Ф А 2.2.1-36-367

MINISTRY OF HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
Pharmaceutical Faculty
Drug Technology Department

QUALIFICATION WORK

on the topic: **«DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF A CREAM-GEL WITH KERATOLYTIC ACTIVITY»**

Prepared by: higher education graduate of group Phm21(4,10d)eng-01
specialty 226 «Pharmacy, industrial pharmacy»
educational and professional program «Pharmacy»
Ayoub CHOUKRI-HAMIOUI
Supervisor: associate professor of the drug technology department, candidate of pharmaceutical sciences, associate professor Tetiana KOVALOVA
Reviewer: head of the department of industrial technology of drugs and cosmetics, doctor of pharmacy, professor Halyna SLIPCHENKO

Kharkiv – 2026

ANNOTATION

Theoretical studies have confirmed the feasibility and relevance of developing an extemporaneous cream-gel with keratolytic activity intended for topical dermatological application. For the purposes of the present research, a semi-solid cream-gel system possessing keratolytic, moisturizing, softening, and skin-conditioning properties was selected.

During the practical stage of the study, the composition and technology of the cream-gel with keratolytic activity were developed. The selection of active pharmaceutical ingredients with keratolytic properties, gelling agents, emulsifiers, humectants, and other auxiliary substances was scientifically substantiated, and the expected pharmaco-technological, physicochemical, and organoleptic characteristics of the developed preparation were determined.

The work is presented on 45 pages, contains 3 tables, 3 figures and 31 references.

Key words: cream-gel, keratolytic activity, semi-solid dosage form, extemporaneous technology, quality control.

CONTENT

LIST OF ABBREVIATIONS

API – active pharmaceutical ingredient;

ATC – anatomical and therapeutic chemical classification;

BP – British Pharmacopoeia;

CAS – Chemical Abstracts Service;

DSTU – State Standard of Ukraine;

INCI – International nomenclature of cosmetic ingredients;

NAD^+ – Nicotinamide adenine dinucleotide (oxidized form);

$NADP^+$ – Nicotinamide adenine dinucleotide phosphate (oxidized form);

PHA – Polyhydroxy acids;

SPU – State Pharmacopoeia of Ukraine;

PhEur – European Pharmacopoeia.

INTRODUCTION

Actuality of the topic. The development of semi-solid topical dosage forms with keratolytic activity remains an important area of modern pharmaceutical technology and dermatological practice. Among topical preparations, cream-gels occupy a special place due to their combined advantages of creams and gels, including good spreadability, rapid absorption, non-greasy texture, prolonged skin contact, and improved patient compliance. Such dosage forms are widely used in the management of dermatological conditions associated with hyperkeratosis, excessive keratinization, and impaired epidermal desquamation.

Hyperkeratotic skin disorders, including acne vulgaris, seborrheic dermatitis, psoriasis, ichthyosis, calluses, keratosis pilaris, and localized hyperkeratosis, are highly prevalent and often require long-term topical therapy. Keratolytic agents contribute to the softening and removal of the stratum corneum, facilitate skin renewal, improve penetration of active substances into deeper skin layers, and reduce inflammatory manifestations.

Currently, keratolytic therapy commonly involves the use of active pharmaceutical ingredients such as salicylic acid, urea, lactic acid, glycolic acid, sulfur compounds, and other exfoliating agents. However, conventional ointments and creams may demonstrate disadvantages such as excessive occlusiveness, greasy consistency, poor cosmetic acceptability, and discomfort during prolonged use. In contrast, cream-gel systems combine hydrophilic and lipophilic phases, ensuring balanced moisturizing properties, improved release of active ingredients, pleasant sensory characteristics, and enhanced stability of the formulation.

The development of an extemporaneous cream-gel with keratolytic activity is particularly relevant because it allows flexible adjustment of the concentration of active substances depending on the severity of the dermatological condition, skin type, and individual patient needs. Furthermore, the incorporation of moisturizing,

soothing, and anti-inflammatory excipients may help minimize irritation commonly associated with keratolytic agents and improve skin barrier function.

An important scientific challenge is the selection of optimal excipients, gelling agents, emulsifiers, preservatives, and active pharmaceutical ingredients that ensure the physicochemical stability, efficacy, safety, and microbiological purity of the preparation. Therefore, the development of the composition and technology of a cream-gel with keratolytic activity represents a relevant scientific and practical task aimed at improving topical dermatological therapy and expanding the range of effective semi-solid pharmaceutical preparations.

The purpose of the study. To develop the composition and technology of an extemporaneous cream-gel with keratolytic activity intended for topical dermatological application.

Tasks of the study: - to conduct a systematic review and analysis of scientific literature regarding keratolytic agents and semi-solid topical dosage forms;

- to analyze the current pharmaceutical market of topical preparations with keratolytic activity;
- to justify the selection of active pharmaceutical ingredients and excipients for the development of the cream-gel formulation;
- to develop the technological scheme for the preparation of the cream-gel with keratolytic activity;
- to determine the main pharmaco-technological, physicochemical, and organoleptic characteristics of the developed preparation;
- to evaluate the stability and expected quality indicators of the developed cream-gel.

Research objects. Active pharmaceutical ingredients with keratolytic activity and auxiliary substances used for the preparation of cream-gel systems, such as gelling agents, emulsifiers, humectants, preservatives, and purified water.

The subject of research. Development of the composition, technology, and pharmaco-technological evaluation of a cream-gel with keratolytic activity for topical application.

Research methods. The study employs general scientific methods of analysis, comparison, and synthesis, as well as pharmaco-technological, physicochemical, rheological, organoleptic methods used in the development and evaluation of semi-solid topical dosage forms.

Practical significance of the results. The developed composition and technology of the cream-gel with keratolytic activity provide a scientifically substantiated approach to the creation of effective and safe topical dermatological preparations. The obtained results may be used for further optimization, extemporaneous compounding, and implementation in pharmaceutical and dermatological practice as a preparation intended for the management of hyperkeratotic skin conditions.

Approval of research and publications. The results obtained during the research were reported in the form of an oral presentation at the XXXII International Scientific and Practical Conference of Young Scientists and Students entitled «Topical Issues of New Drug Development» (Appendices A, B).

Structure and scope of qualification work. The work is presented on 45 pages, contains 3 tables, 3 figures and 31 references.

CHAPTER 1. THEORETICAL FOUNDATIONS FOR THE DEVELOPMENT OF A CREAM-GEL WITH KERATOLYTIC EFFECT (Literature review)

1.1 Modern approaches to the use of keratolytic agents in dermatological practice

Keratolytic agents occupy an important place in modern dermatological therapy due to their ability to influence the processes of keratinization, promote desquamation of the stratum corneum, improve skin renewal, and enhance the penetration of active pharmaceutical ingredients into deeper epidermal layers. The use of topical keratolytic preparations is particularly relevant in the treatment of hyperkeratotic skin disorders, including acne vulgaris, psoriasis, seborrheic dermatitis, pityriasis versicolor, calluses, keratosis pilaris, and chronic xerotic conditions. Contemporary pharmaceutical research increasingly focuses on the development of semi-solid dosage forms capable of combining keratolytic efficacy with favorable cosmetic and moisturizing properties [5, 6, 7].

The therapeutic effect of keratolytic agents is mainly associated with disruption of corneocyte cohesion and softening of keratinized tissues. Salicylic acid remains one of the most widely used keratolytic substances because of its exfoliating, anti-inflammatory, and comedolytic activity. Urea is also extensively applied due to its hydrating and keratoplastic properties at lower concentrations and pronounced keratolytic activity at higher concentrations. Recent studies have demonstrated the effectiveness of combining keratolytic compounds with moisturizing and anti-inflammatory ingredients to reduce irritation and improve tolerability of topical therapy [14].

Modern dermatological practice demonstrates growing interest in multifunctional topical preparations. According to Muhammad et al., nanoethosomal keratolytic gels containing urea exhibit improved penetration characteristics and enhanced therapeutic performance in inflammatory skin conditions and diabetic complications [14]. Similar findings were reported in studies

investigating combinations of ketoconazole with adapalene in semi-solid systems, where the keratolytic and comedolytic effects of adapalene improved clinical outcomes in pityriasis versicolor treatment [13, 22].

An important trend in contemporary dermatopharmacy is the transition from conventional ointments toward technologically advanced cream-gel systems characterized by improved patient acceptability, lighter consistency, rapid absorption, and reduced occlusiveness. Comparative investigations of gel-cream formulations demonstrated superior spreadability, rheological stability, and skin sensory characteristics compared with traditional semi-solid preparations [8]. Such systems are particularly advantageous for long-term therapy because they minimize discomfort and excessive skin oiliness.

The use of natural and herbal ingredients in keratolytic and dermatological formulations has also become increasingly widespread. Studies involving Aloe vera, Salvia hispanica, Rosella extracts, and Acmella oleracea confirmed their moisturizing, antioxidant, soothing, and regenerative effects when incorporated into cream and gel systems [9, 10, 17, 24]. These properties are valuable in keratolytic therapy, where irritation and skin barrier disruption frequently occur.

Recent pharmaceutical investigations additionally emphasize the importance of maintaining the physiological skin microbiome during topical treatment. Afzal et al. demonstrated that prebiotic gel-cream systems may improve skin condition in acne management while preserving microbial balance and reducing inflammatory manifestations [21]. Such findings indicate that modern keratolytic preparations should combine exfoliating activity with barrier-supportive and microbiome-friendly characteristics.

Scientific interest in dermatological semi-solid dosage forms has also expanded due to advances in pharmaceutical technology. Researchers are actively exploring nanoemulsions, niosomal carriers, gel-emulsion systems, and multifunctional cream-gel bases capable of improving drug release and enhancing stability of active compounds [10, 11, 14]. Consequently, the development of cream-gels with keratolytic activity represents a promising direction in pharmaceutical

technology aimed at improving both therapeutic effectiveness and patient compliance (Table 1.1).

Table 1.1

Main keratolytic substances used in dermatological preparations

Active substance	Main pharmacological effect	Common concentration range	Dermatological application
Salicylic acid	Keratolytic, anti-inflammatory, comedolytic	1–10%	Acne, psoriasis, hyperkeratosis
Urea	Moisturizing, keratolytic	5–40%	Xerosis, calluses, keratosis
Lactic acid	Exfoliating, hydrating	2–12%	Dry skin, hyperpigmentation
Glycolic acid	Keratolytic, regenerative	5–15%	Acne, photoaging
Mandelic acid	Mild exfoliating, antibacterial	5–10%	Sensitive and acne-prone skin
Azelaic acid	Keratolytic, antimicrobial	10–20%	Acne vulgaris, rosacea
Citric acid	Exfoliating, antioxidant	1–10%	Hyperpigmentation, dull skin
Pyruvic acid	Sebostatic, keratolytic	4–14%	Acne, seborrhea
Adapalene	Comedolytic, anti-inflammatory	0.1–0.3%	Acne vulgaris

The analysis of current scientific literature confirms that keratolytic therapy remains an important component of topical dermatological treatment. Modern

pharmaceutical approaches are focused on the creation of multifunctional cream-gel systems that combine keratolytic efficacy, moisturizing action, physicochemical stability, and improved cosmetic acceptability, making them highly promising for extemporaneous pharmaceutical compounding and individualized dermatological care.

1.2 Physicochemical and pharmacological characteristics of substances with keratolytic activity

Active pharmaceutical ingredients with keratolytic properties are widely used in topical dermatological therapy due to their ability to soften, loosen, and promote the removal of excessive keratinized layers of the epidermis. The therapeutic effectiveness of keratolytic preparations largely depends on the physicochemical properties of the active substances, their concentration, solubility, compatibility with excipients, and ability to penetrate the skin barrier [5, 7].

