Original Research

PHARMACOLOGY

Development of cream bases suitable for personalized cosmetic products

Magdalena Bîrsan[1,2], Ana Caterina Cristofor[3], Cristina Tuchiluș[4], Florina Crivoi[5], Robert Alexandru Vlad[6], Cezara Pintea[6], Paula Antonoaea[6], Adriana Ciurba[6]

1) Medicine and Pharmacy Doctoral School, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Romania

2) Department of Drug Industry and Pharmaceutical Biotechnology, Faculty of Pharmacy, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania

3) Morphofunctional Department I, Faculty of Medicine, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania

4) Department of Microbiology and Parasitology, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania

5) Department of Pharmaceutical Physics, Faculty of Pharmacy, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania

6) Pharmaceutical Technology and Cosmetology Department, Faculty of Pharmacy, George Emil Palade University of Medicine, Pharmacy, Science and Technology of Targu Mures, Romania

Abstract

Background and aims. The individualization of cosmetic products or personalized dermatology preparations are in great demand at the present time.

Methods. 24 emulsifying cream bases were proposed which were prepared by the classical, automatic and semi-automatic methods, respectively, and the physical stability resulted from the three types of homogenization was taken into account. Texture parameters were also studied for the most stable cream bases in the preformulation stage and the t - statistical test was applied. In order to choose the most optimal preservative, the effectiveness of the NipaEster solution 0.1%, Cosgard and Euxyl® PE 9010 was tested on the strains of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans*.

Results. 9 cream bases were stable through all the preparation methods used, and preservation was achieved with Euxyl® PE 9010. Following the texture parameters, significant differences were observed for the same formula in the case of choosing a different preparation method.

Conclusions. Formulas F1, with methyl glucose sesquistearate as emulsifier, F8, with cetearyl glucosite as emulsifier, and F14, with Ceteareth-20 can be used as cream bases for customized products.

Keywords: personalized cosmetic products, antimicrobial agents, texture analysis

DOI: 10.15386/mpr-2765

Manuscript received: 25.05.2024
Received in revised form: 22.06.2024
Accepted: 15.07.2024

Address for correspondence:
Magdalena Bîrsan
magdalena.birsan@umfiasi.ro

Background and aims

In recent years, the demand for compounded pharmaceutical products for dermatological use increased in the pharmacy setting. Despite the pharmaceutical industry offering a plethora of products with high stability and efficacy, the trend toward personalized medication is gaining momentum. Personalized treatments, tailored to individual patient needs, enhance therapeutic efficacy, and strengthen the patient's trust in their healthcare provider [1-3]. This paper outlines the methodology for developing cream bases suitable for such personalized applications in dermatology.

Developing cream bases for personalized dermatological medication or bespoke cosmetic products involves a multi-step process. The goal is to create a stable, effective, and safe base that can be customized with active ingredients to meet specific skin needs [4,5].

The personalization of cosmetic formulations involves the development of products tailored to individual skin types and conditions. This approach leverages well-known natural ingredients at specific concentrations necessary to maintain the skin's physiological functions. In the realm of cosmeceutical products, individualization based on skin type is a highly valued concept globally. This concept, bespoke cosmetics or tailormade cosmetics, represents a niche segment within the contemporary cosmetics industry.

Customization of these formulas focuses on incorporating active ingredients

into a predetermined cream base, meticulously selected to meet consumer specific needs. The efficacy and compatibility of the product are ultimately determined by the consumer, with satisfaction levels directly influencing the product's reputation and acceptance.

Both industrial producers and pharmacists involved in compounding within community pharmacies utilize various cream bases to meet consumer demands. The choice of the base excipient plays a crucial role in the final product's evaluation; hence, selecting the appropriate base is considered pivotal in formulating a successful cosmetic product. Personalized cosmetic products are created by selecting a cream base suitable for the consumer's skin type, into which desired active ingredients are incorporated, generally not exceeding ten compounds. These active ingredients may possess hydrophilic or lipophilic properties, and the chosen cream base must ensure their stable incorporation without destabilizing the final product. The formulator determines the optimal percentage of added ingredients based on their roles, types, and solubility [6].

In summary, personalizing cosmetic products through carefully selecting and incorporating active ingredients into suitable cream bases enhances product efficacy and consumer satisfaction, particularly for individuals with specific skincare needs [7,8].

A fundamental characteristic of cream bases is physico-chemical and microbiological stability, as it is necessary to keep them within optimal parameters even after incorporating the active principles, the incorporation of antimicrobial preservatives being recommended for ointments and O/W creams (Figure 1). The conditioning was correlated with the cosmetic product developed and the method of application. To ensure good microbiological stability over time of cream-type products it is recommended to use a lid container or a airless type container.

Store cream bases must be kept at room temperature, away from heat or moisture. The shelf life of a cream base is variable depending on the type of preservative used and the compatibility between the ingredients. For example, by adding an Ecocert-type preservative, in that case the shelf life of a cream base after opening the container is 9 months, and the shelf life of the final customized product is up to 3 months. Even if the cosmetic/cosmeceutical or master product will retain all its original characteristics for more extended period, in the absence of stability studies, the legislation imposes a maximum validity period of 90 days, provided that studies demonstrate the compatibility between the active principles and between these and the proposed bases [9]. In the absence of compatibility tests, according to good pharmaceutical practice guidelines, customized products will be given a shelf life of up to 30 days.

