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ORIGINAL ARTICLE

Minimalist, bioinspired and sensorial emulsion based on a Ca^{2+} double cone vector system using Design of Experiment (DoE)

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Abstract

Objectives: Innovation is considered a determining factor in the highly competitive environment of the cosmetic industry to introduce products while creating new needs. The goal of the study consisted of developing a highly natural and minimalist emulsion with sensorially pleasant skin application highlighted by an innovative ingredient based on a Ca^{2+} double cone vector system. The desired product characteristics include a creamy, white texture that is not too greasy or excessively whitening, with rapid skin penetration to facilitate its use for skin treatment.

Methods: To determine the ideal composition of the emulsion, a design of experiment (DoE) based strategy was applied in two steps: a screening step followed by optimisation. The screening step aimed to identify the key potential ingredients and process parameters that have a significant impact on the rheological and textural properties of the emulsion. The optimisation step provided the final emulsion formula with the desired physicochemical parameters and sensory characteristics.

Results: After rheological and sensory analysis, the screening of different ingredients revealed that the combination of 0.8% xanthan gum as the thickening agent (TA), glyceryl stearate citrate and polyglyceryl-3 stearate and hydrogenated lecithin as surfactant S1, and 1% of a mixture of C15-19 alkane (plant-based and renewable) - coco-caprylate/caprate as the sensory agent (SA1) provided the best sensorial qualities for the emulsion. The study demonstrated that the deflocculating rod met one of optimisation's target criteria through its process effect.

Conclusion: Based on DoE, the final formulation resulted in a visually white formulation that was neither too greasy nor excessively whitening and highly

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penetrative of the skin, offering a comfortable face or body cream application for adults and children.

KEYWORDS
emulsion, experimental design, formulation stability, skin barrier

RESUME

Objectifs: L'innovation est considérée comme un facteur déterminant dans l'environnement hautement concurrentiel de l'industrie cosmétique, permettant d'introduire de nouveaux produits tout en créant de nouveaux besoins. L'objectif de cette étude est de développer une émulsion très naturelle et minimaliste, offrant une application sensorielle agréable sur la peau, mise en valeur par un ingrédient innovant basé sur un système vecteur en double cône de Ca^{2+}. Les caractéristiques recherchées pour le produit incluent une texture crémeuse et blanche, pas trop grasse, ni excessivement blanchissante, avec une pénétration cutanée rapide facilitant son utilisation dans les soins de la peau.

Méthodes: Pour déterminer la composition idéale de l'émulsion, une stratégie basée sur la méthodologie du plan d'expériences (Design of Experiment, DoE) a été appliquée en deux étapes: une étape de criblage suivie d'une optimisation. L'étape de criblage visait à identifier les principaux ingrédients potentiels et les paramètres du procédé ayant un impact significatif sur les propriétés rhéologiques et texturales de l'émulsion. L'étape d'optimisation a permis d'obtenir la formule finale de l'émulsion avec les paramètres physico-chimiques et les caractéristiques sensorielles souhaités.

Résultats: Après les analyses rhéologiques et sensorielles, le criblage des différents ingrédients a révélé que la combinaison de 0,8 % de gomme xanthane comme agent épaississant (TA) (glycéryl stéarate citrate (et) polyglycéryl-3 stéarate (et) lécithine hydrogénée) comme tensioactif S1, et 1 % d'un mélange d'alcane C15-19 (d'origine végétale et renouvelable) - coco-caprylate/caprate comme agent sensoriel (SA1) apportait les meilleures qualités sensorielles à l'émulsion. L'étude a démontré que l'utilisation de la tige de défloculation répondait à l'un des critères cibles de l'optimisation par son effet sur le procédé.

Conclusion: Sur la base de la méthodologie DoE, la formulation finale a abouti à un produit visuellement blanc, ni trop gras, ni excessivement blanchissant avec une forte pénétration cutanée, offrant une application confortable en crème pour le visage ou le corps, destinée pour les adultes ainsi qu'aux enfants.

INTRODUCTION

The skin is described as the human body's largest organ and within the epidermis, the *stratum corneum*, the first barrier against allergens, pathogens, pollutants and UV [1–3]. Human skin has three main roles: limiting passive water loss, preventing the absorption of chemicals and protecting against physical, chemical and biological threats [4]. According to Rajkumar et al. [5], the skin can be separated into four interdependent layers: physical, chemical, microbiologic and immunologic, which act as the main contributors to structural stability and hydration.

Barnes et al. [6] showed that cosmetic acceptability, which includes greasiness, stickiness, visibility on the skin, tactile sensation, as well as the ease of use or convenience (such as spreadability, time required for

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application and drying, staining of clothes and bedding) is considered an important parameter in the choice of vehicle and the formulation of moisturizing agents. Oliveira and Almeida described that consumer satisfaction tends to be lower with topical treatments compared to systemic ones, with adherence rates (50%–70%), in line with the generally poor cosmetic acceptability of topical formulations [7]. Therefore, novel effective treatment options are required to address the underlying mechanisms contributing to the dysfunction of the ageing skin barrier.

Composed of several layers, the skin is considered complex, with many components involved in its overall function. Keratinocyte differentiation, skin barrier formation and permeability barrier homeostasis all depend on the epidermal calcium concentration gradient [8]. Lee and Lee showed that the gradient of calcium ions [9] (Ca^{2+}) across the epidermis plays a crucial role in the processes of keratinocyte differentiation and the formation of the epidermal permeability barrier. Both Ca^{2+} release from intracellular stores and Ca^{2+} influx from extracellular sources contribute to the regulation of epidermal structures and functions. However, this concentration gradient deteriorates with skin ageing, or when specific diseases (such as psoriasis or atopic dermatitis) arise [10]. A potential treatment option for collapsed skin was a formulation establishing a Ca^{2+} gradient to replenish depleted stores through non-invasive topical application, using a vector system designed to deliver Ca^{2+} into deeper epidermal layers and provide a long-lasting effect. An innovative, bioinspired vector was developed, encapsulating Ca^{2+} within a double-cone vector system composed of a phospholipid bilayer membrane [11]. Its structure is considered bioinspired based on how the skin naturally uses structured gradients, compartmentalisation and controlled release of Ca^{2+} to maintain barrier function. Baumann et al. described the in vitro and clinical effects of a ready-made oil-in-water (O/W) emulsion in optimising calcium distribution in aged or damaged skin [12].

