The Role of Prostaglandins E2 and F2α in Ultraviolet Radiation-Induced Cortical Cataracts In Vivo

Usha P. Andley,*† Carol Fritz,* Aubrey R. Morrison,‡ and Bernard Becker*

Purpose. Previous work has shown that exposure of lens epithelial cells or rabbit eyes in vivo to ultraviolet B (UVB) radiation enhanced prostaglandin (PG)E2 synthesis. Such enhanced PGE2 synthesis was related to the increased DNA synthesis that followed UVB exposure. The current study examined the relationship between enhanced prostaglandin synthesis and UVB-induced cataract formation.

Methods. Seventy albino (New Zealand white) rabbit eyes were exposed to UVB radiation in vivo. Fluence of radiation at the cornea was 2.8 J/cm², 5.6 J/cm², or 11.2 J/cm². Eyes were examined 24 hours after UVB exposure and for as long as 10 days by slit lamp biomicroscopy. Mass spectrometry was used to measure PGE2, PGF2α, and 6-keto-PGF1α content of the lens and iris-ciliary body using authentic standards. To determine the effect of inhibition of prostaglandin synthesis on UVB-induced cataract formation, animals were given indomethacin intraperitoneally. Other pharmacologic agents, such as PGE2, PGF2α, and misoprostol, were applied topically to the eye. The effect of UVB on K⁺ pump was determined by incubating isolated lenses with [³⁸Rb⁺].

Results. Twenty-four hours after UVB exposure, PGE2 and PGF2α concentrations in aqueous humor were increased by 100- and 30-fold, respectively. Lens PGE2 and PGF2α increased by 6- and 4-fold, respectively, after UVB radiation exposure. Pretreatment of animals with indomethacin prevented the rise in lens and aqueous humor PGE2 and PGF2α levels. Furthermore, indomethacin was partially protective against UVB cataract formation and lowered cataract severity from stage 3 to stage 1, but it did not prevent UVB-induced lens changes completely. Topical application of PGE2 before UVB exposure completely prevented cataract formation in the UVB-exposed eye. In contrast, topical administration of PGF2α increased cataract severity. UVB-induced cataract formation preceded changes in [³⁸Rb⁺] uptake in lenses subsequently incubated in K⁺-free Tyrode's.

Conclusions. Enhanced synthesis of cyclooxygenase products of arachidonic acid metabolism in the lens is associated with UVB-induced cataract formation in albino rabbit eyes, and inhibition of cyclooxygenase by indomethacin decreased the severity of cataracts. PGE2, the principal arachidonic acid metabolite, appears to have a protective role because pretreatment of the eye with topical PGE2 completely prevented UVB-induced cataract formation, whereas PGF2α increased the severity of the cataract. The evidence presented for a role of PGF2α in the development of cataract suggests that caution be exercised in the use of PGF2α derivatives in the therapy of glaucoma. Invest Ophthalmol Vis Sci. 1996;37:1539-1548.

Exposure of the eye to ultraviolet B (UVB; 290 to 320 nm) radiation induces cortical cataract formation in acute and chronic models of UVB exposure.¹⁻⁵ Pitts’ work has defined the distinct stages of UVB-induced lens opacities in the rabbit eye and quantitated the response at wavelengths between 295 and 335 nm.¹ The earliest changes in the lens after UVB exposure include the appearance of small granules across the anterior epithelium, with subsequent formation of discrete white dots that coalesce into a larger, uneven permanent opacity. The mechanisms proposed by which UVB radiation induces lens opacity include protein cross-linking and aggregation, DNA damage and epithelial cell death, increased intracellular levels of Ca²⁺, and alteration of function of enzymes such as Na⁺/K⁺-ATPase.³⁻⁵ Because epidemi-
logic studies support the role of chronic UVB radiation exposure in human cortical cataracts, a better understanding of the mechanisms by which UVB induces cataractogenesis is of great interest. Recent evidence suggests that UVB radiation may alter normal membrane lipid function, including regulatory functions such as signal transduction, regulation of cell division, differentiation, and growth.

All experiments were performed in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

**Materials and Methods**

All experiments were performed in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

**Animals**

Eighty New Zealand White albino rabbits (each weighing 2 to 2.5 kg) were used in this study. Animals were obtained from Doe Valley Farms (Bentonville, AR).

