



Characteristics of Biologically Active Properties and Therapeutic Use of *Ulomoides dermestoides* Beetles

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ABSTRACT

Every year there is an increase in patients suffering from autoimmune and immunodeficiency diseases. At the same time, in countries with an underdeveloped pharmaceutical market, insectotherapy is a particularly popular treatment. The purpose of the research work is to study the possibility of using *U. dermestoides* beetles as a source of raw materials for the development of an immunomodulatory agent. The conducted literature search has shown the potential of using *Ulomoides dermestoides* beetles for the treatment of various diseases. During the research work, the biologically active additive "Immutoron" was developed from the biomass of *U. dermestoides*. Moreover, to show the effect of the nutrition quality of *U. dermestoides* beetles on the final product, three samples of the preparation were developed: beetles grown sparingly on a banana peel, sunflower meal, and apple pulp. The resulting drug was given to rats as a dietary supplement, and the following indicators were compared with the control group: body temperature, behavior, white blood cells, erythrocytes, hemoglobin, as well as cholesterol and total protein. It was found that due to the high content of chitin and melanin in the initial product, dietary supplements based on *U. dermestoides* biomass have antioxidant and immunomodulatory properties, while not having any toxic effect on the body of experimental animals.

Keywords: Insectotherapy, *Ulomoides dermestoides*, Biologically active additive, Immunomodulator, Extract.

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INTRODUCTION

The number of patients suffering from autoimmune and immunodeficiency diseases increases every year. In some economically underdeveloped countries, patients are forced to resort to various methods of treatment, one of

the most common is insectotherapy. Most often, the black beetle *Ulomoides dermestoides* is used in insectotherapy. The use of these insects is becoming more and more popular every year, especially in Asia and South America [1, 2]. The effectiveness of their use in chemotherapy, bronchial asthma, oncology, psoriasis, and diabetes has been proven [3]. Substances

contained in the feces of these insects can be used to treat stomach disorders, heart disease, myalgia, kidney diseases, and asthma, as well as against dermatitis, rheumatoid arthritis, hemorrhoids, inflammation, and pain in the liver and kidneys, Parkinson's disease, diabetes, various types of oncology [4-7].

Santos *et al.* [4] conducted a study aimed at evaluating *in vitro* and *in vivo* the anti-inflammatory effect of *U. dermestoides*. A model of acute inflammation by injection of carrageenan into the pleural cavity of rats was used. In experiments with an intrapleural injection of carrageenan-induced by an acute inflammatory reaction characterized by a noticeable accumulation of pleural, plasma exudation and intensive migration of polymorphisms of the pleural cavity. Treatment of animals with *U. dermestoides* extract weakened the inflammatory process: the total number of leukocytes, PMN cells, protein concentration, and volume of pleural exudation after treatment [8-11].

Tobon *et al.* [12] studied a neuropharmacological profile of biologically active substances extracted from *U. dermestoides*. The most significant effect was that the animals presented in this preliminary trial were sleepy and passive; during that time of the experiment, compared with the depressive effect of Diazepam and the

stimulating effect of amphetamine on the central nervous system. Neuropharmacological tests performed showed the depressing effect of *U. dermestoides* extract: on memory, learning, and discrimination. Statistical analysis of the data shows that the extract of *U. dermestoides* produces a noticeable decrease in brain functions in these animals.

The purpose of the research work is to study the possibility of using *U. dermestoides* beetles as a source of raw materials for the development of an immunomodulatory agent.

MATERIALS AND METHODS

Despite the huge volume of biotechnological potencies, *U. dermestoides* beetles have not been used before in the preparation of drugs in the field of immunology, in this regard, there is no detailed description of the technological process of preparation of the drug based on the biomass of these beetles in the available literature. Relying on traditional methods and allowing our modifications, we have prepared an extract from *U. dermestoides*.

The technological process of preparing a biologically active substance from raw materials of animal origin is presented in the block diagram in **Figure 1**.

