

РЕЗЮМЕ

Для улучшения производительности бройлерных цыплят в промышленном птицеводстве крайне важно изучение особенностей пищеварения и метаболизма. Это знание необходимо для поддержания и повышения их жизнеспособности и продуктивности путем обеспечения достаточного поступления энергии и питательных веществ. Основные биохимические показатели крови отражают общее состояние здоровья и функционирование иммунной системы организма. Изменения, связанные с физиологическими процессами роста и развития птиц, напрямую влияют на состав белков в крови. Исследование было выполнено на бройлерах породы Росс-308. В рамках научного эксперимента были созданы три группы бройлеров: контрольная и две экспериментальные, каждая из которых насчитывала по 50 особей. Группы для опыта были сформированы из цыплят, взятых в возрасте одних суток. Цыплятам было предоставлено кормление в соответствии с рекомендованными нормами для данного кросса. Наши исследования показали, что добавление минеральной подкормки в виде опоки к основному корму для бройлеров не только не снижает содержание сырого белка и необходимых аминокислот, но также благоприятно влияет на состав белков крови. Это приводит к увеличению содержания общего белка и его составляющих. При статистическом анализе не было обнаружено значимых различий в биохимических параметрах сыворотки крови между экспериментальными и контрольными группами цыплят. Это показывает, что использование минеральной добавки в виде опоки в кормах для бройлеров является безопасным.

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TOXIC AND ALLERGIC EFFECTS OF ARTEMISIA LERCHIANA INFUSION AND ESSENTIAL OIL ON THE BODY OF LABORATORY ANIMALS

ANNOTATION

As a result of therapeutic and preventive research, in practice with a long history, the need for the use of medicinal plants in medicine and veterinary medicine has acquired an accurate scientific basis. A share of up to 40% of the drugs used in practice medicinal plants are common in many regions of the world. Phytopreparations made from medicinal plants have their own characteristics: the gradual, slow development of the therapeutic effect, the harmless effect on the body, the absence of adverse reactions, even with prolonged use, heal not only individual symptoms of the disease, but the entire organism as a whole by mobilizing various protective forces.

As a research material, an infusion prepared from the dried form of the *Artemisia lerchiana* plant, collected from the region of the West Kazakhstan region, and an essential oil obtained by hydrodistillation were used. The toxic and allergic effect of *Artemisia lerchiana* infusion and essential oil on the body of laboratory animals (white mice, rabbits) was studied.

As a result of the study, a sample prepared in two dosage forms (infusion and essential oil) to study the toxic and allergic effects of *Artemisia lerchiana* did not have a negative effect on the body of laboratory animals, mortality and normal changes in internal organs and tissues showed that *Artemisia lerchiana* infusion and essential oil are harmless to the body.

Key words: *Artemisia lerchiana* infusion, essential oil, white mouse, rabbit, allergic effect, local irritation, poisoning, toxic effect.

Introduction. The study of the pharmacological properties of phytopreparations is becoming more and more relevant, as preparations of plant origin are successfully used in the treatment of various diseases. One of the most important tasks is to increase the arsenal of phytopreparations, search and study of the biological activity of preparations from little - studied plants, and expand the spectrum of action of plant-based medicines.

Health care is experiencing difficulties due to the development of medical and pharmaceutical chemistry, and many natural drugs of irregular action have been replaced by synthetic ones and are being used in the medical field. However, over time, specialists began to identify many side effects that chemical drugs have a toxic effect on the body, have an allergic effect, form new tissue formations (malignant and benign tumors), cause changes in the physiological function of the body.

As the requirements for the quality and safety of medicines increase, one of the directions of pharmaceutical science is the development of medicines with high medicinal properties, low toxicity, allergic and irritating effects [1,2,3,4].

Many chemicals with antimicrobial effects are not effective and reliable. Some are used as a disinfectant, others as an antiseptic for the skin, and some are used to prevent infectious diseases in animals. In addition, many of them have the property of accumulating in organs and tissues, allergic and toxicological side effects.

