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Relationship Between Oxygen Uptake Levels and Capacity of Intestinal Sacs for Sugar Active Transport *

by

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Scientific literature dealing with investigation on the metabolism of intestinal mucosa with relation to active transport is fairly limited. Contrary to some previous negative observations (5, 6) an increase in the oxygen uptake by intestinal mucosa or by strips of small intestine was observed in the presence of glucose, or fructose in the medium (14). This increase in the oxygen uptake is only evident in the presence of sugars that are easily metabolized (glucose, fructose) but not necessarily of the ones that are actively transportable. On the other hand, this increase was not shown by sugars that are transported actively by only shortly metabolized or not at all (3-O-methyl-glucose, galactose) by the intestine (3).

Following our studies on the active transport of sugars (9, 10) the relationship between the oxygen uptake level and the active transport of galactose and 3-O-methyl-glucose were studied in separate everted intestinal sacs.

Materials and Methods

White Wistar rats, weighing 150 g to 200 g were used. Everted sacs 3 cm long were prepared from the middle portion of the small intestine and incubated separately in the Warburg apparatus, following the *in vitro* technique of everted intestinal sacs described by WILSON and WISEMAN (17).

Intestinal sacs previously filled with 0.3 ml of Krebs-Henseleit solution (8) (serosal fluid) were introduced in Warburg flasks containing 4 ml of the same solution (mucosal fluid). The initial concentration of sugar in the serosal and mucosal solutions was 5 mM. The flasks were shaken at 90 oscilations/minute, with an amplitude of 3 cm. The duration of each experiment was 30 minutes, and the oxy-

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gen uptake and the sugar transported were measured within the same time. The results are expressed in micromoles of oxygen used per 100 mg of wet tissue in 30 minutes. The ratio of wet to dry weight was constant, corresponding to 83 ± 0.6 per cent of water. A temperature of 37° C (± 0.001) was maintained during the experiments.

Very pure samples of galactose and 3-O-methyl-glucose, previously tested that they were free of glucose by the glucose oxidase, were utilized in the experiments. The concentrations of sugars were determined by the method of SOMOGYI (15).

Results

The values of oxygen uptake are based on the results obtained utilizing separate everted intestinal sacs of wet weights ranging from 150 to 200 mg. In the absence of substrates, these sacs showed a relative high oxygen uptake, althought a remarkable difference was found to exist between intestinal sacs proceeding from different animals. This variability follows Gaus'law and exhibits distinct levels of oxygen uptake per unit weight of tissues for different sacs. The intestinal sacs also showed an appreciable variability in the active transport of sugars.

The transport, *in vitro* can be determined either by the difference in concentration of the substance in the mucosal solution and its increase in the intestinal wall and the serosal solution, or in the case of active transport, by the quotient between the concentrations of sugar under test in the serosal solutions, before (Si) and after (Sf) the incubation. In our experiments we have used this second method to measure the transport.

A significant correlation was found to exist when comparing values of oxygen consumption in the active transport of galactose and 3-O-methyl-glucose.

Table I shows the results obtained.

The classification of experiments which had an oxygen consumption of the same order of magnitude, demonstrated a lineal regression between the transport of sugar and oxygen uptake. If T is equivalent to the transport of sugar measured in micromoles/100 mg of wet weight of intestine and expressing the oxygen uptake in micromoles/100 mg of wet weight of intestine, the value of T obtained with galactose $T = 0.84 \times O_2$ uptake $- 0.39$ (with a coefficient of correlation, $r = 0.777$, values tabulated for 41 grades of liberty

TABLE I

Relationship between oxygen uptake levels and capacity of intestinal sacs for sugar active transport

Incubation time, 30 minutes. The values represented correspond to the measurement with its respective standard error

