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# Influence of Peptide Bioregulators on Indicators of Hemostasis in Blood of Irradiated Experimental Animals at Low Altitude Conditions

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**Abstract**: In modern biology and medicine, much attention is paid to the study of the hemostasis regulation of some cell populations by substances of a peptide nature. They have the ability to regulate the functional and proliferative activity of cells and ensure communication in normal and pathological conditions. Research data showed that significant violations of the hemostatic system also occur with radiation damage to the body. One of the first radiation responses involves the coagulation cascade's activation, which leads to the breakdown of fibrinogen and the formation of fibrin clots. The potential threat of this is quite evident due to the existence of uranium mining tailings in several regions of the Kyrgyz Republic. Considering that significant disturbances of the hemostatic system occur during radiation damage to the body, and effective means are clearly not enough, the study of the effect of bioregulatory peptides in these conditions is of great importance. In the study, we carried out the total X-ray irradiation of laboratory animals on the X-ray therapeutic apparatus RUM-17. Peptide bioregulators peptide-1 and peptide-2 were administered intramuscularly to irradiated animals. Throughout the research, we used methods characterizing all links of hemostasis: vascular-platelet hemostasis, coagulation hemostasis, and fibrinolysis. The study has shown that the use of the peptide bioregulators in the background of acute radiation pathology leads to a decrease in the intensity of the chronic course of post-radiation thrombo hemorrhagic syndrome, contributing to an increase in the content of antithrombin III in the blood and modulating the versatile effects of endogenous heparin, which undoubtedly have a beneficial effect on the pathogenesis of radiation sickness.

**Keywords:** Experimental animals, Irradiation, Kemostasis, Low altitude, Peptide bioregulators.

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## 1. INTRODUCTION

Much attention in modern biology and medicine is paid to studying the involvement of peptidic nature's substances in regulating the hemostasis of some cell populations and their role as signaling molecules providing communicative links in normal and pathological conditions (1, 2). Such studies include various works on the primary participants in the blood coagulation system and their functioning (3), mechanisms of platelet activation (4), as well as the interaction between them (5) and active agents during thrombosis and thrombo-inflammation (6).

In addition to the main participants of the process of hemostasis regulation, such as blood cells and blood clotting factors, the most interesting are physiologically active peptides, which have been isolated from almost all internal organs. They have the ability to regulate the functional and proliferative activity of tissue cells, which are the starting material for their production (7,8). Our work focuses on the study of the functioning of polypeptides isolated from the spleen (conventionally designated as peptide-1) and erythrocytes (respectively peptide-2) in radiation damage of the organism. The potential threat of radiation exposure is exceptionally relevant to the study due to the presence of uranium mine

tailings in the regions of the Kyrgyz Republic. In addition, the wide use of radioactive sources in production, medicine, and other spheres of life of modern man increases the reality of his contact with radionuclides in various conditions of life and damage to various systems of the organism. Data from several studies (9–11) showed that the many identified violations and stepwise changes occur in the hemostasis system in radiation damage to the body. One of the first reactions to radiation involves the activation of the blood coagulation cascade, which leads to fibrinogen cleavage and the formation of fibrin clots. Effective means of therapy are clearly insufficient, and the study of the state of bioregulatory peptides that eliminate multidirectional changes in plasma hemostasis after irradiation is of great importance, which was the basis for this experiment.

## 2. MATERIALS AND METHODS

The experiments were carried out in the spring-summer and autumn periods of the year on 80 outbred rabbits of both sexes, weighing 2-3 kg, and 350 white outbred laboratory rats of both sexes, weighing 120-180 g, in low-mountain conditions (Bishkek, Kyrgyzstan, 760 above sea level). All animals were kept in the vivarium for at least two weeks on a regular diet before the start of the experiments. Due to the fact that the quality of nutrition and the content of microelements in food have a pronounced effect on hemostasis, the diet and quality of nutrition were the same for both intact and irradiated rabbits and rats in Bishkek. Hemostasis in experimental animals was studied in low altitude conditions on the 8th and 14th days of the experiment (that is, on the 3rd and 9th days after the end of the bioregulator administration).

