STUDY OF CHRONIC TOXICITY OF NARROW-LEAVED LAVENDER EXTRACTS: INFLUENCE ON FUNCTIONAL STATUS AND LABORATORY INDICATORS OF RATS

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Introduction

Despite the widespread use of chemotherapeutic drugs, medicinal plants continue to hold scientific interest among pharmacologists today. The increased interest in medicinal plants is a result of the increased incidence of side effects associated with the use of synthetic drugs [1]. Due to the possibility of combining different groups of biologically active substances (BAS) with a wide spectrum of pharmacological activity, phytomedicines are attractive for the prevention and treatment of various diseases, including chronic ones [2]. Several scientific articles report the widespread therapeutic use of L. angustifolia as an alternative medicine, effective for a wide range of diseases [3, 4].

In order to saturate the domestic pharmaceutical sector with affordable phytopreparations of a wide spectrum of action, scientists of the National University of Pharmacy (postgraduate student Gurina V.O. under the supervision of Doctor of Pharmaceutical Sciences, Professor Georgiyants V.A.) obtained extracts of narrow-leaved lavender grass containing biologically active substances: terpenoids (linalool, linalyl acetate and traces of 1,8-cineole), flavonoids (hyperoside, isoquercitrin) and hydroxycinnamic acids (rosmarinic, chlorogenic). The total content of phenolic substances is 2.02-2.60 mg/g, flavonoids - 1.46-3.17 mg/g, and potentially have antimicrobial, anti-inflammatory, analgesic, chondroprotective effects, i.e. are promising agents for inflammatory diseases of various genesis. The highest number of phenolic compounds was expectedly contained in the extract of narrow-leaved lavender herb obtained by extraction with a 70 % aqueous-ethanol solution (2.60 mg/ml), the lowest in the aqueous extract, the total content of phenolic compounds was 2.02 mg/ml [5, 6]. As a result of experimental microbiological tests, it was found that the herb of narrow-leaved lavender of Ukrainian origin is a promising and affordable source of potential antimicrobial active pharmaceutical ingredients (API). Thus, the lavender extract obtained by extraction with a 70% aqueous-ethanol solution, according to the results of the conducted studies, revealed high antimicrobial and antifungal potential. The results obtained may be useful for the search for original substances for the complex correction of symptoms of neurological deficit of infectious etiology. In addition, the results of such studies may provide an answer to the question of pharmacological markers of lavender since scientists previously noted the leading role of linalool in providing antimicrobial action [5].

However, reports on toxicological studies of narrow-leaved lavender are limited. In addition, when developing new drugs, the assessment of the toxic properties of the substance is of crucial importance for the protection of public health since exposure to chemicals can lead to negative consequences for humans [7]. In addition, at the stage of preclinical studies, the determination of acute and chronic toxicity parameters helps to decide on the feasibility of further studying the new substance [8]. Acute toxicity studies in appropriate animal models are an integral part of studying the toxicological profile of new substances and drugs [9, 10]. Based on the data of our previous experimental studies on the acute toxicity of test samples of narrow-leaved lavender when administered intragastrically to white mice, it was concluded that a single administration of aqueous and two extracts of narrow-leaved lavender herb obtained by extraction with aqueous-ethanol solutions (40 and 70% ethanol) at a dose of 5000 mg/kg does not lead to lethality and any noticeable changes in the physiological state of animals, their body weight and relative weight of internal organs, which allowed us to classify the studied test samples as class V of practically non-toxic substances (LD_{50}>5000 mg/kg) [11]. **The aim of the work.** Experimental study of the toxicological properties of narrow-leaved lavender extracts (chronic toxicity) to substantiate the safety of use in clinical practice.

Materials and methods

The objects of the study were experimental test samples: test sample No. 1 - extract of the narrow-leaved lavender herb, obtained by extraction with purified water; test sample No. 2 - extract of the narrow-leaved lavender herb, obtained by extraction with a water-ethanol solution (40% ethanol); test sample No. 3 - extract of the narrow-leaved lavender herb, obtained by extraction with a water-ethanol solution (70% ethanol). Experimental studies of the toxicological properties of narrow-leaved lavender herb extracts were conducted on 48 white non-linear rats of both sexes weighing 170-190 g and aged 5-6 months in accordance with the recommendations of the State Expert Center (SEC) of the Ministry of Health of Ukraine [12] and the Bioethics Protocol No. 8 dated 02/15/2023.