In recent years, scientific research has confirmed the growth of strains of microorganisms resistant to all classes of chemical compounds. The lack of a single scientific concept of combating microorganisms based on the laws of biology, physics, chemistry does not allow any significant achievements in the sanitary and epidemiological protection of the population and animals [5,6,7,8].

In modern veterinary medicine, more and more attention is paid to plant and natural remedies. Given their abundance on the market, it is difficult to choose the most profitable one from among them. In this regard, recently there has been an increase in interest in medicinal plants of the *Artemisia* family.

The Republic of Kazakhstan has unique reserves of medicinal plant raw materials. In Kazakhstan, 81 species of wormwood grow, of which only a small part has been studied, namely: *Artemisia armeniaca* Lam., *A. atomentella*, *A. annua*, *A. pontica*, *A. tournefortiana*, *A. laciniata*, *A. semiarida*, *A. albida*, *A. marschalliana* et al. [9].

Taking into account the comprehensive use of wormwood species, in our research work, the study of various properties of the *A. lerchiana* plant, which is an endemic species for the West Kazakhstan region, was the main relevant point of our work.

Some components of *A. lerchiana* essential oil (1,8-cineol, borneol a-tuion, borneol, bornyl acetate, a-tuion) serve as protection against pathogens, have fungicidal and bactericidal activity [10,11,12,13,14].

Terpinoline and terpinene in essential oil found in *A. lerchiana* can act as phytoalexins [15] terpinoline and terpinene in essential oil found in *lerchiana* can act as phytoalexins [15]. Hermacrene D, a-pinene found in *A. lerchiana* essential oil has antioxidant activity [16], which are important properties for this species growing in conditions of drought, salinity, high temperature and excess solar insolation [17].

Analyzing the above data, a promising direction is the study of the possibility of using wormwood essential oils as active and auxiliary substances in the development of new drugs for the treatment of infectious and non-infectious diseases, various inflammations associated with stable microflora. The antimicrobial activity of different types of wormwood also depends on the place of growth, extraction

technology. Among the medicinal plants growing on the territory of the Republic of Kazakhstan, only some types of wormwood have been studied.

In this regard, the determination of the antimicrobial effect of biologically active substances contained in the locally grown *Artemisia lerchiana* showed the importance of the study.

At the initial stages of treatment, it was established that the tincture and essential oil prepared from the *Artemisia lerchiana* plant have a high indicator of antibacterial activity. *Artemisia lerchiana* in the form of essential oil, its low concentration also has antibacterial activity. The results of the study showed that *Artemisia lerchiana* can be used in production as an effective antibacterial agent [18].

The general program for studying the harmlessness of new drugs also includes determining their allergic effect.

Guaranteeing the safety of plant raw materials and medicines is possible after conducting the appropriate stages of research in the process of preparing a new product. In this regard, one of the main tasks of our work was to study the toxic and allergic effects of various dosage forms of *Artemisia lerchiana*.

Research materials and methods.

The research work was carried out within the framework of the project AR15473422 "Determination of efficacy of *Artemisia lerchiana* based medication in the treatment of surgical injuries in animals ", funded by the Science Committee of the Ministry of Education and science of the Republic of Kazakhstan.

In the course of the research, the use of laboratory animals was carried out by the decision of the local bioethical Commission of the West Kazakh agrarian and Technical University named after Zhangir Khan.

Toxicological studies of the *Artemisia lerchiana* plant were carried out in accordance with the methodological recommendations of Professor R. U. Habriev [19] on "Toxic-environmental assessment of drugs used in Veterinary Medicine" and "instructions for experimental (preclinical) research of new pharmacological substances, Instructions (part one) of A. N. Mironov [20] "Conducting preclinical studies of drugs". Also, the provisions stipulated by State Standard 32296-2013, the "European Convention for the protection of vertebrates used for practical and scientific purposes" were observed and studied.

As a material for the study, an infusion prepared from the dried form of the *Artemisia lerchiana* plant, collected from the territory of the West Kazakhstan region, and an essential oil obtained by hydrodistillation were used.

