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PROGRAMME and ABSTRACTS

THE PROTECTIVE ROLE OF COENZYME Q_{10} AND VITAMIN E ON ANTIOXIDANT DEFENSE SYSTEM IN THE HEART OF CADMIUM TREATED RATS

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Cadmium (Cd) is an important pollutant of environment which accumulates in the liver and the kidneys, as well as in other tissues (1). Cd induces oxidative damage causing many metabolic, histological and pathological changes, such as nephrotoxicity, cardiotoxicity, increased lipid peroxidation (LP) and alteration of the antioxidant defense system (AOS) (2). Recent studies have shown that coenzyme Q_{10} (CoQ_{10}) and vitamin E (Vit E) are the powerful liposoluble antioxidants, which inhibit lipid peroxidation and thus prevent free radical mediated oxidative injuries. It is well known that CoQ_{10} and Vit E may act synergistically as antioxidants (3, 4). The aim of this study was to investigate a possible protective influence of CoQ_{10} and Vit E in Cd induced oxidative stress in the rat hearts.

Male, *Wistar albino* rats 3 months old, weighing 280±30 g were used in our experiments. The animals were kept at 21±2^{0}C and exposed to 12 h light/dark cycle. All rats were housed in individual cages and given a standard diet and tap water *ad libitum*. The rats injected with (1) $CdCl_2$ (0.4 mg Cd/kg b.m.,i.p., 24^h before the sacrificing), (2) (CoQ_{10}+Vit E) + Cd (20 mg CoQ_{10}/kg b.m., i.m., 48^h before the sacrificing + 20 IU Vit E/kg b.m., i.m., 48^h before the sacrificing + 0.4 mg Cd/kg b.m., i.p., 24^h before the sacrificing), (3) CoQ_{10} + Vit E (20 mg CoQ_{10}/kg b.m., i.m., 48^h before the sacrificing + 20 IU Vit E/kg b.m., i.m., 48^h before the sacrificing. After the treatment all animals were sacrificed by decapitation and heart tissue was isolated and prepared for analysis. The activities of total superoxide dismutase (Total SOD), manganese containing superoxide dismutase (Mn SOD), copper zinc containing superoxide dismutase (CuZn SOD), catalase (CAT), glutathione peroxidase (GSH-Px), glutathione-S-transferase (GST), glutathione reductase (GR), as well as ascorbic acid (AsA), vitamin E (Vit E) and Cd concentrations were analyzed.

The results obtained in our experiments are presented in Table 1. The significance of all experimental groups was compared with control animals (C). Acute intoxication of rats with Cd were followed by significantly increased of all examined antioxidant defense enzymes (total SOD, Mn SOD, CuZn SOD, CAT, GSH-Px, GST and GR), ($p<0.05$, or less), while AsA and Vit E concentrations were significantly decreased ($p<0.05$ and $p<0.02$). A significantly increased accumulation of Cd in heart tissue was observed in animals treated with Cd ($p<0.005$). Recent studies on mammals have shown that Cd stimulates formation of reactive oxygen species and through binding to sulfhydryl groups of enzymes inhibits their activity, consequently causing the peroxidative destruction of cell membranes. These ubiquitous reactions of Cd result as its toxic effects on whole blood (2), liver, kidneys, heart, testes and other tissues and organs (5-8).

The protective role of CoQ_{10} and Vit E in acute Cd intoxication results as decreased activities of total SOD, CuZn SOD, GSH-Px and GST. AsA concentration was also reversed to the control value. However, pretreatment with CoQ_{10} and Vit E induced further increase of CAT and GR activities and Vit E concentration ($p<0.02$). Our results showed that combination of two liposoluble antioxidants such as CoQ_{10} and Vit E resulted as suitable and potent antioxidant action, probably as consequence of quenching of reactive oxygen species, inhibition of LP and prevention of free radical mediated injuries (3, 4). The results of our study suggested that CoQ_{10} and Vit E functions as a potent antioxidants in protection of rat heart against oxidative stress induced by Cd.

Table 1. Total SOD, Mn SOD, CuZn SOD, CAT (U/g w.m.), GSH-Px (nmol NADPH/min/g w.m.), GST (nmol GSH/min/g w.m.), GR (nmol NADPH/min/g w.m.) activities, as well as AsA (mg/100 g tissue), Vit E (μg/g tissue) and Cd (μg/g tissue) concentrations in the heart of control rats (C), treated with Cd, treated with (CoQ_{10}+Vit E)+Cd or treated with CoQ_{10}+Vit E.

	C	Cd	(CoQ_{10} + Vit E) + Cd	CoQ_{10} + Vit E
Total SOD	482.67 ± 4.49	851.40 ± 41.72 ***	697.15 ± 44.56 **	687.49 ± 25.77 **
Mn SOD	149.17 ± 19.05	206.80 ± 13.04 **	212.98 ± 15.67 **	186.14 ± 2.84 *
CuZn SOD	333.50 ± 3.25	644.60 ± 31.28 ***	484.02 ± 32.52 *	501.35 ± 24.59 **
CAT	912.04 ± 34.92	1088.16 ± 27.22 *	1235.90 ± 39.97 **	1284.70 ± 49.06 **
GSH-Px	4259.33 ± 399.29	5528.29 ± 416.96 *	5079.99 ± 410.66	4367.99 ± 293.97
GST	2167.20 ± 31.84	2840.76 ± 90.95 *	2057.92 ± 65.24	2237.50 ± 75.84
GR	654.24 ± 36.59	746.48 ± 65.58 *	883.27 ± 44.54 **	827.65 ± 35.11 **
AsA	8.79 ± 0.69	6.51 ± 0.22 *	8.85 ± 0.38	9.82 ± 0.60
Vit E	15.35 ± 0.21	12.44 ± 0.27 **	17.41 ± 0.26 **	18.96 ± 0.69 **
Cd	N.D.	0.14 ± 0.004 ***	N.D.	N.D.

The values are means ± SE from 7 animals.
*$p<0.05$, **$p<0.02$, ***$p<0.01$ in comparison to the control animals.

References

1. Stohs S.J., Bagchi D., Hassoun E., Bagchi M. *J. Environm. Pathol. Toxicol. Oncol.*, 19, 201-213, 2000.
2. Kostić M.M., Ognjanović B., Dimitrijević S., Žikić R.V., Štajn A., Rosić G.L. *Eur. J. Haematol.*, 51, 86-92, 1993.
3. Beyer R.E. *J. Bioenerg. Biomemb.*, 26, 349-358, 1994.
4. Niki E. *Mol.Aspects Med.*, 18, S63-S70, 1997.
5. Ognjanović B., Žikić R.V., Štajn A., Saičić Z.S., Kostić M.M., Petrović V.M. *Physiol. Res.*, 44, 293-300, 1995.
6. Štajn A., Žikić R.V., Ognjanović B., Saičić Z.S., Pavlović S.Z., Kostić M.M., Petrović V.M. *Comp. Biochem. Physiol.*, 117C, 167-172, 1997.
7. Žikić R.V., Štajn A.Š, Ognjanović B.I, Saičić Z.S., Kostić M.M., Pavlović S.Z., Petrović V.M. *J. Environm. Pathol. Toxicol. Oncol.*, 17, 259-264, 1998.
8. Pavlović S.Z., Ognjanović B.I., Štajn A.Š., Žikić R.V., Saičić Z.S., Petrović V.M. *Jugoslav. Med. Biohem.*, 20, 229-235, 2001.