Biochimica et Biophysica Acta, 552 (1979) 346—357

BBA 78319

INHIBITION OF POTASSIUM CONDUCTANCE BY BARIUM IN FROG SKIN EPITHELIUM

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(Received September 15th, 1978)

Key words: Na^+ transport; Ba^{2+}; K^+ conductance; Conductance inhibition; (Frog skin epithelium)

Summary

The effect of Ba^{2+} (0.5 mM, corial side) upon the transport characteristics of the frog skin epithelium was investigated. It was observed that Ba^{2+} decreased the conductance of the preferably K^+-permeable basolateral border to less than 30% of its control value. Furthermore, Ba^{2+} abolished the K^+ electrode-like behaviour, existing at the basolateral membrane under conditions of zero transcellular current flow, for $[K^+]$ below 10—15 mM. Effects upon other parameters of transepithelial transport (electromotive forces and resistance of outer or basolateral border and shunt pathway, respectively) were small and might represent secondary events. It is concluded that Ba^{2+} inhibits passive fluxes of K^+ across basolateral membranes of tight, Na^+ transporting epithelia, similar to its influence upon membranes of nonpolar cells.

Introduction

Passive movement of potassium accounts for the dominant part of ionic conductance in basolateral membranes of epithelial tissues. This is reflected by an almost ideal K^+ electrode-like behaviour of the transepithelial potential difference of amphibian skins and bladders in response to alterations of the serosal $[K^+]$ [1—4]. As a consequence, the experimental demonstration of other ionic conductances or electrogenic pump components, which might contribute to the electrical properties of the basolateral border, is rather difficult. It could be facilitated, if selective blockage of passive K^+ conductance (g_K) would be possible. Ba^{2+} in low concentrations has been demonstrated to reduce g_K drastically in various excitable membranes (for references see Ref. 5) and gastric mucosa [6].

Ba^{2+} decreases, as several other divalent cations, the transepithelial Na^+

transport in toad bladder [7]. Based upon microelectrode measurements of intracellular potentials, this was attributed to an inhibition of the active Na^+ pump. The validity of microelectrode recordings from toad urinary bladder, however, must seriously be questioned [8,9]. Thus it appeared necessary to reinvestigate the effects of Ba^{2+} upon resistances and electromotive forces of the individual membranes of tight Na^+ transporting epithelia.

The present study was done on frog skin, which can easily be impaled with microelectrodes and allows measurement of stable intracellular potentials from individual cells for long periods of time [9—13]. It will be demonstrated that the influence of Ba^{2+} on basolateral membranes of the frog skin epithelium is similar to effects known from non-polar tissues, i.e. is reasonably described as an interference with passive conductance for K^+. Accordingly, Ba^{2+} might provide a useful tool for the study of basolateral membrane properties of Na^+ transporting epithelia.

A preliminary report of the study has been presented elsewhere [14].

Methods

The experiments were performed on abdominal skins of *Rana temporaria*, mounted in a modified Ussing type chamber for microelectrode impalement which has been described previously [11,12]. Both sides of the skin were continuously perfused with fresh NaCl-Ringer solution of the following composition: 110 mM Na^+, 2.5 mM K^+, 110 mM Cl^-, 2.5 mM HCO_3^-, 10 mM glucose, pH 8.1. The transepithelial potential difference was monitored through Ag/AgCl electrodes and Ringer-filled bridges which ended 0.5 mm apart from the skin. Transepithelial current was fed in through AgCl-coated Ag wires, 5 mm apart from the skin on each side. The skins were short circuited except for periods of 600 ms for measurement of transepithelial conductance and fractional resistance of the apical border by voltage clamping to ±20 mV. The clamping device described by Helman and Fisher [10] was used.

Microelectrodes for intracellular recordings were pulled on a mechanical two-stage microelectrode puller from Omega-dot microfilament capillaries of 1.5 mm outer diameter and 0.8 mm inner diameter (Frederik Haer and Co., Ann Arbor, MI). They were filled from behind with 1.5 M KCl and were used when input resistance and tip potential were between 40 and 60 MΩ and below 5 mV, respectively. The cells were impaled from the epithelial side perpendicular to the surface using an ultra-fast stepping-motor micromanipulator (Fa. Marcinowski, Heidelberg, Germany); stable and reliable intracellular potentials were usually obtained after 10—50 μm electrode advancement from the first contact to the skin surface. Microelectrode potentials were considered to represent intracellular values if the previously discussed criteria [9,11—13] were fulfilled. The microelectrode potentials were monitored via Ag/AgCl electrodes with a Burr-Brown-Instrumentation amplifier (BB 3621), displayed on a Tektronix storage oscilloscope (No. 5113) and recorded continuously on a two-channel strip chart recorder together with the transepithelial clamping current, i.e. usually the short circuit current I_{sc}. At irregular intervals ranging between 1 and 10 min, digital readouts of the intracellular potential and the clamping current at clamping voltages of 0 and ±20 mV were printed on a line printer.

