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Effect of the pH on Intestinal Absorption of Sugars *in vivo*

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Influence of the pH on the absorption rate of sugars by rat intestine *in vivo* has been revised by means of a technique for intestinal lumen perfusion with 1 minute absorption periods. Absorption at pH 2.5, 5, 7, 8.5, and 10 has been compaired in each animal. Absorption rate of D-glucose, D-galactose and D-fructose is highest at pH 7 and decreases at the lower or higher pH values. The pH does not affect the absorption of D-arabinose. The pH effect is attributed to changes in the transport system for sugars.

Old experiments in rat (10) and in human intestine (6) suggested maximum absorption of glucose at pH 7. PONZ and LARRALDE (14, 15), working with rat *in vivo*, showed that the medium pH affected greatly the absorption rate of sugars (D-glucose and D-xylose) with maximums when pH values approached 7, and decreasing thereafter on acidifying or alkalinizing the medium. They further showed a tendency for the intestine to neutralize the solutions.

The findings that acidifying the medium produced inhibition, were confirmed by gastric intubation in rat (1) and by perfusion of human intestine by GOLDENBERG and CUMMINS (4), who observed instead an increase towards an alkaline pH (10, 11.5). Experiments *in vitro* with rat showed that glucose transference decreased with a slightly acidic pH (9). In hamster maximum glucose transport was found at pH 5.9-6.0, followed by a sharp decline with a pH shift to either side (7).

Some differences in these results made advisable the revision of the pH effect on *in vivo* absorptions. This has been done by using sugars capable or uncapable of active transport at low concentrations, and by means of a perfusion technique with just 1 minute absorption periods. The experiments confirmed that glucose, galactose and fructose are clearly pH dependent for their absorption, with

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maximums at about pH 7, while they showed that arabinose absorption is not pH dependent.

Materials and Methods

White Wistar rats, weighing 100-180 g were used after 24 hour fasting. A special technique of successive absorptions with perfusion of the intestine was employed (13, 18). The intestinal segment between the cannulae was about 20 cm long.

The solution perfused in a series of experiments contained 0.9 percent NaCl; the required pH values were obtained by simply adding HCl or NaOH 0.5 N. In another series the pH values were obtained by means of buffer solutions: citrate-phosphate for pH 2.5 and 5; Tris-HCl for pH 7 and 8.5; and carbonate-bicarbonate for pH 10 (5).

The pH was electrometrically measured before perfusion and again at the outlet of the intestine.

Concentrations of D-glucose, D-galactose, D-fructose and D-arabinose in the initial perfusion medium were 2 mM. Perfusion with hexoses was performed without recycling at a rate of 5.6 ml/min, with successive absorption periods of 1 minute. Between one period and the next the intestine was rinsed with a 0.9 percent NaCl solution with pH 7.4. Since arabinose is hardly absorbed, perfusion with this sugar was performed by recycling the solution (10 ml) during successive periods of 5 minutes.

Sugars were determined after NELSON-SOMOGYI (12, 19). Absorption rate is expressed in nmoles of sugar absorbed per cm of intestine per minute.

Results

Ten successive absorption periods, two for each pH assayed value, were performed in each animal. The succession order of pH values was changed in distinct animals without any observable effects on the results.

Table I sums up the results of experiments in the absence of buffer solutions, and table II the corresponding ones with buffer solutions.

As the solution flowed along the intestine, its pH values tended to be neutralized. In the presence of buffer solutions the pH displacements were hardly appreciable (less than 0.1); in their absence, the variation was approximately 0.2 (with pH 5 and 8.5) or 0.9 (with pH 2.5 and 10).

The absorption of D-glucose, D-galactose and D-fructose was maximum at

Table I. *Influence of the pH on the intestinal absorption rate of 2 mM sugars in rat.* Perfusion fluid: NaCl 0.9 % (the pH was adjusted between 2.5 and 10 by adding 0.5 N HCl or OHNa). Mean values with their standard error. Number of experiments between parenthesis.

Sugar	Absorption in successive periods (nmoles/cm/min)				
	1st pH=2.5	2nd pH=5	3rd pH=7	4th pH=8.5	5th pH=10
D-glucose	42 ± 1 (28)	76 ± 1 (28)	89 ± 1 (10)	60 ± 1 (10)	37 ± 2 (10)
D-galactose	47 ± 0.5 (8)	86 ± 2 (8)	111 ± 2 (8)	76 ± 2 (8)	41 ± 2 (8)
D-fructose	40 ± 1 (8)	66 ± 2 (8)	80 ± 3 (8)	64 ± 3 (8)	34 ± 0.5 (8)
D-arabinose	26 ± 0.7 (8)	26 ± 0.4 (8)	25 ± 0.5 (8)	26 ± 0.7 (8)	27 ± 0.7 (8)

Table II. *Influence of the pH on the intestinal absorption rate of 2 mM sugars in rat.* Perfusion fluid: NaCl 0.9 % with buffer solutions. Mean values with their standard error. Number of experiments between parenthesis.

