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# HONEYBEE VENOM, APIS MELLIFERA, AS A MEANS OF PREVENTION AND PROTECTION FROM RADIATION-INDUCED DAMAGE TO LIVING ORGANISMS

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# ფუტკრის შხამი Apis mellifera, როგორც ცოცხალი ორგანიზმების რადიაციული დამარცხებისგან პრევენციისა და დაცვის საშუალება

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## რეზიუმე

კვლევის მიზანი იყო ფუტკრის Apis mellifera L. caucasica-ს შხამის რადიოპროტექტორული ეფექტის შესწავლა თაგვების ერთჯერადი γ-დასხივებისას 60Co-ით D = 1, 3, 5, 7, 10 Gy დოზებით 1 Gy/წთ. შესწავლისთვის გამოვიყენეთ ეკოლოგიურად სუფთა და გამა გამოსხივების მცირე დოზებით დასხივებული შხამი, აზერბაიჯანის ეკოლოგიურად სუფთა ტერიტორიაზე მდებარე საფუტკრეებიდან. ექსპერიმენტები ჩატარდა 5 სერიის „in vitro“ 3 თვის, 18-22 გრამი წონის თეთრ თაგვებზე. თაგვებს ინტრამუსკულარული ინექციით გაუკეთდათ 18-22 გრამი ფუტკრის შხამი, დოზით 0.1, 0.2, 0.4 და 0.5მგ/კგ სხეულის მასაზე გათვლით. 24 საათის შემდეგ, კი ერთჯერად γ-დასხივებით 60Co დოზით D=1, 3, 5 და 7 Gy სიჩქარით 1Gy/წთ დოზით. თაგვების ექსპერიმენტული ჯგუფების გადარჩენის მაჩვენებელი საკონტროლო ჯგუფთან მიმართებაში შხამის შეყვანიდან 24 საათის შემდეგ ერთჯერადი ინტრაპერიტონიალური ან ინტრამუსკულარული ინექციის დროს გაიზარდა 33%-დან 56%-მდე და 35%-დან 50%-მდე დიაპაზონში. შესაბამისად მიგვაჩნია, რომ ფუტკრის შხამის რადიოპროტექტორული ეფექტი დაკავშირებულია არასპეციფიკური ადაპტაციის რეაქციის წარმოქმნასთან. შხამის ინტრაპერიტონიალური ან ინტრამუსკულარული ფრაქციული შეყვანისას, რასაც მოჰყვა 60Co-ს ერთჯერადი γ-დასხივება D = 1, 3, 5 და 7 Gy დოზით 1Gy/წთ, თაგვების ექსპერიმენტული ჯგუფების სიცოცხლის ხანგრძლივობის ზრდა აღინიშნა 33%-დან 56%-მდე 53%-დან 755%-მდე დიაპაზონში. შხამის ერთჯერადი (24 საათი) ინტრაპერიტონეალური ან ინტრამუსკულარული ინექციისას თაგვების ექსპერიმენტული ჯგუფების სიცოცხლის ხანგრძლივობა გაიზარდა შესაბამისად 35%-დან 50%-მდე და 52%-დან 66%-მდე.

The issue of radiation protection is becoming increasingly relevant today. One of the most severe pathologies that requires intensive pharmacotherapy and prevention is radiation injury resulting from acute external radiation exposure [1, 2]. The prevention of adverse effects caused by exposure to hazardous radiation doses is achieved through the use of prophylactic radioprotective agents—radioprotectors. However, existing radioprotectors do not always meet the required standards of effectiveness and tolerability [3,4,5,6]. As a result, both in our country and abroad, the search for new radioprotectors from various classes of chemical compounds continues. Equally active is the study of the radioprotective properties of zootoxins and animal-derived preparations. In the research of A.S. Koryagin (2006), the radioprotective effect of honeybee venom was studied in detail. The author suggests that the radioprotective effect of bee venom is associated with the formation of a non-specific adaptation response [7,8]. However, it is important to note the potential for addressing this issue through the combined use of