In low-mountain conditions, total X-ray irradiation of animals was carried out on an X-ray therapeutic apparatus, RUM-17. Animals were placed in special cages during irradiation. Two rats were exposed simultaneously at a dose of 3–5 Gy (dose rate 26.1 Gy/min, tube voltage 200 kW, current strength 15 mA, filter 0.5 ml, focal length 92 cm). The dose of irradiation of animals (radiation sickness of moderate severity) was chosen to consider the fact that, on the one hand, the maximum radiation effects in irradiated animals could be detected according to the studied parameters, and on the other hand, the maximum radiation effect was estimated during long periods of observation.

Obtaining blood and plasma. Blood was taken through a fluoroplastic cannula in a fluoroplastic dish with sodium citrate (3.8%) in a ratio of 9:1 and immediately centrifuged for 10 minutes at 1500 rpm. The resulting plasma was pipetted into a siliconized test tube and used in the experiment.

Bioregulatory peptides were obtained by acetic acid extraction according to the Khavinson method. Peptide bioregulators peptide-1 and peptide-2 in our experiments were administered to irradiated animals intramuscularly at a dose of 1 mg/kg of bodily weight. Before administration, peptide bioregulators were diluted in sterile saline. The solutions were administered once a day for 5 days. As a control, the animals were simultaneously injected with a sterile 0.9% sodium chloride solution in the same volume.

Throughout the research, we used methods characterizing all links of hemostasis: vascular-platelet hemostasis, coagulation hemostasis, and fibrinolysis (12).

The resulting material was processed by methods of variation statistics for Student's related and unrelated observations, and the confidence score differences (P) were calculated (13 ).

## 3. RESULTS AND DISCUSSION

### 3.1. Results

In the available literature, we did not find any studies on the effect of peptide-1 on the hemostasis of irradiated animals in low-mountain conditions. We studied the effects of peptide-1 on the hemostasis of animals compared to the effect of physiological saline. So, if the number of platelets in irradiated animals (compared to healthy animals) fell and amounted to $282.7\pm12.6x10^9$/L (Table 1), then after a five-day injection of saline, an even more significant decrease in their number was noted ($262.6\pm8.9x10^9$/L – $210.6\pm1.3x10^9$/L) (Figure 1).

In the control group of animals, fluctuations in the adhesive function of blood platelets were statistically insignificant; however, the platelet aggregation time was extended both on the 8th day of the experiment (from 18.6±2.2 to 35.5±6.0 s) (Table 1) and on the 14th day (Table 2) of the examination (from 18.6±2.2 to 24.7±1.3 s).

So, in animals irradiated in the conditions in low mountains, which were injected with physiological saline, pronounced thrombocytopenia, inhibition of the aggregation function of platelets, and an increase in the time of plasma recalcification were determined.

In addition, the kaolin clotting time of plasma in this group of animals changed in different directions - on the 8th day of the examination, it was shortened from 67.2±1.0 to 59.3±1.0 s, and on the 14th day, it was lengthened from 67.2±1.0 to 90.1±4.7 s. According to the autocoagulation test, pronounced hypocoagulation was detected at the specified time. Also, on the 8th day of development of acute radiation sickness, plasma tolerance to heparin decreased (from 23.1±1.3 to 29.3±0.9), while on the 14th day, it increased from 23.1±1.3 up to 16.3±2.0 min. This indicates that thrombin that binds to heparin is apparently formed in the bloodstream of irradiated rabbits. Along with this, on the 8th day of the examination, the prothrombin time was shortened from 22.4±0.7 to 20.0±0.2 s, and the thrombin time remained practically unchanged, the concentration of fibrinogen in the blood plasma decreased from 4.2±0.28 to 3.4±0.06 g/l (Table 1-2).

On the 8th and 14th days of the experiment in the control group of animals, the plasma recalcification time was extended (respectively from 78.5±1.2 to 93.8±1.3 s and from 78.5±1.2 to 86.0±0.2 s).

