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A Methodology for Emulsion Design Based on Emulsion Science and Expert Knowledge. Part 2: An Application in the Cosmetics Sector

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Keywords

Emulsion formulation, chemical product design, cosmetic products, decision methodology, early design stages, Consumer Centered Chemical Products

Abstract

The design of micro-structured chemical products such as emulsions is not a simple task, because they are complex systems in which their components, structures, phenomena, and processes are highly interrelated. Any design decision must be made considering its multiples effects on the next stages of the design, production, use and recycling of the product. The uncertainty and the impact of the decisions are more critical at early design/screening/exploratory stages, when information is scarce and main product characteristics are defined. This study presents an application of a design methodology for early design stages that considers the interrelation between design decisions in oil-in-water (O/W) emulsions. The methodology was explained in detail in the first part of the article containing the conceptual approach. In this second part, the methodology is exemplified through a case study of the cosmetics sector: the design of a moisturizing cream. The case is presented in two parts: First, the decision-making process following the three steps of the methodology is explained. Then, the experimental results are presented and discussed. For the case study, the methodology helped to develop five conceptual alternatives of the product based on the use of a nonionic surfactant system, and prototypes were made and tested. It was found that the elements of the methodology can be used for the generation of product alternatives that correspond to the design problem.

1. Introduction

The chemical industry is changing rapidly in response to new challenges such as strong competition in the chemical market, public concern about environmental impacts and ever-changing customer requirements¹. In this context, many companies are finding new growth opportunities through the development of high added-value products such as consumer chemical products. To seize those opportunities, companies require a systematic product design

methodology, enabling them to generate innovative products efficiently and to respond to a diversified market faster than their competitors.

The development of product design methodologies has been the goal of multiple studies. For example, Cussler and Moggridge proposed a generic methodology for chemical product design^{2,3}, based on the proposal for mechanical product design developed by Ulrich and Eppinger⁴. They divided the chemical product design process into four stages: (1) needs identification, (2) generation of product ideas, (3) selection of the most promising ideas, (4) process design.

Since their seminal work, different approaches have been proposed following a similar set of design stages⁵⁻¹⁰. However, these stages cannot be applied sequentially in all cases. Specifically, in the case of micro-structured chemical products (e. g. emulsions and colloidal products), it is difficult to establish a workflow because of the intrinsic complexity of the system to be designed. Micro-structured chemical products are formed by multiple components interacting in different scales^{1,11}. They must be designed in a manner that guarantees their technical feasibility, the satisfaction of customer needs and the fulfillment of sustainability requirements¹. The achievement of such a design is not straightforward, because the elements forming the product (ingredients, micro-structure, phenomena, packaging) are highly interrelated. Thus, design decisions to be made must consider this complex scenario. This is critical at early design stages when information is scarce and the multiple effects of a decision on final emulsion properties are still vague.

To contribute to the research on Chemical Product Design, this study shows the application of a novel methodology for the design of emulsion type chemical products in the cosmetics sector. The methodology has the following contributions: (1) it is applicable at early design stages, i.e., when ingredients have not been defined and the first decisions about the product are made. (2) It

considers emulsions as systems where any design decision may affect the entire product, and thus their effects must be considered simultaneously. (3) It enables the rapid visualization of the effects of a decision/ group of decisions (solution strategies) in multiple product characteristics (sub-problems). The methodology was explained in detail in a previous publication corresponding to the first part of this paper ¹². This article shows the application of the methodology in a case study: the design of a moisturizing cream. In that case, the methodology is used to explore sets of solution strategies responding to a design problem, to plan an experimental design and to propose design modifications after performing the first experiments to move toward the fulfillment of product specifications.

This article presents the application of the methodology to the design of a moisturizing cream. It begins by explaining the design problem and applying the steps of the methodology. During the design, product specifications are transformed into sub-problems, then into solution strategies and finally into product alternatives. Product alternatives are explored experimentally to create product prototypes. The article ends by presenting and analyzing the conceptual and experimental results.

2. Overview of the Methodology for Emulsion Design Based on Emulsion Science and Expert Knowledge

The methodology comprises the steps presented in Figure 1 and four tools for the different steps: (1) list of sub-problems, (2) list of solution strategies, (3) database of ingredients and (4) two relational matrices connecting the three previously mentioned elements. The inputs of the design process are product specifications, and the outputs are product alternatives meeting these

specifications. Product alternatives are then converted to product prototypes through experimentation, as it is briefly explained below.

- Before the application of the methodology, the design problem must be defined in terms of product specifications, e.g., measurable product properties and characteristics, which are the goals to be achieved in the design. The preparation of the design problem requires interdisciplinary work and in some cases the consultation of experts and/or customers.
- In the first step, the defined product specifications are classified according to a predefined list of 21 general sub-problems (element 1), shown in Figure 2. Sub-problems are emulsion properties, characteristics and phenomena that may be desired or not in a product. They were defined based on emulsion science principles and classified into five groups: appearance, rheology, stability, transport processes and special properties (U.V. protection, antioxidant activity, and so on). Examples of sub-problems in the category emulsion stability are biological stability, stability against lipid oxidation, stability against gravitational separation, among others. A product specification can be classified according to more than one sub-problem and/or switch directly to special functions when its achievement requires a specific functional ingredient. For example, the specification “product odor” comprises two characteristics: odor intensity and fragrance type. The first is classified in the category transport processes and in the sub-problem release of a volatile molecules (Sub-problems D20 or D21 in Figure 2, depending on fragrance nature). Fragrance type is connected to special functions – fragrance and subsequently to a database of ingredients.
- In the second step, sub-problems are connected to solution strategies that could solve them. The connection is done using a predefined relational matrix (element 4), which indicates

the effect of 30 solution strategies (Figure 3, element 2) on the sub-problems. Solution strategies were previously defined based on emulsion science principles and the effects were validated by experts. The matrix and its uses were presented in detail in the previous publication ¹². Solution strategies are design paths related to emulsion structure, phases, and nature of ingredients but not directly to specific ingredients or process variables. Examples include changes in the continuous phase such as pH and electrolyte concentration, or changes in structural variables such as droplet size and droplet size distribution, etc.

- In the third step, solution strategies are connected to ingredient types using a second relational matrix (element 4) and a database of compounds (element 3). In this step, product alternatives are created by selecting ingredients. The experimental exploration of these alternatives enables the generation of product prototypes in a subsequent experimental step.

