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Optimization of cleansing oil formulation containing polyglyceryl-6 caprylate and polyglyceryl-4 caprate using the response surface method

Ayşenur Kılıç [1,2] & Burak Çelik [2]

[1] İstanbul University, Institute of Graduate Studies in Health Sciences, Department of Pharmaceutical Technology, İstanbul, Türkiye
[2] Bezmialem Vakıf University, Department of Pharmaceutical Technology, İstanbul, Türkiye

Abstract

Background and Aims: Natural raw materials used in skin cleansing products have recently become popular. In this study, natural-origin raw materials were used to develop an oil-based cleanser formulation with high foaming ability and stable properties. The researchers attempted to obtain the optimum formulation by determining the optimised polyglyceryl-6 caprylate/polyglyceryl-4 caprate (PG-6/PG-4) ratio.

Methods: Cleansing formulations were prepared using caprylic/capric triglyceride (CCT), hemp seed oil, and PG-6/PG-4. The D-optimal response surface design was used to determine the optimum formulation component ratios. The foaming volumes and the transparency of the formulations were also evaluated. The pH and viscosity of the formulations were also measured. Stability tests of the formulations were carried out at 40°C and 75% relative humidity conditions for 2 months. The optimum component quantities were determined by the Design-Expert software.

Results: The ratios of the formulation components were found to be 4.3% for PG-6/PG-4, 5.6% for water, and 34.1% for CCT as optimised formulation. The foam volume was found to be 1.06 mL, and the transparency was observed to be 4 out of the maximum 5. The pH of the formulation was 6.61. It exhibited pseudoplastic flow properties, and as a result of stability studies, there were no significant changes in its pH, transparency, and foaming properties.

Conclusion: In this study, we obtained a cleansing product composed of natural compounds with acceptable properties and stability.

Keywords Cosmetics · Experimental design · Hemp seed oil · Skincare · Surface-active agents

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Corresponding author: Ayşenur Kılıç ecz.aysenurkilic@gmail.com

INTRODUCTION

Soaps and syndets, also called synthetic detergents, are frequently used for skin cleansing products. The skin cleansing products were initially introduced as bar form, then soft detergents such as shower cream or humective body wash gel formulations were began to be used (Ananthapadmanabhan et al., 2004). The effectiveness of skin cleansers mainly comes from surfactants, because these substances reduce the surface tension of skin, trap dirt, and depollute it (Effendy & Maibach, 1995; Kuehl et al., 2003). In affinity-based cleansing, which is the most basic form of skin cleansing treatment, hydrophobic dirt from the skin can be cleaned with oils, whereas hydrophilic dirt can only be cleaned with water. However, cleaners such as classic soap and contemporary syndets that use surface-active agents dissolve the dirt in the micelles through water, thereby ensuring their removal (Corazza et al., 2010).

Surface-active agents are chemically amphiphilic compounds. This means that they have an oleophobic/polar head and a lipophilic/non-polar tail in their chemical structure. Due to these structures, surface-active substances that can be dissolved in both aqueous media and organic solvents can diminish the surface tension at both the gas–liquid interface and between the liquid and the liquid (oil-water) (Effendy & Maibach, 1995). When surfactants are added to the solution, they form spherical micellar complexes at levels above the critical micelle concentration. In these micelle structures, the long alkyl-chain lipophilic endings in the structure of the surfactant dissolve in oil, and the hydrophilic parts with affinity for water surround the outside of the lipophilic structure (Effendy & Maibach, 1995). Surfactants dissociate in aqueous solutions and are examined under 4 classes: cationic, anionic, non-ionic, and amphoteric, according to the presence of ionic charges and at the hydrophilic end. Of these, cationic, anionic, and amphoteric molecules are charged molecules, whereas non-ionic ones are uncharged molecules (Effendy & Maibach, 1995; Friedman & Wolf, 1996).

