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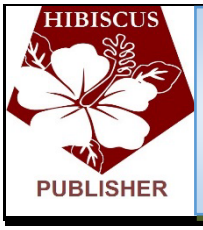

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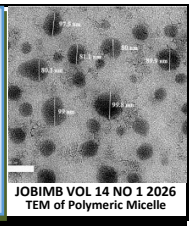

Optimisation and Characterisation of a Kojic Monooleate, Niacinamide and Hyaluronic Acid Facial Cleanser Using Polymeric Micelle Nanocarriers

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Abstract

This study reports the preliminary development and optimisation of a polymeric micelle (PM)-based facial cleanser formulation incorporating kojic monooleate (KMO), niacinamide, and hyaluronic acid (HA) as active components, evaluated mainly through physicochemical testing. Response Surface Methodology (RSM) coupled with a Face-Centred Central Composite Design (FCCCD) was employed to systematically evaluate the influence of three critical process variables, namely stirring time (55–85 min), stirring rate (1000–1500 rpm), and temperature (30–70 °C), on droplet size as the primary response. Optimisation of the formulation yielded an ideal preparation under conditions of 55.155 min stirring time, 1494.301 rpm stirring rate, and 30.123 °C, producing a droplet size of 97.29 nm, a residual standard error (%RSE) ranging from 1.79% to 12.13% and an encapsulation efficiency of 95.82%. Analysis of variance (ANOVA) confirmed satisfactory model fitness, with an F-value of 5.95, a statistically significant p-value ($p < 0.0500$), a non-significant lack-of-fit, and a coefficient of determination of $R^2 = 0.8562$. Physicochemical characterisation of the optimised formulation revealed a zeta potential of -5.18 ± 3.75 mV, a polydispersity index (PDI) of 0.223, and a conductivity of 0.284 mS/cm at pH 5.69, collectively indicating a monodisperse, oil-in-water (O/W) dispersion system. Under the limited stability testing performed, the formulation remained stable under centrifugation but showed transient suspension formation during freeze-thaw cycling, indicating moderate rather than high short-term stability. A preliminary qualitative cleansing assessment (lipstick-stain removal on a glass substrate) showed promising cleansing performance, supporting the formulation's potential as a cosmeceutical delivery system that warrants further investigation.

INTRODUCTION

Cosmeceuticals represent a specialised category bridging pharmaceuticals and cosmetics by providing therapeutic benefits through bioactive components. Current consumer demand favours formulations for skin brightening and hydration that are safe and non-irritating. This is essential because ultraviolet radiation triggers melanogenesis, a tyrosinase-driven process of melanin production that leads to hyperpigmentation and potential carcinogenesis. Consequently, tyrosinase inhibitors such as kojic monooleate (KMO) are vital for regulating melanin overproduction. KMO is a palm-based fatty acid derivative produced from the esterification of kojic acid (KA) and oleic acid (OA). It is extensively studied and reported to act as a tyrosinase inhibitor in treating hyperpigmentation and is far more effective than its source material [1–3]. Simultaneously, sun exposure degrades collagen and elastin, resulting in dryness and wrinkles that require ingredients such as niacinamide and hyaluronic acid (HA) to restore barrier function, repair the skin, and help retain moisture [4,5]. The combination of niacinamide and HA has demonstrated clinical efficacy in improving skin quality, with a two-month topical study reporting significant improvements in wrinkles, fine lines, radiance and smoothness alongside increased dermal glycosaminoglycan and collagen content [4].

Topical delivery of KMO is usually hindered by its greasy nature and large droplet size [3,6]. Nanotechnology, particularly nanocarriers, improves stability and skin penetration. Among these, polymeric micelles have emerged as versatile carriers for poorly water-soluble cosmeceutical actives, offering enhanced solubilisation, controlled release, and improved cutaneous bioavailability [7,8]. The amphiphilic architecture of polymeric micelles is particularly well suited to this multi-active payload [9,10]. The hydrophobic core solubilises the lipophilic KMO, whereas the water-soluble niacinamide and HA are accommodated within the hydrophilic corona and the surrounding aqueous phase. A single micellar system can therefore co-deliver actives of contrasting polarity, avoiding the need for separate carriers and ensuring their uniform distribution throughout the cleanser [11]. In a cleanser context, polymeric micelles emulsify oils, dirt, and impurities in water, disrupting the adhesion between contaminants and the stratum corneum so that they are easily removed during washing [11]. As the cleanser is rinsed away, the hydrophilic micelle shells are swept along, carrying encapsulated debris, sebum, oils, and make-up and leaving the skin clean [12,13]. To prevent micelle disassembly upon dilution below the critical micelle concentration, a mixed system of Poloxamer 407 and PEG 400 is employed to maintain high encapsulation efficiency [14].

Importantly, the choice of cleansing system strongly influences skin-barrier compatibility. Conventional surfactant-based cleansers can disrupt the stratum corneum lipids, denature barrier proteins, and alter skin pH, whereas milder polymer- and micelle-based cleansing technologies have been shown to remove impurities while preserving barrier integrity and minimising irritation [15–17]. Recent studies confirm that surfactant selection determines cleanser mildness, with milder systems showing minimal disruption of the epidermal barrier compared with harsher surfactants [18]. Formulating KMO within a mild micellar cleanser at a mildly acidic pH therefore offers a route to deliver a tyrosinase inhibitor in a rinse-off product without compromising the skin barrier.

Despite growing interest in KMO, prior work has been confined to leave-on nanoemulsion and nanodelivery systems containing KMO as the sole active, for example, optimised O/W nanoemulsions developed for hyperpigmentation treatment and thin-film nanoemulsions incorporating PVA/PG [2,3,6]. To date, no study has incorporated KMO into a polymeric micelle system, combined it with the complementary barrier-supporting actives niacinamide and HA, or delivered it in a rinse-off facial cleanser format. This combination of a polymeric micelle carrier, a multi-active brightening-and-hydrating payload, and a cleanser dosage form constitutes the knowledge gap addressed here. Optimisation is required to ensure a robust formulation. In contrast to one-factor-at-a-time methods, Response Surface Methodology (RSM) offers a cost-effective multivariate approach to predict interactions between stirring time, stirring rate, and temperature, and has been shown to be an effective tool for improving cosmetic formulations [19]. This research therefore aimed to optimise a polymeric micelle-based facial cleanser containing these three actives using this methodology, followed by physicochemical and preliminary stability characterisation.

