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Inhibition of acid secretion of fundus of *Rana pipiens* with a high concentration of potassium on the secretory side

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Inhibition of acid secretion of the frog fundus is generally accompanied by an increase in transmucosal resistance, R_t, and in potential difference, PD (nutrient normally positive). These results are predicted for the intact tissue by an electrogenic proton pump. It has been suggested that the increase in PD with inhibition can also be explained by a neutral proton pump. The latter model postulates a K^+ diffusion potential across the secretory (lumen-facing) membrane tending to make the secretory side positive. Upon inhibition, the $[K^+]$ in the lumen is assumed to increase, which decreases the diffusion potential, resulting in an increase in the positivity of the nutrient side. To test this theory, we determined the effects of inhibition with a high $[K^+]$ on the secretory side. With a high $[K^+]$ in the lumina, inhibition would result in only a small change in the ratio of K^+ in the cell to that in the lumina, and hence a small change in the diffusion potential. We found, however, that inhibition increased the PD essentially the same as in the controls. With inhibition the resistance also increased with high secretory K^+. Elevating the secretory K^+ during secretion produced a 44% decrease in R_t indicating a large increase in luminal K^+. We conclude that the results are not compatible with the K^+ diffusion potential model but are those predicted by the electrogenic concept.

Introduction

Evidence indicates that in intact fundi the proton pump is electrogenic [1–3] while with the gastric $(K^+ + H^+)$-ATPase in vesicles the findings indicate that it is neutral [4–7]. One of the many lines of evidence supporting the electrogenic pump concept is the finding that inhibition of secretion produces an increase in R_t and PD [8]. The emf of the electrogenic pump is oriented to make the secretory side positive and with inhibition the emf and conductance would vanish resulting in an increase in PD and R_t. It has been suggested [9,10] that the increase in PD and R_t could also be explained on the basis of a neutral pump. It has been postulated that a change in the K^+ diffusion potential between the cell and lumen can explain the increase in PD. In the work reported herein, we will examine the postulate that a change in the emf of the K^+ diffusion potential accounts for the increase in PD. It is postulated (a revival of the Conway-Brady theory [11]) that K^+ and Cl^- move from the cell to the lumen via conductive mechanisms and a neutral $(H^+ + K^+)$-ATPase antiport

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in the secretory membrane produces a forced exchange between K^+ and H^+. The K^+ in the lumen is exchanged for H^+ thus resulting in HCl secretion.

It has been suggested that during acid secretion the K^+ concentration in the lumina is low and that with inhibition it increases and that K^+ and Cl^- continue to enter the lumina with a consequent increase in their concentrations in the lumina [9]. Since the Cl^- concentration is high, a small change in the Cl^- concentration would not change significantly the magnitude of the Cl^- diffusion potential between the cell and the lumina. However, a small change in K^+ concentration from 2 to 4 mM or 2 to 6 mM would change substantially the ratio of K^+ in the cell to that in the lumen, and would result in a decrease in the magnitude of this diffusion potential, which is oriented to make the lumen positive. A decrease in this potential would result in the nutrient side becoming more positive, and thus the increase in PD, with inhibition of secretion, could be explained.

To test the K^+ diffusion potential hypothesis, we studied the effect of inhibition on the PD and resistance with a high K^+ concentration in the secretory fluid. With a high K^+ concentration in the lumina, the change in its concentration of a few mM would result in only a small change in the ratio of the K^+ in the cell to that in the lumen and hence there would be only a negligible change in the K^+ diffusion potential. On the basis of the K^+ diffusion potential model, inhibition of secretion under these conditions would be expected to produce only a negligible change in PD. If, with a high K^+ concentration in the secretory fluid, the increase in PD with inhibition was abolished or markedly decreased, this would support the K^+ diffusion potential model. On the other hand, if the PD still increased, and the increase was not significantly different from the appropriate controls (4 mM K^+), this would constitute evidence against the neutral pump model. The main purpose of this paper was to test the K^+ diffusion potential concept.