The study of toxic and allergic effects of *Artemisia lerchiana* infusion and essential oil on the body of laboratory animals (white mice, rabbits) was carried out on white mice of different sexes weighing 19-24.0 g (n=25) and rabbits of the "White and gray giant" breed at the rate of 2-2.5 kg (n=20) in the vivaria of the West Kazakhstan agrarian Technical University named after Zhangir Khan. Laboratory animals were kept in vivarium conditions with a temperature of 20-22°C and a humidity level of 60-62%.

At the first stage of the study, the determination of acute toxicity of *Artemisia lerchiana* tincture was carried out. Based on analog principles, the experiment used white mice contained in the same conditions. The feeding regimen included raw vegetables and fruits (carrots, pumpkin, apples), white and rye bread and vitamin supplements with water regularly, fed twice a day with a grain mixture (wheat, barley, corn).

In order to identify possible deviations from physiological indicators (temperature, pulse, breathing) and monitor the development of pathological changes, all animals were quarantined in advance.

4 hours before the experiment, watering and feeding of white mice was stopped.

Further, animals that met the criteria for inclusion in the experiment were divided into five groups – 4 experimental and Control (n=5) groups.

In experimental groups of rodents, *Artemisia lerchiana* infusion was administered into the oral cavity in a volume of 0,3; 0,5; 0,7 and 0,9 ml. White mice from the control group were given distilled water (distilled) in a volume of 0,9 ml. After the introduction of the infusion, no feeding was carried out for 2 hours.

The technique for administering the infusion is described in Table 1.

Table 1 – Outline of an experiment to study the acute toxicity of *Artemisia lerchiana* infusion on laboratory white mice (n=5)

Groups	Input method	Dose and volume
1-experimental group	oral	0,3 ml 1 time per day for 3 consecutive days
2- experimental group		0,5 ml 1 time per day for 3 consecutive days
3- experimental group		0,7 ml 1 time per day for 3 consecutive days
4- experimental group		0,9 ml 1 time per day for 3 consecutive days
Control group		0,9 ml of distilled water 1 time a day for 3 consecutive days

In the following days of the study, there were no restrictions on food and water. After the last administration of the infusion in white mice, the clinical condition was evaluated daily for 14 days to identify signs of toxicosis. During the first day, control was carried out every hour, then every 8 hours (three days after intoxication). On the rest of the days, an assessment of the condition of white mice was carried out every 24 hours. In this case, it was carried out in order to check the survival rate, the nature of the toxic effect of *Artemisia lerchiana* infusion, behavioral activity, and tactile sensitivity. Feeding and physiological functions, skin reflexes and changes in body weight were monitored.

In the second stage of the study, the allergic effect of *Artemisia lerchiana* infusion was determined by a conjunctival test carried out in rabbits. The scheme of the experiment is presented in Table 2.

Table 2 – Scheme for assessing the irritant effect of *Artemisia lerchiana* infusion in rabbits (conjunctival test)

Number of animals studied, n	10
Input frequency	Once
Input type	Administration of <i>Artemisia lerchiana</i> infusion under the upper eyelid
Dose	1 drop

In the third stage of the study, the determination of the skin resorption effect of *Artemisia lerchiana* essential oil (10%, 15% and 20% essential oil) on 10 rabbits weighing 2-2,5 kg was carried out. In order to determine the effect of essential oil in different concentrations, vaseline was taken as an additive to the base. The study was carried out by applying a smear to the hair-free part of the animal's body. Before applying ether-based ointment to rabbits, the day before the study, a 5*5 cm hair cover was cleaned from one side area of the animal's jaw.

After a day, ether-based *Artemisia lerchiana* ointment was applied to the hairless, degreased skin of animals for research with 10% in the first experimental group, 15% in the second experimental group; 20% ointment in the third experimental group; and Vaseline in the fourth control group.

The use of pharmacological drugs was repeated twice a day for 5 days. The exposure reaction was monitored immediately after application, after 30 minutes, then after 1, 2, 6 hours and up to 24 hours. All animals were kept in separate cages.

During the specified period, edema, hyperemia, itching, pain on palpation, the appearance of cracks and scales, an increase in local temperature were monitored.