Among keratolytic compounds, salicylic acid remains one of the most extensively studied and clinically effective substances. It belongs to the group of beta-hydroxy acids and demonstrates pronounced exfoliating, anti-inflammatory, antimicrobial, and sebostatic activity. Due to its lipophilic properties, salicylic acid readily penetrates sebaceous follicles and contributes to the dissolution of intercellular cement in the stratum corneum, thereby facilitating desquamation processes. The effectiveness of salicylic acid-containing semi-solid preparations has been confirmed in numerous dermatological studies focused on acne, psoriasis, seborrheic dermatitis, and hyperkeratotic lesions [5].

Urea is another important keratolytic substance frequently incorporated into dermatological formulations. At low concentrations, urea acts as a humectant and moisturizer by increasing water retention within the epidermis. At higher concentrations, it exhibits keratolytic effects associated with disruption of hydrogen bonds in keratin structures, resulting in softening and exfoliation of hyperkeratotic tissues. Moreover, urea contributes to improved skin permeability and enhances penetration of other active pharmaceutical ingredients [14].

Alpha-hydroxy acids, including lactic acid and glycolic acid, are also commonly used in dermatological practice. These substances reduce corneocyte adhesion, stimulate epidermal renewal, and improve skin texture. In addition to their keratolytic action, alpha-hydroxy acids demonstrate moisturizing and antioxidant properties, making them valuable components of multifunctional cream-gel systems.

Modern research highlights the importance of combining keratolytic substances with anti-inflammatory, antioxidant, and regenerative ingredients. Herbal extracts and natural biocomponents such as Aloe vera, Salvia hispanica, Rosella extracts, and plant polyphenols have shown significant dermatoprotective potential in semi-solid formulations [9, 17, 20, 24]. Such combinations may reduce irritation associated with keratolytic therapy and improve patient tolerance during prolonged use.

The physicochemical characteristics of keratolytic substances strongly influence formulation development. Solubility, pH stability, hygroscopicity, and compatibility with gelling agents determine the selection of suitable dosage forms and technological methods. According to Sanjeevini et al., the pH of topical cream and gel systems may significantly affect both the stability of active substances and skin compatibility [26]. Therefore, optimization of formulation pH is essential for ensuring efficacy and minimizing irritation.

The incorporation of keratolytic agents into cream-gel systems requires careful consideration of rheological and release properties. Studies investigating gel-cream formulations demonstrated that balanced hydrophilic-lipophilic systems provide improved spreadability, enhanced drug release, and satisfactory physical stability [8, 16]. Furthermore, nano-carrier systems and advanced gel technologies are increasingly employed to optimize skin penetration and prolong therapeutic action [10, 14].

Thus, the analysis of physicochemical and pharmacological characteristics of keratolytic substances confirms the necessity of rational formulation design for semi-solid dermatological preparations. Appropriate selection of active ingredients

and excipients is essential for achieving optimal therapeutic efficacy, stability, and patient acceptability.

1.3 Formulation features and technological aspects of cream-gel dosage forms

Cream-gels represent modern semi-solid dosage forms that combine the structural characteristics of emulsions and gels, providing improved cosmetic properties, enhanced drug release, and satisfactory patient compliance. From a physicochemical perspective, they are typically considered biphasic or multiphase systems in which a dispersed oil phase is incorporated into a structured aqueous gel network, or vice versa, depending on formulation design. Owing to their balanced hydrophilic-lipophilic composition, cream-gels demonstrate favorable rheological behavior, including pseudoplastic flow, thixotropy, and structural viscosity, which ensures ease of application under shear stress and stability at rest. In comparison with conventional ointments and creams, such systems exhibit superior spreadability, rapid absorption, reduced occlusiveness, and a significantly lower greasy feel, which directly influences patient acceptability and adherence to long-term dermatological therapy [8, 10].

In dermatological practice, these properties are particularly important for topical treatment of keratolytic conditions, where repeated application over large skin areas is often required. The sensory profile of the dosage form plays a crucial role in patient compliance, especially in chronic diseases such as acne, psoriasis, and xerosis, where therapy duration may extend for weeks or months. Additionally, cream-gel systems allow more uniform distribution of active substances across the skin surface, improving dose consistency and minimizing localized irritation that may occur with more occlusive semisolid bases.

The technological development of cream-gels requires careful and scientifically justified selection of excipients capable of ensuring physical stability, homogeneity, and controlled release of active pharmaceutical ingredients. Gelling agents such as carbomers, cellulose derivatives, xanthan gum, and tamarind gum are

widely used for the formation of structured gel networks with defined rheological properties and high stability over a wide pH range [16]. Carbomer-based systems, in particular, are valued for their ability to form clear, stable gels with adjustable viscosity depending on neutralization degree. Cellulose derivatives contribute to improved film-forming properties and moisture retention, while natural polysaccharides such as xanthan gum and tamarind gum provide additional biocompatibility and enhanced sensory characteristics.

In addition to gelling agents, emulsifiers play a key role in stabilizing the oil and aqueous phases within cream-gel systems. Non-ionic emulsifiers are often preferred due to their lower irritation potential and compatibility with a wide range of active pharmaceutical ingredients. Humectants such as glycerin, propylene glycol, sorbitol, and polyethylene glycols are commonly incorporated to enhance skin hydration, improve elasticity of the stratum corneum, and reduce transepidermal water loss. These components are particularly important in keratolytic formulations, where disruption of the epidermal barrier may lead to increased dryness and irritation.

Recent pharmaceutical investigations emphasize the importance of optimizing rheological and physicochemical characteristics of semi-solid systems as a critical factor influencing both product performance and patient acceptability. Comparative studies of gel-cream formulations have demonstrated that the ratio between oil and aqueous phases significantly affects viscosity, yield stress, spreadability, structural stability, and organoleptic properties of the preparation [8]. From a technological standpoint, an optimal balance between these phases ensures sufficient mechanical strength of the formulation while maintaining ease of application and satisfactory skin feel. In keratolytic preparations, appropriate rheological behavior is especially important because it determines uniform distribution of active substances, controlled residence time on the skin, and ultimately therapeutic efficacy and patient adherence.

Natural ingredients are increasingly incorporated into cream-gel systems due to their multifunctional biological and technological properties. Plant-derived components such as Aloe vera gel, Salvia extracts, polyphenol-rich plant fractions,

and essential oils have demonstrated antioxidant, anti-inflammatory, moisturizing, antimicrobial, and regenerative activity in various topical formulations [9, 11, 17]. Their inclusion in cream-gel systems may provide a synergistic effect, enhancing overall therapeutic efficacy while simultaneously mitigating potential irritative effects associated with keratolytic agents. Moreover, natural polymers and extracts may also contribute to improved sensory properties and additional stabilization of the formulation matrix.

Technological approaches to cream-gel preparation commonly involve a multi-stage process that includes separate preparation of aqueous and oil phases, followed by controlled emulsification and subsequent incorporation of the gelling system under constant mixing conditions. Key technological parameters such as temperature режим, homogenization intensity, mixing duration, and sequence of component addition significantly influence the final structure and quality of the dosage form. Proper pH adjustment is also essential, as it affects both the stability of active substances and the performance of the gelling agent system. According to Roik et al., optimization of technological stages plays a decisive role in ensuring the stability, reproducibility, and therapeutic effectiveness of dermatological semi-solid preparations [4].

Another important aspect of cream-gel technology is microbiological stability. Due to the relatively high water content in these systems, they are particularly susceptible to microbial contamination during manufacturing, storage, and use. Therefore, the inclusion of preservatives is often necessary to ensure microbiological safety and extend shelf life. At the same time, careful consideration must be given to the compatibility of preservatives with active pharmaceutical ingredients, gelling agents, and other excipients, as potential interactions may affect both stability and efficacy of the final product. Modern formulation approaches increasingly focus on selecting mild, broad-spectrum preservative systems that minimize irritation while maintaining antimicrobial protection.

Modern technological research is also increasingly focused on advanced drug delivery systems incorporated into cream-gels. Niosomal systems, nanoemulsions,

liposomal carriers, and gel-emulsion hybrid structures have shown promising results in enhancing skin penetration, improving solubility of poorly water-soluble drugs, and enabling controlled or sustained release of active compounds [10, 14]. These systems can significantly improve the bioavailability of keratolytic agents and allow for more targeted delivery within the epidermal layers. In addition, such technologies contribute to reduction of dosing frequency and improvement of overall therapeutic outcomes.

Consequently, cream-gel dosage forms represent technologically advanced semi-solid systems with considerable potential for topical dermatological therapy. Their unique combination of favorable physicochemical properties, patient-friendly sensory profile, and high formulation flexibility makes them particularly suitable for modern keratolytic treatment strategies. Rational selection of excipients, careful optimization of formulation parameters, and integration of modern pharmaceutical technologies are essential prerequisites for achieving stable, effective, and clinically acceptable topical preparations capable of meeting current dermatological and pharmaceutical requirements.

1.4 Prospects for the development of extemporaneous cream-gels with keratolytic activity

The growing prevalence of chronic dermatological disorders associated with hyperkeratosis and impaired epidermal renewal has intensified scientific interest in individualized topical therapy. Extemporaneous cream-gels with keratolytic activity represent a promising direction in modern pharmaceutical compounding because they enable flexible adjustment of formulation composition according to the specific therapeutic needs of patients [29].

One of the major advantages of extemporaneous preparations is the possibility of modifying concentrations of active pharmaceutical ingredients depending on disease severity, skin sensitivity, patient age, and concomitant dermatological conditions. This approach is especially valuable in dermatology, where

individualized therapy often determines treatment effectiveness and patient tolerance.

Contemporary pharmaceutical research demonstrates increasing demand for multifunctional topical preparations combining keratolytic, moisturizing, anti-inflammatory, and regenerative effects. Studies focused on dermatological cream and gel systems confirmed that incorporation of natural extracts, antioxidants, and moisturizing agents improves cosmetic acceptability and skin barrier recovery [9, 12, 24]. Such multifunctional properties are particularly important for long-term keratolytic therapy, which may cause irritation and excessive dryness.

The development of extemporaneous cream-gels is also supported by advances in pharmaceutical technology. Modern gelling agents, nano-carrier systems, and optimized emulsification techniques provide opportunities for creating stable and effective semi-solid systems with enhanced bioavailability and improved release characteristics [10, 14]. In addition, recent studies indicate that cream-gel systems possess favorable sensory properties and higher patient adherence compared with traditional ointment bases [8].

An important promising direction is the incorporation of microbiome-supportive and prebiotic components into keratolytic formulations. According to Afzal et al., prebiotic gel-cream systems may contribute to maintaining physiological skin microflora while reducing inflammatory manifestations in acne therapy [21]. This tendency reflects the modern concept of dermatological care focused not only on symptom elimination but also on preservation of skin homeostasis.

Scientific publications additionally emphasize the importance of physicochemical stability and pH optimization in semi-solid systems [26]. Extemporaneous preparations allow pharmacists to adapt formulation parameters to the properties of active substances and the characteristics of individual patients, thereby improving safety and therapeutic outcomes.

Therefore, the development of extemporaneous cream-gels with keratolytic activity represents a highly relevant and promising direction in pharmaceutical

technology and dermatological practice. The combination of individualized formulation design, modern technological approaches, and multifunctional therapeutic action creates favorable conditions for further expansion of such preparations in pharmaceutical compounding and topical therapy.