Methods

Experiments were performed on the gastric mucosae of *Rana pipiens* by an in vitro method in which the mucosa was mounted between chambers [8,12]. The transmucosal resistance and PD, and the H^+ secretory rate were measured. Two pairs of electrodes were used: one for sending current across the mucosa, and the other for measuring the PD. The resistance was determined as the change in PD per unit of applied current. Current (10–20 $\mu A \cdot cm^{-2}$) was applied for 1 s, first in one direction, and then 1–10 s later, in the other direction. No significant rectification was observed. The mucosal resistances were obtained by subtracting the resistance of the fluids between the probe electrodes and the mucosa resistance. The H^+ secretory rate was measured by the pH-stat method. The pH of the secretory solution was generally maintained between 4.6 and 4.9. Both sides of the mucosa were gassed with a mixture of 95% O_2 and 5% CO_2. Histamine was added to the nutrient solution to a concentration of 10^{-4} M. Thiocyanate was added to the nutrient solution to a final concentration of 10 mM unless otherwise specified. Omeprazole was added to the nutrient solution to a final concentration of $1 \cdot 10^{-3}$ to $3 \cdot 10^{-3}$ M. Student's *t*-test for paired data was used for statistical analysis.

The standard chloride nutrient (serosal) solution contained (in mM): 102 Na^+, 4 K^+, 1 Ca^{2+}, 0.8 Mg^{2+}, 81 Cl^-, 0.8 SO_4^{2+}, 25 HCO_3^-, 1 phosphate, and 10 glucose. The standard Cl^- secretory (mucosal) solution contained (in mM): 156 Na^+, 4 K^+, and 160 Cl^-. For a secretory solution with increased K^+ concentration, K^+ was substituted for Na^+, Cl^- remained 160 mM. Other solutions were used and their compositions are given in the text. The effects of SCN are readily reversible, in contrast to those of omeprazole. Omeprazole inhibition is not reversed by simply washing it out of the nutrient fluid. Hersey et al. [9] reported a partial reversibility of omeprazole inhibition by the use of mercaptoethanol, which we confirmed. However, in our hands, there was poor reversibility of acid secretion with mercaptoethanol [13]. Hence, alternating the sequence of SCN^- and omeprazole from mucosa to mucosa was not feasible. We first used SCN^-, then removed it, and after the PD, R_t, and the H^+ rate returned to about their original levels, which was about 100%, we used omeprazole. We wished to compare the effects of SCN^- and omeprazole on the same mucosa (see above and Discussion).

Results

We studied the effects of inhibition of acid secretion with K^+ concentrations that were higher than our normal concentration, which is 4 mM. With 20, 40, or 80 mM K^+ on the secretory side (K^+ replaced Na^+), there were typical increases of the PD and R_t with inhibition. The results, reported in the following, except where indicated, were for those experiments in which 80 mM K^+ was used.

Fig. 1 shows an experiment in which the control secretory solution (156 Na^+, 4 K^+, 160 Cl^-) was changed to one containing 80 Na^+, 80 K^+, and 160 Cl^-. Changing to the 80 K^+ secretory solution resulted in a transient increase in PD. The PD increased, and then declined to a level slightly less than that of the control. The average transient increase in PD (8 experiments) was 8.1 (S.D. $\pm$ 4.1) mV and the steady state PD was less, but not significantly different from that of the controls (see Fig. 3). The resistance declined substantially and reached a new level within about 10 min. At about 39 min, SCN^- was added to the nutrient solution. In about 4 min, the H^+ rate decreased to zero, and the resistance and PD markedly increased. The resistance after reaching a peak, decreased to a lower level, and the PD in contrast to the resistance, after increasing, showed only a small tendency to decrease with time. The increase in PD with SCN^- was essentially the same as that found previously with 4 mM K^+ in the secretory solution (vide infra). The rapid responses of the PD, R_t, and H^+ rate were typical for the SCN^- experiments.

Fig. 2 shows a typical experiment in which omeprazole was added to the nutrient solution with 80 mM K^+ in the secretory solution. The acid secretory rate decreased more slowly than with SCN^- – it took about 20 min for the acid rate to decline to zero. Interestingly, the PD and resistance also increased more slowly than with SCN^- – the PD, R_t and H^+ rate changed concurrently. The PD increased by about 14 mV. The slow changes in the PD, R_t and H^+ rate were typical for omeprazole. The response of the resistance was quite different from that in Fig. 1. Instead of reaching a peak and then declining, it increased and showed only a little tendency to decrease with time.