Research results and analyzes.

Acute toxicity of *Artemisia lerchiana* infusion.

Acute toxicity is a harmful effect of a drug that occurs after its single use or readministration for a short period of time during the day to determine the transportable, toxic and lethal doses of the substance and the causes of death of animals.

According to the work carried out to determine the toxic effect of *Artemisia lerchiana* infusion at the first stage of the study, the following results were obtained. The results of the study are described in Table 3.

Table 3 – Acute toxic effect of *Artemisia lerchiana* infusion on white mice (n=6)

Research groups	Average weight, g	Dose, ml	The introduced substance	Research results
1-experimental group	21,0±0,79	0,3	<i>Artemisia lerchiana</i> infusion	No visible toxic reaction was observed after the administration of the tincture, no abnormalities in the behavior and general state of the animals were detected during all days of the study. Appetite for food and water consumption are obvious. Death of animals did not register.
2- experimental group	22,0±0,93	0,5		
3- experimental group	21,2±0,74	0,7		
4- experimental group	20,8±0,82	0,9		Due to the manipulations carried out, short-term (up to 5 minutes) changes in breathing were observed in mice, no deviations in behavior were observed in the days of the further experimental period. No animal deaths have been identified.
Control group	22,2±0,89	0,9	distilled water	Condition of animals well, mice are active, the appetite for food is pronounced, reflexes are preserved, there are no signs of intoxication

According to the results of the study, the administration of *Artemisia lerchiana* infusion once a day for 3 consecutive days did not cause fatal and acute toxic effects on laboratory animals. The precipitate did not have a negative impact on the general condition and behavior of laboratory animals. White mice in the 4th experimental group showed a change in breathing only for 5 minutes after administration due to the threshold of the amount of injections, in our opinion, these changes were associated with the conduct of manipulation.

During the subsequent control period, white mice from all experimental groups did not have clinical and physiological differences from the control group of animals in all the studied indicators. Experimental animals actively moved in the cage and showed interest in water and food. A similar clinical picture was also observed in the control group.

In all experimental mice (regardless of the group), no significant differences in respiratory rhythm and body temperature indicators were found with the control group. The skin and mucous membranes are pale pink in color, there are no wounds and ulcers.

No abnormalities in digestive and urinary functions were observed: fecal secretions were pronounced, Brown in color, of normal consistency; there were no changes in the color of urine, no fluids or discharge from natural openings were observed.

Taking into account the principles of bioethics, 2 animals were taken from each study group by euthanizing with diethyl ether for pathological slaughter research after 7 days of follow-up from each group. During the slaughter study, a macroscopic examination of internal organs was carried out (Figure 1).

In the course of the slaughter study of white mice in the experimental and control groups, no macroscopic changes in internal organs and tissues were observed. The anatomical arrangement of the internal organs was correct.

The mucous membranes of the digestive system are pink. There was no visible swelling, inflammation in the parenchymal organs. Blood vessels were characterized by full bloodiness.



Figure 1 – View of internal organs during the slaughter study

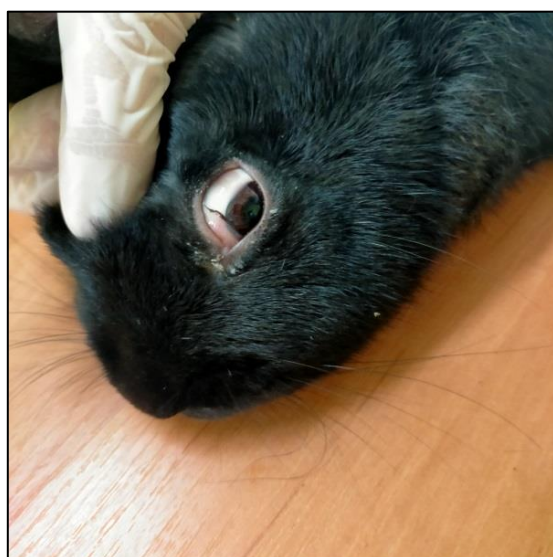
Thus, a study of the acute toxicity of *Artemisia lerchiana* infusion showed that its use in different doses through the mouth did not adversely affect the body of white mice and did not cause functional disorders of various systems of animal organs.