radioprotective agents from various pharmacological groups. The lethal dose of bee venom for humans is 1.4 mg per 1 kg of body weight. Death most often occurs due to paralysis of the respiratory center [9,10,11]. Moreover, studies on experimental animals with inflammatory diseases have shown that bee venom effectively and successfully suppresses inflammation [12,13]. It is important to note that bee venom contains trace elements such as phosphorus, copper, calcium, and magnesium. The venom is well soluble in acids and water, but insoluble in alcohol. It withstands freezing and heating up to 100–115°C but is sensitive to sunlight. The lethal dose of bee venom for humans is approximately 0.2 g. For mice, a single bee sting is toxic—they typically die after being stung once. On average, a bee injects between 0.3 to 0.8 mg of venom per sting. The LD50 (median lethal dose) of bee venom for white laboratory mice is 4 mg/kg of body weight. To study the radioprotective effect of honeybee venom, the control group of mice was irradiated at doses of D = 1, 3, 5, and 7 Gy. Experimental groups of 2–3-month-old white mice with a total body mass of 18–22 grams were pre-treated intraperitoneally with bee venom at doses of 0.1, 0.2, 0.4, and 0.5 mg/kg of body weight once daily for three consecutive days.

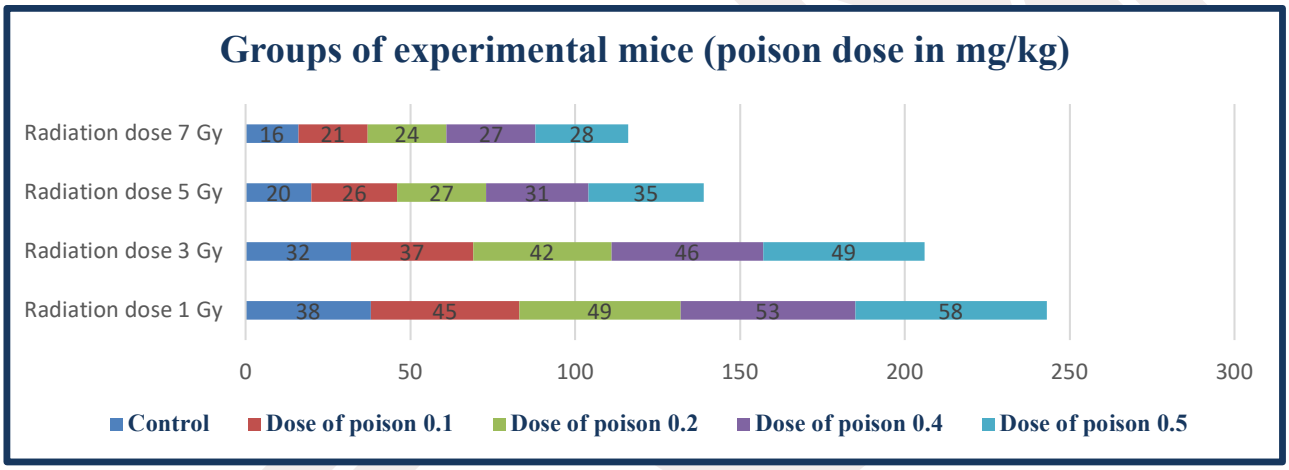


**Figure 1.** Survival of mice when mice were injected intraperitoneally with bee venom at doses of 0.1, 0.2, 0.4, and 0.5 mg/kg body weight, followed by single γ-irradiation with 60Co at doses of D=1, 3, 5, and 7 Gy at an irradiation dose rate of 1 Gy/min.