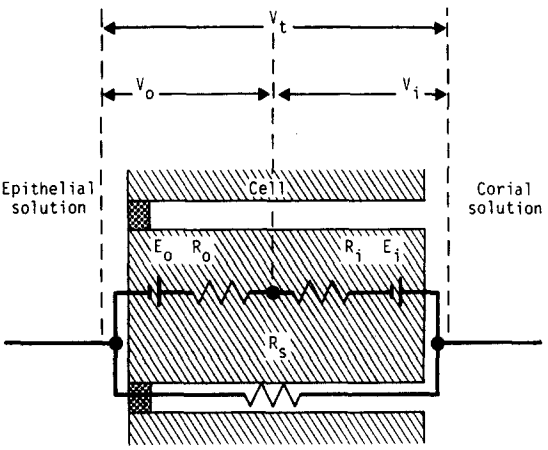

Fig. 1. Electrical equivalent circuit of the frog skin epithelium. V_t, transepithelial potential difference; V_0 and V_i, potential difference across apical and basolateral border, respectively; E_0 and E_i, effective EMF of apical and basolateral border, respectively; R_0, R_i and R_s, resistance of apical and basolateral border and shunt pathway, respectively.

The results are expressed in terms of an electrical equivalent circuit, shown in Fig. 1, using the following abbreviations: I_{sc}, short circuit current; V_{sc}, V_0 ($=V_i$) when $V_t = 0$ mV, i.e. the intracellular potential under short circuit conditions; g_t, transepithelial conductance $\equiv \Delta I_t/\Delta V_t$; given in mS = $10^{-3}\ \Omega^{-1}$; $F(R_0)$, fractional resistance of the apical border $\equiv R_0/(R_0 + R_i) = \Delta V_0/\Delta V_t$; $\Delta V_t = \pm 20$ mV.

In four experiments the measurements could be obtained from the same cell under control conditions and until a new steady state was approached after addition of 0.5 mM Ba^{2+} to the corial side (50—60 min). In three other experiments it was necessary to impale different cells after loss of the initially impaled cell. Amiloride ($0.5—1 \cdot 10^{-4}$ M, epithelial side) was added at the end of each experiment to verify the correct intracellular location of the microelectrode. Furthermore, the following values could be obtained or calculated:

g_s, conductance of shunt pathway $\equiv g_t$ when $g_c \to 0$; assuming, that amiloride affects only the transcellular Na^+ current;

g_c, conductance of the active pathway $\equiv g_t - g_s$;

g_0 and g_i, conductance of apical and absolateral border, respectively. $g_0 = 1/R_0 = g_c/F(R_0)$ and $g_i = 1/R = g_c/(1 - F(R_0))$;

E_{Na}, effective electromotive force of the active transepithelial Na^+ transport $\equiv I_{sc}/g_c$ [15];

E_i, effective electromotive force of the basolateral border calculated from $V_{sc} = E_i - R_i \cdot I_{sc}$ for $I_{sc} \to 0$ [16].

The response of the transepithelial electrical parameters upon addition of 0.5 mM Ba^{2+} was studied in five additional experiments without simultaneous microelectrode measurements. In a second series of eight experiments, the effect of Ba^{2+} on E_i and the response of this potential upon variation of the serosal $[K^+]$ was investigated. Amiloride (10^{-4} M) was added at least 30 min prior to Ba^{2+}. After the V_{sc} had assumed a steady value under Ba^{2+}, the serosal $[K^+]$ was increased stepwise from the usual value of 2.5 mM to concentrations

between 10 and 110 mM. After each step, the serosal side was again perfused with 2.5 mM K^+. If the intracellular potential difference approached the previous control value within ±3 mV, this was considered as an appropriate test for correct intracellular recording and the measurement was accepted. The K^+ of the serosal perfusion solution was analysed after the experiment by flame fotometry (IL 543, Instruments Laboratory Inc., Lexington, MA).

