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General and specific toxicity determination of an extract from the plant *Rhodiola semenovii* Boriss

The study of chronic and acute toxicity pharmacological phenomena with occupational symptoms of intoxication provides essential information on therapeutic activity of the drug. An extract of the *Rhodiola semenovii* Boriss plant was taken to determine toxicity. Phytochemical studies were carried out on the composition of biologically active compounds for medicinal purposes. Based on the statistical data on the chemical composition, substances, such as flavonoids, coumarins, phenolic acids, and polysaccharides, were identified in the root extract of the *Rh. semenovii* plant. To study the chronic and acute toxicity of the extract, preclinical tests were on outbred laboratory rats. After completion of the experiment of acute and chronic toxicity, animals were slaughtered and peripheral blood samples were obtained for hematological and biochemical blood analysis. In addition, macroscopic studies of laboratory animals were performed. There were morphological-structural changes heart, kidneys, liver, heart, and pancreas. An external examination at the autopsy revealed no changes in the vital organs, as well as the digestive, respiratory, excretory systems. According to the studies carried out, *Rh. semenovii* does not have general toxic extracts.

Keywords: toxicity, pharmacology, *Rhodiola semenovii*, extract, phytochemistry, acute toxicity, chronic toxicity, hematology.

Introduction

Currently, researchers, developing priority issues of modern pharmacological science in terms of researching new medicines of natural compounds of various chemical structures and biological action pay great attention to the problem of drug toxicology and the safety of drug use in clinical practice [1]. In accordance with modern concepts, the assessment of the safety of a medicinal herbal preparation (MHP) should take into account all potential risk factors specific to this group of medicinal products. Modern MHP is fundamentally different in terms of the safety of its composition [2]. For successful introduction of new drugs into clinical practice for treatment it is necessary to conduct a preclinical evaluation of the drug based on international standards to implement and accelerate ongoing research [3–5]. Preclinical studies are carried out to eliminate the adverse effects of the drug in the process of clinical trials on target animal species. In the course of preclinical studies, preliminary information is obtained on the toxicity, efficacy, and pharmacological properties of the study drug [6].

The task of preclinical safety studies is description of the toxic effect of the drug depending on the dose and the relationship that occurs when the pharmacological substance interacts with the body of laboratory animals. The obtained data was used to determine the initial non-toxic dose used for clinical studies [7]. All experimental work on laboratory animals must be carried out in accordance with the current rules of laboratory practice and ethical standards for the treatment of animals, based on the standard operating procedures adopted by the research organization, which must comply with international rules for the conduct of research and the protection of experimental animals used in experiments and other scientific purposes [8]. Preclinical evaluation of the safety of natural medicines usually includes pharmacologicol studies, studies on the general toxic effects of the drug, preclinical studies, studies of toxic reactions to reproduction and geno toxicity. For drugs that pose a potential hazard or are intended for long-term use, studies of carcinogenic properties are also necessary [9]. The study of general toxic properties is mandatory for all groups of drugs, and is divided into two stages: the study of acute toxicity (the toxic effect of a substance administered in a single dose or in multiple doses for not more than 24 hours, which can be expressed in a disorder of physiological functions or in a violation of the morphology of the organs of experimental animals, as well as the death of an animal); study of chronic toxicity with repeated administration (a set of functional and/or morphological disorders of the organs and systems of the experimental animal after repeated prolonged administration of the substance [10].

The study of acute and chronic toxicity of pharmacological substances in the professional assessment of the symptoms of intoxication allows one to obtain significant information about the biological activity of the future drug [11].

The purpose of the study is to determine the acute and chronic toxicity of the extract of the plant *Rhodiola semenovii* Boriss.

Experimental

To determine the toxicity of the extract of the plant *Rh. semenovii* Boriss, phytochemical studies were conducted to determine the composition of the BAA in the extract, for therapeutic use. The material was an aqueous extract of *the plant Rh. semenovii* Boriss.

