UDC 615.454.1: 615.322: 616.02
DOI: 10.15587/2519-4852.2025.322855

DEVELOPMENT OF THE COMPOSITION OF A DERMATOLOGICAL PRODUCT IN THE FORM OF A CREAM WITH EXTRACTS OF THE AERIAL PART OF LESPEDEZA BICOLOR

Kate Kiselyova, Liliia Vyshnevska, Tetiana Yudkevych, Liubov Bodnar, Mariia Skybitska, Liudas Ivanauskas, Olha Mykhailenko, Oleksandr Kukhtenko, Victoriya Georgiyants

The aim of the work: *justification of the composition of emulsion cream with extracts of Lespedeza bicolor.*
Materials and methods. *In the development of the emulsion base of the cream, corn oil (Ukraine), propylene glycol (Germany), purified water, emulsifiers: xyliance (France), prolipid 141 (USA) and lamecrem (France) were used. The composition of the emulsion base included oil and liquid alcohol extract of the above-ground part of Lespedeza bicolor, which were obtained from the above-ground part of Lespedeza bicolor, harvested in the Botanical Garden of the Ivan Franko National University of Lviv (Lviv, Ukraine) in the flowering phase. The studies used physicochemical (pH value, identification and quantitative content of BAS), pharmacotechnological (thermo- and colloidal stability, structural-mechanical properties and disperse analysis) research methods. The anti-inflammatory activity of the experimental samples was studied on a burn wound model in outbred sexually mature male rats. The following medicines were used as comparison drugs: Panthenol ointment, "Hemofarm", AD, Serbia, series 138CLA and Calendula ointment, LLC "Pavlova Pharmacy", Ukraine, series 23.0823.*
Results. *Experimental studies of the organoleptic, physicochemical and structural-mechanical properties of samples of emulsion bases showed their dependence on the concentration of the oil phase, the composition and concentration of complex emulsifiers xyliance, prolipid 141 and lamecrem. It was established that the emulsion base of the cream, which contains 15 % corn oil, 7 % of the complex emulsifier xyliance, 5 % propylene glycol and water purified to 100, has satisfactory structural-mechanical properties, the necessary dispersion and homogeneous distribution of particles of the oil phase in the aqueous dispersion medium, withstands the test for thermal and colloidal stability and can be used to develop a dermatological cream with Lespedeza extracts. It was shown that the introduction of extracts into the composition of the developed base does not affect the stability, structural-mechanical properties of the base and the content of BAS. Studies of the anti-inflammatory activity of a cream with a complex of biologically active compounds of the oily and alcoholic extracts of the terrestrial part of Lespedeza bicolor on a burn wound model showed a reduction in signs of inflammation without signs of the joining of an infectious process in laboratory animals with wound healing on the 26th day of the study.*
Conclusions. *The composition of the cream with oil and alcohol extract of Lespedeza, which, due to the BAS complex, has a wider spectrum of pharmacological activity, has been experimentally substantiated. The composition of the emulsion base of the cream with corn oil, xyliance emulsifier, propylene glycol and purified water has been developed. It has been shown that the introduction of extracts into the composition of the developed base does not affect its pharmacotechnological properties, and the quantitative content of biologically active compounds in the cream corresponds to their content in the extracts in terms of the concentration of extracts in SDF, which is a confirmation of the compatibility of BAS with excipients. It has been established that the cream containing the BAS complex of Lespedeza bicolor in terms of anti-inflammatory activity is at the level of the comparison preparations Panthenol ointment and Calendula ointment*
Keywords: *aerial part of Lespedeza bicolor, phenolic compounds, dermatological cream, Lespedeza bicolor extracts, anti-inflammatory activity, drug technology*

How to cite:
Kiselyova, K., Vyshnevska, L., Yudkevych, T., Bodnar, L., Skybitska, M., Ivanauskas, L., Mykhailenko, O., Kukhtenko, O., Georgiyants, V. (2025). Development of the composition of a dermatological product in the form of a cream with extracts of the aerial part of lespedeza bicolor. ScienceRise: Pharmaceutical Science, 1 (53), 26–40. http://doi.org/10.15587/2519-4852.2025.322855

1. Introduction

An important component of the therapy of dermatological diseases is the use of phytopreparations, which have low toxicity and, due to the diversity of their chemical composition, combine a number of pharmacological effects, primarily such as anti-inflammatory, reparative, antioxidant, antibacterial, antifungal, antiviral and, accordingly, can effectively combat a number of dermatological diseases, namely such as pyoderma, acne, herpes, etc. [1, 2].

Lespedeza bicolor Turch (Leguminosae) has a wide spectrum of pharmacological activity, which is due to the presence of various biologically active compounds, such as flavonoids, phenolic compounds [3, 4], phenylpropanoids, steroids, lignans and phenyldilactones [5]. The plant has a high content of widespread flavonoids (quercetin, kaempferol, isoquercitrin, homoorientin, orientin, eriodictyol), isoflavonoids (daidzein), chalcones (isoliquiritigenin), hydroxybenzoic acids (caffeic

and protocatechuic), and the chemical composition of leaves, stems, and flowers is almost the same [6, 7], which allows the use of the aboveground part without separation into components.

Promising medicinal raw materials for the creation of dermatological drugs are plants of the *Lespedeza* genus. It has been experimentally established that extracts of Lespedeza have antioxidant [3, 4], anti-inflammatory [5, 6], reparative [7], antimicrobial [8, 9], antifungal activity [9].

Lespedeza-based drugs are used to treat kidney diseases (uremic syndrome), normalize metabolism, and increase diuresis [10]. Examples are the drugs Lespenephril® and Lespefril®, produced by Lubnypharm in Ukraine, which are used to improve kidney function. However, the leaves and shoots of Lespedeza have not been considered as raw materials for the creation of dermatological drugs until today in scientific pharmacy, and a sufficient number of studies have not been conducted on the possibility of their use in dermatology. There is one patent for the invention for the extract of *L. capitata Michx.* for use in cosmetics and/or dermatology for the treatment and/or prevention of alopecia and/or seborrhea of the scalp [11]. In addition, studies [12] have shown that fermented extract of *L. cuneata G.* is promising for use as an active agent with antioxidant activity in anti-aging cosmetics.

Recent studies show that *Lespedeza bicolor* contains such biologically active substances as flavonoids (rutin, quercetin) [13], which exhibit antioxidant, anti-inflammatory and capillary-strengthening effects; tannins, which provide astringent and antimicrobial effects; phenolic compounds, which promote tissue regeneration. Due to their antimicrobial, anti-inflammatory and antioxidant effects, Lespedeza extracts can be used in the treatment of dermatitis, pyoderma, acne, eczema and to accelerate wound healing.

We have previously conducted studies on obtaining alcohol and oil extracts of the aerial part of *Lespedeza bicolor* [14, 15]. The sensitivity of test strains of *Staphylococcus* microorganisms, which cause such purulent-inflammatory diseases of the skin and mucous membranes as pyoderma, folliculitis, carbuncle, furuncle, to the obtained extracts was established [16]. Experimental studies have established the anti-inflammatory activity of oil and alcohol extracts of *L. bicolor*, which confirms the prospect of creating a dermatological agent with antimicrobial and anti-inflammatory effects [17].

An important task in the development of SDF is to combine the requirements for quality and stability with optimal aesthetic appeal and therapeutic efficacy [18]. Nowadays, a sufficient amount of knowledge has been accumulated regarding the barrier function of the skin and the mechanism of penetration of APIs through the skin [19, 20], the influence of solvents on penetration through the skin [21, 22], which has provided an opportunity to better understand the influence of excipients on the local action of drugs [23].

Despite the wide range of innovative surfactants, the nomenclature of emulsifiers in the composition of creams and ointments on emulsion bases has not changed significantly in recent years [18]. Therefore, for our studies, we chose modern complex emulsifiers containing a mixture of non-ionic surfactants. All of the studied emulsifiers are non-toxic, chemically inert, biodegradable and have the Ecocert certificate. They can form emulsion bases with a lamellar structure similar in structure to the lipid layer of the skin. However, despite a number of advantages compared to the used anionic surfactants and complexes with anionic surfactants, there are no studies on their quantitative content in emulsion bases that can be used for the development of SDF.

In view of the above, research into the development of modern emulsion bases and the use of *Lespedeza bicolor* extracts of different compositions, which, according to their properties, can be introduced into both the oil and aqueous phases, opens prospects for the creation of effective innovative dermatological products with predicted release of APIs, which meets the modern requirements of the pharmaceutical market.

2. Research planning (methodology)

The research methodology was based on the main stages of soft dosage form development – experimental and technological and biological studies [24, 25]. Given the medical and biological requirements for agents for the treatment of infectious and inflammatory processes of the skin and the solubility of the selected extracts, the optimal is the development of a cream on an emulsion base of the oil/water type. The approach to developing the SDF composition was based on creating a base considering the physicochemical properties of the API and the selection of critical excipients that affect the stability of the DF, and for emulsion bases, these are emulsifiers and solvents that increase the release rate of the API. The necessary distribution of selected APIs between the oil and water phases, as well as the presence of surfactants, is known to accelerate and promote a more complete release of BAS dissolved in the external dispersion medium and prolonged release and long-term action of BAS dissolved in the disperse phase [18, 19, 20]. A wide range of surfactants for prompted us to create emulsion bases with modern emulsifying mixtures.

The studies used physical, physicochemical, pharmacotechnological and pharmacological research methods. The results of the study were interpreted, and conclusions were drawn based on the results.

According to the research plan when justifying the composition of the emulsion base, the constant input data are vegeTable oil and purified water, propylene glycol and its concentration in the composition of the emulsion base, the variables are the concentration of oil, the nature of the emulsifier and its quantitative content. The concentration of emulsifiers was varied in the range recommended by the manufacturer. The composition of the bases is given in Table 1.

Variable data are defined by factors influencing the initial parameters that characterize the object. To build an experimental model, samples of emulsion bases were defined as the planning object, and its main properties were defined as the initial parameters (Fig. 1).

