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R E P O R T

on the performed research work on the topic "Study of the radioprotective properties of the drug Donovit-VS"

Assessment of the state of lipid peroxidation (LPO) processes in irradiated animals, as well as the content of very low density lipoproteins (VLDL), low density (LDL) and high density (HDL) in the blood plasma.

The work was carried out jointly in the department of radiobiology of the Institute of Experimental Pathology, Oncology and Radiobiology named after N.N. R.E. Kavetsky National Academy of Sciences of Ukraine (Head of the Department of Doctor of Biology, Prof. Ya.I. Serkiz) and the Laboratory of Radiation Cytology (Head of the Laboratory, Doctor of Biology G.M. Chobotko) of the Institute of Experimental Radiology of the Scientific Center for Radiation Medicine of the Academy of Medical Sciences of Ukraine

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MATERIALS AND METHODS

The studies were carried out on 3-month-old mature male Wistar rats. Animals were irradiated once on a RUM-17 X-ray machine: Cu filters 0.5 mm + Al 1 mm, exposure dose rate 0.529 mA/kg.

Starting from the day of irradiation, animals every day before exposure for 30 days with drinking water they gave the drug "Donovit-VS" (experimental name VS-1). The calculated amount of the drug per animal was twice the dose (calculated on the body weight of the rat) recommended for humans. The drug was given to animals in the form of an aqueous solution in the amount of 10 ml per animal per day.

Animals were divided into 11 groups:

1 - control (intact) animals;
2- irradiated at a dose of 3 Gy;
3- irradiated at a dose of 3 Gy + preparation VS-1;
4- irradiated at a dose of 5 Gy;
5 - irradiated at a dose of 5 Gy + preparation VS-1;
6 - irradiated at a dose of 6 Gy;
7 - irradiated at a dose of 6 Gy + drug BC-1;
8 - irradiated at a dose of 7 Gy;
9 - irradiated at a dose of 7 Gy + preparation VS-1;
10 - irradiated at a dose of 9 Gy;
11 - irradiated at a dose of 9 Gy + preparation VS-1.

Each group consisted of 100 pieces. animals. In all groups of animals, we studied the dynamics of death within 30 days from the moment of irradiation (table 1), which is generally accepted when performing experiments on small laboratory animals. In this series of experiments, 11 groups x 100 animals = 1100 rats were used.

In order to assess the state of lipid peroxidation (LPO) processes in irradiated animals, as well as in the dynamics of taking the BC-1 preparation, the content of very low density lipoproteins (VLDL), low density (LDL) and high density (HDL) in the blood plasma was studied. Blood plasma lipoproteins were extracted by single [1] and successive [2] ultracentrifugation in a saline medium at a given density. Ultracentrifugation was carried out for 60 minutes at a temperature of $15C^{o}$ on an L8-80 Beckman using a TV865 vertical rotor at 65000g. The distribution of lipoproteins was studied using polyacrylamide gel disc electrophoresis [3] using a Camag device for gel densitometry at a wavelength of 560 nm.

To assess the intensity of lipid peroxidation, primary products - diene conjugates (DC) were studied according to the modified method of V.P. Gavrilov [4] at a wavelength of 233 nm, as well as secondary LPO products - malondialdehyde (MDA) according to the method of S.V. Andreeva [3] at a wavelength of 532 nm.

To study lipoproteins and lipid peroxidation products in blood plasma, similar groups of animals were taken in the amount of 7 pcs. in each. The indicators were studied in terms: 0.5; 1;

6; 12; 24 and 720 days after irradiation (Table 2 and H). In this series of experiments used: 11 groups x 6 terms x 7 animals = 462 animals.

In total, 1100+462=1562 animals were used in the experiment.

The research results were processed statistically according to the generally accepted Student's criterion.

RESULTS OF RESEARCH

Course application of the drug VS-1 for 30 days after a single exposure of animals to x-rays significantly reduces their death at non-absolutely lethal doses of radiation (table 1). At a dose of 3 Gy, the use of VS-1 did not lead to the death of animals. At a dose of 5 Gy + VS-1, death was reduced by 70%, at a dose of 6Gy - by 24%. At high doses of radiation 7-9 Gy, the drug was ineffective.

Blood plasma lipoproteins are known to perform a transport function, providing cells and their membrane structures with cholesterol, triglycerides, phospholipids, fat-soluble vitamins, hormones, etc., which significantly affects the functions of individual body systems.