**Chemicals**

PGE$_2$, PGF$_{2\alpha}$, indomethacin, 8-bromocyclic adenosine monophosphate (cAMP), dibutyryl cAMP, N-nitro-L-arginine methyl ester (L-NAME), and forskolin were purchased from Sigma Chemical (St. Louis, MO). Misoprostol was purchased from Searle (St. Louis, MO). RbCl was obtained from Amersham (Arlington Heights, IL). All other chemicals were obtained from Sigma.

**Ultraviolet Exposure**

Animals were confined in an adjustable rabbit retaining cage (Fisher Scientific, Pittsburgh, PA), which protects most of the animal except its head. Right eyes of animals were exposed to UV radiation from a bank of FS20 lamps at a distance of 20 cm. The left eye was patched. This UV source has a maximal output in the UVB region at 310 nm but also emits UVA and a small amount of UVC. UVA fluences are ineffective in producing cataracts, and UVC radiation does not reach the lens because it is absorbed completely by the cornea. Experiments in which a UVC filter was used (Corning 0–53, 2 mm thick) gave identical results to those without the filter. Total exposure was varied by changing time of irradiation from 1 hour to 4 hours, unless indicated otherwise. The irradiance as measured with an International Light radiometer calibrated at the emission maximum of the source (310 nm) was 0.78 mW/cm$^2$. Eyes were irradiated for 1 hour to produce a total fluence of 2.8 J/cm$^2$. In some experiments, effects of pharmacologic agents also were tested at higher doses (5.6 or 11.2 J/cm$^2$), by increasing the time of irradiation to 2 or 4 hours, respectively. Eyes were examined 24 hours after UV exposure and scored for corneal, conjunctival, and lens changes using slit lamp biomicroscopy using a Marco slit lamp (Jacksonville, FL). Eyes were photographed using a Nikon (Tokyo, Japan) AS-15 camera. All experiments were double blind.

Aqueous humor was collected 24 hours after UV exposure under topical anesthesia using Alcaine (Proparacaine hydrochloride; Alcon, Fort Worth, TX) at 0.5% concentration and assayed for PGE$_2$ and PGF$_{2\alpha}$ as described below.

**Cataract Severity in Ultraviolet B-Exposed Lenses In Vivo**

Ultraviolet B cataract development was scored by slit lamp biomicroscopy according to a modified version of the Pitts method$^1$:

Stage 0 = clear lens.
Role of Prostaglandins in UV-Induced Cataract Formation

Stage 1 = loss of normal appearance of anterior lens capsule, small granules across the anterior subcapsular epithelium, prominence of Y-suture line. Changes disappear within 24 hours.

Stage 2 = many small, discrete, white dots in the anterior epithelium. The changes are not restricted to the area irradiated through the iris. A small amount of darkening caused by opacity seen in retroillumination reduced red reflex compared to that in stage 1.

Stage 3 = white opacities coalesced into larger, uneven opacity. Frequently, a band of opacity across the middle of the lens is observed. Approximately three fourths of the lens is affected. There is further reduction of red reflex but no further change up to 10 days after irradiation.

Stage 4 = most of the lens anterior lens is opaque. A large amount of opacity is observed across the lens, and there is poor red reflex. No further change up to 10 days after irradiation.

Ultraviolet B-Induced Changes in Cornea and Conjunctiva

Corneal changes induced by UVB radiation were scored between stage 0 (clear cornea) and stage 4 (completely opaque) by slit lamp biomicroscopy. Conjunctival changes were scored between stage 0 (no hyperemia) and stage 4 (extensive inflammation and reddening of conjunctiva).

Pharmacologic Agents

The effect of inhibition of PGE₂ and PGF₂α synthesis by indomethacin on PGE₂ and PGF₂α levels and clinical changes in the lens in vivo was investigated by treatment of animals with indomethacin. Animals were given indomethacin (50 mg/kg) intraperitoneally three times in a 24-hour period. Indomethacin treatment was started immediately before or after irradiation. The effect on cataract formation was identical under the two conditions.

