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A methodology for emulsion design based on emulsion science and expert knowledge. Part 1: conceptual approach

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Keywords

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

Abstract

Formulated emulsions have a high commercial value due to their multiple applications in several product sectors such as cosmetics, nutrition, medicine, and household products, among others. Their design is not a simple task because emulsions are complex systems in which components, structures, phenomena, and processes are highly interrelated. Thus, any decision must be made with its multiple effects on the final product's properties in mind. Emulsion design is even more challenging at early design stages when information is scarce and critical design decisions are made. In view of the above, this study proposes a decision-making methodology for emulsion formulation applicable to early product design/screening/exploratory stages. It enables product designers to understand the product as a whole system and select a set of complementary solution strategies applicable to their specific emulsion formulation problem. The methodology presented in detail in this article comprises three steps and uses two databases, which were proposed based on emulsion science principles and connected thanks to a database of expert knowledge. In the first step, product specifications are classified according to a list of 21 general sub-problems in emulsion formulation, which are related to physico-chemical phenomena or properties that are to be promoted or limited in the product. In the second step, sub-problems are connected to a list of 30 general solution strategies, which are solution paths related to the emulsion's nature or structure but not initially directly to a specific compound or process technology. In the third step, solution strategies are connected to compound types and processing conditions using a second database with the aim of creating potential design concepts.

1. Introduction

In recent years, opportunities for and challenges in the design of chemical products have increased continuously, mainly with micro-structured chemical products, i.e. emulsions, solids and aerosols that are frequently found in the consumer market ¹⁻³. Opportunities involve the emergence of new information, methods, methodologies, technologies and ingredients that can be used for chemical product design ⁴⁻⁷. Challenges involve new customer demands including individualization and stronger sustainability constraints ⁸⁻¹⁰. For example, at present customers demand bio-sourced or bio-based products. Under this scenario, product designers need a methodology that enables them to visualize suitable design possibilities responding to the design requirements and that helps them to make the best possible design decisions in a systematic and efficient way.

Among the opportunities regarding new methods and methodologies, a relatively new research field called Chemical Product Design has emerged within Chemical Engineering ¹¹⁻¹⁴. Within this field, special emphasis has been placed on Computer Aided Molecular Design (CAMD) and property prediction by Group Contribution (GC). These methods are used to find molecules that satisfy a set of target properties using the reverse design technique, which virtually generates a large number of alternatives and screens them to find candidates corresponding to target values ^{5,15-19}. The use of CAMD methods has been extended to the design of simultaneously functional and safe molecules by using these methods to calculate safety indicators ^{8,9,20}. CAMD methods are mostly used for the design of molecules and homogeneous mixtures, as well as for the prediction of certain emulsion properties ²¹. However, they are not directly applicable to the design of sophisticated products such as micro-structured chemical products, because of their inherent complexity, process operating conditions, and, in many cases, the scarceness of reliable models and information²²

The added value of a micro-structured chemical product does not stem from its chemical nature, but from its functions¹², which are defined by its components, its composition and its micro-structure, the latter being the result of the simultaneous interactions between the production process and the components^{12,23,24}. For this type of product, the trial and error method and random experimentation are the main ways of addressing their design². Companies with significant experience in the market have developed their own methods for product design based on their know-how and staff experience. However, this type of knowledge is difficult to develop, transmit and maintain over time²⁵.

In order to support the consumer chemical industry in the creation of chemical products for the consumer market, researchers are actively working to expand their knowledge on the relation between ingredients, micro-structure, functions and process conditions in formulated products (mixtures of ingredients, e.g., homogeneous liquid mixtures) and more specifically in micro-structured chemical products (mixtures of ingredients in which their arrangement at the nano- and micro- scale is fundamental in their functionality e.g., emulsions)^{14,26-28}.

