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Properties of Biologically Active Compounds and Medicinal Applications of *Ulomoides dermestoides* Beetles

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ABSTRACT

The incidence of immunodeficiency and autoimmune diseases continues to increase annually, especially in countries with an underdeveloped pharmaceutical market, making insect therapy a widely used treatment. The goal of this research is to investigate the potential of using *Ulomoides dermestoides* beetles as a raw material for the development of an immunomodulatory agent. A review of the available literature revealed the therapeutic potential of *U. dermestoides* beetles in the treatment of various health conditions. During the study, the biologically active supplement “Immutoron” was created from *U. dermestoides* biomass. To evaluate the effect of the beetles' diet on the final product, 3 different formulations were produced using the beetles-fed banana peel, sunflower meal, and apple pulp. The resulting supplement was administered to rats, and several indicators, including behavior, body temperature, white blood cell count, erythrocytes, hemoglobin, cholesterol, and total protein levels, were compared with those of a control group. The results showed that the high content of chitin and melanin in the beetles contributed to the antioxidant and immunomodulatory effects of the supplement, with no observed toxicity in the experimental animals.

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

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Introduction

The number of patients suffering from autoimmune diseases and immunodeficiencies continues to rise each year. In some economically underdeveloped countries, patients are forced to rely on various treatment methods, with one of the most common being insect therapy. The black beetle *Ulomoides dermestoides* is frequently used in this form of treatment. The use of these insects is growing in popularity each year, particularly in South America and Asia [1, 2]. Their effectiveness has been proven in treating chemotherapy, bronchial asthma, cancer, psoriasis, and diabetes [3]. Substances found in the feces of these insects are used to treat heart diseases, stomach disorders, myalgia, kidney diseases, asthma, as well as dermatitis, rheumatoid arthritis, inflammation, hemorrhoids, pain in the kidneys and liver, Parkinson's disease, diabetes, and different types of cancer [4-7].

Santos *et al*. [4] carried out a study to assess the anti-inflammatory effects of *U. dermestoides* both in vitro and in vivo. The researchers used a model of acute inflammation by injecting carrageenan into the pleural cavity of rats. This induced a strong inflammatory response, marked by a notable buildup of pleural fluid, plasma exudate, and significant migration of polymorphonuclear cells into the pleural space. After treating the animals with *U. dermestoides* extract, the inflammation was reduced: the total leukocyte count, PMN cell levels, protein concentration, and pleural exudation volume decreased significantly [8-11].

In a separate study, Tobón *et al*. [12] explored the neuropharmacological effects of biologically active compounds extracted from *U. dermestoides*. The animals in this study showed notable drowsiness and inactivity, with effects similar to those produced by diazepam, in contrast to the stimulating impact of amphetamine on the central nervous system. Neuropharmacological testing revealed that the *U. dermestoides* extract had a depressant effect on learning, memory, and discrimination abilities. Statistical analysis demonstrated a significant decline in brain functions in these animals following the treatment with the extract.

The goal of the current research is to investigate the potential use of *U. dermestoides* beetles as a raw material for developing an immunomodulatory agent.

Materials and Methods

Despite the significant biotechnological potential of *U. dermestoides* beetles, they have not previously been utilized in the development of drugs for immunological purposes. Consequently, there is a lack of detailed documentation regarding the preparation process of a drug based on the biomass of these beetles in existing literature. Using conventional methods along with our modifications, we have successfully prepared an extract from *U. dermestoides*.

The process for preparing a biologically active substance from animal-based raw materials is outlined in the flowchart presented in **Figure 1**.

