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NAS RK is pleased to announce that Bulletin of NAS RK scientific journal has been accepted for indexing in the Emerging Sources Citation Index, a new edition of Web of Science. Content in this index is under consideration by Clarivate Analytics to be accepted in the Science Citation Index Expanded, the Social Sciences Citation Index, and the Arts & Humanities Citation Index. The quality and depth of content Web of Science offers to researchers, authors, publishers, and institutions sets it apart from other research databases. The inclusion of Bulletin of NAS RK in the Emerging Sources Citation Index demonstrates our dedication to providing the most relevant and influential multidiscipline content to our community.

Қазақстан Республикасы Ұлттық ғылым академиясы "ҚР ҰҒА Хабаршысы" ғылыми журналының Web of Science-тің жаңаланған нұсқасы Emerging Sources Citation Index-те индекстелуге қабылданғанын хабарлайды. Бұл индекстелу барысында Clarivate Analytics компаниясы журналды одан әрі the Science Citation Index Expanded, the Social Sciences Citation Index және the Arts & Humanities Citation Index-ке қабылдау мәселесін қарастыруда. Web of Science зерттеушілер, авторлар, баспашылар мен мекемелерге контент тереңдігі мен сапасын ұсынады. ҚР ҰҒА Хабаршысының Emerging Sources Citation Index-ке енуі біздің қоғамдастық үшін ең өзекті және беделді мультидисциплинарлы контентке адалдығымызды білдіреді.

НАН РК сообщает, что научный журнал «Вестник НАН РК» был принят для индексирования в Emerging Sources Citation Index, обновленной версии Web of Science. Содержание в этом индексировании находится в стадии рассмотрения компанией Clarivate Analytics для дальнейшего принятия журнала в the Science Citation Index Expanded, the Social Sciences Citation Index и the Arts & Humanities Citation Index. Web of Science предлагает качество и глубину контента для исследователей, авторов, издателей и учреждений. Включение Вестника НАН РК в Emerging Sources Citation Index демонстрирует нашу приверженность к наиболее актуальному и влиятельному мультидисциплинарному контенту для нашего сообщества.

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Адрес типографии: ИП «Аруна», г. Алматы, ул. Муратбаева, 75

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doctor of chemistry, professor, academician of NAS RK

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K. D. Rakhimov¹, A. A. Turgumbayeva¹, Zh. B. Abuova², G. O. Ustenova¹, E. A. Egorov³¹Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan,²Kazakh Medical University of Continuing Education, Almaty, Kazakhstan,³N. I. Pirogov Russian National Research Medical University, Russia

DEVELOPMENT OF EYE OINTMENTS COMPOSITION FROM SAFFLOWER EXTRACT

Abstract. In recent years, the growth of self-medication with the help of antibiotics, water and air pollution has led to increasing in the number of allergic and fungal diseases. Synthetic drugs exacerbate pathological processes, in addition, the side effects of these drugs exceed the expected therapeutic effect. Therefore, in recent years, there has been a significant increase in demand for herbal products. The results of the search for promising sources of antimycotic activity among representatives of plant flora also confirm the real possibilities of creating on their basis the effective antifungal agents in ophthalmic practice.

Key words: fungicidal and antibacterial actions, safflower, eye ointments.

At present, the main attention in pharmaceutical activity in the Republic of Kazakhstan is aimed at ensuring an annual increase in the nomenclature and volumes of production of high-quality pharmaceutical products by domestic producers. The drug policy of the Republic of Kazakhstan is based on the principles of providing medical institutions and the population of the republic with effective, high-quality, safe and affordable medicines.

Today, plants are one of the most important sources of medicines (LP) used in various areas of medical practice. This is explained by the fact that herbal preparations have a wide range of pharmacological activity and, as a rule, do not cause side effects with rational application. The most optimal dosage form for the treatment of eye diseases is ointment, since the effect of eye drops and solutions is short-lived, and the ointment forms a film on the eye mucosa and gives a long-term therapeutic effect [2, 6, 24]. The purpose of this study was to study the antibacterial and antifungal activity of the extracts provided and to determine their minimum bactericidal and fungicidal concentrations against museum strains of microorganisms, and to determine the optimal composition of ocular ointment bases.