This work aims to create emulsifying creams W/O and O/W with light texture or rich texture, with optimal texture properties. To create the dispersed system, the use of different types of emulsifiers, with different characteristics and emulsifying properties, in association with other excipients with a functional role, was proposed resulting in 24 cream-based formulations grouped into six formulation groups: Group I - W/O emulsions, Group III - oleogels, and the others being O/W emulsions. Following some preliminary tests and a specific pharmacotechnical screening, the preparation stability with different homogenizing methods, rheological properties, firmness, consistency, adhesiveness, three optimal cream base formulations were finally proposed as suitable bases in order to incorporate various active ingredients in future research phases.

Figure 1. Conditions for a base cream.

Many substances are known to have antimicrobial action, but studies proving their advantages and disadvantages are few. In this study, we aimed to choose a preservative with maximum efficiency from the most common substances with preservative action available on the market. When the pharmacist makes various personalized preparations in the laboratory, few studies confirm which preservative can be added and what effect it can have over time. The proposed study aims to offer some carefully selected and studied formulas to be used in bespoke cosmetic products or personalized dermatological medication.

Materials and Methods

1. Materials

The following ingredients included in table I and table II were used: Olea Europaea Oil (Fagron, Trikala-Larissa, Greece); Euxyl® PE 9010 (Dow Chemical, Midland, MI, USA); Methyl glucose sesquistearate (Lehvoss, Origgio, VA, Italy); Stearic acid (Medchim TM, Bucharest, Romania); Ceteareth-20 (Ethoxylated cetostearylic alcohol 20 ethylene oxide) (Lehvoss, Origgio, VA, Italy); Cetyl alcohol (Medchim TM, Bucharest, Romania); Polyglyceryl 3-methylglucose distearate (Evonik, Germany); Cetyl palmitate (Medchim TM, Bucharest, Romania); Aqua (Medchim TM, Bucharest, Romania); Cetearyl glucoside (Lehvoss, Origgio, VA, Italy); Glyceryl stearate (Fagron, Trikala-Larissa, Greece); Carbomer 971®PNF (Lehvoss, Origgio, VA, Italy); Triethanolamine (Medchim TM, Bucharest, Romania); Glycerin (Medchim TM, Bucharest, Romania); Xanthan Gum (Fagron, Trikala-Larissa, Greece).

2. Methods

Formulation of cream bases

As a general formulation principle, in most groups, the association of the hydrophilic component with the lipophilic component was used in the presence of an emulsifier and a viscosity-increasing agent. In the case of the oleogel-type group, in addition to the hydrophilic and lipophilic phases, the association of a gel structure-forming polymer with a pseudo emulsifier was used.

Preparation of cream bases

The laboratory of the community pharmacy has evolved. Although preparation of an emulsifying system was done only using mortar and pestle until a century ago, there are several options nowadays.

The preparation of the 24 cream bases was carried out according to the general rules for their preparation, namely, heating the lipophilic phase until it liquefies, bringing the hydrophilic phase to the same temperature as the lipophilic phase, mixing the two phases, and homogenizing until the system cools down. The cream bases homogenization was done either manually (classic preparation method) or mechanically, choosing a semi-automatic (Mechanical Stirrer SBS-MR-40, Germany) or automatic device with a predetermined number of revolutions per minute (Gako Unguator EM, Scheßlitz, Germany).

Each formula among the 24 proposed in table I and table II was prepared by three different methods: the classical method, incorporating the components by manual homogenization with the pestle, the semi-automatic method by using a mechanical stirrer at a speed of 1000 rpm for 10 minutes and the automatic method, using a homogenizer with advanced mixing technology, with speed steps between 300-2400 rpm. Visual characteristics and physical stability were taken into consideration to select optimal formulations after preparation.

3. Assessment of appearance and homogeneity

Appearance and homogeneity were determined by visual examination of 1 g of sample pressed between two 10 x 25 cm glass slides until a uniform layer of 0.5 mm was obtained. All formulas made by the three preparation methods were evaluated. Formulas that proved inhomogeneous, with signs of phase separation, were excluded from the following tests. For the appropriate formulas from the point of view of homogeneity and appearance, the centrifugation test is proposed as a crucial step. This test allows the selection of stable formulations to mechanical actions imposed by the manufacturing technology, aiming for them to be subjected to further studies. All formulas were subjected to the stability test 14 days after preparation.

4. Preformulation study to select an effective preservative for a cosmetic product

Methyl parabenzoate and propyl parabenzoate are still used to formulate master preparations. However, in recent years, the paraben mixture has been replaced with other broad-spectrum antimicrobial preservatives, such as a combination of benzyl alcohol, salicylic acid, sorbic acid and glycerin (Cosgard®, Geogard® ECT), a preservative approved by Ecocert and Cosmos, or phenoxyethanol (Euxyl® PE 9010) for topical products that are applied to sensitive skin.

In order to choose the suitable preservative which would be further incorporated in the proposed cream-bases, in the preformulation stage the antibacterial efficacy was assessed using different concentration of the preservative solutions. The study was conducted on three microorganisms *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Candida albicans* from those recommended by the in-force European Union stipulations.

This requires special attention to the quality of raw materials and packaging containers, which must not be contaminated. In addition, further contamination of the product must also be avoided. Considering that cosmetic creams are conditioned in multi-dose containers, and by daily opening the possibility of contamination is

very high, the choice of preservative is one of the most important decisions to be made.

