Effect of Ubiquinone-10 on the Blood System in Rats Exposed to Radiation

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The use of synthetic ubiquinone-10 (2 and 10 mg/kg) as a therapeutic food additive normalized the counts of erythrocytes, reticulocytes, and leukocytes and the content of hemoglobin in the blood and inhibited lipid peroxidation in erythrocytes in irradiated rats (3 Gy).

Key Words: *radiation injury; blood cells; lipid peroxidation; ubiquinone-10*

Intensification of free radical processes and disintegration of membrane structures play a role in the pathogenesis of radiation sickness [7,13]. These changes are followed by alteration of membrane processes and inhibition of energy metabolism. The major component of the respiratory chain ubiquinone plays an important role in these processes. This compound is easily solubilized after impairment of membrane permeability. These data suggest that the therapy with ubiquinone would completely or partially normalize disturbances in energy-synthesizing and energy-depended functions of cells. Exogenous ubiquinone passes through hypoxia-labilized biological membranes, incorporates into the respiratory chain, and recovers electron transport in this chain [9]. Previous studies showed that ubiquinones possess antioxidant activity, which is similar to that in tocopherols [2]. Ubiquinone has not only antihypoxic, but also antioxidant properties. These properties of synthetic ubiquinone-10 were revealed in our experiments with myocardial ischemia in animals [6]. Moreover, ubiquinone-9 (Co Q-9) displays radioprotective activity [5]. Since ubiquinone-10 (Co Q-10) is synthesized in humans [4], studies of radioprotective activity of synthetic ubiquinone-10 are of considerable importance [6,10,11]. The state of the blood system reflects the development of moderate radiation injury (bone-marrow form) [8,15]. Here we studied the effects of ubiquinone-10 synthesized at the BVK Plant (Kstovo) on peripheral blood parameters in rats during irradiation. Experiments were performed by the method developed at the Sintezbelok Institute (Russian Academy of Sciences).

MATERIALS AND METHODS

Experiments were performed on outbred albino female rats weighing 150-180 g. The animals were exposed to single whole-body γ-irradiation with 3.0 Gy (^{60}Co) on an Agat device. The dose rate was 1 Gy/min. The therapy started 1 h after irradiation and lasted 7 days. Ubiquinone-10 obtained by microbiological synthesis [6] was dissolved in olive oil and administered through a probe in daily doses of 2 and 10 mg/kg. Control animals received olive oil. Reference group consisted of untreated irradiated rats. All rats fed a standard diet. The blood was taken from the sublingual vein on days 7, 14, and 21 after irradiation.

The content of hemoglobin and counts of erythrocytes, reticulocytes, and leukocytes in the blood were measured by routine techniques [13]. The intensity of lipid peroxidation (LPO) in erythrocytes was estimated by the content of malonic dialdehyde (MDA) [3]. The results were analyzed by Student's *t* test.

RESULTS

The development of radiation sickness was accompanied by suppression of erythro- and leukopoiesis.

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TABLE 1. Blood Parameters in Rats Irradiated in a Dose of 3 Gy and Receiving 2 mg/kg Ubiquinone-10 for 7 Days (*M*±*m*)

Parameter	Intact	Days after irradiation					
		7		14		21	
		control	ubiquinone	control	ubiquinone	control	ubiquinone
Hemoglobin, g/liter	130.60±8.91	114.40±2.62	126.40±6.16	103.40±2.29	152.80±7.19	110.0±3.2	153.60±10.91
Reticulocytes, per 10^3 erythrocytes	20.2±1.0	15.80±1.28	21.0±1.5	9.8±0.6	19.9±1.1	10.40±1.16	19.3±1.1
Erythrocytes, 10^{12}/liter	3.41±0.44	2.93±0.02	2.46±0.09	2.89±0.06	3.80±0.05	3.17±0.05	3.90±0.19
Leukocytes, 10^9/liter	8.94±0.07	4.13±0.18	8.32±0.40	6.14±0.32	13.44±1.84	7.50±0.28	9.76±0.01
Neutrophils, 10^9/liter	3.22±0.36	1.65±0.12	1.91±0.12	3.64±0.11	5.3±0.2	3.30±0.24	3.27±0.21
Lymphocytes, 10^9/liter	4.68±0.38	2.10±0.09	6.05±0.12	2.31±0.11	7.90±0.06	3.84±0.17	6.31±0.22

Severe anemia, erythropenia, and leukopenia were found in untreated animals ($p<0.05$). Ubiquinone-10 used as a food additive abolished the anemic effect of radiation (day 7 of therapy). In these rats the content of hemoglobin and erythrocyte count in the peripheral blood did not differ from that in intact animals and markedly surpassed the control (Table 1). In rats exposed to irradiation and receiving ubiquinone-10 reticulocyte count in the peripheral blood did not differ from that in intact animals, which indicates that the antianemic effect of this compound is associated with stimulation of hemopoiesis (Table 1).

The radioprotective effect of ubiquinone-10 was dose-independent ($p>0.05$ for 2 and 10 mg/kg).

