Comparative Study of the Effect of Cd on the Oxidative Phosphorylation of Liver and Kidney Mitochondria of Rat

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Abstract: Cd (10 mg/Kg of body weight) uncoupled the oxidative phosphorylation of liver and kidney mitochondria *in vivo*. MgCl_2 administered intraperitoneally immediately after injection of Cd into rat had protective effect against uncoupling dysfunction of liver mitochondria, but did not against uncoupling dysfunction of kidney mitochondria *in vivo*. A similar phenomenon was observed *in vitro*.

Keywords: Liver and kidney mitochondria—Oxidative phosphorylation—Uncoupling action of Cd—Protective effect of Mg

INTRODUCTION

It has already been reported that Cd uncoupled isolated normal mitochondria *in vitro*¹⁾ and also *in vivo* liver mitochondria²⁾. The uncoupling action of Cd was suppressed by Zn administered simultaneously with Cd³⁾. Ogata *et al.* reported that the presence of MgCl_2 suppressed the uncoupling effect of Cd on liver mitochondria⁴⁾. However, there is no comparative study of the protective effect of Mg on liver and kidney mitochondria from the uncoupling action of Cd. We found that *in vivo* liver mitochondria were protected from the uncoupling effect of Cd by Mg administered simultaneously with Cd intraperitoneally, but that *in vivo* kidney mitochondria were not protected. This report describes our findings.

MATERIALS AND METHODS

Donryu male rats (weighing about 200 g) were used. Rats were divided into two groups. One group was administered CdCl_2 (10 mg/Kg of body weight) intraperitoneally. The other group was administered simultaneously MgCl_2 (50 mg/Kg of body weight) intraperitoneally in addition to Cd. Two hours later, rats were decapitated, and liver and kidney were isolated quickly; mitochondria

were prepared according to the method described previously⁵⁾ and oxidative phosphorylation was measured in a medium containing mitochondria (3–5 mg protein/ml), 0.15 M KCl, 10 mM Tris-HCl buffer (pH 7.5), 2.5 mM potassium phosphate buffer (pH 7.5) 5 mM sodium succinate, and 0.3 mM sodium ADP at 25°C with a Galvanic oxygen electrode. Cadmium content of isolated liver and kidney mitochondria of rat was determined by atomic absorption spectroscopy. Mitochondrial protein was determined by a biuret method.

RESULTS AND DISCUSSION

Table 1 shows the main results of this experiment. In the control group, liver mitochondria show that respiratory control index (RCI) was 5.8 and ADP/O ratio was 1.9, indicating a tightly coupled state. On the contrary, kidney mitochondria were shown to be in a less coupled state than liver mitochondria due to damage in preparation.

When 10 mg/kg body weight of Cd was injected into rats, liver mitochondria were uncoupled (RCI was decreased from 5.8 to 3.6, ADP/O ratio was also decreased from 1.9 to 1.6) and mitochondrial Cd content increased from 5.3 to 173 ng/mg protein. Kidney mitochondria were also uncoupled, and decreases in RCI and ADP/O ratio and increase in Cd content were also observed.

When MgCl_2 was administered simultaneously RCI and ADP/O ratio of liver mitochondria in the Cd-administered group showed normal values, indicating that liver mitochondria were protected from the uncoupling effect of Cd. However, RCI and ADP/O ratio of kidney mitochondria in the Cd-administered group were not changed by the simultaneous administration of Mg, indicating that, unlike liver mitochondria, kidney mitochondria were not protected. These results were confirmed *in vitro* where the presence of Mg (5 mM) protected the normal isolated liver mitochondria from the uncoupling action of Cd, but did not protect the normal isolated kidney mitochondria.

Table 1. Effect of Cd on oxidative phosphorylation of liver and kidney mitochondria in vivo and protective effect of Mg on the uncoupling action of Cd.

		Control	CdCl_2	$\text{MgCl}_2 + \text{CdCl}_2$
Liver	RCI	5.8 ± 0.26	3.6 ± 0.92	5.7 ± 0.66
	ADP/O	1.9 ± 0.09	1.6 ± 0.09	1.9 ± 0.17
	Concentration of Cd*	5.3 ± 7.5	173 ± 90	74 ± 37
Kidney	RCI	3.6 ± 0.27	2.3 ± 0.54	2.3 ± 0.47
	ADP/O	1.8 ± 0.08	1.5 ± 0.10	1.5 ± 0.16
	Concentration of Cd*	trace	29 ± 21	36 ± 13

* ng/mg protein

All values are expressed as the average of six animals $\pm$ standard deviation.

These results suggest that the uncoupling mechanism of liver and kidney mitochondria induced by Cd is not the same and that in the case of liver mitochondria, Mg-binding site is the same as the uncoupling site of Cd, but that this is not the case in kidney mitochondria.

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