To control the effectiveness of antimicrobial preservatives, those strains that are most frequently encountered as possible contaminants in the manufacturing process, during preservation and at the time of product use, representing a contamination risk for cosmetic preparations, were used as test microorganisms. The trial period lasts at least 28 days. The test was carried out under conditions that must avoid accidental contamination.

Culture mediums used: Nutrient agar medium (Biolab®, Greece) for bacteria and Sabouraud agar medium (Biolab®, Greece) for fungi.

Test microorganisms: *Staphylococcus aureus* ATCC 25923; *Pseudomonas aeruginosa* ATCC 27853; *Candida albicans* ATCC 10231.

Solutions with preservative action tested, in order to select them in the formulation stage (in the proposed cream bases).

- Solution 1: Cosgard® 1% solution
- Solution 2: Methyl- and propylparaben solution 0.1%
- Solution 3: Euxyl® PE 9010 1% solution

The preservative solutions mentioned above were evaluated regarding the antimicrobial effect.

Parameters for inoculum preparation

The stock cultures of the test microorganism were inoculated on the surface of the solid culture medium. The bacteria incubated at 35°C for 24 hours, and the fungi at 20-25°C for 7 days.

To obtain *Candida albicans* bacterial suspensions, the surface of the cultures was washed with sterile isotonic sodium chloride solution (9 g/L NaCl) and diluted to a concentration of 108 microorganisms per milliliter.

The antimicrobial method

The evaluation of viable microorganisms inoculated into the product to be examined was done on the media used for the initial cultivation of each microorganism.

For every 20 ml of the sample to be analyzed, 0.1 ml of the inoculum from the test microorganism suspensions was introduced, so the final concentration is 105-106 per milliliter or gram. The samples were kept in the dark at room temperature (20-25°C).

Samples of 1 g were taken at 0 h, 6 h, 24 h, 7 days, 14 days and 28 days after inoculation and the number of CFU (colony forming units) that developed per milliliter was identified [8,9]. In the beginning, live bacteria were inoculated from each test microorganism, and the role of the preservative is to act on these microorganisms in the shortest possible time. It is ideal to act immediately, or according to the production sheet, within 24 hours.

5. Textural analysis method applied for the evaluation of cream bases

Considering their appearance the obtained results in a previous study regarding the rheological properties [10], consistency and the intention to select both W/O and O/W cream bases, three formulations were chosen, being considered optimal as cream bases: F1, F8, and F14 which highlighted a good homogeneity, by classical preparation method and by the automated and semiautomated methods, good consistency and a pleasant texture. Taking into account that the most frequent preparation methods are the classical one and the automated one (in the microproduction laboratories and in the cosmetic industry) in the further studies the three formulations were evaluated by applying the classical and the automated method.

Formulas prepared by the semi-automatic method were excluded because at the industrial level, automatic mixers are used in particular, semi-automatic preparation is not used, and for manufactured cosmetic products it is preferable to use a cream base prepared by a traditional or automatic method. For the six evaluations, the appearance was identical.

The textural properties of the prepared formulations were examined using a TA.XT Plus texture analyzer (Stable Micro System, Godalming, UK) for reverse extrusion measurements. This method involves lowering a disk (35 mm diameter) over the sample which has been pushed at a speed of 2 mm·s-1 a distance of 5 mm into the sample (30 g) and withdrawn. Data collection and data analysis were performed using the Texture Exponent 32 software package. Parameters such as hardness, consistency, cohesiveness, and viscosity index were determined from force-time plots using the inverse extrusion method for semisolid products. Each formulation was placed in a special container and the test was performed according to the set parameters, pre-test speed 1.5 $mm \cdot s^{-1}$ test speed 2 $mm \cdot s^{-1}$, post-test speed 2 $mm \cdot s^{-1}$, distance 5 mm, trigger force 0.294 N (30 g) [10,11].

Results

1. Formulation of cream bases

The synthetic presentation of the six groups of formulations made according to the type and nature of the emulsifier, respectively, the type of dispersed system obtained can be found in tables I and II.

Within each group, four formulas were proposed by using different concentrations/ratios of hydrophilic, lipophilic, and emulsifier phases, as well as other excipients with a functional role.

2. Assessment of appearance and homogeneity

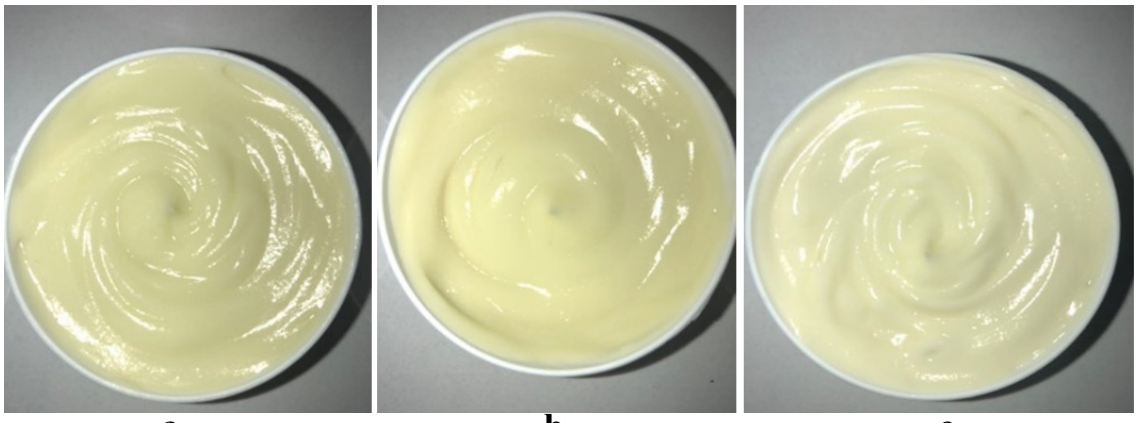
24 cream bases were obtained by applying the previously mentioned preparation methods: classical, semi-automatic, and automatic, manufacturing cream-type products, that had the color and the components characteristics (Figure 2).