Mean values are given ± S.E.; when appropriate, comparison was done using matched samples of the same skin.

Results

(a) Effects of Ba^{2+} upon transepithelial parameters

Fig. 2 shows the typical response of I_{sc} and g_t upon serosal Ba^{2+} (0.5 mM). The initial decrease of I_{sc} and g_t was followed by a secondary recovery. Thus, the final steady-state values of I_{sc} and g_t were only slightly less than the respective control values. Addition of amiloride ($5 \cdot 10^{-5}$ M) before and after Ba^{2+}

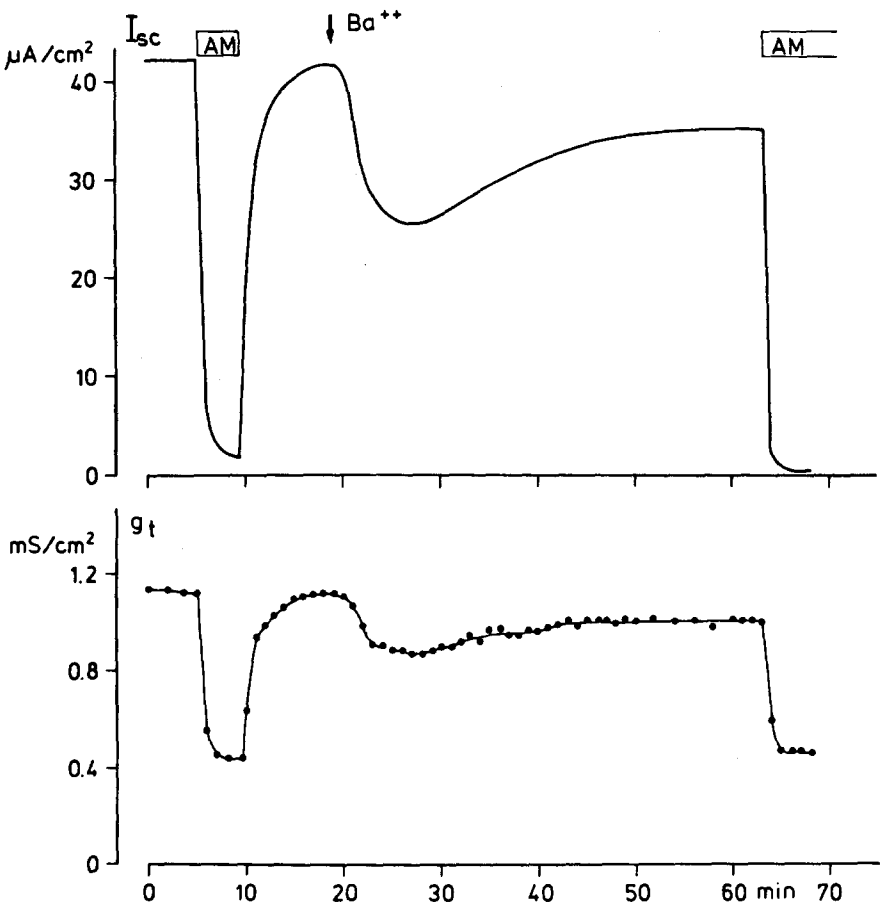

Fig. 2. Effect of Ba^{2+} (0.5 mM, corial side) upon I_{sc} and g_t of frog skin. Amiloride was applied to the epithelial side during the periods indicated by AM.

TABLE I

EFFECT OF Ba^{2+} (0.5 mM, CORIAL SIDE) UPON TRANSEPITHELIAL ELECTRICAL PARAMETERS OF FROG SKIN

The results are expressed in mean values ± S.E. from 12 skins.

	I_{sc} ($\mu A/cm^2$)	g_t (mS/cm^2)	g_c (mS/cm^2)	g_s (mS/cm^2)	E_{Na} (mV)
Control	49.4 ± 3.4	0.715 ± 0.055	0.436 ± 0.053	0.277 ± 0.025	116.4 ± 7.6
Ba^{2+}, 8—10 min	31.7 ± 3.3	0.590 ± 0.062	0.298 ± 0.042	—	114.8 ± 5.6
Ba^{2+}, 25—40 min	40.5 ± 4.2	0.729 ± 0.090	0.416 ± 0.050	0.319 ± 0.040	102.6 ± 4.7

indicated that neither the sensitivity of the apical border to the inhibitor nor the remaining transepithelial conductance ($=g_s$) were measurably affected.

