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EFFECT OF BODY VITAMIN K LEVEL ON COLLAGEN METABOLISM IN THE SKIN

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In rats with secondary avitaminosis-K induced by Pelentan the collagen content in the skin is reduced and the content of free hydroxyproline increased. The rate of acid hydrolysis of collagen is increased. Vitamin K (Vikasol*) prevents the development of the changes in collagen metabolism.

KEY WORDS: collagen; vitamin K; avitaminosis-K.

Vitamin K and its synthetic analogs have been used with success in the treatment of diseases accompanied by lesions of the connective tissue [4, 7]. The therapeutic value of vitamin K in these diseases and during administration of anticoagulants with indirect action can be explained by its ability to restore disturbances of fibrillogenesis and of the resistance and permeability of the tissues [1, 3, 5, 8, 9]. The state of these tissue functions is known to be largely dependent on collagen and mucopolysaccharide metabolism.

It was accordingly decided to study collagen metabolism in the skin of rats receiving vitamin K (Vikasol*) and its antagonist, Pelentan.

EXPERIMENTAL METHOD

Experiments were carried out on rats weighing 130-150 g, receiving daily intramuscular injections of Vikasol solution in a dose of 10 mg/kg for 10 days or Pelentan by mouth in a dose of 40 mg/kg for 15-20 days, or both preparations together for 20 days. In special experiments rats with avitaminosis-K, at the conclusion of their course of Pelentan, received Vikasol in a dose of 10 mg/kg daily for 8 days. Some rats after developing avitaminosis-K were kept under ordinary conditions. The development of avitaminosis-K was monitored by determining the prothrombin time. The rats were decapitated at the end of the experiments. A weighed sample of skin was homogenized and collagen was extracted from it with hot TCA solution [11]. Hydrochloric acid was added to the resulting extracts (up to a concentration of

*Bisulfite derivative of 2-methyl-1,4-naphthoquinone — Translator.

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TABLE 1. Indices of Collagen Metabolism (in μmoles/g dry tissue) in Skin of Rats with Different Vitamin K Levels (M ± m)

Experimental conditions	Free hydroxyproline	Hydroxyproline of collagen	
		hydrolysis for 2 h	hydrolysis for 6
Control (n = 14)	1,67± 0,097	272,9± 6,7	594,3± 5,5
Vikasol (n = 10)	1,60± 0,10	267,1± 6,8	622,6± 16,9
Pelentan (n = 13)	3,73± 0,31*	325,2± 4,9*	452,2± 10,1*
Pelentan followed by Vikasol (n = 11)	1,76± 0,15	289,2± 2,9	559± 36,6
8 Days after end of course of Pelentan (n = 10)	1,97± 0,26	302,5± 10,8	534,8± 26,3
Pelentan together with Vikasol	1,62± 0,10	276,3± 7,4	586,5± 12,3

*These values differ by a statistically significant degree from the control ($P < 0.05$).

6 N) and they were hydrolyzed in sealed ampules at 120°C for 2 and 6 h. The hydroxyproline content was determined in the digests [2, 13]. The hydroxyproline level in 2-h digests reflected the rate of hydrolysis of collagen, and in the 6-h digests the total quantity of collagen in the skin. To determine the free hydroxyproline content, 100 mg of skin, freed from other tissues, was minced with scissors and homogenized in 1 ml water. After 30 min 1 ml of 10% TCA solution was added to the mixture and it was centrifuged at 3000 rpm for 5 min. The residue was washed twice with 0.5 ml of the same TCA solution. The resulting supernatants were pooled and the hydroxyproline content in them was determined.

EXPERIMENTAL RESULTS AND DISCUSSION

The results are given in Table 1. Administration of Vikasol had virtually no effect on the collagen content in the skin, in agreement with the data in the literature [12].

In avitaminosis-K, however, the total collagen content in the skin was reduced, and there was a parallel increase in the rate of its hydrolysis and in the level of free hydroxyproline.

In the modern view, during collagen biosynthesis hydroxyproline is formed only by oxidation of peptide-bound proline residues [6, 10, 14]. Free hydroxyproline is not incorporated into the polypeptide chain of collagen. Consequently, the accumulation of free hydroxyproline observed in avitaminosis-K is evidently the result of increased catabolism of collagen. Evidence of this is given by the decrease in the total collagen content in the skin and also in the rate of its acid hydrolysis.

Changes in the skin of rats with avitaminosis-K were reversible. They disappeared when the Pelentan was stopped and, especially quickly, during subsequent saturation with vitamin K. During combined administration of Pelentan and Vikasol the collagen content in the skin did not decrease. This points to a causative role of vitamin K deficiency in the development of disturbances of collagen metabolism in the skin.

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