Table I. The composition (g) of the proposed formulas F_1-F_{12}.

	INCI	Function	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Group I W/O	Olea Europaea Oil	Lipophilic phase	23	21	23	21								
	Aqua	Hydrophilic phase	68	68	66	66								
	Stearic acid	Emulsier stabilizer	4	6	4	6								
	Methyl glucose sesquistearate	Emulsifier	5	5	7	7								
Group II O/W	Olea Europaea Oil	Lipophilic phase					23	22	23	21				
	Aqua	Hydrophilic phase					68.5	68.5	68	68				
	Cetearyl glucoside	Emulsifier					1	1	1.5	1.5				
	Glyceryl stearate	Emulsifier stabiliser					6.5	7.5	6.5	8.5				
Group III oleogel	Olea Europaea Oil	Lipophilic phase									23	23	23	23
	Carbomer 971®-PNF	Matrix forming polymer for oleogels									0.5	0.5	0.5	0.5
	Triethanolamine	Gel structuring agent									1	1	1	1
	Glycerin	Humectant									2	2	2	2
	Xanthan gum	Viscosity agent									0.5	1	1.5	2

Table II. The composition (g) of the proposed formulas F_{13}-F_{24}.

	INCI	Function	F_{13}	F_{14}	F_{15}	F_{16}	F_{17}	F_{18}	F_{19}	F_{20}	F_{21}	F_{22}	F_{23}	F_{24}
Group IV O/W	Olea Europaea Oil	Lipophilic phase	23	23	23	23								
	Aqua	Hydrophilic phase	68	66	64	62								
	Cethyl alcohol	Emulsifier stabiliser	6	6	6	6								
	Ceteareth-20	Emulsifier	3	5	7	9								
Group V O/W	Olea Europaea Oil	Lipophilic phase					23	23	23	23				
	Aqua	Hydrophilic phase					68	66	64	62				
	Cethyl palmitate	Emulsifier stabiliser					7	7	7	7				
	Ceteareth-20	Emulsifier					2	4	6	8				
Group VI O/W	Olea Europaea Oil	Lipophilic phase									23	23	23	23
	Aqua	Hydrophilic phase									61.5	61	60.5	60
	Cethyl alcohol	Emulsifier stabiliser									3	3	3	3
	Cethyl palmitate	Emulsifier stabiliser									3	3	3	3
	Ceteareth-20	Emulsifier									6	6	6	6
	Xanthan gum	Viscosity agent									0.5	1	1.5	2
	Glycerin	Humectant									3	3	3	3



a **b** **c**

Figure 2. Aspect of the F_1 formula prepared by the three preparation methods (**a**) Classic Method; (**b**) Semi-automatic Method; (**c**) Automatic Method.

Table III. Appearance of the formulations made.

F	Preparation method			F	Preparation method		
	Classic	Semi-automatic	Automatic		Classic	Semi-automatic	Automatic
F_1	O	O	O	F_{13}	O	O	H
F_2	O	O	O	F_{14}	O	O	O
F_3	O	O	O	F_{15}	O	H	O
F_4	O	O	O	F_{16}	O	O	H
F_5	O	O	O	F_{17}	O	O	H
F_6	O	O	O	F_{18}	O	O	H
F_7	O	O	O	F_{19}	O	O	H
F_8	O	O	O	F_{20}	O	H	O
F_9	O	H	H	F_{21}	O	H	H
F_{10}	O	H	H	F_{22}	O	H	H
F_{11}	H	H	H	F_{23}	O	O	H
F_{12}	O	H	H	F_{24}	O	O	H

*Homogeneous, Stable=O; Heterogeneous=H (signs of phase separation)