Some polyglyceryl fatty acid esters such as polyglyceryl-4 caprate, polyglyceryl-6 caprylate, and polyglyceryl-10 caprylate/caprate are preferred in cosmetics and are often used to dissolve perfumes or as foam enhancers in cosmetic products. However, polyglyceryl-4 caprate should be combined with different substances to remove makeup or transparent/subtransparent cosmetic products from the skin (Zhang et al., 2020).

Cosmetic preparations examined under the name of cleansing oils can often be used to remove makeup from the skin. Cleansing oils, which involve oils of natural or synthetic origin, can dissolve products used for cosmetic purposes and readily clean them from the skin while also standing out because of their softening properties (Ertel, 2005; Sakamoto et al., 2017). Naturally sourced oils are preferred for use as cleansing oils. The reason is that natural oils may contain skin-specific active ingredients and biological substances like essential fatty acids. In addition, they have antioxidant activity (Raknam et al., 2020).

Herbal oils are principally used to form the oil phase of emulsions in cosmetic products, and the oils with unsaturated fatty acids are particularly diverse. Hemp seed oil extracted from *Cannabis sativa* L., is of great importance in this context. Hemp seeds contain abundant amounts of α-linolenic acid, linoleic acid, β-carotene, minerals, and vitamins. Along with the γ-linolenic acid it contains, hemp seed oil is used as an excellent oil in light body oils and lipid-rich creams and is remarkable for its ability to penetrate through the skin. Lack of essential fatty acids in the body manifests itself as dermatological disorders, such as atopic dermatitis, acne, and scaly skin (Muggli, 2005; Tadić et al., 2021). In addition, essential fatty acids, when applied to the skin, improve its appearance and to protect its function (Nicolaou, 2013). Due to these properties of hemp seed oil, it is used in cosmetics.

Yucca schidigera Roezl ex Ortgies, which is examined under the Agavaceae family and grows mainly in Mexico and Southwest America, has been used by the public for many years because of its therapeutic effects. Because of its saponins, yucca extract is widely used in pharmaceutical, beverage, and cosmetic industries (Tanaka et al., 1996). Yucca extract is a natural raw material with foaming properties owing to its high saponin content (Oleszek et al., 2001). The purpose of using yucca extract in this study was to evaluate its contribution to the foaming ability of the formulations.

The purpose of conventional formulation design is to change one variable while keeping the other variables constant and realise a design in this way. However, such a design requires numerous trials to determine the optimum formulation components. Due to significant work and time, the research and development costs increase. The response surface methodology (RSM) examines the connections among various variables and evaluates their impacts on output. This statistical model is effective for determining optimum rates in formulation design (Ge & Ge, 2015; Ravar et al., 2016; Wang et al., 2014). This study aimed to develop a skin cleansing formulation with high foaming ability and stable properties using natural raw materials. In addition, D-optimal design was used to determine the optimum ratios in the formulation design. The formulations are prepared by adding the oil phase to the water phase using a mechanical mixer. The foaming abilities of the resulting formulations were measured, and the degree of transparency was determined. As a result, the viscosity of the optimised formulation was measured in addition to these measurements.

MATERIALS AND METHODS

Materials

Glycerine was purchased from the Manolya Natural and Aromatic Products Company (Isparta, Türkiye). CCT, hemp seed oil, PG-6/PG-4, and yucca extract were purchased from Croda, Phoenix Chemical, Evonik – Personal Care, and Bio-Botanica, respectively.

Preparation of Makeup Removal Formulations

All formulations were prepared at a room temperature of 25ºC. Glycerine and PG-6/PG-4, which form phase A, are weighed separately and combined in a beaker. The water and yucca extract in phase B are weighed in separate beakers. CCT and hemp seed oil are weighed in separate beakers to form phase C. Phase A was placed under the overhead mixer, mixing began at 650 rpm, and phase B was added and mixed for 1 min. Afterward, the C phase containing the oil phase was added dropwise to the mixture, stirring at 650 rpm for 20 min, to ensure that the oil phase was incorporated into the mixture. When the oil phase is added, the mixing continues under the same conditions for another 5 min. The prepared formulation was transferred to a glass vial (Alchemy, 2024).

