ROLE OF VITAMIN K IN BIOSYNTHESIS OF SOME EXOENZYMES OF THE DIGESTIVE ORGANS

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Avitaminosis K was produced in albino rats either by keeping them on a special diet (primary avitaminosis) or by ligating the bile duct (secondary avitaminosis). The pancreatic lipase and amylase activity and the alkaline phosphatase and enterokinase activity in the duodenal mucosa were significantly lowered in these rats.

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Most workers who have studied the mechanism of action of vitamin K in the body have concentrated their attention on the part played by vitamin K in the synthesis of certain proenzymes of the blood clotting system. At the same time, there is convincing evidence that the action of vitamin K in the body covers a wider spectrum. Views on the possible pathways of its participation in metabolic processes must be clarified. In face of changes in the metabolism of certain biogenic amines determining the character of secretion of the digestive glands accompanying vitamin K deficiency [1, 2], we decided to investigate the role of vitamin K in the synthesis of exoenzymes by the digestive organs.

In the present investigation the effect of vitamin K on pancreatic lipase and amylase activity and on the activity of enterokinase and alkaline phosphatase in the duodenal mucosa was studied.

EXPERIMENTAL METHOD

Experiments were performed on 105 male albino rats weighing 160-180 g. Activity of the enzymes was determined in extracts from homogenates of the pancreas and duodenal mucosa. Pancreatic lipase activity was determined by the method of G. E. Shlygin, L. S. Fomina, and Z. M. Pavlova [5], and pancreatic amylase activity by the classical Wohlgemuth method modified in the laboratory of Normal and Pathological Physiology of Digestion, Institute of Nutrition, Academy of Medical Sciences of the USSR; enterokinase was investigated by G. K. Shlygin's method [6], and alkaline phosphatase by the method of L. S. Fomina and coworkers [4].

In the animals of group 1 lipase, enterokinase, and alkaline phosphates activity was studied in avitaminosis E produced by ligation and excision of the bile duct [3], during treatment of such avitaminosis by the synthetic vitamin K vikasol in a dose of 2.5-5 mg/kg body weight daily by subcutaneous injection and in control intact animals. This group of rats received the ordinary vivarium diet.

The animals of group 2 were kept in special cages preventing the possibility of coprophagy, on a vitamin K-deficient diet [7]. Rats kept under the same conditions on an artificial vitamin K-deficient diet but receiving vikasol in addition at the rate of 10 mg/100 g diet served as controls for this group of experiments. The development of avitaminosis K was judged from prolongation of the prothrombin time measured by Quick's one-stage method [11].

EXPERIMENTAL RESULTS

In secondary avitaminosis K (Table 1) caused by ligation of the bile duct, a marked decrease of activity of all enzymes studied in this group of experiments was observed ($P < 0.001$ for all enzymes). The

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TABLE 1. Activity (in conventional units/g tissue) of Pancreatic Lipase and of Enterokinase and Alkaline Phosphatase from the Duodenal Mucosa of Rats with Secondary Avitaminosis K (M±m)

Series of rats	Enzyme		
	lipase	entero-kinase	alkaline phosphatase
Control (n = 28)	11,729±758	5348±306	12,405±504
Animals with avitaminosis K (n = 30)	1475±132	1840±139	3068±195
Animals with avitaminosis K receiving vikasol (n = 19)	1722±152	2815±285	7009±979

Note. Here and in Table 2, n denotes number of animals.

TABLE 2. Activity (in conventional units/g tissue) of Pancreatic Lipase and Amylase and of Enterokinase and Alkaline Phosphates from the Duodenal Mucosa of Rats with Primary Avitaminosis K (M±m)

Series of rats	Enzyme			
	lipase	amylase	entero-kinase	alkaline phosphatase
Control (n = 15)	10,227±879	24,130±2896	6154±411	9217±730
Animals with avitaminosis K (n = 13)	7186±784	8318±808	2832±264	2565±249

pancreatic lipase activity, for instance, was 13% of the activity of this enzyme in the intact animals, the enterokinase activity 34%, and alkaline phosphatase activity 25%. Injection of vikasol into rats with avitaminosis K did not restore the initial activity (the activity of the corresponding enzyme in the control animals), although the lipase activity increased by 20%, the enterokinase activity by 50%, and the alkaline phosphatase activity by 130%. The increase in lipase activity under the influence of vikasol was not statistically significant ($P > 0.05$).