Next, the first experimental group of mice was subjected to a single γ-irradiation with ^60Co at a dose of D = 1 Gy with a dose rate of 1 Gy/min, three days after the initial treatment. The second experimental group was subjected to single γ-irradiation with ^60Co at a dose of D = 3 Gy with the same dose rate, also three days after treatment. The third experimental group received a single γ-irradiation with ^60Co at a dose of D = 5 Gy, and the fourth experimental group was irradiated with ^60Co at a dose of D = 7 Gy — both groups also three days after the initial treatment with bee venom, and at a dose rate of 1 Gy/min (see Fig. 1). Subsequent 5, 6, 7 and 8 groups of experimental mice were injected intramuscularly with bee venom at a dose of 0.1 mg/kg of body weight followed by a single γ-irradiation with 60Co irradiation at a dose of D=1 Gy at a dose rate of 1 Gy/min at a frequency of once a day.

Survival data of mice with intramuscular injection of bee venom at doses of 0.1, 0.2, 0.4 and 0.5 mg/kg body weight followed by single γ-irradiation with 60Co at doses of 1, 3, 5 and 7 Gy at a dose rate of 1 Gy/min are shown in Figure 2.

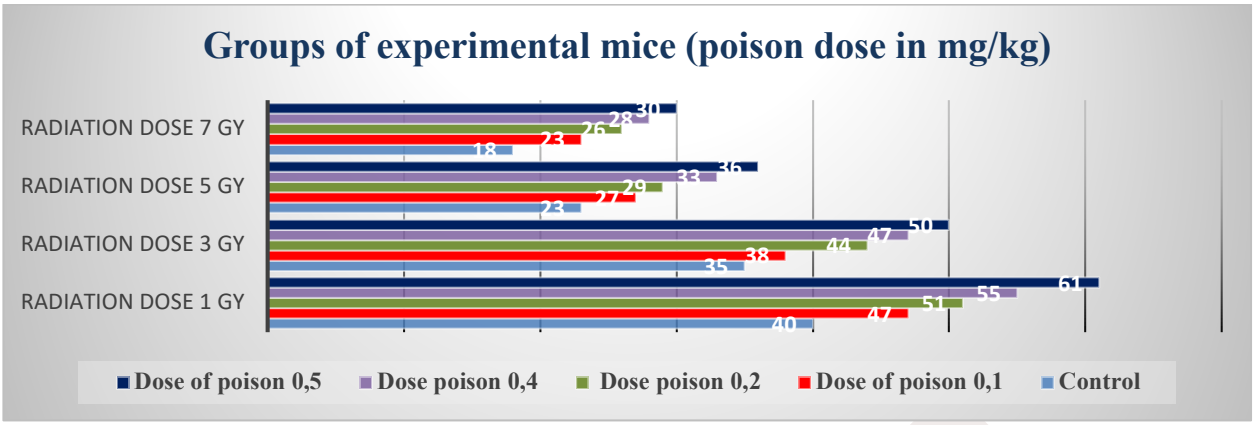


**Figure 2.** Survival of mice after intramuscular administration of bee venom at doses of 0.1, 0.2, 0.4, and 0.5 mg/kg body weight followed by single γ-irradiation with ^60Co at doses of D = 1, 3, 5, and 7 Gy, with an irradiation dose rate of 1 Gy/min.

Survival data of mice after intraperitoneal administration of bee venom at doses of 0.1, 0.2, 0.4, and 0.5 mg/kg body weight, followed by single γ-irradiation with ^60Co at doses of D = 1, 3, 5, and 7 Gy with a dose rate of 1 Gy/min, are shown in Figure 3. The survival of mice after intraperitoneal administration of bee venom at doses of 0.1, 0.2, 0.4, and 0.5 mg/kg body weight, followed (after 24 hours) by single γ-irradiation with ^60Co at doses of D = 1, 3, 5, and 7 Gy with a dose rate of 1 Gy/min, is presented in Figure 4. Subsequently, mice in groups 14, 15, 16, and 17 were intramuscularly injected with bee venom at doses of 0.1, 0.2, 0.4, and 0.5 mg/kg body weight, and after 24 hours were subjected to single γ-irradiation with ^60Co at doses of D = 1, 3, 5, and 7 Gy at a dose rate of 1 Gy/min.