CONCLUSIONS TO CHAPTER 1

1. The analysis of scientific literature demonstrated that cream-gels represent a modern and promising group of semi-solid dosage forms widely used in dermatological practice due to their favorable organoleptic properties, improved patient compliance, and ability to ensure effective delivery of active pharmaceutical ingredients into the skin. Current trends in formulation development are focused on optimizing therapeutic efficacy, physicochemical stability, and dermatological safety of such systems.

2. It was established that keratolytic agents remain a key group of active substances in the treatment of hyperkeratotic skin conditions, including acne, psoriasis, xerosis, and other disorders associated with impaired keratinization. The literature confirms that substances such as salicylic acid, urea, and alpha-hydroxy acids exhibit pronounced keratolytic, moisturizing, and skin-renewing effects, while their rational combination allows reduction of irritation and improvement of therapeutic outcomes.

3. The reviewed sources indicate that the physicochemical properties of keratolytic substances, including solubility, lipophilicity, stability at different pH levels, and compatibility with excipients, play a crucial role in the design of effective topical formulations. Proper selection of active ingredients and their concentrations significantly influences the safety, efficacy, and stability of cream-gel systems.

4. It was determined that cream-gel dosage forms possess significant technological advantages compared with traditional semi-solid preparations, including improved rheological characteristics, enhanced spreadability, controlled release of active substances, and higher patient acceptability. The structure of cream-

gels, based on the interaction of emulsified and gel networks, ensures balanced physicochemical and sensory properties of the final product.

5. Scientific literature also confirms that the incorporation of natural bioactive components, modern gelling agents, and advanced pharmaceutical technologies contributes to the development of multifunctional dermatological systems. Such approaches enable the creation of stable, effective, and cosmetically acceptable keratolytic cream-gels that meet contemporary requirements of pharmaceutical practice and dermatological therapy.

CHAPTER 2. MATERIALS AND RESEARCH METHODS

2.1 Materials used in the research

The development of a topical semisolid dosage form with keratolytic activity requires a rational selection of both active pharmaceutical ingredients and excipients that ensure not only therapeutic efficacy but also physicochemical stability, biopharmaceutical performance, and patient acceptability. In the present study, the formulation of a cream-gel system is based on a combination of modern dermato-active substances and well-established pharmaceutical excipients that provide synergistic effects in terms of keratolysis, hydration, barrier restoration, and antimicrobial protection. Each component was selected considering its pharmacological profile, compatibility within a hydrogel-emulsion matrix, and technological functionality in the final dosage form. The following section provides a detailed description of the active substance and excipients used in the development of the proposed cream-gel formulation.

Active pharmaceutical ingredient

Lactobionic acid, Acidum lactobionicum (CAS No.: 96-82-2). Lactobionic acid is a white or almost white crystalline, odorless, hygroscopic powder belonging to the class of polyhydroxy acids. Chemically, it is a disaccharide acid composed of D-galactose and gluconic acid linked via an ether bond. Its molecular formula is $C_{12}H_{22}O_{12}$, and molecular weight is 358.30. The substance is freely soluble in water, slightly soluble in ethanol, and practically insoluble in lipophilic solvents. Aqueous solutions demonstrate weak acidity with a pH typically ranging from 2.5 to 4.0 depending on concentration [16, 31].

From a physicochemical standpoint, lactobionic acid is characterized by high hydrophilicity and multiple hydroxyl functional groups, which provide strong hydrogen-bonding capacity and pronounced water-binding properties. These characteristics determine its ability to form a hydration layer on the skin surface and reduce transepidermal water loss. Unlike classical alpha-hydroxy acids, lactobionic acid exhibits a significantly lower penetration rate due to its larger molecular size,

which contributes to a reduced irritation potential while maintaining keratolytic efficacy.

Pharmacologically, lactobionic acid demonstrates mild keratolytic activity through gradual disruption of corneodesmosomal structures in the stratum corneum, leading to controlled desquamation of corneocytes. In addition, it exhibits antioxidant properties associated with metal ion chelation and reduction of oxidative stress in epidermal tissues. It also contributes to skin barrier support and hydration, acting as both a humectant and osmoprotective agent. In dermatological practice, it is applied in formulations intended for acne, xerosis, hyperkeratotic conditions, and sensitive skin, where gentle exfoliation and barrier preservation are required simultaneously.

Excipients

Urea, Ureum (CAS No.: 57-13-6). Urea is a white crystalline, odorless, highly hygroscopic compound with the molecular formula CH_4N_2O and molecular weight 60.06. It is freely soluble in water, soluble in ethanol, and practically insoluble in non-polar solvents [2, 16, 31].

Urea is a natural constituent of the skin's natural moisturizing factor and plays a fundamental role in maintaining epidermal hydration and elasticity. At the molecular level, it acts by disrupting hydrogen bonding within keratin structures of the stratum corneum, resulting in increased water binding and softening of the skin. At higher concentrations, it demonstrates keratolytic activity, while at lower concentrations it functions primarily as a humectant.

From a pharmacotechnological perspective, urea enhances skin permeability and facilitates penetration of other active ingredients. It is widely used in the treatment of xerosis, ichthyosis, psoriasis, and other hyperkeratotic disorders. However, it is chemically sensitive to alkaline conditions and elevated temperatures, where it may decompose into ammonia and carbon dioxide, which is an important consideration in formulation development.

Niacinamide, Nicotinamidum (CAS No.: 98-92-0). Niacinamide is a white crystalline, odorless, water-soluble compound with molecular formula $C_6H_6N_2O$ and

molecular weight 122.12. It is stable in neutral and slightly acidic aqueous environments [16, 31].

Niacinamide represents the amide form of vitamin B3 and functions as a precursor of nicotinamide adenine dinucleotide (NAD^+) and $NADP^+$, which are essential coenzymes in cellular metabolism. It plays a key role in redox reactions, energy production, and cellular repair mechanisms.

Dermatologically, niacinamide exhibits multiple beneficial effects, including anti-inflammatory activity, reduction of sebum production, improvement of epidermal barrier function through stimulation of ceramide synthesis, and reduction of transepidermal water loss. It also inhibits melanosome transfer from melanocytes to keratinocytes, contributing to a mild depigmenting effect. Due to its excellent tolerability, it is widely used in acne-prone, sensitive, and hyperpigmented skin conditions.

Carbomer, Carbopolum Ultrez 21 (INCI: Acrylates/C10-30 Alkyl Acrylate Crosspolymer). Carbomer is a white, fluffy, hygroscopic powder without odor, representing a high-molecular-weight crosslinked polymer of acrylic acid. Its molecular weight exceeds 1×10^6 Da [2, 16, 30, 31].

In aqueous media, carbomer remains in a compact structure under acidic conditions; however, upon neutralization, ionization of carboxyl groups leads to electrostatic repulsion and rapid swelling of polymer chains, resulting in the formation of a three-dimensional gel network.

Carbomer is widely used as a rheology modifier, gelling agent, and stabilizer in semisolid pharmaceutical systems. It provides high viscosity at low concentrations, pseudoplastic flow behavior, good spreadability, and excellent clarity of gels. These properties make it particularly suitable for topical dermatological formulations, ensuring uniform distribution of active substances and controlled release characteristics.

Triethanolamine, Triethanolaminum (CAS No.: 102-71-6). Triethanolamine is a colorless to pale yellow viscous liquid with a mild ammoniacal odor, having the

molecular formula $C_6H_{15}NO_3$ and molecular weight 149.19. It is fully miscible with water and ethanol [16, 31].

In pharmaceutical technology, triethanolamine is primarily used as a neutralizing agent for carbomer-based systems. It induces gel formation by converting carboxylic acid groups into their salt form, thereby enabling polymer swelling and network formation. Additionally, it serves as a pH regulator, ensuring optimal conditions for stability of acid-sensitive active substances such as lactobionic acid and urea. Its concentration must be carefully controlled to avoid excessive alkalinity, which may compromise formulation stability and skin compatibility.

Glycerin, Glycerolum (CAS No.: 56-81-5). Glycerin is a clear, colorless, viscous, hygroscopic liquid with molecular formula $C_3H_8O_3$ and molecular weight 92.09. It is fully miscible with water and ethanol [2, 16, 30, 31].

Glycerin is a trihydric alcohol widely used as a humectant in topical pharmaceutical formulations. It acts by attracting and retaining water molecules through hydrogen bonding, thereby increasing hydration of the stratum corneum. This leads to improved skin elasticity, reduced dryness, and enhanced comfort during application of keratolytic agents. In addition, glycerin contributes to improved rheological stability and sensory characteristics of semisolid formulations.

Polysorbate 80, Polysorbatum 80 (CAS No.: 9005-65-6). A viscous, clear to slightly opalescent liquid ranging from pale yellow to amber in color, practically odorless or with a faint characteristic odor. It is a non-ionic surfactant belonging to the class of polyoxyethylene sorbitan fatty acid esters. Polysorbate 80 is produced by the ethoxylation of sorbitan followed by esterification with oleic acid. Its empirical formula is variable due to its polymeric nature; the average molecular weight is approximately 1310. It is freely soluble in water, ethanol, and several organic solvents, forming stable colloidal systems. The pH of a 5% aqueous solution is approximately 5.5–7.0 [2, 16, 31].

Polysorbate 80 is a pharmacologically inert excipient with pronounced emulsifying, solubilizing, and stabilizing properties. In pharmaceutical technology,

it is widely used as a non-ionic emulsifier for oil-in-water systems and as a solubilizing agent for lipophilic active substances in aqueous media. It reduces interfacial tension, enhances physical stability of dispersed systems, and ensures uniform distribution of active ingredients in semisolid dosage forms. It is extensively applied in dermatological, cosmetic, and parenteral formulations.

Caprylic/Capric triglyceride (CAS No.: 65381-09-1). A clear, colorless to slightly yellow oily liquid with a faint characteristic odor or odorless appearance. It is a mixture of triglycerides of glycerol with medium-chain saturated fatty acids, mainly caprylic (C8:0) and capric (C10:0) acids, typically derived from fractionated coconut or palm kernel oil. Its molecular formula is variable due to its mixed composition; the average molecular weight is approximately 470–520. It is practically insoluble in water but miscible with oils and organic lipophilic solvents [16].

Caprylic/Capric triglyceride is a pharmacologically inert excipient with strong emollient properties. In pharmaceutical and cosmetic formulations, it is used as a skin-conditioning agent, solvent for lipophilic substances, and lipid phase component in emulsions. It improves skin softness, reduces transepidermal water loss, enhances sensory properties of formulations, and contributes to the overall stability and spreadability of semisolid dosage forms [30].

Squalane, Squalanum (CAS No.: 111-01-3). A clear, colorless, lightweight oily liquid with a neutral or very faint odor. It is a saturated hydrocarbon (triterpene derivative) obtained by hydrogenation of squalene, a natural component of human sebum. Its molecular formula is $C_{30}H_{62}$, with a molecular weight of 422.81. Squalane is practically insoluble in water but highly soluble in organic solvents and lipid phases [16, 31].

Squalane is a biomimetic lipid excipient with excellent emollient and skin barrier-replenishing properties. It is widely used in pharmaceutical and cosmetic preparations to restore the lipid barrier of the epidermis, reduce transepidermal water loss, and improve skin elasticity and smoothness. Due to its high oxidative stability,

it enhances the physicochemical stability and shelf life of emulsion-based and semisolid formulations.

Phenoxyethanol, Phenoxyethanolum (CAS No.: 122-99-6).