In this respect, Bernardo and Saraiva defined the product as “a system depending on a set of components, their organization (structure), and a specific interaction with the environment”. In their proposal, the product function (quality model) is defined in part by the ingredients and in part by their micro-structure (property model), with the latter being highly dependent on the process (process model)^{6,29}. This approach was extended with the use of heuristics for its more precise application to the cosmetics sector³⁰. Although it is not a holistic approach (only some variables related to the micro-structure are considered and their interrelations and their effects in multiple product characteristics are not addressed), their results show the advantage of a simultaneous product/process design. Similarly, Fung et al.⁵ presented a

simultaneous product and process design methodology, in which the net present value is maximized subject to constraints represented by six models: process, property, quality, cost, pricing and economic. Their proposal is a global framework that combines a great diversity of tools (knowledge base, model base and database), but it does not model the product as an integrated system. It was extended in order to be applicable to all types of formulated products ³¹. On their part, Kontogeorgis et al. ³² presented a systematic methodology specifically applicable to emulsified products. In their proposal, the design steps and tools are exhaustively explained, but as in the previous cases, the relationship between structure/multiple-product-properties/process is not completely explored. In contrast to the previous developments, Hada et al. ³³ proposed a multivariable analysis of the product, exploring interrelations between variables to solve a complex formulation design problem through the use of a multivariate statistical analysis tools. That proposal is holistic and considers the product as an integrated system, but it is only applicable with a large amount of data, i.e., at an advance design stage. The described product design methodologies are summarized and compared in Table S1 of the supplementary material.

All the examples previously mentioned show the advantage of a simultaneous product and process design and the application of modelling and computer optimization to deal with its difficulties. Nevertheless, these methods require realistic property models and a huge amount of data to simulate factual product design problems, which are not available at very early design stages. From our knowledge, a methodology for the design of micro-structured chemical products that considers both the product as a multi-variable integrated system and can be applied to early design stages has not been published. Most of the reported methodologies adapt the design to what can be accurately modeled, not considering the

intrinsic complexity of the product as a system, thus limiting the search of possible solutions. For example, viscosity of emulsions is frequently modeled as a function of the viscosity of the continuous phase, droplet size, volume fraction of the disperse phase and viscosity of the dispersed phase. The effects of intermolecular forces (electrostatic and steric interactions), and of phenomena such as flocculation are not taken into account.

With the objective of visualizing a wider solution space from early design stages, this study proposes a design methodology for emulsified products (a case within the set of micro-structured chemical products) where the product is described as a system formed by the interrelation of ingredients and a micro-structure. The elements of this scope were selected based on emulsion science principles and their interrelation was done with the aid of experts.

The methodology is holistic and enables a decision-making process based on the understanding of the emulsion nature. This approach is based on the QFD methodology (Quality Function Deployment)^{34,35} and is inspired by a decision methodology applied in the field of process intensification⁷.

2. General description of the methodology

The methodology workflow comprises the following steps and uses two databases, as shown in Figure 1:

- In the first step, product specifications are classified according to five categories and subsequently to a list of 21 general sub-problems, which were previously identified based on emulsion science principles (Figure 2). Sub-problems are phenomena or interactions that are desired or not to happen within the product. The categories of

sub-problems are appearance, rheology, stability, transport process and special functions. The latter corresponds to specific functions that are directly connected to an active ingredient, while the other categories are related to characteristics of the product as a system. Examples of sub-problems in the category of rheology are emulsion viscosity and emulsion viscoelasticity behavior, among others.

The input of this step corresponds to product specifications, and the output to sub-problems and special functions. Product specifications can be related to one or more sub-problems and/or to the category of special functions. For example, in the case of a sunscreen, the product should have a sun protection factor (SPF) and a thixotropic rheological behavior. In that case, the first specification is connected to the category special functions and later to a database of ingredients, while the second is connected to the sub-problem – thixotropic behavior (to be enhanced) in the category rheology.

- In the second step, sub-problems are connected to seven categories and subsequently to a list of 30 general solution strategies using a predefined connection matrix. Solution strategies are general solution paths predefined based on emulsion science principles and related to the emulsion's structure and nature, but not initially directly related to a specific compound or processing technology. Examples include the use of a type of surfactant system (promoting electrostatic or steric interactions), increasing/decreasing droplet, particle size, pH, among others. The connection between sub-problems and solution strategies is made using a first relational matrix developed by gathering expert knowledge. The matrix indicates the solution strategies that most affect the sub-problems, allowing designers to define sets of compatible solution strategies for a specific product design problem. The input of this step is a list of sub-problems and the output is a set of solution strategies.

- In the third step, solution strategies are connected to ingredient categories and processing conditions thanks to a second relational matrix. This matrix links solution strategies to a database of ingredients categories to create possible design concepts. The input of this step is a list of solution strategies and the output is a list of ingredients categories (design concept) which can be later related to specific ingredients and composition using databases and heuristics to generate product possibilities. When experiments are made from the possibilities, prototypes are created.