The research was conducted in the Educational and Scientific Training Laboratory of Medical and Biological Research of NUPh, certified by SE "Kharkivstandardmetrology" (certificate dated 06.08.2021 No. 01-0084). During the experiment, the animals were kept in the vivarium of the Educational and Scientific Training Laboratory of Medical and Biological Research of NUPh as a research base in experimental pharmacology, in accordance with standard sanitary standards on the required food ration. All research was conducted in accordance with the EU Council Directive 86/609 EEC of 24 November 1986 on the application of laws, regulations and administrative provisions of the EU Member States regarding the protection of animals used for experimental and other scientific purposes [13].

The animals were kept in separate rooms with controlled microclimate parameters. For rats, the air temperature was +20-24 °C, humidity was 45-65%, and the light regime was “12 hours day/night”, in standard plastic cages of 6 animals each. The room was ventilated, and the air was sterilized using a quartz lamp daily. The animals had free access to water. For drinking, they used settled tap water from the drinkers. The rats were fed with granulated complete compound feed for mice and rats, TM “GORA” (TU.U15.7-2123600159-001:2007). Animal care was carried out in accordance with standard operating procedures and recommendations for the maintenance of laboratory

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animals and work with them [14]. Chronic toxicity studies of narrow-leaved lavender extracts were conducted on 48 white non-linear rats of both sexes with an initial weight of 170-190 g with daily intragastric administration for 90 days. All animals were divided into 4 experimental groups of 12 animals as follows: group 1 - intact control; group 2 - animals that received intragastric test samples No. 1; group 3 - animals that received intragastric test samples No. 2; group 4 - animals that received intragastric test samples No. 3. Test samples were used at a dose of 100 mg/kg, which corresponds to 1/50 of the LD_{50} of the test agents, which was determined at the previous stage of the studies.

Before the start of the study, rats were weighed, randomized, and individually tagged. Then, all animals were given daily intragastric administration of lavender extracts in appropriate doses for 90 days. Test samples were administered in the form of solutions that were previously prepared by dissolving the dose of the agent in the required amount of purified water. Intact animals received purified water in an equivalent amount.

Animals were withdrawn from the experiment in two stages, 6 animals from each group, on the 45th and 90th day of the study. At the same time, the rats were weighed, and their spontaneous daily diuresis was determined using individual metabolic chambers. After the end of the observation period, the animals were euthanized under light chloroform anesthesia by cervical dislocation to obtain biomaterial for laboratory and biochemical studies. In the collected urine, general properties (colour, transparency, pH, density), total protein content (by reaction with sulfosalicylic acid), and glucose content (by glucose oxidase method) were determined, and urinary sediment was examined [15, 16]. Next, a complete laboratory blood test was performed using standard haematological methods and the following were determined: haemoglobin and erythrocyte content, colour index (CI), leukocyte content, leukocyte formula, erythrocyte sedimentation rate (ESR) [15, 16]. Also, the animals were determined to have creatinine content (by reaction with picric acid) [15, 16] in blood and urine. To assess glomerular filtration rate (GFR), endogenous creatinine clearance was calculated using the formula:

$C_{cr} = U_{cr} \cdot V / P_{cr}$,

where C_{cr} – creatinine clearance;

U_{cr} – creatinine concentration in urine;

P_{cr} – creatinine concentration in blood plasma;

V – daily urine output.

Also, in the blood serum of rats, using test kits from the company "Filisit" (Ukraine), the urea content (diacetylmonooxime method), total protein (biuret method), glucose content (glucose oxidase method), the activity of cytolysis marker enzymes - alanine aminotransferase (AlAT) and aspartate aminotransferase (AsAT) (by the Reitman-Frankel method), bilirubin content (by the Jendrassik-Grof method), cholesterol content (by the modified Liebermann-Burchard method) were determined [15, 16]. The significance of differences between samples was assessed using the Kruskal-Wallis method and the Mann-Whitney test in comparison with the intact control group [17, 18].