Phenoxyethanol is a colorless to slightly oily liquid with a mild aromatic odor, having molecular formula $C_8H_{10}O_2$ and molecular weight 138.16. It is slightly soluble in water and freely soluble in ethanol and glycols [16, 31].

It is widely used as a broad-spectrum preservative in pharmaceutical and cosmetic formulations. Its antimicrobial activity is based on disruption of microbial cell membrane integrity and inhibition of enzymatic systems, leading to suppression of bacterial and fungal growth. Phenoxyethanol is stable over a wide pH range and compatible with most hydrophilic gel systems, ensuring microbiological safety of aqueous semisolid preparations.

Purified water, Aqua purificata. Purified water is a clear, colorless, odorless liquid with molecular formula H_2O and molecular weight 18.02. It serves as the primary solvent and dispersion medium in pharmaceutical formulations [2, 16, 30, 31].

It forms the continuous phase of gel systems and enables homogeneous distribution of hydrophilic substances, ensuring system uniformity and stability. Purified water used in pharmaceutical preparations must comply with pharmacopoeial requirements regarding microbial purity, conductivity, and absence of contaminants, as its quality directly influences the safety, stability, and efficacy of the final dosage form.

2.2 Research methods

In this study, general scientific theoretical methods were used, as well as marketing, physicochemical, pharmacotechnological, rheological, analytical, statistical, and organoleptic methods.

The organoleptic properties of the cream-gel were evaluated in accordance with the requirements of the State Pharmacopoeia of Ukraine. The assessment included the determination of appearance, color, odor, consistency, and

homogeneity. The evaluation was performed under standard laboratory conditions by visual and sensory inspection to confirm the absence of phase separation, lump formation, and any undesirable odor characteristics [1].

The colloidal stability was studied in accordance with DSTU 4765:2007 "Cosmetic creams. General technical requirements." Methodology: two test tubes were filled with the investigated sample to 2/3 of their volume and weighed (the mass difference between samples should not exceed 0.2 g). The samples were kept in a thermostat at 42–45 °C for 20 minutes. Centrifugation was performed using a clinical centrifuge LabAnalyt DM 0412 at a rotation frequency of 100 s^{-1} for 5 minutes. Stability was evaluated visually. The sample is considered stable if no more than one drop of water is released in each test tube after centrifugation [3].

Thermal stability was determined in accordance with DSTU 4765:2007 "Cosmetic creams. General technical requirements." Methodology: three test tubes (14 × 120 mm) were filled with the sample to approximately 2/3 of their volume, avoiding air entrapment. The samples were then kept in a thermostat at 40–42 °C for 24 hours. Stability was evaluated visually. The sample is considered stable if no more than one drop of water is observed in each test tube after the test [3].

Rheological studies were performed using a rotational viscometer Reotest-2 with coaxial cylinders at temperatures of 20 ± 2 °C and 37 ± 2 °C according to standard pharmacopoeial methodology [1].

The determination of pH was carried out in accordance with DSTU 4765:2007 "Cosmetic creams. General technical requirements." Methodology: 10.00 g of cream-gel was weighed into a 100 mL volumetric flask, and the volume was adjusted to the mark with purified water while stirring. The mixture was heated to 80 ± 2 °C and then cooled to 20 ± 2 °C. After cooling, the supernatant liquid was separated, and the pH was measured in it. The prepared solution was transferred into a 50 mL beaker, and the electrodes were immersed without touching the walls or bottom of the vessel. The pH value was recorded using the instrument scale. The final result was calculated as the arithmetic mean of two parallel measurements, with an allowable difference not exceeding 0.1 pH units [1, 3].

Statistical processing of the results was performed in accordance with the requirements of the State Pharmacopoeia of Ukraine. Standard parametric and non-parametric methods were used, with the choice depending on the nature of the obtained data, normality of distribution, and the specifics of the research task. Data processing was carried out using Microsoft Excel 2021 software [1].

CONCLUSIONS TO CHAPTER 2

1. The physicochemical and pharmacotechnological characteristics of the selected components for the development of a keratolytic cream-gel were analyzed. The properties of lactobionic acid, urea, niacinamide, carbomer, triethanolamine, glycerin, phenoxyethanol, and purified water were considered in terms of their functional role in the formation of a stable semisolid gel system and in ensuring the therapeutic efficacy of the final formulation.

2. A set of appropriate methods for quality evaluation of the developed dosage form was substantiated and systematized. The selected methodologies enable the determination of key quality attributes, including organoleptic characteristics, pH value, colloidal and thermal stability, rheological behavior, as well as overall homogeneity and physical stability of the system under storage and mechanical stress conditions.

CHAPTER 3. FORMULATION AND TECHNOLOGICAL DEVELOPMENT OF A KERATOLYTIC CREAM-GEL

3.1 Analysis of the pharmaceutical market of topical keratolytic preparations

The analysis of the pharmaceutical market of topical keratolytic preparations was performed based on the study of commercially available dermatological and dermocosmetic products presented in pharmacy chains and online distribution platforms. The evaluation included classification by active pharmaceutical ingredients, dosage forms, and countries of origin, which allowed identification of the main formulation trends and technological approaches in this product category [4].

The distribution of keratolytic preparations by pharmacological category shows that hydroxy acid-based products account for approximately 38% of the analyzed market segment, urea-containing formulations represent about 26%, retinoid-based topical agents constitute around 18%, while combined multifunctional dermocosmetic systems, including hybrid keratolytic-moisturizing formulations, account for approximately 18%. This distribution reflects the current shift toward milder, better tolerated keratolytic systems with improved safety profiles for long-term dermatological use.

When analyzed by country of origin, the market demonstrates significant geographic diversity. Products manufactured in South Korea constitute approximately 24% of the total assortment, reflecting strong development of dermocosmetic technologies in this region. Italian manufacturers account for about 16%, while German and French products represent approximately 12% and 10%, respectively. Products originating from China occupy around 14% of the market, mainly in the dermocosmetic segment. Ukrainian manufacturers account for approximately 8%, demonstrating a stable presence in the regional pharmaceutical market with a focus on urea-based and combined dermatological formulations.

Products from the United States represent about 9%, while the remaining 7% is distributed among Poland, Spain, and other European countries (Fig. 3.1).

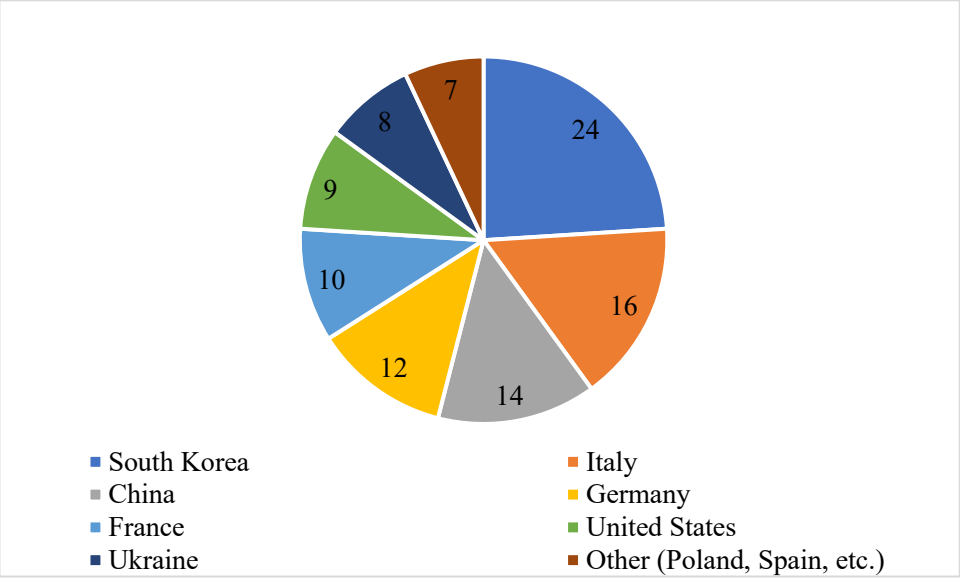

Fig. 3.1 Geographic distribution of keratolytic products, %

From the perspective of dosage form distribution, topical keratolytic preparations are predominantly represented by semisolid and liquid dermal systems with clearly differentiated market shares. Cream formulations constitute the largest segment, accounting for approximately 42% of the total market, which is associated with their balanced sensory properties, good skin compatibility, and suitability for both therapeutic and dermocosmetic applications.

Gel-based preparations represent the second largest group with about 28%, which is explained by their non-greasy texture, rapid absorption, and high patient acceptability, particularly in the treatment of acne-prone and seborrheic skin. Serum formulations account for approximately 18% of the market and are mainly positioned within the dermocosmetic segment, where high concentrations of active ingredients and lightweight textures are preferred.

Emulsion-based systems, including classical oil-in-water and water-in-oil formulations, represent around 10% of products and are mainly used in dermatological therapy requiring enhanced emollient and barrier-supporting properties. Patch systems constitute the smallest segment, accounting for

approximately 2%, and are primarily used in localized treatment approaches, where controlled and occlusive delivery of keratolytic agents is required.

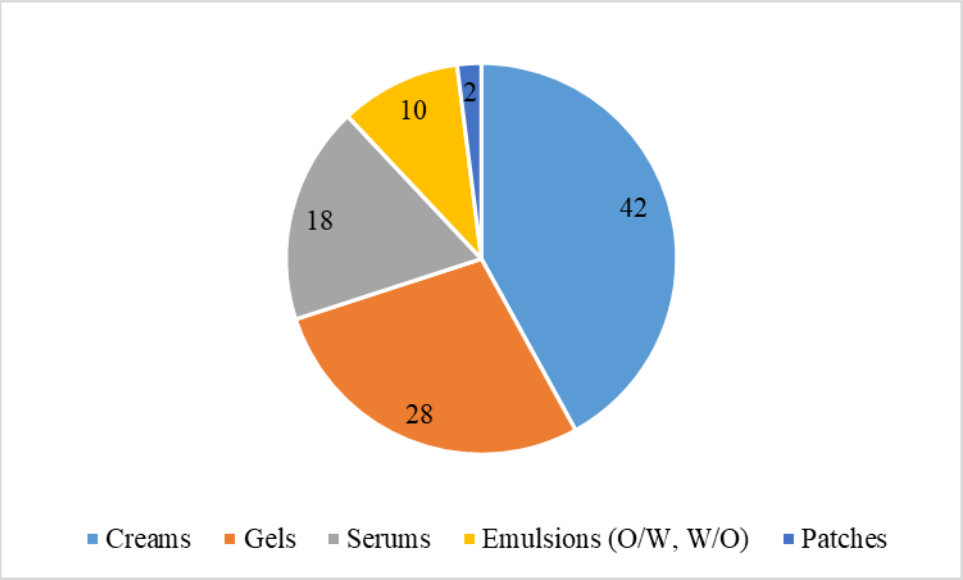

Fig. 3.2 Distribution of topical keratolytic preparations by dosage form, %

From the perspective of active pharmaceutical ingredients, the most frequently used keratolytic agents include glycolic acid, salicylic acid, lactic acid, urea, and retinoid derivatives such as adapalene and tretinoin. Among these, salicylic acid remains the most widely used beta-hydroxy acid due to its lipophilic nature and comedolytic activity, while glycolic acid is predominant among alpha-hydroxy acids due to its strong exfoliating effect. Urea is particularly important in dermatological formulations intended for xerosis and hyperkeratotic conditions due to its dual humectant and keratolytic properties. In modern dermocosmetic products, polyhydroxy acids such as lactobionic acid are increasingly incorporated due to their reduced irritancy and additional antioxidant effects (Fig. 3.3).