Cathamus tinctoris (Safflower *C. tinctorius*) belongs to Asteraceae family in the order of Asterales which contains about 22,750 genera and more than 1,620 species. The *Carthamus* species probably originated from Southern Asia and is known to have been cultivated in China, India, Iran and Egypt, almost from prehistoric times. During the Middle Ages it was cultivated in Italy, France, and Spain, and was introduced into the United States in 1925 from the Mediterranean region. *C. tinctorius* has been known as ‘Golrang’ in Iran. It is grown for the red/orange pigment in the flower petals which is used for colouring rice and bread, and for dyeing cloth. The flowers of *C. tinctorius* are an important medicinal material in prescriptions used for cardiovascular, cerebrovascular and gynecological diseases. In China, the water extract of *C. tinctorius* has been developed as an intravenous injection, which is extensively applied to treat cardiovascular diseases clinically [5]. Its dye is mainly used as a colouring agent [6].

The objects of the study were samples of CO₂-extracts obtained from flowers of safflower (*Carthamus tinctorius* L.), collected during the flowering phase.

Determination of antimicrobial and fungicidal activity of extracts was carried out by disco-diffusion method (DDM). This method was realized by applying the discs processed with the test drug to Petri dish, using sterile tweezers at a distance of 15-20 mm both from the edge of the cup and from each other. The

results of DDM were taken into account by counting the diameter of the delay / growth inhibition zones with an accuracy of 1 mm.

The test samples were CO₂-extracts No 1 and No 2. Sample No 1 was an oily liquid of limpid color. Sample No 2 was a bright orange liquid. Due to the lack of data concerning the concentration of the active substance, the stock solution was the initial concentration. The method of serial dilution was carried out.

As test microorganisms, the following groups of strains were used: 1. for the research of antibacterial activity: *Staphylococcus aureus* ATCC 6538-P (museum sensitive strain); *Staphylococcus aureus* ATCC BAA-39; *Staphylococcus epidermidis* ATCC 12228; *Escherichia coli* ATCC BAA-196. 2. for the research of antifungal activity: *Candida albicans* ATCC 10231 (museum sensitive strain).

Testing was carried out on liquid nutrient media: Mueller-Hinton broth (standard antibiotic sensitivity medium) and RPMI 1640 medium (medium recommended by CLSI M27-A2: «Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeast» for testing fungicides).

To determine the antimicrobial activity, 10 tubes of the Eppendorf type were used. In all test tubes, except for the 1st (from 2 to 10), the nutritious broth of MHB was dispensed in the amount of 0.5 ml. The working solution (sample No 1 and sample No 2) was added in pure form (in a volume of 0.5 ml) to the first tube, with the MXB (0.5 ml) already present in it. Next, serial dilutions were made, which were carried out by taking the mixture (MXB (0.5 ml) + test preparation (0.5 ml)) from the 2nd tube in the amount of 0.5 ml into the 3rd tube already containing 0.5 ml of broth. 0.5 ml of the test sample in the broth was thoroughly mixed and transferred from the 3rd tube to the 4th also containing initially 0.5 ml of broth. This procedure has being repeated until the required amount of dilution was achieved. 0.5 ml of the mixture from the last tube was removed. Thus, the following dilutions were obtained: 1: 1; 1: 2; 1: 4; 1: 8; 1:16; 1:32; 1:64; 1: 128; 1: 256, which corresponds to the tubes from the 1st to the 10th. After conducting a series of dilutions, 0.05 ml of test strains of microorganisms at a concentration of 1.5×10^6 COE / ml were added to all the tubes. The procedure was repeated for all test samples.

All samples have being incubated for 18-24 hours at 37°C. On the expiry of incubation the sowings were carried out onto Petri dishes to determine the living cells. After seeding, the dishes were placed in a thermostat for 18-24 hours at 37° C for bacteria.

The results were taken into account by the presence of visible growth of microorganisms on the surface of a dense nutrient medium. The minimum bactericidal concentration (MBC) was the smallest dilution in a test tube that suppressed the growth of microorganisms.

The results of the research of antibacterial and fungicidal activity of extracts in respect of five strains of pathogenic microorganisms *S. aureus* ATCC 6538-P, *S. aureus* ATCC BAA-39, *S. epidermidis* ATCC 12228, *E. coli* ATCC BAA-196 and *C. albicans* ATCC 10231 are presented in tables 1, 2 and figures 1, 2.

From the data presented in Table 1 for the serial dilution method, it can be seen that the test sample No 1 exhibits an expected bactericidal activity against the susceptible strain of *S. aureus* ATCC 6538-P at 1: 128 dilution, as well as fungicidal activity against *C. albicans* ATCC 10231 in 1:1 dilution (MBC at this dilution).