Sugar	Absorption in successive periods (nmoles/cm/min) 1st pH=2.5	2nd pH=5	3rd pH=7	4th pH=8.5	5th pH=10
D-glucose	35 ± 1 (10)	64 ± 2 (10)	84 ± 3 (10)	59 ± 2 (10)	22 ± 1 (10)
D-galactose	33 ± 1 (8)	80 ± 2 (8)	106 ± 2 (8)	69 ± 1 (8)	28 ± 1 (8)
D-fructose	34 ± 0.5 (8)	58 ± 1 (8)	79 ± 2 (8)	56 ± 1 (8)	26 ± 0.5 (8)
D-arabinose	26 ± 1 (8)	25 ± 1 (8)	27 ± 7 (8)	28 ± 0.6 (8)	24 ± 1 (8)

pH 7, and decreased with acidic or alkaline pH values, the decrease becoming more and more pronounced as the pH values moved further away from 7. Alterations in pH did not affect the absorption rate of D-arabinose, although changes in pH at the end of the periods were slightly greater since the perfusion medium with this sugar was subjected to 5 minute recyclings (fig. 1).

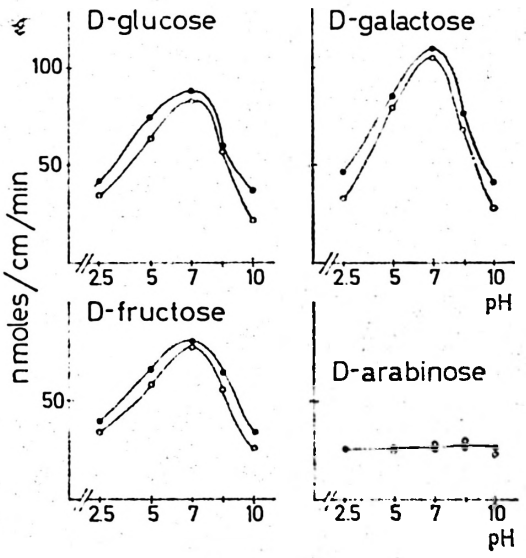

Fig. 1. *Influence of the perfusion fluid pH on the intestinal absorption rate of 2 mM sugars in rat. Successive periods of 1 min for hexoses and of 5 min for arabinose, with* (○) *or without* (●) *buffers.*

The effect of pH on absorption in the presence of buffer solutions presented no significant differences, except with some hexoses with pH 2.5 and 10. In these cases absorption was inferior in the presence of a buffer solution. The reason for this is that only in these cases the differences in the displacement of the pH towards neutrality during 1 minute perfusion, become sufficiently significant.

Absorption inhibitions in relation to the corresponding ones at pH 7, taken as control, were greatest with D-galactose, slightly inferior with D-glucose, and somewhat lower with D-fructose.

Discussion

pH influence on the absorption of D-glucose, D-galactose and D-fructose in these experiments presents very similar characteristics to those described by PONZ and LARRALDE (14, 15). These had also used *in situ* rat intestine with a successive absorption technique, but unlike the present method, they used 0.3 M glucose in distilled water and kept static the solution in the intestine during 30 minutes. Under such conditions, diffusion constituted an important absorption component (8, 11),

and the transport system worked with low Na^+ concentrations. As a result a marked displacement of the solution pH towards neutrality took place during those 30 minutes.

With the technique followed in this work, absorption is due mainly to transference by the transport system, since sugar concentrations are very low, inferior even to the values of their transport constants (K_T), and which in the case of glucose imply flow towards blood against concentration gradient (8). Furthermore the high level of Na^+ favours the use of the transport system (2, 3, 16, 17).

With 1 minute absorption periods the absorption inhibitions produced by non-neutral pH disappeared completely on the following period when neutral pH is restored. This indicates that the pH effect cannot be assigned to unspecific perturbations of the enterocytes. The fact that pH variations do not affect the absorptions of D-arabinose, a sugar uncapable of using the transport system, points to the same conclusion.

These results suggest that the pH influence on the absorption rate of glucose, galactose and fructose must be related to changes in the affinity of the transport system towards its substrates, or in the lessening of its operative capacity to translocate sugar. These changes in the transport system, owed to the pH, are quite understandable if their proteic nature is admitted.

Resumen

Se ha revisado la influencia del pH sobre la velocidad de absorción de azúcares por el intestino de rata *in vivo* utilizando una técnica de perfusión de la luz del intestino y períodos de absorción de 1 minuto. Se ha comparado en cada animal la absorción a pH 2,5, 5, 7, 8,5 y 10. La velocidad de absorción de D-glucosa, D-galactosa y D-fructosa es máxima a pH 7 y disminuye a los pH más bajos o más altos. La absorción de D-arabinosa no se influye por el pH. El efecto del pH se atribuye a cambios en el sistema de transporte de los azúcares.

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