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ELIMINATION DYNAMICS OF CADMIUM, ADMINISTERED BY A SINGLE INTRAPERITONEAL INJECTION, IN COMMON CARP, *CYPRINUS CARPIO* L.

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Background. Chemical substances, including heavy metals, introduced into aquatic ecosystem can disturb the homeostasis of a habitat. The aim of this study was to assess the effects of cadmium compounds on common carp, *Cyprinus carpio* L. and to follow the toxicodynamics of cadmium elimination from intoxicated fish once they were transferred to a clean ambience.

Material and methods. Common carp were given a single intraperitoneal injection of a sub-lethal cadmium dose (10 μg · kg^{-1} body weight) to assess their detoxification potential following transfer to uncontaminated habitat. The 60-day experiment was divided into 8 stages during which various organs and tissues of the fish (liver, kidneys, skin, gills, alimentary tract, and muscles) were examined and subjected to assays for cadmium contents at pre-set times. Cadmium was determined with flameless graphite furnace atomic absorption spectrometry (GF-AAS) in a ZL 4110 Perkin Elmer spectrometer after wet digestion in concentrated HNO_3 in CEM MDS 2000 microwave oven.

Results. The fish intoxicated with Cd were sluggish, their responses to light and sound were much slower than those of the control fish. The cadmium level was observed to change with time: after initial cadmium accumulation in the tissues, the xenobiotic was eliminated. The experiment explains changes in the intoxicated carp system during the process of detoxification. The highest biological half-life ($t_{1/2}$) of cadmium was recorded in the muscles (37 days), the lowest being typical of the liver (3.4 days).

Conclusion. During detoxification, cadmium was observed to be redistributed among the organs. Metal elimination rate was depended on organ and varied from 0.001 to 0.006 μg · day^{-1}. A long-term effect of sub-lethal intoxication was an about 10-percentage-point reduction of the fish body weight.

Key words: fish, carp, *Cyprinus carpio*, cadmium, intoxication, elimination, dynamics.

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INTRODUCTION

When released to or introduced into ecosystems as a result of multifaceted human activity, various chemical elements, including heavy metals, become pollutants which adversely affect the natural environment. Chemical changes disturb the homeostasis of an ecosystem, thus preventing it from proper functioning. This in turn, affects individual development of both plants and animals. Biological effects of disturbed chemical homeostasis appear in the environment much earlier, before symptoms and biochemical changes appear in individual organisms.

Environmental pollution and the resulting changes are related to the constant transport and exchange of materials. Depending on their properties, pollutants and contaminants of various kinds differ in the pathways and intensity of their transfer to the soil, water, and air, and thence to plant and animal bodies. All pollutants affect the health state of organisms as a result of direct or indirect effects, the latter ensuing through accumulation of toxic compounds ingested with food. The fish are directly associated with water; they are an important component of human diet. For humans, they can be a source of xenobiotics that adversely affect human life functions (Żmudzki and Szkoda 1996).

The aim of the present study was to assess effects of cadmium compounds on common carp, *Cyprinus carpio* L. exposed to cadmium via an intraperitoneal injection, and to follow the toxicodynamics of cadmium elimination from intoxicated fish once they were transferred to a clean ambience. Specifically, dynamics of absorption, transfer, and—especially—elimination of toxic substances after a single intraperitoneal injection were followed and changes in the fish body during those processes were observed.

MATERIALS AND METHODS

The study involved individuals of common carp, *Cyprinus carpio* L. obtained from the experimental station of the Agricultural University of Szczecin. A total of 120 individuals measuring 17.5–20.2 cm and weighing 88.3–138.7 g were used. At the onset and on termination of the experiment, the carp were 3- and 5.5 month-old, respectively. After their delivery to the laboratory, the fish were placed in six 120-l aerated tanks, 20 individuals in each; the tanks were filled with tap water. To dechlorinate the tank water and to bring its temperature to the ambient level, the tanks were filled and aerated for 48 hours prior to fish release. Under such conditions, the fish were acclimated for 14 days. The tank water was changed daily; during acclimation, the fish were in condition. The carp were fed the Aller pelleted feed mix containing 37 % protein and 12 % fat; the feed was identical to that applied in culture at the experimental station. The daily food ration was 3.4 ± 0.2 g per fish. Throughout the experiment, the tank water temperature oscillated around 21 ± 2°C; the dissolved oxygen content, pH, and hardness of the water were 8.0–9.0 $mg \cdot l^{-1}$, 7.0–7.5, and 10.71 $mval \cdot l^{-1}$, respectively.