Table 1

Composition of emulsion base samples

Ingredients	Sample numbers/Quantitative content, %											
	1	2	3	4	5	6	7	8	9	10	11	12
Corn oil	8	8	10	10	15	15	15	15	15	20	20	20
Xyliance	4	5	4	5	4	5	6	7	8	6	7	8
Propylene glycol	5											
Purified water	up to 100											
Ingredients	Sample numbers/Quantitative content, %											
	13	14	15	16	17	18	19	20	21	22	23	24
Corn oil	8	8	10	10	15	15	15	15	15	20	20	20
Prolipid 141	4	5	4	5	4	5	6	7	8	6	7	8
Propylene glycol	5											
Purified water	up to 100											
Ingredients	Sample numbers/Quantitative content, %											
	25	26	27	28	29	30	31	32	33	34	35	36
Corn oil	8	8	10	10	15	15	15	15	15	20	20	20
Lamecreme	5	6	5	6	5	6	7	8	9	7	8	9
Propylene glycol	5											
Purified water	up to 100											

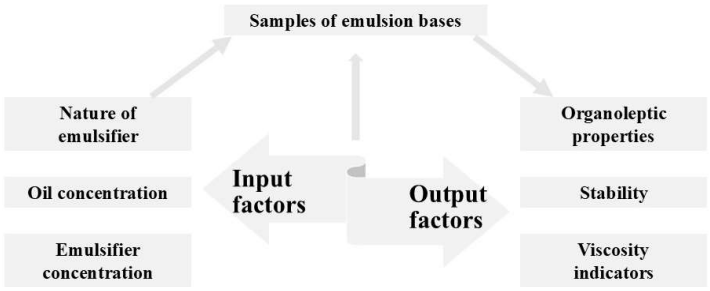


Fig. 1. Model of the planned experiment

The main factors that can affect the initial parameters were the quantitative content of oil and emulsifier in the emulsion base, considering these variables for each of the emulsifiers. Having analyzed the nature of each of the initial factors, the following response functions were determined: organoleptic properties (visual stability and consistency), stability (colloidal and thermal stability), viscosity indicators (Pa·s, at 20 rpm and 20 °C). For the convenience of statistical data processing, non-numeric indicators were converted into points, where the stability of the samples is denoted by 1, the absence of stability is 0, and the visual consistency is characterized as liquid (1), creamy (2), viscous (3).

To study the logic of the interaction of input and output data, in particular the influence of factors on the response functions, a two-factor experiment plan was proposed, which reflects the combination of the specified factors (Fig. 2), it is also advisable to investigate their independent influence.

Thus, a two-factor plan with 4–5 levels for quantitative variables was used, where the quantitative content of the emulsifier is factor A, the quantitative content of the oil is B. Therefore, for one emulsifier for each of the response functions, it is necessary to conduct 12 separate experiments, consisting of 3 parallel experiments.

The introduction of API into the base can lead to changes in the properties of both the base and the active substances, so we investigated the effect of API on the pharmacotechnological properties of the base, identified and determined the quantitative content of BAS marker groups, which makes it possible to confirm their compatibility and stability in the developed base.

A mandatory stage of confirming the effectiveness of the developed drug is conducting pharmacological studies, so we investigated the anti-inflammatory activity of the developed cream compared to reference drugs.

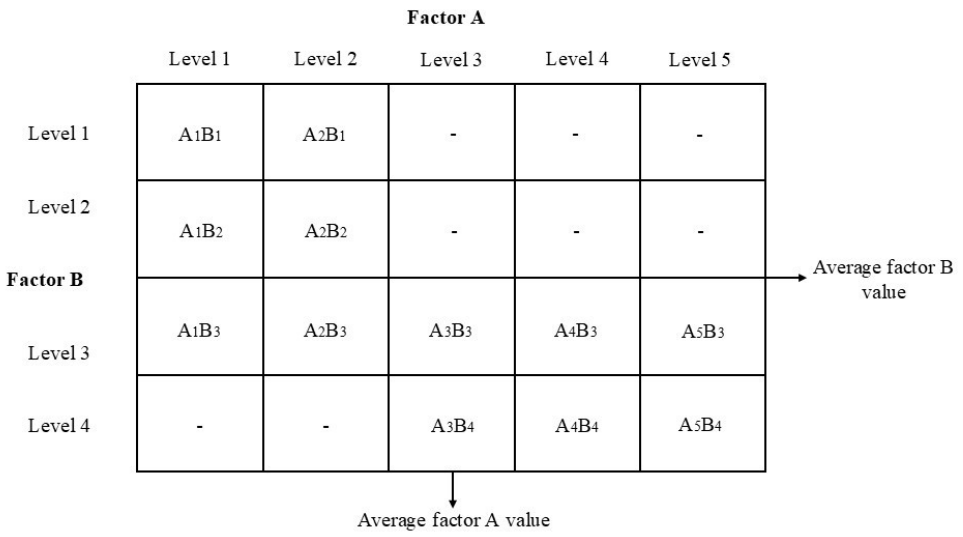


Fig. 2. Factorial experiment plan

3. Materials and methods

When developing the cream base, corn oil (Ukraine), propylene glycol (Germany), purified water and complex emulsifiers (cetearyl glycoside and cetearyl alcohol), HLB 8, (France), prolipid 141 (glyceryl stearate, behenyl alcohol, palmitic acid, stearic acid, lecithin, lauryl alcohol, myristyl alcohol, cetyl alcohol), HLB 7.8 (USA) and lamecreme (glyceryl stearate, glyceryl stearate citrate), HLB 7.6 (France) were used. The oil phase (corn oil) was chosen considering the nature of the extractant and, accordingly, chemical compatibility with the extractant used in obtaining the Lespedeza oil extract.

The emulsion base was composed of an oily and liquid alcoholic extract of *Lespedeza bicolor*, which was obtained from the aerial part of *Lespedeza bicolor*, harvested in the Botanical Garden of the Ivan Franko National University of Lviv (Lviv, Ukraine) in the flowering phase.

Experimental samples of emulsion bases and cream were emulsified using a MI-2 mixer for 15 min at a speed of (2000 rpm).

Microscopic studies and determination of the linear dimensions of the dispersed phase in the dispersion medium were carried out by microscopy [26] using a Granum R-40 laboratory microscope (China) with a built-in digital video camera DCM 310 and an achromatic objective 40x/0.65 (at a magnification of 400 times), which made it possible to measure linear dimensions in real time and on a static image. For image visualization, the taken pictures were displayed on the screen and processed using the Toup View 3.7 program.

Structural and mechanical properties were investigated with a Rheolab QC rheoviscosimeter (Anton Paar, Austria) using a system of coaxial cylinders C-CC27/SS. The device meets the requirements of the ISO 3219 standard. The Rheolab QC rheometer is equipped with RheoPlus software, which allows you to set the necessary conditions for performing the experiment (shear rate range, number of measurement points and measurement duration of one point, temperature). The rheological curve was measured in three stages:

a) linear increase in the shear rate gradient from 1 s^{-1} to 350 s^{-1} with 106 measurement points and a measurement point duration of 1 s;

b) constant shear at a shear rate of 350 s^{-1}, one measurement point with a duration of 1 s;

c) linear decrease in the shear rate gradient from 350 s^{-1} to 1 s^{-1} with 106 measurement points and a measurement point duration of 1 s.

The shear rate gradient range of 1–350 s^{-1} corresponds to a speed range of 0.78–271 rpm. The temperature of the study of the rheological properties of the samples was 25±0.5 °C, each sample was thermostated for 20 min.

To identify substances of polyphenolic (chlorogenic and caffeic acid) and flavonoid (rutin and hyperoside) structure, the method of thin-layer chromatography [26] was used in the solvent system anhydrous formic acid – water – ethyl acetate (5:10:85) with subsequent detection with a solution of 10 g/L *diphenylboronic acid aminoethyl ester in methanol*, then with a solution of 50 g/L *macrogol 400 R in methanol R*. The chromatograms were viewed in UV light at a wavelength of 365 nm.

To identify pigments, the method of thin-layer chromatography was used in the solvent system – petroleum ether-diethyl ether (10:3.5) with subsequent development of chromatograms with a 10 % solution of phosphoromolybdic acid when heated at a temperature of 60 °*C* for at least 10 minutes.

The amount of substances of polyphenolic structure was determined by absorption spectrophotometry in the visible region after reaction with phosphorus-molybdenum-tungsten reagent in a saturated sodium carbonate solution according to the method of the State Pharmacopoeia of Ukraine [26]. The reaction product, colored in blue, is characterized by the presence of a rather shallow absorption maximum at a wavelength of 760 *nm*, which corresponds to the absorption maximum of the pyrogallol solution under these conditions.

The content of the amount of substances of polyphenolic structure, in terms of pyrogallol, in milligrams, is calculated by the formula:

$$X, MG = \frac{625 \cdot A_1 \cdot m_2}{A_2 \cdot m_1},$$

where m_1 – weight of a portion of cream, in grams; m_2 – weight of a portion of pyrogallol, in grams.

The pharmacological activity of the cream was studied on outbred sexually mature male rats kept in the vivarium of the Educational and Scientific Institute of Applied Pharmacy of the National University of Pharmacy in accordance with sanitary and hygienic standards. The animals were kept in accordance with the current regulations on the devices, equipment and maintenance of vivariums. The animals received standard food in accordance with the current regulations [27, 28]. The animals were treated in accordance with the rules of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Scientific Purposes" (Strasbourg, 1986) [28]. The draft plan for the preclinical study of the pharmacological properties of the test samples was approved by the Bioethics Committee of the National University of Pharmacy (protocol No. 10 dated 03.10.2023).

The study was conducted in accordance with methodological recommendations (Stefanov, 2001) and Orders of the Ministry of Health of Ukraine No. 944 dated December 14, 2009 and No. 95 dated February 16, 2009, in compliance with the requirements of Good Laboratory Practice (GLP) [27, 29].

The animals were kept in a separate room with controlled microclimate parameters: air temperature 18–22 °C, relative air humidity 50–65 %, light regime "12 hours day/night", in plastic cages with individual ventilation [27]. Sterilization of the room using a UV lamp was carried out daily. The animals had free access to water (pre-settled tap water from drinking bowls). Granulated balanced compound feed (TU.U15.7-2123600159-001:2007) was used to feed the animals. Animal care was carried out in accordance with the standard operating procedures of the Educational and Scientific Institute of Applied Pharmacy

of NUPh. Before conducting the experiment, the animals underwent acclimatization for 7 days. During the acclimatization period, each animal was examined daily (behavior and general physical condition were assessed), and the animals were observed for possible morbidity or mortality.