A detailed analysis of formulation composition demonstrates that topical keratolytic preparations contain a complex system of functional excipients designed to ensure stability, efficacy, and patient acceptability. Due to the limited aqueous solubility of many keratolytic agents, co-solvents such as glycerin, ethanol, and propylene glycol are commonly used to enhance solubilization and improve dermal

penetration. These components also act as humectants, contributing to hydration of the stratum corneum and reduction of skin irritation.

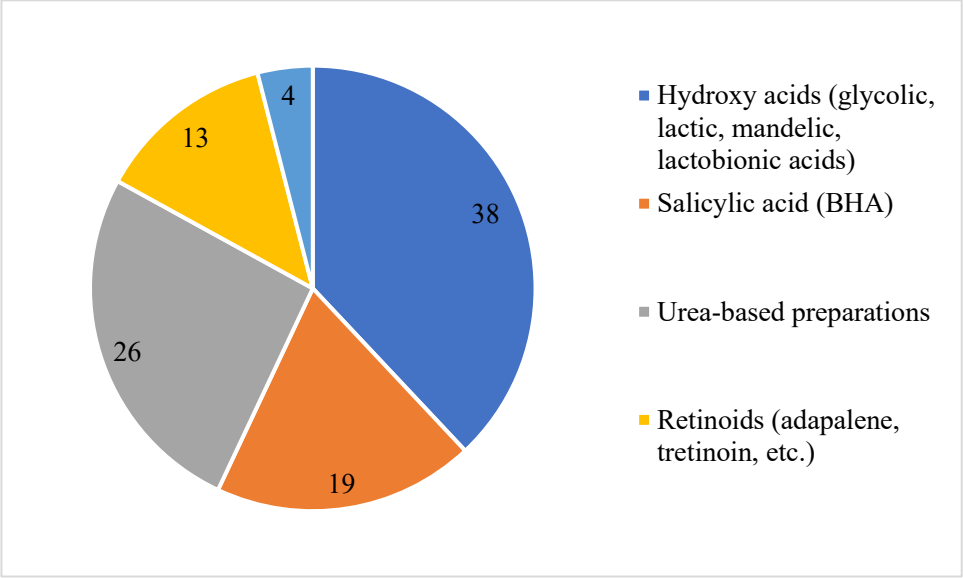

Fig. 3.3 Distribution of keratolytic preparations by active pharmaceutical ingredients, %

Rheological modifiers and gelling agents, including carbomers, cellulose derivatives, xanthan gum, and polyacrylate crosspolymers, are widely used to provide structural integrity and desired viscosity of semisolid systems. These excipients ensure uniform distribution of active substances, prevent phase separation, and improve application properties. Emulsifying agents such as polysorbates and fatty alcohol derivatives are used in cream-based systems to stabilize oil-in-water emulsions and improve sensory characteristics.

Emollients, including caprylic/capric triglycerides, squalane, and plant-derived oils, are frequently incorporated to restore lipid barrier function and reduce potential irritant effects associated with keratolytic therapy. In advanced formulations, ceramide complexes are included to support epidermal barrier repair and enhance long-term skin tolerance.

Preservative systems are essential components of aqueous keratolytic formulations due to their susceptibility to microbial contamination. Commonly used preservatives include phenoxyethanol and organic acid-based systems, selected

based on their compatibility with acidic pH environments typical for keratolytic products. Additionally, antioxidant components are sometimes introduced to prevent oxidative degradation of active substances and maintain formulation stability over time.

pH adjustment plays a critical role in the performance of keratolytic systems, as it directly influences both chemical stability and biological activity of active ingredients. Buffer systems or neutralizing agents are therefore carefully selected to maintain an optimal pH range that ensures therapeutic efficacy while minimizing skin irritation.

Overall, the current pharmaceutical market of topical keratolytic preparations demonstrates a clear trend toward multifunctional, well-tolerated dermocosmetic systems, particularly cream-gel formulations, which integrate keratolytic, moisturizing, and barrier-repairing functions within a single dosage form.

3.2 Selection and justification of active pharmaceutical ingredients and excipients of the cream-gel

The development of a topical keratolytic cream-gel requires a scientifically justified selection of active pharmaceutical ingredients and functional excipients that ensure a balanced combination of efficacy, safety, physicochemical stability, and patient acceptability. The formulation design is based on a multifunctional approach, where keratolytic, moisturizing, anti-inflammatory, and barrier-repairing effects are achieved through the rational combination of complementary substances (Table 3.1).

Table 3.1

Experimental design of cream-gel compositions with keratolytic activity

Component	1 (%)	2 (%)	3 (%)	4 (%)	5 (%)
1	2	3	4	5	6
Lactobionic acid	5.00	5.00	5.00	5.00	5.00
Urea	7.00	7.00	7.00	7.00	7.00
Niacinamide	2.00	2.00	2.00	2.00	2.00

Continuation of tab. 3.1

1	2	3	4	5	6
Carbomer	0.60	0.70	0.80	0.90	1.00
Triethanolamine	0.40	0.50	0.60	0.70	0.80
Glycerin	5.00	5.00	5.00	5.00	5.00
Polysorbate 80	1.00	1.00	1.00	1.00	1.00
Caprylic/Capric triglyceride	5.00	5.00	5.00	5.00	5.00
Squalane	3.00	3.00	3.00	3.00	3.00
Phenoxyethanol	0.10	0.10	0.10	0.10	0.10
Purified water	to 100	to 100	to 100	to 100	to 100

Lactobionic acid was selected as a modern representative of polyhydroxy acids (PHA), characterized by a gentle keratolytic effect combined with pronounced humectant and antioxidant properties. Due to its large molecular structure and multiple hydroxyl groups, it provides controlled exfoliation of the stratum corneum with minimal irritation potential, making it suitable for sensitive and compromised skin. In addition, lactobionic acid contributes to the improvement of epidermal hydration and supports skin barrier integrity through water-binding mechanisms.

Urea is a physiologically relevant component of the natural moisturizing factor of the skin and is widely used in dermatological practice due to its dual mechanism of action. At the selected concentration, it exhibits both keratolytic and humectant effects, promoting the softening of hyperkeratotic tissue through disruption of hydrogen bonding within keratin structures. It also enhances skin permeability, thereby improving the penetration of other active substances into the epidermis.

Niacinamide (nicotinamide), a biologically active form of vitamin B3, was included due to its multifunctional dermatological activity. It demonstrates anti-inflammatory properties, reduces sebum production, and plays a key role in the restoration of the epidermal barrier by stimulating ceramide synthesis. Furthermore,

niacinamide contributes to the regulation of pigmentation processes and improves overall skin tolerance to active keratolytic agents.

Carbomer was chosen as the primary gelling agent due to its ability to form stable three-dimensional polymer networks upon neutralization. It provides optimal rheological properties, including pseudoplastic flow behavior, high viscosity at low concentrations, and good spreadability, which are essential for uniform application of topical preparations. Carbomer also ensures physical stability of the dispersed system and prevents phase separation.

Triethanolamine serves as a neutralizing agent for carbomer, enabling the formation of a stable gel structure through ionization of carboxyl groups and subsequent polymer swelling. Additionally, it allows precise adjustment of the pH of the formulation, which is critical for maintaining the stability and activity of acid-sensitive components such as lactobionic acid and urea.

Glycerin was incorporated as a classical humectant with strong hygroscopic properties. It enhances hydration of the stratum corneum by attracting and retaining water molecules, reduces transepidermal water loss, and improves the sensory properties of the formulation. Glycerin also contributes to improved skin comfort during keratolytic therapy, reducing the risk of irritation.

Polysorbate 80 was selected as a non-ionic surfactant and emulsifying agent due to its excellent ability to stabilize oil-in-water systems and solubilize lipophilic components within hydrophilic gel matrices. It reduces interfacial tension between phases, ensuring thermodynamic stability of the dispersion system and preventing phase separation during storage. In addition, Polysorbate 80 is chemically stable over a wide pH range and demonstrates good compatibility with hydroxy acids, urea, and niacinamide, which is essential for maintaining the integrity of the multifunctional keratolytic formulation. Its inclusion enables uniform distribution of lipid phase components and contributes to the formation of a physically stable cream-gel system with improved texture and application properties.

Caprylic/Capric triglyceride was incorporated as a physiologically compatible emollient and lipid phase component. It is characterized by a lightweight, non-greasy

sensory profile and high dermal tolerability, which makes it suitable for dermatological preparations intended for sensitive or compromised skin. Functionally, it acts as a skin-conditioning agent, reducing transepidermal water loss and improving skin softness and elasticity. Moreover, it serves as a solvent for lipophilic components and enhances the spreadability of the formulation. Its chemical similarity to naturally occurring skin lipids supports restoration of the skin barrier function and improves patient comfort during keratolytic therapy.

Squalane was selected as a biomimetic lipid due to its close structural and functional similarity to endogenous sebum components. It plays an important role in reinforcing the epidermal lipid barrier and reducing transepidermal water loss without producing an occlusive effect. Squalane exhibits high oxidative stability, which contributes to the long-term physicochemical stability of the formulation. Additionally, it improves skin elasticity, smoothness, and overall tolerance of active keratolytic agents. Its inclusion is particularly important in formulations containing exfoliating acids, as it helps to balance potential irritant effects and enhances the overall dermatological acceptability of the cream-gel system.

Phenoxyethanol was selected as a broad-spectrum preservative due to its effectiveness against bacteria and yeasts, as well as its stability over a wide pH range. It ensures microbiological safety of the aqueous gel system during storage and repeated use, while maintaining compatibility with the selected active substances and excipients.

Purified water acts as the dispersion medium and continuous phase of the cream-gel system, ensuring homogeneous distribution of hydrophilic components and enabling the formation of a stable semisolid system. Its quality directly influences the stability, safety, and overall performance of the final dosage form.

3.3 Development of the extemporaneous preparation technology of the cream-gel

The development of the extemporaneous preparation technology of the keratolytic cream-gel is based on the principles of sequential formation of a

hydrophilic gel matrix and separate preparation of an aqueous solution of active substances followed by controlled phase integration. This approach ensures complete solubilization of water-soluble components, uniform distribution of active ingredients within the system, and stability of the rheological characteristics of the final dosage form.

The technological process begins with preparatory operations, including calculation of required quantities of all components, accurate weighing using analytical balances, and preparation of working equipment. Particular attention is paid to maintaining process cleanliness and preventing contamination or loss of active substances.

Step 1. Preparation of the gelling base (Solution A). Carbomer is dispersed in a portion of purified water under continuous stirring using a mechanical mixer equipped with an anchor-type impeller. The polymer is added gradually to ensure uniform wetting and to prevent agglomerate formation. The dispersion is left for complete hydration of carbomer until a homogeneous viscous system is formed.

Control point 1: absence of lumps, uniform polymer dispersion, stable swelling of carbomer.

Step 2. Preparation of the aqueous solution of active substances (Solution B). In a pre-measured amount of purified water, lactobionic acid, urea, and niacinamide are sequentially dissolved under continuous stirring until a clear or slightly opalescent solution is obtained. Separate preparation of the aqueous phase ensures complete solubilization of active substances and prevents local overconcentration in the final system.

Control point 2: complete dissolution of active substances, absence of precipitate and mechanical impurities.