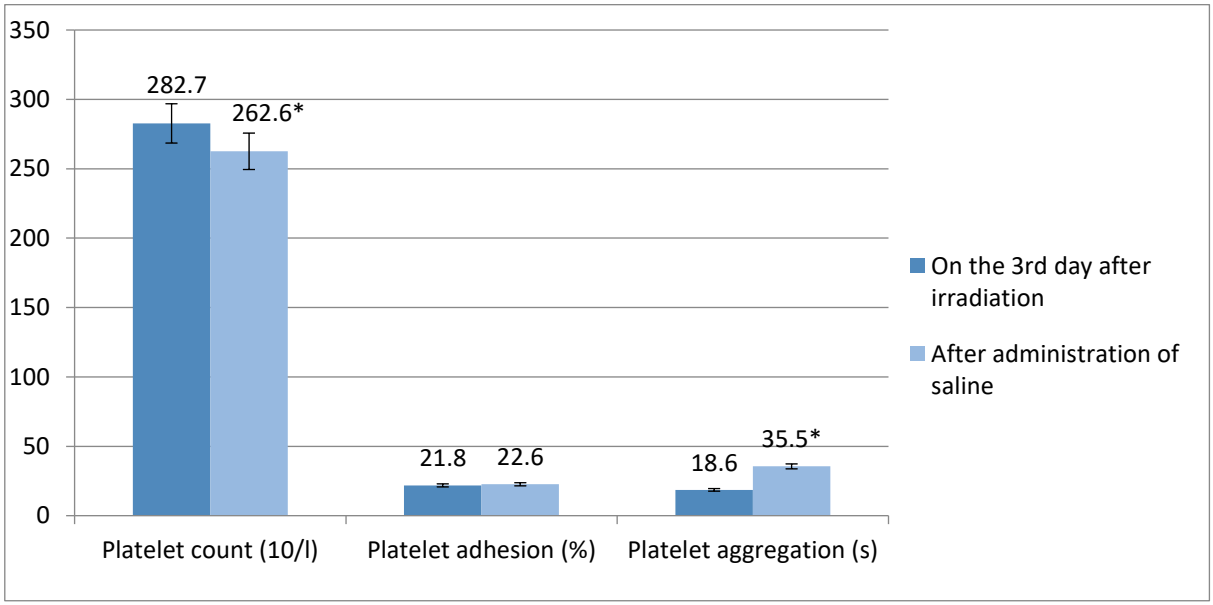


**Figure 1:** Influence of saline solution on hemostasis of irradiated animals in low mountains (on the 8th day of examination)

**Table 1:** Influence of saline solution on hemostasis of irradiated animals in low mountains (on the 8th day of examination)

| Indicators | On the 3rd day after irradiation | After administration of saline |
|---|---|---|
| Plasma recalcification time (s) | 78.5±1.2 | 93.8 ±1.3 |
| Kaolin clotting time (s) | 67.2±1.0 | 59.3±1.0* |
| Autocoagulation test (c) | | |
| at 6th minute | 12.5±0.4 | 14.8±0.2* |
| at 8th minute | 11.3±0.3 | 12.6±0.2* |
| at 10th minute | 9.1±0.6 | 11.5±0.1* |
| Prothrombin time (s) | 22.4±0.7 | 20.0±0.2 |
| Thrombin time (s) | 25.7±0.3 | 26.2±1.2 |
| Kaolin-cephalin clotting time (s) | 33.7±0.8 | 108.7±5.4* |
| Plasma tolerance to heparin (min) | 23.1±1.3 | 29.3±0.9* |
| Antithrombin III (c) | 47.1±0.6 | 88.6±15.3* |
| Fibrinogen (g/l) | 4.2±0.2 | 3.4±0.06* |
| Euglobulin fibrinolysis (min) | 141.1±7.2 | 150.0±10.8 |
| Ethanol test (%) | 55.0 | 62.5 |
| Protamine sulfate test (%) | 44.0 | 50.0 |

NOTE:* P<0.05 when compared with control (3rd day after irradiation)

Based on the fact that in irradiated animals (who received and did not receive saline), in addition to the above changes, positive ethanol, and protamine sulfate tests were also noted in 55% and 44% of cases, respectively, we can talk about the formation of post-radiation thrombohemorrhagic syndrome on the indicated days of observation. At the same time, total fibrinolysis was sharply activated in these animals, which indicated that the plasminogen activator entered the bloodstream from the vascular wall and tissues.

