EFFECT OF THYROID HORMONE ON BLOOD AND LIVER GLUCOSE-6-PHOSPHATASE ACTIVITY

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In recent years considerable attention has been paid by biochemists and endocrinologists to hepatic glucose-6-phosphatase, because changes in its activity may contribute to the elucidation of certain obscure problems of the pathogenesis of disturbances in carbohydrate metabolism.

Not much work has been done on the effect of hormonal factors on glucose-6-phosphatase, and the results have mostly been contradictory. Thus adrenalectomy caused an appreciable fall in the activity of this enzyme, which was restored to normal following administration of cortisone or corticosterone. These hormones also activated hepatic glucose-6-phosphatase of unoperated rats [9,10]. Hepatic glucose-6-phosphatase activity was also depressed in hypophysectomized animals, and adminstration of cortisone or thyroxine to such animals caused less reactivation of the enzyme than when they were given simultaneously [6].

Enhancement of hepatic glucose-6-phosphatase activity has been reported by one worker (referring to unpublished data) in thyrotoxic rats [7]. The opposite effect was found in young rats under prolonged treatment with small doses of thyroxine [8].

In the present research we examined the effect of thyroid hormone on the activity of glucose-6-phosphatase in the liver and blood plasma of rats and mice. Parallel measurements of alkaline phosphatase activity were made.

TABLE 1. Glucose-6-phosphatase and Alkaline Phosphatase Activities of the Liver and Blood Plasma of Normal and Thyrotoxic Rats (as Micronomes of Phosphate per 1 g in 1 hour)

Serial No. of animal	Glucose-6-phosphatase				Alkaline phosphatase			
	liver		plasma		liver		plasma	
	normal	thyrotoxicosis	normal	thyrotoxicosis	normal	thyrotoxicosis	normal	thyrotoxicosis
1	368	395	0,13	0,13	—	—	—	—
2	271	314	0,00	0,00	31,0	81,3	1,42	2,32
3	243	325	0,26	0,00	31,0	42,6	—	—
4	252	334	0,00	0,00	69,5	46,5	3,61	2,45
5	209	325	0,38	0,00	31,0	42,6	7,43	2,77
6	255	310	0,00	0,00	27,0	42,6	9,89	2,45
7	341	465	0,26	0,45	31,0	50,3	8,00	6,95
8	332	446	0,19	0,26	27,0	42,6	11,60	3,88
9	243	368	0,00	0,13	42,6	50,3	—	—
10	352	368	0,00	0,19	27,0	31,0	5,35	1,42
Mean	286,6± 18,7	365,0± 19,0	0,122± 0,047	0,116± 0,050	35,2± 2,62	47,7± 2,81	6,75± 1,45	3,17± 0,74
	$t = 2,96$		$t = 0,08$		$t = 3,26$		$t = 2,20$	
	$P<0,01$		$P>0,5$		$P<0,01$		$P<0,05$	

EXPERIMENTAL METHOD

For our experiments we used 20 rats and 22 mice. Thyrotoxicosis was induced in half of the animals by feeding daily doses of thyroidin (0.2 g to rats, and 0.1 g to mice) for a month [1]. The remaining animals served as controls.

Pairs of rats or mice (one from the thyroidin-fed group, and one from the control group) were killed by decapitation. Blood was collected in centrifuge tubes containing heparin, the cells were spun down, and the plasma was collected.

The liver was removed without delay, chilled on ice, and homogenized in a glass homogenizer at 0°, in 10 volumes of physiological saline. Undiluted plasma was taken for assay.

Glucose-6-phosphatase activity [5] was assessed in homogenate and plasma from the amount of inorganic phosphate liberated from glucose-6-phosphate after 10 min of incubation with liver homogenate, or after 1 hr of incubation with plasma. Alkaline phosphatase was estimated under the same conditions, by Bodansky's method [2].

Enzyme activity was expressed as micromoles of phosphate released from the respective substrates under optimum conditions during 1 hr of incubation at 37° with 1 g of liver tissue or with 1 ml of plasma.

EXPERIMENTAL RESULTS

Experimental thyrotoxicosis in rats (Table 1) and in mice (Table 2) was associated with significant rises in hepatic glucose-6-phosphatase activity ($P<0.01$ and $P< 0.001$). In order to ascertain whether this effect might not have been due to direct action of the hormone on glucose-6-phosphatase activity we incubated homogenates of normal rat liver, as described above, with different amounts of thyroxine. No change in the activity of the enzyme was observed in the presence of $0.5 \cdot 10^{-3}$M, $0.5 \cdot 10^{-5}$M, and $0.5 \cdot 10^{-7}$M thyroxine.

We could find no evidence of the release of glucose-6-phosphatase into the blood of animals of the experimental groups.

The opinion of some authors [3,4] that enzymes may be released into the blood stream when their content in tissues is greatly increased is thus not confirmed by our results. Glucose-6-phosphatase activity varied within very wide limits in the blood of normal and thyrotoxic rats, but the mean values were practically identical (0.122 ± 0.047 and 0.116 ± 0.050).

Parallel measurements of hepatic alkaline phosphatase activity showed changes similar to those found for glucose-6-phosphatase (Table 1).

The alkaline phosphatase activity of plasma did not vary parallel with that of liver. In the given case, rise in alkaline phosphatase activity of the liver was associated significantly ($P<0.05$) with a fall in plasma.

TABLE 2. Glucose-6-phosphatase Activity of the Liver of White Mice (as Micromoles of Phosphate per 1 g/h).

Serial No. of animal	normal	thyrotoxicosis
1	275	410
2	357	360
3	282	482
4	**407**	407
5	**388**	486
6	**542**	463
7	**336**	604
8	**380**	646
9	254	636
10	339	627
11	334	570
Mean	$354 \pm 22,7$	$516 \pm 30,1$

$t = 4,31$
$P<0,001$

Activation of glucose-6-phosphatase of the liver in experimental thyrotoxicosis may partly account for the disturbances in carbohydrate metabolism observed during thyroid hyperactivity.

SUMMARY

Experimental thyrotoxicosis of mice and rats causes a significant ($P< 0.01$ and $P< 0.001$) rise in hepatic glucose-6-phosphatase activity, but did not affect that of blood plasma. Hepatic alkaline phosphatase activity was raised in thyrotoxic rats, while plasma alkaline phosphatase activity was lowered.

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