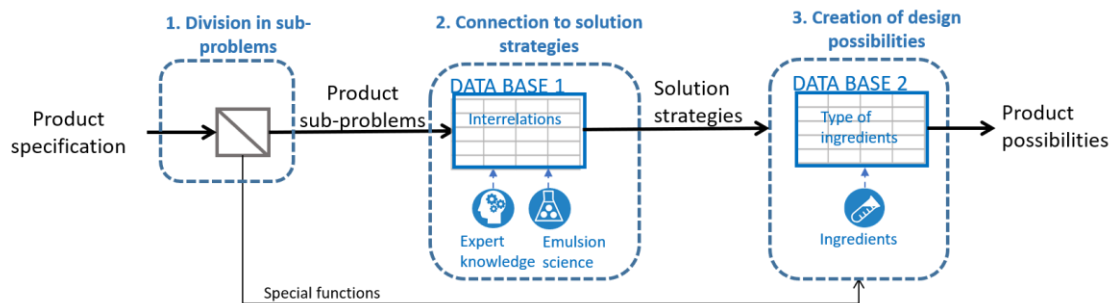


Figure 1. Workflow of the decision methodology for emulsion formulation

In the following sections the elements of the methodological framework will be presented in the following order: sub-problems, solution strategies, ingredients and relational matrices. Subsequently, how these elements can be used to make design decisions will be explained. The elements of the methodology presented here can be applied for the design of oil in water (O/W) emulsions of low and intermediate concentration. Heuristics and ingredients of the databases are specifically of the cosmetics sector. Despite the above, this approach can be adapted to other emulsion types (water in oil (W/O) emulsions, nano-emulsions, concentrated emulsions, multiple emulsion) or to other micro-structured products by adapting the

relational matrices to those cases. It can also be transferred to other product sectors, using the appropriate ingredient databases and heuristics.

3. Sub-problems for emulsion formulation

The lists of sub-problems and solution strategies were defined based on a comprehensive literature review conducted on the body of knowledge of emulsion science. The search was focused on physicochemical aspects of O/W emulsions of low and intermediate concentrations (maximum 30% oil concentration). The objective was to be as exhaustive but also as general as possible. Therefore, publications containing the basic principles of emulsion science were prioritized. It is worth mentioning that emulsion science is a huge and complex discipline and there are many non-typical examples of emulsion behaviors that could not be covered by the methodology presented here.

The sub-problems identified are presented in Figure 2 and are explained in Table 1. An extended explanation can be found in the supplementary material. They are classified into five categories: appearance, rheology, stability, transport process and phase behavior, and special functions. The latter category corresponds to those functions connected to special ingredients, *e.g.* U.V. protection or antioxidant effect. The 21 sub-problems in Table 1 help designers to formalize their design problem in relation to the characteristics and behaviors of the emulsion system.

