Effect of Diethylstilbestrol on Glucose Absorption by Rat Small Intestine in vitro

The diphenolic synthetic estrogen, diethylstilbestrol, is a potent inhibitor of sugar transport in the erythrocyte membrane[1]. Since it has been postulated that the carrier for active transport of sugars in the small intestine has a phenol binding site[2], we have studied the effect of diethylstilbestrol in that system.

Material and methods. Sacs of everted mid-small intestine from non-fasted male rats were prepared as described by WILSON and WISEMAN[3]. Each sac (3–4 cm in length) was filled with a measured volume (about 1 ml) of gassed Krebs-Henseleit bicarbonate saline, and incubated with agitation for 1 h at 37 °C in 10 ml of the same medium. Diethylstilbestrol had been previously added to the 'experimental' flasks dissolved in 0.1 ml of 0.1 N KOH, and the same amount of KOH was placed in the 'control' flasks. Following incubation, the final serosal fluid was determined by weighing the sacs before and after emptying.

Glucose concentration was initially the same (5 mM) on both sides of the intestinal wall. In experiments with xylose and arabinose, the sugars were initially placed (20 mM) on the mucosal side only. Glucose was estimated by a glucose-oxidase method[4], xylose and arabinose by the method of SOMOGYI-NELSON[5], and lactic acid by the BARKER and SUMMERSON[6] method.

Results and discussion. The results of experiments with glucose are shown in Table I. Diethylstilbestrol inhibits glucose accumulation on the serosal fluid, so that at $2\times 10^{-4}M$ the drug, already, has practically abolished net transfer of sugar to the serosal side. However, diethylstilbestrol does not prevent the entry of glucose into the cells from the mucosal fluid (Table I, mucosal uptake). Thus, these results suggest that the main effect of the drug in that system is to inhibit the energy-dependent accumulation component of the transfer process[7,8], although they do not exclude some lesser effects on the entry component by binding to the phenol site of the membrane carrier[2].

As shown in Table I, diethylstilbestrol does not modify the rate of glucose utilization and lactic acid production by the tissue, but it has been shown previously that this drug uncouples oxidation from phosphorylation in cyclophorase preparations[9]. Since the produced lactic acid is accumulated on the serosal side against a concentration gradient in both the control and experimental sacs (Table I), it seems that the active accumulation of lactic acid is not so tightly dependent on this last type of energy-yielding process as glucose accumulation.

Finally, Table II shows that diethylstilbestrol hastens passive diffusion of L-arabinose and L-xylose in the small intestine. This fact also seems to be a consequence of the action of diethylstilbestrol on cell metabolism, since a similar effect was found to take place for transfer of L-sorbose and D-ribose in anaerobic conditions[10].

Table I. Effect of diethylstilbestrol on transfer and utilization of glucose, and on production and accumulation of lactic acid

Concentrations of diethylstilbestrol	No. of sacs	Glucose Ser./Muc. ratio[a]	Mucosal uptake[b]	Tissue utilization[b]	Lactic acid Tissue production[b]	Ser./Muc. ratio[a]
Control	20	5.18 ± 0.42	1.95 ± 0.10	1.41 ± 0.09	0.80 ± 0.11	8.76 ± 1.53
$5\times 10^{-4}M$	12	1.19 ± 0.09				
$2\times 10^{-4}M$	20	1.64 ± 0.11	1.43 ± 0.08	1.42 ± 0.09	0.85 ± 0.05	5.43 ± 0.28
$1\times 10^{-4}M$	20	2.12 ± 0.11	1.31 ± 0.07	1.29 ± 0.06	0.67 ± 0.06	5.11 ± 0.42

[a] Ratio of the concentrations in the serosal and mucosal fluids, at the end of the incubation period. Means ± S.E.M. [b] mg/100 mg of fresh tissue. Means ± S.E.M.

Table II. Effect of diethylstilbestrol on passive transfer of L-arabinose and L-xylose

Concentration of diethylstilbes	Ser./Muc. concentration ratio[a] Arabinose	Xylose
Control	0.14 ± 0.01 (10)	0.18 ± 0.01 (6)
$2\times 10^{-4}M$	0.25 ± 0.02 (8)	0.26 ± 0.01 (6)
$5\times 10^{-4}M$	0.29 ± 0.02 (10)	0.28 ± 0.01 (6)

[a] Ratio of the concentrations in the serosal and mucosal fluids at the end of the incubation period. The sugars were initially placed on the mucosal fluid only. The values are means ± S.E.M. Number of sacs in brackets.

Resumen. El dietilestilbestrol inhibe la absorción activa de glucosa en el intestino de rata in vitro, aunque no impide la entrada del azucar en las células de la mucosa. La difusión pasiva de arabinosa y xilosa es facilitada por la droga.

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