From the data presented in Table 5 for the serial dilution method, it can be seen that the test sample No 2 exhibits bactericidal activity against sensitive and resistant strains. For instance, for multidrug resistant *S. aureus* strain ATCC BAA-39, sample No 2 is active at a dilution of 1: 4, for *S. aureus* sensitive *S. aureus* ATCC 6538-P in a ratio of 1:128, for epidermal staphylococcus *S. epidermidis* ATCC 12228 - in the dilution 1: 2, and for *E. coli* ATCC BAA-196 - 1: 4. Sample No 2 was not active against fungi of the genus *Candida*.

To make ointments, you need to go to marketing analysis. In the next study, the data obtained from plant substances for ophthalmic ointments from the State Register of medicines of 2018 are indicated. The collected results were included in computer forecasts and market share analysis models.

Tables 1 – The results of the research of antibacterial and fungicidal activity

Test sample	<i>S. aureus</i> ATCC 6538-P	<i>S. aureus</i> ATCC BAA-39	<i>S. epidermidis</i> ATCC 12228	<i>E. coli</i> ATCC BAA-196	<i>C. albicans</i> ATCC 10231
Sample No 1	1:128	Not active	Not active	Not active	1:1

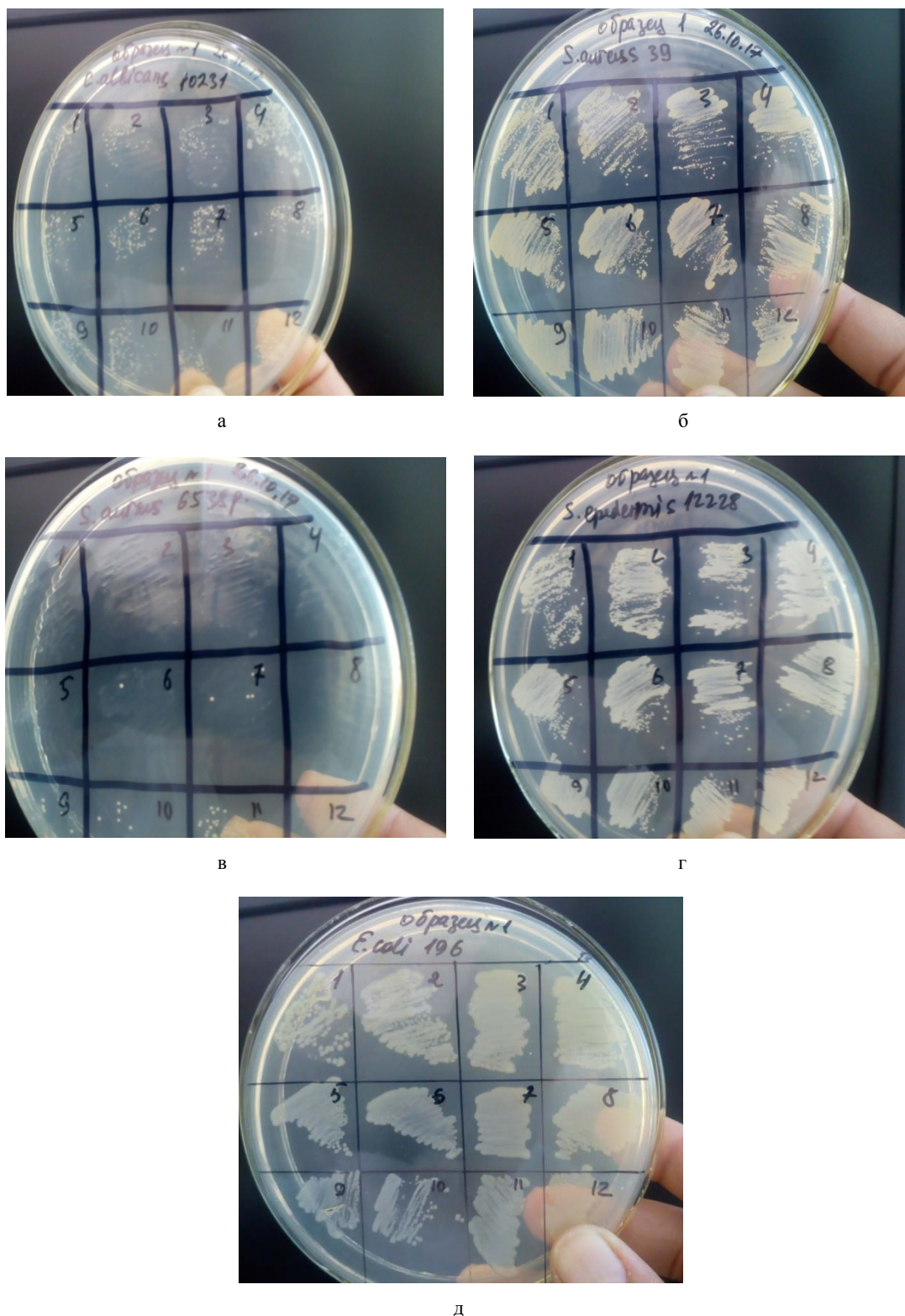


Figure 1 – The results of the antimicrobial activity of sample No. 1 in relation to museum test strains:
 а – *C. albicans* ATCC 10231, б – *S. aureus* ATCC BAA-39, в – *S. aureus* ATCC 6538-P,
 г – *S. epidermidis* ATCC 12228, д – *E. coli* ATCC BAA-196

Table 2 – Results of the antimicrobial activity of sample No. 2 obtained by the serial dilution methods

Test sample	<i>S. aureus</i> ATCC 6538-P	<i>S. aureus</i> ATCC BAA-39	<i>S. epidermidis</i> ATCC 12228	<i>E. coli</i> ATCC BAA-196	<i>C. albicans</i> ATCC 10231
Sample No 2	1:128	1:4	1:2	1:4	Not active