Allergic effects of *Artemisia lerchiana* infusion.

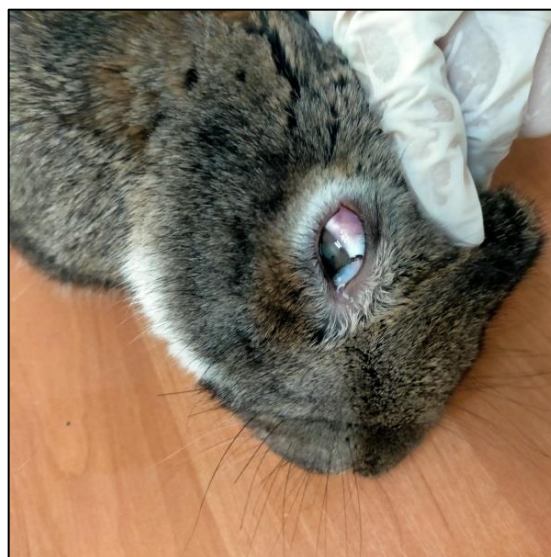
An allergic reaction is a type of immune response that occurs when the immune system is compromised. According to the rate of development, two types of allergic reactions are distinguished: reactions of the acute type and delayed type. The first symptoms appear a few minutes after contact with the allergen.

In the process of determining the allergic effect of *Artemisia lerchiana* infusion in the second stage of the study, the following results were obtained.

5 rabbits of the experimental group were injected with a drop of *Artemisia lerchiana* infusion under the upper eyelid of the left eye, and at the same time one drop of distilled water (distilled water) was administered in a similar way to the left eye of animals of the control group (n=5) (Figure 2, A, B).



A



B

Figure 2 – Making an allergy test for the eyes of laboratory animals
a – experimental group, right eye, b-control group, left eye

Accounting for the reaction was carried out after 5 and 15 minutes (rapid reaction) and after 24-48 hours (delayed-type hypersensitivity) according to the following indicators: the condition of the sclera, conjunctiva, cornea, hyperemia of the vessels of the sclera and cornea, the release of tears from the tear glands.

According to the results of the study, the blink reflex was observed in a rabbit of one experimental group immediately after administration of *Artemisia lerchiana* infusion, while the process of tear production lasted about 1 minute. However, during subsequent studies, redness (hyperemia), swelling of the mucous membrane of the eyes were not observed, the animals were in good general condition, and no side effects were observed.

Local irritating effect of *Artemisia lerchiana* essential oil.

The local effect of the pharmacological drug occurs in direct contact with body tissues, that is, with the skin, mucous membranes, the surface of the wound, drugs with an irritating effect Act both locally and remotely. These effects are associated with reflex reactions and indicate reflex action. Sensitive nerve endings (interoreceptors) of mucous membranes, skin and subcutaneous formations are stimulated, impulses in afferent nerve fibers reach the central nervous system, excite nerve cells, and then through the efferent nerves the action spreads to organs or throughout the body.

The clinical picture of the use of *Artemisia lerchiana* essential oil in different concentrations is presented in Figure 3 (A,B,C,D).

During the experiment, edema, hyperemia, itching, pain on palpation, the appearance of cracks and scales, an increase in local temperature were observed.