Experimental Design Using the RSM

Make-up remover formulations containing natural ingredients with high stability were optimised by the RSM. In this study, the hemp seed oil concentration was kept constant at 5% in all formulations, the PG-6/PG-4 concentration varied between 3% and 5%, the amount of water varied between 4% and 10%, and the CCT concentration varied between 30% and 50%. The amount of glycerine varies according to these variables. Three factors were studied using a response surface D-optimal design with 5 lack of fit points and 5 replicates.

Design-Expert software (version 13.0.5.0; Stat-Ease, Inc., Minneapolis, MN, USA) was used for the experimental design and statistical analysis. The response was estimated using the following quadratic polynomial equation:

$$Y = \beta_0 + \beta_1 A + \beta_2 B + \beta_3 C + \beta_{12} AB + \beta_{13} AC + \beta_{23} BC + \beta_{11} A^2 + \beta_{22} B^2 + \beta_{33} C^2$$

where Y is the predicted response; A, B, and C are independent variables; β_0 is the intercept; β_1, β_2 and β_3 are linear coefficients; β_{12}, β_{13} and β_{23} represent interaction coefficients; and β_{11}, β_{22} and β_{33} represent quadratic coefficients (Ravar et al., 2016).

Analysis of variance (ANOVA) was used to interpret the impact of independent variables on the responses and $P<0.05$ was accepted as statistically significant. The predicted (pred.) and adjusted (adj.) determination coefficients (R^2) were calculated to interpret the suitability of the model. Three-dimensional surface graphs were created to illustrate the experimental region and the impacts of independent variables on the output.

Foam Test

The procedure was followed the study by Schreiner et al. with some modifications (Schreiner et al., 2021). To perform the foam test, 0.5 g of the prepared formulation was weighed and filled with up to 5 mL of water to prepare a 5 mL sample of 10% (w/v) in a 15 mL falcon tube. The falcon tube was capped and shaken vigorously upside down 10 times. The height of the volume as a result of shaking (T_0) was recorded. Foam stability was determined by measuring the foam volume after 15 min (T_{15}).

Transparency Evaluation

To assess transparency, the formulations (Run 1-24) were placed in transparent glass bottles and optically assessed against a white background under a light source (Hussein, 2014). Evaluation was performed by scoring from 1 to 5 points (1, 2, 3, 4, 5) according to the degree of transparency. The formulations with the least transparency received 1 point and those with the highest transparency received 5 points.

Measurement of pH

The pH value of the optimised formulation was diluted with distilled water at a ratio of 1:10 and measured using a bench-type pH metre (AB33PH-F, Ohaus Aquasearcher™, Switzerland).

Viscosity Measurements

To evaluate the flowability of the optimised skin cleansing formulation, the viscosity of the optimum formulation was measured by oscillation tests at different shear rates using a rheometer (Anton Paar MCR 102, Switzerland). Viscosity measurements were carried out at a constant temperature of 24ºC and a parallel plate with a radius of 25 mm was used with a space of 0.5 mm between the plates. 0.15 mL of the sample was used on the measuring plate to measure the viscosity. Viscosity studies were conducted by taking 110 samples at shear rates ranging from 0.01 to 100 s^{-1}.

Evaluation of Cleansing Effectiveness

To evaluate the cleaning effectiveness of the optimum formulation, the method used by the Raknam group was used with minor modifications (Raknam et al., 2020). The goal is to compare the cleansing effectiveness of the formulations applied on makeup against water. First, a lipstick (Deluxe Cashmere, Türkiye) and a liquid foundation (Pretty Beauty Matte Finish, Türkiye) were applied to glass slides and left to dry for 10 min. Photographs of the slides were taken before applying the product. Afterward, the optimised formulation was added to cover the make-up area and gently massaged with a gloved hand 10 times. Afterwards, 5 mL of water was added to each of them separately and they were massaged again 10 times. 5 mL of water was added to slides treated with water only, and slides were massaged 20 times each. After these procedures, the slides were photographed again, and the cleaning effectiveness of the product was evaluated in comparison with water.