A summary of the experiments (a total of 8) on the PD with SCN^- and omeprazole are presented in Fig. 3. The PD before 80 mM K^+ was not significantly different from the PD immediately before addition of SCN^- or omeprazole. Both SCN^- and omeprazole significantly increased the PD ($P < 0.001$). The ΔPD for SCN^- was 15 (S.D. $\pm$ 5.1) and for omeprazole was 14 (S.D. $\pm$ 3.2)

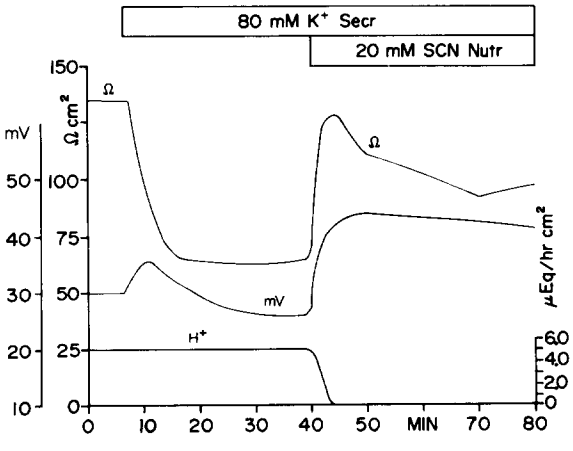

Fig. 1. Resistance, PD, and H^+ rate of frog fundus versus time. Effect of increasing K^+ on the secretory side from 4 to 80 mM. Effect of 20 mM SCN^- to the nutrient side with 80 mM K^+ on the secretory side. The standard nutrient solution ($K^+ = 4$ mM) with 10^{-4} histamine was on the nutrient side. The standard secretory solution was 156 Na^+, 4 K^+ and 160 Cl^-. 0.2 ml of 1 M NaSCN was added to 10 ml nutrient.

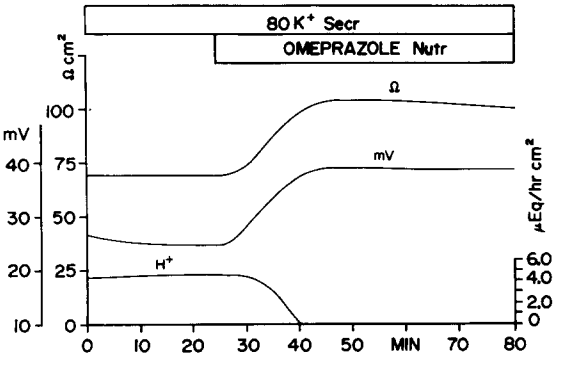

Fig. 2. The effect of the addition of omeprazole (10^{-3} M) to the nutrient side on PD, resistance, and H^+ rate with 80 mM K^+ on the secretory side. The standard nutrient solution ($K^+ = 4$ mM) with 10^{-4} M histamine was on the nutrient side and the standard secretory solution was used.

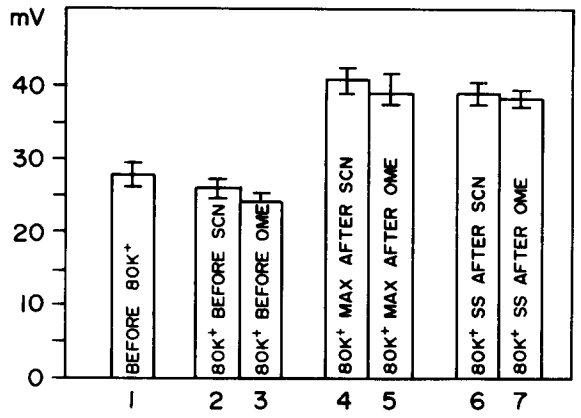

Fig. 3. Summary of eight experiments on the effect on the PD of increasing K^+ from 4 to 80 mM on the secretory side. Effect of SCN^- and omeprazole (OME) with 80 mM K^+ on the secretory side. Max, maximum and ss, steady-state PD.