N-nitro-L-arginine methyl ester (L-NAME, 10 mg/kg) was given intraperitoneally before UV exposure. Forskolin (50 μl of 1% solution), dibutyryl cAMP, 8-bromo-cAMP (50 μl of 4% solution), and misoprostol (5 μg) were applied topically to the eye 30 minutes before UV exposure to indomethacin-treated animals. Treatment with the drug was repeated 5 and 24 hours after exposure. Animals untreated with indomethacin were treated with misoprostol (5 μg), PGE₂ (10 μg), and PGF₂α (10 μg). Prostaglandins were applied topically to the eye 30 minutes before and immediately after UVB exposure. Treatment with prostaglandins was repeated 5 and 24 hours after UVB exposure. Prostaglandins (1 mg) initially were dissolved in 0.1 ml ethanol and 0.9 ml deionized water. Ten microliters of this solution was applied to the eye. The contralateral eye was given 10 μl of the vehicle.

Prostaglandin Assays

PGE₂ was assayed routinely by radioimmunoassay using specific antisera as described. The limit of

FIGURE 1. The effect of indomethacin on slit lamp images of rabbit lenses in albino rabbits. Animals were untreated or given indomethacin (50 mg/kg), exposed to ultraviolet B radiation for 1 hour (2.8 J/cm²), and examined 24 hours after irradiation. Magnification, ×24. (top) Unirradiated eye of the rabbit. (middle) Irradiated eye shows lens changes, including clefts, vacuoles, and opacity covering the entire lens. (bottom) Irradiated lens in animal treated with indomethacin, as described in Materials and Methods. The unirradiated eye of the indomethacin-treated animal was the same as in the control and showed no changes in the lens (not shown).
detection of PGE₂ by RIA is 2 pg. PGF₂α was assayed by enzyme-linked immunosorbent assay using a kit from Cayman Chemicals (Ann Arbor, MI). The limit of detection of PGF₂α by the kit is 2 pg. Aqueous humor and conditioned medium of lenses were assayed routinely using these assays.

Mass spectroscopy was used to determine product identity and product profile with and without indomethacin. Deuterated PGE₂, PGF₂α, and 6-ketoPGF₁α were added as internal standards, and proteins were removed using 50% methanol. The extracts were diluted to 10% methanol with Tris acetate, pH 4, applied to Baker octadecylsilane C₁₈ columns and were washed with water. The lipids were eluted with methyl formate, dried under N₂, and derivatized with 25 μL of 3% methoxamine hydrochloride in pyridine. After reapplying to C₁₈ columns, the pentafluorobenzyl derivatives were prepared by adding pentafluorobenzyl bromide and then derivatized to the trimethylsilyl ether. The pentafluorobenzyl ether, methoxamine trimethylsilyl ether, of the prostaglandin was measured by negative ion chemical ionization detection using a Nermag 1010H mass spectrometer surfaced with a Delsi gas chromatograph. The reagent gas was methane, and the carrier gas was helium. The column used was a 25-m Ultra-1 cross-linked OV-1 capillary column (Hewlett-Packard, Dallas, TX). The injection temperature and interface was 280°C. The oven was programmed from 150°C to 270°C at 25°C per minute. Data were collected on a Spectral 30 software (Delsi). (D₄) Prostaglandin standards were added at a concentration of 10 ng. (D₀) and (D₄)PGE₂ were monitored at m/z 524 and 528, respectively; (D₀) and (D₄)PGF₂α were monitored at m/z 569 and 573, respectively; (D₀) and (D₄)6-keto-PGF₁α were monitored at m/z 614 and 618, respectively.

At an optimal time after UVB exposure, eyes were enucleated, and lenses were dissected and incubated in K⁺-free Tyrode's solution containing 0.1 μCi ⁸⁶RbCl per milliliter, as described by Becker. Lenses were placed in vials in a 37°C water bath shaker, and aliquots were withdrawn at 1 hour to 6 hours. The amount of ⁸⁶Rb⁺-uptake by the lens was determined and expressed as a ratio of tissue-medium counts. Tissue-medium ratios were compared for irradiated and contralateral control eyes.

Data Analysis
Data were expressed as mean ± standard error. Data were analyzed by the Sigma plot program using the Student's t-test.

RESULTS
Ultraviolet B Radiation and Cataract Formation
Figure 1B shows the effect of UV radiation on the lens of an albino rabbit eye exposed in vivo to 2.8 J/cm² UV radiation 24 hours after irradiation. Slit lamp microscopy of the eyes showed stage 3 cortical cataracts (Fig. 1B). Approximately three fourths of the lens was affected, and the opacity was not limited to the area irradiated through the pupil. Contralateral eyes of the animals were used as internal controls. The lens of the contralateral eye remained unchanged (Fig. 1A). Clinical changes were followed for as long as 10 days for a group of six animals. Corneal and conjunctival-lid changes were prominent in the first 2 days after UV radiation, but both returned to a more normal appearance thereafter. The lens opacities, however, were unaltered during the 10-day observation period (Fig. 2).