The experiment involved a single intraperitoneal injection of cadmium. Each fish was randomly assigned to one of three groups, 40 individuals each; each group was subdivided into two sub-groups of 20 individuals per tank. The first group was a control and consisted of individuals, which were not subject to any treatment; this was the so-called physiological group (W_{Fiz}). The second group (W_{H_20}) consisted of fish that received a single intraperitoneal injection of 1 ml deionised water. The fish in the third group (W_{Cd}) were given a single injection of aqueous cadmium (Cd^{2+}) solution in the form of cadmium (II) nitrate (V), applied at a dose of 10 μg Cd · kg^{-1} body weight.

The experiment took 60 days after the injection. The water used for injection and for preparing the cadmium solution to be injected was deionised and UV sterilised in an EASY Pure UV apparatus (Barnstead). Random samples of 5 fish each were collected from each group prior to the injection (hour 0) and 6 hours post injection as well as after 1, 3, 7, 14, 30, and 60 days.

Chemical assays were performed on samples of gills, anterior and mid-posterior parts of the alimentary tract, liver, kidneys, skin, and muscles, dissected from each fish. The tissues were frozen and kept at –20°C until analysed.

Cadmium effects on carp behaviour were observed throughout the experiment. External morphological changes in those individuals selected for assays were recorded; during necropsy, the appearance and consistence of gills and viscera was described as well.

Prior to the actual assay, 1-g tissue samples (weighed to 0.001 g) were mineralised wet in 3 ml concentrated HNO_3 in a CEM MDS 2000 microwave oven. The solution obtained was quantitatively transferred to polyethylene bottles and brought to 30 g with deionised water. The samples prepared this way were assayed for Cd content.

Cadmium was determined with flameless graphite furnace atomic absorption spectrometry (GF-AAS) in a ZL 4110 Perkin Elmer spectrometer.

The tissue cadmium content was calculated from a relevant calibration curve, accounting for data produced by blind samples. Cadmium contents are reported in μg·g^{-1} wet weight (μg·g^{-1} ww).

The data obtained were used in toxicokinetic calculations utilising formulae given by Grabowski (2003). The following toxicokinetic and toxicodynamic parameters were calculated: area under curve (AUC), area under first moment curve (AUMC), mean retention time (MRT), distribution coefficient (V_d), biological half-life ($t_{1/2}$), organ clearance (Cl), elimination rate constant (β), initial concentration, recorded at the start of the experiment (C_o), maximum concentration (C_{max}), time of maximum concentration (t_{max}), last recorded concentration (C_{last}), time of last sampling (termination of the experiment) (t_{last}).

The results were subjected to statistical treatment with the aid of Statistica 6.0 software. The data were tested for normality of distribution with the Kolmogorov–Smirnov test and were subject to one- and multi-way analysis of variance (ANOVA, Scheffé's test) at the significance level of $P = 0.05$.

RESULTS

Cadmium intoxication induced changes in carp behaviour. The fish affected were sluggish and tended to stay near the bottom of a tank; their responses to light and sound were much slower than those of the control fish and the fish injected with deionised water. As of day 14 of the experiment, some cadmium-injected fish developed ecchymoses on the fins. The autopsy revealed liver hyperaemia and ecchymoses on the kidneys 7 days post-injection, while after 14 days the gill lamellae were anaemic. After 14 days, the cadmium-injected carp (W_{Cd}) lost appetite, their feed consumption until the termination of the experiment being lower than that in the remaining groups (W_{Fiz}, W_{H_2O}). On the other hand, behaviour, external appearance, and feed consumption of the control fish (W_{Fiz}) and those injected with deionised water only (W_{H_2O}) did not change. The fish receiving both types of injection developed, during 24 h, clearly visible changes at the injection site.

Cadmium contents were assayed in the kidneys, anterior and mid-posterior parts of the alimentary tract, gills, muscles, and the skin. Statistically significant differences between cadmium contents in the injected fish and those of the control and water-injected groups were found in all the organs except muscles (Table 1). Throughout the experiment, cadmium contents in the organs of the intoxicated carp, generally higher than those in the other two groups, were observed to change.