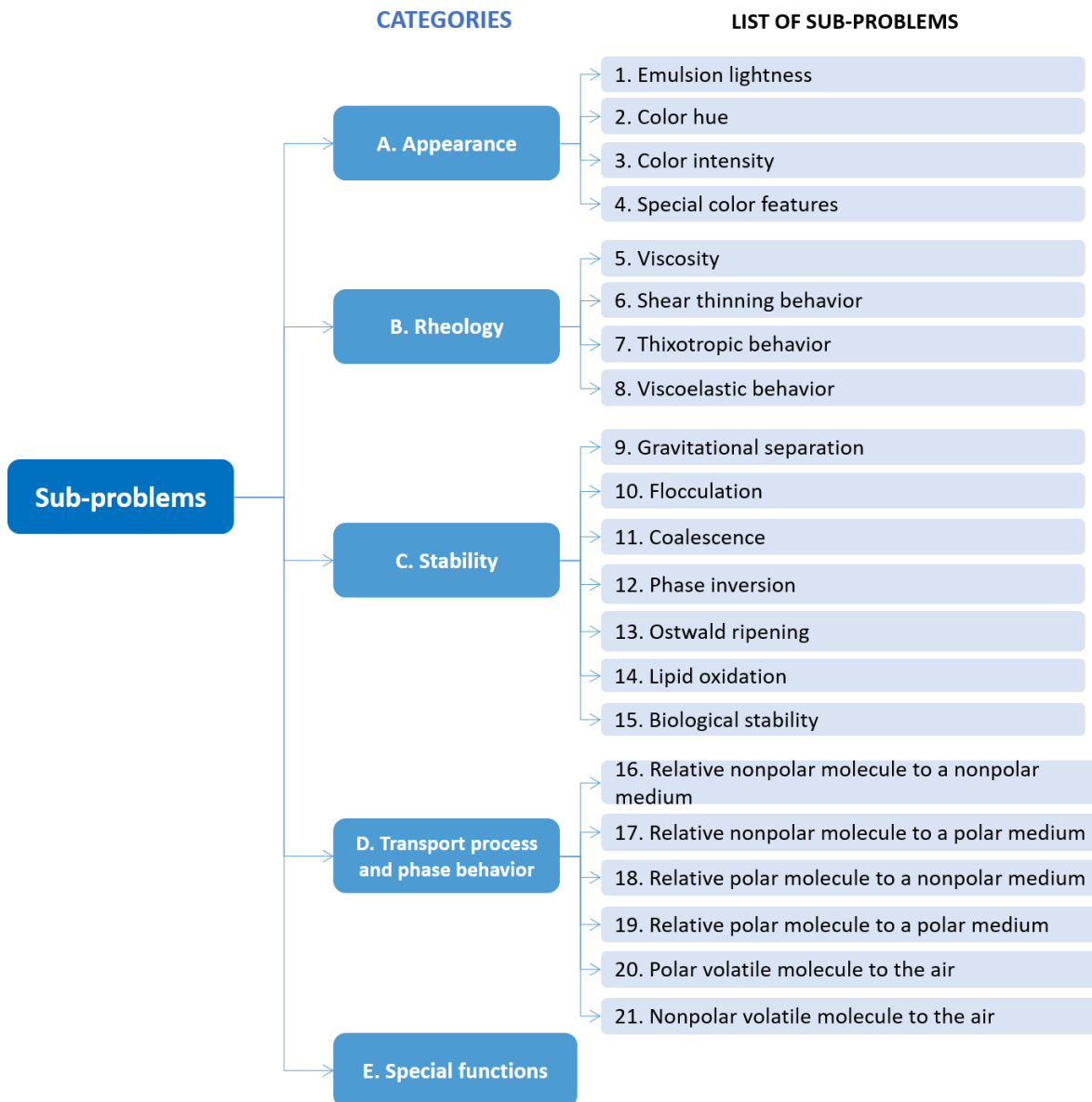


Figure 2. List of sub-problems for emulsion formulation

Table 1. Explanation of the selected sub-problems for emulsion formulation according to the methodology proposed

A. Appearance	A1. Emulsion lightness	This is the emulsion's whiteness or milky appearance. It is caused by light scattering, a phenomenon whereby light is driven in multiple directions other than the incident angle when it encounters a surface (in this case, emulsion droplets) ³⁶ . It is strongly related to the emulsion's micro-structure.
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	A2. Color hue	This is defined as spectrally pure color (i.g. red) without any considerations of intensity (i.g. from light pink to bright red). It is caused by light absorption of a colorant molecule ³⁶ .
	A3. Color intensity	This is a colorant property. It can be described in terms of absorbance (A), which is proportional to the concentration (c) of the colorant and its absorptivity (α) ³⁶
	A4. Special color features	They are created by selecting additives with special functions.
B. Rheology	B5. Emulsion viscosity	It is related to adjectives such as thick (high viscosity) and fluid (low viscosity) ³⁷ . It increases with the dispersed phase volume fraction, the viscosity of the continuous phase ³⁸ , the forces between particles, the presence of flocs, and, depending on the concentration, with smaller droplet sizes ³⁶ .
	B6. Shear thinning	It describes a behavior in which viscosity decreases as the emulsion is sheared. When shearing is stopped, the fluid recovers its original viscosity immediately ³⁷ . The main factors promoting this behavior are an increase in the dispersed phase volume fraction, rheological modifiers ³⁶ .
	B7. Thixotropic behavior	It describes the reversible decrease of the viscosity with time under a constant shear rate ³⁹ . The main factors enhancing this behavior are an increase in the dispersed phase volume fraction, weak flocculation, rheological modifiers ³⁶ .
	B8. Viscoelastic behavior	When a force is applied, part of the energy is stored and part is dissipated ³⁶ . Thus, the material behaves solid-like and liquid-like simultaneously. The main factors enhancing this behavior are an increase in the effective dispersed phase volume fraction ³⁸ , weak flocculation ³⁶ and rheological modifiers ³⁷ .
C. Stability	C9. Gravitational separation	It happens when droplets or particles move upwards or downwards within the emulsion and form a visible layer ⁴⁰ . It can be controlled by adjusting the density of the phases, reducing the dispersed phase volume fraction, reducing the droplet size, increasing the viscosity of the continuous phase, avoiding flocculation, and a narrow droplet size distribution ³⁶ , among others.
	C10. Flocculation	It is the process whereby droplets associate with each other before they merge ³⁶ . It can be controlled by decreasing the dispersed phase volume fraction, increasing the droplet size, and increasing the viscosity of the continuous phase ³⁶ , among others.
	C11. Coalescence	It is the process where two or more droplets merge together ^{36,39} . This process is thermodynamically favorable. It can be controlled by avoiding flocculation and gravitational separation, and increasing inter-particle repulsive forces, among other ³⁶ .
	C12. Phase inversion	It is the phenomenon in which the emulsion structure overturns, i.e., the continuous phase becomes the disperse phase and vice versa ⁴¹ . It is prevented by not exceeding the critical level in disperse phase concentration and selecting a proper surfactant system ⁴² .
	C13. Ostwald ripening	It consists in the diffusive transfer of the disperse phase from small to large droplets. The driving force behind the phenomenon is the difference in chemical potential of the disperse phase in the continuous phase, which is larger for material contained in small than in large droplets ^{39,41} .
	C14. Lipid oxidation	It is a complex sequence of chemical reactions that results from the interaction of lipids with oxygen active species ⁴³ . It can be controlled by reducing the concentration of oxygen, selecting oils with a low tendency to oxidize, avoiding the presence of oxidant agents.

