Six rabbits received NaF1 solution as a SC injection. A tuberculin syringe was used with a 26-gauge, 0.5-in. needle. The needle was inserted subconjunctivally in the superior temporal quadrant 2 to 3 mm away from the limbus, and ballooning of the conjunctiva was observed. The injection site was compressed by using a cotton swab before the needle was removed. Six rabbits were injected with NaF1 solution intravenously using the marginal ear vein.

Seven rabbits were injected with NaF in the PST space. A tuberculin syringe was used with a 30-gauge, ½-in. needle. Four rabbits were injected with NaF1 and three rabbits were injected with NaF2. The solution was injected in the superior temporal quadrant. The rabbit eye was rolled down, and the needle was advanced along the sclera beyond the equator. There was a localized ballooning of the Tenon’s space 5 to 6 mm away from the limbus. The injection site was compressed by using a cotton swab after the injection. A fluorophotometer reading was taken within 5 to 10 minutes of the injection to detect any leakage of the solution from the bleb.

A total of 29 animals were used in the study. None of the eyes received more than 1 ocular injection. If the same animal was used for two experiments, the injection was given in the other eye. There was a gap of at least 1 week between experiments, and the baseline fluorescence was always measured in both eyes. The PST injections were given by the same ophthalmologist (DG), and the other injections were given by two of the authors (DG, BM).

An external ocular examination, slit lamp examination, and fundus examination was performed before and immediately after the injection, to evaluate any inflammation or drug reaction.

Fluorophotometry. Baseline fluorescence in the anterior segment, vitreous, and the choroid-retina was measured in all rabbits in both eyes (Fluorotron Master fluorophotometer; OcuMetrics, Mountain View, CA) with the standard objective lens. Ocular fluorescence was measured in the anterior segment, vitreous, and choroid-retina in both eyes immediately after the injection (5 minutes): 30 minutes, 1 hour, and 2, 3.5, and 5 hours afterward; and then daily until the fluorescence reached baseline fluorescence levels (usually 1–2 days). After the initial anesthesia for the periocular injections, all the measurements were taken in nonanesthetized animals. Three fluorophotometric scans of both eyes were taken at each time point. The individual results of the three scans per time point were used to determine the mean.

The fluorescein concentrations in various ocular tissues (choroid/retina, vitreous, lens, anterior chamber, cornea, and tear film) were obtained at data points that were 0.25 mm apart along an optical axis by the fluorophotometer. The fluorophotometer has an internal standard and gives absolute fluorescein concentrations at each data point. It provides linear fluorescence concentration values between 0 and 2000 ng/mL. Beyond 2000 ng/mL, the values are nonlinear due to quenching. For concentrations beyond 2000 ng/mL, the numbers are not representative of the actual fluorescence values. All that can be deduced is that the NaF concentrations are very high in that particular reading.

The standard objective lens was used in the experiments to measure the fluorescein concentrations from the cornea to the choroid/retina. Figure 1 represents the fluorescence level in the ocular tissues along a central axis from the cornea to the retina, as measured by the fluorophotometer and illustrates our measurement technique. The raw data from the fluorophotometer was transferred to a spreadsheet (Excel; Microsoft Corp., Redmond, WA) and graphed. Figure 1A is an example of natural tissue fluorescence. The choroid/retina fluorescence peak and the anterior segment peak are easily observed on the graphs. The midvitreous fluorescence levels were defined as the maximum fluorescence between 20 to 36 data points anterior to the choroid/retina peak. Figure 1B demonstrates the tissue fluorescence 2 hours after a PST injection of NaF1. The choroid/retina fluorescence value in the test eye has increased to 1278 ng/mL; the values at the midvitreous and anterior segment have increased to 704 and 469 ng/mL, respectively. In the contralateral eye (Fig. 1C), the choroid/retina concentration is 32 ng/mL and represents systemic NaF levels.

RESULTS

Table 1 is a summary of the compiled results (mean ± SD) of all the experiments. The maximum fluorescence values (ng/mL) of the anterior segment, midvitreous and retina/choroid were analyzed (the mean peak values are shown in bold). This data is also plotted in Figures 2 to 5.