Similar behaviour was observed in 12 experiments which are summarized in Table I. Ba^{2+} exerted its maximal effect upon I_{sc} and g_t about 8—10 min after addition to the serosal solution. The final steady-state values were approached 25—40 min after Ba^{2+}. The shunt conductance g_s, estimated from g_t after amiloride increased by 15% upon Ba^{2+}, but this change was statistically not significant ($2P > 0.3$). The conductance of the active transcellular pathway, g_c, showed a bi-phasic response. During the initial period of the Ba^{2+} response it was found to decrease by about 30%. This is similar to the change of the I_{sc}. Within the framework of the above equivalent circuit, this allows to calculate that the effective EMF of the transcellular transport, E_{Na}, remained unchanged during the initial period after Ba^{2+}. After approach to the final steady state, g_c assumed almost control values, while the I_{sc} remained clearly reduced compared to the control values. Consequently, it must be concluded that E_{Na} was reduced by about 10% in the late period after Ba^{2+}. This change is statistically not significant ($2P > 0.1$).

(b) Effect of Ba^{2+} upon intracellular potentials and individual membrane conductances

Fig. 3 shows the response upon Ba^{2+} of the intracellular potential under short circuit conditions, V_{sc}, and the fractional resistance of the apical border, $F(R_0)$, compared to the change of the I_{sc}. From a control value of —97 mV, V_{sc} decreased concomitantly with the I_{sc}. At the time when the I_{sc} had assumed the minimal value, the V_{sc} was reduced to —46 mV. In contrast to the behaviour of the I_{sc}, which increased considerably until the final steady state was reached, the V_{sc} continued to decrease under the influence of Ba^{2+}, approaching a steady value of —39 mV. The decrease of the V_{sc} was associated with a decrease of the $F(R_0)$ to about 70% of the control value. Addition of amiloride ($5 \cdot 10^{-5}$ M) resulted in an immediate increase of the V_{sc} and the $F(R_0)$ to —84 mV and 0.97, respectively. These values are characteristical for successful impalements under the influence of Ba^{2+} according to the recently described criteria [9,11—13]. Note, that V_{sc} decreased under the influence of amiloride thereafter within 3—4 min to a steady value of —71 mV. Similar behaviour was observed in all experiments.

