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THE EFFECTS OF CADMIUM AND SELENIUM ON THE ASCORBIC ACID AND VITAMIN E CONTENTS IN THE PLASMA AND LIVER OF YOUNG AND ADULT RATS

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Young and adult Wistar albino rats were given cadmium (15 mg Cd /day/kg), selenium (7 μg Se/day/kg) and both cadmium and selenium (15 mg Cd + 7 μg Se/day/kg) in drinking water in the cours of 30 days. Cadmium caused the decrease of ascorbic acid (AsA) concentration in the liver and the increase of vitamin E (vit E) concentration in the liver and plasma of both young and adult rats. In the liver and plasma of both experimental groups exposed to selenium the concentrations of AsA and vit E were significantly increased. However, by concomitant exposure both to cadmium and selenium, the single effects of cadmium and selenium on the AsA and vit E concentration in plasma were annulled. In the liver, these single effects were diminished.

Key words: Rats, cadmium, selenium, ascorbic acid, vitamin E, plasma, liver.

INTRODUCTION

Cadmium induces different toxic effects if it is present as a free or non-protein bound (Webb, 1979). It acumulates in organism,

particularly in the liver and kidneys, causing metabolic and histological alterations in the liver, kidneys, heart, testes and in other tissues and organs (Kopp et al., 1983; Bomhard et al., 1984). Cadmium significantly decreases the body growth in rats (Štajn et al., 1992), induces anemia (Kostić et al., 1993), influences the membrane transport (Verbost et al., 1989) and the synthesis of protein (Dudley et al., 1984).Cadmium induces the increased production of superoxid anion radicals (Amoruso et al., 1982) and increased lipid peroxidation (Jamall and Smith, 1985). Because of the inhibition of antioxidant defense system enzymes (Jamall and Smith, 1985a; Jamall and Sprowls, 1987) induced by cadmium, the oxidative injuries in different tissues and organs evolve (Hussain et al., 1987; Shukla et al., 1987).

Previous investigations have shown that cadmium significantly reduces the concentration of AsA in the liver (Patnaik, 1971; Shukla and Chandra, 1989). AsA as a nonenzymatic component of antioxidant defense system may have an important role in scavenging of radicals (reactive oxygen species) (Halliwell and Foyer, 1976; Bodannes and Chan, 1979), as well as in process of regeneration of reduced form of vit E (Padh, 1990). Vitamin E is an important biological oxidant (Chow, 1989) that stabilises the cell membranes maintaining its permeability (Lucy, 1972; Molennar, 1980). Moreover, it is known that ascorbic acid and vit E may act synergically as antioxidants (Burk, 1983; Chow, 1985; Weiss, 1986).

Selenium is a necessary trace element in diet of animals, but in higher concentrations it becomes toxic and even lethal (Rosenfeld and Beath, 1964). Selenium is a constituent of enzyme glutathion peroxidase (Se-GSH-Px) that has an important biological role in scavenging of lipid peroxides and in preserving of the integrity of cell membrane (Flohe et al., 1973). It is also known that selenium demonstrates some defense role against the toxic influence of cadmium in biological systems (Chung and Maines, 1987; Štajn et al., 1992). The presence of selenium induces the alteration in the distribution of cadmium in tissues and the forming of protein Se-Cd complexes (Gesiewicz and Smith, 1976). Selenium and vit E may interact to act synergically against the development of some tumors (Liebovitz et al., 1990).

In this work the influence of cadmium and selenium on the ascorbic acid (AsA) and vitamin E (vit E) content in plasma and in the liver of young and adult rats was analyzed.

MATERIALS AND METHODS

Male young rats (Wistar albino) 30 days old and adult rats 60 days old were dayly given cadmium (15 mg Cd/day/kg), selenium (7μg/day/kg) and both cadmium and selenium (15mg Cd + 7μg Se/day/kg) in drinking water during 30 days. The rats were fed with chow pellets. The control groups of animals were fed by the same food but drunk by the tap water.

Each experimental group consisted of six animals. The animals were sacrificed by decapitation between 8 and 10 a.m. The fresh heparinized blood was colected. Liver tissues were dissected within 3 min. placed in ice-cold 155 mM NaCl and washed with the same solution. The liver tissues were minced and homogenized in 10 volumes of 25 mM sucrose containing 10 mM Tris-HCl, pH 7.5 at 1500 rpm using Thomas sci. Comp. glass homogenizer (Teflon pestle), 8-10 up-and down-strokes. Homogenates were then centrifuged at 4°C at 100.000 g for 90 minutes. The ascorbic acid (AsA) contents in plasma was measured by the method of Day at al.(1979) with 2,4,6-Tripyridyl-S-Triazine (TPTZ), while ascorbic acid content in the liver was measured by dinitrophenyl-hydrazine method (Roe, 1957) and vitamin E (vit E) by the method as suggested by Desai (1984).