MATERIALS AND METHODS

Chemicals

Kojic monooleate (KMO), Brij 93, Polyvinylpyrrolidone (PVP), Polyvinylpolypyrrolidone (PVPP), Polyethylene Glycol 400 (PEG-400), Pluronic F127 (Poloxamer 407) were purchased from Sigma-Aldrich (St. Louis, USA), Polyoxyl-35 castor oil (Cremophor EL), methanol, Tween 80 (HLB = 15.0) was purchased from Merck Chemicals (Germany), Safflower oil, Olive oil, Potassium hydroxide, Citric acid monohydrate, Distilled water (DH_2O), Hyaluronic acid (HA), Niacinamide, Germall Plus™ Liquid, Cocamidopropyl betaine, Geranium oil, Coco glucoside, Sulfosuccinate, Polyglucose, Sodium methyl cocoyl taurate. Chemicals used were all analytical, food or cosmetic grade classes.

Preliminary Screening on the Solubility of KMO with Polymers and Their Encapsulation Efficiency (EE%)

To determine the standard curve of KMO, pure KMO was diluted with methanol to get the concentration of 0.003125, 0.0125, 0.025, 0.05 and 0.1 M. The diluted KMOs have then undergone UV-VIS spectroscopy at 255.5 nm using UV-VIS spectrophotometer (Shimadzu 1650PC, Japan) and their absorbances were recorded. KMO solubility in various polymers, such as Brij 93, PVP, PVPP, Poloxamer 407 and Cremophor EL was investigated to determine which polymers had the best solubilizing ability as a carrier. 2% w/w each of the polymers and 1% w/w KMO were mixed into an ointment jar for 50g in total and distilled water was added for the remaining. All the six mixtures were stirred for 24 hours at 60 °C and 400 rpm.

The suspension of the six mixtures was centrifuged at 2000 rpm for 15 min, and visual inspections of each mixture including phase separation and precipitations were observed and recorded. The supernatant of the soluble polymer(s) was then filtered through a 0.45 µm PVDF membrane filter (Whatman, Kent, UK). The solubility of KMO in the corresponding polymers was observed and recorded their absorbance at 255.5 nm using UV-VIS spectrophotometer (Shimadzu 1650PC, Japan) as indicated the amount of the KMO released from the lyophilised polymer. Based on the graph equation obtained, the encapsulation efficiency of KMO in the polymer was calculated and determined. Polymer with the highest encapsulation efficiency proceeded as the copolymer for PMs system.

Preparation of Polymeric Micelle Facial Cleanser Formulation Containing KMO, Niacinamide and HA

The preparation of polymeric micelle formulation containing KMO was using low energy emulsification method. This formulation had been through preliminary test beforehand, and the best formulation was selected for this optimisation stage. The formulation of polymeric micelle facial cleanser was prepared with 2% w/w Poloxamer 407. For the aqueous phase, Tween 80, PEG-400, Coco Betaine, and distilled water were stirred at 1500 rpm and heated at 50 °C. Poloxamer 407 was added to the solution and stirred until dissolved. The oil phase which consists of KMO, Olive oil and Safflower oil was gradually added dropwise and stirred for 10 mins. KOH and Citric acid that both acted as pH stabilisers were added and stirred for 10 minutes until dissolved followed by actives, niacinamide and hyaluronic acid.

The final mixture was further stirred while adding Germall Plus™ Liquid which worked as non-toxic preservative and geranium oil was added dropwise [2,20,21]. The Poloxamer 407 concentration (2% w/w) was maintained well above its reported critical micelle concentration, promoting self-assembly into a mixed micellar system with the co-surfactants. As this study focused on formulation optimisation and physicochemical characterization, detailed structural confirmation of micelle formation such as critical micelle concentration determination or cryo-TEM was not undertaken and is acknowledged as a limitation to be addressed for future work.

Table 1. Compositions of PMs facial cleanser formulations containing KMO, niacinamide and HA.

Formulation ingredients	Composition (%*w/w*)
Poloxamer 407	2
Tween 80	2
PEG-400	5
Coco-betaine	15
DH_2O	q.s
KMO	1
Olive oil	2
Safflower oil	2
KOH	0.3
Citric acid	0.5
Niacinamide	5
HA	0.5
Germall Plus™ Liquid	0.2
Geranium oil	0.2

q.s = *quantum satis* (to make 50 g).

Optimisation of Polymeric Micelle Formulation Containing KMO, Niacinamide and HA

Experimental design of Response Surface Methodology (RSM)

A Face Centred Central Composite Design (FCCCD) was utilised via Response Surface Methodology (RSM) to optimise the process parameters of three independent variables: stirring time (55 to 85 min, X1), stirring rate (1000 to 1500 rpm, X2), and temperature (30 °C to 70 °C, X3). The droplet size of the polymeric micelles (Y1) served as the primary response to evaluate variable effects. Using Design Expert version 13.0 software (Stat Ease Inc., Minneapolis, USA), 20 experimental runs were generated based on the FCCCD to identify optimised levels and the relationships between process variables. These three independent factors were investigated at three distinct levels (−1, 0, +1), with their respective coded forms detailed in **Table 2**.

Table 2. Variables and their coded levels utilised in the FCCCD matrix.

Independent variables	Units	Coded levels of variables		
		−1	0	1
Stirring time, A	min	55	70	85
Stirring rate, B	rpm	1000	1250	1500
Temperature, C	°C	30	50	70

Statistical Analysis

Statistical analysis was conducted using analysis of variance (ANOVA) to evaluate the significance of independent variables and the fit of the second order polynomial model [14]. The probability value of $p < 0.05$ was utilised to identify significant factors and refine the final reduced model. The optimised polymeric micelle composition was ultimately determined based on the parameters that yielded the minimum droplet size.