The results of seven experiments are summarized in Table II. Values are

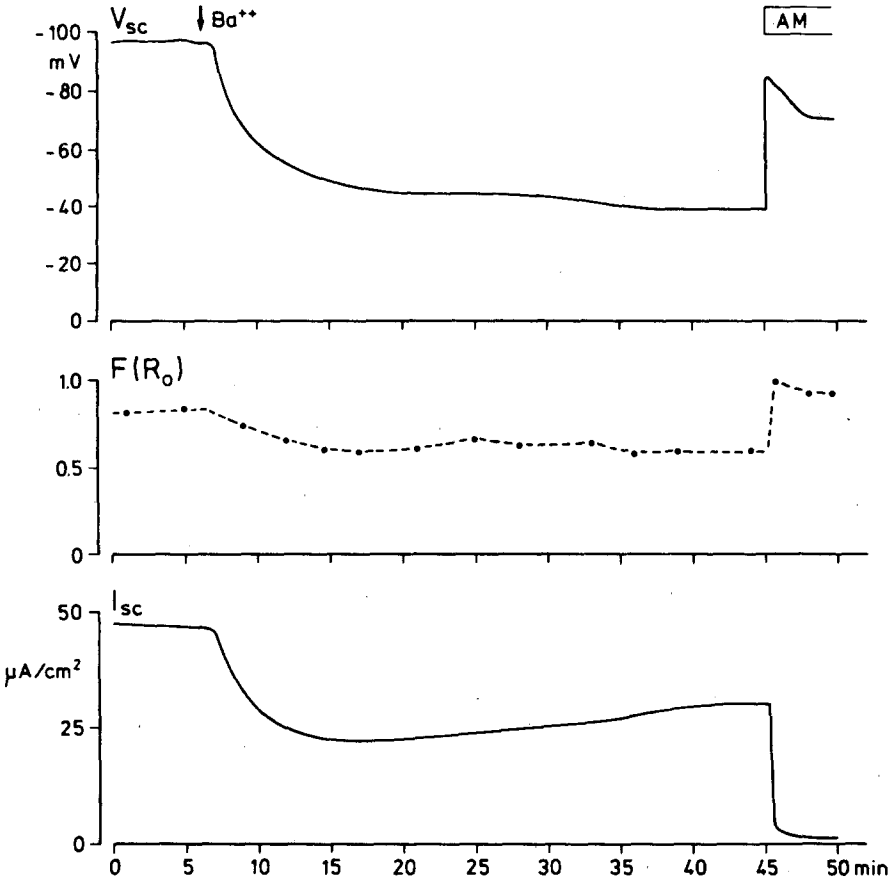

Fig. 3. Response of V_{sc} and $F(R_0)$ upon addition of Ba^{2+} (0.5 mM, corial side), compared to the decrease of the I_{sc}. AM, $5 \cdot 10^{-5}$ M amiloride, epithelial side.

given for the early period (8—10 min after Ba^{2+}) when the I_{sc} was minimal, and for the final steady state (25—40 min after Ba^{2+}). It is evident, that the V_{sc} and the $F(R_0)$ decreased in the early period after addition of Ba^{2+} and remained essentially unchanged at this reduced level.

The specific conductance of the outer membrane, g_0, showed the same

TABLE II

RESPONSE OF INTRACELLULAR POTENTIAL DIFFERENCE AND SPECIFIC MEMBRANE CONDUCTANCES OF THE INDIVIDUAL MEMBRANES OF FROG SKIN TO ADDITION OF Ba^{2+} (0.5 mM, CORIAL SIDE)

The results are expressed in mean values ± S.E. from seven skins.

	V_{sc} (mV)	$F(R_0)$	g_0 (mS/cm²)	g_i (mS/cm²)
Control	−78.5 ± 7.1	0.797 ± 0.040	0.547 ± 0.108	2.41 ± 0.42
Ba^{2+}, 8—10 min	−31.9 ± 4.5	0.578 ± 0.018	0.475 ± 0.120	0.656 ± 0.158
Ba^{2+}, 35—45 min	−33.0 ± 3.7	0.536 ± 0.036	0.710 ± 0.194	0.739 ± 0.111

bi-phasic response as reported above for I_{sc} and g_t. The initial decrease by some 15% was followed by an increase to about 130% of the control value. These changes, however, were statistically not significant. In contrast, considerable and highly significant changes ($2P < 0.001$) were observed at the inner border. The specific conductance g_i decreased to about 30% in the initial period and remained at this level.

Similar conclusions regarding the behaviour of g_i can be obtained using a different approach to calculate the specific resistance of the inner border. Using the equivalent circuit model shown in Fig. 1, it can be demonstrated that $V_{sc} = E_i - R_i \cdot I_{sc}$. This equation allows to calculate R_i from $\Delta V_{sc}/\Delta I_{sc}$, provided E_i and R_i remain unaffected by the manoeuvre to change I_{sc}. This condition is most likely fulfilled, if the outer border resistance is increased by amiloride and if only the instantaneous values of V_{sc} and I_{sc} after addition of the inhibitor are used for computation. Calculated in this way, R_i was found to increase from a control value of 0.72 ± 0.11 k$\Omega \cdot$ cm^2 ($n = 4$) to 1.90 ± 0.13 k$\Omega \cdot$ cm^2 ($n = 7$). These changes are equivalent to a decrease in g_i to about 40%.

Using the same equation and assumption, the effective EMF of the inner border, E_i, can be estimated from the value of V_{sc} when I_{sc} approached zero. It was found, that E_i decreased from a control value of 113 ± 4 mV ($n = 4$) to a value of 89 ± 4 mV ($n = 7$) after Ba^{2+}.

(c) Effects of Ba^{2+} upon basolateral membrane properties under non-transporting conditions (Amiloride)

Addition of Ba^{2+} to the corial bathing solution in the presence of amiloride ($5 \cdot 10^{-5}$ M at the epithelial side) results in a decrease of the V_{sc} ($=E_i$). Fig. 4 shows the time course of this decrease in terms of the mean values from eight experiments. Before addition of Ba^{2+}, amiloride was present until the temporary hyperpolarisation had disappeared. At that time, V_{sc} had assumed a value of -93.8 ± 3.4 mV. 20 min after Ba^{2+}, a new steady value of -61 mV was approached. The decrease of the V_{sc} occurred with a half-time of about 4 min, which is only slightly higher than the half-time of diffusion of Na^+ through the corial tissue layers [17].