To exclude the influence of biliary stasis and of changes associated with the interruption of entry of bile into the duodenum, a series of experiments was performed on rats with primary alimentary avitaminosis K (Table 2).

The experiments with alimentary avitaminosis K revealed the same relationship as the series of experiments with secondary avitaminosis. Pancreatic lipase activity amounted to 70% of the activity of this enzyme in control animals (kept on a vitamin K-deficient diet with vikasol), the pancreatic amylase activity was 34%, and the enterokinase and alkaline phosphatase activities 46 and 28% respectively. We are inclined to attribute the small difference in alkaline phosphatase activity of individual animals of both groups (12,405±504 and 9217±730, see Tables 1 and 2) to defects in the salt mixture No. 446 [13].

The undoubted role of vitamin K in the biosynthesis of exoenzymes of the digestive organs revealed by experiments on rats with primary and secondary avitamosis K is a new fact. It is difficult at present to explain the role of vitamin K in this process. It is probably too early to accept the hypothesis of Quick and Collentine [12] regarding the formation of an active enzyme responsible for prothrombic synthesis by vitamin K with a hypothetical apoenzyme. In experiments using actinomycin D, Olson [10] concluded that vitamin K stimulates DNA-dependent synthesis of the corresponding messenger RNA, thereby inducing prothrombin formation. There is more abundant evidence of the participation of vitamin K in oxidative phosphorylation [8, 9, 14].

The most likely explanation of the results obtained is that vitamin K, by taking part in oxidative phosphorylation, makes available a certain quantity of high-energy compounds required for synthetic processes in the body.

LITERATURE CITED

1. N. G. Bogdanov, Z. V. Urazaeva, and N. I. Yalovaya, Abstracts of Scientific Proceedings of the Tenth All-Union Congress of the I. P. Pavlov Physiological Society [in Russian], Vol. 2, No. 1, Moscow-Leningrad (1964), p. 107.

2. N. G. Bogdanov and B. V. Polushkin, Byull. Éksp. Biol., No. 11, 28 (1965).
3. B. A. Kudryashev, Dokl. Akad. Nauk SSSR, 60, No. 8, 1469 (1948).
4. L. S. Fomina, In the book: Modern Methods of Biochemistry [in Russian], Vol. 1, Moscow (1964), p. 292.
5. G. K. Shlygin, L. S. Fomina, and Z. M. Pavlova, In the book: Modern Methods in Biochemistry [in Russian], Vol. 1, Moscow (1964), p. 298.
6. G. K. Shlygin, In the book: Modern Methods in Biochemistry [in Russian], Vol. 1, Moscow (1964), p. 282.
7. M. S. Mameesh and B. C. Johnson, Proc. Soc. Exp. Biol. (New York), 101, 467 (1959).
8. C. Martius and D. Nitz-Litzow, Biochim. Biophys. Acta, 13, 152 (1954).
9. C. Martius and R. S. Beyer, Biochim. Biophys. Acta, 28, 663 (1958).
10. R. E. Olson, Canad. J. Biochem., 43, 1565 (1965).
11. A. J. Quick, J. Biol. Chem., 109, P23 (1935).
12. A. J. Quick and G. Collentine, J. Lab. Clin. Med., 36, 976 (1950).
13. H. Spector, J. Biol. Chem., 173, 659 (1948).
14. M. M. Weber, In the book: Abstracts of Section Proceedings of the Fifth International Biochemical Congress [in Russian], Vol. 2, Moscow (1961), p. 383.