Physicochemical Characterisation of PMs Facial Cleanser Formulation Containing KMO, Niacinamide and HA

Droplet size analysis

Droplet size, stability, and size distribution of the polymeric micelle system were determined using Dynamic Light Scattering (DLS) via a Zetasizer Nano ZS90 (Malvern Instruments, UK) at a 173° scattering angle and a temperature of 25 °C [3]. Samples (0.01 mL) were diluted with distilled water (9.99 mL), corresponding to a 1:1000 dilution, before being transferred into a folded capillary cell (DTS1070, Malvern Instruments, UK). Dilution is necessary in dynamic light scattering to suppress multiple scattering and particle-particle interactions that would otherwise bias the measured size distribution [22]. The dilution factor was selected to bring the sample within the instrument's optimal count rate range (100-300 kcps) while maintaining the Poloxamer 407 concentration above its reported critical micelle concentration, thereby limiting micelle dissociation, while the inclusion of PEG 400 further stabilises the micellar assemblies against disassembly at high dilution. The diluted samples underwent 15 minutes of sonication. The count rate was maintained between 100 and 300 kcps, and droplet sizes within the 20 to 200 nm range were analysed based on intensity weighted distribution (Z-average). Zeta potential was determined through electrophoretic mobility measurements of particles in a charged field. All measurements were performed in triplicate to calculate mean values.

pH and conductivity measurement

The pH and conductivity of the optimised polymeric micelle formulation were measured directly on the undiluted sample using a Eutech pH 700 (Thermo Scientific) and a Zetasizer Nano ZS90 (Malvern Instruments, UK), respectively. The pH meter was calibrated using standard buffers (pH 4.00, 7.00, and 10.00) before triplicate measurements were recorded to determine mean values [2]. The pH evaluation was done to indicate that the product is skin compatible whereas the conductivity measurement was made to verify the formation of continuous phase and to determine the system as either oil in water (O/W) or water in oil (W/O) emulsion [23,24].

Morphology study

The optimised polymeric micelle size and morphology in their polymeric form were characterised using Transmission Electron Microscopy (TEM) on a JEOL JEM 1210 (Tokyo, Japan). A 0.1 ml sample of solution was homogenised in 0.9 ml deionised water (a 1:10 dilution) and a single drop of dilution applied to a formvar coated copper grid for 3 min at 25 °C. The grid was stained with 2% uranyl acetate for 2 min and air dried before imaging.

Stability study: accelerated stability test

The stability testing of the optimised formulation involved the following: (i) stability test under centrifugation and (ii) freeze-thaw cycles. Regarding the test for stability under centrifugation, triplicate samples were subjected to centrifugal force for 15 min at a speed of 4000 rpm and were investigated to check for phase separation. Thermal stability was assessed using modified freeze thaw cycle that included 22 hours of exposure to -7 °C followed by 2 hours of thawing at 40 °C in water bath for three consecutive days [25]. The samples were observed to check for the phase separation periodically, and at the end of each cycle the final droplet size was determined after the completion of the third day.

Organoleptic physical evaluation

Organoleptic properties including colour, odour, texture, foaming, and appearance were evaluated in triplicate. Visual assessment was performed by placing the formulation on a glass surface against a black background [2]. Cleansing performance was assessed qualitatively by applying three drops of the PM formulation to a lipstick stain on a glass substrate, providing a preliminary visual indication of cleansing action.

RESULTS AND DISCUSSION

Preliminary screening on the solubility of KMO with polymers and their encapsulation efficiency (EE%)

The preliminary screening on the solubility of KMO was carried out by mixing selected polymers (Brij 93, PVP, PVPP, Poloxamer 407 and Cremophor EL) at a ratio of 1:2. Under centrifugal force, all mixtures showed signs of phase separation, precipitation, and low homogeneity towards active ingredient KMO except for Cremophor EL and Poloxamer 407 as depicted in **Fig. 1**. Both Cremophor EL and Poloxamer 407s' supernatants

were then filtered, and their absorbance were recorded at 255.5 nm for the encapsulation efficiency determination. For Cremophor EL, the absorbance was 1.387 while for the Poloxamer 407, the absorbance was 0.283.

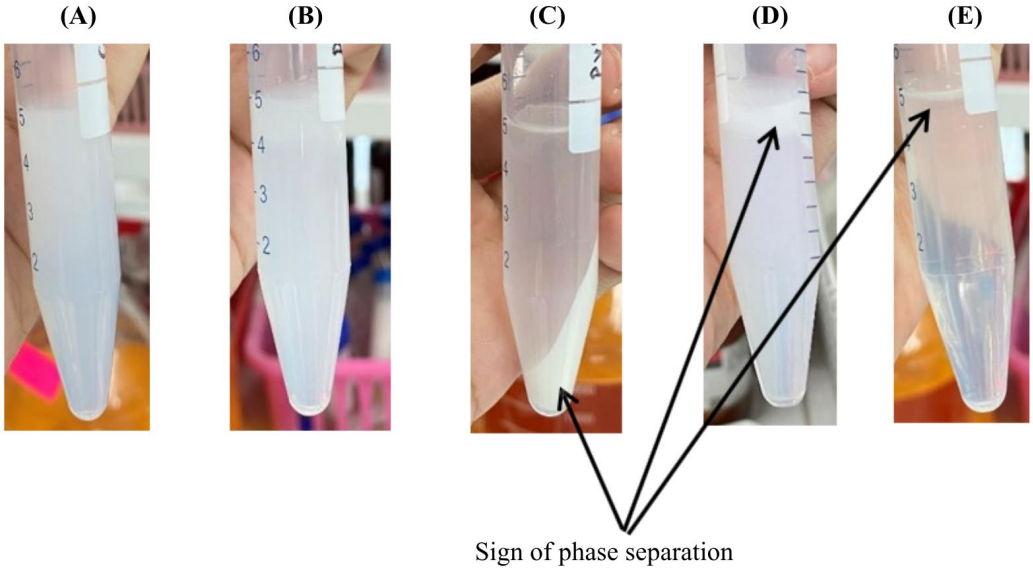

Fig. 1. Preliminary screening on the solubility of KMO with selected polymers (A: Cremophor EL; B: Poloxamer 407; C: PVPP; D: Brij 93; E: PVP).

$$Encapsulation\ efficiency\ (EE\%) = 100 \times \frac{Amount\ of\ KMO\ in\ micelle)}{Amount\ of\ KMO\ initially\ taken\ to\ prepare\ micelle} \quad \text{(Eqn. 1)}$$

The equation of the calibration between KMO concentration and absorbance obtained based on Equation (1) above was y = 13.551x. The value of x was determined for Cremophor EL and Poloxamer 407 to obtain the encapsulation efficiency as tabulated in **Table 3**. Based on **Table 3**, with the 0.5 ml/ml concentration of KMO initially taken to prepare the polymer solution, the encapsulation efficiency for the Cremophor EL and Poloxamer 407 was 79.53 and 95.82% respectively. Therefore, Poloxamer 407 was selected to be used as a copolymer for the PMs system.

