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EFFECT OF PROSTAGLANDINS ON CONDUCTIVITY OF MODEL MEMBRANES

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Prostaglandins (PG) with their broad spectrum of action on various functional states of cells, exert their influence indirectly through the cell membrane. To understand the membrane mechanism of the action of PG it is important to study their effects on model membranes.

In the present investigation the effect of PG E_1 and $F_{2\alpha}$ and of prostacyclin on conductivity of model membranes formed from gangliosides, phosphatidylcholine, and proteolipids, was studied.

EXPERIMENTAL METHOD

Bilayer membranes were formed from phosphatidylcholine by the method of Mueller et al. [4], and membranes from gangliosides and proteolipids isolated from bovine brain containing 28% protein and 72% lipids were prepared by the method suggested by the present writers previously [2, 4]. Electrical measurements were made with a high-ohmic electrometer, using a pair of Ag—AgCl electrodes [1]. The ionic selectivity of the model membranes was determined by the method suggested by Lev [3]. The measurements were made in solutions containing 0.1 M KCl, NaCl, LiCl, CsCl, and $CaCl_2$ at 26°C.

All points used to plot curves shown on the graphs represent mean values of at least six measurements on two or three different films.

The phosphatidylcholine was from the Kharkov Bacterial Preparations Factory, the PG from the Upjohn Company (USA).

EXPERIMENTAL RESULTS

Model membranes formed from components of cell membranes, namely phosphatidylcholine and gangliosides, had low conductivity. Conductivity of bilayers of phosphatidylcholine for potassium and calcium ions was $(2.3 \pm 0.3)\cdot 10^{-8}$ and $(3.5 \pm 0.2)\cdot 10^{-8}$ $\Omega^{-1}\cdot cm^{-2}$, respectively. The conductivity of ganglioside membranes was low for potassium ions and high for calcium ions — $(1.8 \pm 0.2)\cdot 10^{-8}$ and $(36.5 \pm 0.3)\cdot 10^{-6}$ $\Omega^{-1}\cdot cm^{-2}$, respectively. Membranes modified by PG E_1 and $F_{2\alpha}$ and by prostacyclin increased conductivity by several orders of magnitude depending on the PG concentration. The highest conductivity of model membranes made from phosphatidylcholine and gangliosides, modified by PG E_1 and $F_{2\alpha}$, for potassium ions (an increase of 2-3 orders of magnitude) occurred in the presence of PG in a concentration of 10^{-10}-10^{-6} M (Fig. 1a, b, curves 1 and 2), whereas the conductivity of lecithin membranes for calcium ions (increased by 3-4 orders of magnitude) was highest when modified by concentrations of 10^{-9}-10^{-5} M, and that of ganglioside membranes (an increase of one or two orders of magnitude) was highest when modified by PG in concentrations of 10^{-9}-10^{-6} M (Fig. 1c, d, curves 1 and 2). Conductivity of membranes modified by prostacyclin (Fig. 1, curves 3) differed from that of membranes modified by PG E_1 and $F_{2\alpha}$. The highest conductivity was created by prostacyclin in the case of phosphatidylcholine bilayers for all ions in a concentration of 10^{-8} M (an increase of four orders of magnitude) and in the case of ganglioside membranes for po-

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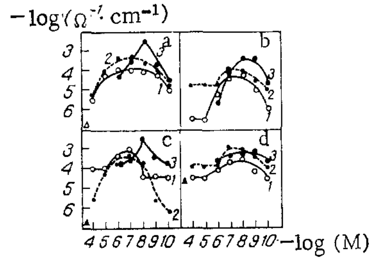

Fig. 1

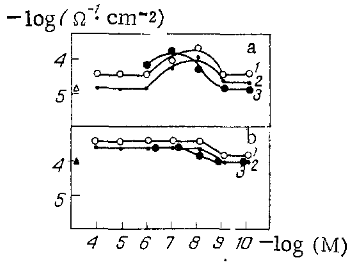

Fig. 2

Fig. 1. Effect of PG on conductivity of model membranes formed from phosphatidylcholine (a, c) and gangliosides (b, d) in solutions of 0.1 M KCl (a, b) and 0.1 M $CaCl_2$ (c, d). Triangles denote conductivity of unmodified membranes; 1) PG E_1; 2) PG $F_{2\alpha}$; 3) prostacyclin. Here and in Fig. 2: abscissa, logarithm of PG concentration; ordinate, logarithm of conductivity.

Fig. 2. Effect of PG on conductivity of model membranes formed from proteolipids in solutions of 0.1 M KCl (a) and $CaCl_2$ (b). Legend as to Fig. 1.

tassium ions in concentrations of 10^{-9}-10^{-8} M. As the data given above show, PG increased the conductivity of the model membranes within a wide range of concentrations, and prostacyclins had the most powerful action.

To elucidate the mechanism of action of PG on cell membranes, besides investigations on models made of lipid bilayers, it was also necessary to study the effect of PG on the protein components. For this purpose the effect of PG on proteolipid model membranes was studied.

The proteolipid membranes had comparatively high conductivity: $(2.1 \pm 0.2)\cdot10^{-6}\ \Omega^{-1}\cdot cm^{-2}$ for potassium ions and $(4.3 \pm 0.2)\cdot10^{-5}\ \Omega^{-1}\cdot cm^{-2}$ for calcium ions (Fig. 2). Conductivity of proteolipid membranes modified by PG showed only a small increase compared with lipid membranes. In the case of potassium ions conductivity changed by one order of magnitude by the action of a concentration of 10^{-8}-10^{-7} M, that of calcium ions changed by half an order of magnitude in the presence of concentrations down to 10^{-9} M, and no change in conductivity was found with the other concentrations tested.

Analysis of the results shows, first, that the greatest increase in conductivity was observed on membranes formed from lipid fractions and the smallest increase on membranes formed from a mixture of the lipid–protein complex. Second, of the various modifiers examined, prostacyclin had the strongest action.

The conductivity of membranes modified by prostacyclin was higher in all concentrations tested than or equal to the conductivity of membranes modified by PG E_1 and $F_{2\alpha}$. Conductivity of proteolipid membranes for calcium ions was the exception (Fig. 2b). These results suggest that PG increase ion transport in membranes mainly through their effect on the lipid fractions.

In a series of experiments to determine bi-ionic potentials, the PG-modified membranes examined above were shown to exhibit specificity toward cations; cations of the alkaline metals can be arranged in the following order of permeability:

$$K^+ > Na^+ > Cs^+ > Li^+$$

PG thus increase the conductivity of model membranes formed from different membrane components predominantly for cations.

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