



Radioprotective and anti-stress properties of the drug "Pronumol"

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The key role of nitric oxide (NO) in maintaining vascular tone, normal blood circulation and tissue fluids, regulating the activity of immune cells, signaling in the nervous system, as well as in the development of shock, inflammation, and cell apoptosis is established. At physiological concentrations, NO is an antioxidant that inhibits the development of radical oxidative reactions (Odonnell V.B. 1997). In the body, nitric oxide is synthesized enzymatically from l-arginine. Mice of F1 hybrids (CBAx57Bl) weighing 18–20 g were used in experiments. Irradiation of animals was carried out on the Gamma-Cell facility (Canada) with an absorbed dose rate of 1 Gy / min. As a stressful effect, the animals were kept for a long time (within 24 hours) in conditions of limited mobility in narrow individual cells without food and water. Mice were fed for 7 days before exposure to irradiation or stress with food enriched with l-arginine or "Pronumol" (0.8 mg/g and 2.0 mg/g feed, respectively) equivalent in l-arginine content. Studies were performed immediately after the stress exposure or 24 hours after irradiation. The degree of DNA damage was estimated by the kinetic method, determining the percentage of double-stranded fragments after controlled alkaline unwinding of DNA. The level of lipid peroxidation (LPO) in the body was assessed by the content of MDA in the blood serum. For statistical processing, the methods of variation statistics were used. The significance of differences between groups was assessed using Student's t-test and the Wilcoxon-Mann-Whitney U-test.

Results. Exposure to radiation and stress led to the emptying of lymphoid organs, increased the level of DNA degradation in the thymus, and increased the content of MDA in the serum of mice (table 1,2,3). A day after irradiation at a dose of 1 Gy, the number of cells in the thymus decreased by 57.4%, and after stress exposure by 33.3%. Feeding animals with l-arginine did not have a significant effect on the thymus cellularity, while "Pronumol" protected the thymus from emptying under both effects, and it was much more effective under stress. The content of double-stranded DNA fragments decreased from 83.4% (control) to 68.9% (irradiation) and to 71.4% (stress). The level of POL in the body increased by 36.3% (exposure) and 28.1% (stress). Arginine and Pronumol protected thymus DNA from degradation induced by radiation and stress, had an antioxidant effect.

The results indicate that arginine is a moderate protector in its activity. The most pronounced anti-radiation and anti-stress properties of the drug "Pronumol", which is based on nucleic acids and protein protamine, enriched with l-arginine. The advantage of arginine and "Pronumol" is the absence of toxicity.

Table 1 - The effect of l-arginine and "Pronumol" on the thymus cellularity of mice irradiated at a dose of 1 Gy or exposed to stress

animal group	Thymus cell count, $\times 10^{-7}$		
	Control	1 Gy exposure	Stress
exposure without substances	10,8 \pm 0,5	4,6 \pm 0,5 *	7,2 \pm 0,7 *
L-arginine + exposure	-	4,8 \pm 0,6	6,9 \pm 0,8
"Pronumol" + exposure	-	7,3 \pm 1,0 **	11,1 \pm 1,1 **

* - P < 0,05 significant differences from control; ** - P < 0,05 from substances

Table 2 - The effect of l-arginine and "Pronumol" on the DNA degradation of mouse thymocytes irradiated at a dose of 1 Gy or exposed to stress

animal group	content of double-stranded DNA fragments, %		
	control	1 Gy exposure	stress
exposure without substances	83,4 \pm 0,6	68,9 \pm 1,3 *	71,4 \pm 1,1 *
L-arginine + exposure	-	75,8 \pm 2,5 **	77,1 \pm 1,5 **
"Pronumol" + exposure	-	78,0 \pm 0,8 **	82,5 \pm 0,7 **

* - P < 0,05 significant differences from control; ** - P < 0,05 from substances

Table 3 - The effect of l-arginine and "Pronumol" on the concentration of MDA in the serum of mice irradiated at a dose of 1 Gy or exposed to stress

animal group	the concentration of MDA in the serum of mice, μ M		
	control	1 Gy exposure	stress
exposure without substances	40,8 \pm 1,3	55,6 \pm 2,1 *	52,3 \pm 1,6 *
L-arginine + exposure	-	50,7 \pm 1,2 *	43,8 \pm 2,3 **
"Pronumol" + exposure	-	49,3 \pm 2,2 **	44,9 \pm 2,5 **

* - P < 0,05 significant differences from control; ** - P < 0,05 from substances