Glucose Amino Acid and Urea Insorption from the Canine Intestine.* (27801)

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Previously, the insorption† rate for urea exceeded that for chloride(2) whereas chloride and glucose insorption rates were similar (3) when these solutes were perfused through isolated bowel loops in unanesthetized dogs. Since several amino acids left the *in vivo* rat intestine more rapidly than did urea(4,5) the present study was designed to evaluate amino acid insorption in the dog and to test whether glucose and glycine affected the insorption of one another.

Methods. A range of concentrations of glucose, amino acid or urea were perfused through upper jejunal or lower ileal Thiry-Villa loops in unanesthetized dogs at the rate of about 2 ml/minute for one hour. In one series, the perfusates were made up to the desired total osmolarity by addition of NaCl. Glucose plus glycine or urea was perfused in the second series. At least 24 hours elapsed between successive perfusions of each dog and the order of testing the various solutes was randomized. The volume, glucose concentration(6) and total N (micro Kjeldahl after filtration to remove gross mucus) of test solutions were measured before and after perfusion, and unabsorbed solute remaining in the loop was estimated as before(3). Since passage of reducing material into hexose-free perfusates was relatively minute(3), glucose insorption was assumed to be approximately equal to glucose absorption. Nitrogen enterosorption, however, ranged from averages of 18 to 32 mg/hr when 11 nitrogen-free perfusates were given. The appropriate value for each dog was added to nitrogen absorption in order to approximate nitrogen insorption as before(2).

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† Code's terminology(1). Insorption and exsorption mean unidirectional movement from and into the bowel lumen, respectively. Absorption and enterosorption mean net movement from and into the bowel.

Results. The effects of the concentration of the test substance and of the total osmolarity of the perfusate on insorption rate of the test substance are summarized in Table I. Each value is an average for 4 jejunal and 4 ileal loop dogs since no consistent differences were found between these sites. The second column estimates the concentration of test substance to which the loop was exposed as the average before and after traversing the loop. The third column lists approximate total osmolar concentration of the perfusates obtained by adding NaCl to the test substance. The fourth column lists fluid absorption (−) or enterosorption (+). The initial pH values of the glucose, glycine, lysine, histidine and urea solution were 7.0, 6.0, 6.0, 4.0 and 7.4, respectively. The relatively large standard deviations in column 5 reflect consistent differences among the dogs as well as wide random variations. In subsequent statistical evaluation the average values were used.

Table I shows that glucose and glycine insorption rates increased with increasing perfusate concentration. Multiple regression analysis(7), in which glucose or glycine and NaCl concentrations were assumed to be independent variables and non-electrolyte insorption rate the dependent variable, showed that only the non-electrolyte concentration significantly affected its insorption rate. Urea insorption rate increased in nearly linear fashion with increasing urea concentration when total mOsmolar concentration was 250-380. However, urea insorption at given urea concentrations decreased when the total osmolarity of the perfusate was increased. Thus, multiple regression analysis revealed a significant independent effect of NaCl concentration on urea insorption rate. The physiological significance of the finding that urea insorption is affected by NaCl concentration and/or associated fluid absorption or enterosorption is obscure because higher

TABLE I. Glucose, Amino Acid and Urea Insorption Rates.