All the organs of the cadmium-exposed fish showed increasing cadmium contents at the initial phase of the experiment, compared to the physiological and water-injected groups (Table 1). As of the moment of injection, cadmium was absorbed by, distributed among, and accumulated in various fish organs; the metal was subsequently eliminated (Table 1). The fastest response to cadmium injection was observed in the gills the cadmium content of which peaked (0.122 $\mu g \cdot g^{-1}$ ww) as early as after 24 hours post injection.

Following intoxication, the highest cadmium accumulation was observed in kidneys (0.402 $\mu g \cdot g^{-1}$ ww) and liver (0.328 $\mu g \cdot g^{-1}$ ww), the peak values being observed 7 days post injection.

It has to be added that once the maximum content had been reached in the liver, the cadmium content dropped as a result of the metal being eliminated and was observed to increase again. Therefore, on day 60 post-injection, the liver cadmium content was still high; this was related to cadmium metabolism and its transfer from other organs (Table 2).

The anterior part of the alimentary tract absorbed and accumulated cadmium until day 7 of the experiment when the maximum value (0.091 $\mu g \cdot g^{-1}$ ww) was recorded. Between day 7 and 14, cadmium was distributed within the anterior part of the alimentary tract, while as of day 14, the metal began to be eliminated. On day 30, cadmium was transported from the anterior part of the alimentary tract to the liver. That process continued until the end of the experiment (Table 2, Fig. 1).

Table 1

Cadmium contents in organs of the intoxicated and non-intoxicated fish

Organ	Fish Group	Cd content [μg·g^{-1} ww*]			Statistical significance of differences, $P < 0.05$	
		$\bar{x} \pm s$	Min.	Max.	BG	WG
Kidney	W_{Fiz}	0.031 ± 0.006	0.021	0.046	a	–
	W_{H_2O}	0.032 ± 0.007	0.022	0.048	a	–
	W_{Cd}	0.252 ± 0.102	0.033	0.416	b	+
Liver	W_{Fiz}	0.053 ± 0.007	0.041	0.067	a	–
	W_{H_2O}	0.056 ± 0.015	0.006	0.089	a	–
	W_{Cd}	0.245 ± 0.107	0.036	0.450	b	+
AAT	W_{Fiz}	0.019 ± 0.003	0.014	0.031	a	–
	W_{H_2O}	0.022 ± 0.003	0.016	0.032	a	–
	W_{Cd}	0.046 ± 0.021	0.021	0.097	b	+
MAT	W_{Fiz}	0.040 ± 0.009	0.026	0.065	a	–
	W_{H_2O}	0.042 ± 0.009	0.027	0.063	a	–
	W_{Cd}	0.076 ± 0.020	0.041	0.102	b	+
Gills	W_{Fiz}	0.039 ± 0.006	0.025	0.053	a	–
	W_{H_2O}	0.042 ± 0.007	0.030	0.054	a	–
	W_{Cd}	0.080 ± 0.031	0.040	0.127	b	+
Muscles	W_{Fiz}	0.004 ± 0.001	0.002	0.006	a	–
	W_{H_2O}	0.004 ± 0.001	0.002	0.006	a	–
	W_{Cd}	0.005 ± 0.003	0.002	0.012	a	+
Skin	W_{Fiz}	0.022 ± 0.003	0.018	0.028	a	–
	W_{H_2O}	0.024 ± 0.005	0.018	0.035	a	–
	W_{Cd}	0.063 ± 0.066	0.018	0.237	b	+

$\bar{x}$, mean; s, standard deviation; sample size: n = 40; letters mark similarity (a) or differences (b) between groups; –, changes over time non-significant; +, changes over time significant; BG, between groups; WG, within groups changes over time; AAT, anterior part of alimentary tract; MAT, mid-posterior part of alimentary tract.

The mid-posterior part of the alimentary tract showed the maximum cadmium content (0.100 μg·g^{-1} ww) on day 3 post-injection. Distribution of the metal proceeded between day 3 and 7, while elimination began on day 7. Redistribution occurred between day 14 and 30, further elimination beginning as late as on day 30 (Fig. 1). On day 60, the cadmium content dropped to the initial value observed at the start of the experiment.