For ease of use of the data given in Tables 2 and 3, the numbers of groups of animals in these tables are aligned with the numbers of groups and the conditions of the experiment indicated in Table 1.

The research results (Table 2) indicate that the drug mainly for all classes of lipoproteins exhibits a protective effect, starting from 12 hours after irradiation (provided that it was administered to animals before irradiation). The maximum effect of the drug was noted by the end of the observation period (30 days). It was also established that, similarly to the criterion of survival of animals, the drug has a stabilizing effect at doses including 6 Gy.

According to the content of primary and secondary lipid peroxidation products (Table 3), the radioprotective properties of the preparation VS-1 also remain in the range of radiation doses of 3 and 5 Gy.

Thus, as a result of the work performed, it was found that the preparation VS-1 has radioprotective properties. According to the criterion of survival of animals, which is the main one in such tests, these properties of the drug manifest themselves significantly at doses of 3-5 Gy. At a dose of 6 Gy, the effect of the drug is insignificant, and at high doses of radiation of 7–9 Gy, the restorative properties of the drug do not appear. It should be taken into account that the preparation VS-1, close to the survival test, has a stabilizing effect on the radiogenic changes in individual LPO parameters. This allows us to draw an important conclusion about the possible mechanism of its action. Judging by the direction of changes in the content and ratio of different classes of lipoproteins and peroxidation products over time in irradiated animals, the VS-1 preparation obviously has a positive effect on the system of regulation of cellular metabolism and, first of all, on the membrane complex, on the synthesis and transport of constituent lipids, hormones, vitamins and other substances.

Tab. 1. The number of dead animals after a single irradiation, as well as after the action of radiation and the drug VS-1.

Group	Experience conditions	Days after irradiation																Total died by 30 days
		0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	
1	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	3 Gy	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	2
3	3Gy+VS-1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	5Gy	0	1	1	1	2	3	3	1	2	1	0	1	0	1	0	0	17
5	5Gy+VS-1	0	1	0	0	1	1	1	0	1	0	0	0	0	0	0	0	5
6	6Gy	1	2	3	4	4	5	6	6	5	4	3	2	2	1	0	1	49
7	6Gy+VS-1	1	3	2	3	3	4	4	4	3	4	2	1	2	0	1	0	37
8	7Gy	3	5	8	7	9	9	8	6	7	4	5	3	2	4	1	2	83
9	7Gy+VS-1	4	4	6	8	9	8	10	7	6	5	4	2	4	3	0	1	81
10	9Gy	8	8	10	16	15	13	16	8	5	1							100
11	9Gy+VS-1	7	9	12	15	14	17	13	7	4	2							100

Table 2. The content of very low density lipoproteins (VLDL), low density lipoprotein (LDL) and high density lipoprotein (HDL) in the blood plasma of animals after a single irradiation and after exposure to radiation and the drug VS-1, % to control.

№ group	Lipoproteins	Time after irradiation, hours					
		0.5	1.0	6.0	12	24	720
2	VLDL LDL HDL	107±П 101±9 97±7	142±16 105±8 95±11	149±10 108±11 89±9	154±14 113±10 83±6	162±17 119±12 77±8	167±13 121±8 81±9
3	VLDL LDL HDL	105±11 103±10 101±9	141±13 105±9 94±11	145±15 101±8 102±9	134±13 102±11 95±8	112±14 100±9 92±7	104±11 108±12 97±10
4	VLDL LDL HDL	113±12 103±9 93±8	167±18 107±И 89±10	179±17 П6±12 80±9	186±19 125±14 65±7	192±20 130±13 58±6	198±21 133±15 56±9
5	VLDL LDL HDL	114±13 102±11 95±8	169±18 108±9 92±9	167±16 105±11 88±11	160±15 112±10 77±8	148±13 117±12 79±9	141±16 119±13 71±10
6	VLDL LDL HDL	116±11 104±9 91±8	172±19 109±10 86±9	190±21 121±12 74±8	198±21 131±14 58±9	205±23 139±15 49±7	213±24 142±17 47±8
7	VLDL LDL HDL	117±10 105±8 92±9	171±18 112±11 88±10	192±21 119±13 71±8	191±20 116±13 62±8	186±21 125±14 50±7	182±19 131±15 54±8
8	VLDL LDL HDL	119±12 102±9 90±8	178±19 113±12 82±9	194±21 120±11 75±8	205±22 133±14 53±9	212±23 144±15 40±5	218±19 151±18 38±5
9	VLDL LDL HDL	116±13 103±11 91±9	179±18 114±10 79±9	197±16 116±11 73±8	201±23 135±14 54±7	203±21 138±15 43±9	201±19 140±13 39±8
10	VLDL LDL HDL	129±14 103±11 86±10	185±17 112±10 80±9	206±21 125±13 б7±8	213±24 137±15 49±7	222±26 148±16 31±5	
11	VLDL LDL HDL	132±15 104±11 85±9	181±19 115±12 82±11	209±22 128±10 71±7	207±20 134±15 50±8	219±19 145±1 29±5	