Test substance	mM/l	Total, mOs/l	V, ml/hr	Avg insorption rate, mM/hr ± S.D.
Glucose	14	250	−60	1.71 ± .64
"	15	370	−16	1.91 ± .85
"	23	250	−68	3.07 ± 1.96
"	30	370	−21	3.36 ± 1.13
"	61	250	−71	5.11 ± 2.87
"	64	370	−34	5.20 ± 4.78
"	132	370	−22	6.63 ± 3.60
"	248	370	+ 4	7.81 ± 4.15
"	260	260	−15	9.02 ± 3.60
Glycine	20	450	+ 9	1.57 ± .13
"	21	300	−21	2.09 ± .67
"	34	450	+20	3.10 ± 1.37
"	37	300	−32	3.54 ± 1.28
"	66	450	+15	3.63 ± 1.43
"	73	300	−31	5.17 ± 2.72
"	125	450	+ 9	6.45 ± 2.82
"	138	300	−30	7.35 ± 3.30
"	220	450	+19	8.67 ± 3.48
"	280	300	− 7	8.42 ± 2.91
L-lysine HCl	42	175	− 1	1.00 ± .30
"	75	200	+13	1.45 ± .58
L-histidine HCl	43	380	−15	2.15 ± .71
	91	500	+11	3.72 ± .91
Urea	16	475	+21	1.18 ± .28
"	17	380	−10	1.73 ± .44
"	32	300	−28	3.14 ± 1.17
"	60	525	+26	3.92 ± 1.25
"	61	380	− 7	6.40 ± 2.58
"	113	575	+36	7.17 ± 3.45
"	115	400	− 1	9.80 ± 4.76
"	118	380	−26	12.80 ± 4.76
"	119	290	−50	12.50 ± 4.12
"	210	650	+16	10.20 ± 4.82
"	230	500	+ 5	16.10 ± 5.94
"	232	380	−54	31.50 ± 9.70
"	250	250	−70	30.50 ±16.45

total osmolar concentrations were required to produce similar changes in fluid shifts for urea than for glucose or glycine solutions (Table I). Nevertheless, this effect on the insorption of a solute should be considered along with the effects of solute concentration and chemical identity(2,3).

Possible differences between glucose and amino acid insorption rates were tested as follows: curvilinear relationships between glucose or glycine insorption and concentration were rectified by plotting reciprocal insorption rate against reciprocal concentration. Covariance analysis of the rectified data furnished tests of significance for differences between the slopes and between the intercepts, the latter being the reciprocal of the theoretical maximum insorption rates. Since the slopes but not the intercepts differed ($p<.05$), glucose tended to be insorbed at a higher rate than was glycine at relatively low perfusate concentrations, but both approached the same maximum rate. Lysine and histidine insorption rates were below the fiducial limits for glucose or glycine rates. Urea, glucose and glycine were insorbed at similar rates below 100 mM/l perfusate concentration, but urea insorption rates exceeded those for glycine or glucose as the concentration increased (Table I). These findings do not confirm previous rat experiments wherein glycine(4,5) and histidine(5) absorption rates exceeded those for urea.

Insorption rates for glucose, glycine and urea when a non-electrolyte was substituted for NaCl in 7 dogs are averaged in Table II. Comparison with Table I suggests that glycine and urea reduced glucose insorption rates and that glucose reduced glycine insorption rates. This conclusion was validated statistically by reaveraging all available data on the same 7 dogs, plotting reciprocal insorption rates against reciprocal concentrations as shown in Fig. 1 and 2 and comparing the resulting pairs of straight lines by covariance analysis. Thus, the slope constants for glucose insorption with NaCl present and for glucose with glycine present, .613 and .822, respectively, differ ($p<.01$). Also, the slope for glucose with urea present, .816, differs ($p<.05$) from the former but not from the latter. Similarly, the glycine insorption slope constants differ (.953 *vs* 3.17; $p<.01$). Fi-

TABLE II. Insorption Rates for Mixtures of Glucose and Glycine or Urea.

Perfusate composition, mM/l			Insorption rate, mM/hr		
Glucose	Glycine	Urea	Glucose	Glycine	Urea
18	282	—	1.63	7.23	—
65	273	—	3.11	9.25	—
68	147	—	3.29	4.71	—
128	266	—	3.79	5.96	—
233	200	—	6.85	4.35	—
244	120	—	4.51	3.78	—
284	74	—	5.67	2.15	—
16	—	240	1.56	—	22.69
71	—	233	2.84	—	25.60
130	—	250	5.91	—	27.31
242	—	210	7.35	—	19.21