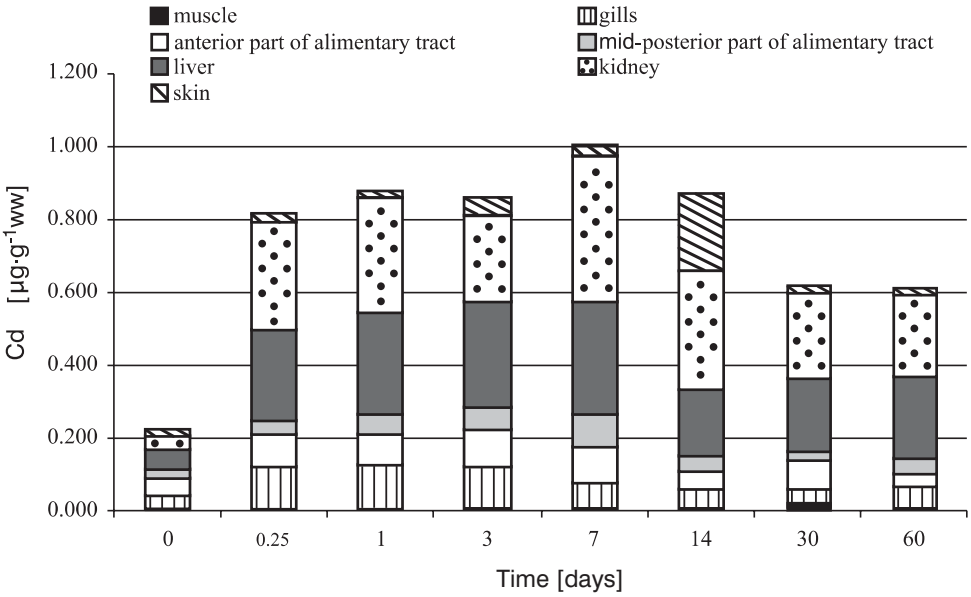

Fig. 1. Cadmium contents [µg·g^{-1} wet weight] in the carp organs during detoxification

Table 2

Initial, maximum, and final contents of cadmium [µg·g^{-1} ww] in carp organs following a single intraperitoneal injection

Organ	C_0 [t_0] $\bar{x} \pm s$	C_{max} $\bar{x} \pm s$	t_{max} [days]	C_{last} $\bar{x} \pm s$	t_{last} [days]
Kidneys	0.034 ± 0.001	0.402 ± 0.010	7	0.225 ± 0.003	60
Liver	0.044 ± 0.007	0.328 ± 0.010	7	0.434 ± 0.011	60
AAT	0.023 ± 0.002	0.091 ± 0.004	7	0.045 ± 0.002	60
MAT	0.047 ± 0.005	0.100 ± 0.002	3	0.032 ± 0.001	60
Gills	0.042 ± 0.002	0.122 ± 0.006	1	0.066 ± 0.005	60
Muscles	0.004 ± 0.001	0.011 ± 0.001	30	0.003 ± 0.001	60
Skin	0.024 ± 0.002	0.212 ± 0.015	14	0.020 ± 0.002	60

$\bar{x}$, mean; s, standard deviation; sample size: n = 5; C_0 , content at the start of experiment; t_0 , time of the start of experiment; C_{max}, maximum content; t_{max}, time of the maximum content; C_{last}, content at final assay; t_{last}, time of termination of experiment; AAT, anterior part of alimentary tract; MAT, mid-posterior part of alimentary tract.

In the liver, absorption and accumulation proceeded until day 7 when the cadmium content was observed to peak (0.328 $\mu g \cdot g^{-1}$ ww). Between day 7 and 14, the metal was being distributed within the organ (Fig. 1). On day 14, cadmium redistribution, involving the enterohepatic cycle, began and proceeded until the end of the experiment. By day 60, the liver had not eliminated all the cadmium; on the contrary, after the absorption and elimination, the cadmium content increased again above the maximum level recorded on day 7, as a result of transport from other organs.

The kidneys, similarly to the liver, showed absorption and slow accumulation of cadmium until day 7, distribution proceeding between day 7 and 14 (Fig. 1). The kidneys began to eliminate cadmium on day 14; by day 60, the cadmium content was halved, relative to the maximum value.

Absorption and accumulation of cadmium in the skin proceeded until day 14. Between day 14 and 60, cadmium was distributed and completely eliminated (Fig. 1).