Figure 2 is a plot of the mean NaF concentration levels in intraocular tissues after periocular injection of NaF1. The maximum fluorescein concentration (nanogram per milliliter) in the choroid/retina after the PST injection was 757 ± 549 (at 2 hours); after the RB was 906 ± 1104 (at 1 hour), after the SC was 320 ± 462 (at 2 hours) and after the IV was 865 ± 363 (at 5–10 minutes). The duration of high NaF levels (>400 ng/mL)
in the choroid/retina was >4 hours with the PST, between 2 and 3 hours with the RB, zero minutes with the SC and <30 minutes with the IV injections (Fig. 2).

The vitreous levels with the RB, SC, and the PST peaked at 3.5 hours. The maximum vitreous NaF concentration after NaF1 was reached with the PST (270 ± 226 ng/mL). The peak vitreous NaF concentration after the SC was 207 ± 233 ng/mL, RB was 154 ± 435 ng/mL and IV was 17 ± 11 ng/mL.

The anterior segment NaF concentration after the SC was the highest at 5364 ± 2840 ng/mL. The SC injection was also the only injection wherein the vitreous NaF levels exceed the choroid/retina NaF levels at the 4 to 7-hour time points.

Figure 3 is a plot of the peak NaF concentrations of the choroid/retina in the test and contralateral eye. The peak fluorescein levels in the choroid/retina (ng/mL) of the contralateral control eye with the RB (279 ± 242), SC (170 ± 285), and IV (865 ± 363) injections were 7, 4, and 21 times greater than that of the PST (41 ± 10) injection. The choroid/retina value for the IV injection is specified in Figure 2.

Figure 4 is a plot of the NaF concentration after RB injection in the live and euthanatized animal. After RB injection in the euthanatized rabbit, the peak NaF concentration in the choroid/retina was 1.8 times higher than in the in vivo experiment and the peak NaF concentration in the vitreous was 13.2 times
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<td>14.6 ± 9.3</td>
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Data are the mean concentration of fluorescein (ng/mL) ± SD. Peak levels are in bold. Beyond a concentration of 2000 ng/mL, fluorophotometer measurements were nonlinear, due to quenching.
The NaF level in the choroid/retina increases after 30 minutes and continues to rise in a linear fashion up to 3.5 hours. The NaF levels in the vitreous and the anterior segment also increase at 30 minutes and continue to rise for 5 hours after the injection.

Figure 5 is a graph of the NaF levels after PST with NaF1 (2.5 mg NaF in 0.1 mL) and NaF2 (2.5 mg NaF/0.5 mL). Maximum NaF levels with NaF1 and NaF2 were respectively 757 ± 549 and 1414 ± 336 ng/mL in the choroid/retina; 270 ± 226 and 350 ± 269 ng/mL in the vitreous; 199 ± 255 and 474 ± 169 ng/mL in the anterior segment. The peak NaF levels with NaF2 compared to NaF1 were two times greater in the choroid/retina and anterior segment; 1.3 times greater in the vitreous and equal in the retina of the contralateral control eye. The PST injection with NaF2 was also the only experiment in which NaF levels were higher than 400 ng/mL for >24 hours.

**DISCUSSION**

**Movement of the Drug from the Periocular Depot to the Choroid/Retina**

NaF can reach the choroid of the test eye from the periocular depot either by direct diffusion across the sclera or by systemic absorption and subsequent hematogenous dissemination and recirculation back into the eye. Previous studies had reported conflicting results on the main drug delivery route after periocular injections. In the present study, we used the NaF levels in the contralateral choroid/retina as a marker for systemic levels and the recirculation pathway.

The NaF levels in the choroid/retina in the test eye and the contralateral eye paralleled each other for the first half hour (Fig. 3). There appears to be an initial bolus of NaF released into the systemic circulation from the depot since NaF appears in the choroidal circulation of both eyes simultaneously. The NaF in the systemic circulation then decreases and the concentration in the test eye choroid/retina increases and reaches its peak 1 to 2 hours after injection.

If the systemic recirculation route was the predominant route of drug delivery after a periocular injection, the vasculature should supply the NaF to the choroid of both the eyes simultaneously and in equal concentration. The large difference in peak concentration values between the eyes in the current experiments supports a local diffusion process rather than systemic absorption and recirculation. The time delay between the choroid/retina peaks of the NaF concentration in the two eyes also indicates that transscleral diffusion (which causes the peak in the test eye) is the major route of drug delivery to the choroid/retina after periocular injections compared to the hematogenous route (which causes the peak in the contralateral eye).