The anti-inflammatory activity of the test samples was studied in a burn wound model [30, 31]. The study was conducted on 30 male rats weighing 240–262 g, aged 4–4.5 months [27]. The following drugs were used as comparison drugs: Panthenol ointment, "Hemopharm", AD, Serbia, series 138CLA (for pharmacological action) and Calendula ointment, LLC "Pavlova Pharmacy", Ukraine, series 23.0823 (for plant origin).

To exclude the possibility of the effect of the cream base on the results of the study, it was studied on a separate group of animals. Animals in the control group were not treated. All animals were divided into 5 groups of 6 each:

– group 1. Control group of animals that did not receive treatment (n=6);

– group 2. Control group of animals that were treated with the cream base (n=6);

– group 3. Group of animals that were treated with a cream with extracts of Lespides bicolor (n=6);

– group 4. Group of animals that were treated with the drug Panthenol, ointment (n=6);

– group 5. Group of animals that were treated with the drug Calendula, ointment (n=6).

Randomization of animals by groups and between groups was carried out by weight, not exceeding ±10 %.

Burn wounds were performed under thiopental anesthesia (40 mg/kg) on a previously depilated area of skin measuring 4×4 cm. The burn was initiated using a device with a set temperature scale and an electric soldering iron with a contact plate with a diameter of 2.5 cm, which allows obtaining standard burns with a size of 490.0 mm^2. The exposure time of the contact plate was 4 seconds at a temperature of 200 °C. Under these conditions, the skin burn corresponds to the second degree according to the clinical classification [29].

The test agent and comparison drugs (CD) were applied to the skin of the animals once a day in a thin layer in sufficient quantity without rubbing. Treatment was started immediately after thermal action and continued until complete healing of the wounds [29].

The main indicators of verification of the expressiveness of the anti-inflammatory effect of the test agents and CD were the change in the area of burn wounds (S, mm^2), the coefficient of healing rate and the percentage of rats with healed wounds compared to the control group. The effectiveness of the test agents and CD was studied in dynamics – on the 2^{nd}, 6^{th}, 9^{th}, 13^{th}, 16^{th}, 20^{th}, 21^{st}, 22^{nd}, 23^{rd}, 24^{th}, 25^{th}, 26^{th}, 27^{th}, 28^{th}, 29^{th} and 30^{th} day of treatment until complete healing. The area of the wounds was measured in mm^2 (L. N. Popova's method [32]), applying transparent graph paper to the wound. The quantitative percentage of animals with complete wound epithelialization on the current day of measurement was calculated [29].

The results were expressed as the arithmetic mean (M) and standard error of the mean (SEM). Comparisons between the study groups were performed using nonparametric analysis methods (Mann-Whitney U-test) and alternative methods (Fisher's angular transformation φ). The probability of differences was determined at a significance level of P<0.05. Experimental design and statistical processing were performed using the basic MS Excel 2007 and IBM SPSS Statistics 22 software packages [33].

4. Research results

The optimal form of the drug for topical application is the form of a cream on an emulsion basis [25, 34]. The choice of the emulsion basis was based on the study of the organoleptic physicochemical and pharmacotechnological properties of samples of emulsion bases in accordance with the developed research plan.

The results obtained (Table 2) allowed us to visualize the influence of the established factors, which led to a narrowing of the range of initial parameters.

It was found appropriate to study the influence of quantitative factors for each of the emulsifiers on the visual consistency and viscosity indicators (Pa·s, at 20 rpm and 20 °C), since no relationship was found between the influence factors and all types of stability. At first glance, for samples containing the emulsifier lamecreme, the influence of the quantitative content of the emulsifier on stability was observed, however, according to the results of statistical analysis, these data were not confirmed. To establish the dependence between the studied indicators, a correlation analysis of the obtained data was performed (Table 3). The studied samples are characterized by normal distribution (p>0.05 according to the Shapiro-Wilk test), so the Pearson linear correlation coefficient (r) was used for the analysis.

The highest correlation indicators are characterized by the group of samples containing the emulsifier xyliance. The concentration of the emulsifier lamecrem on the studied indicators does not have a statistically significant effect.

Finally, to assess the reproducibility and reliability of the experiment, as well as to assess the adequacy of the obtained model, a regression analysis was conducted using the diagram construction method (Fig. 3–5).

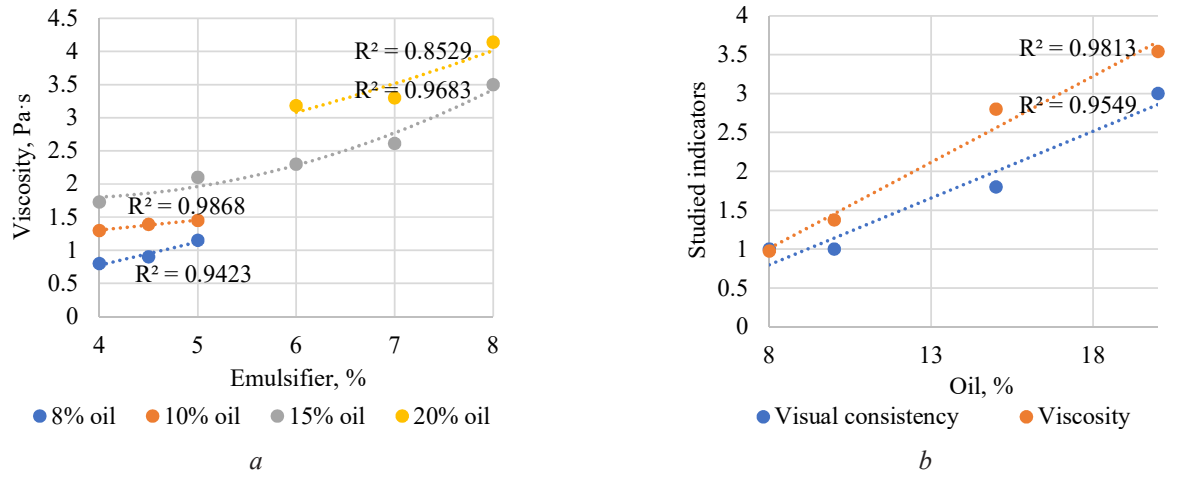
It was found that the vast majority of models correspond to linear regression, with the exception of the effect of the quantitative oil content on the visual consistency of the group of samples containing the emulsifier prolipid 141 (polynomial regression), the effect of the quantitative emulsifier content on the viscosity indicators of the group of samples containing the emulsifier xyliance with 15 % oil content (polynomial regression), and the effect of the quantitative emulsifier content on the viscosity indicators of the group of samples containing the emulsifier xyliance with 20 % oil content (exponential regression). Each of the regression models has a high level of approximation reliability (>80 %), so the experimental data obtained are reliable, and the experiment itself is reproducible.

Table 2

Properties of emulsion base samples, *n*=3

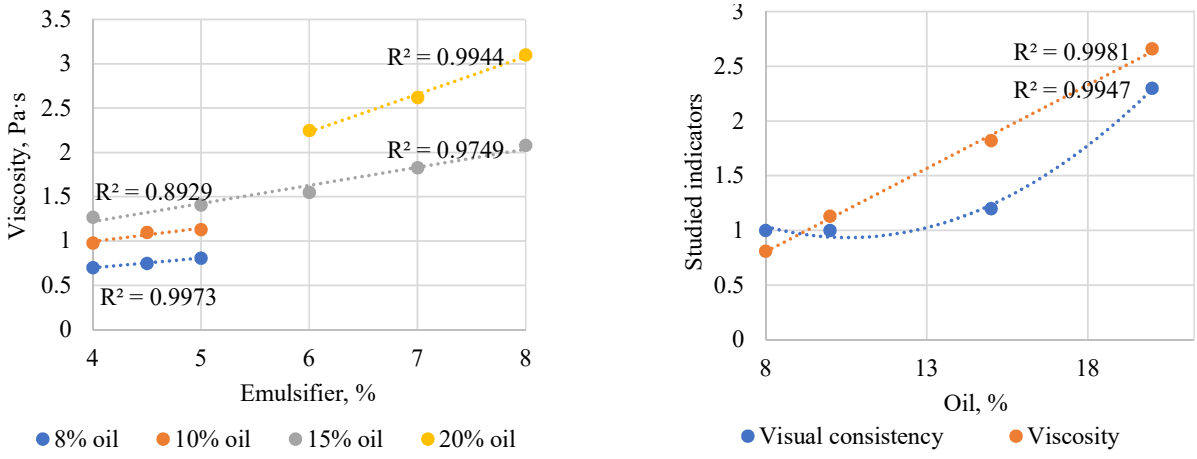
Sample properties	Sample number					
	1	2	3	4	5	6
Bases with xyliance emulsifier						
Visual consistency	1	1	1	1	1	1
Visual stability	1	1	1	1	1	1
Thermal stability	1	1	1	1	0	0
Colloidal stability	1	1	1	1	0	0
Viscosity, Pa·s, at 20 rpm and 20 °C	0.80±0.05	1.15±0.10	1.30±0.12	1.45±0.13	–	–
Sample properties	Sample number					
	7	8	9	10	11	12
Visual consistency	2	2	3	3	3	3
Visual stability	1	1	1	1	1	1
Thermal stability	1	1	1	1	1	1
Colloidal stability	1	1	1	1	1	1
Viscosity, Pa·s, at 20 rpm and 20 °C	2.30±0.10	2.61±0.08	3.50±0.08	3.18±0.06	3.30±0.08	4.14±0.07
Bases with emulsifier prolipid 141						
Sample properties	Sample number					
	13	14	15	16	17	18
Visual consistency	1	1	1	1	1	1
Visual stability	1	1	1	1	0	1
Thermal stability	0	1	0	1	0	0
Colloidal stability	0	1	0	1	0	0
Viscosity, Pa·s, at 20 rpm and 20 °C	–	0.81±0.05	–	1.13±0.03	–	–
Sample properties	Sample number					
	19	20	21	22	23	24
Visual consistency	1	1	2	2	2	3
Visual stability	1	1	1	1	1	1
Thermal stability	1	1	1	1	1	1
Colloidal stability	1	1	1	1	1	1
Viscosity, Pa·s, at 20 rpm and 20 °C	1.55±0.06	1.83±0.08	2.08±0.07	2.25±0.08	2.62±0.06	3.10±0.07
Bases with emulsifier lamecreme						
Sample properties	Sample number					
	25	26	27	28	29	30
Visual consistency	0	0	0	0	0	1
Visual stability	0	0	0	0	0	1
Thermal stability	–	–	–	–	–	1
Colloidal stability	–	–	–	–	–	0
Viscosity, Pa·s, at 20 rpm and 20 °C	–	–	–	–	–	–
Sample properties	Sample number					
	31	32	33	34	35	36
Visual consistency	1	1	2	2	2	3
Visual stability	1	1	1	1	1	1
Thermal stability	1	1	1	1	1	1
Colloidal stability	1	1	1	1	1	1
Viscosity, Pa·s, at 20 rpm and 20 °C	1.55±0.06	1.78±0.05	2.15±0.08	2.21±0.06	2.75±0.05	3.30±0.07