Results and discussion

Observations of animals were carried out for 90 days during the administration of test samples. For an objective assessment of the effect of extracts upon repeated administration on the body of experimental animals, in addition to indicators of general toxic action, indicators of laboratory and biochemical blood and urine tests were used. During the study, it was found that intragastric administration of lavender test samples in selected doses throughout the observation period did not have a significant negative effect on the general condition, appearance (condition of the skin and mucous membranes) and behaviour of rats. Food and water consumption in animals in the experimental groups did not differ from that of animals in the intact control group. During the entire experiment, no cases of animal death were recorded.

One of the integral indicators studied was the dynamics of rat body weight. According to this indicator, during the entire experiment, no significant differences were recorded in the indicators of rats of the intact and experimental groups under the influence of lavender test samples. All bodyweight indicators of the animals were within the physiological norm for this age group of rats.

Toxicological characteristics of test samples of extracts of *L. angustifolia* during chronic intragastric administration were also evaluated according to clinical urine analysis parameters of rats based on data as of days 45 and 90 of the study (Tab. 1). Thus, during the experiment, no statistically significant effect of extracts was recorded compared to the intact group on the indicators of spontaneous daily diuresis, specific gravity and pH of urine of animals. All these parameters were within the physiological norm.

The use of lavender test samples also had no significant effect on the indicators of the level of glucosuria in rats of all experimental groups, while this indicator was not determined by generally accepted methods of quantitative and qualitative analysis, which is within the physiological norm. During the analysis of the urinary sediment of animals receiving lavender extracts in the studied doses, no signs of urinary syndrome and pathophysiological changes in the ratios of formed elements were determined. The content of erythrocytes, leukocytes, epithelium, and cylinders was within the physiological norm, and at the level of intact animals, it was 0-3 in the field of view.

The results of studying the effect of lavender extract test samples on nitrogen metabolism in rats during chronic administration are given in Tab. 2. These indicators reflect both the functional capabilities of the urinary system of experimental animals and the state of protein and nitrogen metabolism. The results obtained indicate that with prolonged use of lavender test samples, there is no statistically significant effect on nitrogen metabolism in animals. Fluctuations in blood urea and creatinine are within the physiological norm.

The results of the analysis of biochemical blood parameters of rats under the influence of chronic administration of lavender test samples are given in Tab. 3. The obtained data indicate that the test samples of lavender in the studied doses did not have a statistically significant effect on the level of the biochemical parameters studied in comparison with intact animals.

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In general, all the studied parameters: glucose, total protein, cholesterol, bilirubin, AlAT and AsAT activity in the intact and experimental groups are within the range of normal values for rats and do not exceed the physiological norm.

Table 1. Clinical analysis parameters of urine of rats under the influence of chronic administration of test samples of L. angustifolia (n = 48)

Clinical urine analysis indicators	Intact control	Test sample №1, 100 mg/kg	Test sample №2, 100 mg/kg	Test sample №3, 100 mg/kg
45 days				
Diuresis, ml/day	8,5±0,2	8,6±0,2	8,9±0,2	8,9±0,3
Specific density	1,021±0,006	1,023±0,005	1,025±0,006	1,022±0,007
pH	5,95±0,16	6,00±0,16	5,96±0,14	5,85±0,16
Total protein, mg/day	1,34±0,07	1,38±0,07	1,35±0,08	1,41±0,08
Glucose, mmol/day	0	0	0	0
90 days				
Diuresis, ml/day	10,2±0,4	10,4±0,5	11,6±0,4	12,2±0,3
Specific density	1,022±0,004	1,020±0,005	1,021±0,005	1,024±0,005
pH	5,91±0,12	5,85±0,17	5,80±0,15	5,90±0,15
Total protein, mg/day	1,44±0,10	1,41±0,08	1,39±0,09	1,46±0,09
Glucose, mmol/day	0	0	0	0

Note: n is the number of animals in the group

Table 2. Effect of test samples of narrow-leaved lavender on nitrogen metabolism in rats under conditions of chronic administration (n=48)