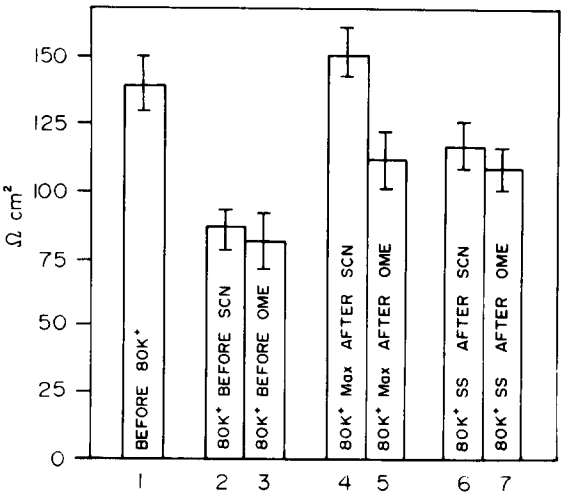

Fig. 4. Summary of the same eight experiments of Fig. 3, on the effect of increasing K^+ from 4 to 80 mM on the transmucosal resistance. Effect of SCN and omeprazole on the fundus with 80 mM K^+ on the secretory side. SCN^- was removed from the nutrient solution, and then omeprazole (OME) was added ($1 \cdot 10^{-3}$ to $3 \cdot 10^{-3}$ M) to nutrient solution.

mV. The difference in PD values, for both SCN^- and omeprazole, between their maximum and their steady-state values was not significant. Also the difference in the ΔPD values of SCN^- and omeprazole was not significant. So it is clear that both SCN^- and omeprazole produced a significant increase in PD with 80 mM K^+ in the secretory fluid. The H^+ rate before SCN^- was 4.7 (S.D. $\pm$ 1.0) and that before omeprazole was 4.2 (S.D. $\pm$ 0.6) μequiv. $\cdot h^{-1} \cdot cm^{-2}$.

Fig. 4 shows the results on R_t of increasing K^+ on the secretory side from 4 to 80 mM (the Cl^- concentration was maintained at 160 mM). The value of R_t decreased significantly ($P < 0.01$) by about 60 ohm $\cdot$ cm^2. Fig. 4 also shows the results on the effect of SCN^- and omeprazole on the resistances with 80 mM K^+ in the secretory fluid. The maximum ΔR_t for SCN^- was 64 (S.D. $\pm$ 16) ohm $\cdot$ cm^2 ($P < 0.001$) and that for omeprazole was 32 (S.D. $\pm$ 16) ohm $\cdot$ cm^2 ($P < 0.001$). The steady-state ΔR_t for SCN^- was 29 (S.D. $\pm$ 17) ohm $\cdot$ cm^2 ($P < 0.01$) and that for omeprazole was 27 (S.D. $\pm$ 15) ohm $\cdot$ cm^2 ($P < 0.01$). The maximum ΔR_t for SCN^- was significantly greater than the steady-state ΔR_t for SCN^- ($P < 0.01$) and also it was greater than the maximum and steady-state ΔR_t for omeprazole ($P < 0.01$). The steady-state ΔR_t for SCN^- was not significantly different from that for omeprazole ($P > 0.1$).

Effect of elevation of K^+ in the secretory fluid on the K^+ concentration in the lumina

Calculations presented in the Appendix indicate that the K^+ concentration in the lumina is markedly elevated when a high K^+ concentration is present in the secretory fluid. The question arises as to whether other evidence supports this conclusion. As shown in Figs. 1 and 4 elevating the K^+ from 4 to 80 mM in the secretory fluid produces a marked decrease in R_t of the secreting fundus. An obvious explanation for this decrease in R_t is that the resistance of the tubular cells is decreased due to an elevation of the K^+ concentration in the lumina. However, it could be argued that the elevation of secretory K^+ decreases the resistance of the pathways parallel to the lumina-tubular cell pathway. It has been shown that the resistances of these parallel pathways i.e., the surface cells and TIC (transintercellular) pathways, are much higher than the lumina-tubular cells pathway, [12,14–17], and it seems unlikely that a decrease in these parallel pathways could explain the decrease in R_t. Nevertheless a very marked decrease in the resistance of the parallel pathways (due to a high K^+ concentration in the secretory fluid) could explain the decrease in R_t.

A method (referred to as hypotonic) for determining the effect of substances on these parallel pathways has been recently developed [14]. Changing the secretory solution from a hypertonic to a hypotonic one has only a small effect on R_t in the secreting fundus, but produces a marked increase in R_t in the inhibited fundus. Evidence indicates that in the inhibited fundus the area of the tubular lumina decreases with a hypotonic solution resulting in a marked increase in R_t in the inhibited fundus. Evidence indicates that in the inhibited fundus the area of the tubular lumina decreases with a hypotonic solution resulting in a marked elevation of the resistance via the lumina-tubular cell pathway [14]. With this preparation the effect of substances on the parallel pathways can be determined. Four experiments were performed with this technique and one is presented in Figs. 5 and 6. In these experiments, the order of procedures was reversed from that of Fig. 1. SCN^- was used first and then the K^+ was increased to 80 mM. The PD and resistance responded to SCN^- in typical fashion. R_t increased by about 115 ohm · cm^2 and then decreased by about 45 ohm · cm^2 while the PD increased by about 18 mV and showed little tendency to decrease.