The results of the study showed that the stability of emulsion bases depends on both the composition and concentration of the emulsifier and the concentration of the oil phase. It was found that, with a content of 8–10 % of the oil phase and 4–5 % of the emulsifier xyliance, sTable but liquid bases are formed. Increasing the content of the oil phase to 15 % and introducing 4–5 % of this complex emulsifier does not ensure emulsion stability, the test samples do not withstand the colloidal stability test. It was shown that increasing the content of xyliance from 6 to 8 % stabilizes the emulsion base. Emulsion bases containing 20 % of the oil phase and 6–8 % of the emulsifier are also stable. It was found that increasing the content of the oil phase and emulsifier contributes to an increase in viscosity. Bases containing 15 % oil phase and 8 % emulsifier, as well as 20 % oil phase and from 6 to 8 % emulsifier have a viscous consistency. The results obtained show that the use of the complex emulsifier xyliance without co-emulsifiers stabilizes emulsion bases of the o/w type, which contain 8–20 % oil phase in a concentration of from 4 to 8 %. Increasing the content of the oil phase requires increasing the content of the emulsifier.



a *b*

Fig. 3. Model of the influence of factors on the viscosity indicators of the group of samples, which include the emulsifier xyliance: *a* – factor A; *b* – factor B



a *b*

Fig. 5. Model of the influence of factors on the viscosity indicators of the group of samples containing the emulsifier prolipid 141: *a* – factor A; *b* – factor B

Table 3

Results of correlation analysis

Responces / Factors	Visual consistency	Viscosity
Emulsifier	Xyliance	
Quantitative content of oil	*r*=0.82019 (*p*=0.00109)	*r*=0.89706 (*p*=7.6406E-5)
Quantitative content of emulsifier	*r*=0.88174 (*p*=0.00015)	*r*=0.90816 (*p*=4.4041E-5)
Emulsifier	Prolipid 141	
Quantitative content of oil	*r*=0.72837 (*p*=0.00722)	*r*=0.91864 (*p*=2.4467E-5)
Quantitative content of emulsifier	*r*=0.75555 (*p*=0.00448)	*r*=0.85851 (*p*=0.00035)
Emulsifier	Lamecreme	
Quantitative content of oil	*r*=0.76603 (*p*=0.04463)	*r*=0.81293 (*p*=0.02621)
Quantitative content of emulsifier	*r*=0.67937 (*p*=0.09322)	*r*=0.72907 (*p*=0.06302)

The results of the study showed that 4 % of the complex emulsifier prolipid 141 does not stabilize the emulsion at an oil concentration of 8 to 15 %, and 5 % of the emulsifier at 15 % of the oil. 5 % of prolipid forms stable, but liquid emulsion bases with 8–10 % of the oil phase. Increasing the emulsifier concentration from 6 to 9 % using an oil phase of 15–20 % contributes to the formation of sTable emulsion bases of different viscosities. Samples No. 20–23, containing 15 % of oil and 7–8 % of the emulsifier and 20 % of the oil at 6–7 % of the emulsifier, have a satisfactory creamy consistency.

The results of the study showed that the use of the emulsifier lamecreme at a concentration of up to 6 % does not stabilize the emulsion with 8–15 % of the oil phase. Increasing the concentration of the complex emulsifier from 7 to 9 % stabilizes emulsion systems

with an oil phase content of 15–20 % with the formation of bases of different viscosity. Samples No. 33–35, containing 15 % oil and 9 % lamecreme, as well as 20 % oil and 7–8 % emulsifier, have a satisfactory creamy consistency.

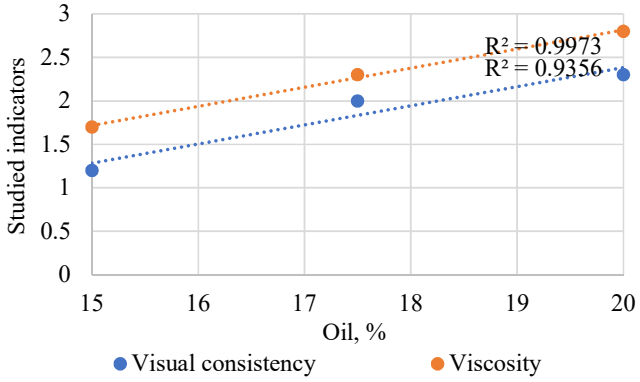


Fig. 6. Model of the influence of factor B on the studied indicators of the group of samples, which include the emulsifier lamecreme

Given the stability, satisfactory organoleptic, physicochemical indicators and viscosity required for SDF in the form of creams, one of the bases stabilized by different emulsifiers, namely samples No. 8, 22 and 34, was selected for further studies.

Rheological and microscopic studies were conducted for these samples. Rheological studies showed that all the formed systems are heterogeneous dispersion systems stabilized by complex emulsifiers containing nonionic surfactants, emulsifiers of the 1st and 2nd kind, which are distributed at the interface of two phases, thereby reducing the surface tension, and also form micelles that contribute to increasing the viscosity of the aqueous dispersion medium and the stability of the system (Fig. 6–11).

Experimental samples of emulsion bases have a pseudoplastic type of flow, since they are characterized by a yield point and certain thixotropic properties, and the restoration of the structure occurs gradually over time [35]. It is noted that a sample of an emulsion base stabilized by complex emulsifiers lamecreme demonstrates a sharp decrease in shear stress with increasing shear rate, which may indicate insufficient stability of the sample, despite the fact that it has passed the colloidal stability test.

The microphotographs of the samples shown in Fig. 12 demonstrate a uniform distribution of particles of the oil dispersed phase in the dispersion medium with the majority of phase particles having a size from 0.02 to 0.20 nm. The photographs demonstrate a certain dependence of the phase distribution and its size on the total concentration of the oil phase and emulsifier, as well as on which emulsifier was used. The particle size of the oil phase of test sample No. 8 was in the range from 0.03 to 0.15 nm, No. 22 – 0.02–0.20 nm and No. 34 – 0.09–0.16.

Considering the organoleptic indicators, the stability of the obtained samples and the structural and mechanical properties, the use of a base containing corn oil 15.0 %, xyliance 7.0 %, propylene glycol 5.0 % and purified water to 100.00 is justified for the development of a dermatological product with lespedeza extracts in the form of a cream.

The concentration of Lespedeza extracts was selected based on data from literary sources and our own research with further confirmation by experimental pharmacological studies. The antimicrobial effect of a cream containing oily and alcoholic extracts of Lespedeza against test strains *S. aureus* ATCC 25923, *S. aureus* ATCC 6538-P, and *C. albicans* ATCC 885-653, and clinical isolates *S. aureus* 16, *S. epidermidis* 14, *S. pneumoniae* 14, *S. pyogenes* 2432 and *S. aureus* 124 was experimentally established [16].

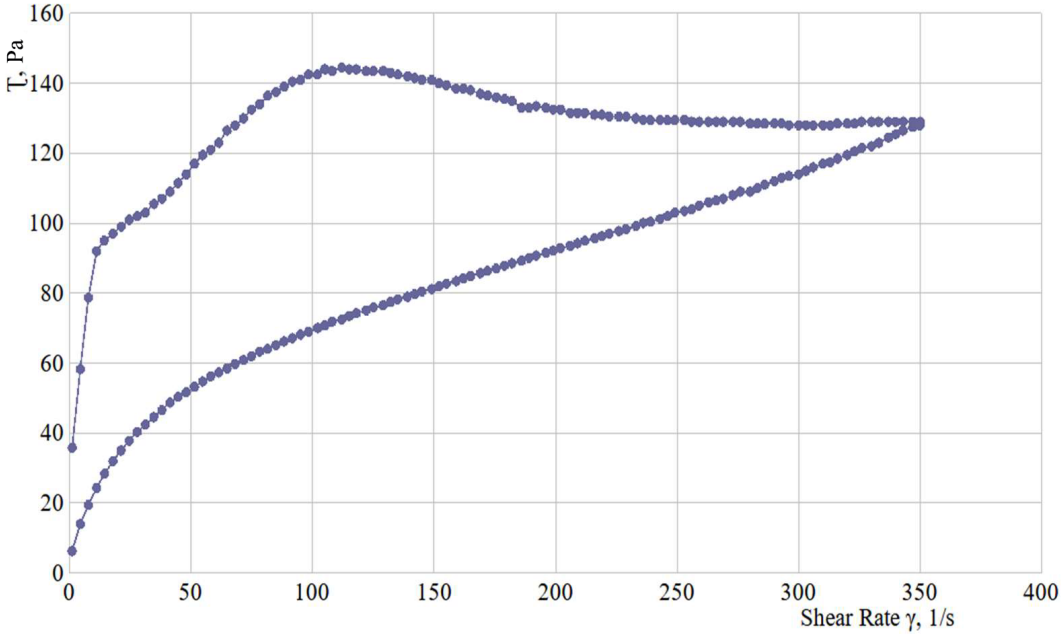


Fig. 6. Dependence of shear stress (τ, Pa) on shear rate gradient (γ, 1/s) of sample 8, with xyliance emulsifier

