ROLE OF CHOLINERGIC AND ADRENERGIC MECHANISMS IN REGULATION OF INTESTINAL ABSORPTION OF MONOSACCHARIDES

I. A. Drzhevetskaya and L. V. Mukhina

UDC 612.332.72:612.89

Experiments carried out on rats by Verzar's method showed that the most marked inhibition of absorption of glucose and arabinose is observed after blocking of the nicotine-like cholinergic structures of the autonomic ganglia and of the autonomic nervous system of the intestine by dicoline. A significant inhibition of resorption of these sugars was also observed after blocking of the central adrenergic structures by chlorpromazine. Blocking of the central muscarine-like and nicotine-like cholinergic mechanisms by administration of benactyzine and gangleron (by intracarotid injection) did not affect the intensity of absorption of these monosaccharides.

* * *

Numerous facts indicate that the absorption of monosaccharides in the intestine is under nervous control [6, 8]. However, the role of the individual chemoreceptors has received little study. Data have been published [7, 9] showing that injection of chlorpromazine, which blocks mainly the adrenergic structures of the reticular formation of the brain stem, into dogs depresses glucose absorption from the small intestine. According to our investigations on dogs with a portal vein fistula of the London [3] type, considerable slowing of glucose absorption is observed during pharmacological blocking of nicotine-like cholinergic (N-cholinergic) systems of the autonomic ganglia by gangliolytic drugs. The importance of other chemosensitive structures has not been investigated.

The object of the present investigation was to compare the effect of pharmacological blocking of adrenergic, muscarine-like cholinergic (M-cholinergic), and N-cholinergic structures of the autonomic ganglia on the intestinal absorption of two monosaccharides: glucose, which undergoes active absorption as a result of its phosphorylation, and arabinose, a pentose whose absorption is determined mainly by its concentration in the digestive canal.

EXPERIMENTAL METHOD

Altogether 66 experiments were carried out on rats by Verzar's method [14]. After laparotomy under thiopental anesthesia, the proximal part of the duodenum was ligated and the intestine was irrigated with several milliliters of physiological saline toward the large intestine. A second ligature was then applied at the boundary between the small and large intestines. Glucose and arabinose were introduced into the intestine as a 5% solution in a dose of 200 mg/100 g body weight. The sugar concentration in the solution injected was measured precisely. The intestine was excised 30 min later, and the volume of fluid contained in it and its sugar concentration were determined by the method of Frank and Kirberger [12]. To determine the absorption, the difference between the quantity of sugar introduced into the intestine and removed from it was determined and expressed as a percentage.

Adrenergic structures were blocked with chlorpromazine (10 mg/kg, intramuscularly), M-cholinergic structures with benactyzine hydrochloride (10 mg/kg, intramuscularly), and N-cholinergic structure with gangleron (1, 2-dimethyl-3-diethylaminopropyl p-isobutoxybenzoate hydrochloride)(10 mg/kg, by intracarotid injection to avoid any effect on peripheral structures). The N-cholinergic systems of the autonomic ganglia were blocked by intramuscular injection of dicoline (dimethiodide of the 2-diethylaminoethyl ester of pipecolic acid) (2 mg/kg). All these compounds were injected 20-30 min before injection of thiopental.

Department of Pathological Physiology, Donetsk Medical Institute (Presented by Academician of the AMN SSSR V. V. Zakusov). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 4, pp. 66-68, April, 1969. Original article submitted May 12, 1968.

TABLE 1. Effect of Neurotropic Drugs on Glucose Absorption (in percent) in the Small Intestine of Rats

Character of experiment	Number of experiments	Glucose absorbed in 30 min (M±m)	P
Control	8	88.0± 5.1	
Injection of chlorpromazine	10	59.0± 1.1	<0.001
Injection of benactyzine	7	84.5± 4.2	>0.6
Injection of gangleron	6	85.0± 4.0	>0.6
Injection of dicoline	10	38.0± 3.0	<0.001

TABLE 2. Effect of Neurotropic Drugs on Arabinose Absorption (in percent) in the Small Intestine of Rats

Character of experiment	Number of experiments	Arabinose absorbed in 30 min (M±m)	P
Control	5	29.0± 2.2	
Injection of chlorpromazine	5	19.3± 1.1	<0.001
Injection of benactyzine	5	27.5± 1.0	>0.5
Injection of gangleron	5	27.0± 1.3	>0.4
Injection of dicoline	5	11.3± 1.0	<0.001

EXPERIMENTAL RESULTS

The results given in Table 1 show that the gangliolytic dicoline caused the greatest inhibition of glucose absorption.