Costa et al. described one of the strategies to develop cosmetic formulations using the design of experiment (DoE) as one type of experimental design. DoE is described as a statistical tool widely used to identify which factors influence the studied parameters, leading to the desired results while reducing both industrial costs and the number of required experiments [13]. An emulsion consists of two or more partially or completely immiscible liquids, where the dispersed phase exists as droplets suspended in the continuous phase, as described by our team for optimised formulas designed using DoE [14].

Among the different parameters, the surfactant (S) is considered one of the main parameters improving emulsion stability by acting at the interface between hydrophobic and hydrophilic layers, thereby reducing interfacial tension. Our previous results [14] showed that the choice of thickening agent (TA) contributed to lowering the creaming instability. Finally, the choice of the sensory agent (SA) contributed to the overall application towards increased cosmetic acceptability.

The main purpose of this study was to develop a DoE-based minimalist formulation and gain a deeper insight into the stability of such emulsions. We assessed the synergy between the surfactant (S)–TA and SA, coupled with different process modalities, and compared the emulsion characteristics to a moisturising benchmark. This minimalist formulation featured a reduced International Nomenclature of Cosmetic Ingredients (INCI) list, a high percentage of naturality and a rich sensoriality to valorise a new calcium-phospholipid complex-based active ingredient.

MATERIALS AND METHODS

Chemicals and reagents

Glycerin, coco oil (*Cocos nucifera* oil), white beeswax (Cera Alba) were purchased from Cooper (Paris, France), xanthan gum was purchased from Jungbunzlauer (Basel, Switzerland), acacia gum was purchased from DKSH (Zurich, Switzerland), Surfactant 1 composed of (glyceryl stearate citrate (and) polyglyceryl-3 stearate (and) hydrogenated lecithin) was provided by Lucas Meyer Cosmetics by Clariant (Massy, France), Surfactant 2 composed of (arachidyl alcohol (and) behenyl alcohol (and) arachidyl glucoside) and the Sensory agent 1 composed of (C15-19 Alkane (plant-based & renewable) - coco-caprylate/caprate) were purchased from SEPPIC (Courbevoie, France), Sensory agent 2 (propanediol dicaprylate), stearic acid, calcium vector (hydrogenated lecithin (and) calcium chloride (and) glycerin (and) pentylene glycol (and) aqua / water) was provided by Mibelle Group Biochemistry (Buchs, Switzerland), pentylene glycol was purchased from Minasolve (Paris, France), tocopherol was purchased from BASF (Ludwigshafen, Germany) and sodium hydroxide was purchased from Fisher Scientific (Illkirch, France). Milli-Q water (Millipore Corp.) (Burlington, MA, USA) had a specific resistivity of 18.20 MΩ.cm at 25°C.

Formulation protocol

The aqueous phase (water, glycerin and xanthan gum) was prepared separately from the oily phase (coconut oil,

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white beeswax, Surfactant 1, Sensory agent 1 and stearic acid). The aqueous phase was subdivided: first, a "pre-mix" was made with water and the xanthan or acacia gum, which thickened for 10 minutes; then the rest of the water and the glycerin were added. To mix the two phases, each phase was heated to 70°C before placing the water phase under shearing on a Rayneri VMI machine (VMI, Montaigu-Vendée, France), either with a rotor-stator at 1500 rpm or with the deflocculating rod at 1000 rpm. The mixing lasted for 10 min. Then, the emulsion was cooled to 40°C. At this point, the innovative Ca^{2+} vector could be added under light shearing (300 rpm), in consideration of its sensitivity to high temperature and shear stress, following the protocol described by Düring [15]. Another cooling down to 25°C was necessary before adding the pentylene glycol and the tocopherol at 300 rpm, both being sensitive to temperature. Finally, the sodium hydroxide solution (20%) was added drop by drop to reach the pH of the skin (5.5) by hand mixing. The formulation protocol is presented in Figure 1.

Design of experiment

Two DoE were performed: a screening design and an optimisation design (Figure 2). The first screening phase aims to identify the influence of the ingredients on the emulsion's parameters. Three variation factors were chosen: the TA with either xanthan gum or acacia gum; the surfactant (S) with either Surfactant 1 or Surfactant 2 and the SA with Sensory agent 1 or Sensory agent 2. To conduct this screening, a two-level full factorial design 2^3 with