Table 3. Encapsulation efficiency (%) of KMO in the polymer.

Polymer	Encapsulation efficiency (%)
Cremophor EL	79.53
Poloxamer 407	95.82

Optimisation of PMs Formulation Containing KMO, Niacinamide and HA Using Response Surface Methodology (RSM)

Fitting of Response Surface Model

Experimental values across 20 runs closely aligned with predicted outcomes. Analysis of variance (ANOVA) performed using Design Expert software Version 13.0 confirmed that the droplet size of the formulation containing KMO, niacinamide, and HA followed a quadratic model. The quadratic model was significant, characterised by an F-value of 5.95 ($p < 0.0500$), with only a 0.70% probability that such an F-value resulted from noise. However, its overall fitness and predictability are considered moderate, as reflected in an R^2 of 0.8562 and a significantly lower predicted R^2 of 0.4820. This suggests that the model's ability to predict untested conditions is not very strong. Consequently, the model serves as a useful empirical tool within the selected ranges. The lack-of-fit F-value of 0.48 was non-significant relative to pure error, with a 75.17% probability of noise interference, further validating the model's accuracy within the design space. The final polynomial equation describing the droplet size in terms of coded factors is expressed in Equation 2:

$$\text{Droplet size} = +102.26 - 0.1310A - 7.06B + 0.6380C + 1.70AB + 1.98AC + 4.91BC + 3.82A^2 + 4.08B^2 - 5.24C^2 \quad \text{(Eqn. 2)}$$

where A is Stirring Time, B is Stirring Rate and C is Temperature.

Based on **Table 4**, the predicted and the actual values of the droplet size obtained showed that there was not much difference, and the model shows an acceptable correlation between the experimental and predicted values. This can be displayed in **Fig. 2(A)** whereby only a few points were far from the diagonal line which is still within the range. The normal probability plot of residuals in **Fig. 2(B)** showed that the data points lay close to the straight line, indicating that the residuals were normally distributed and the assumption of normality for the quadratic model was satisfied. The randomness of the residuals was further examined using the residuals versus predicted plot (**Fig. 3**). All data points were scattered randomly within the control limits with no discernible pattern, confirming that the model satisfies the assumptions of constant variance and independence of errors.

Table 4. Actual and predicted values of droplet size of the PMs facial cleanser formulation containing KMO, niacinamide and HA.

Std order	Run order	A (min)	B (rpm)	C (°C)	Actual droplet size (nm)	Predicted droplet size (nm)
15	1	70	1250	50	96.83	102.26
10	2	85	1250	50	106.7	105.94
4	3	85	1500	30	93.06	91.89
1	4	55	1000	30	121.6	120.05
8	5	85	1500	70	105.9	106.94
19	6	70	1250	50	99.19	102.26
14	7	70	1250	70	99.05	97.65
17	9	70	1250	50	108.4	102.26
16	10	70	1250	50	106.6	102.26
6	11	85	1000	70	107.3	107.85
13	12	70	1250	30	92.94	96.38
2	13	85	1000	30	112.1	112.44
5	14	55	1000	70	106.9	107.56
18	15	70	1250	50	103.9	102.26
7	16	55	1500	70	100.7	99.85
12	17	70	1500	50	97.23	99.27
20	18	70	1250	50	102.7	102.26
3	19	55	1500	30	93.77	92.71
9	20	55	1250	50	103.4	106.2

Table 5. ANOVA for the response surface quadratic model of droplet size of the PMs facial cleanser formulation containing KMO, niacinamide and HA.

Source	Sum of squares	df	Mean square	*F*-value	*p*-value	Remark
Model	787.37	9	87.49	5.95	0.0070	significant
A–Stirring time	0.1716	1	0.1716	0.0117	0.9163	
B–Stirring rate	417.08	1	417.08	28.38	0.0005	
C–Temperature	4.07	1	4.07	0.2770	0.6114	
AB	23.09	1	23.09	1.57	0.2417	
AC	31.24	1	31.24	2.13	0.1788	
BC	192.77	1	192.77	13.12	0.0056	
A^2	33.96	1	33.96	2.31	0.1628	
B^2	29.59	1	29.59	2.01	0.1896	
C^2	64.07	1	64.07	4.36	0.0664	
Residual	132.27	9	14.70			
Lack of fit	36.69	4	9.17	0.4798	0.7517	not significant
Pure error	95.58	5	19.12			
Cor total	919.64	18				