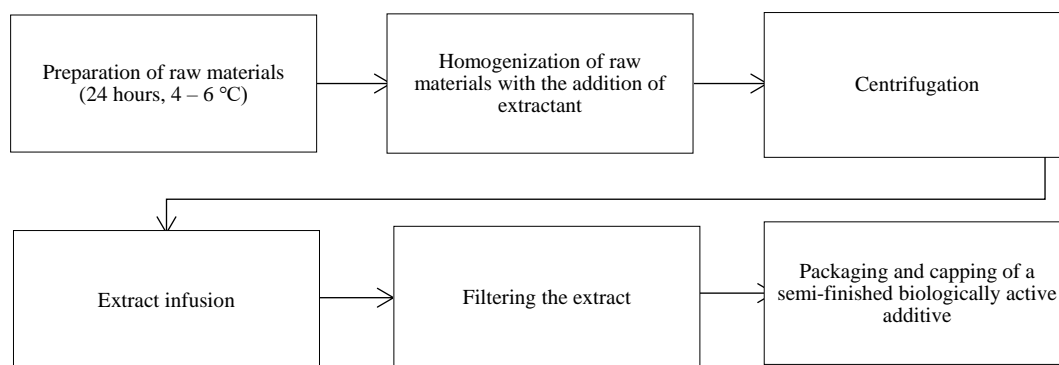


Figure 1. The technology of preparation of the dietary supplement "Immutoron" from *U. dermestoides* biomass.

At the preparatory stage, beetles were grown in a laboratory, while part of the beetles was fed only banana peel (sample 1), part only sunflower meal (sample 2), and part only apple pulp (sample 3). Then the beetles were placed in a refrigerator for a day at a temperature of +4-6 °C for preservation. The cooled bodies of beetles improved the structural and mechanical

properties and facilitated the subsequent homogenization process.

The need for homogenization (grinding) is since extraction is a mass transfer process, and its speed will depend on the contact area between the raw material and the extractant. After homogenization, extracts obtained from raw materials of animal origin *U. dermestoides* were placed in test tubes and subjected to

centrifugation at a speed of 4000 revolutions per minute for five minutes, to separate into fractions according to density. Due to centrifugal forces, the primary juice is removed from the cellular material, a fresh extractant is supplied in its place, which is again removed from the material. The extractant circulates until saturation and then is replaced with a new one.

A saline solution was selected as an extractant. The production of the extract was carried out as follows: homogenate from beetle raw materials in a ratio of 1:10 was poured with saline solution. To prepare the extract taking into account the dry matter content in the homogenate, we took 20 g of homogenate and poured 350 ml of saline solution. The extract was infused for a week at room temperature 20-25 °C, humidity 40-45%, and at normal atmospheric pressure. After the infusion of the extract, a two-time filtration was carried out through a sterile bandage folded in three layers. According to external characteristics, the extract is a viscous liquid of a light yellow color with a pungent odor.

In the final stage of extraction, packaging, and capping of semi-finished products in sterile bottles of 100 ml, as well as labeling, was carried out. Thus, when developing the technology for preparing the extract of the biologically active additive "Immutoron", based on the raw materials of *U. dermestoides* beetles, the most rational method of preparing the extract was used, allowing to preserve the immunomodulatory properties from the original raw materials, and also to develop several biologically active substances that improve the quality of the raw semi-finished product.

The rats are housed in cages mounted on metal racks. Experiments on Wistar rats (n = 40) were carried out following the rules for the protection of vertebrates used for scientific purposes.

After the animals were admitted to the laboratory, they were placed in clean, disinfected cages for quarantine for fourteen days. During the quarantine period, daily clinical observation and registration of the general condition of the animals were carried out. The animals were kept in rooms with a constant temperature of +20-22 °C and air humidity not exceeding 40-45%. The rats had free access to food and water. The rats received a standard vivarium diet recommended by the Research Institute of Nutrition of the Russian Academy of Medical Sciences for

Animals, balanced by the main macronutrients and micronutrients, and chilled boiled water.