The subsequent elevation of K^+ from 4 to 80 mM produced, as expected, a decrease in R_t. This was followed by replacing the 80 mM K^+, 80 mM Na^+ hypertonic solution by an 80 mM KCl solution (a hypotonic solution). After this replacement, R_t increased from 90 ohm · cm^2 to 780 ohm · cm^2. In the other three experiments, R_t increased from 107, 111 and 146 ohm · cm^2 to 630, 550 and 610 ohm · cm^2, respectively.

The 80 mM KCl solution was then replaced with an 80 mM NaCl solution, and then returned to the 80 mM KCl solution. In all four experiments, the value of R_t was slightly higher, with 80 mM NaCl than with 80 mM KCl. Subsequent changes were made (see Fig. 6) in the secretory solution, in which a 40 mM KCl solution was alternated with a 40 mM NaCl solution, and a 20 mM KCl solution was alternated with a 20 mM NaCl soltuion. It can be seen that there were substantial increases in R_t in going from 80 to 40 mM and from 40 to 20 mM solutions. R_t was slightly greater with 40 mM NaCl than with 40 mM KCl. This was also true for the other three experiments. R_t was approxiamtely the same with the 20 mM NaCl solution as with the 20 mM KCl solution in all four experiments. The values for R_t with the 20 mM solutions were 1005, 1015, 1300 (Fig. 6) and 1378 ohm · cm^2. These values were approximately the same as found in the past with other hypotonic solutions [13,14,17].

The main point in the hypotonic experiments is that with hypotonic 80 mM KCl, R_t increases substantially – this means that 80 mM K^+ per se does not produce a marked decrease in resistance

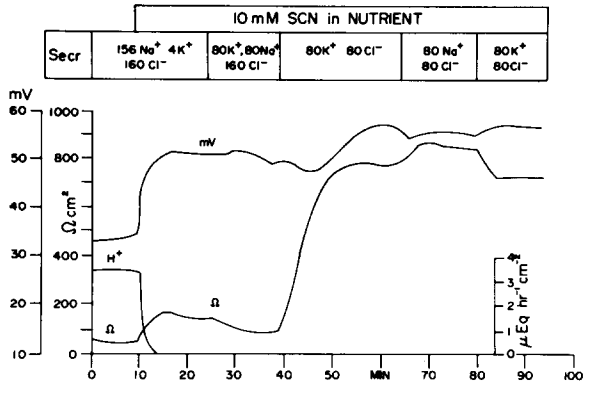

Fig. 5. Effect of changing the secretory solution during SCN inhibition. Regular nutrient solution with 10^{-4} M histamine was used. 0.1 ml of 1 M NaSCN was added to 10 ml of nutrient solution. The composition of the secretory solutions is in mM.

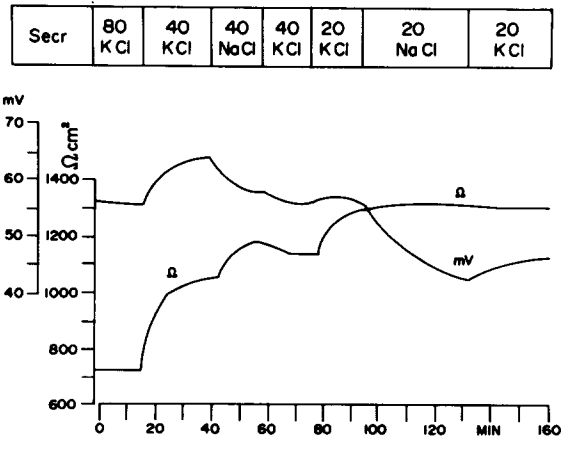

Fig. 6. Continuation of the experiment of Fig. 5. The composition of the secretory solution is in mM.

in the pathways parallel to the lumen-cellular pathway. Further evidence supporting this conclusion is found in experiments with microelectrodes (see Discussion). During inhibition, the large increase in R_t with hypotonic secretory solutions is due to an increase in the resistance of the lumen-cellular pathway resulting from a decrease in the area of the lumina [13,14,17]. During SCN^- inhibition, elevation of secretory K^+ from 4 to 80 mM produces a small increase in PD of 4.0 (S.D. $\pm$ 4.2) mV (which is not significant, $P > 0.1$) and a decrease in R_t of 66 (S.D. $\pm$ 34.8) ohm $\cdot$ cm^2. The latter value is significant, $P < 0.05$, and is about the same magnitude as that found before SCN^- inhibition (see Figs. 1 and 4). In other words, elevation of secretory K^+ decreases R_t during secretion and during inhibition.

