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THE INFLUENCE OF COENZYME Q_{10} (CoQ_{10}) ON THE GROWTH OF BODY MASS AND SOMATIC INDEXES IN CADMIUM TREATED RATS

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ABSTRACT. Male 30 days old *Wistar albino* rats were treated with cadmium (Cd, 17 mg/day/kg body mass in drinking water + 100 μL olive oil, i.m., every fifth day), coenzyme (CoQ_{10},16 mg/kg, dissolved in olive oil, i.m., every fifth day), Cd+CoQ_{10} (17 mg Cd/day kg body mass in drinking water + 16 mg/kg CoQ_{10}, dissolved in olive oil, i.m., every fifth day) and with olive oil (100 μL, i.m., every fifth day) during 30 days. The changes of the body mass growth and somatic indexes were calculated.

Our results show that Cd causes significant decrease of body mass growth when administered alone, as well as, in combination with CoQ_{10}. At the same time, treatment with olive oil induces the elevation of the body mass growth. It is established that Cd and Cd+CoQ_{10} induces significant increase of the mass of kidneys, while CoQ_{10} increases the mass of all investigated tissues (e.g. liver, kidneys, heart and testes). Treatment with olive oil induces the increase the mass of kidneys and testes. In Cd treated animals somatic indexes were significantly increased for the liver, kidneys and heart. In rats treated with CoQ_{10} somatic index was increased only for the liver, while cotreatment with Cd+CoQ_{10} induces the increase of somatic index only for the kidneys. At the same time, concentration of Cd in the liver, kidneys and testes significantly increased in animals treated with Cd and rats treated concomitantly with Cd+CoQ_{10}.

INTRODUCTION

Cadmium (Cd) is a commonly occuring environmental contaminant of food, water and air [1]. Oral exposure to Cd is the major route in the nonindustrially exposed individual where food consumption constitutes the main environmental source of Cd for the nonsmoking general population [2]. Another major source of Cd intake for the general population is the inhalation [3]. From the total amount of food Cd intake, only about 6 % is absorbed in the gastrointestinal tract of animals [4]. After absorption, cadmium penetrate in the blood stream and bound to the erythrocyte membranes and serum albumines [3]. Cadmium accumulates mostly in the liver and kidneys, but it can be also accumulated in other organs and tissues [5]. In the blood and tissues Cd binds to low-molecular mass proteins producing metallothioneins. It must be pointed that toxic effects exerts only "free", e.g. non-bound Cd, while Cd which is bound to metallothioneins become inactive [6]. In the liver cadmium induced difficulties in protein metabolism [7] and increased activities of gluconeogenetic enzyme [8]. The accumulation of Cd in the kidneys causes alterations in tubular

cells, as well as the secondary nephropathy of cortex [9]. As a result of chronic exposure to cadmium, "Itai-itai" disease occurs which is characterized mainly by the renal dysfunctions and osteomalacia [10]. In testes, as target organs, Cd induces increased of lipid peroxidation and hemorrhagic lesions [11]. In mammalian species cadmium causes the onset of anemia [12], cardiotoxic effects associated with increased lipid peroxidation, histopathological alterations and decreased force of heart contractions [13,14]. In the living organisms cadmium also causes decreased body growth [5,15], and reduction of mass of particular organs in rodents [16]. Cadmium also affects various metabolic processes, especially processes of energy metabolism [17], membrane transport [18] and protein synthesis [19].

Coenzyme Q_{10} (CoQ_{10}, ubiquinone) is a lipid-soluble molecule which was discovered as an obligatory component of mitochondrial electron transfer chain [20], and have antioxidant properties too [21]. It is the only lipid-soluble antioxidant which is normally synthetized by the organism [22]. Besides its bioenergetic role, CoQ_{10} is also a component of extra-mitochondrial redox chains [23] whose functions would be to remove excess of reducing power formed by glycolysis when mitochondrial respiration is decreased [24]. Coenzyme Q_{10} in its reduced form ($CoQ_{10}H_2$, ubiquinol) is a powerfull antioxidant. As an antioxidant it is exploited either directly upon superoxide or indirectly on lipid radicals [21]. $CoQ_{10}H_2$ can also act together with Vitamin E by regenerating the active form from the tocopheroxyl radical [25]. The antioxidant action of reduced form of CoQ_{10} yields the CoQ_{10} radical ($CoQ_{10}^{\cdot}$) or ubisemiquinone radical, and this species converted back to its antioxidant form by reduction (which occurs through the electron transfer chain in mitochondria), and operated by various quinone reductases represent in different cell fractions [26]. It appears that CoQ_{10} may prevent both the initiation and propagation of lipid peroxidation [21], protects DNA from oxidation causing by lipid peroxidation [27], and protects organism from oxidative stress induced by various toxic agents [28].