**Table 2:** Influence of saline solution on hemostasis of irradiated animals at low mountain conditions (on the 14th day of examination)

| Indicators | On the 3rd day after irradiation | After administration of saline |
|---|---|---|
| Platelet count (10/l) | 282.7±12.6 | 210.6±1.3* |
| Platelet adhesion (%) | 21.8±0.6 | 22.5±0.9 |
| Platelet aggregation (s) | 18.6±2.2 | 24.7±1.3* |
| Plasma recalcification time (s) | 78.5±1.2 | 86.0±0.2* |
| Kaolin clotting time (s) | 67.2±1.0 | 90.1±4.7* |
| Autocoagulation test (c) | | |
| at 6th minute | 12.5±0.4 | 13.2±0.5 |
| at 8th minute | 11.3±0.3 | 11.8±0.5 |
| at 10th minute | 9.1±0.6 | 11.7±0.4* |
| Prothrombin time (s) | 22.4±0.7 | 19.8±0.5* |
| Thrombin time (s) | 25.7±0.3 | 23.1±1.2 |
| Kaolin-cephalin clotting time (s) | 33.7±0.8 | 78.7±2.1* |
| Plasma tolerance to heparin (min) | 23.1±1.3 | 16.3±2.0* |
| Antithrombin III (c) | 47.1±0.6 | 118.8±4.7* |
| Fibrinogen (g/l) | 4.2±0.2 | 3.2±0.3 |
| Euglobulin fibrinolysis (min) | 141.1±7.2 | 113.2±8.7* |
| Ethanol test | 55.0 | 62.5 |
| Protamine sulfate test | 44.0 | 50.0 |

NOTE:* P<0.05 when compared with control (3rd day after irradiation)

Thus, the administration of physiological saline to irradiated animals in the conditions of Bishkek does not significantly affect the state of multidirectional changes in hemostasis parameters, indicating the development of post-radiation thrombohemorrhagic syndrome.

In experiments to study the effect of a 5-day administration of peptide-1, it was shown that on the 8th day of the examination, the number of platelets in the blood of irradiated animals increased (from 262.6±8.9 to 286.0±9.6x$10^9$ g/l) (Figure 2) and their adhesion increased against the background of unchanged platelet aggregation.

From the data in Table 3, it can be seen that against the background of the use of peptide-1 in irradiated animals, the time of plasma recalcification was prolonged (from 93.8±1.3 to 128.3±2.0 s), as well as the kaolin time of plasma (from 59.3±1.0 to 107.6±3.3 s). However, according to the autocoagulation test, at the 6th minute, an acceleration of the fibrin clot formation time was detected.

Shortening (from 20.0±0.2 to 17.5±0.1 s) of prothrombin and thrombin (from 26.2±2.2 to 24.0±0.4 s) plasma time also testified about hypercoagulation shifts in hemostasis after the administration of peptide-1. The addition of cephalin significantly shortened (from 108.7±5.4 to 73.3±0.8 s) the kaolin-cephalin clotting time. At the same time, plasma tolerance to heparin increased (from 20.3±0.9 to 24.2±0.6 min), and the content of antithrombin III, fibrinogen in the blood, and the time of euglobulin clot lysis did not change.

**Table 3:** Effect of bioregulatory peptide-1 on hemostasis of irradiated animals in low mountains (on the 8th day of examination)

| Indicators | After administration of saline | After administration of peptide 1 |
|---|---|---|
| Plasma recalcification time (s) | 93.8 ±1.3 | 128.3±2.0* |
| Kaolin clotting time (s) | 59.3±1.0 | 107.6±3.3* |
| Autocoagulation test (c) | | |
| at 6th minute | 14.8±0.2 | 13.1±0.8* |
| at 8th minute | 12.6±0.2 | 12.2±0.6 |
| at 10th minute | 11.5±0.1 | 11.5±0.4 |
| Prothrombin time (s) | 20.0±0.2 | 17.5±0.1* |
| Thrombin time (s) | 26.2±1.2 | 24.0±0.4 |
| Kaolin-cephalin clotting time (s) | 108.7±5.4 | 73.3±0.8* |
| Plasma tolerance to heparin (min) | 20.3±0.9 | 24.2±0.6* |
| Antithrombin III (c) | 68.6±15.3 | 39.2±0.9* |
| Fibrinogen (g/l) | 3.4±0.06 | 3.5±0.2 |
| Euglobulin fibrinolysis (min) | 150.0±10.8 | 141.8±13.5 |
| Ethanol test | 62.5 | 25.0 |
| Protamine sulfate test | 50.0 | 25.0 |

NOTE:* P<0.05 when compared with control (after administration of saline)