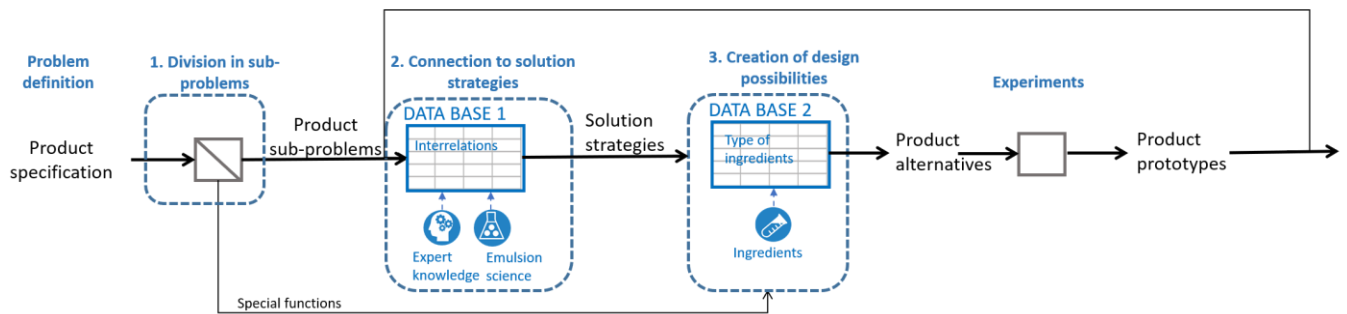


Figure 1. Workflow of the decision methodology for emulsion formulation

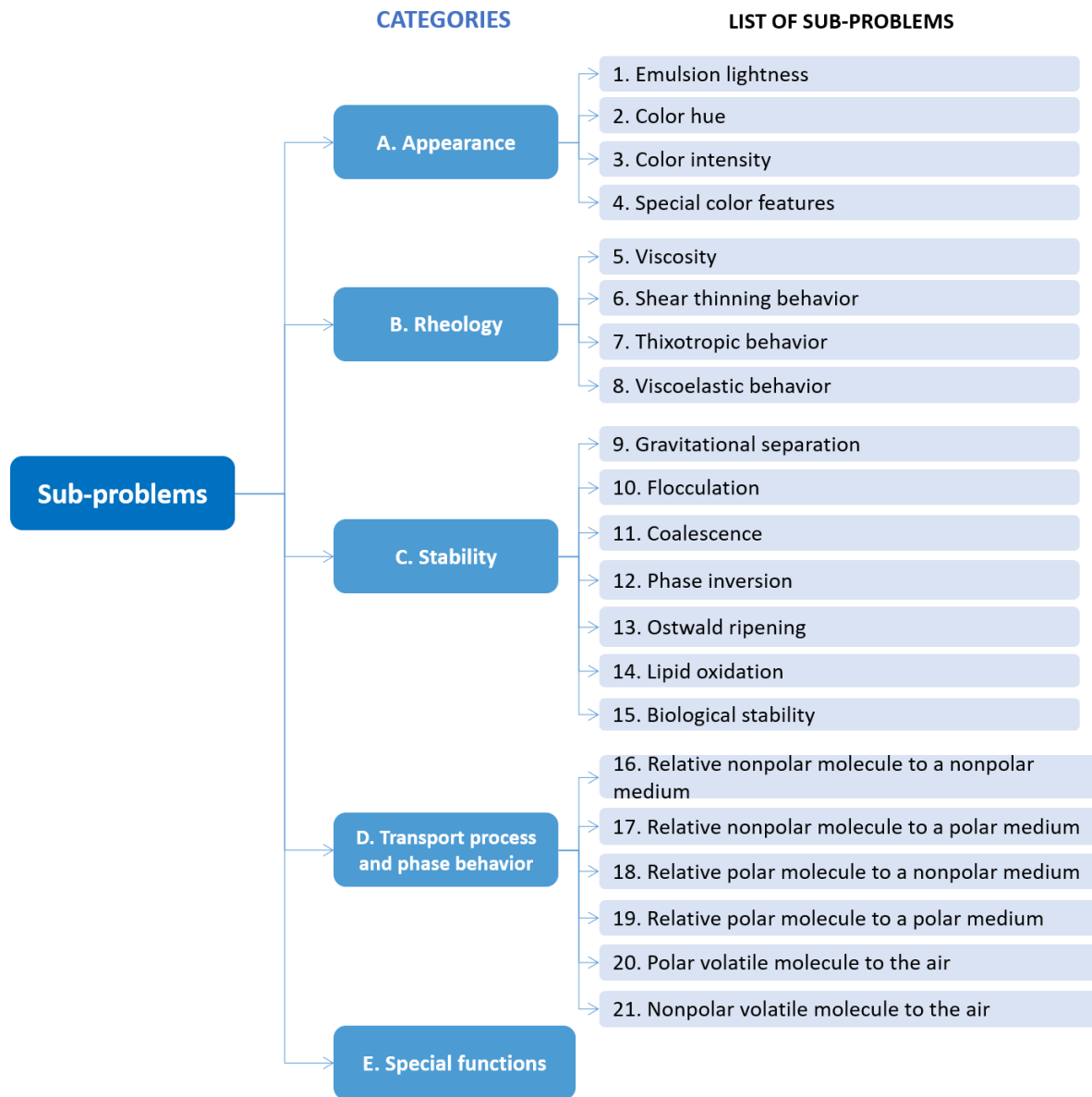


Figure 2. List of sub-problems for emulsion formulation

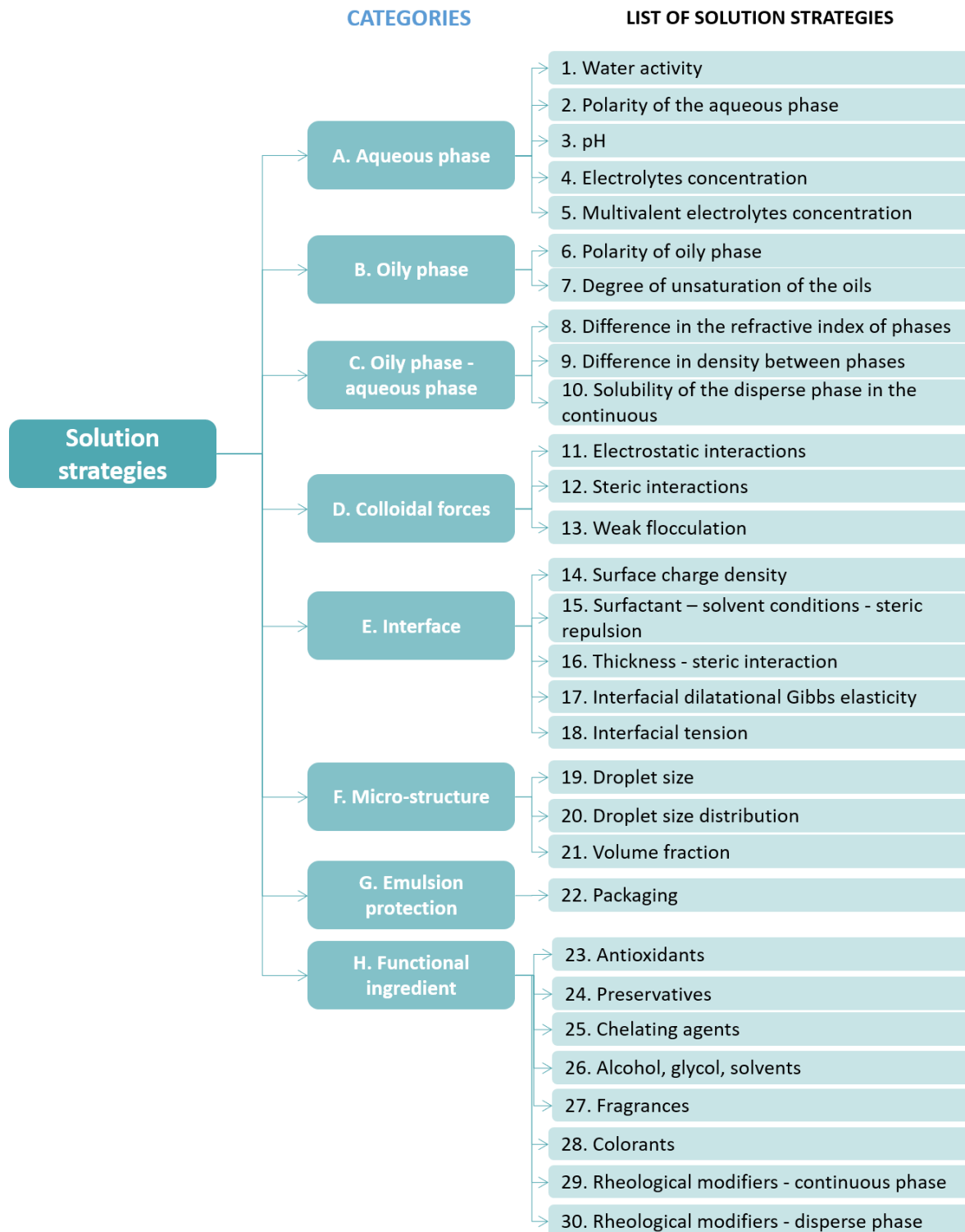


Figure 3. List of solution strategies for emulsion formulation

3. Design problem description

The design problem is described through product specifications and their respective target values. Both form the goals that guide the design process. Product specifications are a set of properties or characteristics that describe the product performance through measurable variables. Target values of specifications can be numbers, intervals, integers, or precise adjectives corresponding to the product desired behavior.

The case study is the design of a facial moisturizing cream containing calendula oil as a natural antioxidant. This example was chosen in line with the objective of the entrepreneurial project “Xiu Aguee - *Aceites esenciales* - Colombia”, which aims to confer added value to the current products of the company, mainly essential oils and hydrosols (water of essential oils) extracted by steam distillation. Calendula essential oil one of the flagship products of the company, traditionally used to treat skin inflammation^{13,14}. In addition, studies have shown that it has significant antioxidant activity^{15,16}, which makes it an interesting ingredient for cosmetic application.

Product specifications were determined based on an exploratory study of potential customers. In that study, needs were identified through a survey on 213 respondents. Subsequently, the needs were analyzed by applying the Kano model^{17,18} to 32 respondents. Next, the needs were translated into product specifications with target values applying the Quality Functional Deployment (QFD)¹⁹ with the participation of 20 experts from the cosmetics sector (of whom 60% have more than five years of experience)²⁰ and 58 customers consulted about the sensation a set of creams with different rheological profiles generates. Based on the answers of customers, a target rheological profile was selected.

Table 1 presents the specifications of the facial moisturizing cream containing calendula oil, along with the target values for the case study. Figure 4 presents the target rheological profile selected with the participation of customers.

Table 1. Design problem definition: Product specifications of a facial moisturizing cream containing calendula oil

Categories of product specifications	of	Product specification	Target values
Safety and Regulation	1	Physical/chemical stability	6 months
	2	Toxicology	Only allowed cosmetic substances are used ²¹
	3	Microbiological quality	less than 10 ³ cfu/g ²²
	4	Use of allowed substances	Only allowed cosmetic substances are used ²¹
	5	Dermal tolerance and non-irritability	Use of substances that do not irritate skin ²³
Sensorial evaluation	6	Product odor – intensity and fragrance type	Qualitative characteristic to be tested with a panel
	7	Low oil skin sensation	Qualitative characteristic to be tested with a panel
Performance evaluation	8	Sensation of hydration just after product application	Measure of skin hydration by corneometry -Hydration index > 60 ²⁴
	9	Sensation of hydration – long term	Measure of skin hydration by corneometry after 8 hours from application-Hydration index > 60 ²⁴
Instrumental tests	10	Light and fluid product - low viscosity and low viscoelastic modulus	A rheological profile was defined based on benchmarking and customer consultation. It is presented in Figure 4.
	11	pH	A slight acid value is preferred to protect the acid mantle of the facial skin. A value of pH 4.5 -5.7 corresponding to normal skin is selected ²⁵ .
Price	12	Product price	7-10 euro (benchmarking)
Additional	13	Antioxidant function	Antioxidant test DPPH

Nature ingredients	of 14	It should contain ingredients of natural origin. Ingredients with low user acceptance such as parabens should be avoided	-
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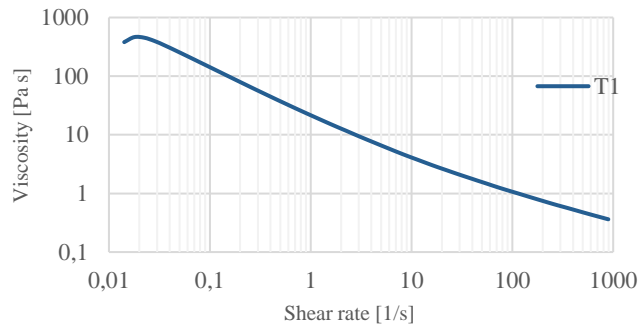


Figure 4. Design problem definition: The target profile was defined with the participation of customers (specification 10)

4. Step 1: Classification of product specifications into sub-problems

Once the product specifications were defined, they were classified according to the list of sub-problems presented in Figure 2. For this connection, product designers must properly understand the meaning of each specification and sub-problem. A specification may correspond to more than one sub-problem, and/or two specifications may correspond to the same sub-problem. Some specifications may require the enlargement of a sub-problem (positive effect) and some may require its diminution (negative effect). Moreover, some specifications may be directly related to a specific ingredient or to a specific solution strategy. Table 2 and Figure 5 show the classification of the specifications into sub-problems. Table 2 shows that specification 1 – physical/chemical stability is related to six sub-problems (C9 to C15) in the stability category. Specification 1 and specification 3 are both related to the sub-problem C15 - biological stability. To meet product specifications, the nature of some ingredients is defined (Figure 5, ingredient types). The viscosity and viscoelastic behavior sub-problems (B5 and B8 respectively) are to be reduced (negative

symbol in Figure 5), while sub-problem B6-sheat thinning behavior is to be enhanced. Additionally, four solution strategies are already fixed due to the design problem statement: A3 - pH, H23 - antioxidants, H26 - alcohols, glycols, solvents and H27 - Fragrances.