Analysis of organic compounds was carried out by gas chromatography with mass spectrometric detection (Agilent 6890N/5973N). Analysis conditions: sample volume 1.0 μl, sample input temperature 260 °C without flow division. Separation was carried out using a chromatographic capillary column DB-35MS 30 m long, 0.25 mm internal diameter and 0.25 μm film thickness at a constant carrier gas (helium) speed of 1 ml/min. Chromatography temperature is programmed from 40 °C (shutter speed 0 min) to 150 °C at a heating rate of 10 °C/min (shutter speed 0 min) and up to 300 °C at a heating rate of 5 °C/min (shutter speed 10 min). Detection is carried out in scan m/z mode 34-850. Agilent MSD ChemStation software (version 1701EA) was used to control the gas chromatography system, record and process the results and data obtained. Data processing included determination of retention times, peak areas, as well as processing of spectral information obtained using a mass spectrometric detector. To decipher the obtained mass spectra, the Wiley 7th edition and NIST'02 libraries were used (the total number of spectra in the libraries is more than 550 thousand).

According to the available data on the chemical composition in the extract of the root of the plant *Rh. semenovii* B., such substances as flavonoids — 74.8 %, coumarins — 11 were identified. 7 %, phenolocyslots — 6.1 %, polysaccharides — 7.4 %, the main biologically active component of flavonoids was rhodioflafonoside.

The study of acute, chronic toxicity of the extract was conducted on white mongrel laboratory rats. Animals (males) were kept in cages in groups of 10 individuals of group 3. Sawdust was used as a litter. The air temperature in the vivarium premises was maintained in the range of 18-20 °C at a relative humidity of 60–70 %. Animals were kept under standard conditions on the vivarium diet. To assess the chronic toxicity *of the extract Rh. semenovii*, the animals were administered the extract orally for 21 days.

To analyze the different significance between samples, Student's T-criterium at $p<0$ was used. 05 (Statistica 12, StatSoft Inc., Tulsa, USA). The fluorimeter data was processed and graphed using MS Excel capabilities. Atypical values based on the T-criterion were excluded from the data, a standard sample average error was calculated. Plus/minus signs in the tables show a standard average error. The graphs show average values with standard error bars. Signs * and ** indicate the reliability of the results with significance levels of 0.05 and 0.01, respectively (unless otherwise indicated). When determining the reliability of the difference between the indicators of the compared groups, the t-confidence criterion was calculated, the p value was determined from the Student's table of values, the changes were considered reliable at $p\leq0.05$. All data were calculated in the MS Offis Excel 2010 software package.

Results and Discussion

Table 1 represents the results of the Acute Toxicity experiment. Data presents the survival of animals in acute toxicity experiences, depending on the dosage of the extract. *Rh. semenovii* in the acute toxicity groups 0.5 g and 1.0 g, in both groups there was a 100 % survival rate, only 10 % of the animals dropped out of the experiment due to fighting and injuries on the body, from which it follows that the extract of *Rh. semenovii* in a dosage of 0.5−1.0 g does not cause death of animals and is not toxic.

Table 1

Survival of animals in acute toxicity experiments, depending on the dosage of *Rhodiola semenovii* extract

Extract Dosage	0.5 g	1.0 g
Survived	90 %	90 %
Eliminated from experience*	10 %*	10 %*
* — *out of the experience due to fighting and body injuries*		