**Clearance of the Periocular Depot**

A NaF depot injected periocularly can be cleared by either the conjunctival, orbital vessels and lymphatics or by the choroidal vasculature. Once the NaF is cleared from the test eye, it passes into the systemic circulation and can be measured in the choroidal circulation of the contralateral eye. Thus, the time and duration of the NaF peaks in the choroid of the contralateral eye are a good measure of NaF clearance from the periocular depot.

The peak NaF level in the contralateral eye was reached in all cases within the first hour. The concentrations then decreased, and none of the experiments had contralateral NaF levels over 10 ng/mL at 5 hours.

The choroid has been traditionally thought to have an important role in drug elimination. If the choroidal vasculature had the dominant role in clearance of the NaF depot, the...
NaF peak in the contralateral choroid/retina (point of maximum NaF clearance) should coincide or follow the choroid/retina NaF peak in the test eye. The data from the present study show that the NaF levels in the test eye choroid/retina were maximum at 1 to 2 hours after the peak NaF in the contralateral choroid/retina (Fig. 3) and the NaF values in the contralateral choroid/retina were decreasing when the choroid NaF levels of the test eye were the maximum. Thus, most of the NaF depot clearance had already taken place (by the conjunctival and orbital vessels/lymphatics) before the NaF reached the choroid of the test eye.

This explanation is further confirmed by the peak systemic NaF levels with the RB, SC, and IV injections being 7, 4, and 21 times greater than that of the PST injection (Table 1) which is more secluded from the orbital and conjunctival vessels/lymphatics than the RB or SC injections but has the same exposure to the choroidal vasculature. The corollary is that the PST injection will have the least systemic side effects. Our results concur with the findings of Robinson et al.4 who reported that a conjunctival window increased drug delivery to the vitreous whereas cryotherapy did not. Pontes de Carvalho et al.12 also found that an episcleral exoplat that prevents any drug–orbital vasculature contact results in higher posterior segment drug levels.

Movement of Drug into the Vitreous

Once the NaF has diffused to the choroid, it has to cross the blood–retinal barrier to the vitreous. The NaF levels in the midvitreous peaked at 3.5 hours in all the experiments (except the IV and euthanasia group), 1 to 2 hours after the choroid/retina peaks (Fig. 2). Previous human studies have shown that dexamethasone levels in the subretinal fluid peaked earlier and higher than did the vitreous levels (peak at 3 hours) after peribulbar injection.7,10

The choroid/retina peak in the IV group was 865 ± 363 ng/mL which is comparable to the 757 ± 549 ng/mL peak with PST and 906 ± 1014 ng/mL with RB (Fig. 2). However, the NaF in the choroid/retina stayed elevated over 400 ng/mL for <30 minutes in the IV, 4 hours in the PST and 2 to 3 hours in the RB (Fig. 2). The vitreous peak NaF concentration was proportional to the duration of high NaF levels in the choroid/retina. PST had the highest peak vitreous NaF levels (270 ± 226 ng/mL) followed by the RB (154 ± 435 ng/mL) and IV (17 ± 11 ng/mL).

The exception was SC that had comparable peak vitreous NaF levels (207 ± 233 ng/mL), even though the choroid/retina NaF levels were never higher than 400 ng/mL. The SC had extremely high anterior segment NaF levels (greater than 2000 ng/mL) for the duration of the experiment.

The ciliary body is considered to be the zone of least resistance to transscleral drug delivery.2 The pars plana–pars plicata region should allow transscleral diffusion into both the aqueous and vitreous either simultaneously or first into the aqueous followed by diffusion to the vitreous. This appears to be the case with the SC injection, which was anatomically closest to the ciliary body. The anterior segment values with the SC injection were above 5000 ng/mL (Fig. 2) and the vitreous NaF levels reached a maximum 1.5 hours after the anterior segment and the choroid/retina peaks. SC is also the only injection in which the vitreous NaF concentration was higher than the choroid/retina indicating that the most of the NaF in the vitreous diffused from the anterior segment.

The RB injection (live and euthanatized animal) had vitreous peaks before the aqueous humor peaks (Fig. 2). The PST injection had simultaneous choroid/retina and aqueous humor peaks followed by the vitreous peak 1.5 hours later, and the NaF levels in the vitreous were higher than those in the aqueous. The NaF appears to reach the vitreous predominantly from the choroid/retina in the RB and the PST injection. Diffusion
from the anterior segment to the vitreous may also occur but not to the same extent as the SC injection.