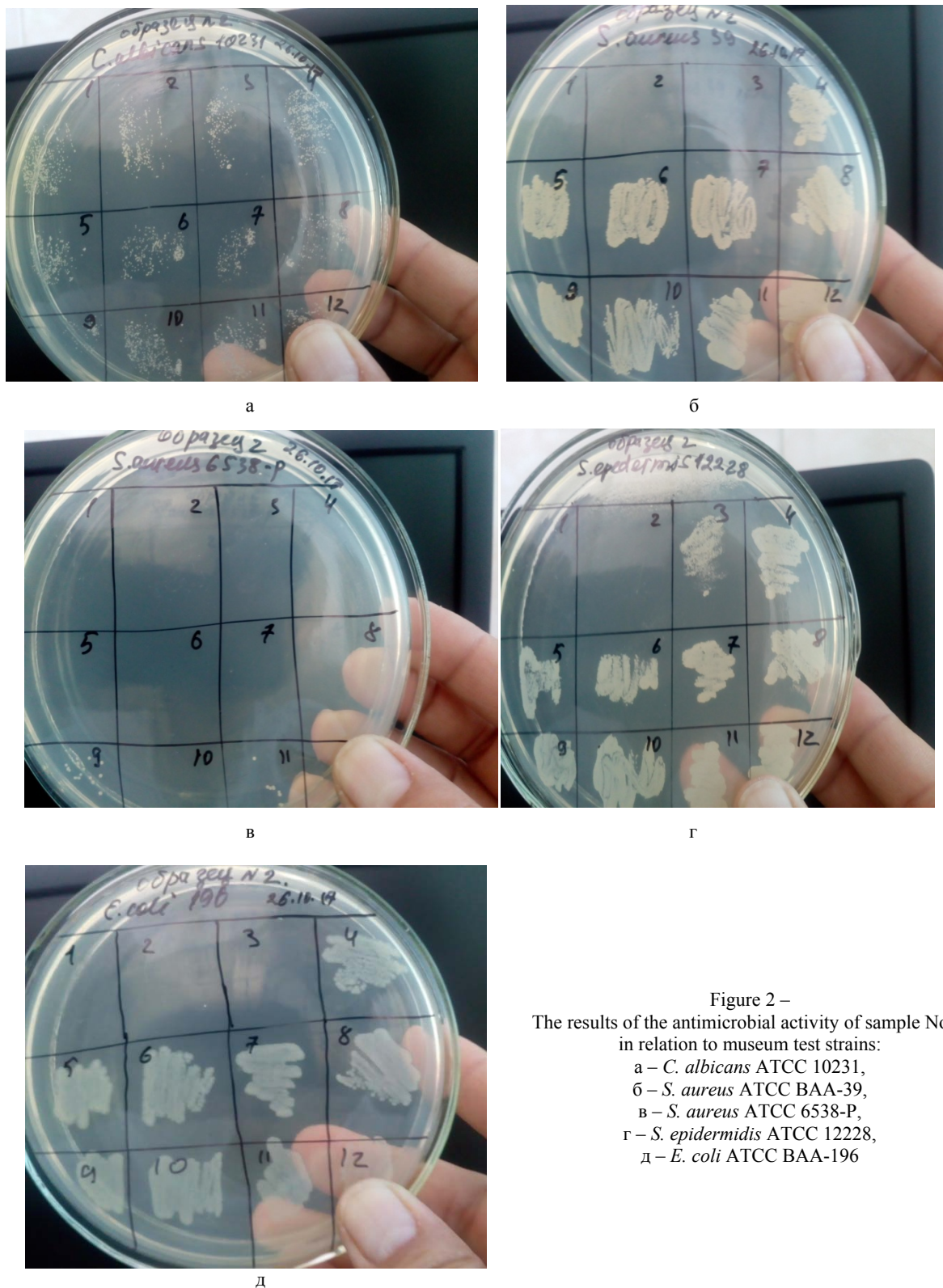


Figure 2 –
The results of the antimicrobial activity of sample No. 2
in relation to museum test strains:
а – *C. albicans* ATCC 10231,
б – *S. aureus* ATCC BAA-39,
в – *S. aureus* ATCC 6538-P,
г – *S. epidermidis* ATCC 12228,
д – *E. coli* ATCC BAA-196

17 types of ophthalmic ointments have been registered in the state register, of which 35% are produced by Russia, 18% by Belgium, 17% by Germany, 12% by Egypt and 18% by other countries. As you can see, according to the results of the study there are no ophthalmic ointments of domestic production. Analysis of the studies suggests that it is extremely relevant now to search for new antimycotic agents of plant origin in ophthalmology in the Republic of Kazakhstan. Given these marketing studies, we must produce a domestic ophthalmic ointment, but first we need to choose the optimal composition of ophthalmic ointments.

Ointments are manufactured on the basis specified in private articles. For the preparation of a soft dosage form, the bases permitted for medical use are used. Obtaining ophthalmic ointments, we developed 5 models using various auxiliary substances that form hydrophilic and hydrophobic bases (table 3).

Table 3 – Selection of the model

Basics	№1	№2	№3	№4	№5
Oil vaseline	2-3	2-3			
Lanolin anhydrous	1,0	1,0	1,0		
Vaseline grade (for eye ointments)	Before 10,0		9,0	Before 10,0	9,0
Paraffin liquid				2,0	1,0
Vegetable oil				2,0	

The optimal composition of the ointment of the following composition was chosen: lanolin anhydrous-1.0, vaseline oil-2-3 drops, vaseline grade (for ophthalmic ointments) -to 10.0.

Test sample No 1 exhibits an estimated bactericidal activity against a susceptible strain of *S. aureus* ATCC 6538-P at 1:128 dilution, as well as fungicidal activity against *C. albicans* ATCC 10231 in a 1:1 dilution (MBC at this dilution).