Stability Studies

In order to evaluate the stability of optimised formulation, 10 mL of the formulation was taken into a 15 mL falcon tube. It was kept in the stability cabinet (Pol-Eko KKS 115, Poland) at 40ºC and 75% relative humidity for 2 months. At the beginning and at the end of 7th, 15th, 30th, and 60th days, the pH, phase separation after centrifugation, foaming ability, and transparency of the optimised formulation were evaluated at both temperature (25ºC and 40ºC). Centrifugation test was performed at 4000 rpm for 20 min on the samples, then the phase separation of the formulation by the centrifugal force method was evaluated.

Table 1. D-optimal design matrix and corresponding responses

Run	Variables				Responses	
	A: PG-6/PG-4 (%)	B: Water (%)	C: CCT (%)	D: Yucca (%)	R_1: Foaming (mL)	R_2: Transparency
1	3.9	6.5	30.0	1	1.5	5
2	4.2	9.9	30.0	0	2.25	4
3	4.0	10.0	39.0	1	1.0	2
4	4.9	4.3	37.5	1	1.5	3
5	3.0	4.0	40.0	0	0.25	3
6	3.9	7.0	45.6	1	0.5	5
7	4.0	10.0	39.0	1	1.25	2
8	3.7	7.9	49.1	0	0.5	4
9	4.9	4.3	37.5	1	1.5	3
10	5.0	9.7	30.0	1	2.5	3
11	5.0	8.0	50.0	1	1.0	3
12	3.7	4.0	50.0	1	0.25	4
13	4.8	7.7	38.8	1	1.5	5
14	4.3	6.1	30.8	0	2.0	5
15	3.0	7.2	38.6	1	0.5	5
16	3.0	10.0	50.0	1	0.5	1
17	3.0	7.2	38.6	1	0.5	5
18	5.0	10.0	39.9	0	2.0	2
19	3.7	7.9	49.1	0	0.5	4
20	4.3	6.1	30.8	0	2.0	4
21	5.0	4.0	50.0	0	0.5	1
22	3.1	4.0	30.0	1	0.75	2
23	3.4	9.5	30.0	1	1.25	3
24	3.0	10.0	30.0	0	0.75	2

Abbreviations: CCT, caprylic/capric triglycerides; PG-6/PG-4, polyglyceryl-6 caprylate, polyglyceryl-4 caprate.

RESULTS AND DISCUSSION

Experimental Design

Design Model and Data Analysis

The D-optimal design setup and results from 24 experiments are exhibited in Table 1. The following quadratic second-order equation was used to estimate the maximum foaming:

$$R_1 = 0.9726 + 0.6014A + 0.1865B - 0.5822C + 0.0610AB - 0.2974AC + 0.0927BC - 0.0157A^2 - 0.0017B^2 + 0.1620C^2$$

where R_1 is foaming (mL), and *A*, *B*, and *C* are coded values for PG-6/PG-4, water, and CCT weight ratios (%), respectively. The regression model was tested using ANOVA for foaming (Table 2) and transparency (Table 3). The *P* values of the ANOVA results in Table 2 indicate that changes in the ratio of PG-6/PG-4 (surfactant) to CCT (oil phase) were the factors that most influenced the foaming of the formulations. According to the results in Table 3, when we examine the *P* values, it is assessed that the water content is the factor that directly affects transparency the most. In addition, the water-to-CCT ratio was also considered as an important parameter affecting transparency.

