Atti Accademia Nazionale dei Lincei

Classe Scienze Fisiche Matematiche Naturali

Rendiconti

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The mechanism involved during D-glucose transport across the basolateral membrane of the enterocyte in the rat jejunum "in vitro"

Atti della Accademia Nazionale dei Lincei. Classe di Scienze Fisiche, Matematiche e Naturali. Rendiconti, Serie 8, Vol. **70** (1981), n.1, p. 29–32.

Accademia Nazionale dei Lincei

<http://www.bdim.eu/item?id=RLINA_1981_8_70_1_29_0>

Atti della Accademia Nazionale dei Lincei. Classe di Scienze Fisiche, Matematiche e Naturali. Rendiconti, Accademia Nazionale dei Lincei, 1981.

Fisiologia. — *The mechanism involved during* D-*glucose transport across the basolateral membrane of the enterocyte in the rat jejunum "in vitro"* (*). Nota di VITTORIO CAPRARO, GIOVANNI ESPOSITO, ALIDE FAELLI e MARISA TOSCO, presentata (**) dal Corrisp. V. CAPRARO.

RIASSUNTO. — In una precedente nota è stato concluso che l'estrusione dagli enterociti del D-glucosio appare dovuta o a un meccanismo metabolico-dipendente o a un meccanismo di mobilità passiva direttamente o indirettamente correlata con il trasporto di sodio. In questa nota, esaminando il comportamento del transito transepiteliale della acetamide, che risulta linearmente proporzionale al trasporto transepiteliale di glucosio, si conclude che anche la seconda ipotesi non può essere esclusa.

In a previous paper [1], we presented evidence that D-glucose entry across the brush border membrane of the enterocyte is just balanced by glucose metabolism and glucose exit across the basolateral membrane so that the intra-

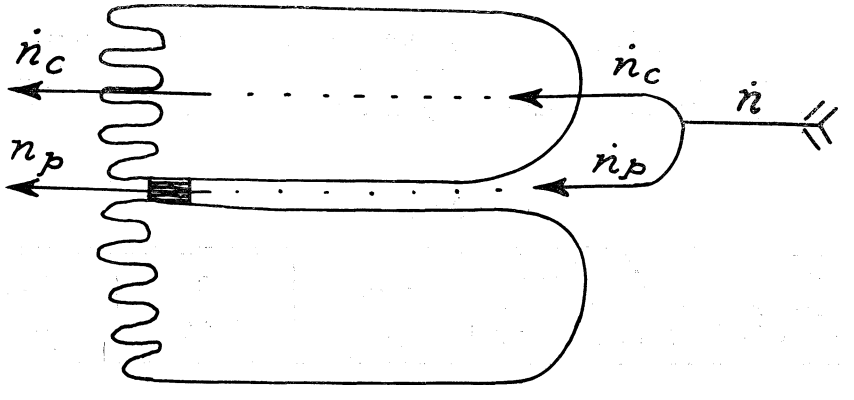

Fig. 1. – Schematic representation of transcellular and paracellular pathways for acetamide serosa-to-mucosa unidirectional movement ($\dot{n}$). $\dot{n}_c$: cell transmembranes movement; $\dot{n}_p$: paracellular movement.

cellular glucose concentration undergoes practically no increase with the net transepithelial glucose transport. One explanation of this observation is that an active extrusion mechanism is present in the basolateral membrane. Alternatively, a direct or indirect correlation between glucose mobility coefficient across the basolateral membrane and the active Na^+ extrusion across the same membrane, could exist.

(*) Lavoro eseguito nell'Istituto di Fisiologia Generale e di Chimica Biologica dell'Università degli Studi di Milano

(**) Nella seduta del 16 gennaio 1981.

This latter hypothesis is supported by the fact that the permeability coefficient of acetamide—a small non-electrolyte and hydrosoluble molecule—through the cell as well as through the basolateral and the apical membranes of rat jejunal enterocyte is strictly proportional to the net glucose transport through the same epithelium. Technical details have been reported elsewhere [2].

The unidirectional serosa-to-mucosa flux of acetamide ($\dot{n}$) is the sum of a transcellular ($\dot{n}_c$) and a paracellular flux ($\dot{n}_p$) (Fig. 1):

$$\dot{n} = \dot{n}_c + \dot{n}_p .$$

This equation, disregarding the negative convective component, is described by the following equations:

$$\dot{n} = P_c \, \Delta C_{sm} + P_p \, \Delta C_{sm}$$

$$\dot{n} = P'_c \, \Delta C_{sc} + P_p \, \Delta C_{sm}$$

$$\dot{n} = P''_c \, \Delta C_{cm} + P_p \, \Delta C_{sm}$$

where "P_c", "P'_c", "P''_c" and "P_p" are the permeability constants through the cell, the basolateral and the apical membranes and through the tight junctions respectively, referred to 1 hour and 1 g. of dry weight of total intestinal tissue (Table I).