Research group	Blood urea, mmol/l	Blood creatinine, μmol/l	Urine creatinine, mmol/L	GFR, ml/day
45 days				
Intact control	4,38±0,12	43,52±3,03	2,07±0,23	393,4±27,3
Test sample №1, 100 mg/kg	4,39±0,11	42,28±3,05	1,92±0,22	378,9±26,9
Test sample №2, 100 mg/kg	4,49±0,14	46,88±3,25	2,05±0,21	382,4±26,6
Test sample №3, 100 mg/kg	4,55±0,15	43,94±2,88	1,98±0,23	387,6±27,8
90 days				
Intact control	4,75±0,33	44,22±3,08	1,81±0,17	493,9±23,7
Test sample №1,100 mg/kg	4,57±0,32	45,20±3,14	1,79±0,18	472,6±22,3
Test sample №2, 100 mg/kg	4,22±0,29	43,79±3,04	1,73±0,16	488,5±24,1
Test sample №3, 100 mg/kg	4,71±0,30	44,67±3,12	1,73±0,16	484,7±23,7

Note: n - the number of animals in the group

Table 3. Biochemical parameters of blood in rats under the influence of chronic administration of test samples of extracts of *L. angustifolia* (n = 48)

Biochemical blood test results	Intact control	Test sample №1, 100 mg/kg	Test sample №2, 100 mg/kg	Test sample №3, 100 mg/kg
45 days				
Glucose, mmol/l	3,72±0,18	3,74±0,19	3,85±0,19	3,59±0,17
Total protein, g/l	73,25±2,12	73,40±2,13	73,15±2,11	73,35±2,15
Cholesterol, mol/l	1,52±0,08	1,56±0,08	1,58±0,09	1,51±0,08
Bilirubin, μmol/l	6,46±0,17	6,10±0,17	5,78±0,16	6,12±0,14
AlAT, μκατ/L	0,42±0,01	0,41±0,01	0,39±0,02	0,36±0,01
AsAT, μκατ/l	0,72±0,02	0,70±0,02	0,70±0,03	0,68±0,03
90 days				
Glucose, mmol/l	3,85±0,19	3,66±0,17	3,97±0,18	3,90±0,18
Total protein, g/l	72,36±2,10	71,88±2,09	71,84±2,09	72,33±2,11
Cholesterol, mol/l	1,64±0,07	1,58±0,07	1,55±0,06	1,50±0,05
Bilirubin, μmol/l	6,06±0,18	5,90±0,17	5,69±0,18	5,34±0,16
AlAT, μκατ/L	0,38±0,01	0,35±0,01	0,34±0,02	0,33±0,01
AsAT,μκατ/l	0,73±0,02	0,69±0,01	0,68±0,01	0,69±0,02

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Note: n - the number of animals in the group

This indicates that the test samples of narrow-leaved lavender in the studied doses with intragastric administration do not affect the parameters characterizing the functional state of the liver and kidneys of rats.

During the study, observations were also made of the peripheral blood pattern of animals under the influence of intragastric administration of experimental lavender extracts. Analysis of the obtained haematological indicators of animals (Tabs. 4, 5) shows that chronic use of test samples of narrow-leaved lavender in the studied doses does not have a toxic effect on the peripheral blood parameters of rats. All indicators are within the physiological norm and do not have significant differences from the intact group.

Table 4. Clinical blood test results of rats exposed to chronic administration of L. *angustifolia* test samples (n=48)

Research group	Hemoglobin, g/l	Erythrocytes, 10^{12}/l	CI	Leukocytes, 10^9/l	ESR, mm/h
45 days					
Intact control	147,4±3,9	5,06±0,12	0,88±0,01	8,95±0,24	4,32±0,37
Test sample №1, 100 mg/kg	145,5±3,8	5,13±0,13	0,86±0,01	8,76±0,23	4,31±0,34
Test sample №2, 100 mg/kg	147,9±3,9	5,11±0,11	0,87±0,01	8,75±0,22	4,14±0,31
Test sample №3, 100 mg/kg	148,8±3,8	5,16±0,12	0,85±0,01	8,45±0,25	4,06±0,33
90 days					
Intact control	145,1±3,8	5,11±0,09	0,84±0,02	9,18±0,24	4,12±0,36
Test sample №1, 100 mg/kg	146,4±3,7	4,98±0,10	0,88±0,01	9,10±0,25	4,06±0,39
Test sample №2, 100 mg/kg	147,2±3,9	5,10±0,10	0,86±0,02	9,02±0,25	4,02±0,42
Test sample №3, 100 mg/kg	146,9±3,8	5,05±0,09	0,87±0,02	8,88±0,24	4,02±0,40

