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THE EFFECT OF CADMIUM ON ASCORBIC ACID, VITAMIN E AND COENZYME Q CONCENTRATIONS IN RAT KIDNEYS: A POSSIBLE PROTECTIVE ROLE OF COENZYME Q_{10}

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Cadmium (Cd) is a commonly occurring environmental pollutant (Forrester *et al.* 2000). It induces oxidative stress, resulting in oxidative deterioration of biological macromolecules. Cd depletes glutathione and protein-bound sulfhydryl groups what results in enhanced production of reactive oxygen species which leads to increased lipid peroxidation, enhanced excretion of urinary lipid metabolites, modulation of intracellular oxidized states, DNA and membrane damages, altered gene expression and apoptosis (Stochs *et al.* 2000). Kidneys are one of the most critical organs for the toxicity of Cd (Štajn *et al.* 1997). The accumulation of Cd in these organs causes alterations of tubular cells, as well as the secondary nephropathy of the cortex (Oishi *et al.* 2000) and "Itai-itai" disease, characterized mainly by various renal disfunctions (Hiratsuka *et al.* 1997).

The main antioxidant properties of coenzyme Q_{10} (CoQ_{10}) are: to inhibit the process of lipid peroxidation (Ernster *et al.* 1992), to regenerate the active form of vitamin E (Ernster and Beyer 1991) and to stabilize the extracellular ascorbate in the organism (Gomez-Diaz *et al.* 1997). CoQ_{10} protects DNA from oxidation caused by lipid peroxidation (Beyer 1990) and also protects organism from oxidative stress induced by various toxic agents (Ernster and Dallner 1995).

The experiments were carried out with male 60 days old Wistar albino rats, weighing 190 ± 20 *g* at the onset of experiments. They were kept in individual cages under controlled conditions (light on: 5 a.m. - 5 p.m.; temperature 23 ± 2°C) and had free access to water and food. The animals were divided into four experimental groups and treated during 30 days. The first group of animals was the control (C, drinking tap water). The second group was treated with cadmium (Cd, 200 *mg* $CdCl_2$ x $5H_2O$/L of drinking water during 30 days + 100 μL of olive oil, i.m., every fifth day). The third group was treated with coenzyme Q_{10} (CoQ_{10}, 40 *mg* CoQ_{10}/mL dissolved in olive oil, i.m., every fifth day, drinking tap water) and the fourth group was treated concomitantly with cadmium and coenzyme Q_{10} (Cd+CoQ_{10} in the above mentioned amounts). The average intake of 17 *mg* Cd/day/kg body mass was calculated from the water consumed during the 30-day treatment. The average intake of CoQ_{10} was 16 *mg/kg* body mass every fifth day. All animals were decapitated always between 8 and 10 a.m. to avoid any possible rhythmic variations in the antioxidant level. The kidneys were dissected out within 3 min and prepared for further analysis. All chemicals were Sigma (St. Louis, MO, USA) products. The concentration of ascorbic acid (AsA) was determined spectrophotometrically by dinitrophenylhidrazine method (Roe 1957). Vitamin E (Vit E) concentration was assayed by the method of Desai (1984) using bathophenanthroline and that of coenzyme Q (CoQ) by the method of Beyer (1989). Protein content was determined by the method of Lowry *et al.* (1951) using bovine serum albumin as a reference. Statistical analysis of the results was based on the Student's t test considering the significance at a level of $p < 0.05$ (Hoel 1966).

In Table 1. the data on AsA, Vit E and CoQ concentrations are listed and compared to the controls (C). The concentration of AsA was significantly increased with respect to the controls in all experimental groups, *i.e.* treated with Cd, with CoQ_{10} and concomitantly treated with Cd+CoQ_{10} ($p < 0.005$). Our previous investigations showed that Cd did not change AsA concentration in kidneys when administered alone (Štajn *et al.* 1997). However, in present experiments, we administered Cd together with olive oil, which contains an increased level of polyphenolic antioxidants that can increase AsA concentration in the kidneys (Manna *et al.* 1997). Increased concentration of AsA in the kidneys of CoQ_{10} treated animals fits well increased concentration of Vit E in these organs. It is known, that AsA and Vit E may act synergistically as

Table 1. Concentrations of ascorbic acid (AsA), vitamin E (Vit E) and coenzyme Q (CoQ) in the kidneys of: control rats (C), treated with cadmium (Cd), with coenzyme Q_{10} (CoQ_{10}) and concomitantly with cadmium and coenzyme Q_{10} (Cd+CoQ_{10}). Values are Means ± S.E. from 7 animals.

	AsA (mg/100 g tissue)	Vit E (μg/g tisue)	CoQ (nmol/*mg* proteins)
C	9.06 ± 0.49	8.24 ± 0.11	589.54 ± 14.78
Cd	17.70 ± 0.63*	14.12 ± 0.26*	571.33 ± 18.02
CoQ_{10}	28.55 ± 1.61*	12.91 ± 0.21*	616.84 ± 5.61
Cd+CoQ_{10}	19.27 ± 0.27*	15.59 ± 0.27*	587.99 ± 20.22

*$p < 0.005$ by Student's t test.

antioxidants and that each can exert sparing effects to the other (Tanaka *et al.* 1997). The data of Gomez-Diaz *et al.* (1997) also showed, that CoQ_{10} and its NADH-dependent reductase stabilized the extracellular ascorbate in the organism. The concentration of Vit E was significantly higher in animals treated with Cd, with CoQ_{10} and concomitantly with both Cd and CoQ_{10} in relation to the controls ($p < 0.005$). The increased concentration of Vit E in the kidneys could be explained by its protective role against the toxic influence of cadmium, which is the physiological adaptation of an organism to toxic cadmium effects. On the other hand, Vit E radical (Vit E·, α-tocopheroxyl radical) formed in the reaction with free lipid radicals (LOO·) would be regenerated by reduced form of CoQ_{10} ($CoQ_{10}H_2$) and this could be an explanation for an increased concentration of Vit E in the kidneys of rats treated with CoQ_{10} (Ernster and Fosmark-Andree 1993). Contrary to AsA and Vit E the concentration of CoQ in the kidneys was not significantly changed in any of the investigated groups of animals in comparison with the controls. Other authors performing dose- and time- dependent studies demonstrated that CoQ concentration after parenteral administration was increased only in the plasma and liver of rats (Scalori *et al.* 1986).

It can be concluded that CoQ_{10} administration to rats chronically exposed to exogenous Cd exerts beneficial effects on AsA and Vit E concentrations in the kidneys, resulting in improved antioxidant protection against Cd toxicity.

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