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PERCHLORIC ACID-SOLUBLE PROTEINS IN BLOOD SERUM AND IN TISSUES OF RATS INTOXICATED WITH CADMIUM

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Rats were treated with cadmium chloride (0.030 mM Cd^{2+}/kg body weight) orally, daily for six weeks. An increase of perchloric acid soluble proteins and protein bound carbohydrates (hexosamines, sialic acids) was shown in the serum, liver, lungs and kidneys. A decrease of these indices was observed in the skin.

Cadmium compounds are highly toxic to human beings and animals (4, 5, 11, 12, 23). Acute poisonings are rare but chronic or subchronic exposure to cadmium-containing substances is relatively frequent as a result of industrial or environmental pollution. Cadmium turnover in the living organism is very slow. The element is cumulated in the kidneys and liver (2, 7, 17, 19, 24), and certain amounts are localized in other organs.

The toxic action of cadmium was found to resemble an acute phase reaction and an increased level of seromucoid was observed after acute cadmium intoxication (10, 27, 28, 29). These observations suggested that glycoproteins play part in the biochemical mechanism of tissue injury induced by cadmium. The aim of the present study was to estimate the effect of subchronic cadmium intoxication on perchloric acid soluble protein content in rat's tissues.

MATERIAL AND METHODS

Male Wistar rats (160 g body weight) obtained from the Central Experimental Animal House of the Silesian School of Medicine were used for investigations. The exposed group (20 animals) was given a cadmium chloride solution as drinking water for six weeks. The solution conta-

ined 1.5 mM Cd^{2+}/dm^3 (= 168.62 mg Cd^{2+}/dm^3). The mean consumption of the solution by a single rat was 3.2 cm^3/24 h. The daily dose of cadmium given orally was 0.0048 mM per animal, i. e. 0.03 mM Cd^{2+}/kg of body weight (= 3.37 mg Cd^{2+}/kg of body weight). The control group (20 animals) received tap water only. Both groups were fed standard rat food.

When the experiment was over, the rats were killed by decapitation, and the blood was taken. Samples of the liver, lungs, kidneys, heart muscle and skin (from the abdominal region) were taken at autopsy.

Perchloric acid soluble proteins were estimated according to *Winzler* (26), protein bound hexosamines were determined according to *Schmidt* (22) and protein bound sialic acids were assayed with the thiobarbituric method of *Warren* (25). Statistical differences between the groups were estimated with Student's »t« test.

RESULTS

Table 1 shows the results of perchloric acid soluble protein content in the blood serum and tissues. Cadmium intoxication increased the seromucoid concentration in the blood serum and perchloric acid soluble protein content in the liver, lungs and kidneys. A decrease of these proteins was shown in the skin.

Table 1
Perchloric acid-soluble proteins

	Control group	Cadmium-intoxicated group
Serum	137.2 ± 8.4	176.5 ± 7.2*
Liver	0.715 ± 0.045	0.845 ± 0.072*
Lungs	0.423 ± 0.025	0.475 ± 0.033*
Kidneys	0.878 ± 0.086	1.390 ± 0.105*
Heart muscle	0.520 ± 0.045	0.522 ± 0.072
Skin	0.520 ± 0.035	0.305 ± 0.038

Results expressed as μmol of tyrosine/dm^3 of serum or g of wet tissue.
*Statistical significance $p < 0.01$

The content of protein bound hexosamines is presented in Table 2. The changes are similar to those observed for the content of perchloric acid soluble proteins. An increase was observed in the serum, liver, kidneys and a decrease was found in the lungs and skin.

Protein bound sialic acids content is shown in Table 3. An increase was found in the blood serum, liver, lungs, kidneys and heart muscle.

Table 2
Protein-bound hexosamines

	Control group	Cadmium-intoxicated group
Serum	2125.0 ± 38.4	2475.0 ± 69.7*
Liver	27.5 ± 2.2	34.3 ± 3.0*
Lungs	12.5 ± 1.3	8.8 ± 0.8*
Kidneys	10.1 ± 0.5	12.4 ± 0.7*
Heart muscle	10.0 ± 1.5	10.1 ± 2.6
Skin	11.3 ± 0.8	7.5 ± 1.2*

Results expressed as mg of glucosamine/dm^3 of serum or g of wet tissue.
*Statistical significance $p < 0.01$

Table 3
Protein-bound sialic acids

	Control group	Cadmium-intoxicated group
Serum	547.5 ± 35.4	707.5 ± 52.7*
Liver	0.575 ± 0.089	0.724 ± 0.102*
Lungs	1.050 ± 0.125	1.357 ± 0.137*
Kidneys	0.634 ± 0.112	1.124 ± 0.154*
Heart muscle	0.570 ± 0.117	0.711 ± 0.095*
Skin	0.525 ± 0.065	0.530 ± 0.157

Results expressed as mg of N-acetylneuramic acid/dm^3 of serum or g of wet tissue.
*Statistical significance $p < 0.01$

DISCUSSION

The mechanism of toxic action of cadmium in animals and in the human body seems to be very complicated and multidirectional. Cadmium ions act as inhibitors or activators of the activity of numerous enzymes and lead to significant disturbances in metabolic pathways. The obtained results suggest that tissue glycoproteins are influenced by cadmium. Changes in the blood serum may be connected with liver injury. *Koj* and co-workers (14, 15) suggested that serum glycoproteins were produced in the liver as a response to various types of injury (inflammation, intoxication etc). Serum glycoproteins inhibit some proteinases

and protect tissues against damage caused by lysosomal proteolytic enzymes. The role of tissue glycoproteins is unknown but it is suggested that they may act like serum compounds. The described changes suggest that subacute intoxication with cadmium leads to changes similar to chronic inflammation. Significant changes in the kidneys are probably caused by cadmium accumulated in this organ (2, 10, 13, 20, 24). The kidneys and the liver are tissues rich in glycoproteins. Evident changes were observed in the lungs. The lungs are also rich in proteins bound to carbohydrates, but these complexes are different than those in the kidney or liver (1, 3, 6, 8, 9).

The mechanism of the described changes is unknown. A direct action of cadmium on protein (and glycoprotein) biosynthesis is postulated (18, 21, 29). An indirect action is also possible. Cadmium compounds may inhibit various enzymes and these cause liberation of lysosomal enzymes. The liberation enzymes according to *Koj* (15) modify glycoprotein synthesis in the liver. This indirect mechanisms does not explain tissue changes of perchloric acid soluble proteins and further studies are needed.

Relatively small changes in the skin glycoprotein content suggest that structural glycoproteins, i. e. glycoproteins firmly bound to collagen fibres are not affected by cadmium (16). This phenomenon is also unclear because there are observations indicating cadmium influence upon collagen metabolism in the skin (own unpublished data).

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Sažetak

PROTEINI TOPLJIVI U PERKLORNOJ KISELINI U KRVNOM SERUMU I TKIVIMA ŠTAKORA OTROVANIH KADMIJEM

Svakodnevno, tijekom šest tjedana, štakori su primali otopinu kadmijeva klorida (0,030 mM $Cd^{2}+$/kg tjelesne težine) u vodi za piće. U serumu, jetri, plućima i bubrezima tretiranih štakora došlo je do porasta sadržaja proteina topljivih u perklornoj kiselini kao i ugljikohidrata vezanih za proteine (heksosamini i sijalična kiselina). U koži štakora primijećeno je smanjenje spomenutih proteina i ugljikohidrata.

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