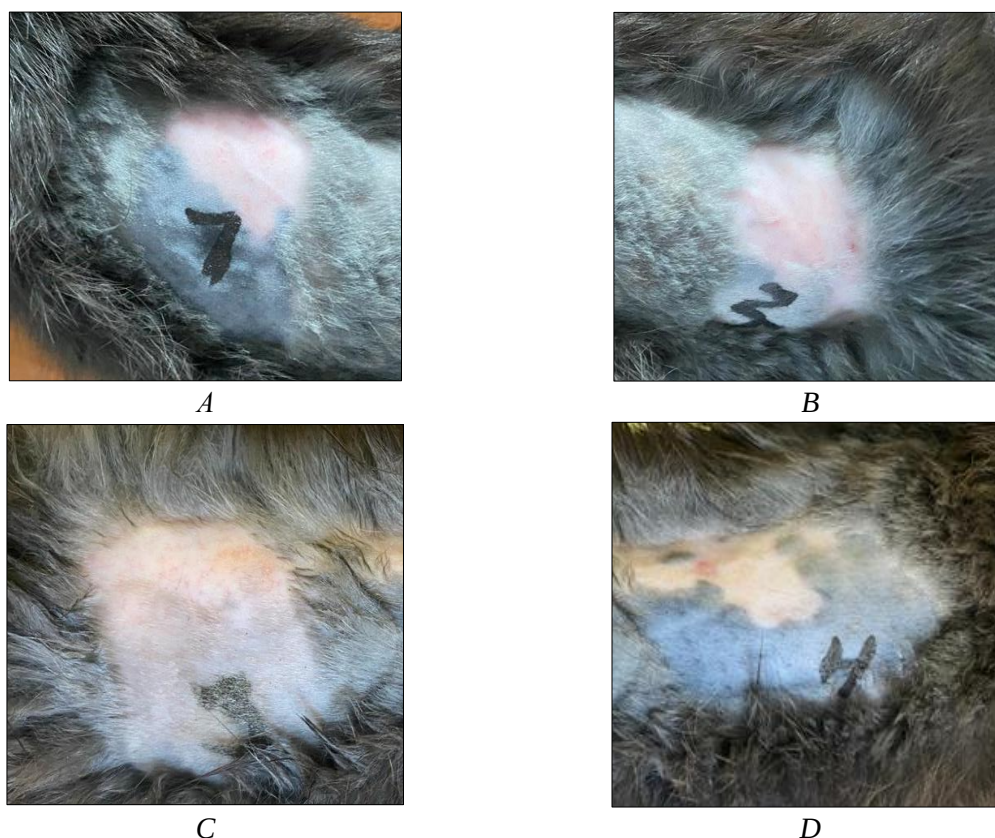


Figure 3 – Local irritating effect of *Artemisia lerchiana* essential oil
A - 10% ointment; B - 15% ointment; C - 20% ointment; D - Vaseline

Assessment of the irritating effect of ointment in different concentrations was evaluated by the effect of ointment on the skin cover.

Analyzing the results, a 20% *Artemisia lerchiana* essential oil-based ointment showed a slight reddening mark on the periphery during the initial 30-minute control in one rabbit and a spontaneous disappearance in the amount of 1 hour. At other stages of the study, these changes in the state of

secondary burning were also not observed. In all the animals in the study, no swellings were formed on the surface of the skin. At other stages of the study, no changes in the state of secondary burnout were observed. Not all of the animals under study developed swelling in the surface area of the skin.

Conclusion. Summing up the research stages, a sample prepared in two dosage forms (infusion and essential oil) was used to study the acute toxic, allergic and local irritating effects of *Artemisia lerchiana* and their effect on laboratory animals (white mice, rabbits) was determined.

At the first stage of the study, acute toxic effects of *Artemisia lerchiana* infusion were prescribed to white mice by oral administration in different doses (0,3; 0,5; 0,7; 0,9 ml). Administration of *Artemisia lerchiana* infusion once a day for 3 consecutive days did not give fatal and acute toxic effects to laboratory animals. There was no negative impact on the general condition and behavior of laboratory animals. In white mice of the 4th group, respiratory changes were observed only for 5 minutes after administration, depending on the threshold of the amount of administration. This was due to manipulation.

Pathoanatomic slaughter studies of white mice showed no macroscopic changes in the internal organs and tissues of animals in the experimental and control groups.

In the second stage of the study, the allergic effect of *Artemisia lerchiana* infusion was detected in rabbits by means of a conjunctival sample. After the solutions were instilled into the rabbits' eyes, the blink reflex was observed in one experimental rabbit in the right eye and the tear process continued for 1-2 minutes. However, in subsequent studies, redness (hyperemia), swelling of the mucous membrane of the eyes were not observed, the animals in the study were in good general condition, and there were no side effects.