According to the responses, a high *F* value (54.41) and low *P* value (0.0001) indicated that the model equation was statistically significant. The lack of fit value of the model was statistically insignificant (*P*=0.0517), which implies that the model fits well. The confidence level of the regression model was verified by an R^2 value of 0.9722, which indicated that 97.22% of the variability in the response can be explained by this model. The pred. R^2 value of 0.8602 is in close agreement with the adj. The R^2 value of 0.9543 demonstrated a high correlation between the observed and predicted values in this case.

Table 2. ANOVA for response R_1 (Foaming)

Source	Sum of squares	df	Mean square	*F*-value	*P*-value
Model	10.33	9	1.15	54.41	< 0.0001
A: PG-6/PG-4	4.33	1	4.33	205.26	< 0.0001
B: Water	0.4209	1	0.4209	19.96	0.0005
C: CCT	4.27	1	4.27	202.64	< 0.0001
AB	0.0298	1	0.0298	1.41	0.2545
AC	0.5037	1	0.5037	23.88	0.0002
BC	0.0518	1	0.0518	2.46	0.1394
A^2	0.0009	1	0.0009	0.0421	0.8404
B^2	0.0000	1	0.0000	0.0005	0.9826
C^2	0.1181	1	0.1181	5.60	0.0329
Residual	0.2953	14	0.0211		
Lack of fit	0.2640	9	0.0293	4.69	0.0517
Pure error	0.0313	5	0.0063		
Corrected total	10.62	23			

Note: R^2=0.9722, adj. R^2: 0.9543, pred. R^2: 0.8602.
Abbreviations: adj., adjusted; ANOVA, analysis of variance; pred., predicted; CCT, caprylic/capric triglycerides; PG-6/PG-4, polyglyceryl-6 caprylate, polyglyceryl-4 caprate.

Table 3. ANOVA for response R_2 (Transparency)

Source	Sum of squares	df	Mean square	*F*-value	*P*-value
Model	36.44	9	4.05	19.62	< 0.0001
A: PG-6/PG-4	0.9415	1	0.9415	4.56	0.0508
B: Water	2.25	1	2.25	10.91	0.0052
C: CCT	1.09	1	1.09	5.28	0.0375
AB	0.8635	1	0.8635	4.18	0.0601
AC	1.80	1	1.80	8.73	0.0104
BC	3.56	1	3.56	17.23	0.0010
A^2	0.5752	1	0.5752	2.79	0.1172
B^2	23.96	1	23.96	116.09	< 0.0001
C^2	0.6882	1	0.6882	3.33	0.0892
Residual	2.89	14	0.2064		
Lack of fit	2.39	9	0.2655	2.65	0.1474
Pure error	0.5000	5	0.1000		
Corrected total	39.33	23			

Note: R^2=0.9265, adj. R^2: 0.8793, pred. R^2: 0.6870.
Abbreviations: adj., adjusted; ANOVA, analysis of variance; pred., predicted; CCT, caprylic/capric triglycerides; PG-6/PG-4, polyglyceryl-6 caprylate, polyglyceryl-4 caprate.

The following second equation was used to estimate the maximum transparency:

$$R_2 = 5.17 - 0.2805A - 0.4314B - 0.2940C + 0.3287AB - 0.5626AC - 0.7680BC - 0.3995A^2 - 2.52B^2 - 0.3910C^2$$

where R_2 is the transparency, and *A*, *B*, and *C* are the coded values for PG-6/PG-4, water, and CCT weight ratios, respectively. The model's *F* value (19.62) and low *P* value (0.0001) implied the significance of the model equation, as displayed in Table 3. The lack of fit of the model (*P*=0.1474) was not significant. According to the coefficient R^2 value of 0.9265, 92.65% of the variability in transparency could be explained by the model. There was a correlation between adj. R^2=0.8793 and pred. R^2=0.6870, which ensured the predictability of the model, as the difference was less than 0.2.

The Formulation Optimization Study

The optimum rates were determined by the Design-Expert software based on the obtained results from the D-optimal design study. While optimising, yucca extract was neglected because it did not have any effect. The variables tried to be optimised in this study were PG-6/PG-4, water, and CCT.