Euthanasia, as a model to study ocular drug delivery and the effects of local diffusion versus hematogenous dissemination by eliminating both hematogenous and lymphatic clearance, has been evaluated before. In this study, the elimination of ocular and orbital blood flow resulted in NaF concentrations that were 1.8 times higher in the choroid/retina, 13.2 times greater in the vitreous and 6.8 times higher in the anterior segment after RB injection than in the in vivo study (Fig. 4). The levels in the choroid/retina increased linearly after half an hour. It takes approximately 30 minutes for the NaF to diffuse into the choroid across the sclera from the periocular depot site. In the live rabbits, the NaF in the choroid/retina parallels the concentration in the contralateral choroid/retina for 30 minutes and then increases above the contralateral eye (Fig. 3). The NaF reaches the choroid/retina by the recirculation pathway in the first 30 minutes.

Effect of Depot Volume with the PST Injection

A larger weight depot periocularly is known to lead to higher intraocular drug levels. We studied the effect of the depot volume on NaF delivery to the intraocular structures. The same amount of drug (2.5 mg NaF) was injected PST in either 0.1 mL (NaF1) or 0.5 mL (NaF2) solution. The NaF concentration graphs paralleled each other (Fig. 5) and the NaF in all ocular tissues was higher with the larger volume depot. The larger volume depot was also the only experiment group with NaF levels above baseline after 24 hours. The PST, because of its location, is more isolated from the orbital vessels and lymphatics than the other periocular injections. Therefore, slower clearance occurs with a larger volume of NaF depot and transscleral drug delivery occurs more readily.

The high standard deviations (SD) in the present study were a cause of concern. After reviewing the literature, we found that this pattern was repeated in all studies dealing with drug delivery to the posterior segment (SD often larger than the absolute concentration values in ocular tissues in animal models and humans), perhaps because of the difficulty of positioning the injections in the same location each time, even though the PST injections were given by the same ophthalmologist (DG). Freeman et al. showed with echography that after a PST injection, the corticosteroid was deposited over the macula in only 11 of 24 cases. The proximity to blood vessels and lymphatics can vary with the positioning of the injection, as could the proximity to the pars plana/pars plicata region, which has been reported to have the minimum resistance to transscleral drug delivery to the posterior and anterior segment. This may explain variable clinical responses to periocular depot injections. The data also support the benefits of a delivery device like fibrin sealant, collagen, or an implant, to keep the drug localized and adjacent to the sclera.

The rabbit model is commonly used in ocular pharmacokinetics. The rabbit scleral thickness is 0.25 mm compared with the human scleral thickness 0.39 ± 0.17 mm at the equator. The rabbit has a vitreous volume of 1.5 to 2.5 mL compared with the vitreous volume of 4 mL in humans. The rabbit has similar scleral permeability to several compounds. It also has a communicating blood vessel between the orbits, which may result in higher contralateral eye NaF levels than in humans. Based on the data in this study, even after assuming higher systemic absorption in the rabbit, we find that our conclusions on the pharmacokinetics of different periocular injections and the comparisons between them allow reasonable extrapolation to humans.

To summarize, NaF diffuses to the choroid/retina by transscleral diffusion rather than by the systemic absorption of the
depot and subsequent recirculation. The data in the present study also show that the orbital and conjunctival vasculature and lymphatics have a larger role in ocular clearance of NaF than does the choroidal vasculature. NaF can diffuse to the vitreous from both the choroid after crossing the blood-retinal barrier and from the anterior segment. The position of the periocular injection determines which route is predominant, and the duration of high NaF levels in the choroid/retina or the aqueous humor determines the vitreous drug concentration. A larger volume of NaF depot injected into the PST space decreases aqueous humor determines the vitreous drug concentration. A aqueous and enhances transscleral drug delivery. The results of this study illustrate the diffusion characteristics of a small-molecular-weight compound (NaF) when injected periocularly. The dynamic barriers to transscleral drug delivery can be better studied in these in vivo experiments than with in vitro studies with isolated scleral tissue. If a drug is formulated with a sustained-delivery vehicle, large vitreous concentrations could be obtained over long periods. Such is the case with carboplatin in a fibrin sealant. The study also demonstrates that the PST route of drug delivery has the highest vitreous concentrations with the lowest systemic drug levels. Transscleral drug delivery would of course be limited by molecular weight, radius, the drug’s logP (partition coefficient), and charge. Nevertheless, the perilobital injection, particularly the PST injection, is an excellent route of drug delivery to the posterior segment of the eye.

References