Discussion

With 80 mM K^+ in the secretory solution, both SCN^- and omeprazole produced an increase in PD, which only decreased by a small amount with time (Fig. 3) – the average steady-state value for the ΔPD for SCN^- is 15.0 mV and for omeprazole 14.0 mV. These values are not significantly different from those obtained in a group of ten experiments in which the K^+ concentration in the secretory fluid was 4 mM [13]. In these ten experiments the steady-state ΔPD for SCN^- was 11.9 mV and for omeprazole 11.4 mV. The increases in PD with SCN^- and omeprazole were not less with 80 mM K^+ than with 4 mM K^+ in the secretory solution.

The increase in PD by either SCN^- or omeprazole is not that predicted by the K^+ diffusion potential hypothesis. However, it could be argued that a change from 4 mM to a high K^+ concentration in the secretory fluid would not produce a large increase in the K^+ concentration in the lumina. It could be pointed out that by use of a similar analysis to that presented in the Appendix, we previously concluded that, in the case of the in vivo secreting fundus of the dog, the concentrations of ions in the lumina are essentially independent of the composition of the mucosal bathing fluid [18]. In other words, increasing the K^+ concentration in the secretory fluid of the secreting dog fundus would not appreciably change that in the lumina. However, the secretory rate of the dog's fundus with an intact blood supply is almost two orders of the magnitude of 10 greater than that of the in vitro frog fundus [18]. The velocity of bulk flow via the lumina for the dog's stomach is very high, and movement of solutes by bulk flow is overriding – movement by diffusion is very low. In sharp contrast, as is pointed out in the Appendix, using the same type of analysis for the frog fundus, it is apparent that a high K^+ in the secretory fluid would result in a large increase in the K^+ concentration in the lumina. Stated another way the velocity of bulk flow in the lumina of the frog fundus is relatively very low; hence, increasing the concentration of a solute in the secretory fluid would lead to a substantial increase in its concentration in the lumina.

Evidence, indicating that the K^+ concentration in the lumina is substantially increased when the K^+ concentration in the secretory fluid is increased from 4 to 80 mM, is presented in Figs. 1 and 4. Increase in K^+ concentration in the secreting fundus produces a marked decrease in R_t. In other words, if the K^+ concentration did not increase significantly in the lumen, how would the decrease in R_t be explained (vide infra)?

However, as pointed out above, the increase in the K^+ concentration of the secretory solution might markedly decrease the resistance of the surface cells and/or the TIC pathway. Evidence (see Figs. 5 and 6) indicates that the resistance of the surface cells and TIC pathways are still large in the presence of 80 mM K^+. Supporting evidence for the above conclusion has been obtained with microelectrodes in the surface cells [19]. During short-circuiting the ratio, $R_{\text{secretory}}/R_{\text{nutrient}}$ and the intracellular potential of the surface cells are essentially unchanged by elevating the secretory K^+ from 4 to 80 mM (Cl^- is maintained at 160 mM).

On the basis of the foregoing, it is difficult to see how the K^+ diffusion model is a viable model. It should be noted that after publication of the Conway-Brady model [11], experiments quite different from the present ones were devised to test it in the frog gastric mucosa [12,20,21]. The results of these experiments were not compatible with the model and are briefly reviewed in Ref. 14.

As pointed out above, on the basis of the K^+

diffusion model, if with 80 mM K^+ in the secretory fluid, inhibition of secretion led to essentially no change in the PD or R_t, this would be evidence in support of it. However, it is clear that with 80 mM K^+ concentration in the secretory fluid, the change in PD due to inhibition is essentially the same as with the regular 4 mM K^+ in the secretory fluid.