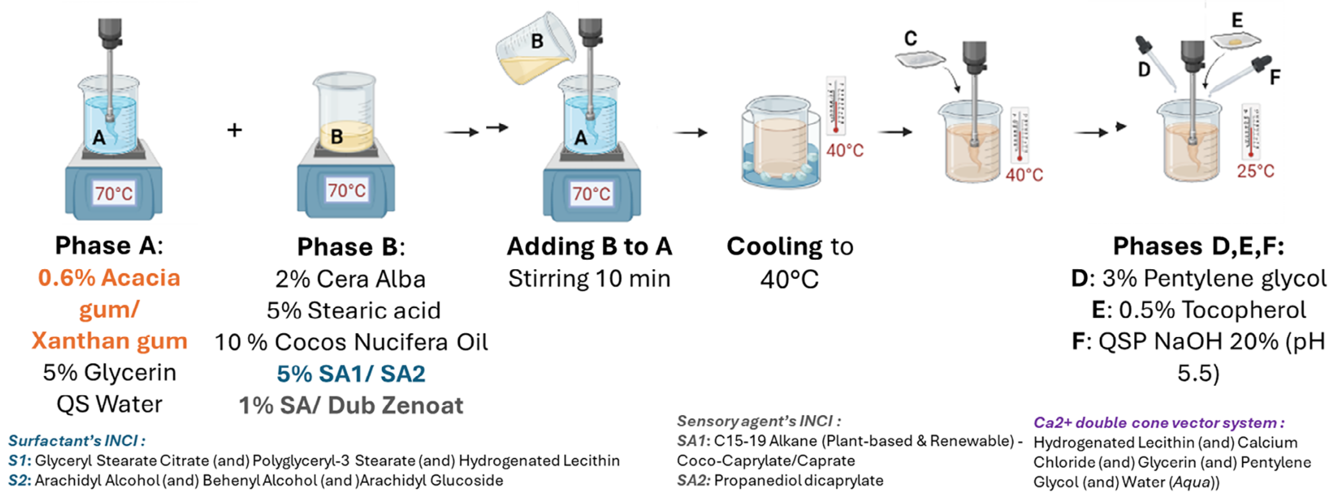

FIGURE 1 Protocol for the formulation of various O/W emulsions.

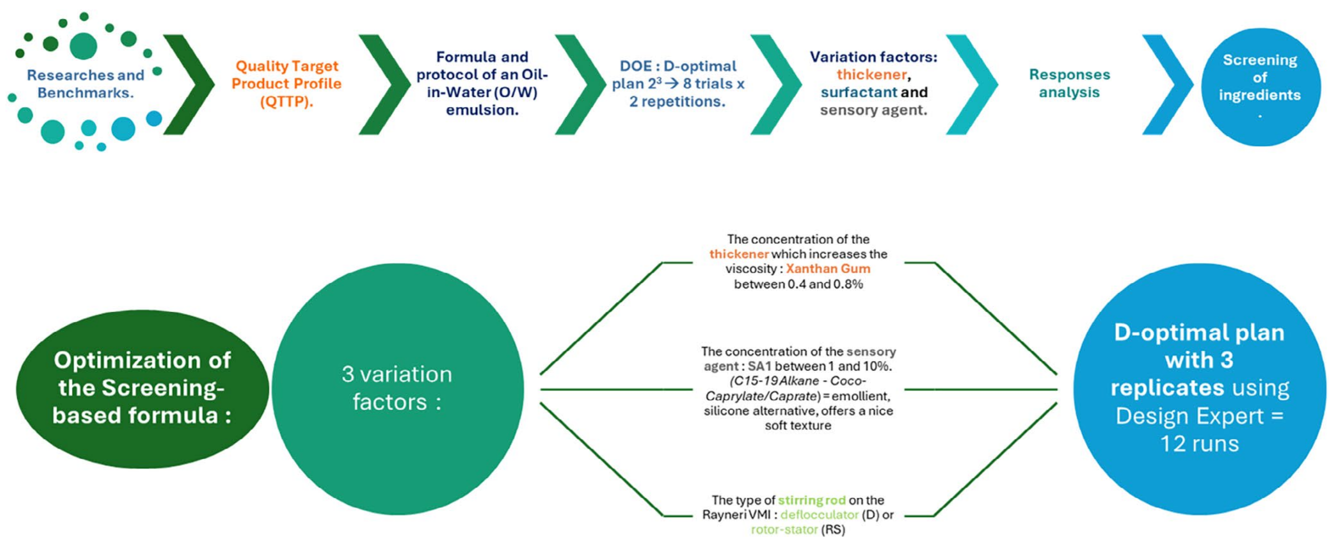

FIGURE 2 Two stages for the formulation design, starting with the screening step, followed by the optimisation step.

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TABLE 1 Composition of each formulation (Run).

Std	Run	Factor A Thickening agent (TA)	Factor B Sensory agent (SA)	Factor C Surfactant (S)
1	12	Xanthan gum	Sensory agent 1	Surfactant 1
2	16	Xanthan gum	Sensory agent 1	Surfactant 1
3	13	Acacia gum	Sensory agent 1	Surfactant 1
4	8	Acacia gum	Sensory agent 1	Surfactant 1
5	4	Xanthan gum	Sensory agent 2	Surfactant 1
6	5	Xanthan gum	Sensory agent 2	Surfactant 1
7	7	Acacia gum	Sensory agent 2	Surfactant 1
8	10	Acacia gum	Sensory agent 2	Surfactant 1
9	1	Xanthan gum	Sensory agent 1	Surfactant 2
10	6	Xanthan gum	Sensory agent 1	Surfactant 2
11	2	Acacia gum	Sensory agent 1	Surfactant 2
12	3	Acacia gum	Sensory agent 1	Surfactant 2
13	14	Xanthan gum	Sensory agent 2	Surfactant 2
14	11	Xanthan gum	Sensory agent 2	Surfactant 2
15	9	Acacia gum	Sensory agent 2	Surfactant 2
16	15	Acacia gum	Sensory agent 2	Surfactant 2

two repetitions was implemented. Sixteen formulas were generated by the Design-Expert® software by StatEase® (Minneapolis, MN, USA, Version 13) (Table 1).

For the optimisation phase, a D-optimal design based on the point exchange algorithm was implemented to fit a quadratic model. [16]. This design, as well as the statistical analysis, was generated using Design-Expert®. The variation factors were: (A) TA content (the percentage of xanthan gum in total solute, %w/w), (B) amount of the SA, in this part, the selected ingredient was the Sensory agent 1 content (%w/w), and (C) the type of the stirring rod (SR). The percentage of xanthan gum could vary from 0.4 to 0.8%, and the percentage of SA1 from 1 and 10%. For the stirring rod, either a rotor-stator (RS) or a deflocculating rod (D) was used. DoE produced 12 different formulas, with various central points (Table 2).