Note: n - the number of animals in the group

Table 5. Effect of test samples of narrow-leaved lavender on leukocyte formula indices in rats during chronic administration (n=48)

Research group	mmature neutrophils, %	Rod-shaped neutrophils, %	Segmented neutrophils, %	Eosinophils, %	Basophils, %	Monocytes, %	Lymphocytes, %
45 days							
Intact control	—	1,00±0,16	21,65±0,50	1,00±0,03	—	3,56±0,30	72,76±0,82
Test sample №1, 100 mg/kg	—	0,81±0,18	22,25±0,40	0,84±0,20	—	3,29±0,32	72,70±0,76
Test sample №2, 100 mg/kg	—	1,15±0,20	22,18±0,45	1,07±0,10	0,09±0,10	3,18±0,40	72,34±0,90
Test sample №3, 100 mg/kg	—	0,98±0,18	21,91±0,45	0,89±0,18	—	3,36±0,36	72,88±0,78
90 days							
Intact control	—	1,20±0,20	20,64±0,57	0,80±0,14	—	3,74±0,22	73,70±0,60
Test sample №1, 100 mg/kg	—	1,12±0,18	20,82±0,58	1,00±0,15	—	3,96±0,22	73,20±0,60
Test sample №2, 100 mg/kg	—	1,48±0,27*	22,22±0,55	0,94±0,32	0,12±0,11	3,60±0,27	71,44±0,68
Test sample №3, 100 mg/kg	—	1,44±0,33	22,08±0,60	0,68±0,23	—	4,37±0,38	70,92±1,10

Note: * – p≤ 0,05 relatively intact animals;
n - the number of animals in the group

The hemogram parameters of rats given in Tab. 5 indicate that on the 45th and 90th day of the study, the levels of haemoglobin, erythrocytes, leukocytes, CI and ESR in animals against the background of the use of test samples of lavender extracts did not differ from those of intact rats and were within the physiological norm. In the leukocyte formula of rats of the experimental groups (Tab. 5) under the influence of chronic use of lavender test samples, the

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percentage ratio of different forms of leukocytes also corresponded to intact animals and did not differ from the norm. The only exception can be considered an increase in the content of rod-shaped neutrophils under the influence of test sample No. 2 as of the 90th day of the study, which probably exceeds the intact level but, despite this, is within the physiological norm for rats.

Conclusions

With chronic (90 days) intragastric administration, test samples of narrow-leaved lavender at a dose of 50 mg/kg do not cause death in rats.

It has been established that under conditions of chronic use, test samples of narrow-leaved lavender do not have a toxic effect on the general condition, behaviour and dynamics of body weight, do not cause significant differences in laboratory test parameters of urine and blood, and practically do not affect the functional state of the urinary and hepatobiliary systems of animals.

Study of chronic toxicity of narrow-leaved lavender extracts: influence on functional status and laboratory indicators of rats