	C15. Biological stability	It is broken when the emulsion is contaminated with biological agents (microbes and fungi). Measures to prevent it include sterile manufacturing conditions, hostile environment (e.g., low pH), preservatives ^{44 45} .
D. Transport process and phase behavior	D16. Release of a relative nonpolar molecule (KOW >1) to a nonpolar medium	It is favored when the difference in polarities between the active and the oily phase (where the nonpolar active is mostly) is larger than the difference between the active and the target medium ⁴⁶ . Other factors are the active concentration, the volume fraction, the droplet size, if the active binds physically or chemically with other component within the emulsion, etc ^{36,46} .
	D17. Release of a relative nonpolar molecule to a polar medium	It occurs as the active diffuses through the droplet, partitions to the aqueous phase, and then diffuses to the polar medium. Nonpolar molecules transfer in low proportions to a polar medium. The main factor affecting this release is the active concentration ^{36,46} .
	D18. Release of a relative polar molecule (KOW <1) to a non-polar medium	It occurs as the active partitions from the aqueous phase to the non-polar medium. Polar molecules diffuse to a non-polar medium in low proportions. The main factor affecting this release is the active concentration ^{36,46} .
	D19. Release of a relative polar molecule to a polar medium	It occurs as the medium dilutes the emulsion and the active molecule diffuses due to the difference in chemical potential created by the dilution. In this case partitioning is not relevant and diffusion is favored ³⁶ . Factors affecting the transport include continuous phase viscosity.
	D20. Release of a relative polar volatile molecule to the air	When this occurs, the properties of the volatile molecule are the main factors determining its transport ³⁶ . For example, as the molecular weight of the active increases, its volatility decreases ³⁶ .
	D21. Release of a relative nonpolar volatile molecule to the air	As in the previous case, the properties of the volatile molecule are the main factors determining its transport ³⁶ . Formulation factors that may affect its transport include the presence of binding molecules and micelles, the volume fraction, and the droplet size.
E. Special functions		They are related to specific functional ingredients or actives. Examples of actives in the cosmetic sector are antioxidants, moisturizers, UV filters, among others. Their behavior in relation to the emulsion system should be analyzed during design.

4. Solution strategies for emulsion formulation

The solution strategies are presented in Figure 3 and are explained in Table 2. An extended explanation can be found in the supplementary material. They are classified into eight categories: A aqueous phase, B oily phase, C relationship between oily and aqueous phase, D colloidal forces, E interface, F micro-structure, G emulsion environment, and H functional ingredients. The 30 solution strategies presented in Table 2 helps the designer to identify the

potential solution set and to understand the chemical and physical variables to be studied for all the sub-problems they have to overcome.

