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The effects of cytochrome C and uranyl on the active transport of sugars by the intestine *

by
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The active transport of sugars by membranes implies a coupling of energy supplied by cellular metabolism. The mechanism of this coupling is still unknown. The procedure by which the molecule of certain sugars is transported into the interior of the cell is not known either, in spite of the various theories emited.

On previous works (1, 4, 5, 6, 7, 8, 9), we tested numerous metabolic inhibitors trying to establish relations between the bloqued metabolic processes and their role in the active transport of sugars by the intestine. It has also been determined precisely, in many cases, weather the inhibitor acted on the cellular surface proper — non-penetrating inhibitors — or if their action was preferably intracellular. The results showed that practicaly all the metabolic inhibitors tested, with easy penetration through the membrane, inhibit the absorption of selective sugars, and their places of action on the metabolism were either on the first steps on the utilization of glucose, along the tricarboxylic cycle, or on the process of oxidative phosphorylation. The absorption is also inhibited when the oxygen supplied to the mucose by the blood decreases for any reason (3). This makes it clear that the metabolic production of energy is really important for the active transport of sugars. On the other hand, the use of non penetrating inhibitors shows that this energy is utilized on the membrane through processes

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of transference to the mechanism of active transport, as yet unknown.

In the present communication we demonstrate that cytochrome o notably stimulates the intestinal absorption of sugars and that this effect can be inhibited by uranyl which is a non penetrating ion.

The experiments have been done on rats, using our method of successive absorptions (SOLS and PONZ, 12) on the intestine in situ. The cytochrome was administered intravenously after a control absorption and the absorbed glucose during the following ones increased up to 40 %. Figure 1 shows a typical record.

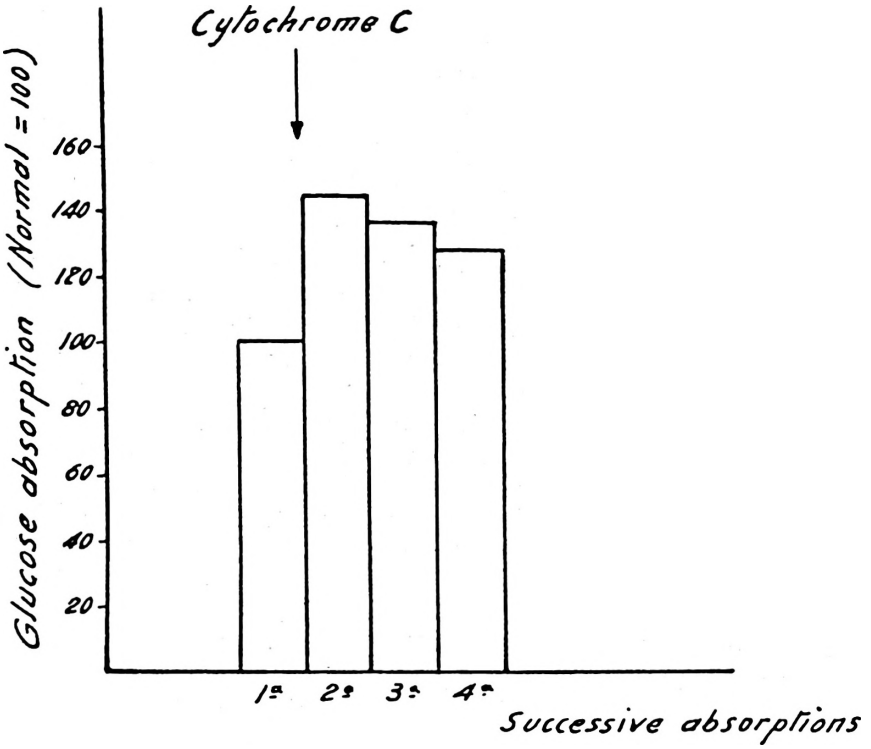

Fig. 1. — Cytochrome effect on the intestinal absorption (5.4 %). Absorption time, 30 min.

The effect keeps a relation with the amount of cytochrome injected and does not take place with denatured cytochrome (Fig. 2).

Cytochrome is not effective either if it is dissolved in the solution of sugar which is to be absorbed.

Experiences with galactose showed a similar behaviour.