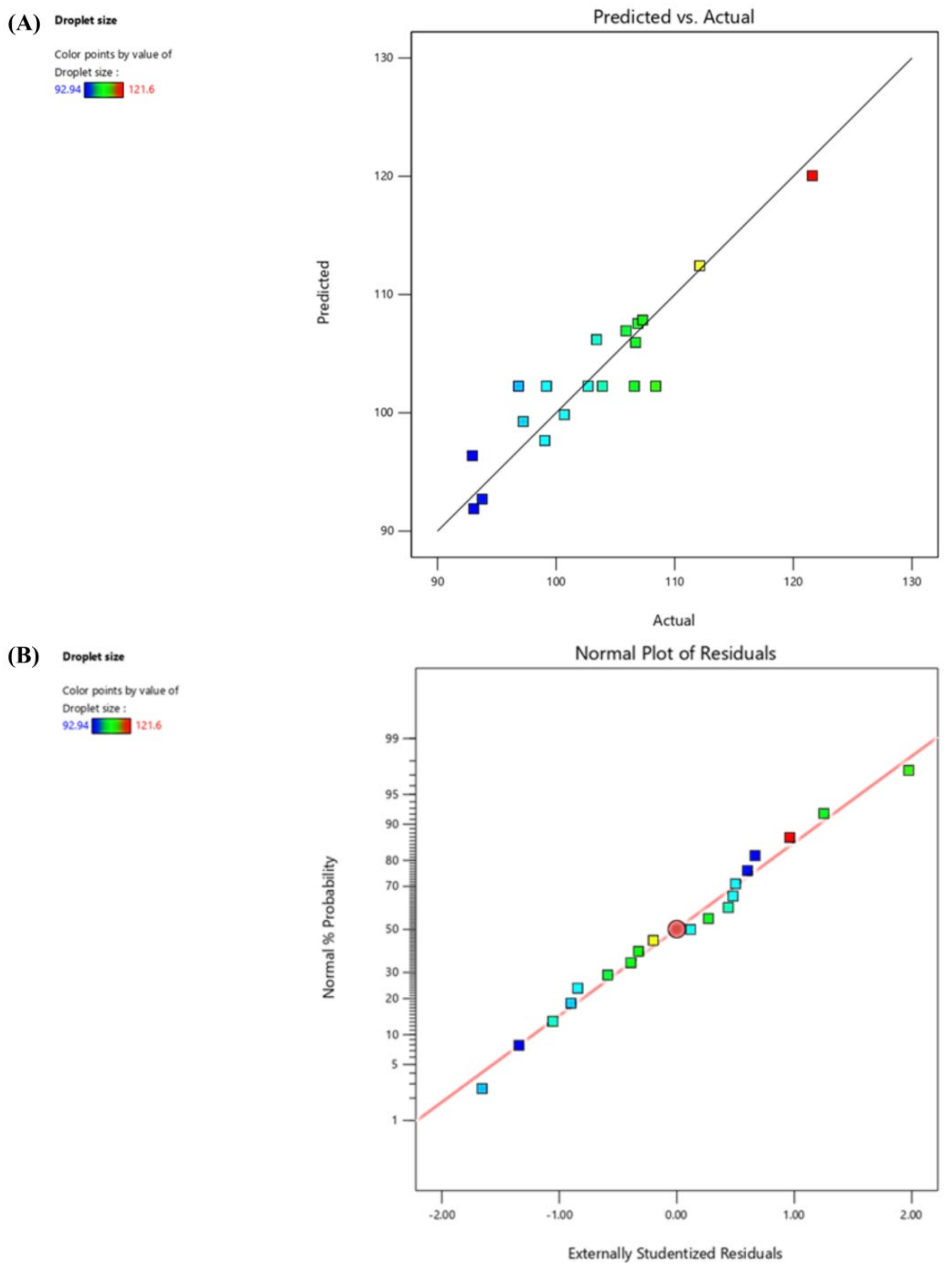

Fig. 2. Model validation plots for droplet size: **(A)** linear correlation between predicted and actual values; **(B)** normal probability distribution of residuals for the optimised facial cleanser formulation.

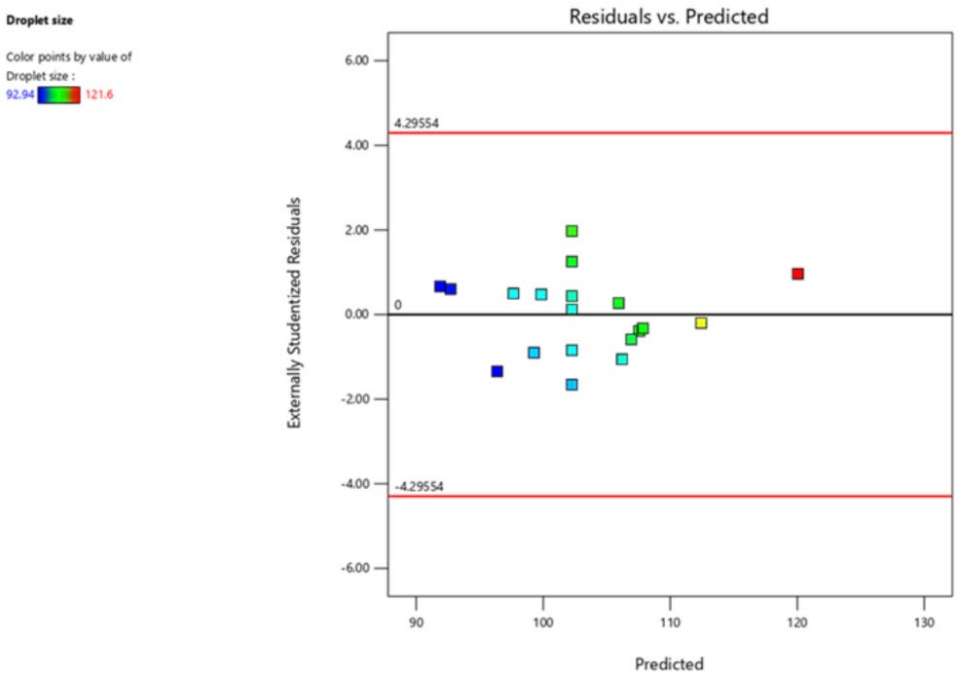

Fig. 3. Residuals versus predicted values of droplet size of the PMs facial cleanser formulation containing KMO, niacinamide and HA.

The quadratic model fit statistics (**Table 6**) showed an R^2 of 0.8562 and an adjusted R^2 of 0.7123. These results indicate that the RSM model effectively explains over 80% of the particle size response variation as a function of stirring time, stirring rate, and temperature. Furthermore, the Adeq Precision value of 10.125 indicates an adequate signal to noise ratio, significantly exceeding the desirable threshold of four and confirming the model's suitability to navigate the design space.

Table 6. Fit statistics of the quadratic model.

Parameter	Value	Parameter	Value
Standard deviation	3.83	R^2	0.8562
Mean	103.07	Adjusted R^2	0.7123
C.V. %	3.72	Predicted R^2	0.4820
		Adeq Precision	10.125

Although the quadratic model was statistically significant and the lack-of-fit was non-significant, the adjusted R^2 of 0.7123 and predicted R^2 of 0.4820 indicate that the model explains the studied response reasonably well but has more limited predictive strength for untested conditions. Therefore, the model should be interpreted as an empirical optimisation tool within the selected ranges rather than a mechanistic model of micelle formation. This caution is relevant because droplet size in polymeric micelle and emulsion systems can also be affected by formulation composition, dilution, viscosity, surfactant-polymer interactions, and storage conditions that were not included as RSM factors in this study [11].

Response Surface Analysis

In response surface, **Fig. 4(A)** illustrates the 3D response surface interaction between stirring time (A) and stirring rate (B) on droplet size at a constant temperature (C) of 50 °C. Within the tested ranges (55 to 85 min and 1000 to 1500 rpm), increasing the stirring rate resulted in smaller droplet sizes, reaching a minimum at approximately 1500 rpm. As shown in **Fig. 4(A)**, stirring time exhibited a U-shaped trend where droplet size decreased from 55 to 70 min but increased slightly from 70 to 85 min. This suggests system saturation at extended stirring durations, causing droplet enlargement, a finding consistent with previous studies [26,27].