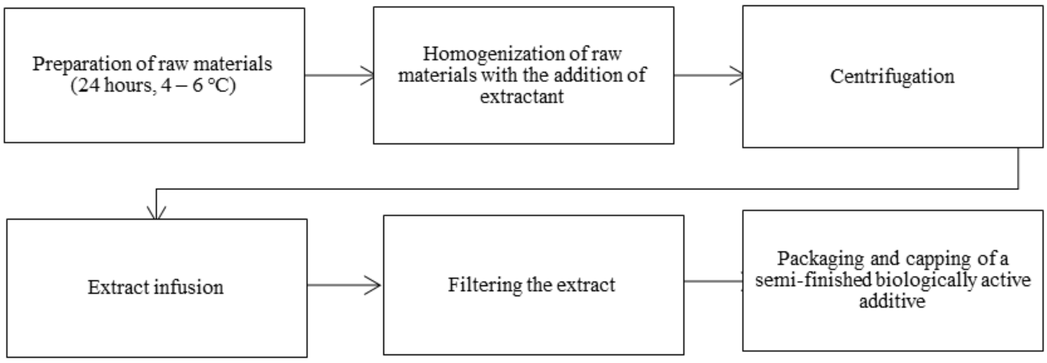

Figure 1. The process for producing the dietary supplement “Immutoron” from the biomass of *U. dermestoides*.

During the initial phase, beetles were cultured in a laboratory environment, with different groups receiving specific diets: one group was fed only banana peel (sample 1), another only sunflower meal (sample 2), and the last only apple pulp (sample 3). The beetles were then refrigerated at a temperature of +4-6 °C for one day to preserve them. This cooling process enhanced the structural and mechanical characteristics of the beetles, facilitating the homogenization procedure that followed.

Homogenization (or grinding) is essential because extraction is a mass transfer process, and its efficiency depends on the surface area between the raw material and the extractant. After homogenizing the beetles, the resulting extracts were transferred into test tubes and centrifuged at 4000 rpm for 5 minutes to separate them into different fractions based on their density. The centrifugal force helped remove the primary juice from the cellular material, after which a fresh extractant was introduced. This cycle continued until the material was saturated, after which the extractant was replaced.

A saline solution was chosen as the extractant for the process. To prepare the extract, a homogenate of beetle raw materials was mixed in a 1:10 ratio with the saline solution. Specifically, 20 grams of homogenate were combined with three hundred fifty ml of saline solution. The mixture was left to infuse for one week at room temperature (20-25 °C), with a humidity level of 40-45%, and under normal atmospheric pressure. Following the infusion, the extract was filtered twice through a sterile bandage folded into three layers. The resulting extract was a viscous, light yellow liquid with a strong odor.

In the last step, the extract was packaged in 100 ml sterile bottles, sealed, and labeled. The developed technology for preparing the biologically active supplement "Immutoron" from *U. dermestoides* raw materials was optimized to maintain the immunomodulatory properties of the original raw material, while also enhancing the final product with additional biologically active substances to improve its quality.

The rats used in the experiments (n = 40) were kept in cages on metal racks. The procedures followed complied with ethical guidelines for the protection of vertebrates used for scientific purposes.

Upon arrival at the laboratory, the animals were placed in disinfected, clean cages for a 14-day quarantine period. During this time, daily clinical monitoring and documentation of their overall health were conducted. The animals were housed in rooms with a stable temperature range of +20-22 °C and a humidity level not exceeding 40-45%. They had unrestricted access to both water and food. The rats were provided with a standard diet recommended by the Research Institute of Nutrition of the Russian Academy of Medical Sciences, which met their nutritional requirements for essential macronutrients and micronutrients, along with chilled boiled water.

The animals were divided into four groups, consisting of three experimental groups and 1 control group, with 10 animals in each group. The experiment lasted for 14 days. Rats in the experimental groups received the "Immutoron" dietary supplement orally once a day at a dosage of 0.5 ml. Rats in the control group did not receive the supplement **(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 monitored in all rats as it serves as a key indicator of the health status of warm-blooded animals. The temperature ranged from 37.0 ± 0.2 °C to 37.5 ± 0.3 °C, which is considered normal. To assess the effects of the immunomodulatory agent on the animals, a cold stress model, developed by V.A. Dorovskikh, was utilized [13].

The animals were observed daily over 14 days. Various aspects of the immunomodulatory response were evaluated, including general health, behavior, motor activity levels, signs of intoxication, and any potential mortality. The results showed that the administered doses did not lead to any fatalities or cause significant toxicity in the rats. In the evaluation of efficacy, factors such as body temperature, physical and feeding activity, immune system parameters, and hematological and biochemical blood tests were considered.

