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CADMIUM AND MERCURY RAT BODY BURDEN FOLLOWING COPPER SUPPLEMENTS

RETENCJA KADMU I RTĘCI W ORGANIZMIE SZCZURA KARMIONEGO PASZĄ Z DODATKIEM MIEDZI

Abstract: Studies involved the influence of a diet containing 10-times increased copper concentrations (50 µg/kg) in comparison with a standard diet on the absorption of mercury and cadmium (mercury-203 and cadmium-109) given intragastrically for 28 days to Wistar male rats at doses corresponding to 10 mg of cadmium or mercury/kg of feedstuff. Concentrations of radiomercury and radiocadmium were determined in the carcass 1 h, 3 h, 12 h, 1 d, 2 d, 4 d, 8 d and 16 d postdosing. Moreover, feed intake and body weight gains were evaluated during the experimental period. A ten-time increase in copper dietary intake did not produce statistically significant differences in the distribution of cadmium in the carcass of rats. On the other hand, copper reduced the retention of mercury in the carcass within the experimental period and significant differences were found 1 d and 2 d postdosing. Treatment of the rats with cadmium and mercury decreased body weight gains in comparison with those reported in normal rats. The supplementation of dietary copper reduced decreases in body gains when compared with those in the rats exposed only to mercury and or cadmium. The results indicate a beneficial role of supplements of dietary copper in decreasing the bioavailability of inorganic mercury *via* the gastrointestinal tract. Lack of differences in the bioavailability of cadmium in the presence of supplemental copper suggests that the mechanisms of mercury-copper and cadmium-copper interactions may vary. Increased body weight gains in rats intoxicated with mercury or cadmium and fed the copper supplemented diet suggested that copper may diminish toxic actions of the two heavy metals.

Keywords: cadmium, mercury, copper, rat, interaction

Cadmium and mercury are natural chemical compounds occurring as residues in food and feedstuffs because of their presence in the environment resulting from human activities such as farming, industry, car exhausts or from contamination during food and feedstuffs processing and storage. Contamination of food and feed by mercury and cadmium cannot be entirely avoided. Current reports of the European Food Safety Authority stress a potential risk of exposure to enhanced levels of cadmium and mercury in food and feedstuffs [1, 2]. The presence of cadmium and mercury in feedstuffs poses a serious toxicological problem even though the influx of these metals into the environment is being limited. People and animals may be exposed during their entire lifespan to dietary cadmium and mercury. It is believed that a frequent consumption of some feeds and feedstuffs may contribute significantly to the overall human and animal exposure to cadmium and mercury. Cadmium and mercury may affect the metabolism of trace elements including copper [3-7]. On the other hand, it seems reasonable that copper supplementation of feeds for animals may influence cadmium and mercury accumulation in the body. The aim of this study was to find the effect of dietary supplements of copper on the body retention of mercury and cadmium given via the gastrointestinal tract.

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Material and methods

Two-month old male Wistar rats from a commercial breeding station (Kozlowska Breeding Station, Warsaw) were used. The rats were kept in group of 5 in stainless steel cages.

Animals were acclimatized under standard laboratory conditions for a one week and then were randomly assigned into four treatment groups comprising 40 rats each: Group 1 and 2 (LSM), the controls, fed a standard pelleted diet LSM for rodents (Fodder Manufacture at Motycz Poland) and were given intragastrically a water solution of cadmium chloride or mercury chloride, respectively, daily for 28 days except weekends at a dose corresponding to 10 mg of cadmium or mercury/kg of feedstuff. Rats in groups 3 and 4 were treated similarly to those in groups 1 and 2 except for a diet which was supplemented with copper chloride 10-times the recommended level in the LSM diet fed in groups 1 and 2. Cadmium and mercury chloride given to rats in all groups were labelled with cadmium-109 and mercury-203, respectively. Daily feed and water consumption was evaluated weekly throughout the experiment. An initial and weekly body gains were evaluated.

All rats were killed by immersion in gaseous carbon dioxide 1 h, 3 h, 6 h, 12 h, 1 d, 2 d, 4 d, 8 d, and 16 d postdosing. The content of cadmium-109 or mercury-203 in the carcass (whole body without the stomach and intestines) was measured in a whole-body counter ZM 701 (Polon, Poland). Reference standards for quantification of carcass were prepared by intraperitoneal injection of the appropriate solution of cadmium-109 or mercury-203 to rats which were killed 30 min thereafter. The area under the curves (AUC) of radiocadmium or radiomercury retention versus time points was calculated by the trapezoidal rule. Data were analysed statistically using Student's *t*-test at $p<0.05$. The experiments were approved by the Local Ethics Committee for Animal Experiments in Lublin, Poland.