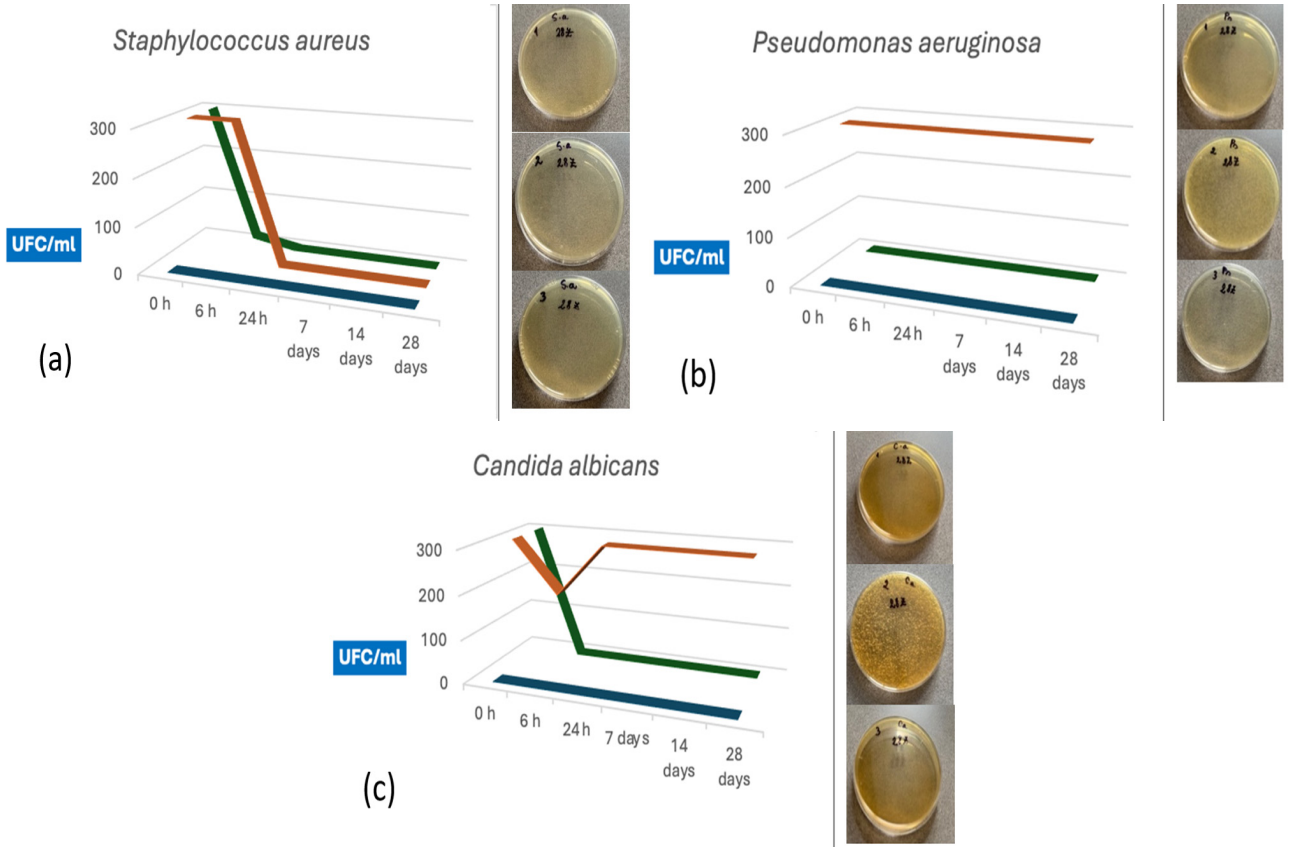


Figure 3. The evolution of the number of UFC/mL (**a**) *Staphylococcus aureus* (**b**) *Pseudomonas aeruginosa* (**c**) *Candida albicans* of the products tested at different time intervals.

The visual characteristics of products are presented in table III.

3. Choosing an effective preservative for a cosmetic product

The results obtained from the microbiological study on the *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans* are shown in figure 3.

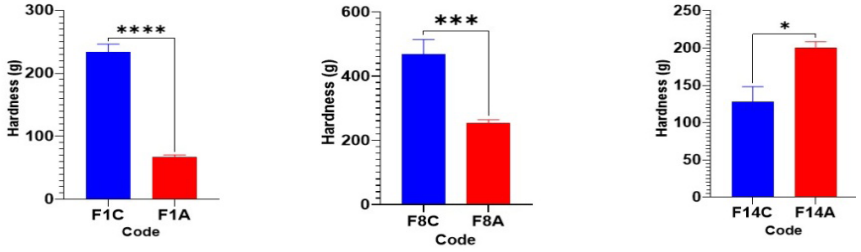
4. Determination of texture characteristics of cream bases

The results obtained from the texture analysis of the products regarding hardness, cohesiveness, consistency and viscosity are presented in table IV.

The obtained data were processed statistically to evaluate the significance of the differences (Figures 4, 5, 6).

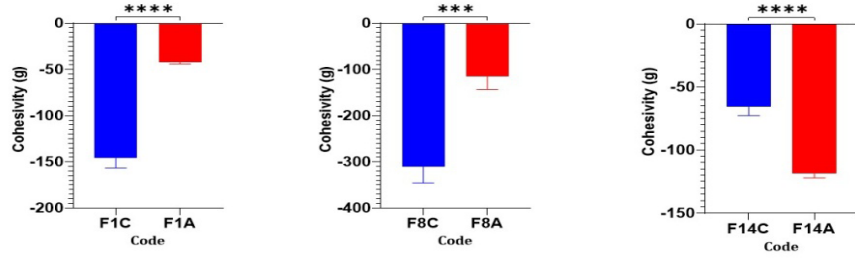
Table IV. Texture parameters for emulsified cream bases made by the traditional (classic)/automatic preparation method.

