As may be seen from Figure 2, the clearance ratio of methylamine to PEG also declined with time. However, in this case, the clearance ratio was considerably greater than one which indicates that methylamine is actively secreted. The clearance ratio from three fish ranged from thirty to seven.

The mean ratio of urine flow for these fish was 0.23 ± 0.05 ml/hr, based on fourteen clearance periods. The mean clearance of PEG was 0.28 ± 0.07 ml/hr. The tissue to plasma ratio of methylamine to that for PEG, determined for one fish, was 16.49 ± 0.51 (n = 5).

The data thus suggests that methylamine is secreted into the lumen by the transport system for weak (organic) cations (see, e.g., Am. J. Physiol. 225:1123, 1973).

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THE RENAL HANDLING OF D-FRUCTOSE BY THE WINTER FLOUNDER (*Pseudopleuronectes americanus*)

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The renal handling of D-fructose by the winter flounder was characterized employing the teased tubule preparation and clearance studies.

The *in vitro* studies, using teased renal tubules, were carried out as previously described (Kleinzeller et al., Am. J. Physiol. 232:F227, 1977). The tissue to medium ratio (T/M) for seven pieces of tissue, incubated for 60 minutes in saline having an initial concentration of 1 mM D-fructose, was 0.61 ± 0.02. (All values are expressed as mean ± the standard error.) No significant difference in the T/M was observed over a concentration range of 0.05 to 5.0 mM; i.e., saturation of a carrier site could not be demonstrated. Glucose, 2-deoxyglucose and mannose, which have previously been shown to share the same carrier at the antiluminal face of the cell, did not inhibit the uptake of D-fructose when present at a fivefold molar excess. Also, 0.5 mM phlorizin, phloretin or ouabain did not significantly reduce the T/M value.

Clearance studies were carried out as previously described (Am. J. Physiol. 231:603, 1976). The clearance of D-fructose was not significantly different from the GFR (clearance of PEG) at a plasma fructose range of 50 to 100 µM. The mean clearance ratio obtained from six fish was 1.05 ± 0.06, based on 29 clearance periods. No correlation was observed between either the GFR or the rate of urine flow and the clearance of D-fructose. An additional load of D-glucose, estimated to be 1 mM, had no effect on the clearance of D-fructose.

In brief, no active reabsorption of D-fructose by the winter flounder kidney was observed. Judging from the results obtained with teased tubules, fructose enters the cells at the antiluminal face by a pathway which is not carrier mediated. This investigation was supported in part by USPHS grant AM 12619 and the Whitehall Foundation. The assistance of Mr. Jonathan Goldstein was appreciated.

THE HANDLING OF D-MANNOSE AT THE BRUSH BORDER OF THE KIDNEY IN THE WINTER FLOUNDER (*Pseudopleuronectes americanus*)

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Studies on the handling of D-mannose by the winter flounder (*Pseudopleuronectes americanus*) were continued in view of persistent reports (Silverman, Biochim. Biophys. Acta 457:303, 1976) that in the brush border of the mammalian kidney a specific carrier is responsible for the phlorizin-insensitive reabsorption of this sugar.

The renal clearance of D-mannose in the winter flounder was examined employing the method described by Pritchard and Kleinzeller (Am. J. Physiol. 231:603, 1976). Over a plasma concentration range of 40 to 100 μM, D-mannose is reabsorbed by the kidney. The mean clearance of D-mannose to that of polyethylene glycol (PEG) obtained from 14 fish was 0.31, with an S.E. of ± 0.02 (n = 74 clearance periods, each of which represents ul of urine). A value of 0.52 was obtained from the slope of the straight line fitted by linear regression to the data points (33 clearance periods) of six fish which showed the best correlation between the clearance of D-mannose and that of PEG, i.e., the coefficient of determination for these six clearance studies was at least 0.90.

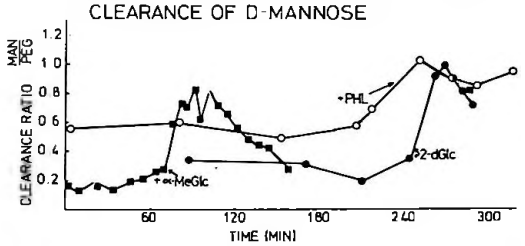
TABLE 1. THE EFFECT OF SELECTED ANALOGS AND PHLORIZIN ON THE RENAL CLEARANCE OF D-MANNOSE

ADDN	n before	n after	RATE OF URINE FLOW before	RATE OF URINE FLOW after	CLEARANCE OF MAN before	CLEARANCE OF MAN after
D-glucose	5	5	0.19±.04	0.39±.03	0.03±.01	0.30±.06
2-deoxy-D-glucose	5	5	0.36±.19	0.85±.06	0.17±.11	0.92±.07
α-methyl-D-mannoside	7	5	0.32±.02	0.33±.03	0.04±.01	0.19±.02
α-methyl-D-glucoside	7	9	0.63±.12	0.84±.11	0.21±.04	0.74±.25
phlorizin	5	4	0.21±.08	0.38±.12	0.24±.11	0.52±.15

ADDN	CLEARANCE OF PEG before	CLEARANCE OF PEG after	CLEARANCE RATIO before (r^2)	PEAK CLEARANCE RATIO after
D-glucose	012±.03	0.44±.04	0.52(0.95)	0.91
2-deoxy-D-glucose	055±.27	1.05±.07	0.38(0.98)	0.99
α-methyl-D-mannoside	017±.02	0.25±.03	0.26(0.58)	0.96
α-methyl-D-glucoside	1.0±.12	1.09±.12	0.26(0.78)	0.84
phlorizin	041±.18	0.56±.18	0.60(0.98)	1.09