Effect of Indomethacin on Ultraviolet B Radiation Cataract Stage and Prostaglandin Synthesis
Clinical changes in the lens, as examined by slit lamp microscopy, were reduced to stage 1 by indomethacin treatment but were not inhibited completely (Fig. 1C). The effect of indomethacin was the same whether it was given before or immediately after UVB treatment. Doubling the dose of indomethacin did not have an additional effect. Figure 3 shows the effect of indomethacin pretreatment on the lens for six different animals in each group. Cornea and conjunctiva-lid changes were prominent in the first 2 days after UV radiation, but both returned to a more normal appearance thereafter. The lens opacities, however, were unaltered during the 10-day observation period.
acrin treatment, as indicated by reduced corneal opacity and decreased conjunctival hyperemia.

PGE\textsubscript{2}, and PGF\textsubscript{2\alpha} concentrations were 125 and 130 pg, respectively, in the control albino lens, and they increased to 845 and 520 pg, respectively, in the UVB-exposed lens 24 hours after UV exposure. PGE\textsubscript{2} and PGF\textsubscript{2\alpha} concentrations remained low or below the limit of detection. Indomethacin lowered PGE\textsubscript{2} and PGF\textsubscript{2\alpha}, in aqueous humor to levels present in unirradiated eyes.

Table 3 shows the prostaglandin product profile of iris–ciliary body from UVB-exposed, contralateral control eyes. Indomethacin abolished prostaglandin levels in UVB-exposed and contralateral control iris–ciliary body.

Effect of Topical PGE\textsubscript{2} and PGF\textsubscript{2\alpha} on Ultraviolet B-Induced Cataract

The effects of PGE\textsubscript{2} were first tested in animals pretreated with indomethacin. These "add back" experiments were performed to identify the major lens prostaglandin responsible for cataract formation. Pharmacologic concentrations of PGE\textsubscript{2} and PGF\textsubscript{2\alpha} topically were administered to the indomethacin-treated eyes. Topical preapplication of exogenous PGE\textsubscript{2} followed

![Figure 3](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933193/ on 11/21/2018)
FIGURE 4. The effect of prostaglandin (PG)E₂, PGF₂α, or misoprostol on ultraviolet B-induced cataract in the rabbit eye. Thirty minutes before UVB exposure, eyes were pretreated with PGE₂, PGF₂α (10 μg), or misoprostol (5 μg). The eyes were exposed to 5.6 J/cm² of UVB radiation, and treatment with the prostaglandin was repeated immediately after UVB exposure and then at 5 and 24 hours after. (A) Right eye of an animal pretreated with PGE₂. (B) Left eye of the same animal treated with PGF₂α. (C) Right eye of an animal treated with misoprostol. (D) Left eye of the same animal with no topical treatment.

by UV exposure completely prevented cataract formation (Table 4). Lenses from UV-irradiated animals appeared normal when PGE₂ was combined with indomethacin. Topical application of PGE₂ was necessary before UVB exposure to produce a protective effect on cataract. There was no protection when PGE₂ was applied after UVB exposure. Unlike PGE₂, PGF₂α not only did not protect against UVB cataract, it enhanced it from stage 1 to stage 5 in the indomethacin-treated animal (Table 4). A synthetic analog of PGE₁, misoprostol, also reduced the severity of cataract (stage 1 in the presence of indomethacin to stage 0 in the presence of indomethacin and misoprostol).

All add back experiments were first conducted at 2.8 J/cm². When the unexpected effect of PGE₂ in protecting cataract formation was observed, these experiments were repeated using a higher fluence of 5.6 J/cm². Table 4 shows the effect of 5.6 J/cm² radiation.

Once we established that topical PGE₂ was protective in the presence of indomethacin, we tested the effect of topical application of prostaglandins in animals exposed to UVB radiation but not treated with indomethacin. PGE₂ or misoprostol also reduced the severity of cataract to stage 0 in the absence of indomethacin (Fig. 4). In contrast, PGF₂α did not reduce, but enhanced, cataract severity.