Table 2. Classification of product specifications into sub-problems of a facial moisturizing cream containing calendula oil - case study

Categories of product specifications	of	Product specification	Classification in sub-problems
Safety and Regulation	1	Physical/chemical stability	Control of all stability sub-problems: C9- Gravitational separation C10- Flocculation C11- Coalescence C12- Phase inversion C13- Ostwald ripening C14- Lipid oxidation C15- Biological stability
	2	Toxicology	Characteristic of ingredients: low toxicology
	3	Microbiological quality	Subproblem C15 – Biological stability
	4	Use of allowed substances	Characteristic of ingredients: only approved cosmetic ingredients
	5	Dermal tolerance and non-irritability	Characteristic of ingredients: approved cosmetic ingredients/avoid the used of allergenics
Sensorial evaluation	6	Product odor – intensity and fragrance type	Subproblem D21 - Release of a relative nonpolar volatile molecule to the air Ingredient type : fragrance. Solution strategy H27 -Fragrance is fixed
	7	Low oil skin sensation	Characteristic of ingredients: oils with low oily sensation
Performance evaluation	8	Sensation of hydration just after product application	Characteristic of ingredients: use of humectants and moisturizers. Common humectants are glycols such as glycerin. Thus, solution strategy H26 – alcohols and glycols is fixed.
	9	Sensation of hydration – long term	Characteristic of ingredients: use of humectants and moisturizers
Instrumental tests	10	Light and fluid product - low viscosity and low viscoelastic modulus.	The sub-problems B5 – LOW viscosity (negative effect), B6 – Shear thinning behavior, B8 – LOW viscoelastic behavior (negative effect) are selected
	11	pH	Solution strategy A3 -pH is fixed

Price	12	Product price	Characteristic of ingredients: price
Functions	13	Antioxidant function	The use of calendula oil is mandatory. Solution strategy H23 -antioxidants is fixed
Natural ingredients	14	It must have ingredients of natural origin. Problem ingredients as parabens are to be avoided	Characteristic of ingredients: At least an ingredient must be of natural origin

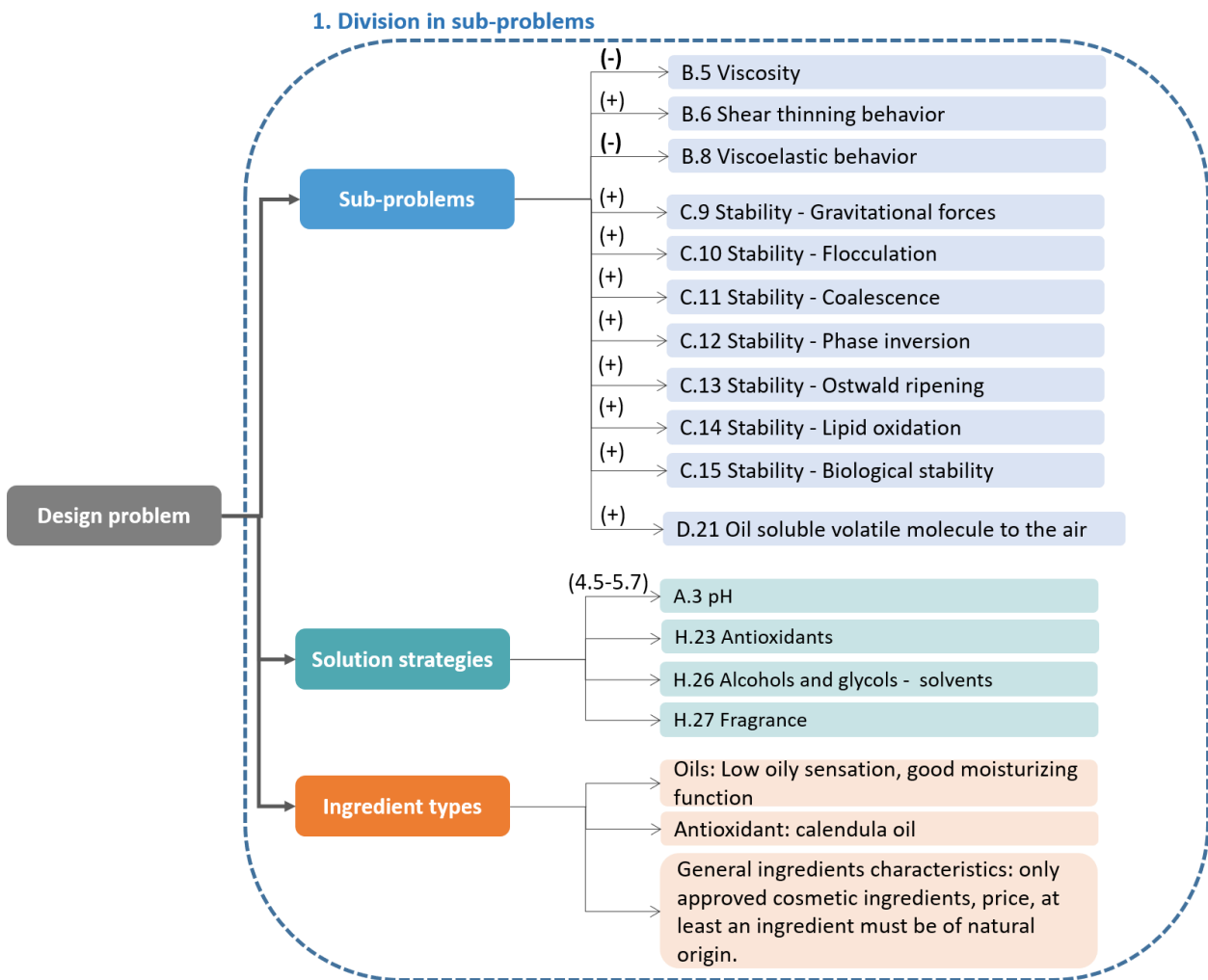


Figure 5. Results of step 1 - Classification of product specifications into sub-problems for the design of a facial moisturizing cream containing calendula oil (The positive symbol means the sub-problem should be enlarged to meet product specifications; the negative symbol means it should be reduced)

5. Step 2-Selection of solution strategies

In this step, sets of solution strategies to solve the identified sub-problems are defined using the first relational matrix presented in the previous publication of the methodology¹². An O/W emulsion is selected to form the product, because it is widely used to create lotions and light creams as defined in the design problem. Five sets of solution strategies are proposed:

Set 1 responds to the following aspects:

- Aspect a: What kind of surfactant best meets the specifications of the problem?: A nonionic surfactant was selected as the basis of the solution set because it tends to be less irritant and milder than ionic surfactants. This was done because the product is for facial use. Thus, the solution strategies D12 – steric interaction and E15- Surfactant solvent conditions are included in the solution set 1.
- Aspect b: Should functional ingredients be included to achieve product specifications? Are there pre-selected solution strategies? Responding to these questions, the preselected solution strategies shown in Figure 5 are included in the solution set 1. That is, the strategies A3 low pH, H23 antioxidants (because of the use of calendula oil as antioxidant), H26 alcohols and glycols (because of the addition of a humectant), and H27 fragrances (because of the use of essential oils, as stated in the design problem).
- Aspect c: Additionally, to respond directly to the group of sub-problems B5, B6 and B8 related to rheology, the solution strategy H29 rheological modifier is selected. As it can be seen in Figure 6, it has a great influence on these sub-problems, and thus it can help to guarantee control over the rheological behavior. Additionally, to act directly on the sub-

problem C15 biological stability and guarantee product safety, the solution strategies H24 preservative system and G22 packaging are also selected.

With the previously mentioned arguments, solution set 1 is proposed. It comprises nine solution strategies, as shown in Figure 6.