The aim of our study was to determined the effects of CoQ_{10} on the growth of body mass and somatic indexes in rats chronically exposed to Cd.

MATERIALS AND METHODS

Two months old male *Wistar albino* rats weighing 190 ± 20 g at the beginning of the experiments were used. The animals were kept at 21 ± 1°C, fed a pellet rat diet, and exposed to 12 h light - 12 h dark cycle. Control rats drunk tap water *ad libitum*. The rats treated with Cd drank water containing 200 mg $CdCl_2$/L for 30 days and injected with olive oil (100 μL, i.m.) every fifth day. The animals treated with CoQ_{10} were injected by i.m. injection, every fifth day, with 20 mg/kg CoQ_{10} dissolved in olive oil, while the rats treated concomitantly with Cd+CoQ_{10} drank water containing 200 mg Cd/L and injected (i.m.) with 20 mg/kg CoQ_{10} dissolved in olive oil, every fifth day. Last experimental group of animals was treated with olive oil (100 μL olive oil, i.m., every fifth day). An average intake of Cd was 17 mg/day/kg body mass, whereas those of CoQ_{10} was 16 mg/kg/dose. The body mass of animals was measured at the beginning, as well as, at the end of treatment and then was calculated an average growth of body mass. After the treatment, the animals were sacrificed by decapitation (without anesthaesia) and following organs: liver, kidneys, heart and testes were isolated and their masses were measured. The somatic index (SI) for particular organ was calculated as follows:

$$\text{somatic index (SI)} = \frac{\text{mass of organ (g)} \times 100}{\text{body mass (g)}}$$

The concentration of Cd in organs was determined in destroyed material [29] in the mixture of nitric and perchloric acid (17:3) by the method of atomic absorption spectrophotometry (AAS, Perkin Elmer, Model 3300) at the wavelength of 228.8 nm, slit 0.1 mm and lamp current 4 mA, in the mixture of air and acetylene.

All obtained data were statistically analyzed and expressed as Mean ± S.E.M. and differences between experimental and control groups were evaluated by Student t-test [30]. The value of $p<0.05$ was taken as the least degree of significance.

RESULTS AND DISCUSSION

At the beginning of the experiments the body mass of rats in each experimental group was between 175 g and 205 g (average 190 ± 20 g), (Table 1). The growth of the body mass of control animals at the end of experiments was 99 ± 4 g (100 %). In animals exposed to Cd was only 75.5 ± 5 g (76.5 %), and was significantly decreased in comparison to the control rats ($p<0.01$). Other authors also demonstrated that Cd induces the decline of body mass in rats [7,16] and mice [31]. The decrease of body mass in Cd treated animals is probably the consequence of the decrease of total mass of muscles and white adipose tissue [5]. When the animals where given Cd and CoQ_{10} concomitantly, the growth of the body mass was significantly decreased ($p<0.025$) when compared with the control animals and was 78 ± 3 g (73.4 %). It can be pointed that CoQ_{10} in dosages administered did not diminish the negative effects of Cd on the growth of the body mass. At the other hand, in animals treated with olive oil the growth of the body mass at the end of the experiments was significantly increased ($p<0.01$) and was 122 ± 5 g (123 %) in respect to the control animals. It is well known that olive oil contains a high level of antioxidants, such as polyphenolic antioxidants [32], as well as Vitamin E and β-carotene [33], which may protect organism from the free radical - mediated injuries and diseases. Olive oil also contains squalene which have beneficial effects on many functions in the organism [34].