On other animals we have studied the effect on the absorp-

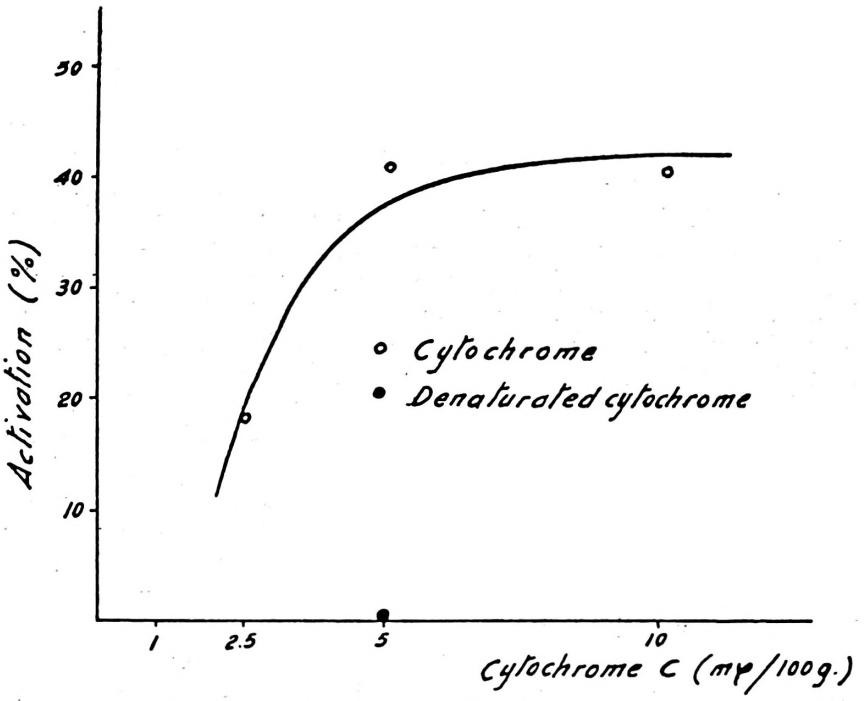

Fig. 2. — Activation of glucose absorption by cytochrome c

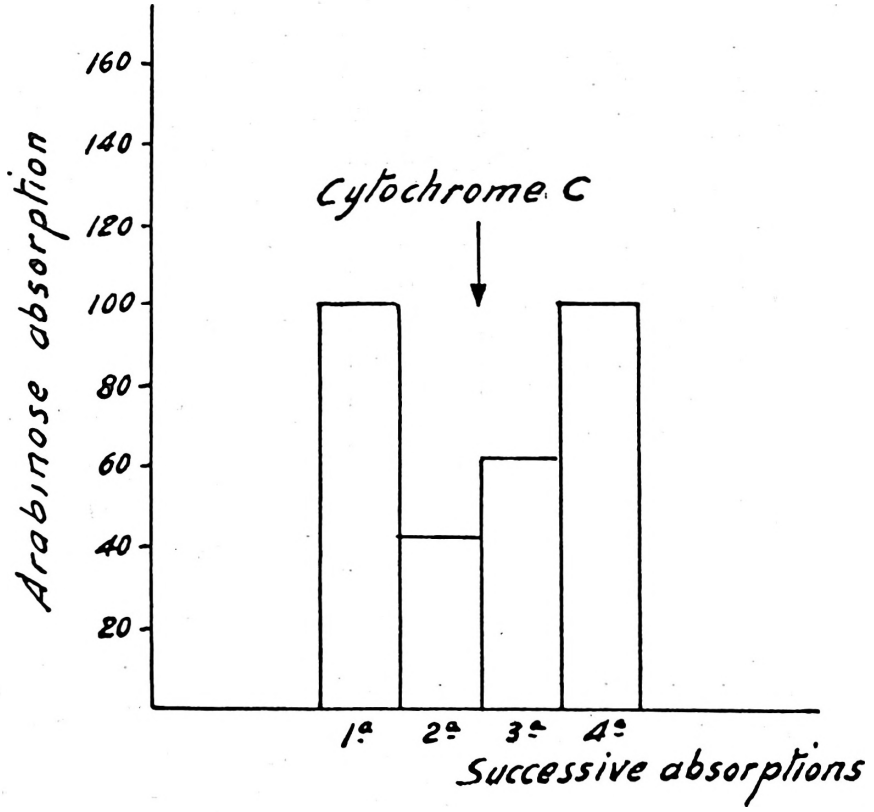

Fig. 3. — Cytochrome effect on the intestinal absorption of arabinose. Absorption time, 60 min.