The maximum cadmium content in the gills (0.122 $\mu g \cdot g^{-1}$ ww) was observed already on day 1, so absorption and accumulation occurred at that time. Distribution proceeded between day 1 and 3, while partial elimination was taking place between day 3 and 30. As of day 30, cadmium was transported from other organs to the gills (Fig. 1).

The maximum cadmium content in carp muscles (0.011 $\mu g \cdot g^{-1}$ ww) was recorded as late as on day 30 (Fig. 1). Absorption, accumulation, and distribution of cadmium in muscles proceeded until day 30 when elimination began. By day 60, the muscle cadmium content dropped to the initial value.

During the experiment, the kidneys, liver, anterior part of the alimentary tract, and the gills failed to completely eliminate cadmium. After 60 days of the experiment, the cadmium contents returned to their initial levels in the mid-posterior part of the alimentary tract, muscles, and skin (Table 2).

Intraperitoneal injection of deionised water to the second group of fish produced no changes in cadmium contents in any of the organs. The small differences observed in the kidney, liver, anterior and mid-posterior parts of the alimentary tract, gills, muscles, and skin during the experiment were statistically non-significant. Similarly, no significant differences were revealed between the deionised water-injected and the control groups, the cadmium contents recorded being similar (Table 1).

Table 3 summarises toxicokinetic parameters of the organs studied after deduction of values calculated for the control.

Values of the parameters: AUC, AUMC, and MTR in the control and water-injected groups were very similar, while those calculated for the cadmium-injected fish were much higher.

The highest AUC value following cadmium intoxication was revealed by muscles (339.4 $\mu g \cdot day^{-1} \cdot g^{-1}$) and gills (253.8 $\mu g \cdot day^{-1} \cdot g^{-1}$), the lowest value being typical of the skin (4.97 $\mu g \cdot day^{-1} \cdot g^{-1}$). An extended mean retention time (MRT) (25.6–29.3 days) was observed in gills, kidneys, muscle, skin, and the mid-posterior part of the alimentary tract, the MRT being much shorter in the anterior part of the alimentary tract (14.7 days) and liver (13.3 days) (Table 3).

Table 3

Toxicokinetic parameters revealed by organs of carp subjected to a single intraperitoneal cadmium injection

Parameter	K	L	AAT	MAT	G	M	S
AUC [μg·day^{-1}·g^{-1}]	339.40	253.85	33.00	36.16	39.34	4.97	54.62
AUMC	218337	178450	20306	12795	25561	3327	17458
MRT [day]	26.8	29.3	25.6	14.7	27.1	27.9	13.3
$t_{1/2}$ [day]	8.5	3.4	8.9	11.1	13.2	37.0	4.5
β [μg·day^{-1}]	0.001	0.002	0.003	0.003	0.003	0.006	0.008
V_d [μg]	0.108	0.117	0.108	0.169	0.030	0.026	1.089
Cl [μl·day^{-1}]	0.009	0.024	0.008	0.11	0.002	0.001	0.169

K, kidneys; L, liver; AAT, anterior part of alimentary tract; MAT, mid-posterior part of alimentary tract; G, gills; M, muscles; S, skin.

The highest biological half-life of cadmium ($t_{1/2}$) was recorded in muscles (37 days), the lowest being typical of the liver (3.4 days). The highest cadmium elimination rate constant (β) was revealed by the liver (0.008 μg·day^{-1}) and skin (0.006 μg·day^{-1}), the lowest constants being typical of gills (0.002 μg·day^{-1}) and muscles (0.001 μg·day^{-1}). Considering the cadmium distribution coefficient (V_d), the highest value was recorded in the skin (1.089 μg), the lowest being typical of gills (0.026 μg). The organ clearance rate (Cl), i.e. the rate at which each organ is cleared of the xenobiotic was at its highest in the skin (0.169 μl·day^{-1}), the lowest rate being found in muscles (0.001 μl·day^{-1}) (Table 3).