Four groups were formed, three experimental and one control group, 10 animals each. The duration of the experiment is 14 days. Rats of the experimental groups were administered orally daily dietary supplement "Immutoron" in a dose of 0.5 ml once. The rats of the control group remained without the introduction of the additive (**Table 1**).

Table 1. Distribution of experimental animals by groups

Group	Type of injected drug
Experience 1	Dietary supplement "Immutoron" (Sample 1, from beetles grown on a banana peel)
Experience 2	Dietary supplement "Immutoron" (Sample 2, from beetles grown on sunflower meal)
Experience 3	Dietary supplement "Immutoron" (Sample 3, from beetles grown on apple pulp)
Control	Control

Body temperature was measured in all rats, as it is an important criterion for assessing the state of the body of warm-blooded animals. The temperature of the animals was within the normal range from 37.0 ± 0.2 °C to 37.5 ± 0.3 °C. To evaluate the immunomodulating drug on the animal body, a cold model of the experiment developed by V.A. Dorovskikh was used [13].

The animals were monitored daily for 14 days. The general immunomodulatory process was evaluated: clinical condition, behavioral characteristics, intensity and nature of the motor activity, signs of intoxication, and possible mortality. It was found that in all tested doses it did not cause the death of rats and did not have a pronounced toxic effect on the body. When evaluating the effectiveness, body temperature, the physical and nutritional activity of animals, immune status indicators, and biochemical and hematological blood tests were taken into account.

RESULTS AND DISCUSSION

The study of blood biochemical parameters is of great diagnostic importance. Even an incomplete hematological and biochemical blood test helps a specialist to reliably determine the state of the animal's body, and periodic examination of the blood composition allows one to determine with high accuracy not only the general condition of

the body but also to predict the outcome of the disease, adjust therapy, study the effect of certain medications. That is why the role of laboratory tests, as well as the range and number of studies required in preclinical studies, is constantly increasing.

A comprehensive analysis of the data obtained during the experiment allowed us to determine the effectiveness of the Immutoron dietary supplement. The effect of biologically active additives on hematological (number of erythrocytes, hemoglobin, leukocytes) and biochemical (total protein, cholesterol, glucose) indicators were studied. The negative influence of the studied "Immutoron" on the conduct and basic clinical parameters (temperature, pulse, respiration) of animals has not been established. Blood samples were taken before the start of the

studies, as well as on the 7th and 14th days of the experiment.

Hematological and biochemical parameters in the second experimental group did not exceed the limits of the physiological norm during the entire study period.

On the 7th day of observation, an increase in the number of red blood cells was noted in the first experimental group – by 9.3%, in the second experimental group – by 8.9%, in the third – by 8.1% compared with the control group. The increase in hemoglobin content in the first experimental group was 11.3%, in the second experimental group – 13.8%, and in the third experimental group – 12.7% (**Table 2**). Biochemical blood parameters in experimental and control animals are shown in **Table 3**.

Table 2. Hematological studies

Indicators	Groups	the beginning of the experiment	after 7 days	after 14 days
White blood cells, ($\times 10^9/l$)	Experience 1	12.3 ± 0.3	12.2 ± 0.2	12.3 ± 0.1
	Experience 2	11.8 ± 0.1	12.2 ± 0.3	12.3 ± 0.3
	Experience 3	12.3 ± 0.2	12.5 ± 0.1	12.1 ± 0.3
	Control	12.1 ± 0.2	12.3 ± 0.2	12.0 ± 0.2
Red blood cells, ($\times 10^{12}/l$)	Experience 1	7.6 ± 0.3	8.7 ± 0.3	8.5 ± 0.3
	Experience 2	7.5 ± 0.2	7.6 ± 0.2	7.5 ± 0.2
	Experience 3	7.7 ± 0.2	8.7 ± 0.3	8.5 ± 0.1
	Control	7.4 ± 0.2	7.4 ± 0.4	7.4 ± 0.2
Hemoglobin, g/l	Experience 1	112.4 ± 5.3	123.4 ± 5.6	127.4 ± 6.3
	Experience 2	112.6 ± 6.1	124.6 ± 5.7	127.4 ± 6.3
	Experience 3	112.4 ± 6.3	123.4 ± 5.6	127.4 ± 6.3
	Control	112.4 ± 5.3	114.8 ± 7.5	112.9 ± 7.7