TABLE 2 D-optimal design generated by design expert for quadratic model.

Run	Factor A Thickening agent (TA)	Factor B Sensory agent (SA)	Factor C Stirring rod (SR)
1	0.8	10	Deflocculator (D)
2	0.4	1	Deflocculator (D)
3	0.6	5.5	Deflocculator (D)
4	0.4	10	Rotor-Stator (RS)
5	0.6	1	Rotor-Stator (RS)
6	0.8	1	Rotor-Stator (RS)
7	0.4	10	Deflocculator (D)
8	0.8	6.85	Rotor-Stator (RS)
9	0.66	10	Rotor-Stator (RS)
10	0.4	5.41	Rotor-Stator (RS)
11	0.4	1	Rotor-Stator (RS)
12	0.8	1	Deflocculator (D)

Viscosity and rheology measurements

Viscosity measurements were performed using a Brookfield viscosimeter (Brookfield Engineering Laboratories, Middleboro, MA, USA) (20 rpm, 1 min). Rheological tests were assessed using an MCR 301 rheometer (Anton Paar, Graz, Austria) at 25°C, controlled by the RheoCompass software (Anton Paar, Graz, Austria). Measurements were made with a new sample loaded for each run. A solvent trap was used to prevent solvent evaporation during measurement. The samples were allowed to relax and acclimatise for at least 2 min after loading and before measurement, following the previously described protocol [17].

Centrifugation test

Centrifugation was performed on the samples at 4000 rpm for 5 min using the laboratory centrifuge Hettich Mikro 185 (Hettich, Tuttlingen, Germany). Following the centrifugation, which simulated accelerated ageing, samples were inspected for any eventual phase separation.

Sensory analysis

Sensory analysis was performed by a sensory panel of nine trained panellists (>6 months of training time). Our team has developed EBITouch™ as an international benchmark for texture analysis, enabling visio-tactile evaluation of skin-applied products used as a reference for the attributes list and the method [18]. Each criterion was graded on a scale from 0 to 10, 10 being the high end of the scale. The analysed visual criteria were opacity, whiteness and light reflection (shininess). The textural criteria were fluidity, spreadability, slipperiness, freshness, whitening effect, softness, stickiness (e.g. adhesive effect), greasiness and no residue. All these criteria were analysed following the EBITouch™ definitions for each attribute [19]. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Ecole de Biologie Industrielle (EBI) for sensory analysis. We followed the recommendations of the ISO standards for sensory analysis and the guidelines of the Ethics Working Group of the French Society for Sensory Analysis (SFAS). A partnership agreement was established between EBI, Mibelle and the panellists involved in the project CAPIDP282022. This agreement specified the ethical conditions, including the requirement to have access to safety data for the raw materials and their recommended usage levels. The products tested were either commercially available cosmetic products or formulations developed using the same ingredient concentrations as those found in commercially available products.

Statistical analysis

Each of the quantitative properties was analysed using an Analysis of Variance (ANOVA). The proposed models were those with the most significant effects, i.e., whose *p*-value was less than 5% or 10%. When no interaction effects were significant, the results were not shown in the corresponding table. Each model was associated with a statistical indicator of estimation: the R^2 indicated the level of correlation between the experimental data and the model, while the standard deviation (SD) and the coefficient of variation (C.V.) provided the fit statistics for the model.

RESULTS

Oil-in-Water (O/W) emulsions with a reduced number of ingredients and specific properties to meet the consumers' expectations were formulated by means of a DoE (Figure 1), based on the Quality Target Product Profile (QTPP) elements and the corresponding Critical Quality Attributes (CQAs), which aligned with the product's intended performance and regulatory requirements (Table S1).

The frame of the O/W emulsion is shown in Table 3, where the main parameters covered the TA, the surfactant (S) and the SA.

TABLE 3 Frame of all the Oil-in-water (O/W) emulsion formulas.

Phase	INCI name		Function	%
Aqueous	Aqua		Solvent	QSP (65.9)
A	Glycerin		Humectant	5
	Xanthan gum	Acacia gum	Thickening agent (TA)	0.6
B	Coconut (Cocos nucifera) Oil		Emollient	10
	Cera Alba		Emollient	2
	(glyceryl stearate citrate (and) polyglyceryl-3 stearate (and) hydrogenated lecithin)	Arachidyl Alcohol (and) Behenyl Alcohol (and) Arachidyl Glucoside	Surfactant (S)	5
	C15-19 Alkane (Plant-based & Renewable) -Coco-Caprylate/Caprate	Propanediol dicaprylate	Sensory agent (SA)	1
C	Stearic acid		Emulsifying/Texturising	5
VS	Hydrogenated Lecithin (and) Calcium Chloride (and) Glycerin (and) Pentylene Glycol (and) Aqua / Water		Active	2
D	Pentylene glycol		Preservative	3
E	Tocopherol		Antioxidant	0.5
F	Sodium hydroxide (20%)		pH Regulator to 5.5	QS

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The results were collected in two phases. First, a screening phase was carried out to select the type of surfactant and SA (Figure 2). In the second phase, an optimisation of the surfactant's quantities and the type of SA was performed according to the type of stirring rod (SR) method.

The results of the screening phase of the study are shown in Table 4. The study aimed to evaluate the influence of three formulation parameters: parameter A, the TA; parameter B, the SA and parameter C, the surfactant (S) on both physicochemical and sensory properties of O/W emulsions. An Analysis of Variance (ANOVA) was conducted to determine the statistical significance of the main effects and their interactions (AB, AC, BC) on each response variable. The model's quality was assessed using R^2 values, standard deviation (SD) and coefficient of variation (C.V).