Step 3. Preparation of the auxiliary lipid–emulsion phase. Phenoxyethanol is first dissolved in glycerin under continuous stirring until a clear and homogeneous solution is obtained, ensuring uniform distribution of the preservative and improving the microbiological stability of the formulation. After complete dissolution, polysorbate 80 is added to the glycerin phase and thoroughly mixed until a uniform

system is formed. Subsequently, caprylic/capric triglyceride and squalane are introduced under continuous stirring until a homogeneous lipid mixture is obtained. This phase contributes to improved sensory properties and stabilization of the dispersed system.

Control point 3: complete dissolution of phenoxyethanol in glycerin, homogeneity of the glycerin–surfactant system, absence of phase separation after addition of lipid components.

Step 4. Formation of the cream-gel system. The aqueous solution of active substances (Solution B) is introduced into the hydrated carbomer dispersion (Solution A) under continuous stirring. After that, the prepared lipid phase is added. The mixture is homogenized until a uniform emulsion–gel system with no visible heterogeneity is obtained.

Control point 4: system homogeneity, absence of phase separation, and uniform consistency.

Step 5. Neutralization and gel structure formation. Triethanolamine is added dropwise under continuous stirring. Neutralization of carbomer carboxyl groups leads to the formation of a three-dimensional polymer network and an increase in system viscosity. Mixing is continued until the gel structure is stabilized.

Control point 5: achievement of target pH, formation of stable gel structure, reproducible viscosity.

Step 6. Final mixing and system stabilization. After gel formation, slow mixing is performed to ensure complete homogeneity of the system and uniform distribution of all components.

Control point 6: mass homogeneity, absence of local inconsistencies.

Step 7. Sampling for intermediate quality control. Samples are taken for evaluation of organoleptic properties, pH, viscosity, and overall system uniformity.

Step 8. Packaging and labeling. The finished cream-gel is packed into 30.0 g containers with dosing applicators. Labeling includes information on composition, batch number, and storage conditions.

Thus, the proposed technology is based on the separate preparation of aqueous and auxiliary phases followed by their controlled combination, ensuring complete solubilization of active substances, stability of the gel structure, and reproducibility of pharmaceutical properties of the cream-gel under laboratory manufacturing conditions.

3.4 Determination of quality parameters and technological characteristics of the developed formulation

The evaluation of quality parameters and technological characteristics of the developed cream-gel formulation is a key stage in substantiating its pharmaceutical suitability, stability, and potential for further dermatological application. A comprehensive assessment was carried out to determine the influence of carbomer concentration on the structural, rheological, physicochemical, and organoleptic properties of the system. The obtained results allow for the selection of an optimal formulation with balanced consistency, acceptable skin compatibility, and high colloidal stability (Table 3.2).

Table 3.2

Quality and technological characteristics of cream-gel samples

Parameter	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
1	2	3	4	5	6
Appearance	Light semi-fluid gel	Soft gel	Uniform gel	Dense homogeneous gel	Very dense gel
Homogeneity	Satisfactory	Good	Very good	Excellent	Acceptable
Color	White, uniform	White	White	White	White, slightly opaque
Odor	Neutral	Neutral	Neutral	Neutral	Neutral
pH (20°C)	5.47 ± 0.04	5.50 ± 0.03	5.52 ± 0.02	5.48 ± 0.02	5.46 ± 0.03

Continuation of tab. 3.2

1	2	3	4	5	6
Viscosity (20°C), Pa·s	7.8 ± 0.4	11.5 ± 0.6	16.2 ± 0.8	22.8 ± 1.1	31.5 ± 1.5
Spreadability	High	Good	Good	Optimal	Reduced
Colloidal stability	Stable	Stable	Stable	Stable	Stable
Thermal stability	Stable	Stable	Stable	Stable	Stable

Sample 1, containing 0.60% carbomer, demonstrated insufficient structural strength. Although it exhibited good spreadability and acceptable organoleptic properties, its low viscosity and moderate thermal stability indicate an underdeveloped gel network, which limits its suitability for prolonged topical application.

Sample 2 (0.70%) showed improved rheological characteristics compared to Sample 1, with better homogeneity and stability. However, the gel structure remained relatively weak, and the system lacked optimal mechanical resistance, which may affect its long-term physical stability.

Sample 3 (0.80%) demonstrated a well-balanced set of properties, including good homogeneity, satisfactory viscosity, and stable colloidal behavior. Nevertheless, the sensory profile and spreadability, although acceptable, were not optimal for patient comfort and uniform application.

Sample 4 (0.90%) exhibited the most favorable overall profile among all tested formulations. It combined excellent homogeneity, optimal pseudoplastic flow behavior, high thermal and colloidal stability, and balanced spreadability. The system formed a stable, structurally organized gel matrix that ensured uniform distribution of active substances and optimal sensory characteristics. These properties make Sample 4 the most suitable formulation for further development.

Sample 5 (1.00%) demonstrated excessive gel structuring, resulting in reduced spreadability and slightly impaired sensory acceptability. Although its stability was generally satisfactory, the overly dense structure may negatively affect ease of application and patient compliance.

Thus, Sample 4 was identified as the optimal formulation due to its balanced rheological behavior, high physicochemical stability, and favorable organoleptic properties, which together ensure its suitability as a keratolytic cream-gel for topical use.

CONCLUSIONS TO CHAPTER 3

1. The pharmaceutical market of topical keratolytic preparations was analyzed, demonstrating its steady expansion and high level of diversification. It was established that modern dermatological products are increasingly oriented toward multifunctional systems combining keratolytic, moisturizing, anti-inflammatory, and barrier-repairing effects, which ensures their wide use in both therapeutic and dermocosmetic practice.

2. The segmentation of topical keratolytic dosage forms was determined, revealing the predominance of cream-based formulations as the largest market segment, followed by gels and serums, while emulsion systems and patch technologies occupy smaller shares. A clear trend toward lightweight, non-greasy, and patient-friendly formulations with improved skin tolerability was identified.

3. Lactobionic acid, urea, and niacinamide were scientifically substantiated as the key active pharmaceutical ingredients of the developed cream-gel. Their combined action provides a synergistic keratolytic, moisturizing, anti-inflammatory, and barrier-supporting effect, which is essential for the safe and effective management of hyperkeratotic and sensitive skin conditions.

4. Carbomer was justified as a suitable gel-forming agent due to its ability to form stable three-dimensional polymer networks with controlled rheological behavior. Triethanolamine was selected as a neutralizing agent ensuring optimal gel structuring and pH adjustment, while glycerin and phenoxyethanol provide moisturizing and antimicrobial protection of the system.

5. The experimental formulations of the cream-gel were developed with variation in carbomer concentration, and their comparative physicochemical and technological evaluation was performed. It was established that formulation 4

demonstrates the most balanced characteristics in terms of viscosity, spreadability, homogeneity, and overall technological performance.

6. The extemporaneous preparation technology of the keratolytic cream-gel was developed and scientifically justified. The process is based on the sequential preparation of a hydrated gel base, aqueous solution of active substances, and controlled incorporation of components, which ensures homogeneity of the system and reproducibility of quality parameters.

7. The technological scheme of cream-gel preparation was elaborated, including the preparation of the gel base, dissolution of active ingredients in the aqueous phase, controlled mixing of phases, and neutralization step to form a stable polymeric gel network. Critical technological parameters such as mixing intensity, order of component addition, and pH control were defined.

8. The quality and technological characteristics of the developed cream-gel were evaluated using organoleptic, physicochemical, rheological, and statistical methods. The obtained results confirmed the stability of the system, acceptable pH within the physiological range, optimal rheological behavior, and satisfactory organoleptic properties, indicating the suitability of formulation 4 as the optimal variant for further development.

CONCLUSIONS

1. The analysis of scientific literature demonstrated that cream-gels represent a modern and promising group of semi-solid dosage forms widely used in dermatological practice due to their favorable organoleptic properties, improved patient compliance, and ability to ensure effective delivery of active pharmaceutical ingredients into the skin. Current trends in formulation development are focused on optimizing therapeutic efficacy, physicochemical stability, and dermatological safety of such systems.

2. It was established that keratolytic agents remain a key group of active substances in the treatment of hyperkeratotic skin conditions, including acne, psoriasis, xerosis, and other disorders associated with impaired keratinization. The literature confirms that substances such as salicylic acid, urea, and alpha-hydroxy acids exhibit pronounced keratolytic, moisturizing, and skin-renewing effects, while their rational combination allows reduction of irritation and improvement of therapeutic outcomes.

3. The reviewed sources indicate that the physicochemical properties of keratolytic substances, including solubility, lipophilicity, stability at different pH levels, and compatibility with excipients, play a crucial role in the design of effective topical formulations. Proper selection of active ingredients and their concentrations significantly influences the safety, efficacy, and stability of cream-gel systems.

4. It was determined that cream-gel dosage forms possess significant technological advantages compared with traditional semi-solid preparations, including improved rheological characteristics, enhanced spreadability, controlled release of active substances, and higher patient acceptability. The structure of cream-gels, based on the interaction of emulsified and gel networks, ensures balanced physicochemical and sensory properties of the final product.

5. Scientific literature also confirms that the incorporation of natural bioactive components, modern gelling agents, and advanced pharmaceutical technologies contributes to the development of multifunctional dermatological

systems. Such approaches enable the creation of stable, effective, and cosmetically acceptable keratolytic cream-gels that meet contemporary requirements of pharmaceutical practice and dermatological therapy.

6. The physicochemical and pharmacotechnological characteristics of the selected components for the development of a keratolytic cream-gel were analyzed. The properties of lactobionic acid, urea, niacinamide, carbomer, triethanolamine, glycerin, phenoxyethanol, and purified water were considered in terms of their functional role in the formation of a stable semisolid gel system and in ensuring the therapeutic efficacy of the final formulation.

7. A set of appropriate methods for quality evaluation of the developed dosage form was substantiated and systematized. The selected methodologies enable the determination of key quality attributes, including organoleptic characteristics, pH value, colloidal and thermal stability, rheological behavior, as well as overall homogeneity and physical stability of the system under storage and mechanical stress conditions.

8. The pharmaceutical market of topical keratolytic preparations was analyzed, demonstrating its steady expansion and high level of diversification. It was established that modern dermatological products are increasingly oriented toward multifunctional systems combining keratolytic, moisturizing, anti-inflammatory, and barrier-repairing effects, which ensures their wide use in both therapeutic and dermocosmetic practice.

9. The segmentation of topical keratolytic dosage forms was determined, revealing the predominance of cream-based formulations as the largest market segment, followed by gels and serums, while emulsion systems and patch technologies occupy smaller shares. A clear trend toward lightweight, non-greasy, and patient-friendly formulations with improved skin tolerability was identified.

10. Lactobionic acid, urea, and niacinamide were scientifically substantiated as the key active pharmaceutical ingredients of the developed cream-gel. Their combined action provides a synergistic keratolytic, moisturizing, anti-

inflammatory, and barrier-supporting effect, which is essential for the safe and effective management of hyperkeratotic and sensitive skin conditions.

11. Carbomer was justified as a suitable gel-forming agent due to its ability to form stable three-dimensional polymer networks with controlled rheological behavior. Triethanolamine was selected as a neutralizing agent ensuring optimal gel structuring and pH adjustment, while glycerin and phenoxyethanol provide moisturizing and antimicrobial protection of the system.

12. The experimental formulations of the cream-gel were developed with variation in carbomer concentration, and their comparative physicochemical and technological evaluation was performed. It was established that formulation 4 demonstrates the most balanced characteristics in terms of viscosity, spreadability, homogeneity, and overall technological performance.