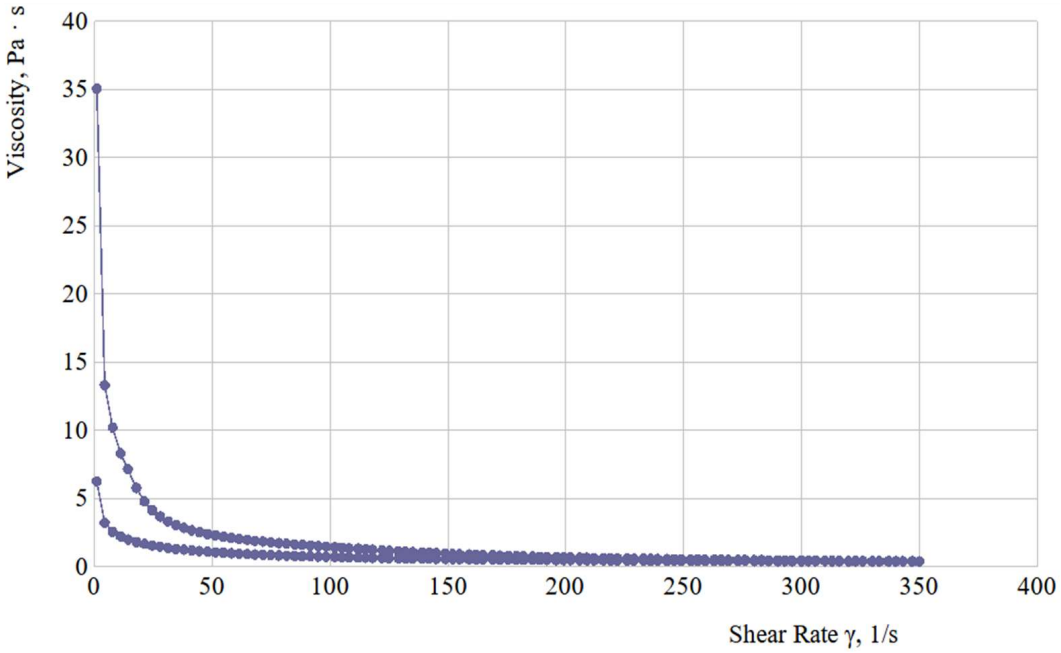


Fig. 7. Dependence of structural viscosity (η, Pa·s) on shear rate gradient (γ, 1/s) of sample 8, with xyliance emulsifier

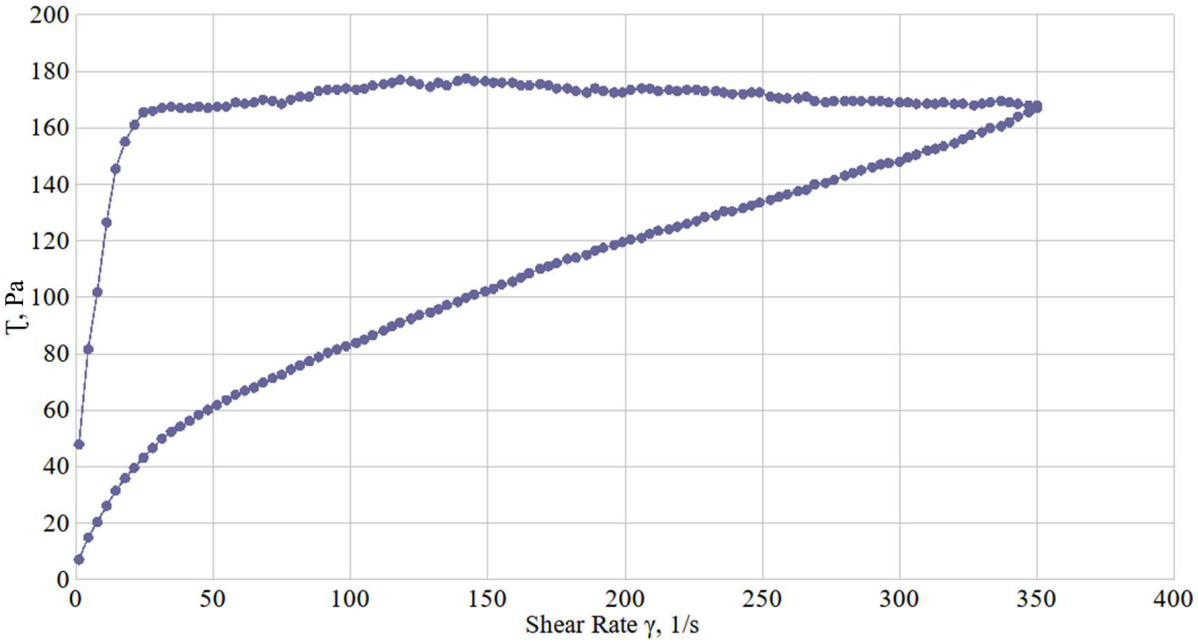


Fig. 8. Dependence of shear stress (τ, Pa) on the shear rate gradient (γ, 1/s) of sample 22, with emulsifier prolipid 141

The study of the properties of the cream base when introducing extracts was carried out to indicate their potential impact on the emulsion system. According to the data given in Table 4, the introduction of extracts does not affect the stability, that is, their colloidal and thermal stability. The change in organoleptic properties (color and odor) is due to the properties of the API itself. When introducing extracts into the base, the samples retain a homogeneous creamy consistency and acquire a greenish-cream color and a characteristic odor.

Table 4

Properties of the studied cream samples compared to the base, *n*=3

Sample properties	Base	+10 % oil extract	+5 % alcohol extract	Cream with extracts
Thermal stability	stable	stable	stable	stable
Colloidal stability	stable	stable	stable	stable
pH value	5.89±0.01	5.70±0.02	5.62±0.01	5.57±0.02
Viscosity, Pa·s, at 20 rpm and 20 °C	2.61±0.08	2.60±0.05	2.52±0.15	2.55±0.10
Quantitative content of the sum of polyphenolic compounds in terms of pyrogallol, mg/100 g	–	–	–	16.55±0.06

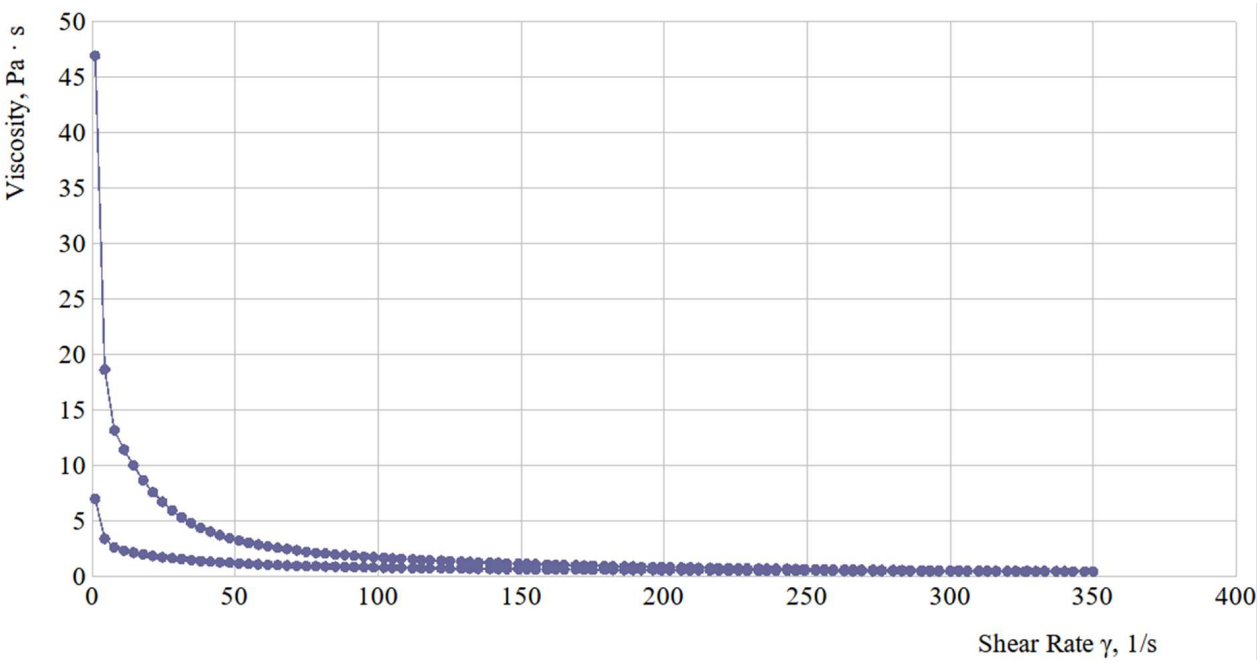


Fig. 9. Dependence of structural viscosity (η, Pa·s) on the shear rate gradient (γ, 1/s) of sample 22 with emulsifier prolipid 141

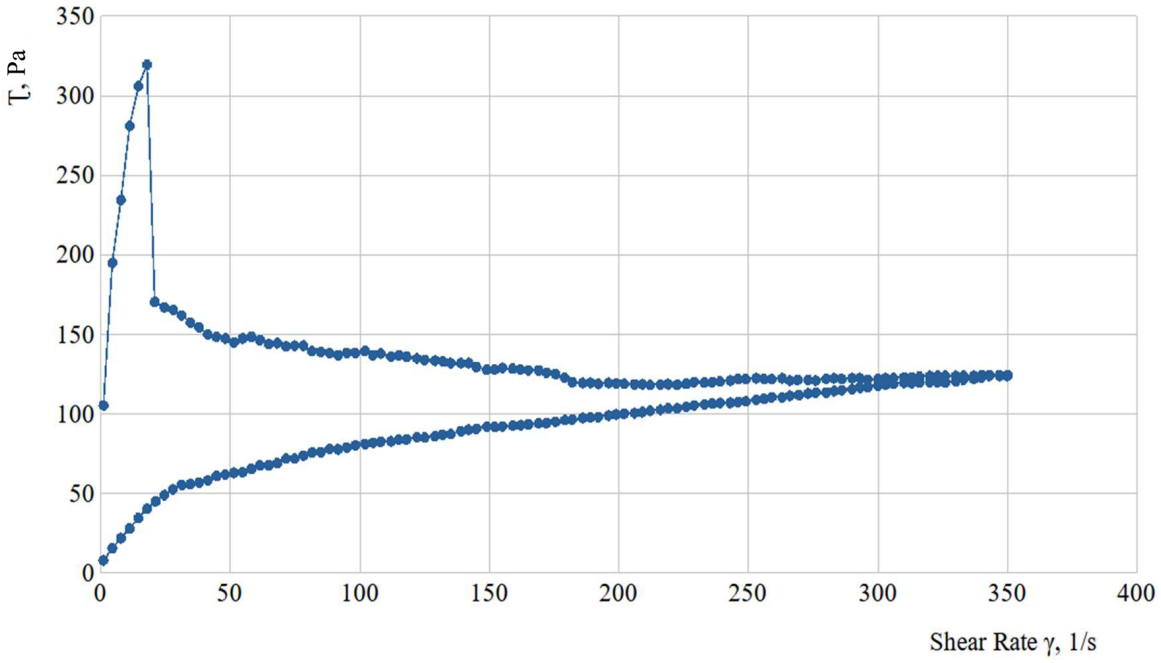


Fig. 10. Dependence of shear stress (τ, Pa) on the shear rate gradient (γ, 1/s) of sample 33, with the emulsifier lamecreme

For properties expressed in numerical values (pH and viscosity), statistical processing of the obtained results was carried out by pairwise comparisons of two samples, where the first sample was the properties of the emulsion base, the second – the properties of the sample with API. The comparison was carried out using the t-test for independent samples, which are characterized by a normal data distribution (according to the Shapiro-Wilk criterion $p>0.05$) (Table 5).