The optimisation phase aimed to refine the formulation by adjusting the quantities of the TA and SA and evaluating the effect of the stirring rod type (SR) on the final product performance. The formulation used the surfactant (S1) and sensory agent (SA1) based on the results of the screening phase. The results of the optimisation phase are described in Table 5. An Analysis of Variance (ANOVA) was conducted to determine the statistical significance of the main effects and their interactions (AB, AC, BC, A^2 and B^2) on each response variable. The model's quality was assessed using R^2 values, standard deviation (SD) and coefficient of variation (C.V).

The contour plots derived from the D-optimal DoE conducted during the screening phase are described in Figure 3. These contour plots illustrated the influence of two formulation variables: xanthan gum (A) and emollient (B) on two key sensory attributes: whitening effect (left) and absence of residue (right). The analysis was performed separately for two types of stirring rods (SR): the deflocculator (top) and the rotor-stator (bottom). These contour plots provided a visual interpretation of how these variables interacted to influence product performance in terms of whitening and after-feel.

DISCUSSION

The main objective of this study was to develop a minimalist oil-in-water (O/W) emulsion formulation using a

TABLE 4 Screening phase results—with ANOVA (analysis of variance), R^2 (level of correlation between the real data and the model), SD (standard deviation) and C.V. (coefficient of variation).

	p-value	Parameters			Parameter interactions			Fit statistics		
ANOVA	**Model**	**A TA**	**B SA**	**C S**	**AB**	**AC**	**BC**	R^2	**SD**	**C.V. %**
Viscosity	<0.001	<0.001	0.439	<0.001	—	—	—	0.89	3307.39	25.35
Droplet size	<0.001	<0.001	0.018	<0.001	0.248	0.258	0.077	0.95	1.08	6.87
White colour	<0.001	0.077	0.335	<0.001	—	—	—	0.83	0.28	3.35
Fluid	0.003	0.017	0.531	0.002	—	—	—	0.67	1.04	17.65
Whitening	0.018	0.093	0.786	0.003	0.583	0.036	0.187	0.76	0.69	25.79
Spreading	0.037	0.176	0.333	0.012	—	—	—	0.49	0.78	9.83
Stickiness	0.055	0.013	0.287	0.543	—	—	—	0.46	0.51	28
Greasiness	0.015	0.15	0.126	0.007	—	—	—	0.57	0.51	10.41
No residue	0.071	0.386	0.48	0.017	—	—	—	0.43	0.97	12.88

Abbreviations: S, surfactant; SA, sensory agent; TA, thickening agent.

TABLE 5 Optimisation phase results. Surfactant (S) 1 and the Sensory agent (SA) 1 were used.

	p-value	Parameters			Parameter interactions					Fit statistics		
ANOVA	**Model**	**A TA**	**B SA**	**C stirring rod (SR)**	**AB**	**AC**	**BC**	A^2	B^2	R^2	**SD**	**C.V. %**
Fluid	0.002	0.002	0.006	0.892	—	—	—	—		0.82	0.89	17.0
Whitening	<0.001	<0.001	0.01	0.901	—	—	—	—		0.87	0.63	12.7
Spreading	0.429	0.128	0.423	0.564	0.536	0.321	0.79	0.16	0.445	0.79	0.4	5.3
Stickiness	0.119	0.77	0.254	0.033	—	—	—	—	—	0.5	0.39	17.4
Greasiness	0.801	0.898	0.618	0.437	—	—	—	—	—	0.11	0.95	17.3
No residue	0.297	0.26	0.266	0.731	0.199	0.111	0.618	0.575	0.118	0.85	0.77	10.5

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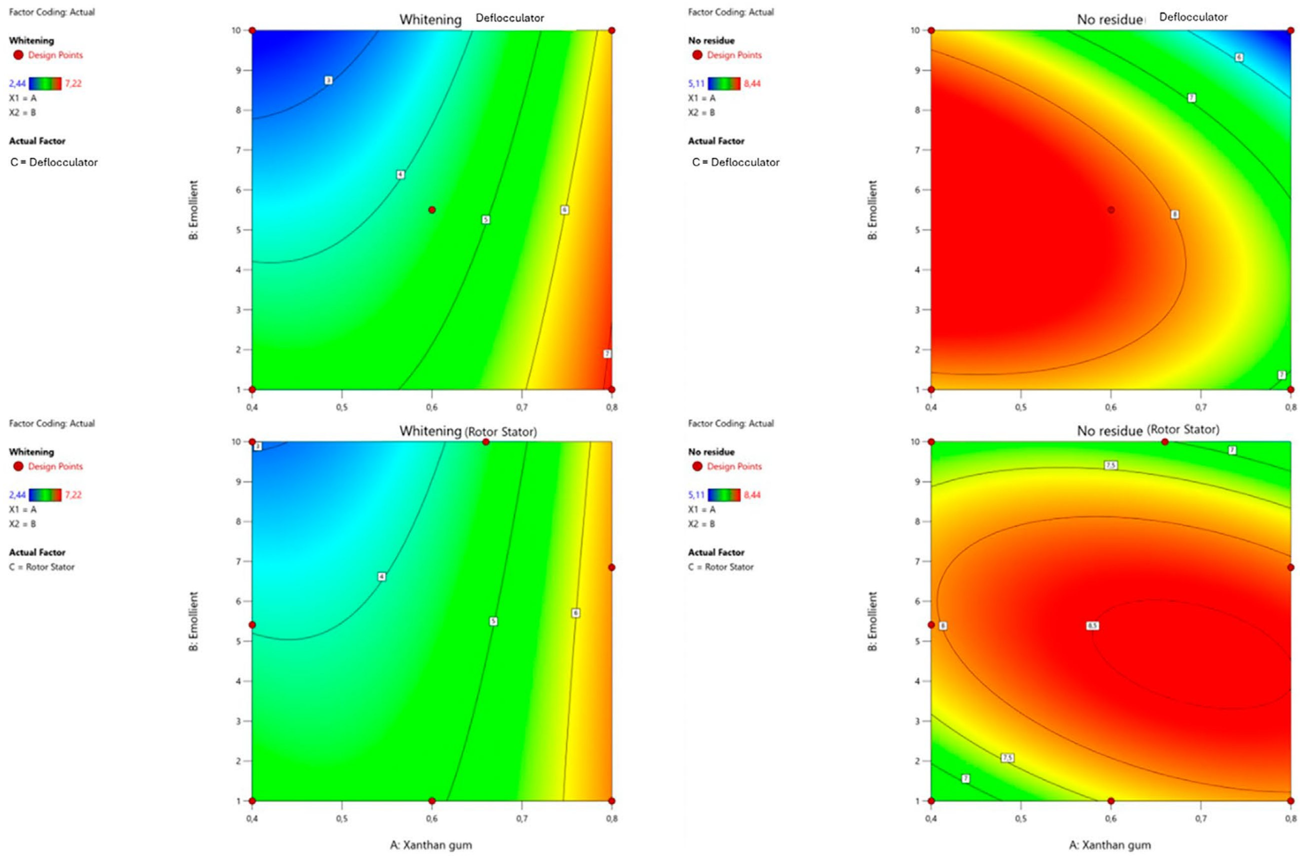