DISCUSSION

When analysing intoxication effects, attention should be paid to such a basic concept as biochemical damage, which can be defined as a biochemical change, or defect that immediately precedes a pathological change or functional disorder. In addition to the target tissue a xenobiotic affects, there are also locations responsible for the processes of absorption, activation, metabolic detoxification, and elimination of xenobiotics. Toxicological diagnostics and toxicokinetic s relies also on other types of analyses, e.g. haematological, biochemical, enzymatic, and genetic assays. As they are applied to evaluate, i.e. parameters of a compartment, which is a site of toxicokinetic processes, they are useful in comparisons with control groups. Such analyses supply, among others, a structural assessment of individual parameters, e.g. haemoglobin content, haematocrit, enzyme contents, and disorders within genes (Pawelski and Maj, 1987).

Until now, vertebrates, including fish, have been in the focus of attention of toxicologists who performed multifaceted studies on toxicity of various metal-

containing compounds and analysed both the pathways along which the compounds penetrated organisms and the duration of exposure to a toxicant. Very few studies, however, were devoted to fish detoxification following exposure to a harmful substance administered directly into the body, e.g. via an intraperitoneal injection. The present study highlights changes in cadmium-intoxicated carp during the process of detoxification. Processes related to cadmium elimination dynamics are relatively poorly known at present.

In this study, dynamics of absorption, distribution, and, especially, elimination of cadmium from carp bodies as well as processes taking place during fish recovery were followed. Those processes are affected by either environmental factors or the internal ones.

Under natural conditions, there are three pathways along which harmful substances can be taken up into the body: respiration, nutrition, and contact. In the present experiment, the harmful substance was administered via intraperitoneal injection so that a fish received a strictly defined xenobiotic dose, which made it possible to accurately follow changes in chemical parameters.

The experiment involved intoxication resulting from a single intraperitoneal injection with a sub-lethal cadmium dose. Cadmium was regarded as a strongly toxic metal the effects of which on animals would be exclusively detrimental.

In the present experiment, the fish were intraperitoneally injected with a cadmium solution, the cadmium dose amounting to 10 $\mu g \cdot kg^{-1}$ body weight. The dose was selected based on research described by Morsy (1991) who demonstrated that cadmium content of 10 $\mu g \cdot l^{-1}$ water produces no toxic changes in carp. It should be remembered that a half of that content, i.e. 5 $\mu g \cdot l^{-1}$, is the allowed cadmium content in waters assigned to quality class I (Anonymous 1991). Thus the dose used in the experiment doubles the concentration regarded as allowed in a non-polluted aquatic environment.

The toxic effect observed in the cadmium-intoxicated carp was visible on necropsy of gill lamellae and internal organs. During the first 14 days of the experiment, the lamellae showed blood extravasations, while ecchymoses were observed on the fins; this may evidence insufficient oxygen supply. The initial effect was most probably caused by irritation of the gill cavity mucosa, which resulted in increased frequency of opercular movements, accompanied by intensified excretory function of the gills and skin, which is likely to prevent increased permeation of these tissues (Antychowicz 1999). Changes in a fish body as a result of exposure to salts of heavy metals involve mainly gills, skin, liver, and kidneys. When affected by cadmium, cells of the gill epithelium and epidermis are frequently necrotic and swollen. The mucus layer covering the gills and skin of the cadmium-affected carp was found to contain peeled-off cells, while the gills and the pectoral fins and tail showed ecchymoses. At a low toxicity, such changes are not visible in the internal organs, but metabolic processes and enzyme function become disturbed.

It was also observed that intraperitoneal cadmium injection resulted in slowing down fish movements and responses to external stimuli. As the fish were exposed to

the toxic substance administered directly into the body, pathologic symptoms in the internal organs appeared very rapidly, at the beginning of the experiment, changes in the external organs (gill lamellae and skin) ensuing at the terminal phase of the experiment. Subsequently, the process of cadmium elimination from the body began. The elimination was probably associated with increased demand for oxygen because, as reported by Prost (1994), harmful effects of metal salts in fish lead to increased oxygen demand. Consequently, respiratory movements of gill lamellae are accelerated and mucus production is increased.

The cadmium dose administered was very low and did not cause any lethal effect. No fish died naturally during the experiment and all survived until its termination in good condition and the fish remaining in the tanks until termination of the experiment were in good condition. In humans, cadmium exposure induces headaches and dizziness, weakening, shivering, increased body temperature; pulmonary oedema develops within 24 hours and can result in kidney and liver failure (Chmielnicka 1999).