As may be seen from Table 1, and from Figure 1, the clearance ratio of D-mannose over PEG was increased by D-glucose, 2-deoxy-D-glucose, α-methyl-D-glucoside and α-methyl-D-mannoside in doses of 2.5 mmol/kg of fish. (The minimum estimate of the final plasma concentration resulting from an

FIGURE 1 THE EFFECT OF α-METHYL-D-GLUCOSIDE, 2-DEOXY-D-GLUCOSE AND PHLORIZIN ON THE CLEARANCE OF D-MANNOSE



addition of that size is 1 mM; thus, the plasma glucose concentration would have increased from 5 to 6 mM.) The ability of each of these sugars to interfere with mannose reabsorption varied from fish to fish and, therefore, they cannot be arranged in any strict order of relative effectiveness. However, of the four analogs, 2-deoxy-glucose was apparently the most effective. In any event, the antagonistic effect of these sugars on mannose reabsorption does suggest that they have a transport site in common with mannose at the luminal face of the renal cell.

Phlorizin, which is a competitive inhibitor of the Na^+-dependent glucose carrier, increased the clearance ratio of mannose over PEG to one, at a dose of 2.5 umole/kg of fish (Table 1 and Figure 1).

Mannose at a dose of 2.5 mmole/kg of fish had no significant effect on the clearance of α-methyl-glucoside, although it did cause a diuresis. The plasma concentration of α-methyl-glucoside ranged from 50 to 100 μM. If these two sugars do share a carrier at the brush border, then the affinity of mannose for the carrier must not be as great as that of α-methyl-glucoside. Also, it must be assumed that much of the reabsorption of mannose occurs in a portion of the nephron distal to where absorption of α-methyl-glucoside takes place. Alternatively, it may be argued that the effect of α-methyl-glucoside on mannose reabsorption is mediated indirectly, i.e., via an increase in the glucose concentration within the nephron (see below).

In order to determine how much mannose was accumulated by the kidney, the kidneys of six fish were extracted at various times after injecting the labelled mannose and PEG (1-8 hrs). Each kidney was sectioned into five pieces of near equal weight, and processed, so that the amount of radioactivity could be measured. It was found that accumulation of the free sugar was low. From 30 kidney pieces, the mean tissue to plasma ratio of D-mannose over that for PEG was 1.6, and the standard error ± 0.10. Since accumulation was low, and scatter considerable, there was no detectable effect of any of the sugars listed in Table 1, or of phlorizin.

There are three possible models which can be proposed to account for the results of these clearance studies. First, glucose, 2-deoxy-glucose and mannose may share a (passive) carrier at the brush border of the renal cell, just as they do at the antiluminal face (Am. J. Physiol. 232:F227, 1977). The difference, however, would be that the former also transports α-methyl-mannoside, while the latter does not. If this were the case, then the effect of phlorizin and α-methyl-glucoside could be explained as an indirect one, since they could conceivably bring about an increase in the effective concentration of glucose, by blocking its uptake via the active carrier. A second explanation is that mannose may be reabsorbed by two separate pathways, one specific for mannose (and α-methyl-mannoside) and the other, the Na^+-dependent glucose carrier. A third explanation, is that there is a carrier for glucose, 2-deoxy-glucose and mannose at the luminal face of the renal cell, identical to the one found on the peritubular side; but, in addition, it may be that the Na-activated glucose carrier is able to accommodate mannose.

Preliminary studies on mannose uptake by vesicles prepared from the brush border of renal cells suggest that either the second or third model may be correct. Evidence was obtained which indicates the existence of a high and low affinity transport site for mannose at the luminal border of the flounder kidney. Uptake of D-mannose by the vesicles showed an overshoot when D-mannose was present at a concentration of 10 uM. This overshoot was reduced by the removal of sodium from the incubation medium. Furthermore, uptake was depressed in the presence of 1 mM glucose, 2-deoxy-glucose and α-methyl-glucoside, as well as mannose. No overshoot in the uptake of mannose was observed when it was present at 100 μM. 10 mM glucose, 2-deoxy glucose, α-methyl-mannoside and α-methyl-glucoside did retard the initial rate of uptake of mannose at the higher concentration. However, more work will need to be done before the pathways for mannose reabsorption are fully defined. This work was supported in part by USPHS grant AM 12619 and the Whitehall Foundation.

AN APPARENT SCN:Cl BI-IONIC POTENTIAL DIFFERENCE OF THE GASTRIC MUCOSA

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Subsequent to the report that the isolated gastric mucosa of the dogfish generates but a meager transepithelial potential difference (PD) (Hogben, Science 129:1224-1225, 1959), SCN, a potent inhibitor of H^+ secretion, has been employed to modulate the PD by applying it only to the serosal aspect (Rehm, Am. J. Physiol. 203:63-72, 1962; Kidder, Am. J. Physiol. 231:1240-1245, 1976). For the gastric mucosa of *Squalus acanthias*, an anion concentration asymmetry results in an apparent bi-ionic PD which has the opposite orientation to that for the isolated mucosa of *Rana catesbiana*.

Experiments were conducted on paired segments of mucosae. A matched pair of Radiometer calomel cells made contact with the two solutions bathing the surfaces of a mucosal segment through 1 M KCl and a pair of iso-osmotic NaCl-3% agar bridges. The signal between the calomel cell pairs was registered with a recording potentiometer, input impedance greater than 1 meg Ω. The observed PD was corrected for the calomel cell-bridge asymmetry PD encountered at the start and end of each experiment, usually negligible and never greater than 1 mV. The composition of elasmobranch saline was Cl 240, HCO_3 30, HPO_4 2, SO_4 4, Na 252, K 10, Ca 10, and Mg 4 mEq/L. Amphibian saline had Cl 92, HCO_3 20,