Table 1. Growth of the body mass in control animals (C), treated with cadmium (Cd), with coenzyme Q_{10} (CoQ_{10}), treated concomitantly with cadmium + CoQ_{10} ($Cd+CoQ_{10}$) and animals treated with olive oil (o. oil).

	BODY MASS (g)			
	before treatment	after treatment	Growth of the body mass	
			(g)	(%)
C	175 ± 5	274 ± 3	99 ± 4	100
Cd	182 ± 6	257 ± 7	75 ± 5 ^{C}	76.5 ^{C}
CoQ_{10}	202 ± 4	303 ± 4	101 ± 3	104
$Cd+CoQ_{10}$	205 ± 5	283 ± 5	78 ± 3 ^{B}	83.4 ^{B}
o. oil	179 ± 4	301 ± 7	122 ± 5 ^{C}	123 ^{C}

Significantly different from controls (C): $^{B}p<0.025$; $^{C}p<0.01$.

It is well established that general growth of the body mass does not indicate changes of internal organs, as well as the mass of particular tissues. Therefore, we measured the mass of the liver, kidneys, heart and testes (Table 2) and calculated somatic indexes (Table 3).

The obtained data shows that Cd induces a significant increase of the mass of kidneys ($p<0.05$) when compared to the control rats, and caused a significant increase of somatic index for this organ ($p<0.005$). At the same time, somatic indexes for the liver and the heart were significantly increased ($p<0.01$ and $p<0.005$, respectivelly), which may be the consequence of decreased total body mass in animals treated with Cd [35]. Some authors show that Cd induces a significant decrease of the mass of particular organs and tissues when it was administered alone [7,16,36,37].

Table 2. The mass of organs (liver, kidneys, heart and testes) expressed in the gram (g) in control animals (C), treated with cadmium (Cd), with coenzyme Q_{10} (CoQ_{10}), treated concomitantly with cadmium + CoQ_{10} ($Cd+CoQ_{10}$) and animals treated with olive oil (o. oil).

	MASS OF ORGANS (g)				
	C	Cd	CoQ_{10}	$Cd+CoQ_{10}$	o. oil
LIVER	7.42 ± 0.22	8.69 ± 0.32	9.03 ± 0.23 ^{C}	8.27 ± 0.14	7.96 ± 0.25
KIDNEYS	0.89 ± 0.01	1.01 ± 0.04 ^{A}	1.00 ± 0.02 ^{C}	1.03 ± 0.03 ^{D}	1.03 ± 0.04 ^{A}
HEART	0.91 ± 0.03	0.94 ± 0.03	0.98 ± 0.02 ^{A}	0.93 ± 0.02	0.96 ± 0.02
TESTES	1.37 ± 0.02	1.41 ± 0.04	1.53 ± 0.03 ^{D}	1.41 ± 0.02	1.45 ± 0.03 ^{A}

Significantly different from controls (C): $^{A}p<0.05$; $^{C}p<0.01$; $^{D}p<0.005$.

In our experiments Cd was given concomitantly with olive oil, and it may be the explanation for the differences between our results and those of other authors. The decreased mass of organs and tissues in animals treated with Cd, mainly is the consequence of significant reduction of protein synthesis [5]. In animals treated with CoQ_{10} the significant increase of the mass of liver ($p<0.01$), kidneys ($p<0.01$), heart ($p<0.05$) and testes ($p<0.005$) were observed, while the somatic index was statistically increased ($p<0.05$) only for the liver. The increased mass of examined organs may be explained as the consequence of better cell respiration, energy metabolism, protein synthesis and antioxidant role of CoQ_{10} [12,26]. In animals treated concomitantly with Cd+CoQ_{10} the significant increase of the body mass ($p<0.005$) and somatic index ($p<0.01$) of kidneys was observed. These results are similar to those in animals treated with Cd and olive oil. In rats treated with olive oil statistically significant increased of the mass of kidneys ($p<0.05$), as well as the mass of testes ($p<0.05$) were observed, without any changes of somatic index for both organs.