TABLE I

Transintestinal D-glucose transport μ mole $g^{-1} h^{-1}$	Unidirectional acetamide $s - m$ flux μmoles $g^{1-} h^{-1}$	ΔC_{sm} mM	ΔC_{sc} mM	ΔC_{cm} mM
177.8 ± 39.2	77.8 ± 9.0	5.50 ± 0.25	4.82 ± 0.25	0.87 ± 0.06
$n = 6$	$n = 6$	$n = 6$	$n = 6$	$n = 6$

The table shows the net transintestinal D-glucose transport, the serosa-to-mucosa unidirectional flux of ^{14}C-labelled acetamide and the acetamide concentration difference between the serosal and mucosal space (ΔC_{sm}) as well as between the serosal and cellular space (ΔC_{sc}) and between the cellular and mucosal space (ΔC_{cm}). The everted jejunal tract of semistarved rats (Sprague-Dawley strain, 200–250 g body weight) are incubated at 28 °C in a Krebs-Henseleit bicarbonate solution (5 ml in the serosal space and 40 ml in the mucosal space) with 13.9 mM D-glucose added.

Net transintestinal D-glucose transport and unidirectional acetamide flux are given in μmoles/g dry tissue weight of total intestine per hour, the concentrations are expressed in μ moles per liter of cell water of scraped mucosa.

Values ± M.S.E. with the number of experiments in parentheses are reported.

Though other possibilities can theoretically be taken into account, let us assume a simplified model in which the paracellular permeability constant " P_p " is not dependent on net sugar transport and therefore constant. Since ΔC_{sm} varies very little around the mean value (Table I), the paracellular acetamide flux (n_p) may be also considered nearly constant (K):

$$\dot{n} = P_c \, \Delta C_{sm} + K$$

$$\dot{n} = P'_c \, \Delta C_{sc} + K$$

$$\dot{n} = P''_c \, \Delta C_{cm} + K \, .$$

From these equations the corresponding value of P_c (P_c, P'_c, P''_c) can be derived:

$$P_c = \frac{\dot{n} - K}{\Delta C_{sm}} = \frac{\dot{n}}{\Delta C_{sm}} - \frac{K}{\Delta C_{sm}}$$

$$P'_c = \frac{\dot{n} - K}{\Delta C_{sc}} = \frac{\dot{n}}{\Delta C_{sc}} - \frac{K}{\Delta C_{sc}}$$

$$P''_c = \frac{\dot{n} - K}{\Delta C_{cm}} = \frac{\dot{n}}{\Delta C_{cm}} - \frac{K}{\Delta C_{cm}} \, .$$

If the single values of transintestinal glucose transport (x) are plotted against the corresponding ($\dot{n}/\Delta C$) values [$y = (\dot{n}/\Delta C_{sm})$, $(\dot{n}/\Delta C_{sc})$, $(\dot{n}/\Delta C_{cm})$] the following numerical linear equations (with a high degree of correlation between the two variables) are obtained:

$$y = 6.11 + 0.047 \, x \, (r = 0.92)$$

$$y = 7.83 + 0.050 \, x \, (r = 0.84)$$

$$y = 33.46 + 0.334 \, x \, (r = 0.94) \, .$$

These equations allow the conclusion that the permeability constants of acetamide through the cell, the apical and the basolateral barrier seem to be strictly correlated with the net glucose transport across the whole intestinal barrier, i. e. these permeability constants are also correlated with net sodium transport and the suprabasal O_2 consumption of the cell due to net sodium transport. These relationships do not seem to be specific because the same relationship is present in the apical membrane as well as in the basolateral one. Furthermore, the increase in the mobility coefficient does not seem to be related to an increase in the membrane surface, because a modification of the surface of the microvillous membrane has never apparently been observed. Presumably a modification of the intrinsic characteristics of the cell membrane is involved.

The intercept numerical values of the above equations are $(K/\Delta C_{sm})$, $(K/\Delta C_{sc})$ and $(K/\Delta C_{cm})$ respectively.

From these values very similar paracellular flux values can be calculated, namely 33.5, 37.7 and 29.1 μ moles $g^{-1}\,h^{-1}$ respectively.

By assuming a similar behaviour of D-glucose, the hypothesis that by increasing the absorption activity of the enterocyte (glucose or Na^+ transintestinal net transport rate) the cotransport rate of glucose and Na^+ through the apical membrane or the passive permeability of glucose together with the active extrusion rate of Na^+ through the baso-lateral membrane are increasing proportionally at the same time, can not be excluded.

In any case, whatever the true mechanism, the enterocyte behaves as a homeostatic system. When the energy available for transport increases, the extrusion of D-glucose and of Na^+ through the serosal pole increase together as well and the intracellular D-glucose and Na^+ concentrations remain nearly constant. This behaviour may be due to a parallel modification of the apparent permeability coefficient of the membrane and of the metabolism dependent transport process.

The energy available for transport varies as a consequence of many factors in a normal population of rat everted intestines, first of all as a consequence of the quantity of energy producing molecules present in the epithelium. An increase of the available energy can also be experimentally induced by keeping the animal in a state of hyperglycemia for many hours before the experiment [3].

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