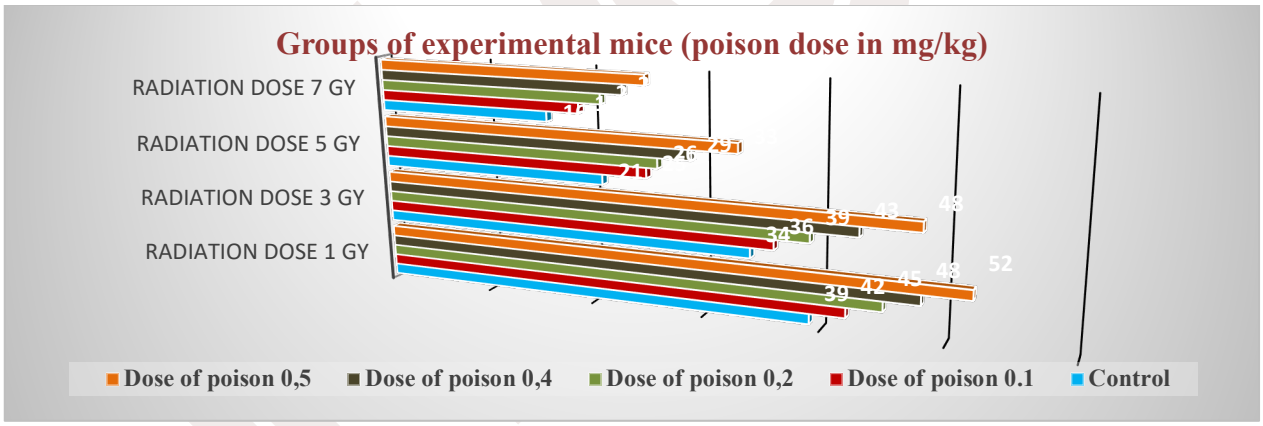


**Figure 3.** Survival of mice by intraperitoneal injection of bee venom followed by single γ-irradiation with 60Co at doses of D=1, 3, 5, and 7 Gy at a dose rate of 1 Gy/min.

In experiments on mice involving intraperitoneal or intramuscular fractional administration of bee venom followed by a single γ-irradiation with ^60Co (at doses of D = 1, 3, 5, and 7 Gy and an irradiation dose rate of 1 Gy/min), an increase in the lifespan of the experimental animal groups was observed. The survival rate of mice in these groups, compared to the control group, increased by: **33% to 56%** with intraperitoneal administration of the venom; **35% to 50%** with intramuscular administration.

Thus, the results of the experiments reliably indicate a radioprotective effect of honeybee venom, manifested in the increased survival and lifespan of animals exposed to γ-irradiation.

It was found that the administration of bee venom is accompanied by prolonged radioresistance, reducing the impact of ionizing radiation on the lifespan of mice under conditions of single gamma irradiation. The study of the radioprotective effect of course-based administration of low doses of bee

venom under conditions of single fractionated gamma irradiation broadens the understanding of nonspecific radioresistance and offers the potential for the development of new drugs based on biologically active substances of animal origin that enhance the body's resistance to radiation.