tion of arabinose. Here the discussion of the results turns out more difficult, because the rate of absorption of the sugar does not stay constant along a certain number of successive absorptions, on the contrary, as GIRÁLDEZ pointed out (2), there is always more absorption on the first than on the following ones. Cytochrome c injected after the second absorption, generally improves the rate of penetration on the following absorptions on which values equal or even greater to the first are reached sometimes (Fig. 3).

If cytochrome c exerts its effect by making the cellular respiration easier, the inhibition of glucose absorption which appears by a certain degree of anoxic anoxia should be able to be compensated. In effect, if the rats breath in an atmosphere whose partial oxygen pressure is of only 60 mm of mercury, the absorption is 35 % inhibited. But if they receive cytochrome posteriously, the absorption, at the same oxygen pressure, becomes normal (Fig. 4).

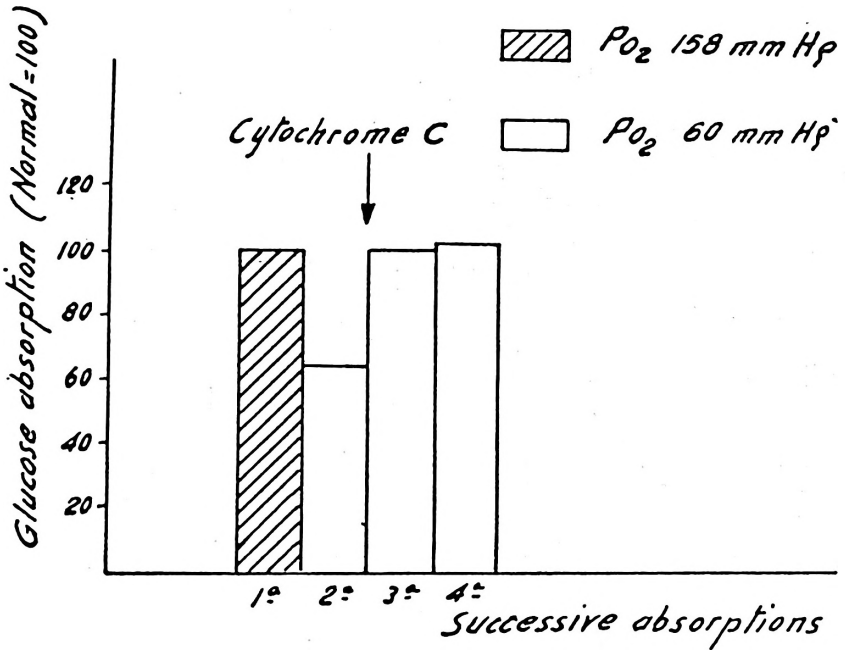

Fig. 4. — Effect of Cytochrome c on the intestinal absorption of glucose in partial anoxic rats. Absorption time, 30 min.

Cytochrome may act facilitating the production of metabolic energy but this must be utilized on the membrane. If through a non penetrating inhibitor this utilization can be bloqued, the cytochrome does not improve the absorption. This is what we have verified through uranyl.

The uranyl ion is a non penetrating inhibitor of the absorption of glucose by yeast (10) and intestine (5). In figure 5 its effects on the intestinal absorption of various sugars are shown. It inhibits the absorption of glucose and galactose but it does not have any effect on fructose and arabinose. The results with arabinose was expected, because this sugar does not seem to be transported. But fructose, which occupies an intermediate position in the selectivity series, must be transported by a mechanism which is not sensible to uranyl, different from that of glucose and galactose.