Test sample No 2 shows bactericidal activity against sensitive and resistant strains. For instance, for multidrug resistant *S. aureus* strain ATCC BAA-39, sample No 2 is active at a dilution of 1:4, for *S. aureus* sensitive ATCC 6538-P in a ratio of 1:128, for *S. epidermidis* ATCC epidermal staphylococcus 12228 - in the dilution 1: 2, and for *E. coli* ATCC BAA-196 - 1: 4.

For optimal composition, model No 1 was chosen. Often the base for eye ointments is Vaseline grade (for eye ointments) that does not contain reducing substances, and also mixes in all proportions with fats, fatty oils (except castor) and waxes. Vaseline is not absorbed by the skin and mucous membranes, slowly and not completely releases the active substances. Therefore, it is advisable to use it in ointments acting superficially. Pure petrolatum has a local effect, as it is hydrophobic and poorly distributed in the conjunctiva. Lanolin is chemically inert enough, neutral and stable when stored. It has a high emulsifying ability.

The test samples show the expected biological activity with respect to opportunistic bacteria and fungi of the genus *Candida*.

The obtained results of the antimicrobial and fungicidal activity of the safflower extract testify to the prospect of its further study and application as an active substance for the development of ophthalmic ointment used in ophthalmic practice.

The composition and technology of the ointment that meet the requirements of the State Pharmacopoeia of the Republic of Kazakhstan have been theoretically substantiated and experimentally developed. The composition of the ointment is represented by the following ingredients; Vaseline varieties (for ophthalmic ointments), lanolin anhydrous and vaseline oil. It is planned to study and standardize the quality of the ointment.