F-formula codification		Classic Method				Automatic Method			
		Hardness (g)	Cohesiveness (-g)	Consistency (g.s)	Index viscosity	Hardness (g)	Cohesiveness (-g)	Consistency (g.s)	Index viscosity
F_1	Mean	240.079	-145.986	344.689	-318.120	67.697	-42.114	138.547	-147.199
	SD +/-	12.303	10.607	46.476	40.766	2.908	1.758	6.525	8.272
F_8	Mean	468.338	-313.804	629.098	-582.387	237.718	-114.973	276.486	-196.703
	SD +/-	45.504	32.174	101.321	47.056	42.297	28.319	36.668	27.523
F_{14}	Mean	127.959	-66.374	224.150	-196.166	211.371	-66.374	393.190	-321.183
	SD +/-	20.375	6.202	33.529	34.655	28.833	6.202	69.818	43.293



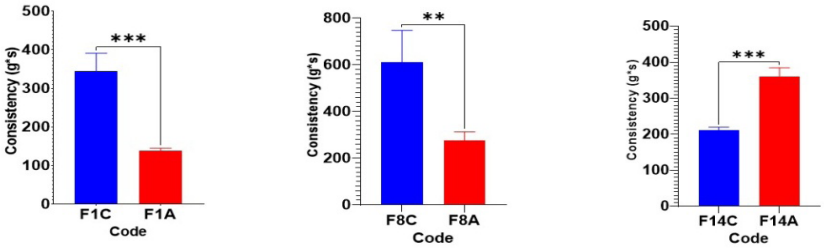
*C-Classical preparation method; A-Automatic preparation method; the significance level of the ~~normality~~ t test between the two values (C/A); without statistical significance (p>0.05), * (p<0,05), **(p<0,01),*** (p<0,001),**** (p<0,0001).*

Figure 4. The hardness (firmness) of the cream bases obtained with the help of the texture analyzer for the formulas F1, F 8 and F14 made by the method of classical preparation vs automatic preparation and the level of significance of the t test between the two values.



*C-Classical preparation method; A-Automatic preparation method; the significance level of the ~~normality~~ t test between the two values (C/A); without statistical significance (p>0.05), * (p<0,05), **(p<0,01),*** (p<0,001),**** (p<0,0001).*

Figure 5. The cohesiveness of the cream bases obtained with the help of the texture analyzer for the formulas F1, F 8 and F14 made by the method of classical preparation vs automatic preparation and the level of significance of the t test.



*C-Classical preparation method; A-Automatic preparation method; the significance level of the ~~normality~~ t test between the two values (C/A); without statistical significance (p>0.05), * (p<0,05), **(p<0,01),*** (p<0,001),**** (p<0,0001).*

Figure 6. The consistency of the cream bases obtained with the help of the texture analyzer for the formulas F1, F 8 and F14 made by the method of classical preparation vs automatic preparation and the level of significance of the t test.

Discussion

The stability of the cream bases made with methyl glucose sesquistearate as an emulsifier (F_1-F_4) can be attributed to the careful selection of the surfactant. This surfactant, with its special water binding capacity, when combined with stearic acid, effectively stabilizes the formed emulsion. The rotation speed and homogenization time the formulas were subjected to when mixing did not negatively influence the appearance of the W/O emulsion cream bases.

The choice of preparation method is crucial for the appearance and homogeneity of the cream bases obtained. Even if the product is homogeneous after preparation by the three proposed methods, the appearance differs considerably. Homogenization with a certain intensity and including a limited amount of air in the stable emulsifying system generates an emulsifying cream base with a desirable appearance, lighter in color, and with different spreading properties on the skin (Figure 2).

In the preparation by the semi-automatic method, a preliminary test was carried out using several rotation speeds of the homogenizer, but because in some formulas, the lipophilic phase solidified before the emulsification process was completed, it was decided to stir continuously without interruption at maximum number of revolutions, 1000 rpm. Furthermore, recent studies have also recommended using a stirring speed of 1000 rpm for 10 minutes for emulsion creams, as illustrated in table III [12-15].

In automatic and semi-automatic preparation only Group I, Group II and Formula F_{14} are stable.

All the formulas prepared by the classic method have a pleasant, homogeneous appearance and present a yellowish-white color and a smell characteristic of the components. They have the right consistency to be applied to the skin. The exception is formula F_{11}, which was excluded from the study.

According to the standards of the European Pharmacopoeia, the reduction in the number of microorganisms in topical preparations must be total 14 days after the insertion of the preservative. Between time 0 and day 14, the number of colonies should gradually decrease, and on day 28, the growth of the studied strains should no longer be observed. The antimicrobial preservative is considered effective if the number of microorganisms is reduced according to cosmetic product standards [1]. The results obtained in the microbiological study for the preservative solutions might be extrapolated to the cream bases, future studies being recommended to confirm this presumption.

The results of the Cosgard® 1% solution (solution 1) efficacy tests are excellent from time 0 of the test on all three strains. Cosgard® 1% solution did not allow the growth of microorganisms and had immediate bactericidal activity. For *Staphylococcus aureus, Pseudomonas aeruginosa* and *Candida albicans* the number of UFC/ml was 0 from the zero time point of testing until the end of the study, 28 days after contamination.

While the parabens solution (solution 2) is widely recognized for its role in ensuring the microbiological stability of topical pharmaceutical and cosmetic products, our findings reveal its limitations. The efficiency of parabens solution is lower compared to the Cosgard® 1% solution or the Euxyl® PE 9010 1% solution. It is important to note that the preservative solution has only bacteriostatic and not bactericidal properties. It inhibited colony growth only in the case of *Staphylococcus aureus*. After 24 hours from the addition of the preservative, the number of UFC/ml of *Staphylococcus aureus* was 0, and by the end of the study (28 days) no more colonies had developed on the culture medium. However, on the *Pseudomonas aeruginosa* strain, the 0.1% parabens solution had no effect, not influencing the development of this microorganism. From time 0 to the end of the study, the UFC/ml of *Pseudomonas aeruginosa*

remained above 300 UFC/ml, demonstrating that solution 2 has no antimicrobial activity for this strain (Figure 3).