FIGURE 3 Contour plots from D-optimal design of experiments (DoE) of the screening step showing the whitening and no residue effect using xanthan gum, and with either a deflocculator or rotor stator.

DoE approach, while assessing its stability and sensory performance.

A specific active component was incorporated in the emulsion, which has shown efficacy in restoring skin barrier function through a novel calcium (Ca^{2+}) delivery system, as demonstrated in both in vitro and clinical studies according to Baumann et al. This effect was particularly relevant for stressed or aged skin, where calcium gradients are compromised [11].

Stabilisation of O/W emulsion, where oil is dispersed in an aqueous phase, occurs with hydrophilic-hydrophobic particles. Therefore, the chemical composition of the formulation and the mixing process impact the emulsion's stability and its physicochemical properties [20].

During the screening and optimisation phases, the effects and interactions among the main parameters were investigated: surfactant (S), TA, SA and the stirring rod type (SR). The DoE approach applied in both phases showed that the results of physicochemical analysis (such as viscosity, droplet size) correlated with the sensory analysis (mainly including fluidity, whitening, stickiness, absence of residue) across different formulations (runs) in comparison to a marketed moisturising benchmark.

In the screening method, all parameters showed at least one significant effect. In almost half of the cases, the R^2 was below 0.8 (fluidity, spreading, stickiness and greasiness), which indicated that these experiments may have overlooked different targeted effects relevant to the consumer's interest in the emulsion formulation.

All three parameters (SA, S and TA) showed a significant effect on the droplet size, with interactions occurring between the SA and the surfactant (S) (Figures S1 and S2). The TA and the SA had a significant impact on the viscosity and fluidity of the emulsion during the setting phase, while the surfactant (S) showed no significant effect.

The droplet size was significantly affected by all three variables, particularly the TA and surfactant, as well as their interaction (AB), with high accuracy. Acacia (TA1) and xanthan (TA2) gums were classified as natural polysaccharides; acacia gum was characterised by amphiphilic properties, whereas xanthan gum exhibited hydrophilic behaviour. [21]. Their chemical differences were described by Kobra et al., showing that acacia gum contained hydrophobic amino acids that interacted with oil droplets, and hydrophilic sugar residues, bringing stability in the aqueous phase compared to xanthan gum, with only free carboxyl groups [22]. Xanthan gum exhibited properties

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of enhancing skin penetration and whitening, due to its coating properties as described by Lv et al. [23].

The choice of the surfactant had a significant effect on the whiteness of the product during application. The use of (S1) resulted in emulsions that appeared less white compared to those formulated with (S2). Jiang et al. explained that the surfactants used in their study exhibited stronger hydrophilic interactions across the entire oil–water interface, contributing to the observed differences in whitening [22]. In the present study, the interaction BC (SA × S) was marginally significant for whitening, suggesting a possible synergistic effect. This could be due to the decrease in the droplet size while improving the emulsion's stability [23].

The process of thickening involves the non-specific entanglement of conformationally disordered polymer chains. For the after-feel, the TA had a significant effect on the stickiness of the emulsion. Due to its coating effects, xanthan gum emulsions showed a higher stickiness than those using acacia gum. These results were consistent with the comparative study described by Saha and Bhattacharya [24]. In their study, the authors reported that xanthan gum helped produce firm, gel-like textures in semi-solid and viscous systems that correlated with the higher observed stickiness. Acacia gum was reported to yield light, fluid textures with no significant contribution to the emulsion's texture [24].

Finally, the SA had a significant effect on the oily residue. Furthermore, the emulsion formulated with SA2 exhibited faster skin penetration and was perceived as less greasy, leaving less residue compared to the emulsion formulated with SA1.

In the second phase of optimisation with DoE, only some sensory properties showed significant differences. There was a significant effect of xanthan gum and emollient on flowability. The influence of the process, using an agitator rod, was observed in relation to the whitening effect of the emulsion upon application, as well as its stickiness after application. These results emphasised a clear influence of xanthan gum on the ease of spreading upon application (Table 5).

The amount of the TA and its relationship with the intensity of oiliness were directly correlated with the emulsion's viscosity. A similar approach was described by Hayakawa et al. [25]. Similarities were observed in the behaviour of the TA and the emollient across both types of mixers, suggesting that their functional roles in the formulation remained consistent regardless of the mixing method.