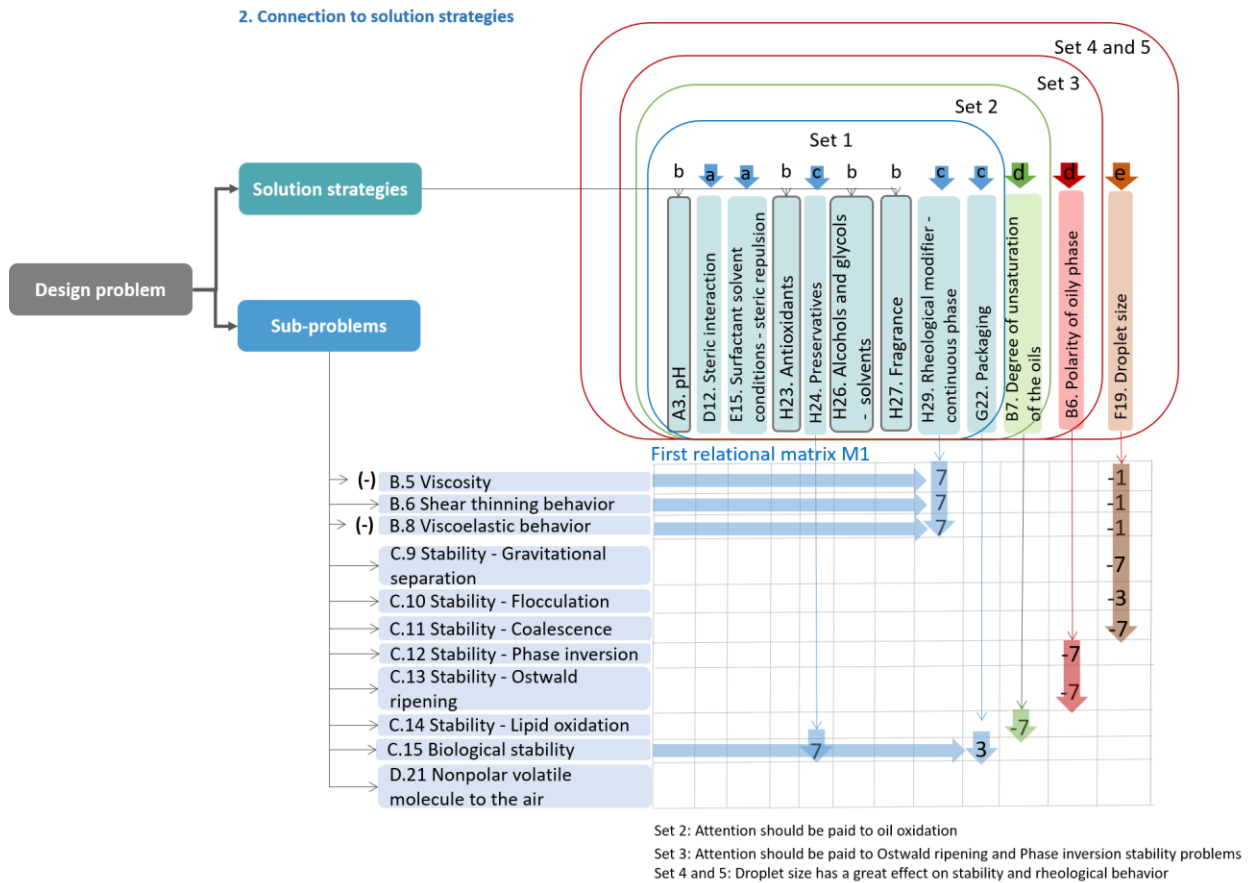


Figure 6. Formation of solution sets for the design of a facial moisturizing cream containing calendula oil

Subsequent sets are established by each time adding a new strategy to this core set 1 to see its effects.

Sets 2 and 3 respond to the following aspect:

- Aspect d: What is the nature of oils that best meets the specification of the problem? Two additional sets were constructed to see the effect of different oil types. Set 2 is formed by adding the effect of oils with unsaturation to the core set 1. Set 3 is formed by adding the effect of oils with relatively high polarity to the previously created set 2.

Sets 4 and 5 respond to the following aspect:

- Aspect e: What is the effect of the micro-structure in the solution of the design problem? Two additional sets were formed with the effect of droplet size in mind. Set 4, by adding the effect of increasing the droplet size, and set 5 by considering the effect of reducing it (in this case the droplet size column is subtracted), both in relation to previously created set 3.

The effect of all solution sets to each sub-problem can be seen in Table 3. A positive symbol means the solution set has a positive response to the sub-problem under consideration. A negative symbol means the solution set may have a negative effect on the sub-problem. In the latter case, the subproblem must be analyzed to see whether it is critical, it can be checked experimentally, and/or an additional solution strategy/ingredient can be selected to turn the sub-problem to positive.

Table 3. Solution sets for a facial moisturizing cream containing calendula oil – case study

APPLIED SOLUTION STRATEGIES AND SETS																	
A3	D12	E15	G22	H23	H24	H26	H27	H29	±	B6	±	B7	±	F19	±	±	±

		Change of pH	Steric interaction (repulsive)	Quality of solvent - steric interaction	Packing	Antioxidants	Preservatives	Rheological modifier continuous phase	Fragrance	Rheological modifier - continuous phase		Polarity of oily phase		Degree of unsaturation of the oils		Droplet size (increase)		
SUB-PROBLEMS																		
B5	Viscosity (-)	0 ^(a)	3	0 ^(e)	0	0	0	0	0	7	(-10)	0	(-10)	0	(-10)	-1	(-9)	(-11)
B6	Shear thinning behavior	0 ^(a)	3	0 ^(e)	0	0	0	0	0	7	10	0	10	0	10	-1	9	11
B8	Viscoelastic behavior (-)	0 ^(a)	3	0	0	0	0	0	0	7	(-10)	0	(-10)	0	(-10)	-1	(-9)	(-11)
C9	Gravitational forces	0	0	0	0	0	0	0	0	7	7	0	7	0	7	-7	0	14
C10	Flocculation	0 ^(b)	3	3	0	0	0	0	0	3	9	0	9	0	9	-3	6	12
C11	Coalescence and partial coalescence	0 ^(b)	3	3	0	0	0	0	0	3	9	0	9	0	9	-7	2	16
C12	Phase inversion	0 ^(b)	0	3	0	0	0	0	0	0	3	-7	-4	-1	-5	0	-5	-5
C13	Ostwald ripening	0 ^(b)	0	0 ^(e)	0	0	0	-3	-1 ⁽ⁱ⁾	3	-1	-7	-8	-1	-9	7	-2	-16
C14	Lipid oxidation and chemical stability of lipids	3 ^(c)	0	0	3	7	0 ^(g)	0	0	0	13	-3	10	-7	3	0	3	3
C15	Biological stability	3 ^(d)	0	0	3	0 ^(f)	7	3	3 ⁽ⁱ⁾	0	19	0	19	0	19	0	19	19
D21	Release of a volatile molecule mainly soluble in the oil phase to the air	0	0	0	-7	0	0	0 ^(h)	7	-3	-3	3	0	0	0	-3	-3	3
Integration degree											1.2		1.1		1		0.9	0.9

Notes: (a) A pH between 4.5 - 5.7 is already fixed. A rheological modifier that works well in acid pH is required. Otherwise, emulsion pH should be checked. (b) A surfactant system that works well in an acid pH is required. Otherwise, emulsion pH should be checked. (c) Acid pH helps to avoid the oxidation of natural oils (Iwata & Shimada, 2013). Thus, the cell takes the value of 3 from the original matrix (first article on the methodology). (d) A relatively acid pH can prevent or reduce the growth of certain microorganisms. Thus, the cell takes the value of 3 from the original matrix (first article on the methodology). (e) The effect of the solution strategy in the problem is unknown, the cell takes the value of 0. The effect can be rechecked once a nonionic surfactant is selected. (f) There is still not a known effect of the solution strategy in this problem, the cell takes the value of 0. The effect can be rechecked once a specific antioxidant is selected. (g) There is still not a known effect of the solution strategy in this problem, the cell takes the value of 0. The effect can be rechecked once a preservative system is selected. (h) The effect of the solution strategy in the problem is unknown, the cell takes the value of 0. (i) Fragrances (in this case essential oils) tend to have a relatively high polarity in comparison to other possible oily components, which may promote Ostwald ripening, the value is set to -1. (j) Calendula oil is part of the fragrance and it has antimicrobial and antifungal activity^{26,27}.

Table 3 also shows the degree of integration of the sets of solution strategies, which is calculated as the number of sub-problems over the number of solution strategies. When it is over 1, there are more sub-problems than solution strategies and the solution set is highly interrelated. This is the case of set 1 with 11 sub-problems and 9 applied solution strategies. In this set, there are four sub-problems with a negative score: Ostwald ripening, release of a volatile compound (in this case, the fragrance), viscosity and viscoelastic behavior. Ostwald ripening is favored due to the use of fragrances, which tend to be relatively polar oils, and the use of glycols, which may favor the transport of oily compounds to the aqueous phase. Both ingredients must be included in the formulation due to design specifications. Ostwald ripening can be prevented by selecting processing conditions that reduce the droplet size distribution (good mixing conditions during homogenization). When checking the factors influencing the release of the fragrance, it was found that the use of a package can highly affect it (strategy G22). In this product, the fragrance is expected to be released once the product is opened (in that moment the package should not interfere), but when it is closed, the release of the fragrance is not desired to preserve essential oils as much as possible within the product. Thus, it is considered that the sub-problem can be controlled by the design of a suitable package (which in turn requires an interdisciplinary design process). Regarding viscosity and viscoelastic behavior, they are expected to be relatively low (reason for the negative symbol), but still much higher than water (the expected rheological profile is shown in Figure 4). The objective is not to reduce but to control them with precision; thus, strategies that independently allow to have a specific control on rheological behavior will respond well to these sub-problems. For example, it is possible to consider the use of more than one rheological modifier to obtain a higher degree of freedom in the control of the product rheology.

Sets 2 and 3 add the effect of polarity and unsaturation of oils, respectively. Natural and biobased oils tend to be more polar than compounds of petrochemical origin and usually contain unsaturated bonds in their molecular structure. Their addition enhances the occurrence of the instability phenomena of phase inversion, Ostwald ripening and lipid oxidation. Phase inversion is unlikely to occur at oil concentrations of 20%, which is usually the percentage used in cosmetic creams. A surfactant system with a high HLB will favor the formation of stable oil in water emulsions. Antioxidants reduce oxidation up to a certain point, but it is highly recommended to avoid or reduce the concentration of unsaturated oils and/or use of a special packing that prevents the entry of oxygen ²⁸. Sets 4 and 5 show the effect of a change in droplet size. A smaller droplet size (set 5) increases the stability of the emulsion overall regarding coalescence, although it enhances Ostwald ripening. Additionally, it could have an important effect on rheological behavior. Table 4 summarizes the results of this step, which are a list of solution strategies to be applied and a list of warning/recommendations to check/consider during the experimental stage. It is decided to continue the design with sets 3, 4 and 5, because they are more complete, they correspond better to the problem definition and they have a lower degree of integration (lower interrelation) than sets 1 and 2.

Table 4. Results of step 2. Solution sets for the design of a facial moisturizing cream containing calendula oil

Solution sets	Solution strategies	Warnings/recommendations
Set 1	A3. Change of pH D12. Steric interaction (repulsive) E15. Quality of solvent - steric interaction G22. Packing H23Antioxidants H24. Preservatives	<ul style="list-style-type: none"> <li data-bbox="932 1654 1401 1833">It would be recommended to guarantee good mixing conditions during homogenization to avoid ostwald ripening.