Appendix

The purpose of this section is to obtain for a given K^+ concentration in the secretory (mucosal) bathing media an estimate of the K^+ concentration at the bottom of the tubular lumina for the frog fundus and also for the in vivo (intact blood supply) dog's fundus. We previously used a distributed parameter model for the frog fundus and found that during secretion the concentration at the bottom of the lumina for solutes like KCl would be about 80% of the concentration in the bathing media [14]. With 80 mM K^+ in the medium the K^+ concentration at the bottom of the lumina would be about 64 mM. In the distributed parameter model the rate of water secretion was assumed to be constant along the tubular lumina. For our present purposes we use a simpler model in which we assume that all of the secretion of water occurs at the bottom of the tubular lumina. A schematic of the model is shown in Fig. 7. It should be intuitively understandable that with the simple model the estimated K^+ concentration at the bottom of the tubular lumina would be less than with the distributed parameter model. We assume that the diffusion of HCl, NaCl and KCl are all independent. This is an assumption suggested by Guggenheim [22] which we have used in the past [23] as has Teorell [24]. We use, as we did for the distributed parameter model, the following well-known equation that combines movement of solute by diffusion and by bulk flow

$$Q = -DA\frac{dC}{dX} + vAC \tag{1}$$

where Q is the rate of KCl diffusion, D is Fick's diffusion coefficient, C the concentration of K^+, A the total area of the lumina of all the tubules for 1 cm^2 gross area of the fundus, X is the distance from the bottom of the tubule and v is the velocity of bulk flow (assumed to be piston-like flow). The transmucosal rate of diffusion of electrolytes is relatively small and for simplicity we assumed that in the steady state Q equals zero. Eqn. 1 becomes

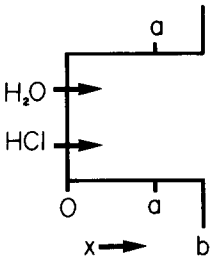

Fig. 7. Schema of the lumina of frog fundus. Bottom of lumina of tubule is at $X = 0$, surface of mucosa is at $X = b$. Tubular lumina extends from $X = 0$ to $X = a$, and pit lumina from $X = a$ to $X = b$. It is assumed that the area of the lumina is constant from $X = 0$ to $X = b$. It is also assumed that all the H_2O and ions of secretion originate at the bottom of the lumina.

$$\frac{dC}{C} = \frac{v}{D}dX \tag{2}$$

Upon integration, where C_0 is the K^+ concentration at $X = 0$ and C is the concentration at X, we have

$$C_0 = C\exp\frac{-vX}{D} \tag{3}$$

and when $X = b$

$$C_0/C_b = \exp\frac{-vb}{D} \tag{4}$$

We used the following values for calculation for 1 cm^2 of gross area: $A = 3.5 \cdot 10^{-2}$ cm^2, $b = 3 \cdot 10^{-2}$ cm, and $D = 1.7 \cdot 10^{-5}$ $cm^2 \cdot s^{-1}$. The values for A and b are from Helander et al. [25] and D from Milazzo [26]. In our previous analysis with the distributed parameter model the calculated velocity of bulk flow in the lumina was $1.5 \cdot 10^{-4}$ $cm \cdot s^{-1}$.

For calculations of v we also use experimental values reported by Villegas for bulk flow [27]. He found, with isotonic fluids (220 mosM) on both sides of the secreting frog fundus, a net water flow from nutrient to secretory side of 11.3 (± 0.9) $\mu l \cdot h^{-1}$ for 1 cm^2 of gross area. He also found that

with a hypertonic fluid on the secretory (mucosal) side of 320 mosM and 220 mosM on the nutrient side (essentially the same as our conditions) a net water transport of 15.9 (± 1.3) $\mu l \cdot h^{-1}$ from the nutrient to the secretory side. Using the latter value and $3.5 \cdot 10^{-2}$ cm^2 for A we obtain the value of v as $1.25 \cdot 10^{-4}$ $cm \cdot s^{-1}$. Using the above values for b, v and D in Eqn. 4, we find $C_0/C_b = 0.80$. With 80 mM K^+ in the secretory solution, the K^+ concentration at the bottom of the tubule would be about 64 mM as found with the distributed parameter model [14]. However, we used a slightly larger value for v in the distributed parameter model. If we use this larger value for v (i.e. $1.5 \cdot 10^{-4}$ $cm \cdot s^{-1}$, see above) we find that the ratio of C_0/C_b is 0.77.