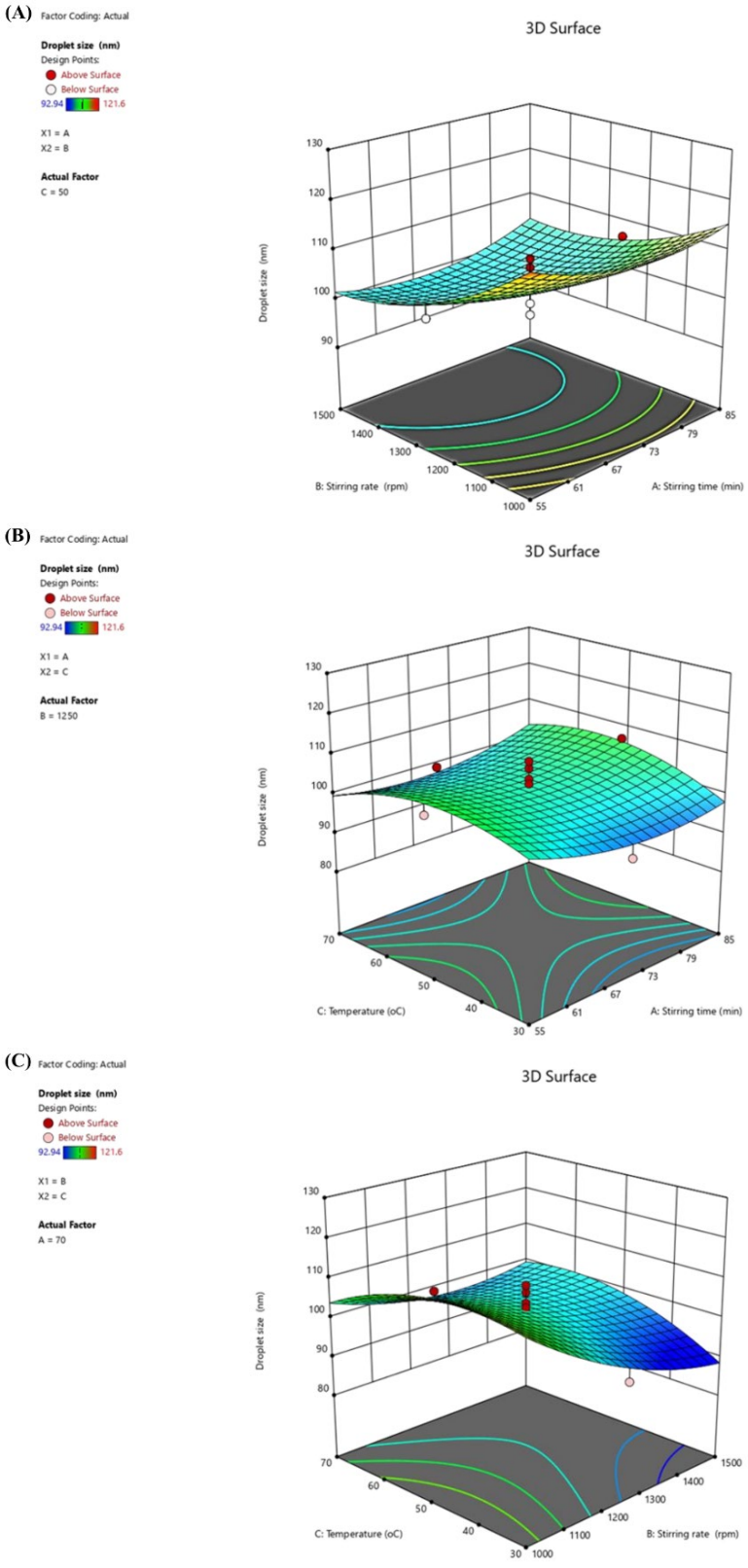

Fig. 4. Three-dimensional response surface plots illustrating the effects on droplet size: **(A)** stirring time versus stirring rate at constant temperature; **(B)** stirring time versus temperature at constant stirring rate; and **(C)** stirring rate versus temperature at constant stirring time.

Fig. 4(B) illustrates the interaction between stirring time and temperature at a constant rate of 1250 rpm. Much like in **Fig. 4(A)**, longer stirring times consistently yielded smaller droplets. The effect of temperature, however, followed a different pattern, droplet size increased as the temperature rose from 30 °C to approximately 48 °C before beginning to drop off; even then, the resulting droplets remained larger than those recorded at 30 °C to 32 °C mark. Consequently, the optimal temperature was

determined to be 30.123 °C. This aligns with existing literature, which suggests that rising temperatures increase the effective volume fraction of the polymeric micelle system, causing the structures to broaden [28]. Finally, **Fig. 4(C)** maps the effects of stirring rate and temperature over a fixed 70-minute period. Following the established trend, higher stirring rates produced smaller droplets, while the temperature repeated its previously observed pattern of an initial swell followed by a decline.

Optimisation of Responses for Formulating PMs Facial Cleanser Containing KMO, Niacinamide and HA

The optimal conditions for the PMs facial cleanser were determined using a desirability function of 1.00 via Design Expert software (Version 13.0), indicating that the predicted solution fully satisfied the defined optimisation criteria. From 48 generated solutions, the optimised formulation was selected based on the software's suggested parameters, as shown in **Table 7**, which compares actual and predicted droplet sizes. Droplet size was minimised to maximise the interfacial area and micellar uniformity of the system, properties that determine the solubilisation and entrapment of sebum, oils, and make-up during cleansing. In a rinse-off cleanser, a small and uniform droplet size within the 20–200 nm range supports efficient emulsification of impurities and consistent product performance rather than transdermal delivery of the actives.

However, it is important to note that the optimised conditions fall at the boundary of the design space, specifically near the lower limits of stirring time and temperature and the upper limit of stirring rate. This represents a limitation of the current study, as a true minimum droplet size may lie beyond the investigated ranges. Consequently, future work should consider expanding the design range towards higher stirring rates and lower temperatures to identify a more definitive and robust optimum.

Table 7. Actual and predicted response values of the optimised PMs facial cleanser formulation containing KMO, niacinamide and HA.