On the 14th day of the examination of irradiated rabbits, after a 5-day administration of peptide-1, an increase in the number of platelets (from 210,6±1,3 to 252.1±4.3) in platelet blood plasma was noted (Figure 2). At the same time, adhesion increased (from 22.5±09 to 25.2±0.6%), and the time of ADP aggregation of platelets shortened (from 24.7±1.3 to 19.8±0.6 s), recalcification time lengthened (from 86.0±0.2 to 109.2±1.8 s) and plasma kaolin time shortened (from 90.1±4.7 to 74.1±1.3 s). According to the ACT indicators, a pronounced hypercoagulation was revealed at the analysis's 6th, 8th, and 10th minutes. It should also be noted that in irradiated animals, the administration of peptide-1 led to prolongation of prothrombin (from 19.8±0.5 to 21.7±0.5 s) and thrombin time. The addition of phospholipids to plasma against the background of activation of the Hageman factor by kaolin caused a sharp shortening (from 78.3±2.7 to 55.3±2.7 s) of the time of formation of a fibrin plasma clot.

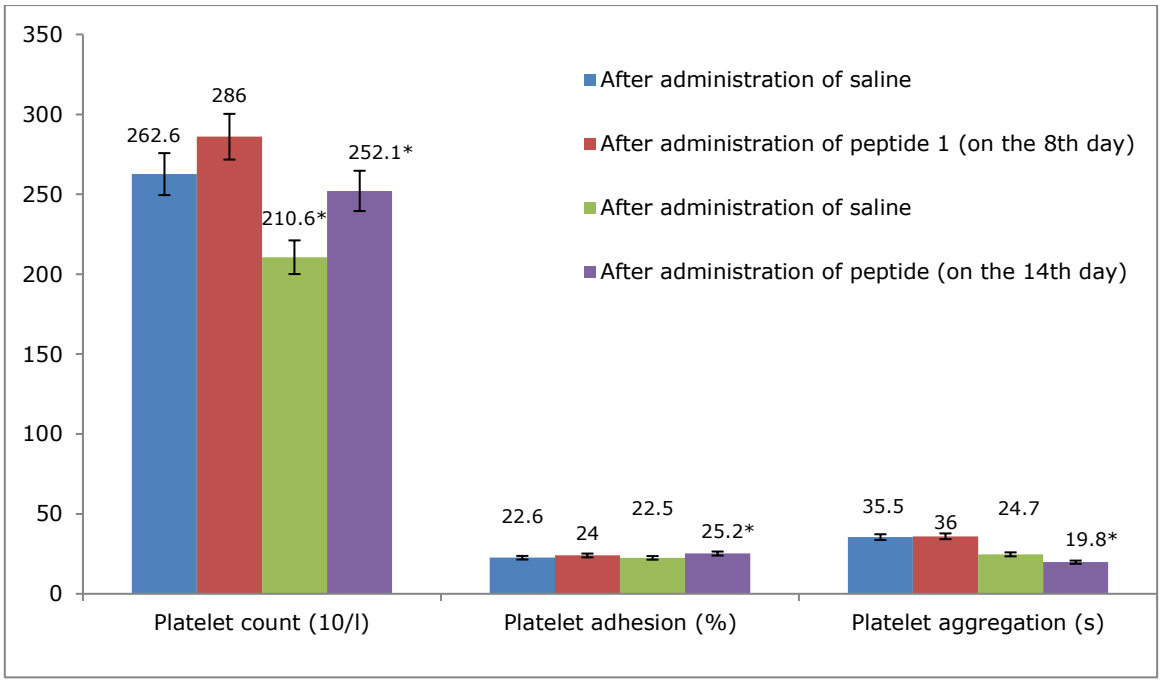


**Figure 2:** Influence of bioregulatory peptide-1 on hemostasis of irradiation of animals in low mountains (on the 8th and 14th day of the examination)

However, the degree of plasma tolerance to heparin in control and experimental animals did not differ much from each other. At the same time, on the 14th day of the examination (the 9th day after the end of the administration of peptide-1), in irradiated animals after the administration of the drug, a decrease (from 118.4± 4.7 to 104.5±1.3 s) was noted in the content of antithrombin III, the concentration of fibrinogen in the blood plasma did not actually change (Table 4).