Table 3. Biochemical parameters of blood serum

Indicators	Groups	the beginning of the experiment	after 7 days	after 14 days
Total protein, g/l	Experience 1	55.4 ± 2.6	56.4 ± 2.6	58.4 ± 2.6
	Experience 2	55.8 ± 2.8	56.1 ± 2.8	62.2 ± 2.9
	Experience 3	56.1 ± 2.6	57.3 ± 2.6	57.9 ± 2.7
	Control	55.7 ± 3.4	54.6 ± 3.2	55.7 ± 4.2
Cholesterol, $\mu\text{mol/l}$	Experience 1	1.1 ± 0.01	1.1 ± 0.01	1.2 ± 0.02
	Experience 2	1.1 ± 0.01	1.2 ± 0.02	1.2 ± 0.01
	Experience 3	1.2 ± 0.01	1.1 ± 0.01	1.2 ± 0.02
	Control	1.2 ± 0.01	1.1 ± 0.01	1.2 ± 0.02

The concentration of total protein in the first experimental group increased by 1.73%, and in the second experimental group – by 5.6%.

At the end of the experiment, the total protein content in the blood serum of group 2 animals

was 13.0 higher compared to the control. No significant differences in cholesterol concentration between the experimental groups and the control were found.

The increase in the total protein content registered in animals of the experimental groups is a consequence not only of the growth of animals but also, in our opinion, is associated with active processes of protein renewal.

Thus, the data obtained during the study allow us to conclude that the scheme of application of the developed dietary supplement used for the first and third experimental groups combines economic and physiological efficiency. As a result of this stage of work to study the effect of the developed dietary supplement on the body of laboratory models, it was found that the drug does not have a depressing effect. The developed dietary supplement improves the immune status and increases the total protein content, which indicates an improvement in the clinical status of experimental animals.

A comprehensive assessment of the data obtained during the study allowed us to conclude that the most effective extract obtained from *U. dermestoides* raw materials, the use of the developed dietary supplement is the first and third option. In addition, we have found that experimental extracts obtained from *U. dermestoides* raw materials are harmless according to the parameters of immunomodulatory ability that correspond to the findings of other researchers [14-16].

CONCLUSION

The use of new effective immunomodulatory drugs derived from insect biomass is of both scientific and practical importance. In the course of studies of literary sources, it was found that *U. dermestoides* beetles have a significant anti-inflammatory effect and can be used in insectotherapy.

During the work, the technology of preparation of the dietary supplement "Immutoron" from raw materials of animal origin, beetles *U. dermestoides* was developed. During subsequent testing for the effectiveness of the Immutoron dietary supplement obtained from *U. dermestoides* raw materials on experimental animals with impaired immune status, it was found that oral administration provides a pronounced acceleration of clinical recovery. The drug does not have a depressing effect. The developed biologically active additive contributes to the improvement of immunity, due to the qualitative improvement of the status of

sick animals. Especially highlighted are the samples of dietary supplements "Immutoron" №1 and №3, derived from the biomass of beetles *U. dermestoides* grown on a banana peel and apple pulp.

Experimentally proved that the dietary supplement "Immutoron" has no toxic effect on animals.

Thus, the research data allows us to consider this type of raw material as a new promising source for immunology.

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ETHICS STATEMENT: The protocol for experiments with laboratory animals complied with the requirements of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes.

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