ROLE OF THE THYROID HORMONES IN REGULATING CONTACT DIGESTION

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Administration of thyroid extract to albino rats by gastric tube or subcutaneous injection of L-thyroxine to the animals for 15 days had no significant effect on invertase, alkaline phosphatase, and dipeptidase activity in a homogenate of the mucous membrane obtained from the proximal portion of the small intestine but did affect transfer of the enzymes from their sites of synthesis in the cytoplasm of the intestinal epithelial cells to the membranes of the microvilli on the brush border. Invertase activity on the surface of the mucous membrane was reduced under these conditions, while alkaline phosphatase activity was increased.

The role of hormones in the regulation of contact hydrolysis in the small intestine may be twofold: first, they control enzyme synthesis in the intestinal epithelial cells [12, 14], and second, they may influence the transfer of enzymes from their sites of synthesis to the membranes of microvilli on the brush border. Information on these aspects of the problem is very limited. Results have been obtained to show the effect of ACTH [9] and adrenocortical hormones [2, 8] on the synthesis and transfer of certain intestinal hydrolytic enzymes.

In the present investigation attention was concentrated on the role of the thyroid gland, whose functions are closely connected with those of the pituitary–adrenal system, in the regulation of these processes.

EXPERIMENTAL METHOD

Experiments were carried on noninbred male albino rats weighing 145-180 g in which a state of hyperthroidism was induced by daily administration of a suspension of dry thyroid extract in a dose of 20 mg/100 g body weight through a gastric tube or by subcutaneous injection of L-thyroxine in a dose of 100 mg/100 g body weight for 15 days. The attainment of the desired effect was judged from the change in the animals' oxygen consumption, which was measured before the beginning and after the end of administration of the substances.

The animals were sacrificed on the day after the last administration of the thyroid preparations. Segments of the proximal portion of the small intestine were cut and turned inside out and their oxygen and glucose consumption measured in a Warburg's apparatus; invertase, alkaline phosphatase, and dipeptidase activity (in a homogenate of the intestinal mucosa and on its surface) was determined as described by Ugolev as a criterion of the state of contact digestion. Invertase activity was determined by Ugolev's modification [10] of Nelson's method alkaline phosphatase activity by a modified Klein's method [13], and dipeptidase activity (with glycine-DL-leucine as the substrate) by the method of Ugolev and Timofeeva [10].

In all the series of experiments at least ten rats were sacrificed at each time. Intact rats from the same batch, kept under identical conditions, were used as the control.

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TABLE 1. Activity of Hydrolytic Enzymes of the Small Intestine in a State of Hyperthyroidism (M ± m)

Experimental conditions	Invertase (in mg% reducing sugars)		Alkaline phosphatase (in international units)		Dipeptidase (in conventional units)	
	surface of mucosa	homogenate	surface of mucosa	homogenate	surface of mucosa	homogenate
Control	43,0±3,3	90,0±9,9	12,9±2,7	65,6±7,5	43,5±2,1	54,3±2,4
Thyroid 15 days	30,6±2,4	81,0±5,2	26,0±5,8	66,0±6,1	39,0±2,5	54,0±2,7
	$P<0,05$		$P<0,05$			
Control	39,0±1,8	60,8±3,6	39,2±5,5	71,6±8,8	50,6±1,5	56,7±3,7
Thyroid 15 days	23,2±3,1	65,3±9,9	65,8±6,1	83,8±4,9	36,2±5,6	55,1±2,2
	$P<0,01$		$P<0,01$		$P=0,02$	

EXPERIMENTAL RESULTS

The oxygen consumption in the rats receiving thyroid extract rose from 303.3 to 357.3 ml/h/100 g body weight ($P=0.05$). The oxygen consumption of the segments of small intestine also rose after thyroid administration from 1112 ±57.3 to 1394 ±61.2 μliter/h/g fresh weight of intestine ($P< 0.01$). No significant changes were found in the glucose consumption of the segments of small intestine in a state of hyperthyroidism (experiment 34.7 ±2.4; control 31.8 ±2.6 mg%/h).

The activity of these three enzymes showed changes of different types. As Table 1 shows, in a state of hyperthyroidism the invertase activity in the homogenate was not appreciably changed, while on the surface of the mucous membrane it rose by 29% ($P < 0.05$) under the influence of thyroid and by 40.5% ($P < 0.01$) under the influence of thyroxine.

Alkaline phosphatase activity on the surface of the mucosa, on the other hand, was almost doubled during thyroid administration ($P < 0.05$). The same effect was found during thyroxine administration, when activity of the enzyme on the surface of the mucosa was increased by 67.9% ($P < 0.01$). Alkaline phosphatase activity in the homogenate of the mucosa like invertase activity, differed very little in a state of hyperthyroidism from its activity in the control animals. In hyperthyroidism no significant changes were found in the dipeptidase activity in the homogenate. In the experiments with thyroxine, activity on the surface of the mucosa was reduced ($P=0.02$), but this was not observed during thyroid administration.

These results show that administration of thyroid or thyroxine had no appreciable effect on the activity of the investigated enzymes in the homogenate of the intestinal mucosa, i.e., it had no effect on the total stock of enzymes, but it caused changes in the activity of certain enzymes on the surface of the mucosa, i.e., in the zone of contact digestion, mainly as the result of transfer of the enzymes. The action of the thyroid preparations was expressed in different ways: the activity of some enzymes on the surface of the mucosa, for example alkaline phosphatase, was increased, whereas that of others (invertase, for example) was inhibited. The varied character of the effect of thyroid hormones on enzyme activity is well known [11, 18], although much of the evidence is contradictory. There are statements to the effect that alkaline phosphatase activity in the succus entericus is increased in dogs with thyrotoxicosis [7].

It is difficult at present to suggest the mechanism of action of thyroid hormones on activity of the intestinal enzymes investigated in these experiments. There is reason to suppose that it may be not only direct, but also indirect, through the pituitary–adrenal cortex system. According to the literature, if thyroid hormones are present in excess, adrenal cortical function is stimulated [4, 15-17], but in severe thyrotoxicosis it is exhausted [1, 5, 6]. L. Ya. Borisova and G. S. Pochechueva, working in the writers' laboratory, found an increase in the corticosterone concentration in the adrenals from 21.7 ±2.2 to 42.9 ± 2.9 mg% in rats in a hyperthyroid state, but a decrease to 13.6 ± 1 mg% in a hypothyroid state.

Thyroid hormones, together with corticosteroids, thus play a role in the regulation of contact digestion, affecting mainly the transfer of enzymes from the sites of their synthesis to the membranes of the microvilli on the brush border, and possibly also on the special arrangement of the enzymes and their molecular structure. These processes play an essential role in the mechanism of compensation of disturbances of the digestive function of the intestinal epithelium. As was reported earlier [3], enzyme activity in the zone of contact digestion can be maintained under certain conditions at a normal or nearly normal level despite deficient enzyme formation. This is a fact of compensatory importance.

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