An external inspection of animals, weighing and fixing the IRR on the "open field" test were held. The test is designed to assess the dynamics of behavioral elements, the psycho-emotional state of animals participating in experiments with a stressful condition. The animal was placed in a structure 100 × 100 cm in diameter with a wall height of 40 cm. The floor was made of white plastic, on which a grid was applied with black paint, dividing the field into 25 (5x5) equal squares. Illumination with a 50 W lamp, which is located at a height of 150 cm above the center of the field. The test was to measure the amount of behavioral components of an animal placed in an open enclosed space enclosed by a wall. When testing, the animal was placed in the center of the facility and the following indicators were visually assessed for 5 minutes: horizontal motor activity — mileage (number of sectors passed), vertical motor activity — stances (number of lifts on the hind legs). Waste from the wall of the arena (number of crossings of the outer concentric circle), exits to the center of the arena (number of crossings of the inner circle), grooming (number of touches of the muzzle with paws, scratching), in the study of pharmacological preparations, a non-stressed open field test was used. The main method for recording test results was continuous or selective recording with time-based recording of animal activity. After 5 minutes of the study, the animal was returned to the cage. The number of spools of manure was counted and the floor was thoroughly washed after each experiment. Testing was repeated for the next four days. Before the start of the drug administration, as well as the dynamics of observation of each experimental group for 3 days, tests were carried out using the "Open field" method to determine the individual typological characteristics of higher nervous activity (HNA) and after tests within 3 days to determine the effect of the drug.

After the completion of the experiment of acute and chronic toxicity, animals were slaughtered and peripheral blood samples were obtained for hematological and biochemical blood analysis (assessment of the function of the liver, kidneys, pancreas in terms of protein, carbohydrate, lipid and pigment types of metabolism, the presence of intoxication). In addition, an autopsy of laboratory animals was performed and the presence of macromorphological changes in the structure of the heart, kidneys, liver, and pancreas. The organs were weighed, the mass coefficients of the organs were calculated, then the material was fixed and placed in a 10 % solution of formaldehyde. Hematological studies were carried out on an automatic hematology analyzer Sysmex XS 550-i (Japan). The blood was centrifuged for 20 min at 1000 rpm to produce plasma. The main biochemical parameters were studied: total protein, g/l, albumin g/l, urea, mmol/l, creatinine, μmol/l, uric acid, μmol/l, alkaline phosphatase, mmol/l, alanine aminotransferase, μkat/l, aspartate aminotransferase, glucose, mmol/l, cholesterol, HDL, LDL, mmol/l, triglycerides, mmol/l. The results of the studies were recorded on the automatic biochemical analyzer BioChem-200.

It can be seen from Table 2 that the total number of leukocytes did not have statistically significant changes in both the control group and the acute toxicity group. Statistically significant changes in the absolute content of monocytes, eosinophils, basophils and neutrophils and in the level of hemoglobin were also not detected. In terms of absolute content, statistically significant changes were also not revealed. It should also be noted that in terms of relative content, no statistically significant changes in the control and experimental groups for acute toxicity were revealed.

However, there were statistically significant changes in the total number of red blood cells in the experimental groups in relation to the control group, and amounted to 6.32 ± 0,7 in the control group 52 *10^{12}/l, in the group of acute toxicity (0.5) — 8.53±0.94 * 10^{12}/ l, and in the group of acute toxicity (1.0) — 8.66 ± 1.01 * 10^{12}/l. Also, there were statistically significant changes in the total number of platelets in the acute toxicity group (0.5) — 698.41 ± 80.10 * 10^{9}/l and in the group of acute toxicity (1.0) — 721.01 ± 54.76 * 10^{9}/l in relation to the control group (413.41 ± 43.03 *10^{9}/l/l).

The absolute lymphocyte count varied between 2.51 ± 0.14 * 10^{9}/l in the control group, 3.83 ± 0.76 * 10^{9}/l in the acute toxicity group (0.5), and statistically significant changes in the acute toxicity group were noted (1.0) in relation to the control group and was 4.19 ± 0.67*10^{9}/l.