In six experiments, the influence of elevating the serosal $[K^+]$ in the presence of Ba^{2+} was investigated. Fig. 5 shows the typical result. In this experiment it

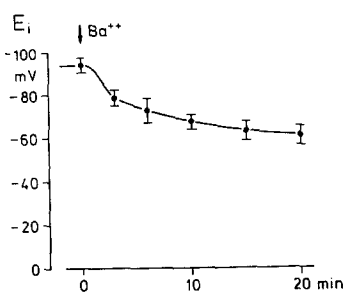

Fig. 4. Time course of the effect of Ba^{2+} (0.5 mM, corial side) upon the effective EMF of the basolateral border E_i. E_i was measured as the V_{sc} at zero transepithelial current ($5 \cdot 10^{-5}$ M amiloride, at the epithelial side). Mean values ± S.E. from eight experiments.

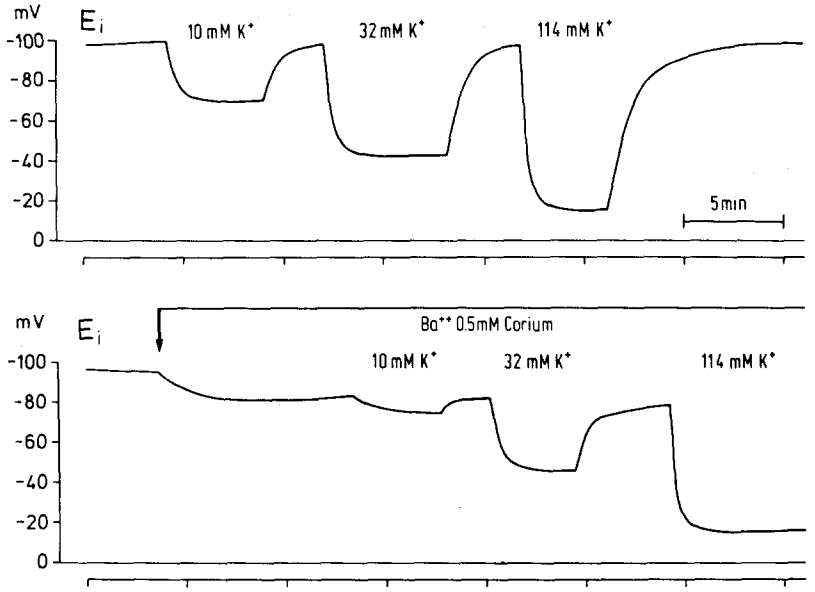

Fig. 5. Effect of elevating the serosal $[K^+]$ upon E_i before (upper panel) and after Ba^{2+} (lower panel).

was possible to study the influence of three different $[K^+]$ upon V_{sc} before and after Ba^{2+} with the microelectrode in the same cell. Before Ba^{2+}, the typical concentration-dependent depolarisation of V_{sc} with a slope of 53 mV per 10-fold change of $[K^+]$ was obtained. After Ba^{2+}, elevating the $[K^+]$ to 10 mM was

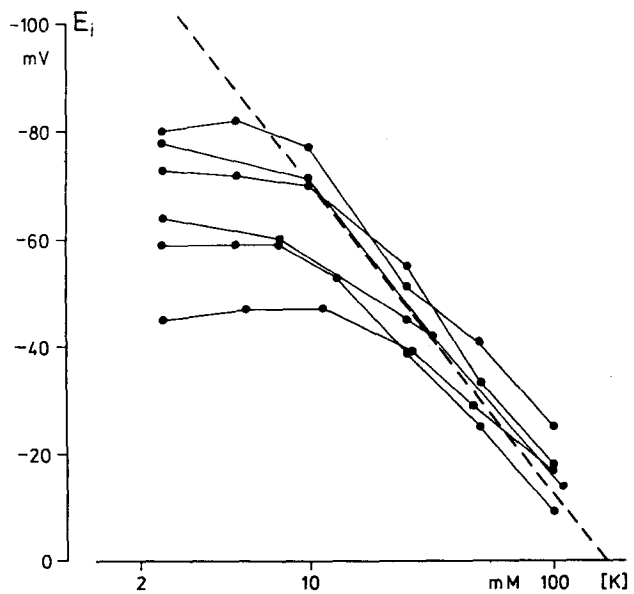

Fig. 6. Semilogarithmic plot of E_i ($=V_{sc}$ at zero transepithelial current) against the serosal $[K^+]$ obtained from skin under the influence of Ba^{2+} (0.5 mM, corial side). Filled circles connected by lines represent measurements from the same experiment (cell).

almost without effect upon V_{sc}. The depolarisation, caused by $[K^+]$ of 30 and 110 mM, however, was essentially the same as before Ba^{2+}.