Results and Discussion

Analyzing blood biochemical parameters plays a crucial role in diagnostics. Even a partial biochemical and hematological blood analysis provides specialists with reliable insights into an animal's health status. Regular blood composition assessments enable precise evaluation of the overall condition, allow for accurate disease outcome predictions, assist in adjusting treatments, and help evaluate the effects of specific medications. This growing importance of laboratory testing, alongside the expanding scope and number of required studies in preclinical research, reflects its vital role.

A thorough analysis of the data obtained from the experiment enabled an assessment of the effectiveness of the Immutoron dietary supplement. The impact of the supplement on hematological parameters (such as erythrocyte count, hemoglobin, and leukocytes) and biochemical markers (including total protein, cholesterol, and glucose levels) was examined. No negative effects of "Immutoron" were observed on the basic clinical parameters of the

animals, including temperature, pulse, or respiration. Blood samples were collected at the beginning of the study and again on the 7th and 14th days for comparison.
Throughout the entire research period, the biochemical and hematological parameters in the second experimental group remained within the normal physiological range.
On day 7 of the observation period, an increase in red blood cell count was observed in the experimental groups: the first group showed a rise of 9.3%, the second group increased by 8.9%, and the third group experienced an 8.1% increase when compared to the control group. Hemoglobin levels also increased, with the first experimental group showing an 11.3% rise, the second group at 13.8%, and the third group at 12.7% **(Table 2)**. The biochemical blood parameters for both experimental and control groups are detailed in **Table 3**.

Table 2. Hematological studies

Indicators	Groups	At the beginning of the experiment	After 7 days	After 14 days
White blood cells ($x10^9$/ 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 ($x10^{12}$/ 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	At 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 (µmol/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 total protein levels in the first experimental group rose by 1.73%, while in the second group, the increase was 5.6%. By the end of the study, the total protein content in the blood serum of animals in the second group was 13.0% higher compared to the control group. No important differences in cholesterol levels were observed between the experimental groups and the control.
The increase in total protein levels in the experimental animals likely reflects not only their growth but also active protein renewal processes.
Based on the findings, it can be concluded that the application regimen of the dietary supplement in the first and third experimental groups offers both economic and physiological benefits. From this phase of the study, it was determined that the supplement didn't have a depressive effect on the animals. It enhances immune function and boosts total protein levels, suggesting an improvement in the overall health of the experimental subjects.
After a thorough analysis of the collected data, we concluded that the most effective extract was derived from *U. dermestoides* raw materials, with the dietary supplement proving most beneficial in the first and third experimental groups. Moreover, the experimental extracts from *U. dermestoides* are safe and exhibit immunomodulatory properties, aligning with the findings of other studies [14-16].

Conclusion

The development of novel, effective immunomodulatory treatments derived from insect biomass holds significant scientific and practical potential. A review of the literature revealed that *U. dermestoides* beetles exhibit notable anti-inflammatory properties and are promising candidates for insect therapy.

Throughout the study, a method for producing the dietary supplement “Immutoron” from *U. dermestoides* beetles was established. Following subsequent testing of the supplement's effectiveness on experimental animals with compromised immune systems, it was observed that oral administration of “Immutoron” significantly expedited clinical recovery. Notably, the supplement did not exhibit any depressive effects. The biologically active additive was found to enhance immune function, contributing to the overall improvement in the condition of the animals. Special emphasis was placed on the formulations of “Immutoron” samples 1 and 3, which were derived from beetles-fed banana peel and apple pulp.

The study confirmed that “Immutoron” poses no toxic risks to the animals.

In conclusion, the findings suggest that *U. dermestoides* beetles represent a promising new source of material for immunological applications.

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Conflict of Interest: None

Financial Support: None

Ethics Statement: The animal experimentation protocol adhered to the principles outlined in the European Convention for the protection of vertebrate animals used for scientific and experimental purposes.

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