13. The extemporaneous preparation technology of the keratolytic cream-gel was developed and scientifically justified. The process is based on the sequential preparation of a hydrated gel base, aqueous solution of active substances, and controlled incorporation of components, which ensures homogeneity of the system and reproducibility of quality parameters.

14. The technological scheme of cream-gel preparation was elaborated, including the preparation of the gel base, dissolution of active ingredients in the aqueous phase, controlled mixing of phases, and neutralization step to form a stable polymeric gel network. Critical technological parameters such as mixing intensity, order of component addition, and pH control were defined.

15. The quality and technological characteristics of the developed cream-gel were evaluated using organoleptic, physicochemical, rheological, and statistical methods. The obtained results confirmed the stability of the system, acceptable pH within the physiological range, optimal rheological behavior, and satisfactory organoleptic properties, indicating the suitability of formulation 4 as the optimal variant for further development.

LIST OF REFERENCES

1. Державна Фармакопея України / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-ге вид. Харків : ДП «Український науковий фармакопейний центр якості лікарських засобів», 2015. Т. 1. 1126 с.

2. Державна Фармакопея України / ДП «Український науковий фармакопейний центр якості лікарських засобів». 2-ге вид. Харків : ДП «Український науковий фармакопейний центр якості лікарських засобів», 2014. Т. 2. 713 с.

3. ДСТУ 4765:2007. Креми косметичні. Загальні технічні умови. Офіц. вид. ; чинний від 01.01.2009. Київ : Держспоживстандарт України, 2008. 12 с.

4. Компендіум. Довідник лікарських препаратів. URL: https://compendium.com.ua/uk/ (дата звернення: 18.01.2026).

5. Обґрунтування складу крему для екстемпорального застосування з антипсоріатичною та протизапальною дією / Ж. М. Полова та ін. *Вісник фармації.* 2025. № 1(109). С. 66–73. DOI: 10.24959/nphj.25.178.

6. Розроблення технології виробництва крему з фотозахисними властивостями / О. Роїк та ін. *Фармацевтичний журна*л. 2025. № 2. С. 50–63. DOI: 10.32352/0367-3057.2.25.05.

7. Фармакологічне обґрунтування складу діючих речовин у складі гелю «Молозоль» / Л. Малоштан та ін. *Фармацевтичний журнал*. 2023. № 2. С. 41–48. DOI: 10.32352/0367-3057.2.23.05.

8. Barve S., Deshpande S., Dhawal P. Cytotoxic, Cytostatic, and Keratolytic Activity of Anti-Dandruff Shampoo Formulations. *International Journal of Research in Dermatology*. 2023. Vol. 9. DOI: 10.18203/issn.2455-4529.

9. Cervadoro G., Cervadoro E., Semeraro R. M. Keratolytic Action of an Emollient Cosmetic Cream. *Giornale Italiano di Dermatologia e Venereologia.* 2003. Vol. 138(6). P. 507–511.

10. Comparative Physicochemical and Pharmacotechnical Evaluation of Three Topical Gel-Cream Formulations / R. Pârvănescu et al. *Gels*. 2025. Vol. 11. P. 532. DOI: 10.3390/gels11070532.

11. Development and Evaluation of Moisturizing Cream Containing Salvia hispanica and Aloe vera and its Antioxidant Potential / R. Deore et al. *Ars. Pharmaceutica (Internet).* 2025. Vol. 66. P. 276–287. DOI: 10.30827/ars.v66i3.32785.

12. Development and Optimization of a Gel-Cream Moisturizer through Acmella oleracea Extract-Loaded Niosomes for Lateral Canthal Rhytides / N. Ali et al. *Particulate Science and Technology*. 2026. Vol. 44. P. 1–16. DOI: 10.1080/02726351.2026.2619478.

13. Development and Stability Study of a Topical Emulsified and Gel-Cream System Containing Syzygium cumini L. Essential Oil / J. José et al. *Science, Society and Emerging Technologies*. 2024. P. 232–246. DOI: 10.51859/amplla.sset.2224-17.

14. Development of the Composition of a Dermatological Product in the Form of a Cream with Extracts of the Aerial Part of Lespedeza bicolor / K. Kiselyova et al. *ScienceRise: Pharmaceutical Science*. 2025. № 1(53). P. 26–40. DOI: 10.15587/2519-4852.2025.322855.

15. Efficacy of Combination of Topical Ketoconazole 2% Cream and Adapalene 0.1% Gel versus Topical Ketoconazole 2% Cream Alone in Treatment of Pityriasis versicolor: Topical Ketoconazole and Adapalene for Pityriasis versicolor Treatment / F. Munir et al. *Pakistan Journal of Health Sciences.* 2024. P. 83–87. DOI: 10.54393/pjhs.v5i04.1395.

16. Exploring the Potent Combination of Quercetin−Boronic Acid, Epalrestat, and Urea Containing Nanoethosomal Keratolytic Gel for the Treatment of Diabetic Neuropathic Pain: In Vitro and In Vivo Studies / H. Muhammad et al. *Molecular Pharmaceutics*. 2023. Vol. 20. DOI: 10.1021/acs.molpharmaceut.3c00236.

17. European Pharmacopoeia. 8th ed. Strasbourg : European Department for the Quality of Medicines, 2013. 3655 p.

18. Formulation Development and Skin Evaluation of Gel-Based Cream Containing Tamarind Gum / M. Phuy et al. *Tropical Journal of Natural Product Research.* 2024. Vol. 8. P. 9256–9264. DOI: 10.26538/tjnpr/v8i11.40.

19. Guetarni H., Ziar N., Khedda R. In Vitro Study of the Physicochemical and Biological Properties of Aloe vera Gel and its Use for the Development of a Cream. *AgriScientia.* 2025. Vol. 42. P. 37–44. DOI: 10.31047/1668.298x.v42.n2.44552.

20. Khanpara P., Sojitra N. Formulation and Evaluation of Anti-Aging Purple Herbal Gel Cream. *Research Journal of Topical and Cosmetic Sciences*. 2023. P. 58–64. DOI: 10.52711/2321-5844.2023.00009.

21. Maqlam T., Kardous A. Antibacterial Activity of Commiphora gileadensis Bark Extract Against Staphylococcus aureus as Cream, Gel and Ointment Formulations. *Yemeni Journal for Medical Sciences*. 2024. Vol. 18. P. 80–85. DOI: 10.20428/yjms.v18i1.2554.

22. Nguyet N., Thao T. Formulation Development and Quality Evaluation of a Topical Cream Containing a Polyphenol-Rich Extract from Spilanthes acmella Murr. *Tropical Journal of Natural Product Research*. 2025. Vol. 9. P. 6190–6196. DOI: 10.26538/tjnpr/v9i12.36.

23. Open-Label, Prospective Study of a Prebiotic Gel Cream on Its Efficacy of Mild to Moderate Acne Management and Effects on the Functional Skin Microbiome / L. Afzal et al. *Journal of Cosmetic Dermatology*. 2025. Vol. 24. P. e70138. DOI: 10.1111/jocd.70138.

24. Parwarish, Ghafoor R. Comparative Study of Efficacy of Combined Treatment with Ketoconazole 2% Cream and Adapalene 0.1% Gel Versus Ketoconazole 2% Cream Monotherapy in Pityriasis versicolor. *Indus Journal of Bioscience Research.* 2025. Vol. 3(5). P. 934–937. DOI: 10.70749/ijbr.v3i5.1702.

25. Pawar R. Development and Assessment of the Anti-Aging Herbal Cream. *TMP Universal Journal of Advances in Pharmaceutical Sciences*. 2025. Vol. 1. DOI: 10.69557/bae4v119.

26. Physicochemical Evaluation and Anti-Aging Activity of the Cream Formulation Containing Aloe Vera and Rosella Extracts / R. Wulandari et al. *Indonesian Journal of Pharmacy*. 2025. Vol. 36(4). P. 611–621. DOI: 10.22146/ijp.16388.

27. Sabe A., Gupta D. Formulation Development and Evaluation of Herbal Cream of Salvia verbenaca for Candidiasis. *International Journal of Drug Delivery Technology*. 2026. Vol. 16(1). P. 49–54. DOI: 10.25258/ijddt.16.1.5.

28. Skin Can Modulate the pH of Topical Creams and Gels / M. Sanjeevini et al. *AAPS Pharm. Sci. Tech*. 2025. Vol. 26(5). P. 166. DOI: 10.1208/s12249-025-03161-0.

29. Synthesis and Determination of the Sun Protection Factor of a Cosmetic Gel-Cream Based on Norbixin / S. Garcia et al. 2023. DOI: 10.56238/globalhealthprespesc-069.

30. The Japanese Pharmacopoeia. 18th ed. The MHLW Ministerial Notification № 220. 2021. 2587 p.

31. The United States Pharmacopeia. The National formulary. Rockville, Md. : United States Pharmacopeial Convention, 2012.

APPENDICES

Appendix A

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ГРАМОТА

нагороджується

Шукрі-Хаміуі Аюб

за участь у секційному засіданні студентського наукового товариства кафедри аптечної технології ліків

XXXII МІЖНАРОДНОЇ НАУКОВО-ПРАКТИЧНОЇ КОНФЕРЕНЦІЇ МОЛОДИХ ВЧЕНИХ ТА СТУДЕНТІВ «АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ»

Ректор закладу вищої освіти **Олександр КУХТЕНКО**

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ * Національний фармацевтичний університет * №02010936 *

15 квітня 2026 р. м. Ужгород

Appendix B

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ
РАДА МОЛОДИХ ВЧЕНИХ
СТУДЕНТСЬКЕ НАУКОВЕ ТОВАРИСТВО
ГО «УКРАЇНСЬКА ФАРМАЦЕВТИЧНА СТУДЕНТСЬКА АСОЦІАЦІЯ»

ПРОГРАМА

XXXII Міжнародної науково-практичної конференції молодих вчених та студентів «АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ»

15-17 квітня 2026 р.

Харків, Ужгород – 2026

Continuation of app. B

9. **Розроблення екстракту сухого для лікування захворювань репродуктивної системи жінок**
Доповідач: Закарлюка Анастасія
Науковий керівник: Марченко М.В., к. фарм. н., доцент
10. **Аналіз підходів до використання рослинних компонентів у складі супозиторіїв**
Доповідач: Зуєва Софія
Науковий керівник: Марченко М.В., к. фарм. н., доцент
11. **Аналіз підходів до фармакотерапії посттравматичного стресового розладу у деяких країнах**
Доповідач: Білозор Ксенія,
Науковий керівник: Вишневська Л.І., д. фарм. н., проф.
12. **Development of the composition and technology of extemporaneous antiseptic liquid soap**
Доповідач: Аллалі Аюб,
Науковий керівник: Вишневська Л.І., д. фарм. н., проф.
13. **Development of the composition and technology of a cream-gel with keratolytic activity**
Доповідач: Шукрі-Хаміуі Аюб,
Науковий керівник: Ковальова Т.М., к. фарм. н., доцент
14. **Development of the composition and technology of an extemporaneous drug based on medicinal plant raw materials**
Доповідач: Агутан Уіам,
Науковий керівник: Іванюк О.І., PhD, асистент
15. **Сучасні напрями виготовлення лікарських препаратів з лікарської рослинної сировини**
Доповідач: Яворська Валерія,
Науковий керівник: Боднар Л.А., PhD, асистент

Ф А 2.2.1-36-366

National University of Pharmacy

Faculty pharmaceutical
Department drug technology
Level of higher education master
Specialty 226 Pharmacy, industrial pharmacy
Educational and professional program Pharmacy

APPROVED
The Head of Department

_____
Liliia VYSHNEVSKA

"07" October 2025

ASSIGNMENT

FOR QUALIFICATION WORK

OF AN APPLICANT FOR HIGHER EDUCATION

Ayoub CHOUKRI-HAMIOUI

1. Topic of qualification work: «Development of the composition and technology of a cream-gel with keratolytic activity», supervisor of qualification work: Tetiana KOVALOVA, Candidate of Pharmaceutical Sciences, Associate Professor

approved by order of NUPh from "06" of October 2025 № 266

2. Deadline for submission of qualification work by the applicant for higher education: May 2026.

3. Outgoing data for qualification work: cream-gel, keratolytic activity, semi-solid dosage form, extemporaneous technology, quality control.