Of the central neurotropic drugs, only chlorpromazine slowed absorption. These results thus suggest that the most important factors regulating glucose absorption are the N-cholinergic structures of the peripheral part of the autonomic nervous system and the central adrenergic structures.

The fact that similar results were obtained with respect to arabinose (Table 2), which is absorbed through processes of osmosis and diffusion, is important in principle. The fact that the neurotropic drugs used had a basically similar effect on absorption of the two monosaccharides indicates that their action is not connected with inhibition of phosphorylation, but with other mechanisms.

When discussing the results of the experiments with dicoline from this aspect, it should be remembered that, like other gangliolytics, it blocks the N-cholingergic structures not only of the autonomic ganglia, but also of the autonomic intramural nervous system of the intestine [2]. Since this latter innervates the villi and controls their motor function, it is evident that administration of dicoline inhibits this important factor essential for the normal course of absorption. This hypothesis is confirmed by the results of an investigation by Ludani and co-workers [13], who demonstrated prolonged inhibition of motor activity of the intestinal villi of dogs after administration of gangliolytics to the animals. Depression of thyroid function by dicoline [4, 5, 10], may also be of some importance, because thyroid hormones activate the absorption of carbohydrates in the intestine [11].

Chlorpromazine blocks mainly the adrenergic structures of the reticular formation, which are abundantly represented in the hypothalamus, stimulation of whose nuclei modifies the intensity of carbohydrate absorption in the intestine [1]. It may therefore be postulated that blocking of the central adrenergic structures by chlorpromazine inhibits the activity of the hypothalamic centers concerned in regulation of the absorption of the intestine. As the results given in Tables 1 and 2 show, blocking of the peripheral N-cholinergic system with dicoline had a much stronger inhibitory action of glucose and arabinose absorption than administration of chlorpromazine. This suggests that the most important factor in the nervous regulation of absorption is the functional state of the intramural nervous system of the intestine, especially the activity of its mediator mechanisms.

LITERATURE CITED

1. P. G. Bogach and Z. A. Dobrovol'skaya, in: Proceedings of a Symposium on the Physiology and Pathology of Absorption in the Gastro-Intestinal Tract [in Russian], Odessa (1964), p. 39.

2. P. P. Denisenko, Gangliolytics [in Russian], Leningrad (1959).
3. I. A. Drzhevetskaya, Fiziol. Zh. SSSR, No. 2, 207 (1962).
4. G. P. Smirnov, Probl. Éndokrinol., No. 4, 18 (1956).
5. G. P. Smirnov, Probl. Éndokrinol., No. 4, 22 (1957).
6. R. O. Faitel'berg, Absorption in the Digestive Apparatus [in Russian], Moscow (1960).
7. R. O. Faitel'berg, V. S. Vasilevskii, and N. K. Bocharova, Fiziol. Zh. (Ukr.), No. 4, 473 (1963).
8. R. O. Faitel'berg, Absorption of Carbohydrates, Proteins, and Lipids in the Intestine [in Russian], Leningrad (1967).
9. V. R. Faitel'berg-Blank and L. S. Grebneva, in: Physiology and Pathology of the Limbico-Reticular Complex [in Russian], Moscow (1968), p. 158.
10. N. F. Shaposhinkova, Vrach. Delo, No. 3, 48 (1961).
11. J. R. Bronk and D. S. Parsons, J. Physiol. (London), 179, 323 (1965).
12. H. Frank and E. Kirberger, Biochem. Z., 320, No. 359 (1950).
13. G. Ludani, T. Gati, J. Rausch, et al., Arch. Int. Pharmacodyn., 127, 402 (1960).
14. F. Verzar, Absorption from the Intestine, London (1936).