It was found that the addition of each of the APIs to the emulsion base has an effect on the pH value, since a statistically significant difference is observed when comparing the samples for this indicator ($p<0.05$). Despite this, the pH value is within the normal range. At the same time, none of the extracts influences the viscosity of the studied samples, as indicated by the absence of a statistically significant difference ($p>0.05$). This demonstrates the ability of the emulsion base to maintain stability and the necessary structural and mechanical properties when changing the pH and introducing APIs with different properties.

Thus, the results of the study of the properties of the samples confirmed that the extracts do not have a negative effect on the main properties of the emulsion base, despite the fact that statistical processing showed an effect on the pH value, but the indicators for SDF do not go beyond the normal range, so it is not negative, but is due to the properties of the API itself, just like color and smell.

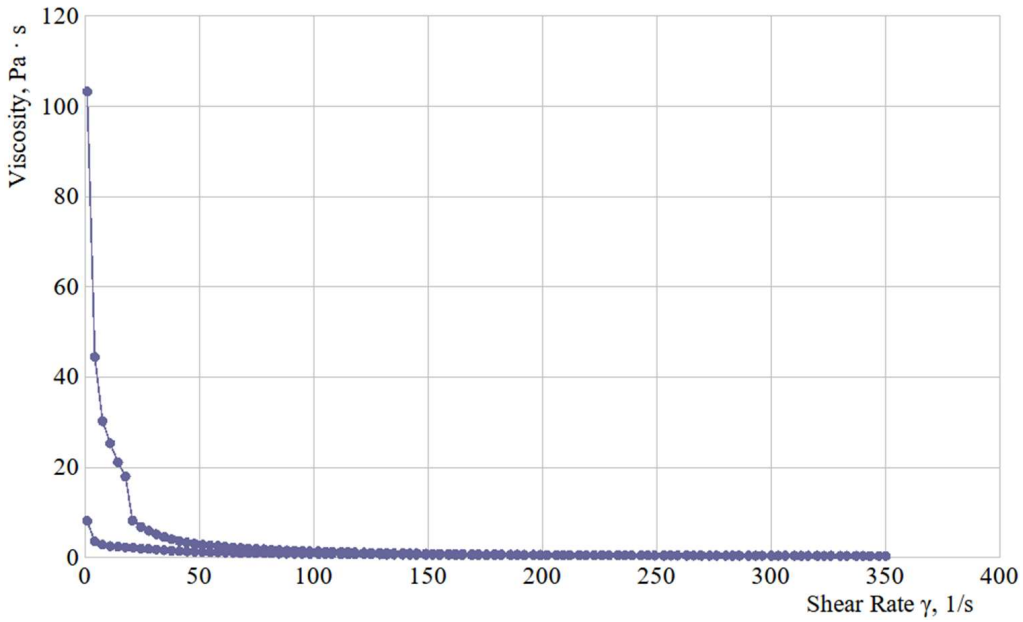
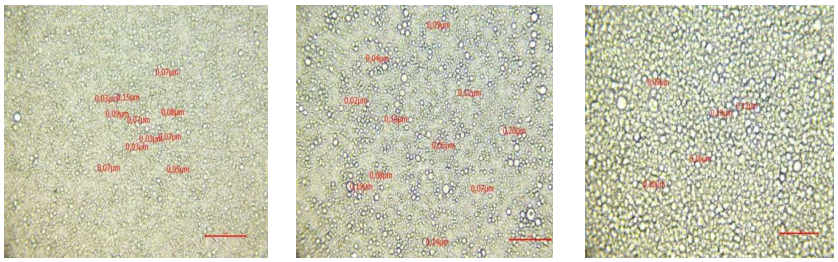


Fig. 11. Dependence of structural viscosity (η, Pa·s) on the shear rate gradient (γ, 1/s) of sample 33, with the emulsifier lamecreme



sample 8 sample 22 sample 33

Fig. 12. Micrograph of experimental samples of emulsion bases with different emulsifiers

It was experimentally determined that the chromatographic profile of the cream is characterized by the presence of a yellow-brown fluorescent zone at the level of the rutin zone (R_f 0.29) and blue fluorescent zones, at the level of the chlorogenic acid zone (R_f 0.43) and caffeic acid (R_f 0.84).

Table 5

Results of pairwise comparison of sample properties (n=3, P=95 %)

Sample properties	Study samples, p-value		
	No. 1–2	No. 1–3	No. 1–4
pH Value	0.02615	0.001885	0.0009221
Viscosity, Pa·s, at 20 rpm and 20°C	0.0551	0.07418	0.2254

When viewed in daylight, the chromatographic profile of the cream is characterized by the presence of blue spots on a green-yellow color with R_f 0.27; R_f 0.36; R_f 0.67; R_f 0.80 (which corresponds to the zones of carotenoids and their derivatives and chlorophylls).

It was determined by the spectrophotometric method that the quantitative content of biologically active compounds in the cream corresponds to their content in the extracts in terms of the concentration of the extract in SDF, which is a confirmation of the compatibility of BAS with excipients and their stability in the emulsion base.

The results of the study of anti-inflammatory activity (Table 6) showed that the next day, after the reproduction of a second-degree burn injury, the size of the wound defect increased by 3–7 % of the declared area of 490.0 mm^2.

In all animals of the experimental groups, a dense gray-brown scab with a clearly limited zone of necrosis and pronounced inflammatory changes in the surrounding tissues was formed [36, 37]. Against the background of the application of the studied samples, a decrease in the burn area was observed at different time intervals in different groups. It should be noted that in each of these groups the healing rate coefficient numerically exceeded the indicator in the control group. Also, a decrease in hyperemia and edema was noted compared to the control group. All experimental animals were active, had a satisfactory appetite. The growth in all animals was positive.

The use of the developed cream and its base also had a positive effect on planimetric indicators. The first signs of complete epithelialization in the group with the cream were determined already on the 20th day of the experiment, compared to the control, where complete scarring of the burn wound was observed in only 1 animal, and in the group receiving the cream base – on the 23rd day. In the period from the 20th to the 25th day, a noticeable acceleration of the reparative process was observed, which was expressed in a significant reduction in the area of burn wounds compared to the corresponding values of the control group. On the 26th day, complete healing was achieved in 100 % of animals, which significantly exceeded the similar indicator in the control group (2 animals out of 6) and in the group receiving

the cream base (3 animals out of 6). The epithelialization period in the group with the comparison drug Panthenol ointment falls on the 21st day (2 animals), the final stage of the reparative process on the 28th day of the experiment, which is inferior to the studied cream. The epithelialization period in the group receiving Calendula ointment began on the 22nd day (2 animals out of 6) and ended on the 26th day, inferior to the studied cream.

According to the results of the studies, it can be concluded that the BAS complex of alcoholic and oily extracts of *Lespedeza bicolor* in the cream provides anti-inflammatory activity that is at the level of comparison drugs.

Table 6

Dynamics of planimetric indicators in rats with burn wounds during treatment with *Lespedeza bicolor* cream, *n*=6, (*M*±*m*)

