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Effect of cadmium ($CdCl_2$) on lipid peroxidation and activities of antioxidant enzymes

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Cadmium is known as one of the most toxic environmental and industrial pollutants [1, 2]. Among the various effects induced by cadmium in biological systems, either *in vitro* and *in vivo*, that most often observed is the destruction of membrane polyunsaturated fatty acids which is dependent on oxygen free radicals. As cadmium, under conditions prevailing in the cells, is a poor electron acceptor and donor, the mechanisms responsible for generation of free radicals in the presence of cadmium are not well understood. Studies on the toxic effects of cadmium following acute exposure concerned, up to date, mainly the testis, liver, and heart [3] but little is known about its effect on gastrointestinal tract.

Besides skin and lung, the gastrointestinal tract is the main portal of entry of xenobiotics in animals, not only for such compounds present in food, or in the form of orally administered drugs but also for a significant amount of environmental chemicals, and among them cadmium seems to play an important role.

The aim of our studies was to investigate the effect of cadmium on the intensity of lipid peroxidation in villus and crypt cells of rat small intestine. The influence of this metal ion on glutathione content and the activities of GSH[1]-dependent enzymes forming an antioxidant system, was also investigated.

The gut sac prepared from rat small intestine was filled with NaCl/P buffer, pH 7.2 (control) or with either 0.5 mM or 1.5 mM $CdCl_2$ and incubated at 37°C. After 60 min, the villus and crypt cells were isolated by the method of Weiser [4]. The cells were suspended in 5 vol. of 50 mM Tris/HCl buffer (pH 7.6) containing 250 mM sucrose and 4 mM $MgCl_2$ and homogenized for 20 s. Lipid peroxidation was measured by the method of Slater [5] directly in the homogenate and expressed as malondialdehyde (MDA). Enzymes activities were measured in supernatant after centrifugation of homogenate at 16000 × *g* for 20 min. Activities of glutathione synthetase [6], γ-glutamyltransferase [7], glutathione peroxidase [8], glutathione-*S*-transferase [9], and glutathione reductase [10] as well as glutathione (GSH + GSSG) content [11] were determined. Protein was measured by the method of Lowry *et al.* [12] using bovine serum albumin as a standard.

Incubation of the rat small intestine with cadmium (Cd^{2+}) resulted, in a dose-dependent manner, in increased production of MDA in both types of the cells studied (Tables 1 and 2).

Cadmium in concentration of 0.5 mM did not affected lipid peroxidation or the activities of glutathione dependent enzymes in either type of the intestinal cells studied. However, in concentration of 1.5 mM cadmium induced peroxidation of lipids, as well as increased glutathione peroxidase and glutathione reductase activities, whereas those of other glutathione dependent enzymes remained unchanged. These effects were observed in both types of cells, but were more pronounced in the villus ones.

[1]Abbreviations: GSH, glutathione; GSSG, oxidized glutathione; MDA, malondialdehyde

Table 1

The effect of cadmium (Cd^{2+}) on lipid peroxidation and activities of antioxidant enzymes in villus cells of rat small intestine

Villus cells	Control	$CdCl_2$	
		0.5 mM	1.5 mM
Lipid peroxidation (MDA/mg protein)	0.18 ± 0.01	0.16 ± 0.01	0.25 ± 0.02
GSH synthetase (IU/mg protein)	4.75 ± 0.77	4.10 ± 0.30	5.25 ± 0.30
γ-Transpeptidase (IU/mg protein)	13.10 ± 1.03	12.60 ± 0.59	14.0 ± 0.43
GSH peroxidase (μmol/mg protein)	1.30 ± 0.20	1.30 ± 0.05	1.80 ± 0.10
GSSG reductase (nmol/mg protein)	0.70 ± 0.04	0.80 ± 0.02	0.95 ± 0.02
GSH transferase (μmol/mg protein)	1.80 ± 0.30	1.80 ± 0.10	1.75 ± 0.10

Table 2

The effect of cadmium (Cd^{2+}) on lipid peroxidation and activities of antioxidant enzymes in crypt cells of rat small intestine

Crypt cells	Control	$CdCl_2$	
		0.5 mM	1.5 mM
Lipid peroxidation (MDA/mg protein)	0.46 ± 0.05	0.44 ± 0.08	0.75 ± 0.08
GSH synthetase (IU/mg protein)	4.65 ± 0.90	4.50 ± 0.85	4.35 ± 0.80
γ-Transpeptidase (IU/mg protein)	9.15 ± 0.30	10.20 ± 0.51	9.70 ± 0.72
GSH peroxidase (μmol/mg protein)	1.18 ± 0.25	1.25 ± 0.18	1.75 ± 0.12
GSSG reductase (nmol/mg protein)	1.15 ± 0.15	1.45 ± 0.10	1.75 ± 0.06
GSH transferase (μmol/mg protein)	0.75 ± 0.06	0.70 ± 0.04	0.70 ± 0.04

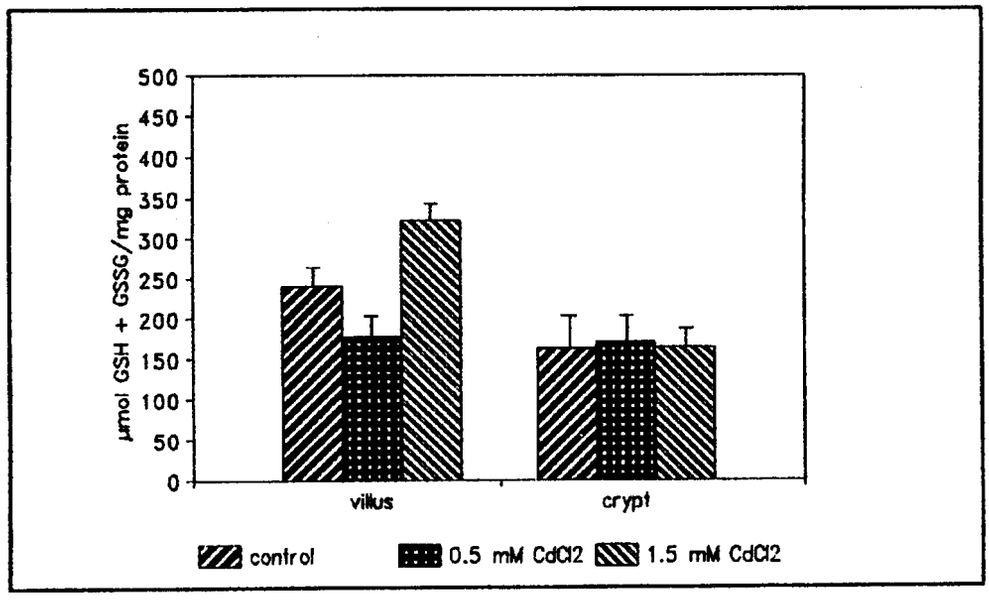

Fig. 1. The effect of cadmium on the content of glutathione in villus and crypt cells of small rat intestine

The incubation of intestine with 1.5 mM cadmium solution resulted also in changes of total glutathione (GSH and GSSG) amount (Fig. 1), but only in villus cells in which activities of glutathione peroxidase and glutathione reductase were also higher than in control.

These data suggest that villus cells are more susceptible to cadmium than the crypt ones. This could be due to their direct contact with cadmium in the experimental conditions. The results obtained indicate that in the intestine, like in other tissues [3], cadmium can induce lipid peroxidation which is accompanied by an adaptive increase in the activities of glutathione dependent antioxidant enzymes.

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