SODIUM-D-GLUCOSE COTRANSPORT IN RENAL BRUSH BORDER MEMBRANES ISOLATED FROM THE SPINY DOGFISH (SQUALUS ACANTHIAS)

Christopher Bevan, Nancy Ehlers Bevan, Rolf Kinne
and Eva Kinne-Saffran
Max-Planck-Institut für Systemphysiologie, 4600 Dortmund, FRG

The reabsorption of D-glucose from the proximal tubule has been well characterized in both mammals and teleosts, and with the exception of the aglomerular toadfish Opsanus tau (Wolff et al., J. Comp. Physiol. 157: 573, 1987), occurs by a Na-coupled cotransport system located at the luminal membrane. In the evolutionary primitive Elasmobranchii, a class of cartilaginous fish which includes the spiny dogfish, little is known about the mechanisms of organic solute reabsorption in the proximal tubule. Therefore, in the present study, we have characterized D-glucose uptake in renal brush border membrane vesicles isolated from the spiny dogfish as previously described (Bevan et al., J. Comp. Physiol. 159: 339, 1989).

D-glucose uptake in the presence of an inwardly-directed sodium gradient was stimulated as compared to a potassium gradient and resulted in an overshoot. This stimulation was specific for Na^+; neither K^+, Li^+, nor choline$^+$ caused significant stimulation of D-glucose uptake. The K_m and V_{max} of the sodium-dependent component of D-glucose uptake were determined using 5 s uptake rates. The results from 3 experiments were 0.26 mM and 0.6 nmol/mg protein/min, respectively. D-glucose uptake was electrogenic and inhibited by phlorizin with an apparent K_i of 5 μM. To characterize the substrate specificity of D-glucose transport, the effect of various sugars was evaluated as inhibitors of the 5 s uptake rate in the presence of a 75 mM NaCl or 75 mM KCl gradient, as shown in Table 1.

Table 1. Inhibition of 0.1 mM D-glucose Uptake into Renal Brush Border Membrane Vesicles by Sugar Analogs

	Percent of Control	
Sugar (5 mM)	Na-dependent	Na-independent
D-glucose	26 ± 7*	111 ± 8
6-deoxyglucose	37 ± 7*	87 ± 4
α-methyl-D-glucoside	52 ± 2*	104 ± 10
5-thio-D-glucose	68 ± 3*	90 ± 16
D-galactose	71 ± 10*	100 ± 16
D-mannose	88 ± 8	101 ± 4
2-deoxyglucose	93 ± 12	96 ± 9
3-O-methylglucose	98 ± 9	105 ± 29
D-allose	99 ± 4	96 ± 16

mean ± S.D., n=3
*Significantly different from control, $P < 0.05$, using t-test

The Na-dependent uptake of D-glucose was strongly inhibited by 6-deoxyglucose and α-methyl-D-glucoside, but only moderately by 5-thio-D-glucose and D-galactose. D-mannose, 2-deoxyglucose, D-allose, and 3-O-methylglucose had little or no effect. In contrast, none of the sugars tested had any specific effect on the Na-independent uptake of D-glucose. From the results shown in Table 1, an equatorial C2-OH and C3-OH group is essential for interaction with the Na-D-glucose cotransport system. Deviations from this steric arrangement are clearly excluded. Pyranose sugars with a change in the OH group at either the C6 (6-deoxyglucose)or the C1 (α-methyl-D-glucoside) position, and to a lesser extent C4 (D-galactose), appear to interact with the Na-D-glucose cotransport system.

These results document the presence of a sodium-D-glucose cotransport system in the proximal tubule of the spiny dogfish with properties similar but not identical to those found in the mammalian kidney. Thus, it seems that Na-coupled transport systems in the renal tubule are established very early in vertebrate phylogenesis.

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