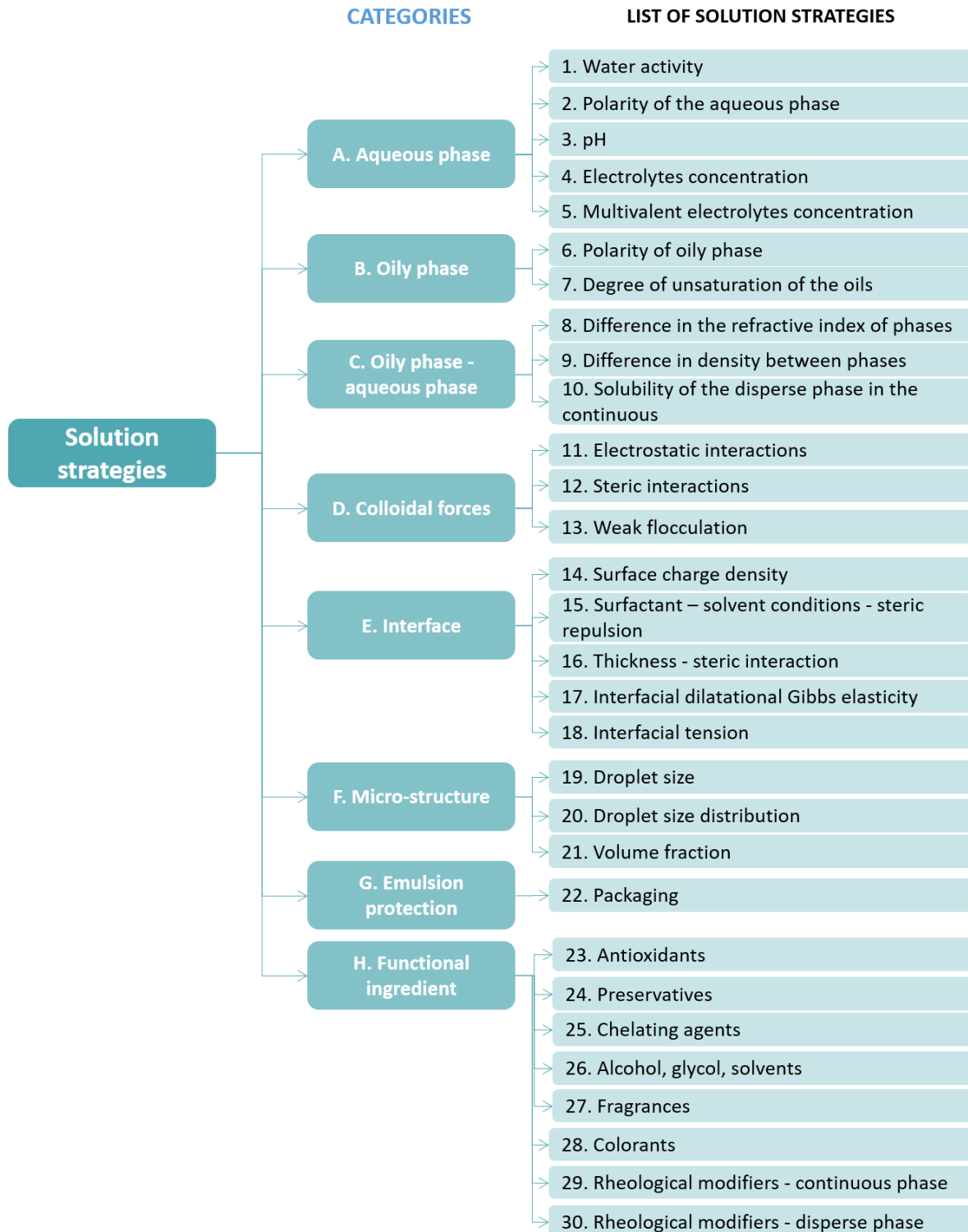


Figure 3. Solution strategies for the formulation of emulsion type products

Table 2. Explanation of considered solution strategies for emulsion formulation

A. Aqueous phase	A1. Water activity	It is related to the capability of organisms to survive and growth. The smaller the water activity, the fewer the possibilities for organisms to live in the media ⁴⁷ . Water activity can be reduced by adding solutes such as sugar, salt, glycerin, among others.
	A2. Polarity of the aqueous phase	It is related to the capability of water to solubilize and transport substances. It can be modified by the addition of solutes.
	A3. pH	It affects the behavior of molecules able to dissociate. It can be changed by the addition of an acid (such as lactic or citric acids) or an alkali (such as sodium hydroxide, potassium hydroxide and triethanolamine)
	A4. Electrolytes concentration	They are compounds that dissociate in water, such as salts. Their concentration affects the behavior of electrically charged species within the emulsion, which may be critical when ionic surfactants are used.
	A5. Multivalent electrolytes concentration	It has a much bigger effect than monovalent ion concentration. Thus, in emulsions stabilized with ionic surfactants, multivalent electrolytes should be avoided or used in very small concentrations. The use of distilled and deionized water is a common practice in the cosmetics industry.
B. Oily phase	B6. Polarity of oily phase	It defines in part the relationship between the oily and aqueous phases. It also determines the solubility and transport of lipophilic actives. It can be changed by selecting a proper mix of oily compounds.
	B7. Degree of unsaturation of the oils	A low degree of unsaturation means a lower propensity to oxidation. Unsaturation is measured through the iodine number, which is high when the degree of unsaturation of the compound is high.
C. Oily-aqueous phase	C8. Difference in the refractive index of phases	It is highly related to appearance. If the difference is zero, the emulsion turns transparent. The refractive index of water can be increased by adding solutes to the aqueous phase ³⁶ . The oily phase refractive index can be modified by changing the oily phase composition.
	C9. Difference in density between phases	It can be decreased by selecting an oily phase with a relatively high density, using weighting agents, increasing the portion of solid oils and using surfactants that form a thick interlayer ³⁶
	C10. Solubility of the disperse phase in the continuous phase	It is related to the phenomenon of Ostwald ripening. In O/W emulsions, the presence of components such as alcohols, or micelles in the continuous phase, increase the solubility of oils in water and in turn the Ostwald ripening rate ^{48 49} .
D. Colloidal forces	D11. Electrostatic interactions	They are generated in the emulsion by adding ionic surface-active agents, which adsorb on the oil-water interface. If they are in their ionized form (which depends on their pKa and the pH of the aqueous phase) a surface potential and a double layer is formed and droplets repel each other ³⁹ .
	D12. Steric interactions	They are generated when nonionic surfactants are added to the emulsion. Nonionic surfactants' molecules have two parts, one of them is highly soluble in the continuous, and defines the curvature of the interfacial layer. The other has a high surface activity and should adsorb efficiently on the droplet interface ³⁹ .
	D13. Weak flocculation	It is generated by the interrelation between attractive and repulsive forces. It may occur when forces acting between droplets create a configuration in which