	H26. Rheological modifier continuous phase H27. Fragrance H29. Rheological modifier - continuous phase	<ul style="list-style-type: none"> It is recommended to consider the use of more than one rheological modifier to obtain a higher degree of freedom in the control of the product rheology
Set 2	Those from set 1 and B6. Polarity of oily phase	<p>The same from set 1</p> <ul style="list-style-type: none"> A surfactant system with a high HLB will favor the formation of stable O/W emulsions. Attention should be paid to the lipid oxidation sub-problem. It is recommended to avoid or reduce the concentration of unsaturated oils
Set 3	Those from set 2 and B7. Degree of unsaturation of the oils	<p>The same from set 1 and</p> <ul style="list-style-type: none"> Attention should be paid to the lipid oxidation sub-problem. It is recommended to avoid or reduce the concentration of unsaturated oils
Set 4	Those from set 3 and F19 Droplet size (increase)	The same from set 3
Set 5	Those from set 3 and F19 Droplet size (reduction)	The same from set 3

6. Step 3: Selection of ingredients using a database of ingredients

Considering the problem specifications and the solution sets selected in the previous sub-section, a list of ingredient types was defined using the second relational matrix presented in the first article on the methodology. The selection process of ingredient types is presented in Figure 7. The results of this step are a list of the ingredients types and a list of warnings/recommendations to be considered for the experimental planning (in Table 5).

3. Creation of design possibilities

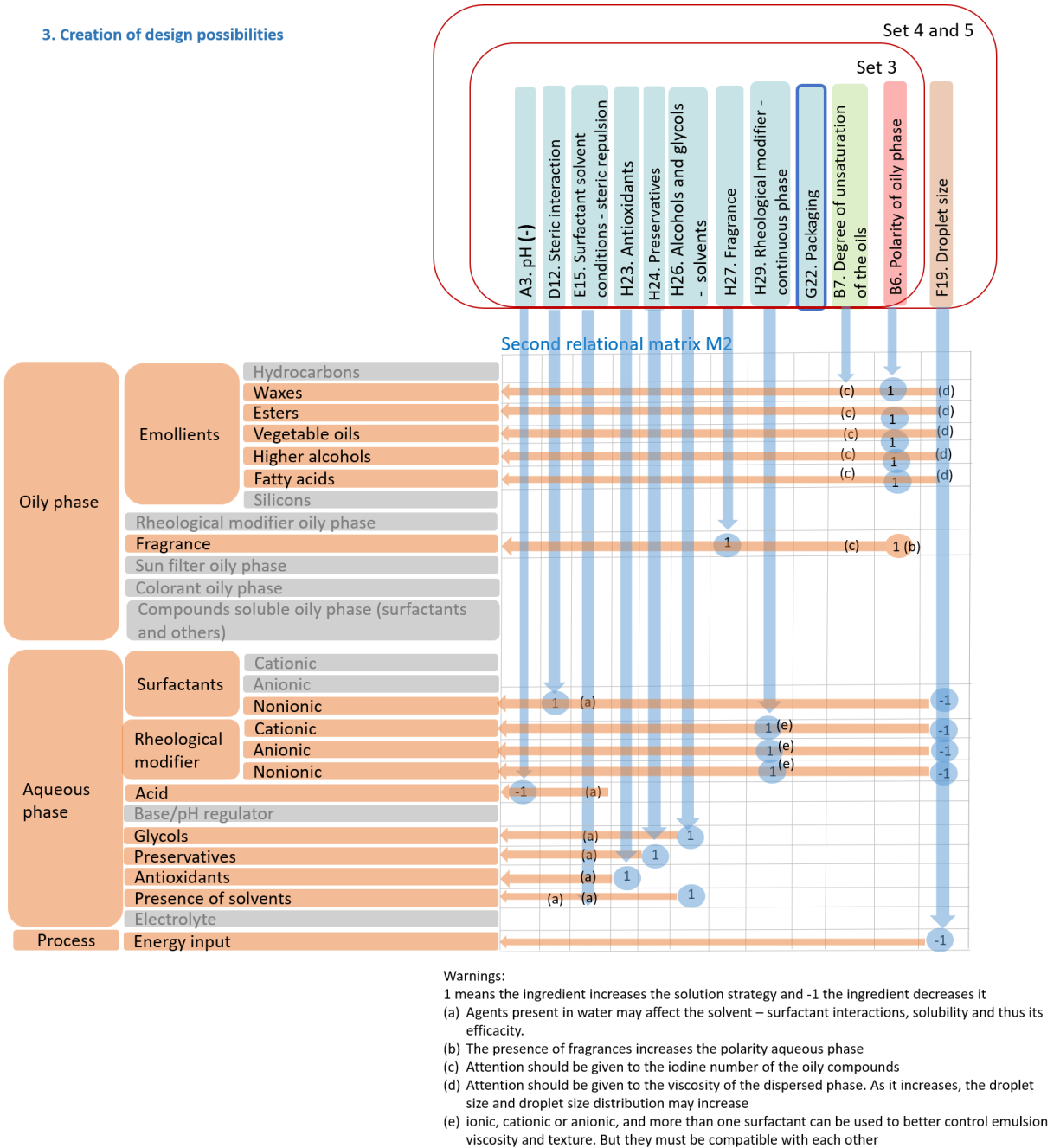


Figure 7. Step 3– selection of ingredient types for a facial moisturizing cream containing calendula oil - case study

Regarding the oily phase, natural and biobased emollients are preferred due to the design specifications. Petrochemical hydrocarbons and silicones are screened out. A fragrance is also

implemented as indicated in the design problem. The pH is adjusted with a weak acid compound. Specific nonionic surfactants that behave well under the emulsion conditions (pH, ionic strength) must be selected to guarantee good solvent interaction. A rheological modifier that works well with acid pH is required. It can be of any nature, ionic, cationic or anionic, and more than one is used to better control emulsion viscosity and texture, but they must be compatible with each other. Ingredient types related to functional solution strategies such as glycols, antioxidants and preservatives are also selected. In the experimental exploration, droplet size can be tuned by modifying surfactant concentration and energy input to control emulsion stability and rheology (application of solutions sets 4 and 5).

Table 5 Results of step 3. Ingredient types for the design of a facial moisturizing cream containing calendula oil

Phase	Ingredient type	Recommendations/warnings
Oily phase	Emollients Can be of the type Waxes, esters, vegetable oils, higher oils, fatty acids	<ul style="list-style-type: none"> • Attention should be paid to the lipid oxidation sub-problem. It is recommended to avoid or reduce the concentration of unsaturated oils (from step 2) • Oils with low oily sensation and good moisturizing function (from step 1) • Attention should be given to the iodine number of the oily compounds. • Attention should be given to the viscosity of the dispersed phase. As it increases, the droplet size and droplet size distribution may increase
	Fragrance	<ul style="list-style-type: none"> • The presence of fragrances increases the polarity aqueous phase.
Surfactants	Nonionic surfactant	<ul style="list-style-type: none"> • A surfactant system with a high HLB will favor the formation of stable O/W emulsions.

		<ul style="list-style-type: none"> Agents present in water may affect the solvent – surfactant interactions, and thus its efficacy
Aqueous phase	Rheological modifiers	<ul style="list-style-type: none"> Ionic, cationic or anionic, and more than one surfactant can be used to better control emulsion viscosity and texture. But they must be compatible with each other It is recommended to consider the use of more than one rheological (from step 2)
	Acid	<ul style="list-style-type: none"> Agents present in water may affect the solvent – surfactant interactions, and thus its efficacy
	Glycols	<ul style="list-style-type: none"> Agents present in water may affect the solvent – surfactant interactions, and thus its efficacy
	Preservatives	<ul style="list-style-type: none"> Agents present in water may affect the solvent – surfactant interactions, and thus its efficacy
	Antioxidants	<ul style="list-style-type: none"> Agents present in water may affect the solvent – surfactant interactions, and thus its efficacy Main antioxidant: calendula oil (from step 1)
	Solvents	<ul style="list-style-type: none"> Agents present in water may affect the solvent – surfactant interactions, and thus its efficacy
Process	Energy input	<ul style="list-style-type: none"> It would be recommended to guarantee good mixing conditions during homogenization to avoid Ostwald ripening (from step 2).
General recommendations/ warnings		Only safe approved cosmetic ingredients will be considered, at least an ingredient must be of natural origin, attention should be given to price of raw materials (from step 1)

Finally, specific ingredients are associated with the identified ingredient types. That task is performed using the databases of ingredients presented in the first article on the methodology¹² and considering recommendations from Table 5 and our availability of raw materials. In some cases, heuristics and references of cosmetics formulation and information from suppliers were

consulted to define specific ingredients. They are presented in Table 6. An extended explanation of their selection can be found in Table S1 in the Supporting Information.

Table 6. Final ingredients for a facial moisturizing cream containing calendula oil - case study

Ingredient type		Ingredient	Concentration	Warnings/recommendations
Oily phase 20%	Emollients/ oils	Caprylic/Capric Triglyceride Isopropyl myristate	6 to 10%	Proportions can be change during experimentation to have a low oily sensation in the final product
	Oil - natural	Shea butter almond oil	Low concentration <2%	
	Fragrance	Lemongrass oil	<0.1%	Attention should be paid to the low resistance of fragrances to high temperature
Surfactants	Surfactant system	System 1: Main surfactant- Polysorbate 80 +Sorbitan stearate +Glyceryl monostearate System 2: Main surfactant- Sucrose palmitate +Cetearyl glucoside +Glyceryl monostearate System 3: Main surfactant-POE 100 stearate +Sorbitan stearate +Glyceryl monostearate	2.5-3.5%	Except for sucrose palmitate, all surfactants are soluble in the oily phase
-	Rheological modifier/ Thickener	Cetearyl alcohol and cetyl palmitate	2-5%, 3%	Soluble in the oily phase
Aqueous phase	Rheological modifier (second)	Xanthan gum	0.1-0.2%	Soluble in water, Dispersible in glycols as glycerin

	Acid	citric or lactic acid	Until pH of (4.5-5.7)	Add after emulsification to adjust the final pH value of the product
	Glycol	Glycerin	3%	Water soluble
	Preservative	Benzyl alcohol and dehydroacetic acid	0.6%	Soluble in polar solvents such as glycerin, Decrease pH of the emulsion
	Antioxidant	Calendula oil Acetate tocopherol		Low resistance to high temperature

7. Experimental step

The experimental phase of the case study was developed in two parts:

First experimental part:

First formulations with the three considered surfactant systems were produced at laboratory scale under the same conditions and their resulting characteristics were compared. This part corresponds to the exploration of solution set 3 (Figure 6). The surfactant system that best meets product specifications is selected for further work. For this first part, emulsions were prepared at a fixed homogenization speed of 7000rpm, surfactant concentration of 2.5%, and cetearyl alcohol concentration of 4%. Table 7 shows the formulations for each case.