Following intoxication, the carp were observed to loose much of their vitality as a likely result of shock as well as distribution and accumulation of cadmium in the body. Such responses to acute metal exposure were also pointed out by Prost (1994). Reduced metabolic activity of the body as a result of metal accumulation in tissues is an underlying cause of reduced metabolic rate of muscle cells (Rice and Harrison 1978). This can be explained by a decrease in the amount of metabolic energy indispensable for enzymatic transformations that accompany detoxification processes. In the present study, the responses were accompanied by a reduction in the amount of food consumed by the cadmium-injected carp.

The changes in the internal organs, observed during autopsy of the cadmium-exposed carp correspond to descriptions of damages in liver and kidneys inflicted by various concentrations of cadmium and nickel, as described by Morsy (1991). It could be assumed that, following cadmium intoxication, metabolic rate would increase in those organs that serve the detoxifying function, the remaining organs restricting their metabolic expenditures. This assumption was borne out by results reported by Heath (1990) who, in an in vitro study of hepatic cells and gills, demonstrated an increased demand for oxygen.

The maximum cadmium contents in various carp organs during the experiment varied markedly. The organs examined can be arranged in the following series of decreasing maximum cadmium contents: kidneys > liver > skin > gills > mid-posterior part of the alimentary tract > anterior part of the alimentary tract > muscles.

The literature shows that the extent of accumulation in and elimination of xenobiotics from various organs vary as well. Sreedevi et al. (1992) who exposed carp for 4 days to nickel dissolved in water in concentration of 20–70 $mg \cdot l^{-1}$, found the highest nickel accumulation in gills, the lowest accumulation being observed in the liver, muscles, and kidney. In a 4-day-long experiment, Ray et al. (1990) followed the rate of nickel deposition in tissues of walking catfish, *Clarias batrachus*. They

arranged the organs studied in the following series of decreasing nickel contents: kidneys > liver > gills > intestine. Carp bream, *Abramis brama* caught in the Vistula River showed the highest mercury contents in the liver, intestine, heart, and gills (Kołacz et al. 1996). Svobodova et al. (1997), too, found high contents of lead and mercury in the liver and gonads of the European wels. Windom et al. (1987) suggested that the extent of heavy metal accumulation is related to fish size and weight and the toxicity of chemicals a fish is exposed to.

When transported to tissues, xenobiotics bind to tissue proteins or are further transported to cells. When in the liver, cadmium binds to the metallothionein thiol groups, which are subsequently eliminated with the body fluids (McCarter and Roch 1984). This results in a reduction of the level of a toxic substance circulating within the body. A single injection of a low cadmium dose (10 $\mu g \cdot kg^{-1}$ body weight) triggered the synthesis of metallothionein involved in the fish detoxification process (Kito et al. 1982). Each xenobiotic occurs simultaneously in both compartments (central and tissue) as two fractions: protein-bound (inactive) and non-bound (free, active). A substance bound to a serum protein may, however, be subjected to biotransformation and capillary excretion in kidneys.

Many authors showed the amounts of heavy metals accumulated in freshwater and marine fish to vary (Protasowicki 1991a, 1991b, Sharif et al. 1991). According to the literature data, the highest heavy metal contents occur in the liver, the lowest contents being typical of muscles, regardless of the metal absorption pathway (Protasowicki and Chodyniecki 1988, 1992, Hellou et al. 1992). Relations between intraperitoneal injection of cadmium and cadmium accumulation from natural environment are "mimic" distribution and detoxification of natural accumulation.

CONCLUSIONS

1. A single intraperitoneal injection of carp with a sub-lethal cadmium dose produced behavioural responses and damage in gills, liver, and kidneys as well as metabolic and haematopoietic disorders.
2. Once the maximum cadmium concentration (C_{max}) had been reached in an organ, the detoxification process began. Gills were the first organ to begin cadmium elimination (24 h post injection), followed by the mid-posterior part of the alimentary tract (after 3 days), kidneys (after 7 days), and skin (after 14 days). During detoxification, cadmium was observed to be redistributed among the organs.
3. Cadmium elimination rate was found to vary from 0.001 to 0.006 $\mu g \cdot day^{-1}$. The biological half-life ($t_{1/2}$) of cadmium calculated for the organs examined ranged from 3.4 to 37 days. After 60 days of detoxification, the cadmium content did not revert to the initial level.
4. A long-term effect of sub-lethal cadmium intoxication was an about 10 % reduction of the fish body weight, relative to the initial weight.

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