		two potential energy minimums are presented. One of them is very deep and corresponds to a very close distance between droplets (primary minimum), and the second one corresponds to a larger distance where droplets can agglomerate reversibly (weak flocculation) ^{40,36} .
E. Interface	E14. Surface charge density (electrolyte repulsion)	It is defined as the amount of electrical charge on the droplet surface. It is mainly affected by the nature of the ionic compounds adsorbed on the droplet surface (ionic surfactants, fatty acids, multivalent ions, charged biopolymers) as well as by the characteristics of the continuous phase such as the pH, ionic composition, temperature ³⁶ .
	E15 Surfactant – solvent conditions (steric repulsion)	Steric repulsion is enhanced when surfactant chains are in good solvent conditions, this is, when the surfactant – solvent interaction is favored over the polymer-polymer interaction ⁴⁰ . Good solvent conditions can be enhanced by selecting an appropriate surfactant with a suitable HLB, by setting the composition of the aqueous phase to enhance solvation.
	E16. Thickness (steric repulsion)	It refers to the range of steric interactions. It can be increased by selecting surfactants with a longer hydrophilic chain. In addition, the strength of steric interactions increases with droplet size and depends on the interfacial layer characteristics ³⁶
	E17. Interfacial dilatational Gibbs elasticity	It gives resistance to the interfacial layer against deformation and coalescence. It can be improved by the implementation of polymeric and biopolymeric surfactants such as proteins and polysaccharides ^{39,36} .
	E18. Interfacial tension	It indicates the free energy required to increase the interfacial area ³⁶ . It is decreased when surfactants or polymers are adsorbed, when temperature is increased until a minimal value (PIT) ^{40, 50} among others.
F. Microstructure	F19. Droplet size	It is defined by components and process conditions. It can be decreased by increasing surfactant concentration, selecting a surfactant with a high adsorption rate, increasing processing temperature, decreasing interfacial tension, and increasing the mechanical energy input, among others ³⁶ .
	F20. Droplet size distribution (DSD)	It depends strongly on the homogenization process. Membrane and micro-channel homogenizers generate narrow DSD, while high shear mixers, high-pressure valve homogenizers, colloid mills, generate broader distributions ³⁶ . Batch systems produce wider DSDs than continuous operation systems ⁵¹ . A more viscous disperse phase generates a broader distribution ^{51,52} .
	F21. Volume fraction	For O/W emulsions, it can be augmented by increasing the oily phase and/or particle concentration if the product contains suspended particles.
G. Emulsion protection	G22. Packaging	It provides protection to the product. It can be designed with U.V. filters or with the purpose of limiting the inlet of air. Attention should be paid to packaging material, its compatibility with the product, and its sustainability performance.
H. Functional ingredients	H23. Antioxidants	They are compounds that prevent oxidation, the formation of free radicals and thus the deterioration of skin cells
	H24. Preservatives	They are substances that inhibit the growth of organisms, preventing the product from getting damaged. Criteria such a safety, regulations and toxicity are fundamental for their selection.
	H25. Chelating agents	They are compounds capable of removing transition metals such as iron and copper from the vicinity of droplets ⁴³ . An example of these agents is EDTA ⁴³ .
	H26. Alcohol, glycol, solvents	This refers to the addition of low molecular weight alcohols (e.g. ethanol) or other solvents. They can affect the spontaneous curvature of the surfactant