Olena Bogatyrova, Olha Naboka

Introduction. Despite the widespread use of chemotherapeutic drugs, medicinal plants continue to maintain the scientific interest of today's pharmacologists. In order to saturate the domestic pharmaceutical sector with affordable phytopreparations of a wide spectrum of action, scientists of the National Pharmaceutical University (postgraduate student Gurina V.O. under the supervision of Doctor of Pharmaceutical Sciences, Professor Georgiyants V.A.) obtained extracts of narrow-leaved lavender containing biologically active substances: terpenoids (linalool, linalyl acetate and traces of 1,8-cineole), flavonoids (hyperoside, isoquercitrin) and hydroxycinnamic acids (rosmarinic, chlorogenic). As a result of experimental microbiological tests, it was established that the herb of narrow-leaved lavender of Ukrainian origin is a promising and affordable source of potential antimicrobial active pharmaceutical ingredients. Also, based on the results of studying the acute toxicity of narrow-leaved lavender extracts when administered intragastrically to white mice, conclusions were drawn that allowed the studied test samples to be classified as class V of practically non-toxic substances (LD_{50}>5000 mg/kg). **The aim of the work.** Experimental study of the toxicological properties of extracts of *L. angustifolia* (chronic toxicity) to substantiate the safety of use in clinical practice. **Materials and methods.** The objects of the study were experimental test samples: No. 1 - extract of narrow-leaved lavender obtained by extraction with purified water; No. 2 - extract of narrow-leaved lavender obtained by extraction with a water-ethanol solution (40% ethanol); No. 3 - extract of narrow-leaved lavender obtained by extraction with a water-ethanol solution (70% ethanol). Test samples of narrow-leaved lavender were used at a dose of 100 mg/kg, which corresponds to 1/50 of the LD_{50} of the experimental agents, which was determined at the previous stage of the study. Chronic toxicity studies of narrow-leaved lavender extracts were conducted on 48 white non-linear rats of both sexes with an initial weight of 170-190 g with daily intragastric administration for 90 days. In the collected urine, general properties (colour, transparency, pH, density), total protein content (by reaction with sulfosalicylic acid), glucose content (by glucose oxidase method) and urinary sediment were determined. Then, a complete laboratory blood test was performed using general scientific haematological methods and the following were determined: haemoglobin and erythrocyte content, colour index, leukocyte content, leukocyte formula, and erythrocyte sedimentation rate. Creatinine content (by reaction with picric acid) in blood and urine was determined. Endogenous creatinine clearance was calculated to assess the glomerular filtration rate. In the blood serum of rats, the urea content (diacetylmonooxime method), total protein (biuret method), glucose content (glucose oxidase method), ALT and AST activity (Reitman-Frankel method), bilirubin content (Jendrassik-Grof method), cholesterol content (modified Liebermann-Burchard method) were determined. The significance of differences between samples was assessed using the Kruskal-Wallis method and the Mann-Whitney test in comparison with the intact control group. **Results and discussion.** According to the results of experimental studies, it was found that intragastric administration of lavender test samples in selected doses throughout the entire observation period did not have a significant negative effect on the general condition, condition of the skin and mucous membranes and behaviour of rats. During the experiment, no case of animal mortality was registered. All indicators of the body weight of rats were within the physiological norm for this age group. On the 45th and 90th day of the study, no statistically significant effect of the extracts was registered relative to the intact group on the indicators of spontaneous daily diuresis, specific gravity and pH of the urine of animals. The use of narrow-leaved lavender test samples did not have a significant effect on the indicators of the level of glucosuria in rats of all experimental groups, while this indicator was not determined by generally accepted methods of quantitative and qualitative analysis, which is within the physiological norm. During the analysis of the urinary sediment of animals receiving narrow-leaved lavender extracts, no signs of urinary syndrome and pathophysiological changes in the ratios of formed elements were detected. The content of erythrocytes, leukocytes, epithelium, and cylinders was within the physiological norm, and at the level of intact animals, it was 0-3 in the field of view. With prolonged use of narrow-leaved lavender test samples, no statistically significant effect was observed on nitrogen metabolism and biochemical blood parameters in animals. Fluctuations in blood urea and creatinine were within the physiological norm. All studied parameters: glucose, total protein, cholesterol, bilirubin, AlAT and AsAT activity in the intact and experimental groups are within the range of normal values for rats and do not exceed the physiological norm. This indicates that lavender test samples in the studied doses with intragastric administration do not affect the parameters characterizing the functional state of the liver and kidneys of rats. During the study, no toxic effect was recorded on the parameters of peripheral blood of rats. In the leukocyte formula of rats of the experimental groups under the influence of chronic use of narrow-leaved lavender test samples, the percentage ratio of

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different forms of leukocytes also corresponded to intact animals and did not differ from the normal values. The only exception can be considered to be the increase in the content of rod-shaped neutrophils under the influence of test sample No. 2 as of day 90 of the study, which probably exceeds the intact level but, despite this, is within the physiological norm for rats. **Conclusions.** With chronic (90 days) intragastric administration, test samples of *L. angustifolia* at a dose of 100 mg/kg do not cause death in rats. It has been established that under conditions of chronic use, test samples of narrow-leaved lavender do not have a toxic effect on the general condition, behaviour and dynamics of body weight, do not cause significant differences in laboratory test parameters of urine and blood, and practically do not affect the functional state of the urinary and hepatobiliary systems of animals.
Keywords: narrow-leaved lavender, dry extracts, chronic toxicity, rats, functional state, laboratory parameters.