In the third stage of the study, the local irritating effect of *Artemisia lerchiana* essential oil (10%, 15% and 20% essential oils) on the skin was studied. To determine the effect of essential oil in different concentrations, Vaseline was taken as a basis as an additional substance. Local irritation effect in an initial 30-minute follow-up of one rabbit using *Artemisia lerchiana* 20% essential oil ointment, a slight sign of redness was observed in the periphery and disappeared on its own within 1 hour. At other stages of the study, the listed changes in the conditions of repeated use were also not observed. Not all of the animals studied developed swelling in the surface area of the skin.

Thus, the results of an allergodiagnostic study showed that the infusion and ointment based on *Artemisia lerchiana* do not have potentially irritating and sensitizing allergenic activity, without causing allergologically significant manifestations identified under the conditions of a toxicological experiment.

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РЕЗЮМЕ

В результате лечебно-профилактических исследований необходимость применения лекарственных растений в медицине и ветеринарии в практике с многолетней историей была обоснована на научной основе. На долю до 40% препаратов, применяемых на практике, лекарственные растения широко распространены во многих регионах мира. Фитопрепараты из лекарственных растений имеют свои особенности: постепенное, медленное развитие терапевтического эффекта, безвредное воздействие на организм, отсутствие побочных реакций, даже при длительном применении, путем мобилизации различных защитных сил, лечат не только отдельные симптомы заболевания, но и организм в целом.

В качестве материала исследования использовались настой из высушенной формы растения *Artemisia lerchiana*, собранной из региона Западно-Казахстанской области, и эфирное масло, полученное гидродистилляционным методом. В исследовании изучалось токсическое и аллергическое действие настоя и эфирного масла *Artemisia lerchiana* на организм лабораторных животных (белые мыши, кролики).

По итогам исследования образец, приготовленный в двух лекарственных формах (настой и эфирное масло) для изучения токсического и аллергического действия *Artemisia lerchiana*, не оказывал негативного воздействия на организм лабораторных животных, летальность и умеренность изменений внутренних органов и тканей показали, что настой и эфирное масло *Artemisia lerchiana* безвредны для организма.

ТҮЙІН

Емдік және профилактикалық зерттеулер нәтижесінде көп жылдық тарихы бар тәжірибеде дәрілік өсімдіктерді медицинада және ветеринарияда қолдану қажеттілігі ғылыми негізде дәлелге ие болды. Тәжірибеде қолданылатын препараттардың 40%-на дейінгі үлесі дәрілік өсімдіктер әлемнің көптеген аймақтарында кең таралған. Дәрілік өсімдіктерден жасалған фитопрепараттардың өзіндік ерекшеліктері бар: терапевтік әсердің біртіндеп, баяу дамуы, ағзаға

зиянсыз әсер етуі, жағымсыз реакциялардың болмауы, тіпті ұзақ уақыт қолданған кезде де, әртүрлі қорғаныс күштерін жұмылдыру арқылы аурудың жеке белгілерін ғана емес, тұтас ағзаны емдейді.

Зерттеу материалы ретінде Батыс Қазақстан облысы аймағынан жинап алынған *Artemisia lerchiana* өсімдігінің кептірілген түрінен дайындалған тұнба мен гидродистилляциялық жолмен алынған эфир майы қолданылды. Зерттеуге алынған *Artemisia lerchiana* тұнбасы мен эфир майының зертханалық жануарлар (ақ тышқан, қоян) ағзасына токсикалық және аллергиялық әсері зерттелді.

Зерттеу қорытындысы бойынша *Artemisia lerchiana*-ның токсикологиялық және аллергиялық әсерін зерттеу үшін екі дәрілік формада дайындалған (тұнба және эфир майы) үлгісі зертханалық жануарлар ағзасына кері әсерін бермеді, өлімге ұшырау және ішкі мүшелер мен ұлпалардағы өзгерістердің қалыпты болуы *Artemisia lerchiana* тұнбасы мен эфир майының ағза үшін зиянсыз екендігін көрсетті.