The observations of all experiments are summarized by the semilogarithmic graph of V_{sc} against the $[K^+]$ of the corial bathing solution shown in Fig. 6. The theoretical slope of a potassium electrode, represented by the dotted line and approximately observed under control conditions (Ref. 18 and unpublished results), provides a reasonable fit for the data after Ba^{2+} only at $[K^+] > 10$ mM. The deviation from the theoretical slope is considerable at lower values of the $[K^+]$.

Discussion

Inhibition of passive transmembranal K^+- fluxes by Ba^{2+} has been demonstrated for non-polar excitable cells (for references see Ref. 5) and the gastric mucosa [6] several years ago. The present study shows that Ba^{2+} in low concentrations has similar effects upon the K^+-permeable basolateral membranes of the tight, Na^+ transporting epithelium of the frog skin. As for other membranes [19], the similarity of the crystallographic radii of K^+ and Ba^{2+} might be suggested to explain the interference between these two ions resulting in a more than 3-fold increase in resistance of the basolateral border. Since passive fluxes of K^+ account for most of the basolateral membrane conductance in frog skin, the decrease of g_i to 27% of the control value (Table II) reflects primarily changes of g_K of this membrane. This change in conductance agrees reasonably with data reported by Hermsmeyer and Sperelakis [5] for frog cardiac muscle. According to their results, 0.5 mM Ba^{2+} decreases g_K from about 3.5—4.2 mS/cm^2 to some 1.2 mS/cm^2, i.e. to about 30% of the control values.

Reduction of the dominating ionic conductance may be expected to unmask significant contributions of other ions to the entire membrane properties. Indeed the deviation of the E_i vs. $\log[K^+]$ plot (Fig. 6) from the theoretical Nernst slope at concentrations below 10—15 mM K^+ seems to support the idea that the equilibrium potential of the basolateral border is considerably influenced by other ions than K^+. Among these, Ba^{2+} itself cannot be excluded as a source of depolarisation since conductance and EMF of Ba^{2+} may be significant. At least three further sources for the observed behaviour must be considered.

(1) Although the conductance of the basolateral border to Na^+ appears to be rather low [20], a small, but finite permeability cannot be excluded. Unfortunately, it is not possible at present to provide a quantitative analysis of this contribution, since reduction of the serosal $[Na^+]$ itself exerts drastic effects upon the basolateral membrane properties (unpublished results).

(2) If Cl^- was permeable at the basolateral membrane, the electrochemical potential of Cl^- could affect E_i. According to electron microprobe results [20], reasonable estimates of chemical potential of Cl^- range around 30—40 mV (intracellular negative) and it could be expected that E_i is depolarized by Cl^- at reduced g_K. This problem is presently under investigation.

(3) Ba^{2+} seems to alter the coupling stoichiometry between the pumped fluxes of Na^+ and K^+ [21]. Although Ba^{2+} has effects upon the electrogenic Na^+ transport [22], which would be in agreement with a reduction of the ratio

between actively transported ions of Na^+ over K^+, this component cannot account for the observed depolarisation. Contribution of the electrogenic Na^+ transport to the E_i is almost abolished after 15—20 min incubation under non-transporting conditions, e.g. with amiloride [23], as it was done in the present study.

Compared to previously published data on epithelial membranes, the present results are in remarkable agreement with results of Pacificio et al. [6]. These investigators report for the frog gastric mucosa, that the resistance in the presence of 0.5 mM Ba^{2+} was about 2.6 times increased over the control values. Furthermore, elevating the nutrient (serosal) $[K^+]$ to 10 mM in the presence of Ba^{2+} has no effects upon resistance and potential difference of the gastric mucosa in contrast to the reversal of the effects of Ba^{2+} by elevating the nutrient $[K^+]$ to 79 mM. The correspondence of these findings and the present results is striking. Thus, the basolateral membranes of the skin and the gastric mucosa appear to be dominated by passive movement of K^+. However, significant contribution of other ionic conductances (Na^+, Cl^-, pump?) appears to exist in both tissues.