The 0.1% preservative solution has neither activity on the *Candida albicans* strain. At 24 hours, 7 days, 14 days, and 28 days after inoculation, the number of UFC/ml of *Candida albicans* was over 300 UFC/ml. A small change in the number of colonies can be seen 6 hours after the application of solution 2, with the number of UFC/ml of *Candida albicans* being 180, but after 24 hours, it increased again to over 300 UFC/ml (Figure 3).

The Euxyl® PE 9010 1% solution (solution 3) has been subjected to rigorous testing and has shown very good activity on all three strains tested. For *Pseudomonas aeruginosa* and *Candida albicans*, the number of UFC/ml was 0 from the plate application of Euxyl® PE 9010 1% solution until the end of the study, 28 days after application. For *Staphylococcus aureus*, Euxyl® PE 9010 1% needed 24 hours to entirely reduce UFC/ml, so after 24 hours of testing the number of UFC/ml was 0 (Figure 3).

Comparing texture properties to identify the structural differences between the emulsion networks formed, can be considered as an indication of the spreadability of a cream-type cosmetic product.

The textural properties of creams are essential in determining consumer preference, where variation in the lipophilic phase content of the formulation has a direct influence on the sensory characteristics of the product [16-20]. The high content of viscosity-increasing agents, such as stearic acid, cetyl alcohol or glyceryl stearate, visibly changes the sensory characteristics of the final product. The compression extrusion test consists of applying a force to the product until it passes through the space between the probe perimeter and the container. Formulations with a higher amount of lipophilic phase, especially with a solid lipophilic component, have an increased flow rate over the piston, forming steeper areas.

The firmness can be defined as the force required to obtain a deformation, the positive area, including the consistency characterized by the internal force of the bonds made in the emulsion system, and the negative area is the force required to "pull" the probe from the sample (aspiration).

Firmness was evaluated for the F_1 formula obtained by the classical preparation method compared to that obtained by automatic preparation (Table IV), and the significance level of the t test between the two values, demonstrates a highly significant correlation, with a $p < 0.0001$ (Figure 4).

The same highly significant correlation, with a $p < 0.0001$ (Figure 5), was also found regarding the cohesiveness of the F_1 formula obtained by the classic preparation method compared to the automatically prepared one.

Also, the consistency which was evaluated for the F_1 formula obtained by the classical preparation method compared to that made by automatic preparation, and the significance level of the t test between the two values, demonstrates a highly significant correlation, with a $p < 0.0001$ (Figure 6).

The preparation method differentiated the cream bases regarding their textural characteristic, through the automatic method lower values of consistency, firmness, and cohesiveness being obtained.

In the case of the F_8 formula, the firmness and consistency show double values, and the cohesiveness is approximately three times higher when prepared by the classic method. The results obtained can be explained by the large amount of glyceryl stearate, 8.5%, a solid lipophilic component that leads to an increased viscosity of the emulsion system.

The results obtained for formula F_{14}, prepared by the two proposed preparation methods, were compared for statistical significance, and a $p<0.001$ was obtained as level of statistical significance. The firmness value for F_{14} made by the automatic preparation method is 60% higher, compared to the value obtained with the same formula made by classical preparation. Ceteareth-20, an emulsifier used mainly by industry, makes emulsifying creams with a texture more suitable for automatic preparation.

Optimal values for firmness, consistency or cohesiveness for various cream bases depend on each skin type.

The final consumer will decide according to the skin typology and his preference the choice of a certain emulsifying cream. In general, for dry, dehydrated, even atopic skin, O/W emulsion bases are recommended, but a higher consistency is preferred to allow the lipophilic phase to restore the intercorneocyte cement and avoid transepidermal water loss. If only a moisturizing action is desired for normal skin, a lighter, almost fluid consistency is recommended for superior spreadability, and in the case of mature, dry skin, a larger consistency is desired, which it allows keeping an occlusive layer on the surface, achieving a superior hydration effect [2-4]. If a cosmetic cream is applied to dry, dehydrated skin, and it does not form an occlusive film, the applied product does not have time to restore the natural skin barrier, and the sensation of dehydration persists [20-22].

All determined texture parameters indicated a real difference between traditional and automatic preparation and significantly changed the consistency, firmness and cohesiveness of the custard bases. Depending on the emulsifier used and the preparation method used, these emulsifying cream bases have different texture parameters and a different appearance, respectively color.

Conclusions

The preparation method is considered an essential criterion for the stability of the emulsion system. Of all the 24 proposed bases only 9 can be integrated to formulate individualized cosmeceutical products or pharmaceutical preparations for dermatologist use in the pharmacy prescription. Secondly, choosing the suitable preservative could be also considered an important criterion for the stability of emulsion bases. According to the results obtained in the present study, the three proposed solutions, Cosgard® and Euxyl® PE 9010 can be used as a suitable preservative. Parabens solution was not shown as effective as previous ones on the strains studied, so we do not recommend it in current practice as a common preservative for cosmetic cream bases.