The desired limits were set as maximised transparency and foaming for formulation. In order to effectively remove the makeup, it is important that the amounts of PG-6/PG-4, water, and CCT are at the optimum ratios. For this reason, the amounts of PG-6/PG-4, water, and CCT were determined as independent variables. Three-dimensional surface plots for R_1 (foaming) as a function of PG-6/PG-4 and water weight percentages at a fixed CCT content, PG-6/PG-4 and CCT weight percentages at a fixed water content, and water and CCT weight percentages at a fixed PG-6/PG-4 content are presented in Figure 1A–C, respectively. Three-dimensional surface plots for R_2 (transparency) as a function of PG-6/PG-4 and water weight percentages at a fixed CCT content, PG-6/PG-4 and CCT weight percentages at a fixed water content, and water and CCT weight percentages at a fixed PG-6/PG-4 content are presented in Figure 1D–F, respectively. Figure 1B shows that as the PG-6/PG-4 ratio used as a surfactant increased, the foaming ability significantly increased. It can be seen from Figure 1D that transparency was at its highest level at a 5% to 8% water ratio.

The coded variables for optimised formulation were *A* = 4.3%, *B* = 5.6%, and *C* = 34.1%. The optimised formulation was prepared in triplicate to assess the model accuracy for the optimum states. According to the foaming and transparency results, the optimised formulation shows 1.5 mL foam, and its transparency score was 4.62. The experimental and predicted results for optimised variables are presented in Table 4.

After the optimised formulation was prepared in three repetitions, the average pH of the formulations was 6.61±0.25. The viscosity measurements, which provide information about