**Table 4:** Influence of bioregulatory peptide-1 on hemostasis of irradiated animals in low mountains (on the 14th day of examination)

| Indicators | After administration of saline | After administration of peptide 1 |
|---|---|---|
| Plasma recalcification time (s) | 86 | 109.2 |
| Kaolin clotting time (s) | 90.1 | 74.1 |
| Autocoagulation test (c) | | |
| at 6th minute | 13.2 | 10.6 |
| at 8th minute | 11.8 | 8.3 |
| at 10th minute | 11.7 | 6.8 |
| Prothrombin time (s) | 19.8 | 21.7 |
| Thrombin time (s) | 23.1 | 30.1 |
| Kaolin-cephalin clotting time (s) | 78.7 | 55.3 |
| Plasma tolerance to heparin (min) | 16.3 | 16 |
| Antithrombin III (c) | 118.8 | 104.5 |
| Fibrinogen (g/l) | 3.2 | 3.4 |
| Euglobulin fibrinolysis (min) | 113.2 | 76.2 |

Particular attention should be paid to the fact that on the 14th day of the examination, the irradiated animals showed a rather sharp activation of total fibrinolysis, as well as a decrease in the number of positive ethanol and protamine sulfate tests, against the background of the use of peptide-1.

Thus, in conditions of low mountains, 5-day intramuscular administration of peptide-1 at a dose

of 1 mg/kg of body weight to irradiated animals, against the background of the existing pronounced post-radiation thrombohemorrhagic syndrome, led to a significant decrease in the intensity of its course. The favorable effect of peptide-1 on the state of the hemostasis and erythropoiesis system was more pronounced on the 14th day of the examination by the preservation of platelets and their dynamic function in the vascular bed, a decrease in the multidirectional hypo- and hypercoagulation shifts in hemostasis, activation of the fibrinolytic activity of the blood, and a decrease in the number of positive ethanol and protamine sulfate tests for paracoagulation products of fibrin and fibrinogen.

The next series of experiments showed that (Table 4) in irradiated animals after a 5-day administration of the peptide-2 polypeptide, the platelet content did not change significantly on the 8th and 14th days of observation.

Although the Lee-White clotting time for this period of examination in animals after the administration of peptide-2 indicated hypercoagulation, the plasma recalcification time and kaolin clotting time remained practically unchanged, and the plasma kaolin-cephalin time shortened (from 108.7±5.4 to 91.2±2.8 s). Shortening on the 8th (12.6±0.2 to 9.0±1.1 s) and 10th minutes (from 11.5±0.1 to 7.5±1.1 c) of fibrin clot formation evidenced the hypercoagulation orientation of hemostasis. At the same time, prothrombin (from 20.02 to 25.0±1.1 s) and thrombin (from 26.0±1.2 to 50.1±4.2 s) plasma time was lengthened. However, the plasma tolerance to heparin in irradiated animals after the administration of peptide-2 (on the 8th day of observation) increased (from 29.3±0.9 to 16.0±1.4 s) and the content of antithrombin III sharply decreased. Hypofibrinogenemia was also detected, and euglobulin fibrinolysis was inhibited (from 150.0±13.5 to 245.0±45.7 min., $P<0.05$). Evidence of the positive effect of peptide-2 on the hemostasis of irradiated animals in Bishkek is the decrease in positive ethanol tests (from 62.5% to 25%).

**Table 5:** Effect of bioregulatory peptide-2 on hemostasis of irradiated animals in low mountains (on the 8th day of examination)

| Indicators | After administration of saline | After administration of peptide 2 |
|---|---|---|
| Platelet count (10/l) | 262.6±8.9 | 280.0±10.0 |
| Platelet adhesion (%) | 22.6±0.6 | 23.2±1.1 |
| Platelet aggregation (s) | 35.5±6.0 | 25.0±2.7 |
| Plasma recalcification time (s) | 93.8 ±1.3 | 90.0±1.8 |
| Kaolin clotting time (s) | 59.3±1.0 | 35.0±8.5* |
| Autocoagulation test (c) | | |
| at 6th minute | 14.8±0.2 | 14.0±1.4 |
| at 8th minute | 12.6±0.2 | 9.2±1.1 |
| at 10th minute | 11.5±0.1 | 7.5±1.1* |
| Prothrombin time (s) | 20.0±0.2 | 25.0±1.1* |
| Thrombin time (s) | 26.2±1.2 | 50.0±4.2* |
| Kaolin-cephalin clotting time (s) | 108.7±5.4 | 91.2±2.8* |
| Plasma tolerance to heparin (min) | 20.3±0.9 | 16.0±1.4* |
| Antithrombin III (c) | 68.6±15.3 | 34.0±8.0* |
| Fibrinogen (g/l) | 3.4±0.06 | 2.3±0.2* |
| Euglobulin fibrinolysis (min) | 150.0±10.8 | 245.0±45.7* |
| Ethanol test (%) | 62.5 | 25.0 |
| Protamine sulfate test (%) | 50.0 | 50.0 |