A previous study of the effects of Ba^{2+} upon Na^+ transporting epithelia [7] led to suggest that Ba^{2+} inhibits the basolateral electrogenic Na^+ pump. The conclusion was primarily based upon three observations: (1) Ba^{2+} did not produce significant changes of the tranepithelial resistance as would be expected if it had influence upon g_K. Table I shows that in the present study g_t decreased also only slightly after Ba^{2+}. Nevertheless, the conductance of the basolateral membrane was remarkably reduced, but this was almost compensated for by a small rise of the other (in series) barrier. (2) Ouabain did not further reduce the I_{sc} in the presence of Ba^{2+} and Ba^{2+} had no effect in addition to ouabain. Unfortunately, ouabain increases the inner and outer membrane resistances considerably [23] which might explain the failure to observe further effects from comparatively small changes of the basolateral border resistance. On the other hand, addition of 10^{-4} M ouabain to Ba^{2+}-treated frog skin results in an instantaneous decrease of the I_{sc} (unpublished observations). This rises the question whether the concentration of 10^{-4} M ouabain used in the toad bladder study might have been too low. (3) Using microelectrode techniques, essentially no change of the resistances of the individual membranes, but identical decrease of the apical and the basolateral potential differences was recorded upon addition of Ba^{2+}. The experimental data, however, must be seriously questioned on theoretical reasons [9] and in view of recent studies on *Necturus* urinary bladders [8] and cannot be used as evidence for or against any mode of action of Ba^{2+}.

The present study demonstrates that the Na^+ transport across the frog skin is reduced due to a remarkable decrease of g_i. Although not directly connected with active steps of the Na^+ transport, the decrease of $g_i = 1/R_i$ must result in a diminution of the I_{sc}, since the intracellular potential of the short circuited epithelium, V_{sc}, is reduced. This latter change is a consequence of the facts that $V_{sc} = E_i - R_i \cdot I_{sc}$ and that the Na^+ uptake across the apical membrane depends upon the potential difference [24].

A slight increase of g_0 was observed 30—40 min after addition of Ba^{2+}. It is most unlikely, that this alteration is due to a direct influence of Ba^{2+} upon the

apical membrane. Ba^{2+} has essentially no effect upon the apical border if applied at concentrations up to 1 mM (Ref. 7 and unpublished observations). Consequently, change of the electrical gradients, the intracellular ionic concentrations or other unknown parameters must be suggested to cause this secondary alteration of g_0 which explains the increase of the transcellular conductance g_c during the late period of Ba^{2+}. In this context, it must be considered that $R_i = 1/g_i$ accounts for only some 20% of the transcellular resistance. A 3-fold increase of R_i changes g_c by a factor of only 1.4. On the other hand, even small alterations of $R_0 = 1/g_0$ have considerable influence upon g_c.

Ba^{2+} had little effect upon the effective electromotive force of the transcellular pathway. E_{Na}, as calculated from I_{sc}/g_c [15], decreased by about 12% in the late period of Ba^{2+}. Only slightly more evident was the decrease of the effective EMF of the inner border by about 25% from its control value. From E_{Na} and E_i, the effective EMF of the outer border, E_0, can be calculated according to $E_0 = E_{Na} - E_i$. Under control conditions, E_0 has a value of +3 mV, which is in agreement with previously published data for control skins [10]. E_0 = +14 mV is obtained for the late period after Ba^{2+}. This change to more positive values resembles the increase of E_0 under the influence of antidiuretic hormone [9]. The absolute values of E_0, however, are much less than would be expected from reasonable values of the Na^+ equilibrium potential. Calculated from the Nernst equation using $[Na^+]$ obtained by electronmicroprobe analysis [20,25], E_0 should be around +40—+70 mV. The reason for this discrepancy is not clear, at present. Nevertheless, it might be important to note that two agents of obviously rather different site of influence as Ba^{2+} and antidiuretic hormone exert similar effect upon the E_0.

Regarding the effect of Ba^{2+} upon active or passive components of the transcellular Na^+ transport, the alterations of the effective EMFs at the invidual membranes and the entire epithelial cell layer are rather small compared to the effects upon the passive conductance of the inner border. A certain inhibition of the active pump cannot be completely excluded, in view of the decrease of E_{Na} and E_i, but these alterations might be a consequence of the increase in g_i or result from a change of the electrogenic mode of transport. Thus, Ba^{2+} in low concentration appears to inhibit primarily passive movements of K^+ at the basolateral membrane of the tight Na^+ transporting frog skin epithelium and might be a useful tool to investigate the transport properties of this membrane.

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