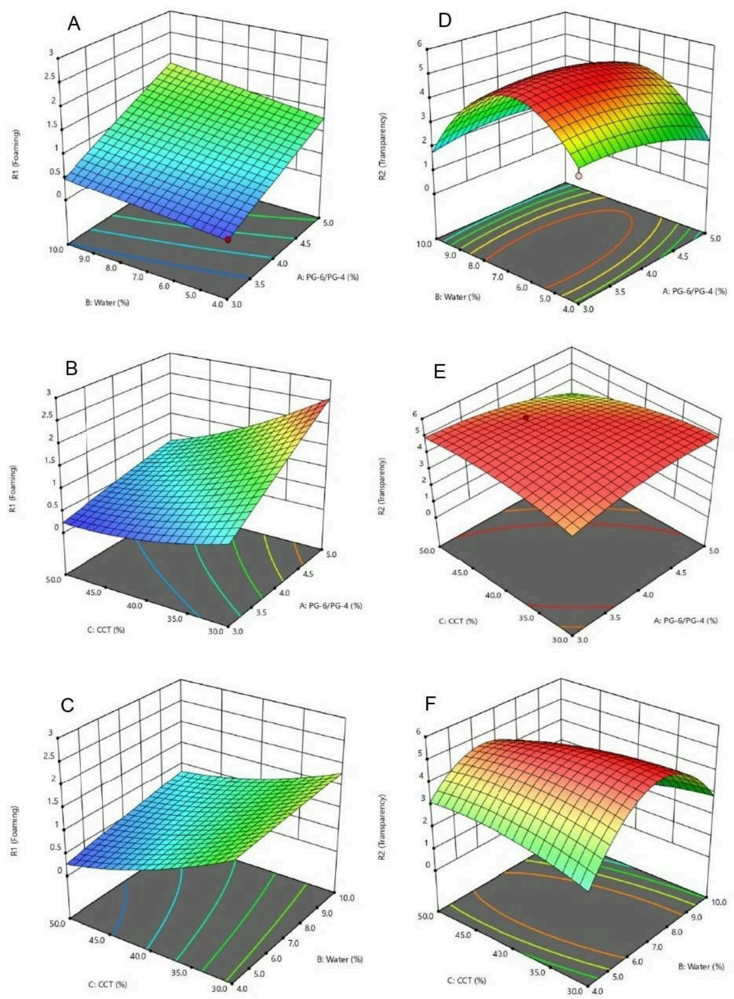

Figure 1. Response surface plot for R1 (foaming) as a function of **(A)** water and PG-6/PG-4 weight ratios at fixed CCT content, **(B)** PG-6/PG-4 and CCT weight ratios at fixed water content, and **(C)** CCT and water weight ratios at fixed PG-6/PG-4 content, for R2 (transparency) as a function of **(D)** PG-6/PG-4 and water weight ratios at fixed CCT content, **(E)** PG-6/PG-4 and CCT weight ratios at fixed water content, and **(F)** CCT and water weight ratios at fixed PG-6/PG-4 content.

Abbreviations: CCT, caprylic/capric triglycerides; PG-6/PG-4, polyglyceryl-6 caprylate, polyglyceryl-4 caprate.

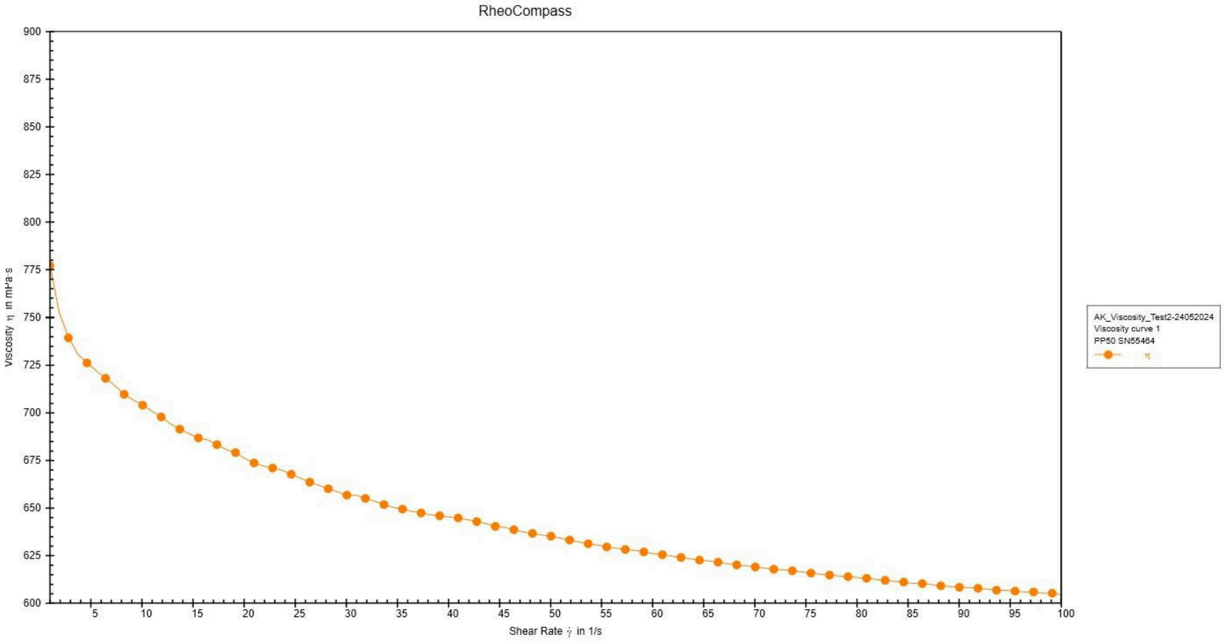

Figure 2. The viscosity of the optimised formulation.

Table 4. Predicted and experimental results of the optimised formulation (n=3)

Result	Predicted value	Experimental value	Prediction error (%)
R_1: Foaming (mL)	1.5	1.06±0.38	29.33
R_2: Transparency	4.62	4	13.42

the flow properties of the optimised formulation, are shown in Figure 2. As seen in the rheograms, a decrease in viscosity is observed in response to increasing shear rate. This indicates that the formulation exhibits pseudoplastic flow properties. In other words, this product exhibits shear thinning features.