Table 2

Hematological parameters of rats in the experiment on acute toxicity

Indicator name, unit of measurement	International abbreviation	Control group	Acute toxicity 0.5 g	Acute toxicity 1.0 g
Total number of Leukocytes, 10^{9}/L	WBC	6.3 ± 0.5	8.4 ± 1.2	7.8 ± 0.8
Total Red Blood Cell Count, 10^{12}/L	RBC	6.4 ± 0.6	8.5 ± 0.8*	8.7 ± 1.1**
Hemoglobin level, g/L	HGB	146.0 ± 4.1	155.0 ± 6.4	153.0 ± 7.9

Total platelet count, 10^3/L	PLT	413.5 ± 43.1	698.5 ± 80.2*	721.1 ± 54.7**
Absolute neutrophil count 10^9/L	Neut	3.2 ± 0.5	3.7 ± 0.7	2.8 ± 0.6
Absolute lymphocyte count 10^9/L	Lymph	2.5 ± 0.1	3.8 ± 0.8	4.2 ± 0.6**
Absolute content of monocytes 10^9/L	Mono	0.6 ± 0.2	0.6 ± 0.2	0.5 ± 0.1
Absolute eosinophil content 10^9/L	Eos	0.3 ± 0.14	0.2 ± 0.1	0.2 ± 0.1
The absolute content of basophils 10^9/L	Baso	0.03 ± 0.1	0.05 ± 0.04	0.06 ± 0.04
The relative content of neutrophils %	Neut	49.1 ± 3.7	45.3 ± 7.3	37.7 ± 7.4
The relative content of lymphocytes %	Lymph	40.4 ± 2.3	46.2 ± 6.5	54.2 ± 6.6
The relative content of monocytes %	Mono	7.6 ± 1.7	6.6 ± 1.8	6.2 ± 1.3
The relative content of eosinophils %	Eos	2.6 ± 0.9	1.6 ± 1.1	1.6 ± 0.9
The relative content of basophils %	Baso	0.5 ± 0.15	0.5 ± 0.5	0.5 ± 0.5
*Note: * — statistically significant changes in the group "Acute toxicity — 0.5 g" relative to the control group, at p≤ 0. 001; ** — statistically significant changes in the group "Acute toxicity — 1.0 g" relative to the control group, at p ≤ 0.001*				

According to Table 3, no statistically significant changes were detected (p≤ 0. 001) in the indicators of hepatic and renal functions in the control and test groups.

Table 3

Indicators of hepatic and renal functions in experimental groups of animals in the experience of acute toxicity

Group - animals	Total bilirubin, μmol/L	AlT, IU/L	AsT, IU/L	ALP, IU/L	Urea, mmol/L	Uric acid, mmol/L	Creatinin, μmol/L
Intact	5.9 ± 0.9	23.0 ± 3.6	11.5 ± 1.9	316.4±120.5	3.9 ± 0.3	340.8 ± 36.9	54.0 ± 3.7
Acute toxicity 0.5 g	5.6 ± 0.2	18.1 ± 5.4	10.8 ± 5.9	332.4±81.21	3.8 ± 0.5	316.9 ± 34.9	52.9 ± 4.5
Acute toxicity 1.0 g	5.5 ± 1.8	14.6 ± 7.9	10.9 ± 5.7	289.2±147.3	3.9 ± 0.9	301.7 ± 51.5	52.0 ± 4.9
*Note: * — statistically significant changes in the group "Acute toxicity — 0.5 g" relative to the control group, at p≤ 0.001; ** — statistically significant changes in the group "Acute toxicity — 1.0 g" relative to the control group, at p ≤ 0.001*							

Thus, considering the results of the "Acute Toxicity Experience", it was revealed that the extract based on *Rh. semenovii* is not toxic and appropriate dosages of the extract were recommended for the formulation of the chronic toxicity experiment.

To study the chronic toxicity extract of *Rh. semenovii* was tested by the IRT — "Open Field". Chronic toxicity was observed for 30 days by oral administration of the extract at a dose of 2.5 mg/ kg. In the dynamics of observation in the experiment on chronic toxicity, changes in the behavior of experimental animals were not revealed. A satisfactory state was noted in all animals based on horizontal and vertical motor activity, waste from the arena wall, exits to the center of the arena, grooming.

During an external examination at the autopsy, no changes were detected from the vital organs, as well as the digestive, respiratory, excretory systems. Table 4 demonstrates the assessment results of body weight of animals.