Table 7. Formulations for the experimental development of a facial moisturizing cream containing calendula oil - case study -first experimental part solution set 3.

Phase	Ingredients	Prototype 1 (P1)	Prototype 1 (P2)	Prototype 1 (P3)
		Surfactant system Main surfactant- Polysorbate 80 +Sorbitan stearate	Surfactant system Main surfactant- Sucrose palmitate +Cetearyl glucoside	Surfactant system Main surfactant- POE 100 stearate +Sorbitan stearate +Glyceryl monostearate

		+Glyceryl monostearate	+Glyceryl monostearate	
A		Isopropyl myristate [%]	2	2
A		Caprylic/capric triglyceride [%]	7	7
A		Shea butte [%]	1	1
A		Cetyl palmitate [%]	3	3
A		Cetearyl alcohol [%]	4	4
A		Almond oil [%]	1	1
A		Surfactants	Glyceryl monostearate [%]	0.5
A	Polysorbate 80 [%]		1.5	
A	Sorbitan stearate [%]		0.5	0.9
A	POE100 stearate [%]			1.1
A	Cetearyl glucoside [%]			0.5
B	Sucrose palmitate [%]			1.5
B		Glycerin [%]	3	3
B		Water [%]	76	76
B		Xantham gum [%]	0.15	0.15
C		Benzyl Alcohol and dehydroacetic acid [%]	0.6	0.6
C		Acetate tocopherol [%]	0.4	0.4
C		Calendula oil [%]	0.09	0.09
C		Lemongrass oil [%]	0.045	0.045

Notes: Concentration of each surfactant is calculated assuming a total surfactant concentration of 2.5% and a required HLB of approx. 11 (calculated based on the oily phase required HLB). The percentage of the oily phase is fixed at approximately 20%, like formulations with similar properties²⁸. Process conditions: A temperature of 70°C can be used for homogenization. At this temperature, all ingredients are melted or dissolved. Components of phase A, the oily phase, are compatible/soluble between each other. They can be weighed and heated together. Components of phase B, aqueous phase are soluble in water. Ingredients such as polymers and gums, even if soluble in water, are difficult to solubilize. They can be pre-dispersed before solubilization. It is recommended to introduce components signed with a C at the end of the homogenization after the cooling process. This because either they are sensible to heating or may affect the homogenization conditions.

Second experimental part:

Second, with the selected surfactant system, a set of experiments varying the concentration of the cetearyl alcohol (rheological modifier and stabilizer), the speed of homogenization (energy introduced into the formulation) and the surfactant concentration was performed. This was done with the purpose of knowing in which proportions these factors affect the emulsion's micro-

structure, and consequently its rheology and stability. This part corresponds to the application of solution sets 4 and 5, where droplet size is intentionally varied. Table 8 shows the applied experimental variations for this part.

Table 8. Experimental conditions for the production a facial moisturizing cream containing calendula oil - case study – second experimental part variation of droplet size - solution sets 4 and 5.

Product prototype	Conditions
P4	Homogenization speed: 7000rpm Surfactant concentration: 2.5% Cetearyl alcohol concentration: 2%
P5	Homogenization speed: 12000rpm Surfactant concentration: 2.5% Cetearyl alcohol concentration: 2%
P6	Homogenization speed: 12000rpm Surfactant concentration: 3.5% Cetearyl alcohol concentration: 4%
P7	Homogenization speed: 12000rpm Surfactant concentration: 2.5% Cetearyl alcohol concentration: 4%

Finally, all emulsions were compared with some product specifications, specifically those related to stability, micro-structure and rheology as a first criteria for prototype screening and for an initial selection at the first design stages. Those prototypes with properties closer to product specifications were selected as functional product prototypes to be improved in further design stages. Table 9 shows the product specifications and the corresponding experimental tests.

Table 9. Experimental tests to verify the achievement of product specifications.

Categories of product specifications	Product specification	Experimental test

Safety and Regulation	1	Physical/chemical stability	1. At this initial stage, two rapid stability tests were done for screening out unstable samples. It is recommended to perform a long-term stability test in further design stages.
	2	Toxicology	<ul style="list-style-type: none"> Only allowed cosmetic substances are used. No further experimental testing is performed on this specification.
	3	Microbiological quality	<ul style="list-style-type: none"> The test is complex and time consuming. It is recommended to apply it in a more advanced experimental phase, when scaling and aseptic process conditions are considered
	4	Use of allowed substances	<ul style="list-style-type: none"> Only allowed cosmetic substances are used. No further experimental testing is performed on this specification.
	5	Dermal tolerance and non-irritability	2. pH of the formulation. The use of essential oils may be irritating. In that case its concentration should be checked
Sensorial evaluation	6	Product odor – intensity and fragrance type	3. Appearance and odor of the product is qualitatively tested. Panel tests are recommended for future design stages
	7	Low oil skin sensation	
Performance evaluation	8	Sensation of hydration just after product application	<ul style="list-style-type: none"> A clinical test with users is required. The test is complex and time consuming. It is recommended to apply it in a more advanced experimental phase.
	9	Sensation of hydration – long term	
Instrumental tests	10	Light and fluid product - low viscosity and low viscoelastic modulus	4. Rheological profile 5. Microstructure to see the effect of droplet size in rheology and stability
	11	pH	Test 2: pH of the formulation

Price	12	Product price	<ul style="list-style-type: none"> Benchmarking product price is relatively high in relation to raw materials cost. A more complete study is needed including other costs such as marketing and production costs in further design stages.
Additional	13	Antioxidant function	<ul style="list-style-type: none"> The test is complex and time consuming. It is recommended to apply it in a more advanced experimental phase.
Nature ingredients of	14	It should contain ingredients of natural origin. Ingredients with low user acceptance such as parabens should be avoided	<ul style="list-style-type: none"> Ingredients of natural origin have already been added to the formulations

7.1. Materials and methods

Materials

The ingredients used for the formulations are:

Isopropyl myristate (Crodamol IPM, Croda, USA), Caprylic/Capric Triglyceride (Crodamol GTCC, Croda, USA), Shea butter (Croda, USA), almond oil (local provider Disproalquímicos Colombia), lemongrass oil (Essential oil - lemongrass oil, Xiu Aguee – Colombia), calendula oil (Essential oil - lemongrass oil, Xiu Aguee – Colombia), Cetearyl alcohol (DISAN, Colombia), Cetyl palmitate (Crodamol CP, Croda), xanthan gum (local provider Disproalquímicos Colombia), glycerin (local provider Disproalquímicos Colombia), benzyl alcohol and dehydroacetic acid (Geogard 221, Lonza, Suisse), acetate tocopherol (Croda, USA). In relation to surfactant system 1: polysorbate 80 (Tween 80, Croda, USA), sorbitan stearate (Span 60, Croda, USA), glyceryl monostearate (Cithrol GMS, Croda, Brazil). In relation to surfactant system 2: sucrose palmitate

(Sucrose palmitate, Modernist pantry. USA), cetearyl glucoside (Emulgade PL 68/50, BASF, Colombia). In relation to surfactant system 3: PEG-100 stearate (Myrj™ 100, Croda)

Emulsification process

Emulsions (100g) were prepared by hot homogenization. The aqueous and oily phases are heated separately and combined under high-speed homogenization. For the preparation of the aqueous phase (phase B), xanthan gum was pre-dispersed in the glycerin and then distilled water was added to the mixture. Subsequently, the phase was heated to 75°C under agitation at 600rpm. Simultaneously, oily soluble ingredients (phase A) were weighed and heated to 75°C. When both phases achieved that temperature, homogenization was started at a speed of 7000rpm, a temperature of 75°C and under agitation at 800rpm. The oily phase was gently added to the aqueous phase (5 minutes of addition) and then homogenization continued for 10 minutes more. After the emulsion was formed, it was cooled to ambient temperature while agitating using a cooling bath at 15°C. pH was checked and lactic acid at a concentration of 70% was added if required. Finally, the samples were stored in a polypropylene package in a dark, and dry place.

The production process is presented schematically in Figure 8. For the first experimental part, homogenization was done under the conditions previously mentioned. For the second experimental part homogenization speed was varied from 7000 to 12000 rpm. Considerations from Table 6 were used to select the phase and form of addition of the ingredients.