The situation for the in vitro frog fundus is substantially different from that for the in vivo dog fundus. Our conclusions for the dog's fundus are not applicable to those of the in vitro frog fundus. The volume rate of the in vivo dog stomach is relatively very large and is easily measured. The volume rate for the dog's fundus, from low to high secretory rates, range (in Villegas' units) from about 200 to 2000 $\mu l \cdot h^{-1}$ for 1 cm^2 of gross area [18]. Using the above values for A and b and substituting in Eqn. 4, we find that the ratio of C_0/C_b for the dog ranges from $0.06 \cdot 10^{-13}$ to $7 \cdot 10^{-13}$. It is apparent that, for the dog's fundus in contrast to that of the frog's, the composition in the luminal fluid is essentially independent of that of the mucosal bathing fluid.

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References

1 Rehm, W.S. (1950) Gastroenterology 14, 401–417
2 Rehm, W.S. (1972) Metabolic Pathways, 3rd Edn., (Hokin, L., ed.), Vol. 6, pp. 187–241, Academic Press, New York
3 Rehm, W.S., Carrasquer, G. and Schwartz, M. (1983) Membrane Biophysics II: Physical Methods in the Study of Epithelia, pp. 313–327, Alan Liss, New York
4 Ganser, A.L. and Forte, J.G. (1973) Biochim. Bophys. Acta 307, 169–172
5 Lee, H.C., Breitbart, H. and Forte, J.G. (1980) Ann. NY Acad. Sci. 341, 297–310
6 Sachs, G., Chang, H.H., Rabon, E., Schackman, R., Lewin, M. and Saccomani, G. (1976) J. Biol. Chem. 251, 7690–7698
7 Sachs, G., Rabon, E., Saccomani, G. and Sarau, H.M. (1976) Ann. NY Acad. Sci. 264, 456–475
8 Rehm, W.S. (1962) Am. J. Physiol. 203, 63–72
9 Hersey, S.J., Sachs, G. and Kasbekar, D. (1985) Am. J. Physiol. 248, G246–G250
10 Reenstra, W., Bettencourt, J. and Forte, J. (1987) Am. J. Physiol. (in press)
11 Conway, E.J. and Brady, T.G. (1948) Nature, London 162, 456–457
12 Rehm, W.S., Davis, T.L., Chandler, C., Gohmann, E., Jr. and Bashirelahi, A. (1963) Am. J. Physiol. 204, 233–242
13 Rehm, W.S., Carrasquer, G. and Schwartz, M. (1986) Am. J. Physiol. 250, G511–G517
14 Rehm, W.S., Chu, T.C., Schwartz, M. and Carrasquer, G. (1983) Am. J. Physiol. 245, G143–G156
15 O'Callaghan, J., Sanders, S.S., Shoemaker, R.L. and Rehm, W.S. (1974) Am. J. Physiol. 227, 273–288
16 Pacifico, A.D., Schwartz, M., Mac Krell, T.N., Spangler, S.G., Sanders, S.S. and Rehm, W.S. (1969) Am. J. Physiol. 216, 536–541
17 Rehm, W.S., Carrasquer, G. and Schwartz, M. (1986) Am. J. Physiol. 250, G639–G647
18 Rehm, W.S., Schlesinger, H.S. and Dennis, W.H. (1953) Am. J. Physiol. 175, 473–486
19 Dinno, M.A., Schwartz, M., Carrasquer, G. and Rehm, W.S. (1986) Biochim. Biophys. Acta 856, 629–633
20 Davis, T.L., Rutledge, J.R. and Rehm, W.S. (1963) Am. J. Physiol. 204, 233–242
21 Sanders, S.S., Noyes, D.H., Spangler, S.G. and Rehm, W.S. (1973) Am. J. Physiol. 224, 1254–1259
22 Guggenheim, E.A. (1930) J. Am. Chem. Soc. 52, 1315–1337
23 Rehm, W.S., Butler, C.F., Spangler, S.G. and Sanders, S.S. (1970) J. Theor. Biol. 27, 433–453
24 Teorell, T. (1947) Gastroenterology 9, 425–443
25 Helander, G.F., Sanders, S.S., Shanbour, L.L. and Rehm, W.S. (1975) Acta Physiol. Scand. 95, 353–363
26 Milazzo, G. (1963) Electrochemistry, Elsevier, New York
27 Villegas, L. (1982) Biochim. Biophys. Acta 685, 249–252