Table 3. The content of lipid peroxidation (LPO) products: diene conjugates (DC) and malondialdehyde (MDA) in the blood plasma of animals after a single irradiation, as well as after exposure to radiation and the drug VS-1, mmol/l.
Norm indicators: DC = 0.79 ± 0.12 mmol/l, MDA = 1.39 ± 0.14 mmol/l

№ group	LPO products	Time after irradiation, hours					
		0.5	1.0	6	12	24	720
2	DC MDA	0.89 ±0.09 1.35 ±0.12	1.71±0.18 1.50±0.17	1.68±0.19 1.61±0.21	1.50±0.13 1.72±0.16	1.41±0.15 2.25±0.24	1.9±0.20 2.60±0.31
3	DC MDA	0.91±0.09 1.29±0.14	1.15±0.20 1.40±0.17	0.93±0.08 1.35±0.12	0.86±0.09 1.41±0.13	0.77±0.08 1.46±0.13	0.72±0.09 1.57±0.19
4	DC MDA	0.92±0.11 1.75±0.18	2.53±0.22 2.10±0.25	2.54±0.27 2.31±0.28	2.32±0.24 2.52±0.27	2.28±0.31 3.25±0.34	2.17±0.24 3.73±0.41
5	DC MDA	0.94±0.11 1.81±0.22	2.43±0.19 2.09±0.21	2.38±0.25 2.24±0.36	2.11±0.20 2.48±0.39	1.75±0.22 2.75±0.32	1.60±0.19 3.16±0.41
6	DC MDA	1.02±0.09 1.76±0.19	2.75±0.26 2.19±0.24	2.74±0.29 2.65±0.28	2.69±0.31 3.03±0.41	2.75±0.26 3.59±0.43	2.26±0.25 4.28±0.56
7	DC MDA	0.98±0.12 1.81±0.17	2.73±0.31 2.18±0.19	2.68±0.24 2.67±0.29	2.71±0.37 3.04±0.33	2.52±0.28 3.51±0.37	2.49±0.52 4.12±0.49
8	DC MDA	1.07±0.13 2.01±0.19	2.85±0.32 2.28±0.33	3.06±0.41 2.75±0.36	3.07±0.36 3.29±0.35	3.14±0.30 3.78±0.40	3.21±0.38 4.63±0.54
9	DC MDA	1.12±0.09 2.36±0.25	2.96±0.28 2.59±0.33	3.11±0.40 2.84±0.31	3.18±0.35 3.49±0.42	3.23±0.34 4.17±0.40	
10	DC MDA	1.12±0.09 2.36±0.25	2.96±0.28 2.59±0.33	3.11±0.40 2.84±0.31	3.18±0.35 3.49±0.42	3.23±0.34 4.17±0.39	
11	DC MDA	0.99±0.12 2.33±0.29	2.91±0.32 2.48±0.31	3.16±0.37 2.79±0.36	3.09±0.34 3.52±0.38	3.34±0.43 4.10±0.55	

CONCLUSIONS

1. According to the criterion of post-radiation death of animals, the VS-1 drug exhibits a significant radioprotective effect in the range of absorbed radiation doses up to 5 Gy.

2. The drug VS-1 significantly reduces the intensity of lipid peroxidation due to radiation exposure in the dose range of 3-5 Gy.

3. The preparation VS-1 in a directed way leads to a certain restoration of the content and ratio of blood lipoproteins, which can have a positive effect on the cellular metabolism of irradiated animals. This effect is also seen in the dose range of 3-5 Gy.

4. At radiation doses of 7-9 Gy, VS-1 is ineffective.

LITERATURE

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