The isocontour curves (Figure 3) of the models predicting the whitening effect (left) and the ease of penetration (right) showed similarities between the two SR methods used: deflocculator (top) and rotor stator (bottom). It can also be noted that the products were more whitening and less penetrating when formulated with the rotor stator compared to the products formulated with the deflocculator.

The use of xanthan gum, a biopolymer (at 0.6%), proved to offer a modification in the rheological properties, under high-shear processing conditions [26]. There was a tradeoff between the amount of the TA and the emollient for both mixers. Differences in the sensory evaluation of the emulsion were observed between the two types of SR used: deflocculator or rotor-stator. The dispersing system used in the optimisation step correlated with the decrease in droplet size due to the surfactant's effect [27] and the absence of residue with improved formulation skin penetration. The results of the chromameter, rheology and viscosity analysis are described in Figures S3 and S4.

Both the screening and optimisation formulations showed a sensory profile approaching the reference products. The radar chart (Figure 4) first displayed the quantitative profile of the O/W emulsions from the screening run 11, followed by the optimisation run 12. These profiles were assessed across seven attributes: fluidity, whitening effect, spreading, stickiness, greasy effect and no residue, in comparison with the marketed benchmark. The benchmark served as a reference, providing standard values against which the screening and optimisation runs were compared, and it exhibited moderate levels across all the attributes without any specific distinctive feature.

Screening run 11 performed well in the fluid and whitening attributes, with less spreadability and stickiness. Screening run 11 showed more variation compared to the optimisation run, with lower performance in the greasy and spreading attributes.

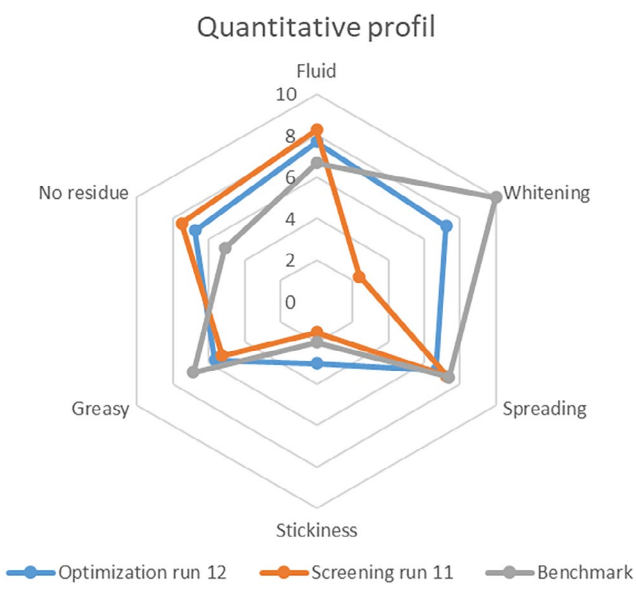

FIGURE 4 Sensory profile of the screening DoE run 11 and optimisation DoE run 12, compared to the Benchmark.

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Optimisation run 12 was more fluid, with a higher whitening effect, no residue and moderate performance for the remaining attributes. Optimisation run 12 demonstrated notably better performance than both the screening run and the benchmark in terms of fluidity and absence of residue, indicating clear formulation improvement during the optimisation step.

Thomas et al. [28] reported similar findings when correlating sensory analysis with the emulsion's functional properties, focusing on attributes such as firmness, spreadability and slipperiness, using 2% of TA.

CONCLUSION

This DoE allowed the optimisation of a screening-based formula to enhance the use of an innovative Ca^{2+} double cone vector system as an active ingredient. The impact of three factors was analysed: the thickener (xanthan gum), the sensory agent (SA1) and the process (rotor stator or deflocculator). The optimal formula had 0.8% xanthan gum and 1% SA1. The optimisation run 12 formulation was chosen as it met the targeted established criteria of the optimisation: a viscosity close to the benchmark's, a creamy product, white, not too greasy or too whitening and highly penetrating the skin. The final bioinspired formula had a reduced INCI list, containing natural ingredients with at least 95% of ingredients from natural origin. Formula optimisation was achieved by varying the shearing process and adjusting the proportions of specific ingredients (SA and thickener) to obtain a cream with optimal properties. The results highlighted the importance of the process tool, where using the rotor stator offered better shearing, resulting in smaller droplet sizes and better incorporation of the oily phase, which improved the sensory experience. The study also highlighted the impact of modulating the concentrations of xanthan gum and SA1, particularly on the sensorial experience. The findings were consistent with the role of xanthan gum in influencing the fluidity of the emulsion, coupled with a synergistic action of the SA1, which reduced skin penetration and decreased the whitening effect.

The cream formulation intended to serve as a model minimalist formula should be completed by further analysis to better analyse the interactions between the selected ingredients in the rheological characterisation and enhanced emulsion stability.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Choi EH. Aging of the skin barrier. Clin Dermatol. 2019;37(4):336–45. https://doi.org/10.1016/j.clindermatol.2019.04.009
2. Ibuki A, Kuriyama S, Toyosaki Y, Aiba M, Hidaka M, Horie Y, et al. Aging-like physiological changes in the skin of Japanese obese diabetic patients. SAGE Open Med. 2018;6:2050312118756662. https://doi.org/10.1177/2050312118756662
3. Nikolakis G, Makrantonaki E, Zouboulis CC. Skin mirrors human aging. Horm Mol Biol Clin Invest. 2013;16(1):13–28. https://doi.org/10.1515/hmbci-2013-0018
4. Camilion JV, Khanna S, Anasseri S, Laney C, Mayrovitz HN. Physiological, pathological, and circadian factors impacting skin hydration. Cureus. 2022;14(8):e27666. https://doi.org/10.7759/cureus.27666
5. Rajkumar J, Chandan N, Lio P, Shi V. The skin barrier and moisturization: function, disruption, and mechanisms of repair. Skin Pharmacol Physiol. 2023;36(4):174–85. https://doi.org/10.1159/000534136
6. Barnes TM, Mijaljica D, Townley JP, Spada F, Harrison IP. Vehicles for drug delivery and cosmetic moisturizers: review and comparison. Pharmaceutics. 2021;13(12):2012. https://doi.org/10.3390/pharmaceutics13122012
7. Oliveira R, Almeida IF. Patient-centric design of topical dermatological medicines. Pharmaceuticals. 2023;16(4):617. https://doi.org/10.3390/ph16040617
8. Rinnerthaler M, Streubel MK, Bischof J, Richter K. Skin aging, gene expression and calcium. Exp Gerontol. 2015;68:59–65. https://doi.org/10.1016/j.exger.2014.09.015
9. Lee SE, Lee SH. Skin barrier and calcium. Ann Dermatol. 2018;30(3):265–75. https://doi.org/10.5021/ad.2018.30.3.265
10. Tu CL, Bikle DD. Role of the calcium-sensing receptor in calcium regulation of epidermal differentiation and function. Best