Table 4

Animal mass values and mass coefficients of organs in chronic toxicity experience

Animal organs / Group of animals	Total body weight	Heart	Kidneys	Liver	Thyroid gland (together with the trachea)	Spleen	Stomach
Control	238.5 ± 8.2	3.5±0.6	2.3 ± 0.2	9.3 ± 0.6	1.1 ± 0.1	4.6±0.4	39.1 ± 3.5
Chronic toxicity	274.0±11.7*	3.7±0.7	2.3 ± 0.2	10.4 ± 0.7	1.1 ± 0.2	4.7±0.4	43.1 ± 0.8
*Note: * — statistically significant changes in the group "chronic toxicity" in relation to the control group, at p≤ 0.001*							

According to the presented data on the masses of internal organs of experimental animals, in comparison with the control group, the group of experience of chronic toxicity did not show statistically significant changes ($p \leq 0.001$). There was a statistically significant ($p \leq 0.001$) increase in the mass of animals from 238.5 ± 8.2 g, to 274.0 ± 11.7 g without changing the mass of organs. In our opinion, the increase in mass is associated with the maturation of experimental animals and the development of musculoskeletal systems.

Table 5 presents the results of studies on comparative assessments of hematological indicators of the observed groups.

Table 5

Hematological parameters of rats of the control group and the group "Experience of chronic toxicity"

Name of the indicator, unit of measurement	MC	Control group	Chronic toxicity
Total Number of Leukocytes 10^9/L	WBC	6.2 ± 0.4	6.7 ± 0.5
Total number of Erythrocytes 10^{12}/L	RBC	6.3 ± 0.5	6.6 ± 0.5
Hemoglobin level, g/L	HGB	146.0 ± 4.1	141.6 ± 3.9
Total platelet count, 10^9/L	PLT	413.4 ± 43.0	496.1 ± 51.6
Absolute content of neutrophils, 10^9/L	Neut	3.1 ± 0.4	2.2 ± 0.4
Absolute content of lymphocytes, 10^9/L	Lymph	2.5 ± 0.1	3.8 ± 0.2
Absolute content of monocytes, 10^9/L	Mono	0.5 ± 0.1	0.5 ± 0.1
Absolute content of eosinophils, 10^9/L	Eos	0.2 ± 0.1	0.2 ± 0.15
Absolute content of basophils, 10^9/L	Baso	0.03 ± 0.05	0.03 ± 0.05
Relative neutrophil content,%	Neut	49.0 ± 3.6	33.0 ± 3.7*
Relative lymphocyte count %	Lymph	40.4 ± 2.3	56.6 ± 3.2*
Relative content of monocytes,%	Mono	7.6 ± 1.8	6.9 ± 1.9
Relative content of eosinophils %	Eos	2.6 ± 0.9	2.9 ± 0.9
Relative content of basophils,%	Baso	0.5 ± 0.9	0.5 ± 0.9
*Note: * — statistically significant changes in the group "chronic toxicity" in relation to the control group, at p≤ 0. 001*			

According to Table 6, with chronic use of extract of *R. semenovii* no change was observed in the indicators of hematopoiesis, there are no pronounced shifts in the leukocyte formula, there is no inhibition of hematopoiesis and allergic reactions according to the level of basophils, eosinophils. There are statistically significant changes in the relative content of neutrophils, which in the control group was 49.0 ± 3.6, in the experimental group — 33.0 ± 3.7. Also, in the relative content of lymphocytes, which in the control group was 40.4 ± 2.3, while in the experimental group — 56.6 ± 3.2.