Results obtained in the sensory analysis further support the selection of the cream bases F_1, F_8 and F_{14}, prepared by the automatic method, for the formulation of the final individual products.

References

1. Ferreira MS, Magalhães MC, Oliveira R, Sousa-Lobo JM, Almeida IF. Trends in the Use of Botanicals in Anti-Aging Cosmetics. Molecules. 2021;26:3584.
2. Potaś J, Wach RA, Rokita B, Wróblewska M, Winnicka K. Evaluation of the impact of tragacanth/xanthan gum interpolymer complexation with chitosan on pharmaceutical performance of gels with secnidazole as potential periodontal treatment. Eur J Pharm Sci. 2024;192:106657.
3. Bîrsan M, Drăgan M, Stan CD, Cristofor AC, Palimariciuc M, Stan CI, et al. Patient satisfaction regarding compounded pharmaceutical products and implication on pharmaceutical practice management. Farmacia. 2021;69:806-812.
4. Manea A, Perju D, Tămaș A. The Method of Studying Cosmetic Creams Based on the Principles of Systems Theory and Mathematical Modeling Techniques. Cosmetics. 2023;10:118.
5. Kulkarni VS, Shaw C. Essential Chemistry for Formulators of Semisolid and Liquid Dosages, 1st ed.; Academic Press: Cambridge, MA, USA. 2016; p.29–41.
6. Saleh MM, Abuhamdan RM, Alshaer W, Amarin M, Abdelnabi H, Abdaljaleel M, et al. Cosmeceutical formulations of pro-vitamin E phosphate: In-vitro release testing and dermal penetration into excised human skin. Int J Pharm. 2023;636:122781.
7. Sznitowska M, Wolska E, Baranska H, Cal K, Pietkiewicz J. The effect of a lipid composition and a surfactant on the characteristics of the solid lipid microspheres and nanospheres (SLM and SLN). Eur J Pharm Biopharm. 2017;110:24-30.
8. Aulton ME, Taylor KMG. Topical and transdermal drug delivery. In Aulton's Pharmaceutics. The Design and Manufacture of Medicines, 4th edition. Churchill Livingstone Elsevier. 2013; p.675-698.
9. Benson HAE. Skin Structure, Function, and Permeation. In Transdermal and Topical Drug Delivery Principles and Practice Edited by Benson HAE, Watkinson AC. Wiley. 2012; p.16-18.
10. Bîrsan M, Gore E, Stan CD, Cristofor AC, Palimariciuc M, Scripcariu ȘI, et al. Development and evaluation of hydrophilic cream bases suitable for custom cosmetic skincare or compounding pharmaceutical dermal products. Farmacia. 2022;70:880-889.
11. Huynh A, Garcia AG, Young LK, Szoboszlai M, Liberatore MW, Baki G. Measurements meet perceptions: rheology-texture-sensory relations when using green, bio-derived emollients in cosmetic emulsions. Int J Cosmet Sci. 2021;43:11-19.
12. Zhang Y, Obuchi H, Toyota T. A Practical Guide to Preparation and Applications of Giant Unilamellar Vesicles Formed via Centrifugation of Water-in-Oil Emulsion Droplets. Membranes. 2023;13:440.
13. Khairnar SV, Pagare P, Thakre A, Nambiar AR, Junnuthula V, Abraham MC, et al. Review on the Scale-Up Methods for the Preparation of Solid Lipid Nanoparticles. Pharmaceutics. 2022;14:1886.
14. Tafuro G, Costantini A, Piatto M, Lucchetti S, Francescato S, Busata L, et al. Eco-Designing Cosmetic Products while Preserving the Sensorial-Application Properties: An Instrumental Approach toward Sustainable Formulations. Cosmetics. 2024;11:60.
15. Bialas I, Zelent-Kraciuk S, Jurowski K. The Skin Sensitisation of Cosmetic Ingredients: Review of Actual Regulatory Status. Toxics. 2023;11:392.
16. Bîrsan M, Cojocaru I, Stamate M, Teodor V, Tuchiluș C. Antifungal action of imidazole derivates from new pharmaceutical forms on various strains of candida. Rev Chim. 2016;67:1385-1388.
17. Gómez-Farto A, Jiménez-Escobar AL, Pérez-González N, Castán H, Clares B, Arias-Santiago S, et al. Development of an Emulgel for the Effective Treatment of Atopic Dermatitis: Biocompatibility and Clinical Investigation. Gels. 2024;10:370.
18. Moussour M, Lavarde M, Pensé-Lhéritier AM, Bouton F. Sensory analysis of cosmetic powders: personal care ingredients and emulsions. Int J Cosmet Sci. 2017;39:83-89.
19. Dumitrașcu DI, Georgescu AV. The management of biofilm formation after hyaluronic acid gel filler injections: a review. Clujul Med. 2013;86:192-195.
20. Nicol NH, Rippke F, Weber TM, Hebert AA. Daily Moisturization for Atopic Dermatitis: Importance, Recommendations, and Moisturizer Choices. J Nurse Pract. 2021;17:920–925.
21. Cheng C, Terreno E. Development of a versatile optical pH sensor array for discrimination of anti-aging face creams. Talanta. 2024;278:126447.
22. Verdier-Sévrain S, Bonté F. Skin hydration: a review on its molecular mechanisms. J Cosmet Dermatol. 2007;6:75-82.