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Pract Res Clin Endocrinol Metab. 2013;27(3):415–27. https://doi.org/10.1016/j.beem.2013.03.002
11. Baumann J, Wandrey F, Sacher R, Zülli F. A novel Ca2+ double cone vector system to treat compromised skin. Int J Cosmet Sci. 2024;46(2):228–38. https://doi.org/10.1111/ics.12926
12. Düring A. s.d. How to formulate with EpiCalsome™. 2025 [En ligne] [cited 2025 February 24]. Available from: https://mibellebiochemistry.com/how-formulate-epicalsometm
13. Costa GMDA, Alves GDAD, Campos PMBGM. Application of design of experiments in the development of cosmetic formulation based on natural ingredients. Int J Phytocosmet Nat Ingred. 2019;6(1):4. https://doi.org/10.15171/ijpni.2019.04
14. Hummel M, Lavarde M, Pages P, Mallard H, Plejewski P, Pense-Lheritier AM. Experimental design and evaluation of the influence of a glucomannan-based thickener on the characteristics of an oil/water emulsion. Int J Phytocosmet Nat Ingred. 2020;7(1):9. https://doi.org/10.15171/ijpni.2020.09
15. Mibelle Biochemistry. MelanoGray™—Delay hair greying and recover natural hair color. n.d. [cited 2025 February 24]. Available from: https://mibellebiochemistry.com/fr/node/249
16. Atkinson AC, Donev AN, Tobias RD. Optimum experimental designs, with SAS. Oxford: Oxford Academic; 2007; online edn. https://doi.org/10.1093/oso/9780199296590.001.0001
17. Imbart S, Laplanche A, Ruzic C, Lavarde M, Marull-Tufeu S, Bernard C, et al. Design of a sensorial-instrumental correlation methodology for a category of cosmetic products: O/W emulsions. Cosmet. 2022;9(4):84. https://doi.org/10.3390/cosmetics9040084
18. Deubler G, Zhang C, Talavera MJ, Swaney-Stueve M. Sensory evaluation in the personal care space: a review. J Sens Stud. 2022;37(6):e12788. https://doi.org/10.1111/joss.12788
19. Vieira GS, Lavarde M, Fréville V, Rocha-Filho PA, Pensé-Lhéritier AM. Combining sensory and texturometer parameters to characterize different type of cosmetic ingredients. Int J Cosmet Sci. 2020;42(2):156–66. https://doi.org/10.1111/ics.12598
20. David MNV, Akhondi H. Emulsions. StatPearls. Treasure Island (FL): StatPearls Publishing; 2023 [Updated 2023 Jul 30].
21. Kobra K, Wong SY, Mazumder MAJ, Li X, Arafat MT. Xanthan and gum acacia modified olive oil based nanoemulsion as a controlled delivery vehicle for topical formulations. Int J Biol Macromol. 2023;253:126868. https://doi.org/10.1016/j.ijbiomac.2023.126868
22. Jiang J, Wang Z, Wang C, Shi L, Hou J, Zhang L. Effect of nonionic surfactants on the synergistic interaction between asphaltene and resin: emulsion phase inversion and stability. Colloids Surf A Physicochem Eng Asp. 2023;675:132056. https://doi.org/10.1016/j.colsurfa.2023.132056
23. Lv X, Wu Z, Qi X. High skin permeation, deposition and whitening activity achieved by xanthan gum string vitamin c flexible liposomes for external application. Int J Pharm. 2022;628:122290. https://doi.org/10.1016/j.ijpharm.2022.122290
24. Saha D, Bhattacharya S. Hydrocolloids as thickening and gelling agents in food: a critical review. J Food Sci Technol. 2010;47:587–97. https://doi.org/10.1007/s13197-010-0162-6
25. Eren NM, Santos PH, Campanella O. Mechanically modified xanthan gum: rheology and polydispersity aspects. Carbohydr Polym. 2015;134:475–84. https://doi.org/10.1016/j.carbpol.2015.07.092
26. Hayakawa F, Tanisawa Y, Hatae K, Shimada A. Relationship between the sensory evaluation for oiliness and physical properties in model emulsions. J Home Econ Japan. 1995;46(8):765–74.
27. Welch CF, Rose GD, Malotky D, Eckersley ST. Rheology of high internal phase emulsions. Langmuir. 2006;22(4):1544–50. https://doi.org/10.1021/la052207h
28. Thomas E, Hurst O, Marsh J, Willcox J, Cunningham N, Jeulin S. Quantitative sensory interpretation of rheological and tribological parameters of emulsions: impact of the nature of the emollient on key sensorial attributes. 2021 In Proceedings of the SCC 75th Annual Scientific Meeting & Showcase. Society of Cosmetic Chemists.

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