Table 6

Indicators of the level of bilirubin and its fractions, transaminases in experimental groups of animals

Group of animals	Total bilirubin, μmol / L	Direct bilirubin, μmol/L	Indirect bilirubin,μmol/L	АлТ, ME/L	АсТ, ME/L
Intact	5.9 ± 0.9	1.5 ± 0.2	7.2 ± 6.4	23.0 ± 3.6	11.5 ± 1.9
Chronic toxicity	5.8 ± 0.9	1.4 ± 0.2	4.3 ± 0.7*	21.4 ± 3.4*	10.7 ± 1.9*
*Note: * — statistically significant changes in the group "chronic toxicity" in relation to the control group, at p≤ 0.001*					

To assess the hepato-, nephrotoxicity, the state of lipid metabolism and the function of the pancreas, biochemical studies of the blood of experimental animals were conducted. The data is presented in (Tab. 6−8).

As can be seen from Table 7, there were statistically significant differences ($p \leq 0.001$) in the content of indirect bilirubin, which in the control group was 7.2 ± 6.4 μmol/L, in the experimental group – 4.3 ± 0.7 μmol / l, and alanine aminotransferase in the control group — 23.0 ± 3.6 IU / l, in the experimental – 21.4 ± 3.4 IU/L. Statistically significant changes were also identified in indicators of aspartate aminotransferase constituting a control group of 11 veins. 5 ± 1.9 IU / l while in the experimental group there is a decrease of 10.7 ± 1.9 IU/L. In the remaining indicators, statistically significant differences ($p \leq 0.001$) were not detected.

Table 7

Indicators of lipid metabolism in experimental groups of animals

Group of animals	Triglyceride, mmol/ L	Total cholesterol, mmol/L	HDL cholesterol, mmol/L	LDL cholesterol, mmol / L	Atherogenic coefficient
Intact	0.8 ± 0.2	1.6 ± 0.3	1.0 ± 0.2	1.0 ± 0.2	0.7 ± 0.2
Chronic toxicity	0.8 ± 0.2	1.6 ± 0.3	0.9 ± 0.1	0.9 ± 0.2	0.7 ± 0.2
*Note: * — are statistically significant changes in the "chronic toxicity" group relative to the control group, at p ≤ 0.001*					

There is no significant changes in the lipid metabolism (Table 7).

Table 8

Indicators of protein and carbohydrate metabolism in experimental groups of animals

Group of animals	Total protein, g/L	Albumin g/L	Urea, mmol/L	Uric acid, mmol/L	Creatinine, μmol/L	Glucose, mmol/L
Intact	66.0 ± 2.4	29.8 ± 2.2	3.9 ± 0.3	340.8 ± 36.9	54.0 ± 3.7	6.7 ± 0.4
Chronic toxicity	64.7 ± 2.3*	28.3 ± 2.1	3.5 ± 0.3	323.8 ± 35.0	53.2 ± 2.9	6.2 ± 0.4
*Note: * — are statistically significant changes in the "chronic toxicity" group relative to the control group, at p≤ 0.001*						

Statistically significant changes ($p \leq 0.001$) were identified by the total protein index, which in the control group was 66.0 ± 2.4 g/l, whereas in experience 64.7 ± 2.3 g/L (Table 8). However, all these data were within the physiological norm. According to the remaining biochemical indicators of blood, statistically significant changes were not detected.

There were no statistically significant changes ($p \leq 0.001$) in the thyroid hormone levels of the control and experimental groups.

Conclusions

Thus, by using open field test, the results of a macromorphological study of experimental animals on the masses of organs, and on the functional indicators of the organs of the digestive, excretory, detoxification systems showed that an extract from the plant *Rh. semenovii* is not toxic.

According to the results of preclinical studies, acute and chronic toxicity experiments, pathomorphological studies of organs, higher nervous activity tests, hematological and biochemical blood parameters, *Rh. semenovii* extract does not have general toxic properties.

