Brief Note

Effects of Prostaglandin A_2 on the Short-Circuit Current across the Isolated Rabbit Iris-Ciliary Body

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The ionic composition of the aqueous humor is characterized by a higher concentration of HCO_3^- and lower concentrations of Na^+ and K^+ than either serum or cerebrospinal fluid. To explain the specific ion composition, active ion transport mechanisms in the ciliary epithelial cells have been postulated by several authors.[1-4] Since water moves accompanied by electrolytes, the disturbance of ion transport mechanisms may possibly produce abnormal intraocular pressure such as that observed in glaucoma. Prostaglandins (PGs) have been known to affect ion transport[3,4] and they have been practically used to lower intraocular pressure.

In my previous work,[5] it was demonstrated that $PGF_{2\alpha}$ and PGD_2 increased the short-circuit current (SCC) in the isolated rabbit iris-ciliary body by modification of anion transport rather than Na^+-K^+ active transport. The present work was carried out to study the action of PGA_2 in comparison with those of $PGF_{2\alpha}$ and PGD_2, because PGA_2 is known to be most effective for the treatment of intraocular pressure elevation.[6]

The method used for the measurement of SCC has been described in my previous paper,[5] but a slight improvement was made in the method for mounting the iris-ciliary body preparation on the Ussing-type chamber. A nylon sheet was stretched tightly over the silicone platform with a small hole of 2.1 mm diameter or 0.035 cm^2 area. The preparation was placed in such a way that the ciliary body would be centered over the small hole. A second nylon sheet was gently placed over the preparation, as illustrated in Fig. 1. An adhesive liquid was used to avoid slipping of the preparation from the silicone platform. The layer of the silicone, nylon sheets and preparation was placed between two plastic plates. The completed preparation-mounting block was then placed between the two halves of the Ussing-type chamber. This improvement in mounting of the preparation helped to minimize the leakage of current. The standard solution contained 118 NaCl, 4.7 KCl, 0.5 KH_2PO_4, 1.2 $MgCl_2$, 2.5 $CaCl_2$, 15 HEPES, 5.5 glucose and 15.5 $NaHCO_3$ (mM) with pH = 7.4. The solution was maintained at 36℃ and was bubbled continuously with a mixture of 95% O_2 and 5% CO_2.

The experiment was commenced about one hour after mounting of the preparation. Upon closing the feedback circuit, a current of 0.3-0.7 μA flowing from the stromal side to the aqueous side was recorded. This is the background

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or basal SCC. Since the area of the fenestration was 0.035 cm^2, it corresponded to 8.5 - 20 $\mu A/cm^2$. The smaller value of the background SCC than that recorded in the previous work was the result of the better mounting.

When 50 μl of 10^{-3} M PGA_2 solution was added to the 5 ml chamber facing the aqueous side, SCC started to increase gradually and attained a steady value in more than 60 min (Fig. 2). Contrary to the findings on $PGF_{2\alpha}$ or

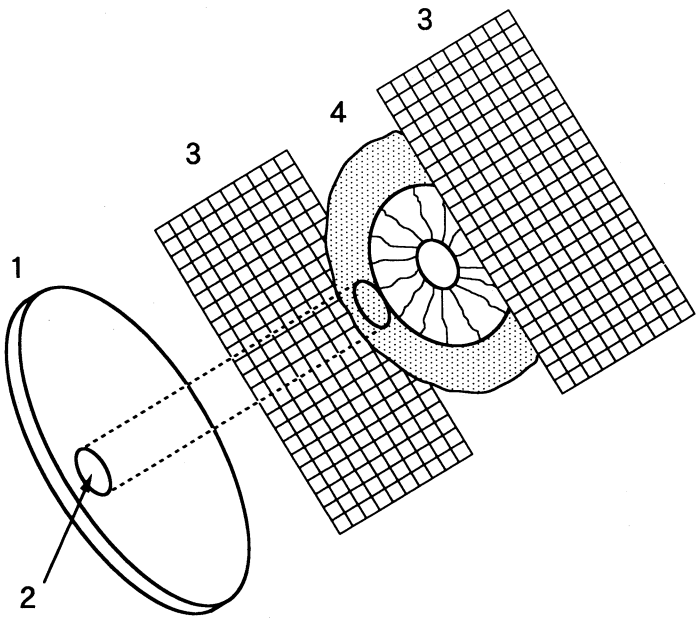

Fig. 1. Schematic diagram of the mounting method for the iris-ciliary body preparation. 1: Silicone plate, 2: Fenestration of an area of 0.035 cm^2, 3 and 4: Nylon nets adhering to the iris-ciliary body.