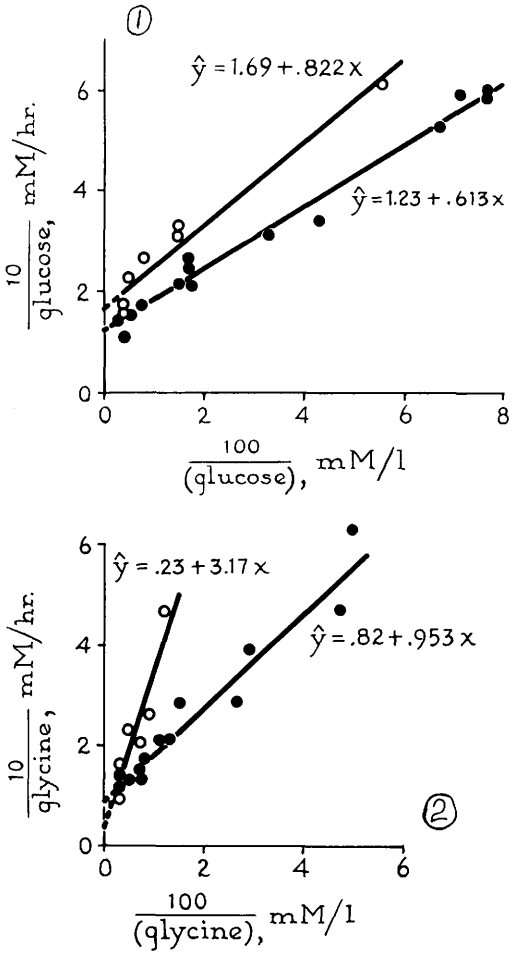

FIG. 1. Double reciprocal plot of glucose insorption rate and concentration. Each point averages same 7 dogs. ● = glucose plus NaCl perfused; ○ = glucose plus glycine perfused.

FIG. 2. Double reciprocal plot of glycine insorption rate and concentration. ● = glycine plus NaCl; ○ = glycine plus glucose.

nally the intercept values for glucose insorption do not differ significantly depending upon whether NaCl (1.23) glycine (1.69) or urea (1.45) was present; neither do the glycine intercepts differ significantly (.82 *vs* .23). These judgments of similar intercept constants are based on estimates of the 95% fiducial limits of each(7).

Discussion. Double reciprocal rectification of the curviliniar relationships between insorption rates and perfusate concentrations was used because it furnished nearly linear data (r = .94 to .99); no necessary implication as to the mechanism(s) of glucose or amino acid absorption is intended. Furthermore, the present method of rectification probably does not apply over a greater concentration range. For example, previous hexose(2) and electrolyte(2,3) data were rectified by plotting insorption rates against log concentration up to 1400 mM/l. Glucose insorption rates averaged 21 mM/hr on 5 similar dogs when 30% glucose was perfused, whereas the present statistical treatment predicts a "maximum" glucose insorption rate of about 12 mM/hr. Thus, the nature of the present inhibitory effects of glucose on glycine insorption and of glycine or urea on glucose insorption are obscure. The evidence suggests, however, that at relatively low concentrations in the bowel lumen these substances may share some common step in their absorptive process(es).

Summary. Glucose and glycine insorption rates increased in similar curvilinear fashion when 20 to 280 mM concentration of each was perfused through isolated bowel loops in unanesthetized dogs. Lysine and histidine were insorbed at lower rates. Urea insorption rates exceeded those for glucose or glycine, but tended to decrease as total osmolarity of the perfusate increased. Glycine and urea interfered with glucose insorption when each was substituted for NaCl in the perfusion fluid, and glucose similarly reduced glycine insorption rates.

1. Code, C. F., Bass, P., McClary, G. B., Jr., Newman, R. L., Orvis, A. L., *Am. J. Physiol.,* 1960, v199, 281.

2. Annegers, J. H., Wakefield, H., *ibid.,* 1962, v203, 563.

3. Annegers, J. H., *ibid.,* 1961, v200, 107.

4. Hober, R., Hober, J., *J. Cell. and Comp. Physiol.,* 1937, v10, 401.

5. Jervis, E. L., Smyth, D. H., *J. Physiol.,* 1959, v149, 433.

6. Folin, O., *J. Biol. Chem.,* 1929, v82, 83.

7. Snedecor, G. W., *Statistical Methods,* Iowa State Coll. Press, 1946.

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