The results of the test conducted to evaluate the cleaning feature of the formulation are shown in Figure 3. As seen in Figure 3D, there was no make-up residue left after the product was applied, and in Figure 3B, there was a lot of residues left in the make-up areas that were tried to be cleaned only with water. These test results show that the optimised formulation has a more effective cleansing ability than that of water, thus it can be considered as an effective make-up remover for daily use.

As a result of the evaluation made within the scope of the stability studies, there was no significant change in the pH of the product on the 7th, 15th, 30th, and 60th days under both temperature conditions, and the product maintained its transparency. In addition, at the end of these periods, the phase separation was not observed after centrifugation test, and the foaming ability was not changed significantly.

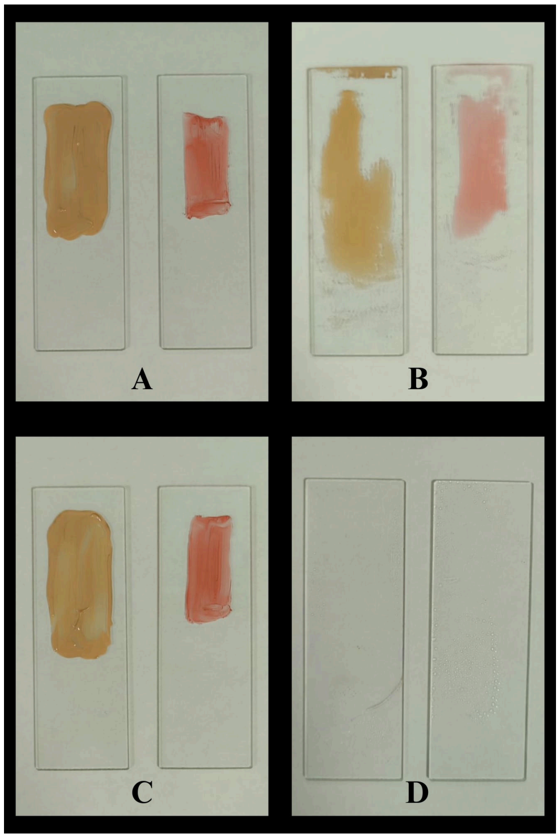

Figure 3. Evaluation of the cleansing effectiveness of the optimised product on make-up versus water (**A:** Images of glass slides to which only water was applied before application, **B:** Images of glass slides to which only water was applied after application, **C:** Images of glass slides to which optimised formulation was applied before application, D: Images of glass slides to which optimised formulation was applied after application).

CONCLUSIONS

The main purpose of the skin cleansing treatment is to remove dead skin and dirt, as well as to maintain the freshness and health of the skin for years through the products used. Thus, it is important to choose a suitable skin and makeup cleansing product according to the skin type and characteristics of the individuals. In recent years, cosmetic products were widely prepared with herbal and non-synthetic raw materials and vegetable oils, which are at the forefront in terms of their advantages and green environment, have been preferred. In this study, we designed a formulation that can be used for skin cleansing, and it has a high foaming ability using natural raw materials. Using CCT, a compound that combines fatty acids from natural oils such as coconut oil with glycerine, PG-6/PG-4, a natural solvent based on completely renewable raw materials, and hemp seed oil, a vegetable oil, we obtained a formulation that is not currently available on the market and, it has effective make-up removal and cleansing properties.

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Author Details

Ayşenur Kılıç

[1] İstanbul University, Institute of Graduate Studies in Health Sciences, Department of Pharmaceutical Technology, İstanbul, Türkiye

[2] Bezmialem Vakıf University, Department of Pharmaceutical Technology, İstanbul, Türkiye

0000-0003-0621-0837 ecz.aysenurkilic@gmail.com

Burak Çelik

[2] Bezmialem Vakıf University, Department of Pharmaceutical Technology, İstanbul, Türkiye

0000-0003-0469-4532

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