Results

Food and water intake was similar in all examined rats although rats intoxicated with mercury or cadmium and fed the copper supplemented diet demonstrated a higher growth rate in comparison with those fed a standard laboratory diet. No visible sign of cadmium or mercury toxicity except some uneasiness noticed at the beginning of cadmium or mercury exposure were found.

The carcass retention of mercury is presented in Figure 1. Results indicate that copper supplemented diet decreased mercury retention in the body of rats throughout the whole experimental period. Significant decreases were found 1 d and 2 d after mercury-203 administration. The AUC values for mercury and mercury plus copper treated rats were 595 (100%) and 473 (79%), respectively. This indicates that mercury retention in rats fed the copper supplemented diet was lower by about 21% as compared with that in rats fed a standard laboratory diet.

The carcass retention of cadmium was show in Figure 2. Data indicate that the retention of cadmium in rats fed the copper fortified diet was not significantly affected by increased intake of dietary copper. Moreover, the AUC values in the controls and copper treated rats were similar, 320 and 340, respectively.

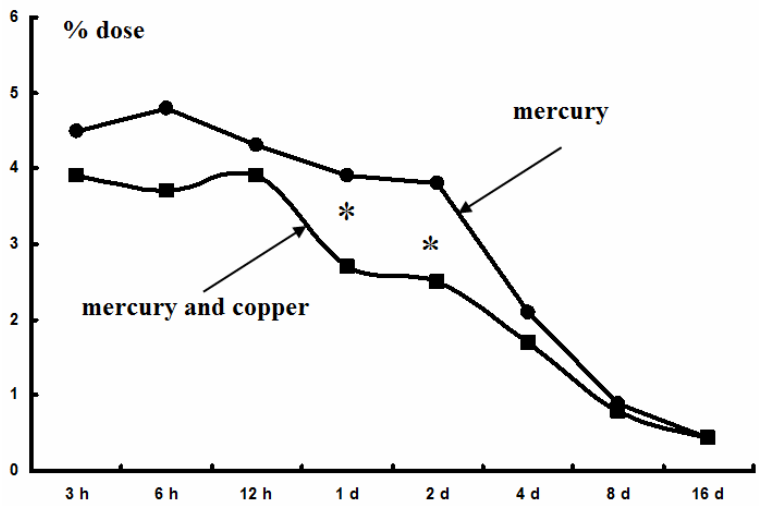

Fig. 1 Carcass retention of mercury (Hg-203) in rats. * - indicates statistically significant differences at $p<0.05$

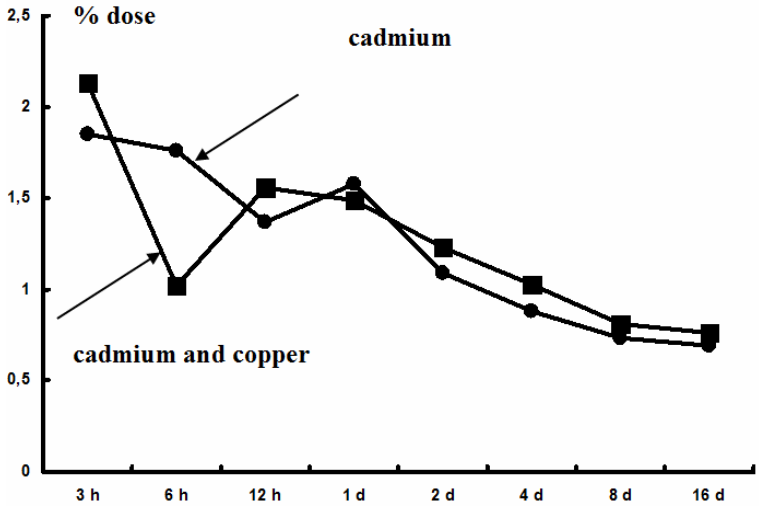

Fig. 2. Carcass retention of cadmium (Cd-109) in rats

Discussion

The bioavailability, retention and consequently toxicity of the metals are affected by several factors such as nutritional status including body trace element stores. Mercury and copper interaction is not well understood. It was found that mercury can replace metallothionein (Mt) bound Cu in *in vitro* studies [9]. Oral intoxication with mercuric chloride increased copper retention in the kidneys [6]. There are not reports which suggest that copper may affect mercury retention in the body. The data presented here show that supplements of copper reduced significantly mercury retention in the body. It may be