Experiment days	Indicators	Control	Cream base	Studied cream	Comparison drugs	
					Panthenol, ointment	Calendula, ointment
Output data	S_{output}, mm²	490.00±0.00	490.00±0.00	490.00±0.00	490.00±0.00	490.00±0.00
2 days	S_{output}, mm²	497.83±26.45	495.83±13.58	490.33±14.28	496.83±22.56	518.00±19.86
	V, c.u.	–0.02	–0.01	0.00	–0.01	–0.06
6 days	*S*, mm²	442.83±32.50	391.67±17.97	373.33±20.24[T1]	431.00±24.48	394.67±39.73
	V, c.u.	0.10	0.20	0.24	0.12	0.19
9 days	*S*, mm²	397.33±33.43	306.50±10.24*[1]	286.67±26.26*[1. T4]	356.83±25.42	320.17±28.76
	V, c.u.	0.19	0.37	0.41	0.27	0.35
13 days	*S*, mm²	307.17±37.28	196.00±20.12	162.83±28.88 *[1. T3]	217.83±24.49	247.00±14.72
	V, c.u.	0.37	0.60	0.67	0.56	0.50
16 days	*S*, mm²	200.33±33.68	136.67±20.57	76.67±23.44*[1. 2]	115.00±20.59*[1]	132.17±20.75
	V, c.u.	0.59	0.72	0.84	0.77	0.73
20 days	*S*, mm²	142.00±34.81	101.67±13.11	39.80±14.04*[1. T2]	70.00±19.15[T1]	91.67±19.18
	V, c.u.	0.71	0.79	0.92	0.86	0.81
	% of animals with scars	–	–	16.7 % (1 animal)	–	–
21 days	*S*, mm²	129.17±33.82	83.17±17.10	37.25±14.53*[1]	55.00±13.08[T1]	65.33±17.87[T1]
	V, c.u.	0.74	0.83	0.92	0.89	0.87
	% of animals with scars	–	–	33.3 % (2 animals)	33.3 % (2 animals)	–
22 days	*S*, mm²	116.33±32.03	73.17±17.76	27.00±11.28*[1]	40.25±12.40*[1]	64.00±14.15
	V, c.u.	0.76	0.85	0.94	0.89	0.87
	% of animals with scars	–	–	33.3 % (2 animals)	33.3 % (2 animals)	33.3 % (2 animals)
23 days	*S*, mm²	104.33±32.69	72.20±14.59	21.67±11.26*[1. T2]	28.25±12.12[T1]	44.75±10.56
	V, c.u.	0.79	0.85	0.96	0.94	0.91
	% of animals with scars	–	16.7 % (1 animal)	50 % (3 animals)	33.3 % (2 animals)	33.3 % (2 animals)
24 days	*S*, mm²	92.83±33.32	65.80±14.07	20.00*[1. 2]	23.67±4.10[T1]	25.00±6.10
	V, c.u.	0.81	0.87	0.96	0.95	0.95
	% of animals with scars	–	16.7 % (1 animal)	83.3 % (5 animals)	50 % (3 animals)	33.3 % (2 animals)
25 days	*S*, mm²	81.50±32.67	53.80±14.20	11.00*[1. 2. 3. 4]	20.33±3.76	16.50±1.50
	V, c.u.	0.83	0.89	0.98	0.96	0.97
	% of animals with scars	–	16.67 % (1 animal)	83.3 % (5 animals)	50 % (3 animals)	66.7 % (4 animals)
26 days	*S*, mm²	71.17±32.37	45.80±14.37	0.00*[1. 2]	17.00±3.61	0.00*[1]
	V, c.u.	0.85	0.91	1.00	0.97	1.00
	% of animals with scars	–	16.67 % (1 animal)	100 % (6 animals)	50 % (3 animals)	100 % (6 animals)
27 days	*S*, mm²	71.00±35.91	44.00±13.08	0.00 *[1 2]	8.50±3.50	0.00 *[1]
	V, c.u.	0.86	0.91	1.00	0.98	1.00
	% of animals with scars	16.7 % (1 animal)	33.3 % (2 animals)	100 % (6 animals)	67.7 % (4 animals)	100 % (6 animals)
28 days	*S*, mm²	78.50±40.42	37.75±13.31	0.00*[1.2]	0.00*[1]	0.00*[1]
	V, c.u.	0.84	0.92	1.00	1.00	1.00
	% of animals with scars	33.3 % (2 animals)	33 % (2 animals)	100 % (6 animals)	100 % (6 animals)	100 % (6 animals)
29 days	*S*, mm²	65.00±38.52	33.00±11.79	0.00 *[1. 2]	0.00 *[1]	0.00 *[1]
	V, c.u.	0.87	0.93	1.00	1.00	1.00
	% of animals with scars	33.3 % (2 animals)	33 % (2 animals)	100 % (6 animals)	100 % (6 animals)	100 % (6 animals)
30 days	*S*, mm²	59.00±44.40	30.00±10.26	0.00 *[1. 2]	0.00 *[1]	0.00 *[1]
	V, c.u.	0.88	0.94	1.00	1.00	1.00
	% of animals with scars	33.3 % (2 animals)	50 % (3 animals)	100 % (6 animals)	100 % (6 animals)	100 % (6 animals)

*Note: *[1] – values are significant relative to the control group (Mann-Whitney test); *[2] – values are significant relative to the baseline group (Mann-Whitney test); *[3] – values are significant relative to the calendula group (Mann-Whitney test); *[4] – values are significant relative to the panthenol group (Mann-Whitney test); *[5] – values are significant relative to the dermatological cream group (Mann-Whitney test); S (mm²) – wound area; V – wound healing rate coefficient, (conditional units); n – number of animals in each group.*

5. Discussion of research results

A prerequisite for a systematic and rational approach to the development of topical drugs is an understanding of the mechanism of API penetration into the skin, including the influence of the drug base on this process [18, 19]. The approach to creating a base based on its compliance with the physicochemical properties of the API helps to ensure the quality of the drug, optimize the API release process, high consumer properties and additional cosmetic effects that contribute to the normalization of the skin condition. The proposed emulsion bases with emulsifying mixtures are promising for the creation of topical DF not only due to the formation of a sTable emulsion base with satisfactory structural and mechanical properties, but also due to the restoration of the lipid barrier, softening and moisturizing the skin due to the reduction of transepidermal moisture loss [19, 25].

Understanding the basic principles of the design of the SDF base formulation made it possible to distribute the API between the oil and water phases, and to select an oil phase compatible with the extractant used to obtain the lespedeza oil extract.

The use of oil and alcohol extracts of the aerial part of *Lespedeza bicolor* in the cream has become an innovative approach to the development of a soft drug, as it has made it possible to maximize the potential of medicinal plant raw materials, which contains different classes of biologically active compounds that have the necessary pharmacological effects.

In previous studies, we have established that Lespedeza liquid extract 1:2 (extractant 40 % water-alcohol solution) contains 1.53 mg/1 g of flavonoids in terms of rutin and 3.51 mg/1 g of polyphenolic compounds in terms of pyrogallol. The oil extract obtained from the raw material after extraction with 40 % ethanol contains 0.078 mg/1 g of carotenoids in terms of β-carotene and 0.16 mg/1 g of total chlorophyll [14, 15]. The necessary distribution of selected APIs between the oil and aqueous phases, as well as the presence of surfactants, accelerates and promotes a more complete release of BAS dissolved in the external dispersion medium and prolonged release and long-term action of BAS dissolved in the dispersed phase [18, 20, 23].

Identification of extracts of Lespedeza BAS in the cream by TLC method demonstrated the presence of the main marker compounds – rutin, chlorogenic and caffeic acids, carotenoids and chlorophylls. Determination of the quantitative content of polyphenolic compounds in the cream may indicate their stability in the emulsion base and compatibility with excipients.

Studies of the anti-inflammatory activity of the cream containing lespedeza extracts on a burn wound model showed a decrease in signs of inflammation, a faster course of wound healing, which may indicate a potentiation of the action of oil and alcohol extracts. The absence of signs of the accession of the infectious process in experimental animals was noted, which confirms the antimicrobial effect of the developed cream [16].

Practical significance. The conducted research will contribute to expanding the range of emulsion bases for dermatological medicines; further use of extracts of the aerial part of *Lespedeza bicolor* in medicines of various dosage forms and expanding the range of dermatological medicines.

Study limitations. The study we planned was completed in full, the results obtained are predicTable and reproducible. The selected methods within the framework of the planned study have no limitations. However, we did not conduct additional studies on the choice of preservative, which should be carried out using microbiological studies.

Prospects for further research. At the next stages of research, it is advisable to study the biopharmaceutical profile of the developed cream *in vitro* and standardize it.

6. Conclusions

The composition of the cream with oily and alcoholic extract of lespedeza has been experimentally substantiated, which, thanks to the BAS complex, has a wider spectrum of pharmacological activity.

Based on the results of the study of the organoleptic, physicochemical and structural-mechanical properties of experimental samples of emulsion bases containing different in composition, complex emulsifiers xyliance, prolipid 141 and lamecreme, the composition of the emulsion base of the 1st type was justified, containing corn oil 15 %, xyliance 7 %, propylene glycol 5 % and water purified to 100.

It was shown that the introduction of oil and alcohol extracts of the aerial part of lespedeza into the composition of the cream does not affect the pharmacotechnological properties of the developed base, and the quantitative content of biologically active compounds in the cream corresponds to their content in the extract in terms of the concentration of the alcohol extract in SDF, which may indicate the stability and compatibility of BAS with excipients.

Studies of the anti-inflammatory activity of the developed cream with the BAS complex of *Lespedeza bicolor* extracts on a burn wound model showed a reduction in signs of inflammation and complete healing of wounds on the 26th day of the study. Visual signs of the accession of the infectious process were not observed in any animal. It was shown that the use of the cream with the BAS complex of *Lespedeza bicolor* in the treatment of wounds contributes to a faster healing process, which may indicate a potentiation of the action of the oil and alcohol extracts in the composition of the developed product. It was established that the developed cream in terms of anti-inflammatory activity exceeds the Panthenol ointment and Calendula ointment, which are at the level of comparison drugs.

Conflict of interests

The authors declare that they have no conflict of interest regarding this study, including financial, personal, authorship or other, that could influence the study and its results presented in this article.

Funding

The study was conducted without financial support.

Data availability

The manuscript has no linked data.

Use of artificial intelligence

The authors confirm that they did not use artificial intelligence technologies when creating the presented work.

References

1. Yazarlu, O., Iranshahi, M., Kashani, H. R. K., Reshadat, S., Habtemariam, S., Iranshahy, M., Hasanpour, M. (2021). Perspective on the application of medicinal plants and natural products in wound healing: A mechanistic review. Pharmacological Research, 174, 105841. https://doi.org/10.1016/j.phrs.2021.105841

2. Ahuja, A., Gupta, J., Gupta, R. (2021). Miracles of Herbal Phytomedicines in Treatment of Skin Disorders: Natural Healthcare Perspective. Infectious Disorders – Drug Targets, 21 (3), 328–338. https://doi.org/10.2174/1871526520666200622142710

3. Ullah, S. (2017). Methanolic extract from Lespedeza bicolor: potential candidates for natural antioxidant and anticancer agent. Journal of Traditional Chinese Medicine, 37 (4), 444–451. https://doi.org/10.1016/s0254-6272(17)30150-4

4. Kim, S. J., Kim, D. W. (2007). Antoxidative activity of hot water and ethanol extracts of Lespedeza cuneata seeds. Korean Journal of Food Preservation, 14, 332–335.

5. Ren, C., Li, Q., Luo, T., Betti, M., Wang, M., Qi, S. et al. (2023). Antioxidant Polyphenols from Lespedeza bicolor Turcz. Honey: Anti-Inflammatory Effects on Lipopolysaccharide-Treated RAW 264.7 Macrophages. Antioxidants, 12 (10), 1809. https://doi.org/10.3390/antiox12101809

6. Lee, S. J., Hossaine, M. D. A., Park, S. C. (2016). A potential anti-inflammation activity and depigmentation effect of Lespedeza bicolor extract and its fractions. Saudi Journal of Biological Sciences, 23 (1), 9–14. https://doi.org/10.1016/j.sjbs.2015.01.016

7. Thuy, N. T. T., Lee, J.-E., Yoo, H. M., Cho, N. (2019). Antiproliferative Pterocarpans and Coumestans from Lespedeza bicolor. Journal of Natural Products, 82 (11), 3025–3032. https://doi.org/10.1021/acs.jnatprod.9b00567

8. Nam, S. H. (2023) Evalution of the anti-caries effect of Lespedeza cuneata extract against Streptococcus mutans. Georgian Med News, 3 (38), 19–22.