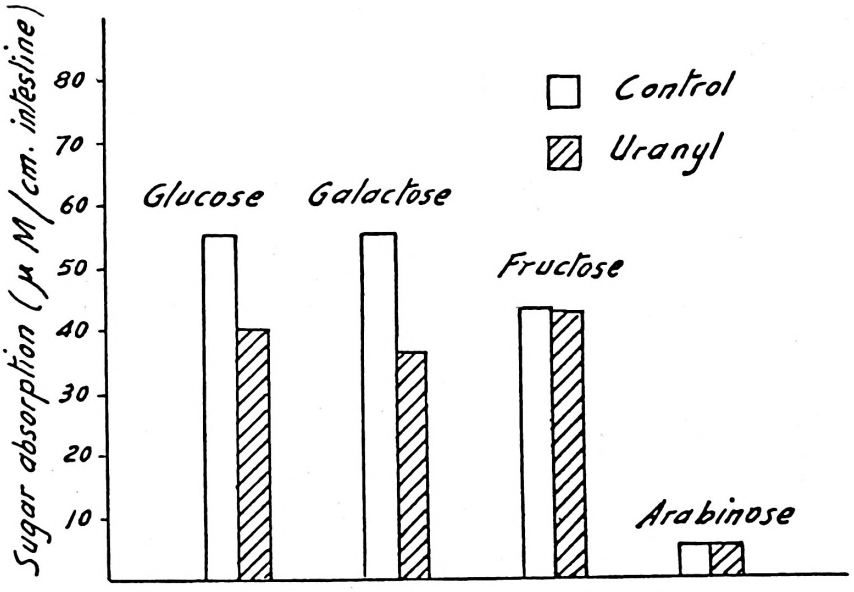

Fig. 5. — Uranyl effect on the intestinal absorption of sugars. Absorption time for glucose, galactose and fructose, 30 min.; for arabinose, 60 min. Uranyl concentration, 5×10^{-4} M.

The inhibition by uranyl is long lasting, it increases with the concentration of the inhibitor up to a certain value (Fig. 6) and it is not reversible upon the habitual intestinal wash out with normal saline solution. On the other hand, the inhibition can disappear with sufficient mucose wash out with versene solution (Fig. 7). This shows that uranyl exerts its action through fixation with determined groups of the cellular membrane from which it can be separated by the deionising action of the versene. According to the experiments of ROTHSTEIN on yeast (11) the bloqued groups probably belong to ATP.

If the rats treated with cytochrome c are subjected to the action of uranyl, the activation of the absorption of glucose by the cytochrome does not appear, but rather the inhbiting effect