The Student's t test was used for data comparison between different groups (Hoel, 1966)

RESULTS

Table 1 depicts the concentration of AsA and vit E in plasma of young and adult rats. In plasma of both groups of animals, cadmium did not change AsA concentration significantly, but it induced significant increase of vit E concentration in young ($p<0,01$) and adult ($p<0,05$) rats. By exposure to selenium the concentrations of AsA ($p<0,02$) and vit E ($p<0,005$; $p<0,02$) were significantly increased in rats of both age groups. By concomitant exposure both to cadmium and selenium the concentration of analyzed vitamins were normalized and did not differ statistically from control values.

Table 1. The ascorbic acid (AsA) and vitamin E (vit E) concentrations in the plasma of young and adult rats after exposure to cadmium (Cd), selenium (Se), and cadmium+selenium (Cd+Se) in respect to controls.

PLASMA		control	Cd	Se	Cd+Se
young	AsA (mg%)	1,06 ± 0,05	1,09 ± 0,08	1,27 ± 0,07**	1,02 ± 0,03
	vit E (µg/ml)	4,06 ± 0,12	6,32 ± 0,42***	6,80 ± 0,24**	3,95 ± 0,34
adults	AsA (mg%)	0,93 ± 0,06	1,01 ± 0,05	1,22 ± 0,04**	1,03 ± 0,06
	vit E (µg/ml)	3,46 ± 0,19	4,39 ± 0,20*	5,27 ± 0,41**	3,47 ± 0,07

Means ±SE of the means of 6 animals in all groups.
* p<0.05; ** p<0.02; *** p<0.01; **p<0.005.

Table 2 shows the concentrations of AsA and vit E in the liver of young and adult rats. Cadmium induced significant decrease of AsA concentration (p<0,01) with concomitant increas of vit E both in young (p<0,05) and adult (p<0,005) rats. By exposure of rats to selenium only, concentrations of AsA (p<0,02; p<0,01) and vit E (p<0,005) in the liver of both age groups were significantly increased. By concomitant exposure both to cadmium and selenium, the concentration of vit E in the liver of young rats was not much different from control values, while in the liver of adult rats it tended to reach control value (p<0,05).

Table 2. The concentrations of ascorbic acid (AsA) and vitamin E (vit E) in the liver of young and adult rats after exposure to cadmium (Cd) selenium (Se), and cadmium+selenium (Cd+Se) in respect to controls.

LIVER		control	Cd	Se	Cd+Se
young rats	AsA (mg%)	38,87 ± 1,01	29,09 ± 1,59***	43,18 ± 1,52**	32,11 ± 1,70**
	vit E (μg/g)	12,26 ± 0,38	15,89 ± 0,49*	19,10 ± 0,88***	13,50 ± 0,58
adults	AsA (mg%)	37,60 ± 0,84	30,01 ± 0,39***	45,23 ± 1,58***	31,53 ± 0,50***
	vit E (μg/g)	13,41 ± 0,69	23,32 ± 0,65**	26,97 ± 1,50**	16,04 ± 0,48*

Means ± SE of the means of 6 animals in all groups.
* p<0.05; ** p<0.02; *** p<0.01; ** p<0.005.

Selenium given in combination with cadmium diminished the effect of cadmium on the concentration of AsA, in some degree, so that concentration of this vitamin in the liver of both age groups remained significantly decreased (p<0,02) in comparison to control values.

DISCUSSION

The results obtained in this work show (Tab. 1) that the concentration of AsA in the liver of young and adult rats is significantly decreased. These data are in accordance with previous investigations on mammals which show that cadmium significantly reduces the concentration of AsA in the liver (Patnaik, 1971; Chatterjee et al.,1973; Shukla and Chandra, 1989). AsA as a significant nonenzymatic antioxidant has an important catalyzing role in metabolic processes and significantly decreases the harmful effects of cadmium in birds and mammals (Fox and Fry, 1970; Chatterjee et al., 1973). It is known that

increased accumulation of cadmium in the liver induces lipid peroxidation and increases the production of malondialdehyde (MDA), which consequently inhibits the enzyme L-gulonolactone oxidase (Chatterjee et al., 1960; Hudecova and Ginter, 1992) necessary for the synthesis of AsA. Ascorbic acid is a potent scavenger of superoxide anion radicals and singlet oxygen and it is shown that in guinea pig marginal AsA deficiency results in intracellular oxidative damage (Chakrabarty et al., 1992).