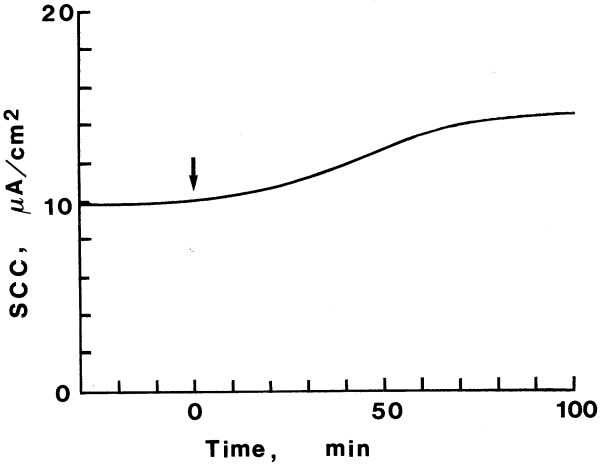

Fig. 2. Effects of PGA_2 (1×10^{-5} M) on the SCC. At the time indicated by the arrow, 0.05 ml of 10^{-3} M PGA_2 was applied to the 5 ml chamber facing the humoral side.

PGD_2 in the previous work, the time course of the increase of SCC caused by PGA_2 was very slow. Delay due to diffusion for added PGA_2 to reach the preparation was excluded because the fluid in the chamber was continuously stirred by bubbling with a gas. Addition of PGA_2 to the chamber of the stromal side resulted in no significant changes in SCC. In Table 1, the increases in SCC caused by PGA_2 obtained from four preparations are summarized together with the results for $PGF_{2\alpha}$ and PGD_2 obtained in my previous work. The increase in SCC caused by 10^{-5} M PGA_2 was smaller and weaker than that in $PGF_{2\alpha}$ at the same concentration. Namely, PGA_2 was less potent than $PGF_{2\alpha}$. On the other hand, the effective concentration of PGA_2 to produce a considerable increase in SCC was 1×10^{-5} M, whereas that of PGD_2 was 1×10^{-4} M. In this regard, PGA_2 was more effective than PGD_2. In summary, the order of the action was $PGF_{2\alpha} > PGA_2 > PGD_2$.

TABLE 1. Changes in the amplitude of SCC ($\mu A/cm^2$) caused by $PGF_{2\alpha}$, PGD_2 and PGA_2 added to the aqueous side

	control	test	% ratio of increase
$PGF_{2\alpha}$	17.0	19.5	
	19.5	26.3	27.6±12.8 (SE)
10^{-5}M	20.3	27.0	
PGD_2	12.8	14.7	
	11.9	20.0	38.8±29.3
10^{-4}M	12.6	18.6	
	12.3	15.1	
PGA_2	9.6	10.9	
	9.8	14.0	23.8±19.1
10^{-5}M	15.9	18.0	
	16.4	20.8	

The nature of the increase in SCC can be explained by inhibition of the Na^+-K^+ pump of the epithelial cell located on the aqueous side or by facilitation of Na^+-HCO_3^- cotransport existing on the same side of the cell. Na^+-H^+ or HCO_3^--Cl^- antitransport may be involved in the change in SCC. Facilitation of either the Na^+-K^+ pump or Na^+-HCO_3^- cotransport would result in an increase in water secretion and a rise in the intraocular pressure. This is contrary to the explanation for application of PGs to practical use. Probably, PGs lower the intraocular pressure by dilating the canal of Schlemm to promote outflow of aqueous humor *in situ*.[7] If PGs increase the production of aqueous humor from the epithelial cells and also promote outflow into the canal of Schlemm, their action on the intraocular pressure stands on the balance of two opposite effects. It has been reported that PGE_2 and $PGF_{2\alpha}$ caused an initial rise preceding a sustained fall of the intraocular pressure when applied through an eye dropper.[8] The initial rise may be due to the strong action on aqueous humor production. On the contrary, PGA_2 and PGD_2 are known to bring about a long-lasting fall in intraocular pressure without an initial rise. The mild effect of PGA_2 on the ion transport and the subsequent water secretion may be advantageous for its practical use to lower the intraocular pressure.

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