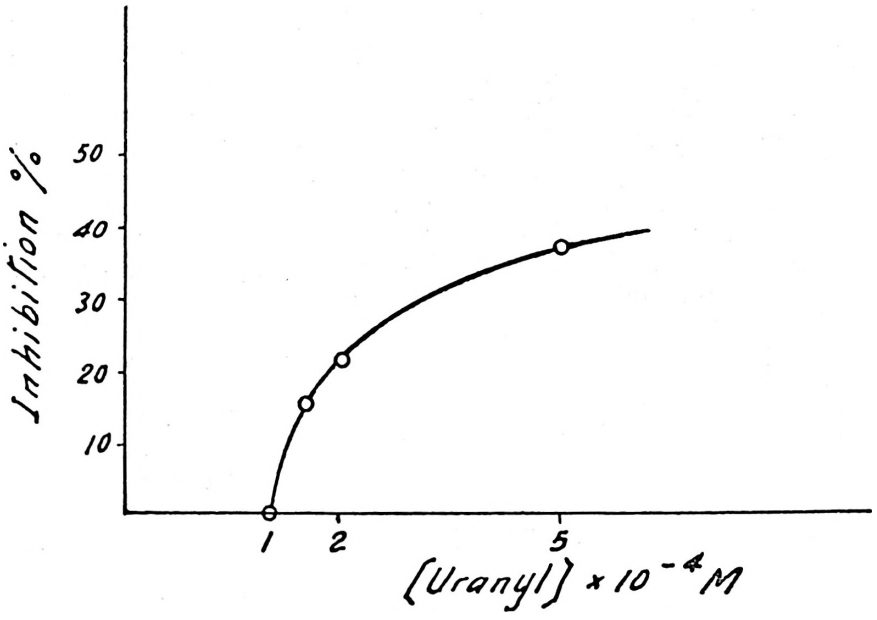

Fig. 6. — Inhibition of the intestinal absortion of glucose by the uranyl

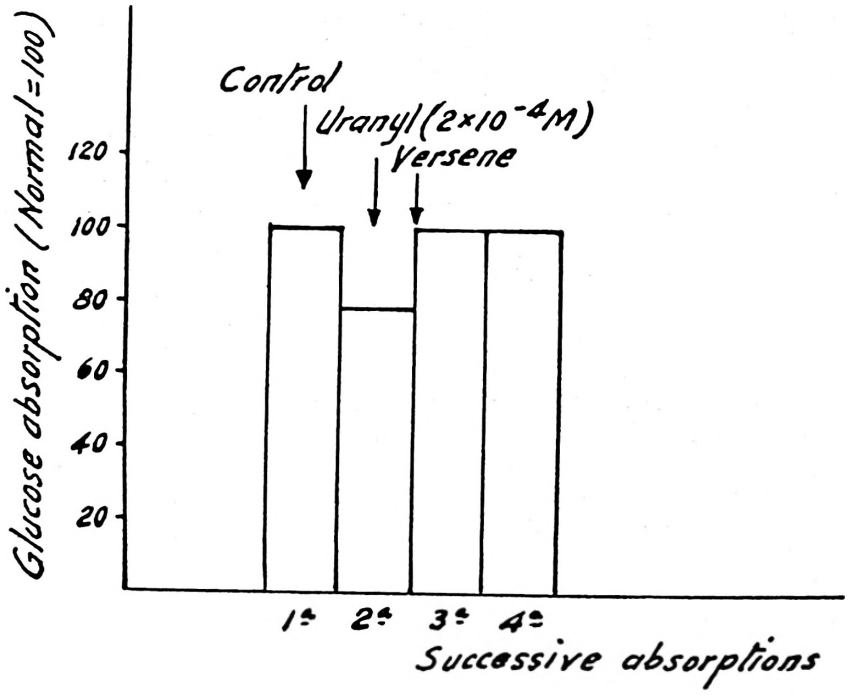

Fig. 7. — Inhibition of the intestinal absorption of glucose by the uranyl and its reversibility by versene. Absorption time, 30 min.

prevails. If the uranyl is posteriously separated from the membrane with versene, the absorption is normalized (Fig. 8).

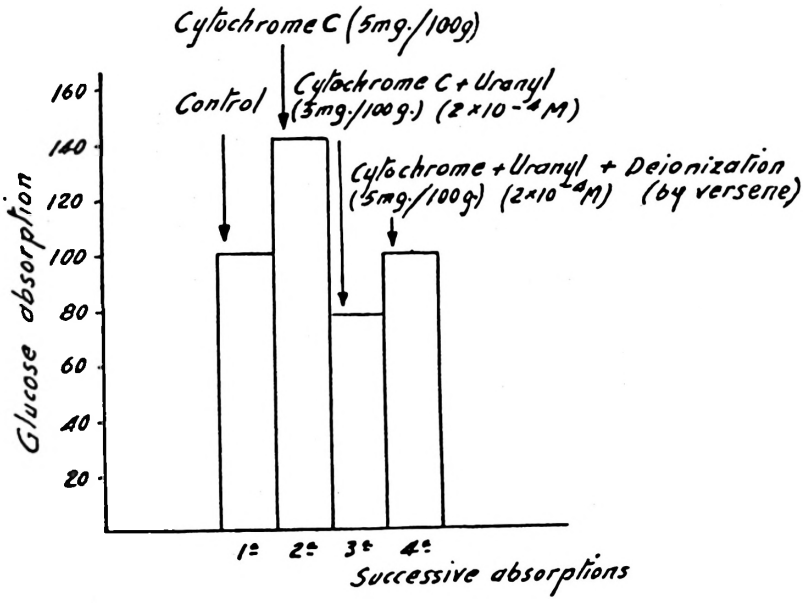

Fig. 8. — Effects of Cytochrome c and Uranyl on the intestinal absorption of glucose. Absorption time, 30 min.

The interpretation of these results is that cytochrome c improves the metabolic productions of energy by the mucose cells, which in part passes to the membrane in the form of energy-rich compounds, from which it is transfered to the transport of sugars facilitating their penetration. This transfer can be bloqued through uranyl by forming complexes with these energy-rich compounds at the membrane level.

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