In the liver of young and adult rats exposed to cadmium, concentration of vit E (Tab. 1) is significantly increased which could be explained by important role of this vitamin in the protection from spontaneous and induced peroxidation in the liver (Shukla and Chandra, 1989; Leibovitz et al., 1990). At the same time, cadmium did not induce significant alteration of AsA content in plasma of both age groups (Tab. 2). However, cadmium induced significant increase of the concentration of vit E in plasma. The increased concentration of vit E in plasma could be explained by its protective role against the toxic influence of cadmium on the erythrocyte membranes. In previous investigations (Chow, 1989) it was shown that plasma vit E was in dynamic equilibrium with vit E in erythrocyte membranes, maintaining the stability and permeability of these membranes. Our results show (Tab. 1 and Tab. 2) that the concentrations of AsA and vit E are significantly increased in plasma and the liver of both age groups exposed to selenium. On the basis of previous investigations (Chow, 1990) it is known that selenium decreases the utilization of vit E in organism. This is achieved by better absorption of vit E in gastrointestinal tract, as well as by increased activity of Se-dependet GSH-Px which in greater extent destroyes lipid peroxides maintaining thus the integrity of cellular and subcellular membranes. Therefore, the increased amounts of vit E are retained (Chow, 1989; Bjørneboe et al., 1990).

In rats exposed to increased concentration of selenium the opposite effect was induced (Tab. 2), and concentration of AsA in the liver was significantly increased. From our results it can be concluded that the inhibitory effect of cadmium on synthesis (concentration) of AsA is expressed more than the stimulatory effects of selenium, cince the concentration of AsA in the liver is significantly lower in rats concomitantly exposed both to cadmium and selenium than in control

animals.

By concomitant exposure of rats both to cadmium and selenium (Cd+Se), in plasma of both young and adult rats (Tab. 1), there are no effects induced by cadmium or selenium separately. This protective effect of selenium could be explained by its interaction with cadmium and by formation of protein complexes with both elements. By binding to protein complex, their separate action is eliminated (Gasiewicz and Smith, 1976). In the liver of young rats which are exposed concomitantly both to cadmium and selenium (Cd+Se), the single effects of cadmium or selenium on the concentration of vit E are also omited. However, selenium only slightly decreased the effect of cadmium on concentration of AsA in the liver of both young and adult rats as well as the effect of cadmium on vit E content in the liver of adult rats (Tab. 1).

It is known that selenium demonstrates certain protective role against toxic action of cadmium and other heavy metals (Bozkurt and Smith, 1981; Magos and Webb, 1980). The protective effects are demonstrated because of the influence of selenium on the redistribution of cadmium from a protein of lower molecular mass into a protein of higher molecular mass (Viljoen and Tappel, 1988).

CONCLUSIONS

After exposure of rats to cadmium, selenium and both to cadmium and selenium it can be concluded that selenium expressed protective effect against toxic influence of cadmium on AsA and vit E contents in plasma of both young and adult rats. At the same time selenium normalized the concentration of vit E in the liver of rats of both age groups, however did not change toxic effects on AsA induced by cadmium.

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EFEKAT KADMIJUMA I SELENA NA SADRŽAJ ASKORBINSKE KISELINE I VITAMINA E U PLAZMI I JETRI MLADIH I ADULTNIH PACOVA

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I Z V O D

Mladi i adultni pacovi soja Wistar albino, izlagani su peroralno kadmijumu (15 mg CdCl/dan/kg), selenu (7 μg Se/dan/kg) i istovremeno kadmijumu i selenu (15 mg Cd + 7 μg Se/dan/kg) tokom 30 dana. Kadmijum je izazvao smanjenje koncentracije askorbinske kiseline (AsA) u jetri uz istovremeno povećanje koncentracije vitamina E (vit E) u jetri i plazmi mladih i adultnih pacova. U jetri i plazmi obe grupe životinja izlaganih selenu, značajno je povećana koncentracija askorbinske kiseline i vitamina E. Međutim, istovremenim izlaganjem kadmijumu i selenu, pojedinačni efekti Cd i Se na koncentraciju AsA i vitamina E u plazmi se poništavaju. U jetri su ovi efekti smanjeni.