Differences in Regulation between Rat Liver and Kidney Tyrosine Aminotransferases

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Rat liver tyrosine aminotransferase (L-tyrosine:2-oxoglutarate aminotransferase; EC 2.6.1.5.) has been studied thoroughly with respect to its inducibility by various hormones. Recently, it has been shown that this enzyme can be stimulated by cyclic AMP [1] and by theophylline [2], which is capable of elevating intracellular levels of cyclic purine nucleotides. Moreover, this enzyme was shown to be induced *in vivo* by administration of quinolinic acid [3, 4], a tryptophan metabolite effecting hypoglycemia [5, 6]. A hypoglycemic agent could act on tyrosine aminotransferase activity at least through two mechanisms. First, the decrease in blood glucose level might result in an enhanced secretion rate of glucagon, which in turn would be able to induce tyrosine aminotransferase [7, 8] via cyclic AMP. Furthermore, low glucose concentrations could effect a sensitization of the mechanism involved in tyrosine aminotransferase formation to glucocorticoids, since it has been demonstrated that glucose depresses the glucocorticoid-dependent induction of amino acid catabolizing enzymes, in particular tyrosine aminotransferase [9].

As shown in Table 1, hepatic tyrosine aminotransferase is induced by theophylline, quinolinic acid, and quinaldic acid as well. Administration of quinaldic acid, which is likewise a tryptophan metabolite, results also in hypoglycemia, however by another mechanism as quinolinic acid [5, 6]. This supports the assumption that no primary actions of these tryptophan metabolites are involved in the induction of the enzyme, but that they are rather acting via hypoglycemia.

By contrast with the hepatic enzyme, rat kidney tyrosine aminotransferase activity is not altered by any of the three agents. This is somewhat surprising in the case of theophylline, since gluconeogenesis appears to be controlled by cyclic AMP levels in the cortical region of the kidney [10]. In the liver, gluconeogenesis and amino acid degradation are clearly co-regulated processes. The non-inducibility of renal tyrosine aminotransferase indicates that this is perhaps not the case in the kidney cortex. The possibility that the concentration of theophylline used in the experiments was too low does not seem to be very probable, as it was high enough to induce a significant increase in the activity of the hepatic enzyme, and as the mechanism which leads to accumulation of cyclic AMP is the same in both organs.

Since the cyclic AMP level of the kidney cortex is not controlled by glucagon, but rather by parathyroid hormone [11], one mechanism by which quinolinic and quinaldic acids could act, was on principle excluded. The second possibility, due to diminution of a glucose effect, does not seem to be realized in this organ as well. Obviously, the rat kidney cortex lacks some of the control mechanisms that are characteristic for liver regulation.

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compound injected	organ	hours after injection			
		0	4	6	8
theophylline	liver	164 ± 14	275 ± 81	304 ± 72	284 ± 84
theophylline	kidney	13.4 ± 3.3	13.8 ± 4.8	12.9 ± 3.6	13.7 ± 4.2
quinolinic acid	liver	164 ± 14	638 ± 114	987 ± 128	1068 ± 125
quinolinic acid	kidney	13.4 ± 3.3	13.4 ± 4.8	13.9 ± 4.5	12.8 ± 4.2
quinaldic acid	liver	164 ± 14	607 ± 72	814 ± 138	715 ± 117
quinaldic acid	kindey	13.4 ± 3.3	12.8 ± 4.2	12.1 ± 4.5	11.6 ± 4.8

Table 1. Rat liver and kidney tyrosine aminotransferase activities after administration of theophylline, quinolinic acid, and quinaldic acid. Injections were given intraperitoneally, at doses of 12 mg per 100 g body weight in the case of theophylline, or 25 mg per 100 g body weight for quinolinic and quinaldic acids. Enzyme activity (expressed as μmoles product/g fresh tissue/hour) was measured according to Diamondstone [12]. Data are given as means ±3-fold standard errors.

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