A: Stirring time (min)	B: Stirring rate (rpm)	C: Temperature (°C)	Actual droplet size (nm)	Predicted droplet size (nm)	Desirability
55.155	1494.301	30.123	97.29	92.839	1

Table 8. Responses of the numerical optimisation.

Responses	Goal	Lower limit	Upper limit	Lower weight	Upper weight
A: Stirring time (min)	Is in range	55	85	1	1
B: Stirring rate (rpm)	Is in range	1000	1500	1	1
C: Temperature (°C)	Is in range	30	70	1	1
Droplet size (nm)	Minimise	92.94	121.6	1	1

Verification of reduced models

To verify model adequacy, the experimental and predicted droplet sizes of five randomised formulations were compared in **Table 9**. The experimental values showed a reasonable degree of alignment with the predicted outcomes, supporting the adequacy of the model within the investigated region. The residual standard error (RSE) for these verification runs ranged from 1.79% to 12.13%. In this context, the RSE represents the percentage deviation between the actual experimental results and the model's predicted values. While these values reflect the moderate predictive strength of the model (as discussed under Fitting of Response Surface Model), the results remain within an acceptable margin for empirical optimization, confirming that the model can effectively guide the development of formulations within the target nano-size range. The RSE percentage was calculated using Equation 3:

$$\text{RSE (\%)} = [(\text{Actual value} - \text{Predicted value}) / \text{Predicted value}] \times 100\% \quad \text{(Eqn. 3)}$$

Table 9. Predicted and actual response values for randomised PMs facial cleanser formulations containing KMO, niacinamide and HA.

Number	Stirring time (min)	Stirring rate (rpm)	Temperature (°C)	Actual droplet size (nm)	Predicted droplet size (nm)	RSE (%)
1	55.155	1494.301	30.123	97.29	92.839	4.79
2	55	1500	30	94.37	92.709	1.79
3	55.989	1499.338	30.012	103.43	92.218	12.16
4	55.51	1498.957	30.169	99.44	92.581	7.41
5	55.024	1497.563	30.101	100.83	92.82	8.63

Physicochemical Characterisation of PMs Facial Cleanser Formulation Containing KMO, Niacinamide and HA

Droplet size, polydispersity index (PDI) and zeta potential analysis

The physical characteristics of the optimised formulation are summarised in **Table 10**, yielding an average droplet size of 97.29 nm, a PDI of 0.223, and a zeta potential of −5.18 ± 3.75 mV. The droplet size falls within the ideal 10 to 200 nm range for nanoscale micellar dispersions [11]. A nanoscale droplet size is advantageous in a cleanser formulation, as the large surface-area-to-volume ratio enhances the solubilisation and dispersibility of the actives, hence, improves the physical stability and textural quality of the product [29]. A PDI of 0.223 indicates a reasonably monodisperse system, reflecting uniformity in droplet size rather than stability. Although previous studies have reported that zeta potential is often taken as an indicator of long-term stability in cosmeceuticals, the

comparatively low value of −5.18 mV recorded here implies that stability in this system is maintained primarily through steric rather than electrostatic mechanisms [3]. Steric stabilisation has been shown to maintain colloidal stability even at near-zero zeta potential, where electrostatic repulsion is negligible, through the repulsive forces generated by adsorbed polymer layers [30]. The polyoxyethylene chains of Poloxamer 407 provide steric hindrance that limits aggregation and accounts for the small particle size [31].

Table 10. Droplet size, polydispersity index (PDI) and zeta potential of the optimised PMs facial cleanser formulation containing KMO, niacinamide and HA.

Property	Value
Droplet size (nm)	97.29
PDI	0.223
Zeta potential (mV)	−5.18 ± 3.75

pH and conductivity measurement

The pH and conductivity values for the PMs facial cleanser are summarised in **Table 11**. The formulation resulted in a pH of 5.69 and was within the optimal range of 4.5 to 6.0 for human skin compatibility and avoidance of irritation [32,33]. The conductivity of 0.284 mS/cm confirms that water forms the continuous phase of the system, consistent with an oil-in-water (O/W)-type dispersion and a value approaching zero would instead indicate a water-in-oil arrangement [34]. Moreover, the mildly acidic pH 5.69 is likewise consistent with a water-continuous, O/W-type dispersion [35,36].

Table 11. pH and conductivity of the optimised PMs facial cleanser formulation containing KMO, niacinamide and HA.

Property	Value
pH	5.69
Conductivity (mS/cm)	0.284

Morphology Study

The TEM imaging of the optimised PMs formulation (**Fig. 5**) revealed spherical droplets dispersed homogeneously without aggregation, corroborating the findings of study before [37]. The morphology and size observed via TEM were consistent with dynamic light scattering (DLS) results. While minor variations in size distribution were visible, these are attributed to the kinetic migration of polymer chains between the aqueous media and individual micelles [38]. TEM preparation involves drying and staining, which may introduce minor artefacts, and TEM measures the dried particle whereas DLS reports a hydrodynamic diameter. The broad agreement in size range between the two techniques, obtained at dilutions differing by two orders of magnitude, nonetheless supports the reliability of the reported droplet size. All observed particles remained below 100 nm, consistent with a uniform, finely dispersed micellar system suitable for a cosmeceutical cleanser formulation.

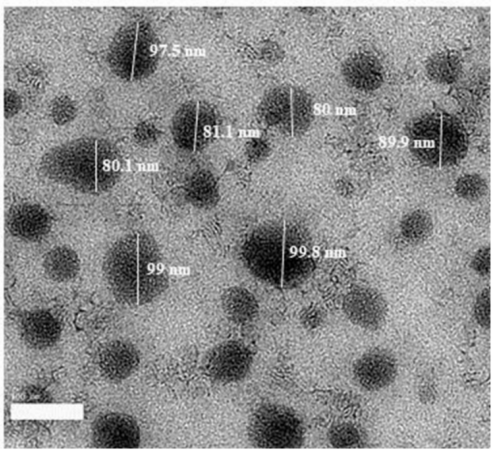

Fig. 5. TEM image of the optimised PMs facial cleanser formulation containing KMO, niacinamide and HA.

Stability study: accelerated stability test

Under centrifugation force of 4000 rpm for 15 min, the optimised PMs facial cleanser formulation containing KMO, niacinamide and HA shown in **Fig. 6** exhibited no phase separation. This indicated that the formulation was in good resistance to gravitational and mechanical stress.

Fig. 6. Centrifugation test of the optimised PMs facial cleanser formulation containing KMO, niacinamide and HA.