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Rhodiola semenovi Boriss өсімдігінің жалпы және спецификалық уыттылығын анықтау

Фармакологиялық заттардың интоксикациялық құбылыстарын кәсіптік деңгейде болдырмау мақсатында қолданылатын жедел және созылмалы уыттылықты зерттеу дәрілік шөптердің құрамындағы биологиялық белсенді заттардың қалыптасуы жайында ауқымды мәлімет бере алады. Уыттылығын анықтау үшін *Rhodiola semenovii* Boriss өсімдігінің сығындысы алынды. Дәрілік мақсаттағы биологиялық белсенді қосылыстардың құрамына фитохимиялық зерттеулер жүргізілді. Химиялық құрамы бойынша статистикалық мәліметтерге сәйкес, *Rh. semenovii* өсімдігінің тамыр сығындысында флавоноидтар, кумариндер, фенол қышқылдары, полисахаридтер сияқты заттар анықталды. Жедел және созылмалы уыттылықты анықтауға арналған материал *Rh. semenovii* өсімдіктерінің сулы сығындысы болды. Сығындының жедел және созылмалы уыттылығын зерттеу үшін ақ тұқымсыз зертханалық егеуқұйрықтарда клиникаға дейінгі зерттеулер жүргізілді. Жануарлармен бірқатар эксперименттер жүргізілді және сығындының мөлшеріне байланысты гематологиялық көрсеткіштер анықталды. Жедел және созылмалы уыттылық эксперименті аяқталғаннан кейін жануарларды сою жүргізіліп, гематологиялық және биохимиялық қан анализін жүргізу үшін перифериялық қан үлгілері алынды. Сонымен қатар, зертханалық жануарларды сойып, жүрек, бүйрек, бауыр, жүрек, ұйқы безі құрылымындағы макроморфологиялық өзгерістердің болуы зерттелді. Сойғаннан кейін сыртқы тексеру кезінде өмірлік маңызды органдардың, сондай-ақ ас қорыту, тыныс алу, шығару жүйелерінің өзгерістері анықталған жоқ. Клиникаға дейінгі сынақ нәтижелеріне сәйкес, *Rh. semenovii* жедел және созылмалы уыттылық тәжірибелеріне, GNI сынақтарына, органдардың патоморфологиялық зерттеулеріне, қанның гематологиялық және биохимиялық көрсеткіштеріне сәйкес жалпы уытты қасиеттерге ие емес.

Кілт сөздер: уыттылық, фармакология, *Rhodiola semenovii*, сығынды, фитохимия, жедел уыттылық, созылмалы уыттылық, гематология.

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Определение общей и специфической токсичности экстракта растения *Rhodiola semenovii* Boriss.

Изучение хронической и острой токсичности терапевтических веществ при внешней оценке признаков интоксикации позволило получить важную информацию о терапевтических свойствах будущего препарата. Для определения токсичности был взят экстракт растения *Rhodiola semenovii* Boriss. Были проведены фитохимические исследования по определению состава биологически активных веществ, для дальнейшего использования в терапевтических целях. Согласно имеющимся данным, по химическому составу в экстракте корня растения *Rh.semenovii* В. были идентифицированы такие вещества, как флавоноиды, кумарины, фенолокислоты, полисахариды. Материалом по определению острой и хронической токсичности служил водный экстракт растения *R. semenovii*. Для изучения острой и хронической токсичности экстракта предклинические испытания проводились на белых беспородных лабораторных крысах. Проведен ряд экспериментов с животными и определены гематологические показатели в зависимости от дозировки экстракта. После завершения эксперимента острой и хронической токсичности проводили забой животных и получали образцы периферической крови для проведения гематологического и биохимического анализа крови. Кроме того, проводилось вскрытие лабораторных животных и оценивание наличия макроморфологических изменений структуры сердца, почек, печени, сердца, поджелудочной железы. При внешнем осмотре на вскрытии не было выявлено изменений со стороны жизненно важных органов, а также пищеварительной, дыхательной, выделительной систем. Согласно результатам доклинических испытаний, экстракт *Rh. semenovii* не обладает обще-

токсическими свойствами по данным опытов острой и хронической токсичности, тестов ВНД, патоморфологических исследований органов, гематологических и биохимических показателей крови.

Ключевые слова: токсичность, фармакология, *Rhodiola semenovii*, экстракт, фитохимия, острая токсичность, хроническая токсичность, гематология.

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