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EFFECT OF COENZYME Q_{10} ON ASCORBIC ACID, VITAMIN E, AND COENZYME Q CONCENTRATIONS IN TESTES OF RATS CHRONICALLY EXPOSED TO CADMIUM.

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Cadmium (Cd) has been recognized as being among the most toxic environmental and industrial pollutants, one that is present in soils, sediments, air, and water (Stoepler, 1991). After penetrating into the organism, mostly through the respiratory and gastrointestinal tracts, Cd accumulates in the liver and kidneys, as well as in other tissues and organs, causing many metabolic, histological, and pathological changes, such as nephrotoxicity, cardiotoxicity, increased lipid peroxidation and hemorrhagic lesions of seminal tubules. In tissues, Cd also binds to proteins of low molecular mass, producing metallothioneins by the induction of metallothionein mRNA synthesis (George *et al.*, 1996). Cadmium depletes glutathione and protein-bound sulfhydryl groups, resulting in enhanced production of reactive oxygen species (ROS). These ROS result in increased lipid peroxidation, enhanced excretion of urinary lipid metabolites, modulation of intracellular oxidized states, DNA damage, membrane damage, altered gene expression, and apoptosis (Kim *et al.*, 2003).

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

Our experiments were carried out with male 60-day-old white rats of Wistar strain weighing 190 ± 20 g at the onset of experiments. They were kept in individual cages under controlled conditions (light on from 5 a.m. to 5 p.m.; temperature of 23 ± 2°C) and had free access to water and food. The animals were divided into four experimental groups and treated for a period of 30 days. The first group of animals was the control (C, drinking tap water). The second group was treated with cadmium (Cd, 200 mg of $CdCl_2$ x $5H_2O$/l of drinking water for 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 of CoQ_{10}/ml dissolved in olive oil, i.m., every fifth day, drinking tap water). The fourth group was treated with cadmium and coenzyme Q_{10} concomitantly (Cd+CoQ_{10} in the above mentioned amounts). The average intake of 17 mg Cd/day/kg body mass was calculated from 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 invariably decapitated between 8 and 10 a.m. to avoid any possible rhythmic variations in the antioxidant level. The testes were dissected out within 3 min and prepared for further analysis. All chemicals were from Sigma (St. Louis, MO, USA). The concentration of ascorbic acid (AsA) was determined spectrophotometrically by the dinitrophenylhydrazine method (Roe, 1957). Vitamin E (Vit E) concentration was assayed by the method of Desai (1984) using bathophenanthroline. Coenzyme Q (CoQ) was determined 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 a level of $p < 0.05$ to be significant (Hoel, 1966).

Data on AsA, Vit E, and CoQ concentrations are given and compared to the control rats (C) in Table 1. The concentration of AsA was significantly increased in relation to the controls in all experimental groups, i.e., treated with Cd, with CoQ_{10} concomitantly ($p<0.005$), and with Cd+CoQ_{10} ($p<0.01$). Our earlier results on rat kidneys (Pavlović *et al.*, 2001) showed that Cd induces elevation of AsA concentration after chronic treatment. Increased concentration of AsA in testes of CoQ_{10}-treated animals tallies nicely with increased concentration of Vit E in these organs. It is known that AsA and Vit E are capable of acting synergistically as antioxidants and that each can exert sparing effects in relation to the other (Tanaka *et al.*, 1997). The data of Gomez-Diaz *et al.* (1997) also showed that CoQ_{10} and its NADH-dependent reductaze stabilize extracellular ascorbate in the organism. The concentration of Vit E was significantly higher in testes of animals treated with Cd, with CoQ_{10}, and with both Cd and CoQ_{10} concomitantly than in testes of the controls ($p<0.005$). Vitamin E radical (Vit E·, α-tocopheroxyl radical) formed in the reaction with free lipid radicals (LOO·) would be regenerated by the reduced form of CoQ_{10} ($CoQ_{10}H_2$), could explain the increased concentration of Vit E in the testes of rats treated with CoQ_{10} (Ernster and Fosmark-Andree, 1993). Increased concentrations of Vit E

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

TESTES	AsA (mg/100 g tissue)	Vit E (mg/g tissue)	CoQ (nM/mg proteins)
K	15.20 ± 0.97	7.76 ± 0.06	626.83 ± 15.81
Cd	22.30 ± 0.79 ****	12.39 ± 0.20 ****	609.41 ± 19.62
CoQ_{10}	32.42 ± 0.88 ****	12.86 ± 0.15 ****	593.37 ± 33.58
Cd + CoQ_{10}	19.03 ± 0.85 ***	14.61 ± 0.20 ****	622.30 ± 15.13

In relation to the controls (C): ***p<0.01; ****p<0.005 by Student's t test.

in the testes have a protective role against the toxic influence of Cd, which represents a physiological adaptation of the organism to toxic Cd effects. Contrary to AsA and Vit E, the concentration of CoQ in the testes 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 (S c a l o r i *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 testes, resulting in improved antioxidant protection against Cd toxicity.

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