Table 3. Somatic indexes of organs (liver, kidneys, heart and testes) expressed in the percent (%) in control animals (C), treated with cadmium (Cd), with coenzyme Q_{10} (CoQ_{10}), treated concomitantly with cadmium + CoQ_{10} (Cd+CoQ_{10}) and animals treated with olive oil (o. oil).

	SOMATIC INDEXES OF ORGANS (%)				
	C	Cd	CoQ_{10}	Cd+CoQ_{10}	o. oil
LIVER	2.78 ± 0.090	3.27 ± 0.110 ^{C}	2.98 ± 0.090 ^{A}	2.99 ± 0.060	2.65 ± 0.100
KIDNEYS	0.33 ± 0.004	0.40 ± 0.005 ^{D}	0.33 ± 0.007	0.36 ± 0.008 ^{C}	0.34 ± 0.008
HEART	0.33 ± 0.006	0.36 ± 0.008 ^{B}	0.32 ± 0.004	0.33 ± 0.005	0.32 ± 0.006
TESTES	0.50 ± 0.010	0.56 ± 0.021	0.51 ± 0.010	0.50 ± 0.010	0.49 ± 0.014

Significantly different from controls (C): $^{A}p<0.05$; $^{B}p<0.025$; $^{C}p<0.01$; $^{D}p<0.005$.

Antioxidant components contained in olive oil, have a protective role on cell metabolism and protein synthesis, and protect tissues from injuries [32,33,34]. These facts may explain the results obtained in our experiments considering kidneys and testes.

The results obtained in our investigations show that Cd was significantly accumulated ($p<0.005$) in the liver, kidneys and testes of rats treated with Cd and rats treated concomitantly with Cd+CoQ_{10} (Table 4).

Table 4. Concentration of cadmium in organs (liver, kidneys and testes) expressed in μg/g in control animals (C), treated with cadmium (Cd), with coenzyme Q_{10} (CoQ_{10}), treated concomitantly with cadmium + CoQ_{10} (Cd+CoQ_{10}) and animals treated with olive oil (o. oil).

Cd (μg/g)	LIVER	KIDNEYS	TESTES
C	0.30 ± 0.026	0.54 ± 0.04	0.24 ± 0.057
Cd	43.40 ± 1.73 ^{D}	39.08 ± 2.72 ^{D}	2.44 ± 0.22 ^{D}
CoQ_{10}	0.31 ± 0.07	-	-
Cd+CoQ_{10}	38.21 ± 1.17 ^{D}	38.41 ± 1.44 ^{D}	1.84 ± 0.070 ^{D}
o. oil	0.31 ± 0.03	0.68 ± 0.07	0.20 ± 0.026

Significantly different from controls (C): $^{D}p<0.005$.

Our results are in accordance with the results of other authors on rats [38]. Cadmium mostly accumulated in the liver and kidneys (about 75 % of total accumulated Cd), where it induces metabolic and structural alterations and decreased protein synthesis [39]. In the kidneys Cd induces tubular disffunction [40] and reduction of renal energy metabolism [41]. Increased accumulation of Cd in kidneys were also found in Japanese quail [42] liver and the kidneys of rats, as well as in the kidneys of rabbits [43]. In testes Cd induces necrosis and atrophy of seminal tubules and lead to the loss of reproductive capacity [44]. In animals treated with Cd and CoQ_{10} concomitantly, CoQ_{10} in the dosage administered did not change the degree of Cd accumulation in investigated tissues.

CONCLUSIONS

Cadmium given through drinking water (17 mg/day/kg body mass) in the course of 30 days causes a significant decrease of the growth of the body mass in rats which is the consequence of the increased accumulation of this metal in the organism. Coenzyme Q_{10} when adiministered concomitantly with Cd (in the dosage of 16 mg/kg, i.m.) did not diminish the toxic effects of this metal. Olive oil treatment induces a significant increase of growth of the body mass in rats.

Cadmium induces increase of mass of kidneys, as well as, the somatic indexes of liver, kidneys and heart. At the same time, CoQ_{10} administration induces a significant increase of mass of all investigated tissues. Our results also show that olive oil may exhibit protective effects in the organism, resulting increased growth of the body mass and mass of kidneys and testes.

In our experiments a significant accumulation of cadmium in all examined tissues was observed.

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