Referring to **Fig. 7**, for freeze thaw cycles, the PMs facial cleanser demonstrated stability during the first and third cycles (A and C). However, the second cycle (B) exhibited temporary instability after thawing, characterised by the formation of a suspension, though the formulation colour remained unchanged. The droplet size increased slightly from 97.29 nm to 107.2 nm, remaining within the nano size range. This slight destabilisation may result from weak thermodynamic interactions between Poloxamer 407 and Tween 80.

The steric stiffness of the oleate chain in Tween 80, caused by its rigid cis double bond, can hinder stabilisation compared to stearate systems [38]. The higher temperature causes more droplet impacts which may lead to droplet coalescences. The other side, larger size in mixed micelle systems (Poloxamer 407, PEG 400, and Tween 80) could be due to hydrogen bonding between of hydrophilic PEO blocks and the hydrophobic forces between PPO blocks on the surface particle [39]. Overall, these observations indicate moderate short-term stability under thermal stress, with full recovery of homogeneity by the final cycle.

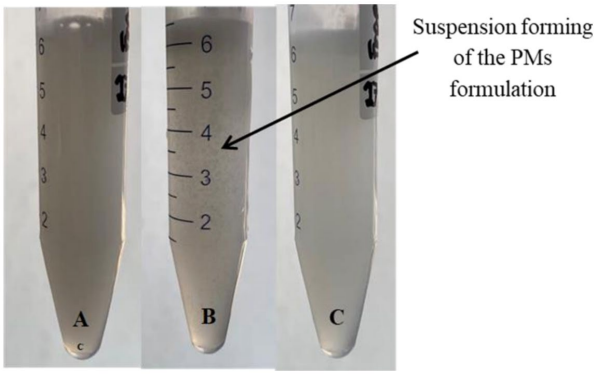

Fig. 7. Freeze–thaw testing of the PMs facial cleanser formulation containing KMO, niacinamide and HA (**A**: after 1 cycle; **B**: after 2 cycles; **C**: after 3 cycles).

Organoleptic physical evaluation

The PMs facial cleanser showed attractive organoleptic characteristics with a homogeneous, uniform and glossy liquid appearance (**Fig. 8**) of uniform texture, pleasant geranium fragrance and dense foam lather formation on its use. In a preliminary qualitative lipstick-removal test (**Fig. 9**), the formulation visibly removed the applied stain, providing an initial indication of cleansing action. These observations suggest that the PMs formulation containing KMO, niacinamide and HA combines acceptable sensory properties with promising preliminary cleansing performance.

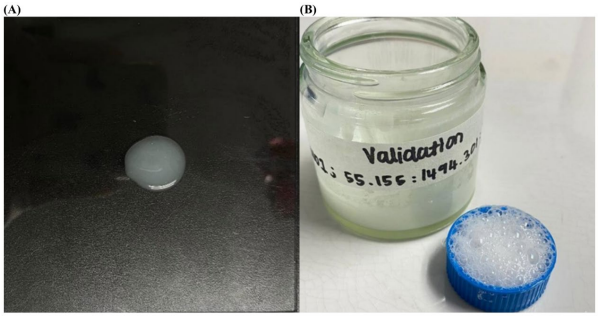

Fig. 8. PMs facial cleanser formulation containing KMO, niacinamide and HA on a glass tile **(A)** and the foaming of the cleanser **(B)**.

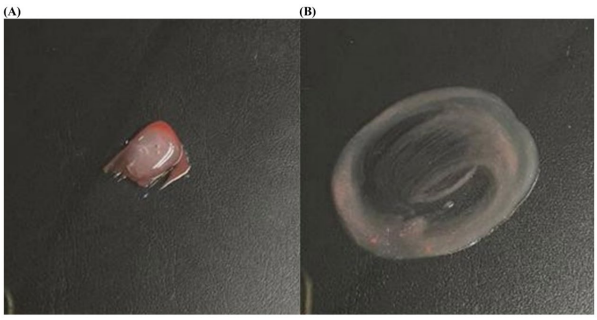

Fig. 9. Lipstick-stain removal test of the PMs facial cleanser formulation containing KMO, niacinamide and HA: before **(A)** and after **(B)**.

The present work establishes the physicochemical basis of the formulation but does not yet address its functional behaviour on skin. As the product is designed to be rinsed off, its cosmeceutical value ultimately depends on the extent to which KMO, niacinamide and HA are retained on or within the skin after washing. Establishing this will require dedicated retention, deposition and *in vitro* permeation studies, complemented by further cleanser characterisation such as viscosity, rheology and foaming behaviour. Together these represent the natural next stage in developing the formulation towards a validated cosmeceutical product. Further work should extend the investigated design space and explore alternative statistical approaches, such as Mixture Experimental Design, to refine the formulation composition. Safety and efficacy evaluation should follow, including *in vitro* cytotoxicity, skin irritation assessment using reconstructed human epidermis models, antimicrobial activity and tyrosinase inhibition assays, before progressing to preclinical pharmacokinetic and pharmacodynamic studies [40]. Such studies would clarify appropriate use levels, expected benefits, and potential adverse effects.

CONCLUSION

This research developed a polymeric micelle facial cleanser incorporating kojic monooleate, niacinamide, and hyaluronic acid, optimised via Response Surface Methodology. The optimised formulation achieved a droplet size of 97.29 nm and an encapsulation efficiency of 95.82%. Physicochemical analysis indicated a reasonably monodisperse oil-in-water system with a pH of 5.69, consistent with skin compatibility. Centrifugation testing showed no phase separation, while freeze-thaw cycling revealed moderate short-term stability, with transient suspension formation in the second cycle. A preliminary qualitative assessment indicated promising cleansing performance, supporting the potential of this formulation as a cosmeceutical delivery system that merits further development.

AUTHOR CONTRIBUTIONS

Abdul Raman, N. A.: Investigation, Formal analysis, Data curation, Validation, Visualisation, Writing original draft; Abdul Wahab, F.: Writing original draft, Resources, Validation, Review & editing; Sufatan, N. F. S.: Software, Formal analysis; Ashari, S. E.: Conceptualization, Methodology, Supervision, Project administration, Review & editing.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

FUNDING STATEMENT

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DATA AVAILABILITY STATEMENT

All data supporting the findings of this study are included within the manuscript.

SUPPLEMENTARY DATA

Not applicable.

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