Ubiquinone-10 produced the radioprotective effect not only on erythropoiesis, it also normalized leukocyte count. In untreated rats radiation sickness was accompanied by severe leukopenia, which developed immediately after irradiation (Table 1). In rats receiving ubiquinone-10 in doses of 2 and 10 mg/kg the count of leukocytes remained unchanged or surpassed that in intact animals. It should be emphasized that normalization of white blood cell count was related to an increase in the number of neutrophils and lymphocytes (Table 2). These results indicate that functional activity of specific (lymphocytes) and nonspecific immune system (neutrophils) in animals treated with ubiquinone-10 remained unchanged. The radioprotective effect of ubiquinone-10 is probably associated with stimulation of the immune system, which is markedly suppressed after radiation injury [14].

The radioprotective effect of ubiquinone-10 can be associated with antioxidant activity. The damaging effect of ionizing radiation is associated with intensification of LPO [1,13]. The formation of free radicals $OH^{\bullet}$, $HO_2^{\bullet}$, and $O_2^{\bullet}$ that initiate peroxidation in cells is related to ionizing radiation-induced water radiolysis and presence of oxygen in the medium. Since ubiquinone acts as a scavenger of free radicals [6, 10,11], its administration during irradiation probably blocks intensification of LPO.

The intensity of LPO in erythrocytes from control and ubiquinone-10-treated rats increased over the first week after irradiation (Table 2). In control rats the concentration of MDA returned to the baseline level by the end of the third week. The intensity of LPO in animals treated with ubiquinone (particularly in a dose of 2 mg/kg) decreased 2 weeks after irradiation.

Our results show that in animals with experimental radiation sickness exogenous biosynthetic ubiquinone-10 produces a hemoprotective effect, prevents the development of anemia, erythropenia, and leukopenia, and stabilizes erythropoiesis, neutrophilopoiesis, and lymphopoiesis.

In irradiated animals ubiquinone-10 repairs the respiratory chain, protects energy activity in cells,

TABLE 2. MDA Content in Erythrocytes from Rats with Radiation Sickness Receiving Ubiquinone-10 (μg/ml, *M*±*m*)

Group		Before irradiation	Days after irradiation		
			7	14	21
Untreated		1.8±0.2	3.12±0.45*	3.39±0.56*	2.03±0.23
Ubiquinone-10	2 mg/kg	1.8±0.2	3.88±0.27*	1.55±0.16	1.28±0.12
	10 mg/kg	1.8±0.2	3.53±0.57*	2.32±0.24	2.11±0.26

Note. *$p<0.05$ compared to intact animals.

blocks intensification of free radical processes and, therefore, attenuates destruction of cell membranes. Thus, ubiquinone-10 prevents disturbances in energy-dependent activity and stimulates proliferation of bone marrow hemopoietic cells in animals with radiation injury. These data indicate that ubiquinone-10 obtained by microbiological synthesis holds much promise for radioprotection.

REFERENCES

1. E. B. Burlakova, A. V. Alesenko, and S. A. Aristarkhova, *Biological Antioxidants in Radiation Injury and Malignant Growth* [in Russian], Moscow (1975).
2. E. B. Burlakova and N. G. Khrapova, *Usp. Khimii*, **54**, 1540-1558 (1985).
3. Yu. A. Vladimirov and A. I. Archakov, *Lipid Peroxidation in Biological Membranes* [in Russian], Moscow (1972).
4. G. V. Donchenko, *Biochemistry of Ubiquinone Q* [in Russian], Kiev (1988).
5. I. K. Kolomiitseva, E. G. Novoselova, N. I. Potekhina, *et al*., *Radiobiologiya*, **25**, No. 1, 53-57 (1985).
6. V. N. Krylov, L. D. Luk'yanova, A. S. Koryagin, and E. V. Yastrebova, *Byull. Eksp. Biol. Med*., **130**, No. 7, 35-38 (2000).
7. A. M. Kuzin, *Structural and Metabolic Theory in Radiobiology* [in Russian], Moscow (1986).
8. V. I. Legeza and V. G. Vladimirov, *Radiats. Biol. Radioekol*., **38**, No. 3, 416-423 (1998).
9. L. D. Luk'yanova, *Itogi Nauki Tekh. Ser. Farmakol. Khimioterapevt. Sredstva*, Moscow (1991), Vol. 27, pp. 11-44.
10. L. D. Luk'yanova, *Byull. Eksp. Biol. Med*., **124**, No. 9, 244-254 (1997).
11. L. D. Luk'yanova, *Vestn. Ros. Akad. Med. Nauk*., No. 9, 3-12 (2000).
12. V. V. Men'shikov, *Laboratory Techniques in Clinical Practice* [in Russian], Moscow (1987).
13. B. I. Polivoda, V. V. Konev, and G. A. Popov, *Biophysical Aspects of Radiation Damage to Biological Membranes* [in Russian], Moscow (1990).
14. A. A. Yarilin and N. I. Sharyi, *Immunity and Radiation* [in Russian], Moscow (1991).
15. S. P. Yarmonenko, *Radiobiology of Humans and Animals* [in Russian], Moscow (1988).