Because PGE₂ increases cAMP levels in lens epithelial cells, the effect of mediators of the adenylyl cyclase on cataract was investigated. Forskolin, a direct stimulator of adenylate cyclase, lowered the severity of cataract slightly, but not to the same extent as PGE₂ (Table 4). DBcAMP and 8-bromo-cAMP did not prevent cataract. IBMX, an inhibitor of phosphodiesterase, which decreases the degradation of cAMP, also did not provide significant protection.

Because it has been suggested that nitric oxide synthase activates the cyclooxygenase pathway, we tested its inhibitor, L-NAME. However, L-NAME did not have a protective effect on cataract. Sodium nitro-

### TABLE 4. Effect of Pharmacologic Agents on UVB-induced Changes in the Lens, Cornea, and Lid-Conjunctiva of Albino Rabbit Eyes

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Lens</th>
<th>Cornea</th>
<th>Lid-Conjunctiva</th>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>UVB</td>
<td>3-4</td>
<td>2-3</td>
<td>3</td>
</tr>
<tr>
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<td>0</td>
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<tr>
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<td>1-2</td>
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<td>0</td>
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<td>3</td>
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<td>L-NAME + UVB</td>
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</tr>
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<tr>
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</table>

Eyes were exposed to 5.6 J/cm² of ultraviolet B radiation (UVB) and examined 24 hours after irradiation. Indomethacin and L-NAME were given intraperitoneally. PGE₂, PGF₂α, IBMX, Forskolin (FS), Misoprostol (MP), dibutyryl cyclic adenosine monophosphate (DBcAMP, 8-bromo cyclic AMP), and sodium nitroprusside (SNP) were applied topically before UVB exposure. * PGE₂ was applied 10 minutes before PGF₂α. † PGE₂ was applied 10 minutes before PGE₂. Four animals were tested under each condition in which pharmacologic agents were used, except L-NAME, IBMX, dbcAMP, and 8-bromo-cAMP. In the latter cases, only three animals were used. Other details are described in Materials and Methods.
prusside, which generates nitric oxide and inhibits Na⁺-K⁺-ATPase, also did not have a potentiating or inhibitory effect on UVB cataract.

Additional experiments were performed to determine the combined effects of PGE₂ and PGF₂α on UVB-induced cataract. Successive pre-application studies showed that pretreatment of eyes with PGE₂
were observed in the lens. However, there was no significant effect of 2.8 J/cm² of UVB radiation on cation uptake (Fig. 5B). At 11.2 J/cm², a 20% decrease in the Rb⁺ uptake was observed in animals tested 3 days after UVB exposure (data not shown). We then tested the effect of higher fluences on cation uptake (Fig. 5B). At 11.2 J/cm², a 20% decrease in the Rb⁺ uptake was observed in animals tested 3 days after UVB exposure. Increasing the UVB radiation reaching the lens by dilating the pupil from 2 to 8 mm did not produce a further decrease in lens cation uptake.

**Histology**

Figure 6 shows the effect of topical PGE₂ on lens histology. Ultraviolet B-exposed lenses showed a marked accumulation of vacuoles, especially in the anterior epithelium. Pretreatment with PGE₂ prevented these changes.

**DISCUSSION**

The current study shows that indomethacin lowers the severity of UVB-induced cataract from stages 3 to 1 but does not prevent it completely. The effect of indomethacin probably results from inhibition of the enzyme cyclooxygenase, thus suppressing the formation of prostaglandins.²⁸ Indeed, the UVB-induced increase in synthesis of PGE₂ and PGF₂α is significantly suppressed in the lens, aqueous humor, and iris-ciliary body by indomethacin treatment. Doubling the dose of indomethacin did not decrease the severity of cataract further. Because indomethacin is inactivated in vivo within 4 to 5 hours, a single dose of indomethacin was not as effective as three doses in the 24-hour study period. The effect of indomethacin on cataract formation was the same whether it was given 1 hour before or immediately after UVB exposure. Indomethacin has been shown to prevent breakdown of the blood aqueous barrier in the rabbit eye.²⁹

Our studies on Rb⁺ uptake by the lens irradiated in vivo indicate that UVB cataract formation precedes changes in cation uptake. This result is in contrast to x-ray cataracts, where loss of Rb⁺ uptake precedes mature cataract formation.³⁰ Because we did not observe a significant change in Rb⁺ uptake, the effect of indomethacin was not investigated.