According to the results of market research revealed that the Kazakhstan pharmaceutical market there is no eye ointments Kazakhstan production and plant origin. This gives the right direction to pharmacists and clinicians who could solve this problem.

Practical use of plant raw materials, from which medicinal preparations are prepared, occupies a special place in medicine, because they are cheaper and can compete successfully with costly synthetic ones, [5, 8, 10].

The advantage of medicinal plants in front of many synthetic drugs is that the plants contain alkaloids, vitamins, microelements and other biologically active substances that are in certain proportions and are less toxic, respectively, adverse adverse reactions are less frequent [7, 9].

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К. Д. Рахимов¹, А. А. Тургумбаева¹, Ж. Б. Абуова², Г. О. Устенова¹, Е. А. Егоров³

¹С. Ж. Асфендияров атындағы Қазақ ұлттық медициналық университеті, Алматы, Қазақстан,

²Қазақ медициналық үздіксіз білім беру университеті, Алматы, Қазақстан,

³Н. И. Пирогов атындағы Ресей ұлттық зерттеу медициналық университеті, Ресей

САФЛОРА СЫҒЫНДЫСЫНАН КӨЗГЕ АРНАЛҒАН ЖАҚПАМАЙ ҚҰРАМЫН ДАЙЫНДАУ

Аннотация. Соңғы жылдары дәрігердің нұсқауынсыз антибиотиктерді қолдану кеңінен таралуда, сонымен қатар судың және ауаның ластануы аллергиялық аурулардың көбеюіне әкелуде. Синтетикалық препараттар патологиялық әсерлерді күшейтеді, осы препараттардың фармакологиялық әсері төмен. Сол себепті дәрілік өсімдік шикізаты негізінде жасалынған препараттарға сұраныс ұлғаюда. Антимикробты белсендігі жоғары және қолжетімді дәрілік өсімдіктердің негізінде саңырауқұлаққа қарсы офтальмология тәдирбиесінде кең сұранысқа ие, отандық өнімді шығару маңызды мәселелердің бірі.

Түйін сөздер: фунгицидті және и антибактериальды әсер, сафлора, көзге арналған жақпамай.

К. Д. Рахимов¹, А. А. Тургумбаева¹, Ж. Б. Абуова², Г. О. Устенова¹, Е. А. Егоров³

¹Казахский национальный медицинский университет имени

С. Ж. Асфендиярова, Алматы, Казахстан,

²Казахский Медицинский Университет Непрерывного Образования, Алматы, Казахстан,

³Российский национальный исследовательский медицинский университет им. Н. И. Пирогова, Россия

РАЗРАБОТКА СОСТАВА ГЛАЗНЫХ МАЗЕЙ ИЗ ЭКСТРАКТА САФЛОРА

Аннотация. В последние годы нарастающие самолечение с помощью антибиотиков, загрязнения воды и воздуха привело к увеличению числа аллергических и грибковых заболеваний. Синтетические препараты усугубляют патологические процессы, кроме того, побочные эффекты этих препаратов превышают ожидаемого лечебного действия. Поэтому в последнее время значительно возрос спрос на препараты растительного происхождения. Результаты поиска перспективных источников антимикотической активности среди представителей растительной флоры также подтверждают реальные возможности создания на их основе эффективных противогрибковых препаратов в офтальмологической практике.

Ключевые слова: фунгицидные и антибактериальные действия, сафлор, глазные мази.

Рахимов К. Д. – заведующий кафедрой клинической фармакологии КазНМУ им. С. Ж. Асфендиярова, академик НАН РК, kdrakhimov@inbox.ru

Устенова Г. О. – профессор кафедры фармация КазНМУ им. С. Ж. Асфендиярова, ustenova@list.ru

Тургумбаев А. А. – PhD КазНМУ им. С. Ж. Асфендиярова, aknurik_88@mail.ru

Абуова Ж. Б. – врач-резидент офтальмолог КазМУНО, zhanar90kz@mail.ru

Егоров Евгений Алексеевич – д.м.н., профессор, заведующий кафедрой офтальмологии им. акад. А. П.

Нестерова и ЦНИИ «Глаукомы и дистрофических заболеваний глаза» Российского национального исследовательского медицинского университета им. Н. И. Пирогова, egorovrgmu@mail.ru

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