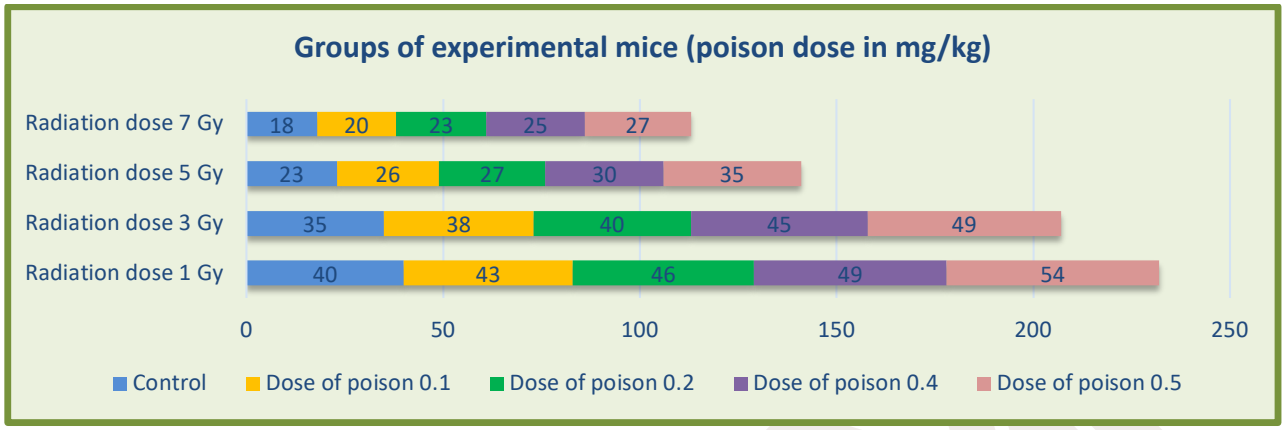


**Figure 4.** Survival of mice by intraperitoneal injection of bee venom followed by single γ-irradiation with 60Co at doses of D=1, 3, 5, and 7 Gy at a dose rate of 1 Gy/min.

Radioresistance, which develops in the organism as a result of repeated injection of bee venom, allows the organism to be successfully protected from fractionated gamma irradiation. Thus, increased longevity of mice varies both with the route of injection and the time of venom injection after γ-irradiation.

**Conclusions:**1. During fractional injection of venom with subsequent γ-irradiation 60Co at doses D=1,3,5, and 7Gy with irradiation dose rate of 1Gy/min, the lifespan of experimental groups of mice was increased from 33% to 56% and from 53% to 75%. 2. At a single (after 24 hours) injection of poison, the life expectancy of experimental groups of mice increased from 35% to 50% and from 52% to 66%, respectively.

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### SUMMARY

This work aimed to study the radioprotective effect of the venom of the honeybee Apis mellifera L. caucasica during a single γ-irradiation of mice with $^{60}$Co in doses of D = 1, 3, 5, 7, 10 Gy at a dose rate of 1 Gy/min. The material of the study was ecologically pure whole venom collected from bees from apiaries located in the ecologically clean territory of Azerbaijan, and venom irradiated with small doses of gamma radiation. The experiments were conducted in 5 series of experiments in vitro on 3-month-old white mice weighing 18-22 grams. We have examined the prevention of radiation damage to experimental animals from honeybee venom, which occurs during external irradiation of mice. Experimental mice were injected intramuscularly with bee venom at a dose of 0.1, 0.2, 0.4 and 0.5 mg/kg of body weight and after 24 hours were subjected to a single γ-irradiation with 60Co at a dose of D = 1, 3, 5 and 7 Gy at a dose rate of 1 Gy/min. An increase in the total number of surviving animals was noted in all studied groups; however, the nature of the change in the lifespan of mice differs both from the method of administration and from the time of administration of the poison after γ-irradiation with $^{60}$Co. The survival rate of experimental groups of mice, compared to the control group, with a single intraperitoneal or intramuscular injection 24 hours after the introduction of the venom, increased within the range from 33% to 56% and from 35% to 50%, respectively. We believe that the radioprotective effect of bee venom is associated with the formation of a non-specific adaptation reaction. With intraperitoneal or intramuscular fractional administration of the poison followed by a single γ-irradiation of 60Co at a dose of D = 1, 3, 5 and 7 Gy at a dose rate of 1 Gy/min, an increase in the life expectancy of the experimental groups of mice was noted within the range from 33% to 56% and from 53% to 75%. With a single (24 hours) intraperitoneal or intramuscular injection of the poison, the life expectancy of the experimental groups of mice increased by 35% to 50% and 52% to 66%, respectively.

**Keywords:** Honeybee, venom, Apis mellifera, radiation, radioprotectors