postulated that copper forming a stable complex with Mt replaces mercury bound to this protein. As a result, mercury may be released into the circulation and then excreted. It was found that cadmium administered at toxic levels decreased copper concentration in several organs except for kidneys [7]. On the other hand, Toshiyuki et al [8] reported that copper given with cadmium increased cadmium retention and toxic action within the body, whereas copper level was unaffected. Based on the current results it was found that copper failed to influence significantly the body burden of cadmium although a higher body rate growth may suggested that that copper reduced a toxic action of cadmium within the body. Thus, these results may support findings presented by Peraza et al [10] who reported that supplements with copper reduced mortality rate and severity of anemia in animals receiving large doses of cadmium. The data presented here indicate that the mechanism of interaction between copper and mercury or copper and cadmium varies with regard to the metal involved. It is worth stressing that copper supplements increased the body weight gains of rats which may suggest a beneficial role of this nutrient in the case of mercury and cadmium intoxication.

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RETENCJA KADMU I RTĘCI W ORGANIZMIE SZCZURA KARMIONEGO PASZĄ Z DODATKIEM MIEDZI

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Abstrakt: Obecność kadmu i rtęci w paszach stanowi poważny problem w toksykologii mimo znacznego ograniczenia dopływu tych metali do środowiska. Z raportu Europejskiego Urzędu do Spraw Bezpieczeństwa Żywności z ostatnich lat wynika, że istnieje potencjalne ryzyko narażenia na zwiększone ilości tych metali zawartych w paszach i żywności pochodzenia zwierzęcego. Dane z piśmiennictwa wskazują, że wchłanianie kadmu i rtęci z przewodu pokarmowego zależne jest od składu diety, w tym zawartości składników mineralnych. W niniejszych badaniach uwzględniono wpływ diety, zawierającej zwiększoną dziesięciokrotnie ilość miedzi (50 µg/kg) w odniesieniu do paszy standardowej na przyswajanie chlorków rtęci i kadmu (znakowanych rtęcią-203 i kadmem-109) podawanych dożołądkowo przez 28 dni szczurom samcom szczepu Wistar w ilościach odpowiadających 10 mg Cd lub Hg/kg paszy. Zawartość radiokadmu i radiortęci oznaczano w korpusie zwierząt

po uprzednim usunięciu przewodu pokarmowego z treścią po 1 h, 3 h, 12 h, 2 d i 4 d, 8 d i 16 d od zakończeniu aplikacji radioizotopów. W trakcie doświadczenia określano dodatkowo spożycie paszy i przyrosty masy ciała. Dziesięciokrotny wzrost zawartości miedzi w paszy nie powodował statystycznie istotnych zmian w rozmieszczeniu radiokadmu w korpusie zwierząt, aczkolwiek obserwowano zauważalne zwiększenie ilości kadmu przez cały okres badań. W przypadku rtęci dodatek miedzi do diety powodował obniżenie zawartości tego metalu w korpusie przez cały okres badań, a różnice statystycznie istotne notowano po 1 d i 2 d od zakończeniu podawania rtęci. Podawanie szczurom rtęci i kadmu zmniejszało przyrosty masy ciała w porównaniu do odpowiednich danych uzyskanych u zwierząt niezatruwanych tymi metalami, nieeksponowanych na te metale ciężkie. Dodatek miedzi do paszy łagodził spadki przyrostów masy ciała u zwierząt zatruwanych rtęcią i kadmem. Uzyskane wyniki wskazują na korzystne oddziaływanie zwiększonych ilości miedzi w paszy, wyrażające się ograniczeniem przyswajania rtęci nieorganicznej podawanej drogą pokarmową. Brak znacznych zmian w biodostępności kadmu w obecności zwiększonych ilości miedzi wskazuje, że mechanizmy interakcji rtęć-miedź i kadm-miedź mogą być zróżnicowane. Warto jednak podkreślić, że dodatek miedzi do paszy powodował ponadto zwiększone przyrosty masy ciała u zwierząt zatruwanych rtęcią i kadmem, co może sugerować ochronne właściwości miedzi w przypadku zatruć testowanymi metalami ciężkimi.

Słowa kluczowe: kadm, rtęć, miedź, szczur, interakcja