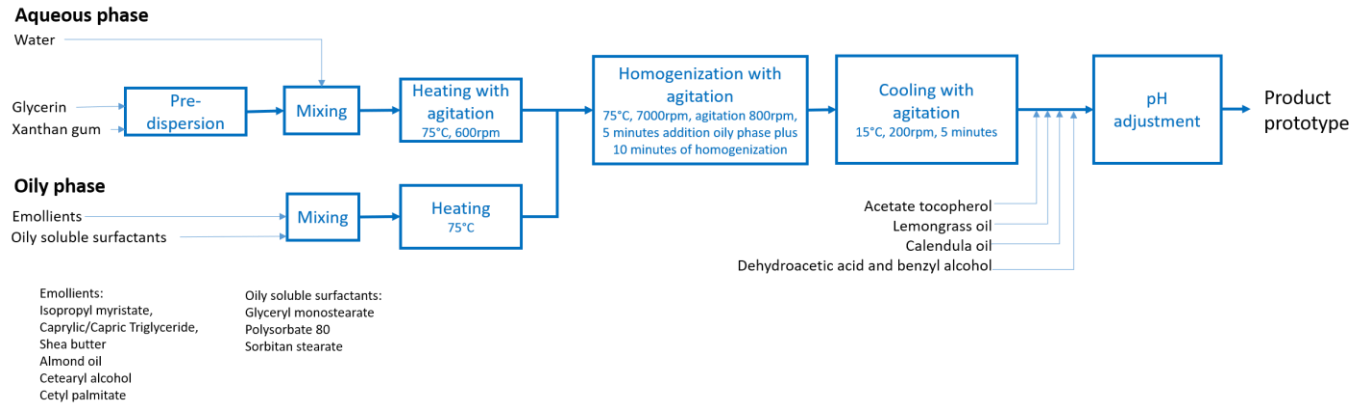


Figure 8. Process diagram of the facial moisturizing cream containing calendula oil - case study - experimental part. This is done considering surfactant system 1: Polysorbate 80, Sorbitan stearate, Glyceryl monostearate. For system 2, the sucrose palmitate is added to the water phase.

7.2. Tests and specifications measurement

The following tests were applied to check the achievement of some of the product specifications and select initial prototypes as presented in Table 9:

1. **Stability :** Two tests were done for screening out unstable samples: a temperature cycle test and a centrifugation test. These are quick tests and cannot replace a long-term stability test. Here, they were used to compare the resistance of product prototypes under stress conditions.

Temperature cycle test: As suggested in ³¹, the samples were subjected to three heating/cooling cycles, changing their temperature to between 40° and 4°C every 24 hours for 6 days. After each 24 h cycle and after the 6 days, the samples were visually checked.

Centrifugation test: As suggested in ³¹, the samples were centrifuged three times for 30 min at a centrifugation speed of 3000rpm. Any change in the emulsions was visually checked.

2. **pH measurement:** pH was measured using a pHmeter MPC 227 Mettler Toledo at 20°C after emulsion preparation. Lactic acid at a concentration of 70% was used to adjust the pH to a value around 5.

3. Appearance, odor, texture: Prototypes are sensorially evaluated by the designers.
4. Rheology profile: The viscosity tests were done using a Bohlin C-VOR rheometer. Tests were done at 25°C using a geometry of cone and plate of 4°, 40 mm in diameter and a gap of 150µm. This geometry was selected due to the rheology of most of the samples (fluids with relative high viscosity that do not flow easily). The shear rate was varied in a continuous increasing ramp from 0.01 to 1000 s⁻¹ for a period of 150s. 40 points were measured in a logarithmic scale. Each sample was evaluated in triplicate.
5. Droplet size distribution: it was calculated based on the optical microscopy determined using a Unico series G380 microscope and an objective of 100X. For better observation, the emulsions were diluted in a 1:4 proportion and the colorant methylene purple was added to the sample. The software Image J was used for image processing. As shown by Sinko et al.³², droplet size and droplet size distribution were determined by considering an image surface containing around 300 to 500 droplets. The samples were examined a week after their preparation.

7.3.Results

First experimental part: Comparison between three nonionic surfactant systems

1. Stability: In the thermal stability test all samples were found to be stable. This means that no emulsion showed a phase separation after the six temperature cycles. In the centrifugation test, emulsion P2 (with sucrose palmitate) showed a separation of phases. Emulsions before and after the latter test are shown in Figure 9.

Before 3 cycles of centrifugation

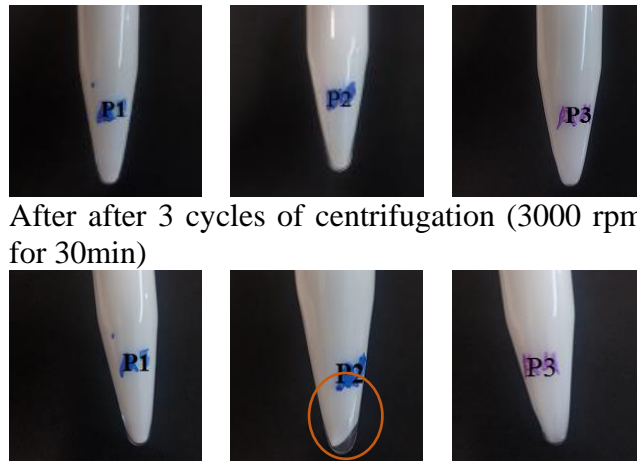


Figure 9. Pictures of product prototypes P1, P2 and P3 before and after the centrifugation test. P1 – main surfactant polysorbate 80, P2 – main surfactant sucrose palmitate, P3 – main surfactant POE-100 stearate.

2. pH: the pH values of all the samples were around 5 after the addition of the preservative system.
3. Appearance: All the samples were creamy and white. Prototype P2 (sucrose palmitate) was slightly more yellowish and less viscous than the other samples. The aroma between samples is similar and it corresponds to product specifications.
4. Rheology test: Figure 10 shows the result of viscosity in relation to shear rate for emulsions P1, P2 and P3. The measurements were made in triplicate and the standard deviations in most of the measurement points were lower than 10%. The figure also shows the viscosity behavior of sample T1 which corresponds to the rheological profile defined as target value with the participation of customers (Problem definition, Figure 4).

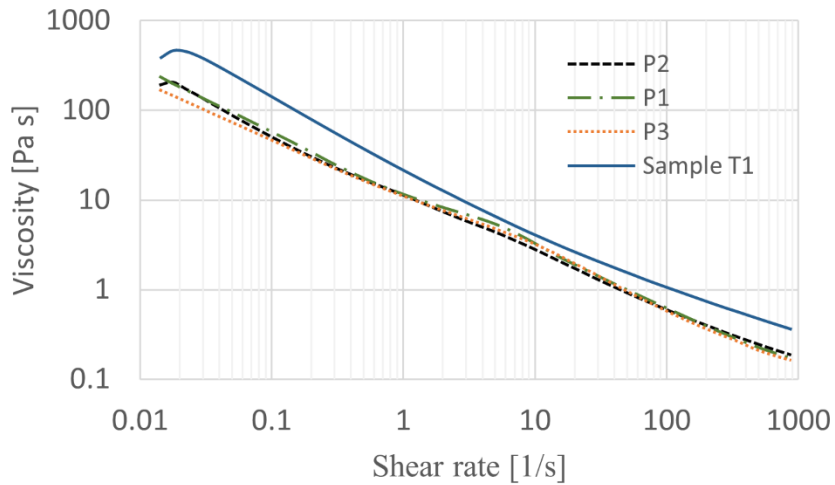


Figure 10. Viscosity vs- shear rate curve of the prototypes of a facial moisturizing cream containing calendula oil - case study. Prototypes P1 – main surfactant polysorbate 80, P2 – main surfactant sucrose palmitate, P3 – main surfactant POE-100 stearate and target value T1

The test shows that the prototypes have a relatively low viscosity in relation to the target value T1. Prototypes P1 and P2 have a viscosity slightly higher than P3.

5. Droplet size: Figure 11 presents the results of the droplet size distribution of prototypes P1 (main surfactant polysorbate 80), P2 (main surfactant sucrose palmitate) and P3 (main surfactant POE 100 stearate). Figure 12 presents the corresponding microscopies at 100X.

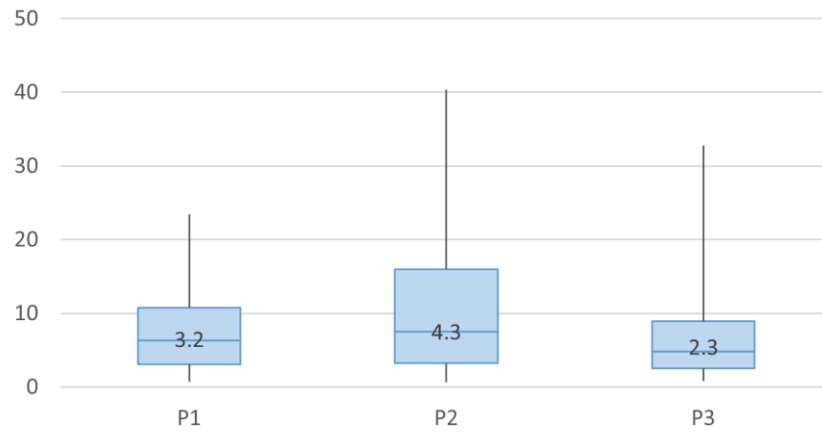


Figure 11. Box plot of droplet size distribution of the prototypes of a facial moisturizing cream containing calendula oil - case study. Prototypes P1 - main surfactant polysorbate 80, P2 - main surfactant sucrose palmitate, P3 - main surfactant POE-100 stearate

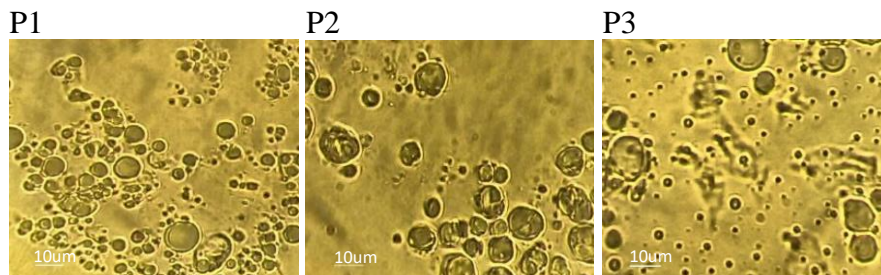


Figure 12. Micrographs at 100X of the prototypes of a facial moisturizing cream containing calendula oil – case study. Prototypes P1 – main surfactant polysorbate 80, P2 – main surfactant sucrose palmitate, P3 – main surfactant POE-100 stearate.

Comparing the median droplet size of the emulsions in Figure 11 and the pictures in Figure 12, prototype P3 (POE-100 stearate) has the smallest median size of all the samples but the widest droplet size distribution. Prototype P2 (sucrose palmitate) has the highest median droplet size of the three emulsions and a wide distribution, and, in the picture, some droplets seem to be formed by the fusion of several half-formed droplets (coalescence), explaining the low stability of P2 in the centrifugation test (Figure 9). This is consistent

with the information given by the first matrix (first article of the methodology), which explains that wide distributions and large particle sizes reduce stability against gravitational separation.