N.° exps.	Sugar 5 mM	Oxygen uptake O_2 µM/100 ww	Active transport Sf/Si
11	D-Galactose	2.59 ± 0.16	1.88 ± 0.13
10		3.28 ± 0.05	2.55 ± 0.15
14		3.74 ± 0.06	2.75 ± 0.12
8		4.39 ± 0.11	3.32 ± 0.15
5	3-O-methylglucose	2.01 ± 0.24	1.19 ± 0.08
13		2.99 ± 0.06	1.60 ± 0.10
7		3.97 ± 0.12	2.50 ± 0.26

and ($P \leq 0.001$, $r = 0.485$) and for 3-O-methyl-glucose a value of $T_1 = 0{,}63 \times O_2$ uptake $- 0.22$ with a coefficient of correlation $r = 0.710$ (values tabulated for 23 grades of liberty and $P \leq 0.001$, $r = 0.619$). Figure 1 illustrates these results.

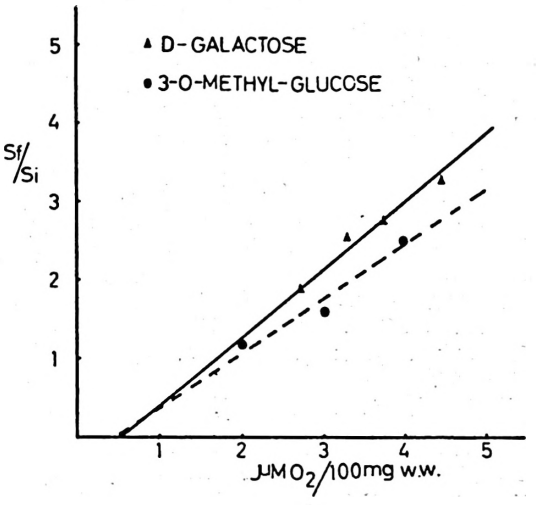

FIG. 1. Oxygen uptake level and capacity of intestine for sugar active transport. The ordinate represents the values of active transport expressed by the gradient between the final (SF) and the initial (SI) concentration of sugar in the serosal solution and the abscissa represents the oxygen uptake in µM/100 mg of intestine wet weight.

Discussion

The energy for the active transport of the intestinal mucosa is supplied by the cellular metabolism. Studies carried out by DICKENS and WEIL-HALHERBE (6) show that the metabolism of the small intestine of the rat and of some other species present very special characteristics with respect to other tissues, in its preponderance of the aerobic in relation to the anaerobic glycolysis and the absence of the Pasteur effect (11).

Whichever the mechanism of active transport by the intestinal epithelial cells, could be, the energy required could be provided by ATP Accordingly, FEHER and col. (7) have studied the role of the ATP content in the intestinal mucosa of rat and the velocity of glucose absorption. Their results show a parallelism between the velocity of absorption of sugars and the ATP content of the intestine and at the same time the ATP is used during the absorption of the sugar.

On the other hand VARRÓ and col. (16) found that hypoxia can produce a diminution in the absorption of glucose with the decrease in the intra-mucosal resintesis of ATP. They studied then the changes of ATP content by the hypoxia produced by a decrease in intestinal blood flow. They also found a direct correlation between the absorption of glucose and the ATP content in the intestinal mucosa.

The influence of hypoxia on the absorption of glucose was investigated *in vivo* by LLUCH (12) several years ago and showed that the hypoxia produced by the decrease in blood flow of the small intestine or by the reduction of inspired oxygen tension, produced an inhibition in the absorption of glucose. These results have received overwhelming confirmation (1, 2, 4, 13). But since the greater or lesser oxygen supply to a tissue does not necessarily signify an identical variation in its oxygen uptake, it was of interest to measure directly and simultaneously the active transport of a substance and the oxygen consumption by the intestinal wall, what has been done in this work.

Our results indicate that the metabolic variability between distinct intestinal sacs is conditioned by multiple factors, but basically this difference measured by the oxygen consumption appears to be directly proportional to the capacity in the transport of the tested sugars. It is very probable that sacs with the greater consumption of oxygen have a greater supply of ATP available for active transport.

Summary

This work includes the study of the influence that the metabolic level of individual intestinal sacs of rats, measured by the oxygen uptake, have on the active transport of galactose and 3-O-methylglucose. The experiments showed a statistically significative correlation between both processes.

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