DISPUTANDUM

Permeability Barrier or Ion Pump?

Sometime ago I presented evidence with DALTON[1] suggesting that aldosterone has an effect on the sodium permebiliaty of the mucosal surface of the isolated toad bladder. This conclusion has reccently been challenged in a review by EDELMAN and FANESTIL[2] on the basis that the conclusion relies on two assumptions 'the first of which is open to question, the second is entirely without experimental support'. In order to answer this criticism and to make my view of this problem quite clear I wish to present the following arguement.

It will be appreciated on reading the review by EDELMAN and FANESTIL[2] that a considerable amount of opinion and evidence has been exchanged between the Boston (LEAF et al.[3]) and California (EDELMAN et al.[2]) groups about whether mucosal permeability or the serosal ion pump normally limits sodium transport cross the toad bladder. The Boston group have favoured the idea that mucosal permeability limits the ion transport and that aldosterone acts to increase this permeability . The California group hold the opposite view, that the pump is normally rate limiting and that effect of aldosterone is to increase the activity of the ion pump independently of any effect on mucosal permeability. Our approach to this problem involved measurement of the temperature coefficient of ion transport across the toad bladder in the absence and presence of aldosterone, vasopressin and amphotericin B, making use of the following model.

The rate at which sodium ions enter epithelial transport cell across the mucosal permeability barrier may be represented by $k_1 n_1$, where k_1 corresponds to the rate constant for this passive process, and n_1 corresponds to the number of ions available for such transport (this allows for saturation of 'carriers' or 'pores'). At the serosal surface the rate of ion transport out of the cell may be represented by $k_2 n_2$, where k_2 corresponds to the rate constant for the active process and n_2 corresponds to the number of ions available for active transport (this allows for saturation of active pumps). These rate constants may be related to the corresponding activation energies E_1 (permeability barrier) and E_2 (ion pump) by the Arrhenius equation.

The short circuit current (SCC) measured across the toad bladder will be equivalent to $k_1 n_1$ and $k_2 n_2$. If the permeability barrier limits the SCC then a plot of log. SCC against reciprocal temperature will give rise to a single activation energy E_a equal to E_1 provided that the pump can move sodium at catalytic rates relative to the permeability barrier i.e. thermal activation of the pump will not affect the measured temperature coefficient. Using a similar argument we expect E_a to equal E_2 if the pump limits the SCC. The observed linearity of the activation plots within the temperature range considered is taken as justification for the use of this model in our analysis.

The measured values of E_a were about 14 kcal/mole in the absence, and 9 kcal/mole in the presence of aldosterone, vasopressin and amphotericin B. It is generally accepted that both vasopressin and amphotericin B cause an increase in the SCC by increasing mucosal permeability to sodium. As aldosterone causes the same lowering of E_a as these agents, it may be supposed on the basis of our model, that aldosterone has a similar effect on mucosal permeability. It may be further argued that if the pump were normally rate limiting, any effect of aldosterone on the supply of ATP or the amount of Na^+/K^+ activated ATPase would not be expected to affect the E_a of the active transport process. No isoenzyme formation or alternative activation system is suggested by any measurements of Na^+/K^+ ATPase in the presence and absence of aldosterone[4,5]. It seems most probable that 9 kcal/mole, the value of E_a observed in the presence of agents accepted as causing an increase in mucosal permeability, corresponds either to a lowering of the permeability activation energy E_1 from 14 kcal/mole to 9 kcal/mole, or to E_2 the pump activation energy.

In conclusion I would like to mention some recent results that have been published[6]. We have limited the pump activity by increasing conditons of anoxia, and have shown that the activation energy for the SCC is thus reduced from 14 kcal/mole to 9 kcal/mole. As this case represents one in which there should be no effect on mucosal permeability, then 9 kcal/mole probably corresponds to the activation energy of the pump and 14 kcal/mole probably represents the activation energy of the permeability barrier. This conclusion represents a modification of previous views[1,5]. In these experiments we obtained intermediate conditions which gave rise to inflection points in the SCC activation plots, at lower temperatures E_a equals 9 kcal/mole, at higher temperatures E_a equals 14 kcal/mole. It is suggested that any effect that predominantly increases the activity of the pump will give rise to an activation energy of 14 kcal/mole, whereas any effect that predominantly increases mucosal permeability will give rise to an activation energy of 9 kcal/mole. This evidence is taken to support the idea that sodium transport across isolated toad bladder is normally limited by the rate at which sodium can cross the mucosal permeability barrier.

Zusammenfassung. An einem einfachen Modell wird die durch Temperatur beeinflusste Aktivität des Natrium-Transportes in biologischen Membranen erklärt. Daraus kann der Schluss gezogen werden, dass der Natrium-Transport in der isolierten Krötenblase normalerweise durch die Ausdehnungsmöglichkeit der mukosalen Zone begrenzt ist und dass Aldosteron in der Lage ist, diese Ausdehnung zu fördern.

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