The behavior of surfactants P2 and P3 can be explained by different factors: incompatibilities between the surfactant systems and other compounds, low absorption speed of the surfactants in the newly formed droplets, low surfactant concentration. To reduce coalescence, when these ingredients are added, it is recommended to explore different homogenization conditions from those used in this study. For example, the use of a higher surfactant concentration, the addition of a co-emulsifier that adsorbs more rapidly or the improvement of mixing conditions during homogenization for better transport of surfactants from the bulk liquid to the interphase.

Besides, prototype P1 has an intermediate droplet size and the smallest droplet size distribution of the group. This surfactant system seems to adsorb fast on the interface, and it forms relatively small droplets.

Prototype P1 showed good stability and better rheological characteristics than the others. Thus, it was selected as the surfactant to be explored in the second experimental part.

Second experimental part: Changes in droplet size distribution

1. Stability test: All emulsions were resistant to the thermal and centrifugation tests without presenting phase separation.
2. pH: As for the first prototypes, the pH of the formulation was around 5.1.

3. Appearance: All the samples were creamy and white. Sample P7 is more viscous than the others. Sample P4 is the least viscous.
4. Rheological test: Figure 13 shows the rheological profile of the prototypes in comparison with the target value sample T1. Product prototypes at small shear rates present different viscosities, being P7, the most viscous of the prototypes and the closest to sample T1. The prototypes are very similar at high shear rates, when they have almost the same viscosity, which is lower than the viscosity of sample T1. This means that in general all prototypes have a higher shear thinning behavior than T1. By reviewing this problem in the first relational matrix it was found that a good solution is the addition of a rheological modifier with a lower shear thinning behavior than the used here (xhantan gum).

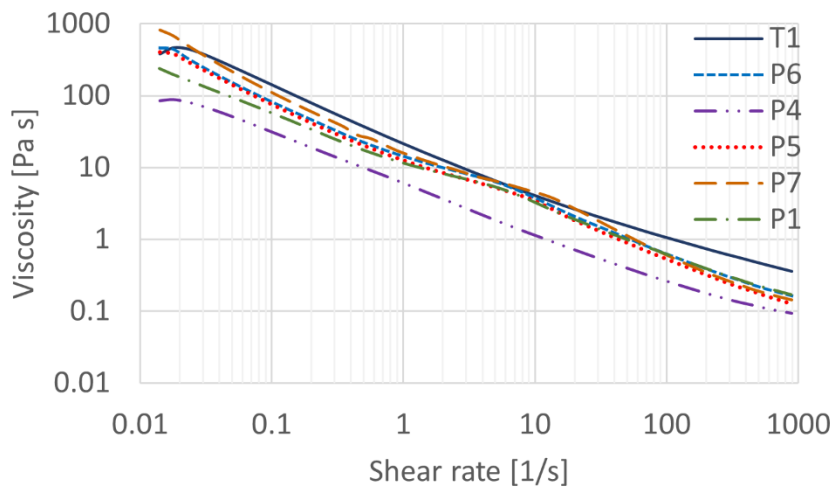


Figure 13. Results of viscosity tests for a facial moisturizing cream containing calendula oil - case study. Plot viscosity –shear rate for product prototypes P1, P4, P5, P6, P7 and the sample T1 that corresponds to customer preference.

5. Droplet size: Figure 14 presents the statistical results of the droplet size distribution of prototypes P1 (the same as the previous part), P4, P5, P6 and P7. Figure 15 presents the corresponding microscopies at 100X.

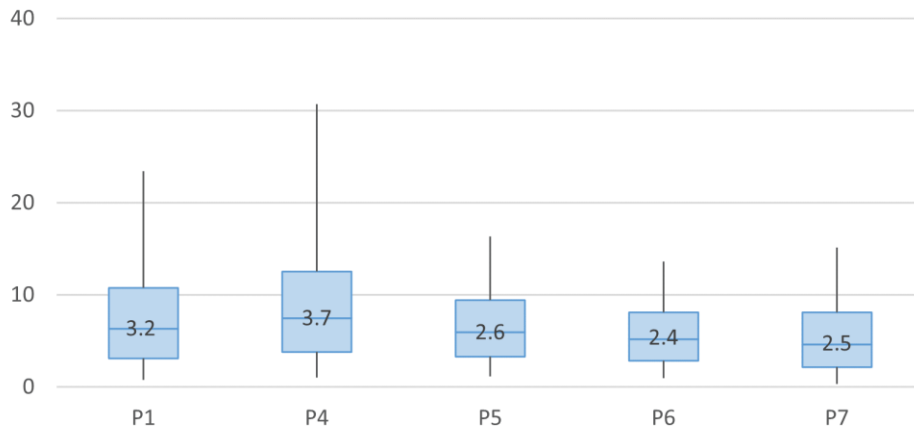


Figure 14. Box plot of droplet size distribution for prototypes P1, P4, P5, P6, P7 for a facial moisturizing cream containing calendula oil - design problem of the case study

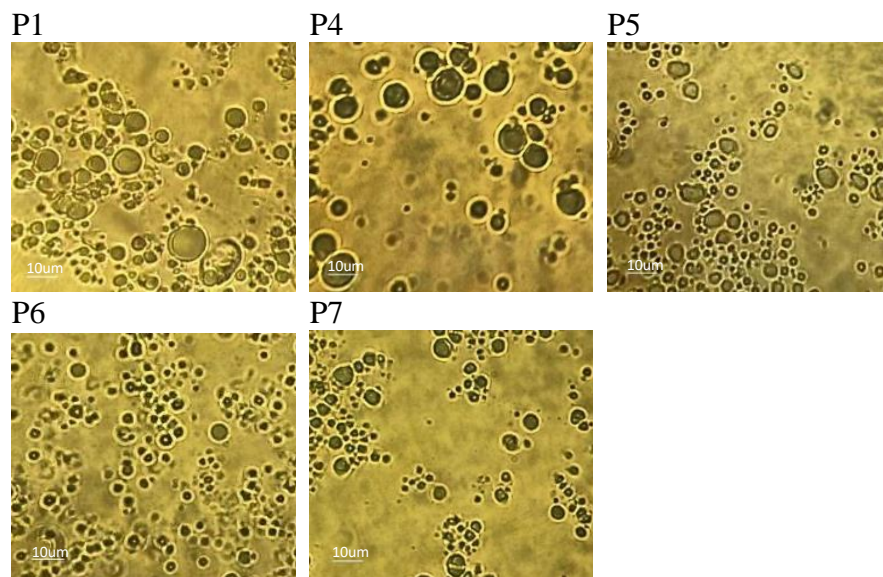


Figure 15. Micrographs at 100X for a facial moisturizing cream containing calendula oil – case study. Prototypes' main surfactant polysorbate 80. P1- 7000rpm, 2.5 surfactant, 4% cetearyl

alcohol, P4 – 7000rpm, 2.5% surfactant, 2% cetearyl alcohol, P5 -12000rpm, 2.5% surfactant, 2%cetearyl alcohol, P6 - 12000rpm, 3.5% surfactant, 4%cetearyl alcohol, P7 12000rpm, 2.5% surfactant, 4%cetearyl alcohol

Figure 15 shows that the emulsions produced at higher homogenization speeds have smaller droplet sizes, as expected. In addition, as the droplet size decreases, the droplet size distribution is also narrower, as can be seen in the boxplot in Figure 14. This can be explained by the fact that at higher speeds both the rate of disruption and the agitation within the homogenizer are increased, which can reduce the droplet size and the droplet size distribution.

The product prototype closest to Sample T1 is P7. It can be tested with customers and further improved to create a product that meets all their requirements.

8. Conclusions

In this article a systematic methodology for chemical product design focused on emulsion formulation was applied to a practical case study: a moisturizing cream with essential oils. Once the design problem is defined, the proposed methodology is applied in three steps: 1. Classification of product specifications into sub-problems; 2. Connection of sub-problems with solution strategies by applying a first relational matrix; 3. Connection of solution strategies to ingredients to create conceptual product alternatives.

Thanks to the application of the methodology to the case study, in a first step five sets of possible solution strategies were proposed using the first relational matrix. In doing so, the effect of each set of solutions in each sub-problem was explored. This showed the complete effect of various solutions in all sub-problems and allowed product designers to identify those which seemed to be

critical before experimentation to be analyzed. As a result of this stage, three sets of solutions were selected based on the use of a nonionic surfactant system and variation in the droplet size of the emulsion (increase, decrease). The sets were transformed into formulations using the second relational matrix, the ingredient database, and the heuristics of the cosmetics sector.

During the experimentation stage, first, three nonionic surfactant systems were applied: one with sucrose palmitate, one with polysorbate 80 and one with POE-100 stearate. It was found that under the conditions explored, emulsions with polysorbate 80 tend to be the most stable with a rheological behavior close to that expected by the product specifications.

In a second experimental part, polysorbate 80 was tested under two different homogenization conditions. It was found that at the highest homogenization speed more viscous creams are created, mainly due to the reduction in droplet size, as predicted by the relational matrices.

The results show that the methodology is applicable to a specific case. In further research, it would be interesting to test the methodology in other cases and to create a program tool based on the methodology presented here. At this time the tools are applicable to the design of O/W emulsions and for the design of cosmetic emulsions. The methodology is systematic and decisions are based on emulsion science, which allows to understand the reason for the experimental results, compare them and improve the prototypes. The methodology can be enriched with more case studies and in the future, its databases can be improved and updated with new cases. Currently, we are working on the digitalization of the tools and the databases proposed. This will allow us to apply the approach in a systematic way to more and more complex cases.

Acknowledgments

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Supporting information

A file containing:

- Table S1 Explanation - Ingredients for a facial moisturizing cream containing calendula oil - case study

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PRODUCT DESIGN METHODOLOGY