The current work shows that in contrast to indomethacin, which only partially protected against UVB cataract formation, excess PGE₂ was fully protective. The lack of complete protection by indomethacin is probably caused by proliferation-independent pathways involved in cataract formation. However, exogenous PGE₂ was protective against these mechanisms. In contrast, PGF₂α counteracted the effect of indomethacin and increased cataract severity to stage 3 when indomethacin was combined with PGF₂α. Synthesis of PGE₂ that follows UVB exposure is ineffective in protecting the lens, perhaps because of the simultaneous production of PGF₂α. It is also possible that at early times after UVB exposure, PGF₂α is the primary product. Because PGF₂α epimers can be synthesized from PGE₂, PGD₂, or directly from the PGH₂ intermediate by the action of an endoperoxide reductase,³¹ future studies should determine the time course of production of prostaglandins during acute cataract formation.

Successive addition experiments showed that if PGE₂ and PGF₂α were applied to the same eye, protection was observed only if PGE₂ was applied first. Eyes pretreated with PGE₂ exhibited no further response to PGF₂α. In contrast, eyes pretreated with PGF₂α exhibited no protective effect of PGE₂. These studies are consistent with reports that a supramaximal concentration of PGE₂ effectively may bind to PGF₂α receptors.³² A synthetic analog of PGE₂, misoprostol, was also protective to the same degree as PGE₂.

Previous studies on lens epithelial cells indicate that PGE₂ modulates lens epithelial DNA synthesis probably through a cAMP-mediated mechanism.¹¹ Furthermore, cAMP concentration of lens epithelial cells increases on treatment with PGE₂, suggesting that PGE₂ receptors of the EP2 or EP4 subtype are present in lens epithelial cells.¹¹ Because PGE₂ and PGF₂α exert effects on cells by receptors coupled to G proteins, the effect of stimulators and mediators of adenylate cyclase was investigated. Of these agents, only forskolin had a small protective effect on UVB-induced cataract. The current studies do not indicate clearly the role of cAMP in the mode of action of PGE₂. Future work aimed at quantifying cAMP levels during acute cataract formation, and the nature and responses of PGE₂ receptors in lens epithelial cells, will be necessary to address this question.

The cytoprotective effects of PGE₂ have been demonstrated in a number of in vivo and in vitro models of injury or wound repair. PGE₂ has a protective role in organs such as stomach and kidney.³³ In rat cortical neurons, PGE₂ is cytoprotective against glutamate toxicity, probably by an EP2 receptor-mediated effect.³⁴ PGE₂ has been reported to induce cell migration of corneal endothelial cells during wound repair.³⁵ In several cell types, PGE₂ and/or increased levels of
cAMP induce changes in actin microfilament organization, which results in alteration of cell shape. In addition, PGE₂ is known to have a chemotactic effect in leukocytes and macrophages. Recent work has shown that UV radiation induces cell apoptosis. It would be interesting to determine whether PGE₂ or indomethacin can protect against apoptosis.

The mechanism of action of PGF₁₀ on lens epithelial cells is unknown at present. In mouse fibroblasts, PGF₁₀ interacts with an FP receptor to stimulate phosphoinositide hydrolysis, with the resultant generation of diacylglycerol and inositol 1,4,5-triphosphate. The IP₃ generated elicits Ca²⁺ transient signals. The FP receptor has particular sensitivity to PGF₁₀α but also is known to recognize other prostaglandins, such as PGE₂ or PGD₂. There is a large body of data on prostaglandin receptors in different cell types. Currently, there is no information on the signaling mechanisms or prostaglandin receptors in the lens.

In summary, this study shows that indomethacin partially protects against UVB cataract formation, whereas topical preapplication of pharmacologic concentrations of PGE₁ was fully protective. The mechanism of action of exogenously added PGE₂ is unknown. It may prevent UVB-induced damage or mediate repair processes in lens epithelial cells. In contrast to PGE₁₂α, exogenous PGF₁₀α counteracted the effect of indomethacin and increased cataract severity when combined with indomethacin. Further studies are necessary to determine whether endogenously synthesized prostaglandins act in the same mode as exogenously added prostaglandins and to understand the role of second messengers, such as Ca²⁺ and cAMP, as well as the receptors for PGE₂ and PGF₁₀α in lens epithelial cells. The evidence that PGF₁₀α has a role in the development of cataract suggests that caution be exercised in the use of PGF₁₀α derivatives in glaucoma therapy.

**Key Words**
cataract, indomethacin, lens, prostaglandins, radiation, ultraviolet

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