References

1. Prusinowska R., Śmigielski K. B. Composition, biological properties and therapeutic effects of lavender (Lavandula angustifolia L): A review. Herba Polonica. 2014;60(2):56-66. doi:10.2478/hepo-2014-0010.
2. Naboka O., Vyshnevska L., Pasynchuk I., Filiptsova O., Tkachenko O., Vislous O. Pharmacological study of original extracts of corn silk. ScienceRise: Biological Science. 2022;(4(33):10-17. doi:10.15587/2519-8025.2022.271049.
3. Cavanagh H. M. A., Wilkinson J. M. Biological activities of lavender essential oil. Phytotherapy Research. 2002;16(4):301-308. doi:10.1002/ptr.1103.
4. Prusinowska R., Śmigielski K. B. Composition, biological properties and therapeutic effects of lavender (Lavandula angustifolia L): A review. Herba Polonica. 2014;60(2):56-66. doi:10.2478/hepo-2014-0010.
5. Bogatyrova O., Hurina V., Naboka O., Filimonova N., Dzhoraieva S., Mykhailenko O., Georgiyants V. Lavandula angustifolia Mill. of Ukrainian origin: a comparative study of the chemical composition and antimicrobial potential of herb extracts. ScienceRise: Pharmaceutical Science. 2024. № 5 (51) P. 4-14. doi:10.15587/2519-4852.2024.313236.
6. Mykhailenko O., Hurina V., Ivanauskas L., Marksa M., Skybitska M., Kovalenko O., Lytkin D., Vladymyrova I., Georgiyants V. Lavandula angustifolia Herb from Ukraine: Comparative chemical profile and in vitro antioxidant activity. Chemistry & Biodiversity. 2024. doi:10.1002/cbdv.202400640.
7. Mir A., Sexena M., Malla M. An acute oral toxicity study of methanolic extract from Tridex procumbens in Sprague Dawley rats as per OECD guidelines 423. Asian Journal of Plant Science and Research. 2013;3:16-20.
8. Ministry of Health of Ukraine. Medicinal Products. Good Laboratory Practice. Kyiv: Ministry of Health of Ukraine; 2009. 27 p.
9. Ministry of Health of Ukraine. Order No. 944: On Approval of the Procedure for Preclinical Studies of Medicinal Products. Kyiv: Ministry of Health of Ukraine; December 14, 2009.
10. Kovalenko V. M., Stefanov O. V., Maksimov Yu. M., Trakhtenberh I. M. Experimental study of the toxic effects of potential medicinal products. Methodical Recommendations. Kyiv; 2000. P. 74-97.
11. Bogatyrova O. O., Naboka O. I. Study of the toxicological profile of lavender narrow-leaved herb dry extracts. Visnyk Farmatsii. 2024;(2(108):78-85.
12. Ministry of Health of Ukraine. Order No. 944: On Approval of the Procedure for Preclinical Studies of Medicinal Products. Kyiv: Ministry of Health of Ukraine; December 14, 2009.
13. European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes. Strasbourg: Council of Europe; 1986. 52 p.
14. Kozhemyakin Yu. M., Khromov O. S., Filonenko M. A., Saifetdinova H. A. Scientific and Practical Recommendations for Keeping and Working with Laboratory Animals. Kyiv: Avicena; 2002. 156 p.
15. Naboka O. I., Khouri S. Z., Koshova O. Yu., Hlushchenko A. V. Pharmacodynamic studies of aqueous and alcoholic extracts of goldenrod. Clinical Pharmacy. 2014;(4(18):58-62 p.
16. Voronina L. M., Desenko V. F., Kravchenko V. M., et al. A Guide to Laboratory and Seminar Classes in Biological Chemistry. Kharkiv: Osnova; 1996. 432 p.
17. Wu F., Zhou Y., Li L., Shen X., Chen G., Wang X., Liang X., Tan M., Huang Z. Computational approaches in preclinical studies on drug discovery and development. Frontiers in Chemistry. 2020;8:546712. doi:10.3389/fchem.2020.00726.
18. Lee S. W. Methods for testing statistical differences between groups in medical research: statistical standard and guideline of Life Cycle Committee. Life Cycle. 2022. 2 p.

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