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Uptake of Radioactive Zinc and Manganese in Damaged Rat Liver. (27180)

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The effect of hepatic damage upon the metabolism of various trace metals has not been well defined. Vallee(1) reported decreased serum and hepatic zinc levels and increased zincuria in patients with post-alcoholic cirrhosis. Butt(2) found decreased hepatic manganese content in patients with hepatic necrosis. On the other hand, Smith *et al.* (3) demonstrated an increased hepatic uptake of Mg^{28} after hepatotoxic doses of CCl_4 in the rat. The present report concerns the uptake of two trace metals, Zn^{65} and Mn^{54} by normal and CCl_4 damaged rat livers.

Methods. Zn^{65} Uptake. A solution of Zn^{65} supplied as the carrier free chloride, was diluted with demineralized water to contain 0.2 μc of zinc per ml and the pH was adjusted to 6.0. Nineteen Holtzman, female, albino rats, weighing 250 g ($\pm$ 3 g) were given 0.5 ml CCl_4 by subcutaneous injection. As a control, an equal number of female rats were injected subcutaneously with 0.5 ml of 0.9% sodium chloride. Forty-eight hours later, 1 ml of the Zn^{65} solution was injected subcutaneously. Animals were sacrificed in equal groups at 1, 3, and 9 hours following injection of the isotope. Tissues were removed, briefly dipped in N. saline to remove blood from the surface, and dried at 100°C for 24 hours. After drying, the tissues were passed through a tissue mill and weighed aliquots were counted in a scintillation well. Whole organ wet weights were recorded for several rats from both control and CCl_4 groups. No significant difference was noted between the two groups for any specific organ.

Mn^{54} Uptake. Mn^{54} supplied as the carrier free chloride was diluted with demineralized water to contain 0.2 μc of manganese per ml and the pH was adjusted to 6.0. Twelve Holtzman, female, albino rats, weighing 237 g ($\pm$ 3 g) were injected subcutaneously with 0.5 ml of CCl_4. As a control an equal number of female rats were injected subcutaneously with 0.9% sodium chloride. Forty-eight hours later, 1 ml of Mn^{54} solution was injected subcutaneously. Animals were sacrificed at 3 hours following injection of the isotope. At sacrifice, tissues were removed and treated in a manner similar to those of the zinc experiment.

Results. Zn^{65} Uptake. Results are reported as % uptake per gram of dry weight, *i.e.*,

$$\left(\frac{\text{NCPM/g dry tissue}}{\text{NCPM injected}}\right) = \% \text{ uptake per g dry wt.}$$

No significant difference in uptake of Zn^{65} in the liver or other tissues was noted at any time period between animals injected with CCl_4 and controls (Table I). Liver tissue sections of animals injected with CCl_4 showed swelling and disruption of mitochondria, diffuse fatty infiltration and centralobular necrosis. Elevation of the dose of isotope failed to bring about any change in distribution or per cent uptake for any given tissue.

As shown in Table II, Mn^{54} uptake was significantly reduced in the livers of rats receiving CCl_4. Elevated doses of Mn^{54} failed to affect the general pattern of Mn^{54} uptake by damaged hepatic tissue.

Discussion. These data indicate that hepatic uptake of zinc is not affected by acute damage to the liver of rats. No studies on the effect of chronic liver damage on zinc uptake have been done to date which would be

TABLE I. Uptake of Zn^{65} in Control Rats and Those with CCl_4 Intoxication.

	Control			CCl_4		
	1 hr	3 hr	9 hr	1 hr	3 hr	9 hr
Blood	.8 ± .7*	.5 ± .1		.8 ± .6	.5 ± .02	
Heart	1.2 ± .4	1.1 ± .1	1.6 ± .1	1.1 ± .3	.9 ± .1	1.4 ± .1
Kidney	4.6 ± 2.0	5.4 ± .1	4.6 ± .4	4.1 ± .8	4.6 ± 1.4	4.9 ± .9
Liver	5.4 ± 2.8	4.1 ± .5	4.5 ± .4	4.1 ± 1.6	3.6 ± 1.2	4.4 ± .8

* Mean % uptake ± S.D.

comparable to the reported change in zinc content in human cirrhotic livers(1).

On the other hand, manganese uptake was significantly decreased in the acutely damaged livers. Decreased manganese content in necrotic human livers has been reported by Butt *et al.*(2). Of further interest is the finding of an increased uptake of magnesium in CCl_4 poisoned rat livers previously reported(3).

The explanation for such difference in behavior of these 3 metals during acute liver damage from CCl_4 is not clear. It is possible that differences in intracellular distribution of trace elements may play an important part in the metabolic characteristics of any given element. Using methods of fractionation and spectrographic analysis, Edwards and associates have reported metal values for several cellular components(4). Manganese was found to be concentrated to the highest degree in the mitochondria and microsomes whereas zinc was found to be in highest concentration in the nuclei and supernatant. Inasmuch as the morphological effects of CCl_4 in our study were most pronounced in the swelling and disruption of the liver mitochondria, alterations in ability of that organ to utilize manganese in a normal manner do not seem surprising. On the other hand, absence of morphological change in the nuclei may in part explain the lack of deviation in zinc uptake between normal and CCl_4 damaged hepatic tissue.

TABLE II. Uptake of Mn^{54} in Control Rats and Those with CCl_4 Intoxication.

	Control	CCl_4	
	3 hr	3 hr	
Blood	.03 ± .03*	.03 ± .02	
Heart	2.7 ± .2	3.7 ± .8	$P = >.05$
Kidney	8.2 ± 1.7	9.0 ± 2.0	$P = >.05$
Liver	6.3 ± 1.1	4.0 ± 1.7	$P = <.02$

* Mean % uptake ± S.D.

Summary. The effect of CCl_4 administration on distribution of Zn^{65} and Mn^{45} in rat liver, heart and kidney was studied. Hepatic uptake of Mn^{54} was significantly decreased from control values with no alteration in other tissues. Zn^{65} distribution did not change.

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