4. Contents of the settlement and explanatory note (list of questions that need to be developed): - to conduct a systematic review and analysis of scientific literature regarding keratolytic agents and semi-solid topical dosage forms;
- to analyze the current pharmaceutical market of topical preparations with keratolytic activity;
- to justify the selection of active pharmaceutical ingredients and excipients for the development of the cream-gel formulation;
- to develop the technological scheme for the preparation of the cream-gel with keratolytic activity;
- to determine the main pharmaco-technological, physicochemical, and organoleptic characteristics of the developed preparation;
- to evaluate the stability and expected quality indicators of the developed cream-gel.

5. List of graphic material (with exact indication of the required drawings): tables 3, figures 3.

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1	Tetiana KOVALOVA, associate professor of the drug technology department	07.10.2025	07.10.2025
2	Tetiana KOVALOVA, associate professor of the drug technology department	23.11.2025	23.11.2025
3	Tetiana KOVALOVA, associate professor of the drug technology department	22.01.2026	22.01.2026

7. Date of issue of the assignment: "07" October 2025

CALENDAR PLAN

№ з/п	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1	Justification of the research design	October 2025	**done**
2	Analysis of literature sources	November 2025	**done**
3	Conducting experimental research	December 2025 – January 2026	**done**
4	Analysis, interpretation, and synthesis of the results	January-March 2026	**done**
5	Designing a work	April 2026	**done**

An applicant of higher education _____ Ayoub CHOUKRI-HAMIOUI

Supervisor of qualification work _____ Tetiana KOVALOVA

ВИТЯГ З НАКАЗУ
По Національному фармацевтичному університету

«06» жовтня 2025 р. **№ 266**
Фармацевтичний факультет

Затвердити теми кваліфікаційних робіт здобувачам вищої освіти 5 курсу 2025-2026 н. р., група Фм21(4,10д)англ-01, освітня програма «Фармація», спеціальність «226 Фармація, промислова фармація», галузь знань «22 Охорона здоров'я», рівень вищої освіти другий (магістерський), денна форма здобуття освіти, термін навчання 4 роки 10 місяців, мова навчання англійська.

Прізвище, ім'я здобувача вищої освіти	Тема кваліфікаційної роботи (українською мовою)	Тема кваліфікаційної роботи (англійською мовою)	Керівник кваліфіка-ційної роботи	Рецензент кваліфіка-ційної роботи
Кафедра аптечної технології ліків				
Шукрі-Хаміуі Аюб	Розроблення складу і технології крем-гелю з кератолітичною активністю	Development of the composition and technology of a cream-gel with keratolytic activity	доц. Ковальова Т.М.	проф. Сліпченко Г.Д.

Підстава: подання декана фармацевтичного факультету доцента Олександра ГОНЧАРОВА

Ректор
Вірно. Секретар

ФА2.8-03-317

ВИСНОВОК

експертної комісії про проведену експертизу

щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

«11» травня 2026 р. № 333812593

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти ШУКРІ-ХАМІУІ Аюба, групи Фм21(4,10д)англ-01, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» очної (денної) форми здобуття освіти на тему: «Розроблення складу і технології крем-гелю з кератолітичною активністю / Development of the composition and technology of a cream-gel with keratolytic activity», експертна комісія дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Заступник голови Комісії,
заступник директора інституту
в складі ЗВО ННІПФ,
доцент Олена НОВОСЕЛ

Ф А 2.2.1-36-353

REVIEW

of scientific supervisor for the qualification work of the master's level of higher education of the specialty 226 Pharmacy, industrial pharmacy

Ayoub CHOUKRI-HAMIOUI

on the topic: «Development of the composition and technology of a cream-gel with keratolytic activity»

Relevance of the topic. Dermatological conditions associated with abnormal keratinization of the skin, such as hyperkeratosis, acne, and certain forms of dermatitis, remain a widespread problem in modern clinical practice. Effective management of these conditions requires topical agents with keratolytic activity that can promote exfoliation of the stratum corneum and improve skin renewal processes. The choice of an appropriate dosage form is crucial for ensuring optimal delivery of active substances, adequate skin penetration, and patient compliance. Cream-gel systems are considered a promising basis for such preparations due to their balanced physicochemical properties, favorable sensory characteristics, and ability to enhance the release and action of active compounds. Therefore, the development of the composition and technology of a cream-gel with keratolytic activity is a relevant task of pharmaceutical technology aimed at improving dermatological therapy.

Practical value of conclusions, recommendations and their validity. The qualification work presents a comprehensive analysis of modern approaches to the development of semisolid dermatological dosage forms with keratolytic properties. The technological aspects of formulation development were studied, including requirements for achieving optimal consistency, stability, and uniform distribution of active substances in the dosage form. As a result, a scientifically justified composition and a rational technology for the preparation of a cream-gel with keratolytic activity under pharmaceutical conditions were proposed. The obtained results may be applied in pharmacy practice for the preparation of effective topical dermatological agents.

Assessment of work. The qualification work is performed at a high scientific and methodological level. The theoretical material is logically structured, well-argued, and

supported by relevant scientific literature. The proposed technological solutions demonstrate a clear understanding of pharmaceutical formulation principles and requirements for semisolid dosage forms. The conclusions are consistent with the objectives of the study and confirm the practical significance of the developed approach.

General conclusion and recommendations on admission to defense. The qualification work meets the requirements for master's level theses and can be submitted for defense to the Examination Commission of the National Pharmaceutical University for the award of the Master of Pharmacy degree.

Scientific supervisor _____ Tetiana KOVALOVA

«13» of May 2026

Ф А 2.2.1-36-356

REVIEW

for qualification work of the master's level of higher education, specialty 226 Pharmacy, industrial pharmacy

Ayoub CHOUKRI-HAMIOUI

on the topic: «Development of the composition and technology of a cream-gel with keratolytic activity»

Relevance of the topic. Keratolytic agents play an important role in dermatological practice, as they are widely used for the treatment of hyperkeratosis, acne, seborrheic dermatitis, and other conditions associated with excessive keratinization of the skin. The effectiveness of such therapy largely depends on the choice of dosage form, which should ensure adequate penetration of active substances into the superficial layers of the skin while maintaining patient comfort during use. Cream-gel systems are particularly promising in this regard, as they combine the advantages of both hydrophilic and lipophilic bases, providing optimal consistency, good spreadability, and enhanced delivery of active compounds. Therefore, the development of the composition and technology of a cream-gel with keratolytic activity is a relevant task of modern pharmaceutical technology aimed at creating effective and patient-friendly dermatological preparations.

Theoretical level of work. The work presents a systematic analysis of modern approaches to the development of semi-solid dermatological dosage forms with keratolytic properties. The author summarized current scientific data on mechanisms of keratolytic action and the role of formulation factors in enhancing skin penetration and therapeutic efficacy. Particular attention was paid to the physicochemical and biopharmaceutical aspects of cream-gel systems, including their structural characteristics, stability, and ability to ensure controlled release of active substances. The theoretical foundation of the study demonstrates a solid understanding of pharmaceutical technology principles and topical drug delivery systems.

Author's suggestions on the research topic. The author independently substantiated the selection of a cream-gel system as a rational dosage form for keratolytic therapy

based on literature analysis. A technologically feasible approach to formulation development under pharmaceutical manufacturing conditions was proposed. The methodological framework of the study includes the selection of appropriate technological stages and considerations aimed at ensuring homogeneity, stability, and consumer acceptability of the final product. The proposed solutions correspond to the objectives of developing an effective dermatological preparation.

Practical value of conclusions, recommendations and their validity. The results of the qualification work have practical significance for pharmaceutical technology and dermatological practice. The proposed approach to the development of a cream-gel with keratolytic activity can be used in pharmacy compounding and small-scale pharmaceutical production. The study contributes to the expansion of available topical dermatological preparations and supports the development of more effective and patient-oriented treatment options for hyperkeratotic skin conditions.

Disadvantages of work. The work contains minor stylistic and technical inaccuracies, as well as isolated formatting issues in the list of references. However, these shortcomings are not significant and do not reduce the overall scientific value of the research.

General conclusion and assessment of the work. The qualification work meets the requirements for master's level research and can be submitted for defense to the Examination Commission of the National Pharmaceutical University for the award of the Master of Pharmacy degree.

Reviewer _____prof. Halyna SLIPCHENKO

«14» of May 2026

Ф А2.2.1-36-230

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ВИТЯГ З ПРОТОКОЛУ № 14
«15» травня 2026 року
м. Харків
засідання кафедри
аптечної технології ліків
(назва кафедри)

Голова: завідувачка кафедри, професор Вишневська Л.І.
Секретар: докт. філ., ас. Боднар Л.А.

ПРИСУТНІ:

проф. Половко Н.П., проф. Семченко К.В., проф. Зуйкіна С.С., доц. Ковальова Т.М., доц. Буряк М.В., доц. Олійник С.В., доц. Марченко М.В., ас. Іванюк О.І.

ПОРЯДОК ДЕННИЙ:

1. Про представлення до захисту кваліфікаційних робіт здобувачів вищої освіти.

СЛУХАЛИ: проф. Вишневську Л. І. – про представлення до захисту до Екзаменаційної комісії кваліфікаційних робіт здобувачів вищої освіти.

ВИСТУПИЛИ: Здобувач вищої освіти групи Phm21(4,10d)eng-01 спеціальності 226 «Фармація, промислова фармація» Ayoub CHOUKRI-HAMIOUI – з доповіддю на тему «Development of the composition and technology of a cream-gel with keratolytic activity» (науковий керівник, доц. Тетяна КОВАЛЬОВА).

УХВАЛИЛИ: Рекомендувати до захисту кваліфікаційну роботу.

Голова
Завідувачка кафедри, проф. _____ Лілія ВИШНЕВСЬКА
(підпис)

Секретар
Асистент _____ Любов БОДНАР
(підпис)

Ф А2.2.1-36-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Ayoub CHOUKRI-HAMIOUI до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньо-професійною програмою Фармація
на тему: «Development of the composition and technology of a cream-gel with keratolytic activity»

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____/ Олександр ГОНЧАРОВ /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Ayoub CHOUKRI-HAMIOUI представив кваліфікаційну роботу, яка за об'ємом теоретичних та практичних досліджень повністю відповідає вимогам до оформлення кваліфікаційних робіт.

Керівник кваліфікаційної роботи

_____ Тетяна КОВАЛЬОВА

«13» травня 2026 р.

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Ayoub CHOUKRI-HAMIOUI допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувачка кафедри
аптечної технології ліків

_____ Лілія ВИШНЕВСЬКА

«15» травня 2026 р.

Qualification work was defended
of Examination commission on
« 09 » of June 2026
with the grade _____
Head of the State Examination commission,
Doctor of Pharmaceutical Sciences, Professor

_____ / Volodymyr YAKOVENKO /