NOTE:* $P<0.05$ when compared with control (after administration of saline)

On the 14th day after the administration of peptide-2 to irradiated animals, according to the hemostasiogram parameters, an elongation (86.0±0.2 to 102.2±2.8 s) of the plasma recalcification time was detected along with a simultaneous shortening (from 80.0±2.8 s) of kaolin and kaolin-cephalin (from 78.7±2.7 to 53.0±1.4 s) plasma time. According to the autocoagulation test, hypercoagulation was detected at the 6th, 8th, and 14th minutes. However, on the 14th day after the administration of peptide-2 in irradiated animals, the prothrombin and thrombin (from 23.1±1.2 to 27, 0±1.4 s $P>0.05$) plasma time lengthened. The content of the natural anticoagulant antithrombin III in the blood decreased (from 118.8±4.3 to 108.0±4.2 s at $P<0.05$). The fact of an increase (from 2.3±0.2 to 3.4±0.6 g/l, at $P<0.05$) of fibrinogen in the blood on the 8th day of examination attracts attention on the 14th day of observation after the administration of peptide- 2 concentration did not change. There was a significant decrease (from 62% to 25%) in positive ethanol and protamine sulfate tests (from 50% to 25%) for fibrin and fibrinogen paracoagulation products (Table 5).

Thus, intramuscular 5-day administration of peptide-2 at a dose of 1 mg/kg of body weight to irradiated animals in low-mountain conditions against the background of post-radiation thrombohemorrhagic syndrome expressed in them led to a significant decrease in the intensity of this syndrome.

**Table 6:** Effect of bioregulatory peptide-2 on hemostasis of irradiated animals in low mountains (on the 14th day of examination)

| Indicators | After administration of saline | After administration of peptide 2 |
|---|---|---|
| Platelet count (10/l) | 210.6±1.3 | 270.0±4.2* |
| Platelet adhesion (%) | 22.5±0.9 | 25.0±0.5* |
| Platelet aggregation (s) | 24.7±1.3 | 25.7±2.8 |
| Plasma recalcification time (s) | 86.0±0.2 | 102.2±2.8* |
| Kaolin clotting time (s) | 90.1±4.7 | 80.0±2.8* |
| Autocoagulation test (c) | | |
| at 6th minute | 13.2±0.5 | 10.2±0.8* |
| at 8th minute | 11.8±0.5 | 8.0±0.5* |
| at 10th minute | 11.7±0.4 | 5.7±0.2* |
| Prothrombin time (s) | 19.8±0.5 | 21.2±0.5 |
| Thrombin time (s) | 23.1±1.2 | 27.0±1.4* |
| Kaolin-cephalin clotting time (s) | 78.7±2.1 | 53.0±1.4* |
| Plasma tolerance to heparin (min) | 16.3±2.0 | 15.7±0.5* |
| Antithrombin III (c) | 118.8±4.7 | 108.0±4.2* |
| Fibrinogen (g/l) | 3.2±0.3 | 3.3±0.3 |
| Euglobulin fibrinolysis (min) | 113.2±8.7 | 125.0±10.0* |
| Ethanol test (%) | 62.5 | 25.0 |
| Protamine sulfate test (%) | 50.0 | 25.0 |

NOTE: * P<0.05 when compared with control (after administration of saline)

This favorable pharmacological effect of peptide-2 in terms of hemostasiogram is manifested by hypercoagulation shifts in the clotting time of whole blood appears in siliconized and non-siliconized tubes and as well as a shortening of the fibrin clot formation time according to the kaolin-cephalin time and autocoagulation test. It is also important to note that this effect in irradiated animals under conditions of low mountains after the administration of peptide-2 persisted on the 14th day of examination of these animals.