9. Hong, H.-J., Son, N.-R., Yang, W.-Y., Lee, J.-M., Kim, J.-H., Jang, S.-M., Nam, S.-H. (2018). Antibacterial and antifungal activities of Lespedeza cuneata extract against Candida albicans. Biomedical Research, 29 (20). https://doi.org/10.4066/biomedicalresearch.29-18-1080

10. Woo, H. S., Lee, K. H., Park, K. H., Kim, D. W. (2024). Flavonoids Derived from the Roots of Lespedeza bicolor Inhibit the Activity of SARS-CoV Papain-like Protease. Plants, 13 (23), 3319. https://doi.org/10.3390/plants13233319

11. Leti, M., Daunes-Marion, S., Leveque, M. (2020). WO2020020791A1; WIPO (PCT). Lespedeza capitata extract for use in the field of hair care. Available at: https://patents.google.com/patent/WO2020020791A1/en

12. Seong, J. S., Xuan, S. H., Park, S. H., Lee, K. S., Park, Y. M., Park, S. N. (2017). Antioxidative and Antiaging Activities and Component Analysis of Lespedeza cuneata G. Don Extracts Fermented with Lactobacillus pentosus. Journal of Microbiology and Biotechnology, 27 (11), 1961–1970. https://doi.org/10.4014/jmb.1706.06028

13. Deng, F., Chang, J., Zhang, J.-S. (2007). New flavonoids and other constituents from Lespedeza cuneata. Journal of Asian Natural Products Research, 9 (7), 655–658. https://doi.org/10.1080/10286020600979894

14. Kiselyova, K. E., Bevz, N. Yu., Mykhailenko, O. O., Yaromiy, M. V., Vyshnevska, L. I. (2024). The substantiation of the choice of an extractant for obtaining extractions of the overground part of Lespedeza bicolor. News of Pharmacy, 107 (1), 58–65. https://doi.org/10.24959/nphj.24.126

15. Kiselyova, K. E., Bevs, N. Yu., Mykhaylenko, O. O., Vishnevska, L. I.; Bessarabov, V., Lubenets, V. (Eds.) (2023). Justification of the conditions for obtaining the oil extract of Lespedecia bicolor. Chemical and biopharmaceutical technologies. Tallinn: Nordic Sci Publisher, 336–342.

16. Kiselyova, K., Osolodchenko, T., Vishnevska, L. (2024). Study of the antibacterial action of Lespedecia bicolor extracts and cream based on them. Annals of the Mechnikov Institute, 2, 69–73. https://doi.org/10.5281/zenodo.11638092

17. Kiselyova, K. E., Vishnevska, L. I. (2024). Study of the anti-inflammatory activity of extracts of Lespedecia bicolor. Industry 4.0: modern directions of development of the pharmaceutical industry. Kharkiv: Publishing House of the National Academy of Sciences, 51–53.

18. Herbig, M. E., Evers, D.-H., Gorissen, S., Köllmer, M. (2023). Rational Design of Topical Semi-Solid Dosage Forms-How Far Are We? Pharmaceutics, 15 (7), 1822. https://doi.org/10.3390/pharmaceutics15071822

19. Dragicevic, N., Maibach, H. I. (2021). Percutaneous Absorption: Drugs, Cosmetics, Mechanisms, Methods. Boca Raton: CRC Press, 1008. https://doi.org/10.1201/9780429202971

20. Grégoire, S., Ribaud, C., Benech, F., Meunier, J. R., Garrigues-Mazert, A., Guy, R. H. (2009). Prediction of chemical absorption into and through the skin from cosmetic and dermatological formulations. British Journal of Dermatology, 160 (1), 80–91. https://doi.org/10.1111/j.1365-2133.2008.08866.x

21. Dias, M., Hadgraft, J., Lane, M. (2007). Influence of membrane–solvent–solute interactions on solute permeation in skin. International Journal of Pharmaceutics, 340 (1-2), 65–70. https://doi.org/10.1016/j.ijpharm.2007.03.030

22. Oliveira, G., Hadgraft, J., Lane, M. E. (2012). The influence of volatile solvents on transport across model membranes and human skin. International Journal of Pharmaceutics, 435 (1), 38–49. https://doi.org/10.1016/j.ijpharm.2012.05.037

23. Herbig, M. E. (2022). Topical Drug Delivery and the Role of Excipients. Chimica Oggi-Chemistry Today, 40, 34–37.

24. ST-N MOZU 42-3.0:2011 «Likarski zasoby. Farmatsevtychna rozrobka (ICH Q8)» (2011). Kyiv: Ministry of Health of Ukraine, 13.

25. Lane, M. E., Hadgraft, J., Oliveira, G., Vieira, R., Mohammed, D., Hirata, K. (2012). Rational formulation design. International Journal of Cosmetic Science, 34 (6), 496–501. https://doi.org/10.1111/j.1468-2494.2012.00747.x

26. Derzhavna Farmakopeia Ukrainy. Vol. 1 (2015). Kharkiv: DP «Ukrainskyi naukovyi farmakopeinyi tsentr yakosti likarskykh zasobiv», 1128.

27. Stefanova, O. V. (Ed.) (2001). Doklinichni doslidzhennia likarskykh zasobiv. Kyiv: Avicenna, 528.

28. Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes (2010). Official Journal of the European Union, L276, 33–79.

29. Medicines. Good laboratory practice (2009). Kyiv: Ministry of Health of Ukraine, 27.

30. Yakovleva, L. V., Tkacheva, O. V., Butko, I. O., Larianovska, Yu. B. (2013). Experimental study of new drugs for local treatment of wounds. Kharkiv: NFaU Publishing House, 52.

31. Trapella, C., Rizzo, R., Gallo, S., Alogna, A., Bortolotti, D., Casciano, F. et al. (2018). HelixComplex snail mucus exhibits pro-survival, proliferative and pro-migration effects on mammalian fibroblasts. Scientific Reports, 8 (1). https://doi.org/10.1038/s41598-018-35816-3

32. Tkachova, O. V. (2014). Pharmacological study of new drugs developed on the basis of natural substances and intended for the local treatment of wound healing process. [Extended abstract of PhD thesis].

33. Indrayan, A., Malhotra, K. R. (2018). Medical biostatistics. Boca Raton: CRC Press, 685.

34. Roberts, M. S., Cheruvu, H. S., Mangion, S. E., Alinaghi, A., Benson, H. A. E., Mohammed, Y. et al. (2021). Topical drug delivery: History, percutaneous absorption, and product development. Advanced Drug Delivery Reviews, 177, 113929. https://doi.org/10.1016/j.addr.2021.113929

35. Kukhtenko, H., GladukhIe, Y., Kukhtenko, O., Soldatov, D. (2017). Influence of Excipients on the Structural and Mechanical Properties of Semisolid Dosage Forms. Asian Journal of Pharmaceutics, 11 (3), 575–578.

36. Bulyha, L. O., Chernykh, V. P., Shtryhol, S. Iu., Movchan, B. O., Butko, Ya. O. (2015). Eksperymentalne doslidzhennia ranozahoiuvalnoi dii heliu z nanochastynkamy sribla ta hliukozaminom. Pharmacology and medicinal toxicology, 2 (43), 49–54.

37. Mayevsky, O. E., Mironov, E. V. (2015). Changes in the skin after thermal burns (literature review). Biomedical and biosocial anthropology, 25, 218–220.

Received 02.10.2024
Received in revised form 15.12.2024
Accepted 13.02.2024
Published 28.02.2024

Kate Kiselyova*, Postgraduate Student**,** Department of Pharmaceutical Technology of Drugs**,** National University of Pharmacy**,** Hryhoriia Skovorody str., 53, Kharkiv, Ukraine, 61002

Liliia Vyshnevska, Doctor of Pharmaceutical Science, Professor, Head of Department**,** Department of Pharmaceutical Technology of Drugs**,** National University of Pharmacy**,** Hryhoriia Skovorody str., 53, Kharkiv, Ukraine, 61002

Tetiana Yudkevych, Deputy Director for Research**,** Educational and Scientific Institute of Applied Pharmacy**,** National University of Pharmacy**,** Hryhoriia Skovorody str., 53, Kharkiv, Ukraine, 61002

Liubov Bodnar, Assistant**,** Department of Pharmaceutical Technology of Drugs**,** National University of Pharmacy**,** Hryhoriia Skovorody str., 53, Kharkiv, Ukraine, 61002

Mariia Skybitska, PhD, Senior Researcher, Botanical Garden of the Lviv National Ivan Franko University, Cheremshyny str., 44, Lviv, Ukraine, 79014

Liudas Ivanauskas, Doctor of Biomedical Sciences, Professor, Head of Department**,** Department of Analytical and Toxicological Chemistry**,** Lithuanian University of Health Sciences**,** A. Mickevic˘iaus str. 9, Kaunas, Lithuania, LT-50162

Olha Mykhailenko, Doctor of Pharmaceutical Sciences, Associate Professor, Department of Pharmaceutical Chemistry, National University of Pharmacy, Hryhoriia Skovorody str., 53, Kharkiv, Ukraine, 61002, Humboldt Research Fellow, Kiel University, Christian-Albrechts-Platz, 4, Kiel, Germany, 24118, Visiting Researcher, Pharmacognosy and Phytotherapy Group, UCL School of Pharmacy, 29-39 Brunswick sq., London, United Kingdom, WC1N 1AX

Oleksandr Kukhtenko, Doctor of Pharmaceutical Sciences, Professor**,** Department of Industrial Technology of Drugs and Cosmetic Products**,** National University of Pharmacy**,** Hryhoriia Skovorody str., 53, Kharkiv, Ukraine, 61002

Victoriya Georgiyants, Doctor of Pharmaceutical Sciences, Professor, Head of Department, Department of Pharmaceutical Chemistry, National University of Pharmacy, Hryhoriia Skovorody str., 53, Kharkiv, Ukraine, 61002

***Corresponding author:** Kate Kiselyova, e-mail: katekiselyova1999@gmail.com*