### 3.2. Discussion

Bioregulatory peptide-1 increases the content of antithrombin III in the blood, apparently modulating the pharmacological and pharmacokinetic parameters of heparin. Also, peptide-1 in all our studies in the low mountains caused the activation of fibrinolysis. Stimulation by peptide-1 of blood fibrinolytic activity in healthy and irradiated animals in low altitude conditions can be carried out with the development of erythrocytosis. Strengthening fibrinolysis leads to the dissolution of fibrinogen and the appearance in the vascular bed of fibrin-monomers with anticoagulant properties. These so-called secondary anticoagulants can prevent the development of thrombohemorrhagic syndrome.

According to our data, after a 5-day administration of peptide-2 in the conditions of the city of Bishkek, pronounced hypocoagulation was noted in the hemostasis of healthy animals. How can one explain the nature of this, at first glance, the paradoxical reaction of animals in low-mountain conditions to introducing the polypeptide used? As we know, the hemostasis system generally reacts very sensitively and subtly to the slightest changes in the strength and nature of disturbing factors, both endogenous and exogenous. In addition, the response of this system and its stability have biorhythmological and specific features of the organism. Therefore, peptide-2, administered parenterally, acts against the background of a pronounced stress state, which necessarily creates the preconditions for increased thrombus formation in the body. It is precisely by acting as a regulator of reciprocal relations in the hemostasis system that, in this case, erythrolin exhibits a hypocoagulant effect in healthy animals in low altitude conditions. The formation of a hypocoagulable state in the hemostasis system is assessed by us as a positive effect of peptide-2 since it prevents stress thrombus formation in low-altitude conditions. This is confirmed by the fact that in this group of animals, there was an increase in the number of platelets in the blood and, most importantly, the content of the natural anticoagulant antithrombin III in the blood increased (on the 14th day of the experiment), and the concentration of fibrinogen increased (from 3.0 ± 0.3 up to 4.1±0.2%). The effect of peptide-2 on hemostasis is associated with the fundamental processes of multilevel regulation of vital functions, including hemostasis of the hemocoagulation system. Based on this, it seems that peptide-2 can block primary and secondary platelet receptors and thereby reduce the "release reaction" of platelets, i.e., keep their number. In addition, depending on the initial physiological state of the hemostasis system, it can either compensate the lack of erythrocyte coagulation factors or reduce their excess activity. As a result, its regulatory function is manifested against the background of the hypercoagulation orientation of hemostasis, peptide-2 forms hypocoagulation, and conversely, against the background of hypocoagulation leads to hypercoagulable shifts.

It is known that profound disorders in the blood coagulation system develop with radiation damage to the body, which usually have a hypocoagulant orientation. In conditions of low mountains after total X-ray irradiation on the 8th and 14th days in rabbits, we revealed pronounced hypocoagulation, a decrease in the content of antithrombin III and activation of fibrinolysis. The presence of

thrombohemorrhagic syndrome explains, in part, a drop in the number of platelets, a decrease in the prothrombin index, an increase in fibrinogen levels, and the appearance of paracoagulation products. Yet, we consider the development of thrombohemorrhagic syndrome to be the main one in the genesis of acute radiation injury, which causes hemorrhagic symptoms in acute radiation sickness.

## 4. CONCLUSION

The introduction of peptide bioregulators in low altitude conditions in healthy animals leads to the development of hypocoagulation, which is expressed in an increase in the number of platelets, the content of fibrinogen and antithrombin III in the blood, an increase in the time of formation of a fibrin clot, kaolin, kaolin-cephalin plasma time. Under conditions of low mountains, bioregulatory peptides peptide-1 and peptide-2 significantly reduce the intensity of secondary post-radiation hypocoagulation, which is manifested by a shortening of the whole blood clotting time in siliconized and non-siliconized tubes, kaolin, kaolin-cephalin time and plasma recalcification time. This effect of bioregulatory peptides is more pronounced on the 14th day of the examination and is manifested by an increase in the number of platelets in the blood with their full function and activation of fibrinolysis. Functional inferiority of hemostasis subsystems can be effectively corrected by peptide bioregulators peptide-1 and peptide-2 in low-mountain conditions.

Thus, the use of peptide bioregulators against the background of acute radiation pathology in low altitude conditions leads to a decrease in the intensity of the chronic course of post-radiation thrombohemorrhagic syndrome, contributing to an increase in the content of antithrombin III in the blood and modulating the versatile effects of endogenous heparin, which undoubtedly have a beneficial effect on the pathogenesis of radiation sickness.

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