		system, increase the solubility of oil in water, reduce surface tension, increase the water refractive index, enhance emulsion preservation, among other effects.
	H27. Fragrances	When selecting them, care must be taken with aspects such as toxicity, compatibility with other components, price, stability to pH and light, and in the case of cosmetics, compatibility with skin.
	H28. Colorants	Their selection depends on aspects such as hue, intensity, solubility in the media, price, safety, stability to different pH, temperature, light chemical agents, among others.
	H29. Rheological modifiers	They are substances that change the rheological behavior of a phase and thus of the emulsion. They can increase viscosity or change the rheological profile to enhance shear thinning behavior viscoelasticity
	H30. Rheological modifiers – disperse phase	Rheological modifiers can be added to both the continuous and the disperse phase, if required.

5. Ingredients for application in the cosmetics sector

As mentioned above, the methodology is focused on O/W emulsions in cosmetics. Therefore, some of the most common ingredients used in this sector are presented below, classified into four groups: oils, surfactants, rheological modifiers, and other ingredients (which include glycols, preservatives, colorants, fragrances, and actives). Properties of a list of some common cosmetic ingredients of each category can be found in Table S1, S2 and S3 in the supplementary information.

5.1. Oils

Oils are used in cosmetic emulsions for several purposes: to act as emollients and make skin and hair softer, and to serve as solvents for liposoluble actives. Some of them can act as occlusive ingredients, i.e., they create a barrier to avoid the loss of water⁵³. Characteristics to be considered in their selection include:

- Polarity, which is related to properties such as the Hansen solubility parameters, octanol-water partition coefficient (K_{OW}) and required HLB.

- Required HLB, which determines the compatibility of oils with the surfactant system.
- Melting point, which determines if the oil is solid or liquid, its consistency and the possible consistency of formulations ⁵⁴.
- Viscosity, which determines the spreadability of the oil and its formulations
- Density, which is related to emulsion stability
- Sensorial profile
- Environmental and safety properties
- Sources, which can be 100% vegetable, vegetable based or synthetic based
- Stability to oxidative agents, pH, temperature
- Capability of solubilization of actives, capability of wetting of dispersible actives
- Interactions with other emulsion ingredients

Oils can be classified according to their chemical nature in esters, fatty alcohols, hydrocarbons, silicones, triglycerides, fatty acids. Figure 4 presents a visual comparison of the polarity, viscosity and spreadability of 21 common oils of different chemical families (other information about these oils is also presented in the supplementary information Table S2). The x-axis is the polarity, expressed in comparative terms (low, medium and high) and the y-axis corresponds to the viscosity in mPa s. Each circle corresponds to an oil, and the radius of the circumference corresponds to its spreadability. Oils of the same category are represented with the same color. In some cases, ingredients in the same category present

similar properties. For example, silicones tend to have a low polarity, high viscosity and low spreadability. In other cases, the same family can have a wide range of properties. For example, it is possible to find esters of medium to high polarity with low to high spreadability. Figure 4 gives information of families of oils and their properties; it can be used for the selection of oils that enable the application of the solution strategies (Figure 3), which can meet design requirements. In this selection, it is also possible to implement heuristics^{30,55}.

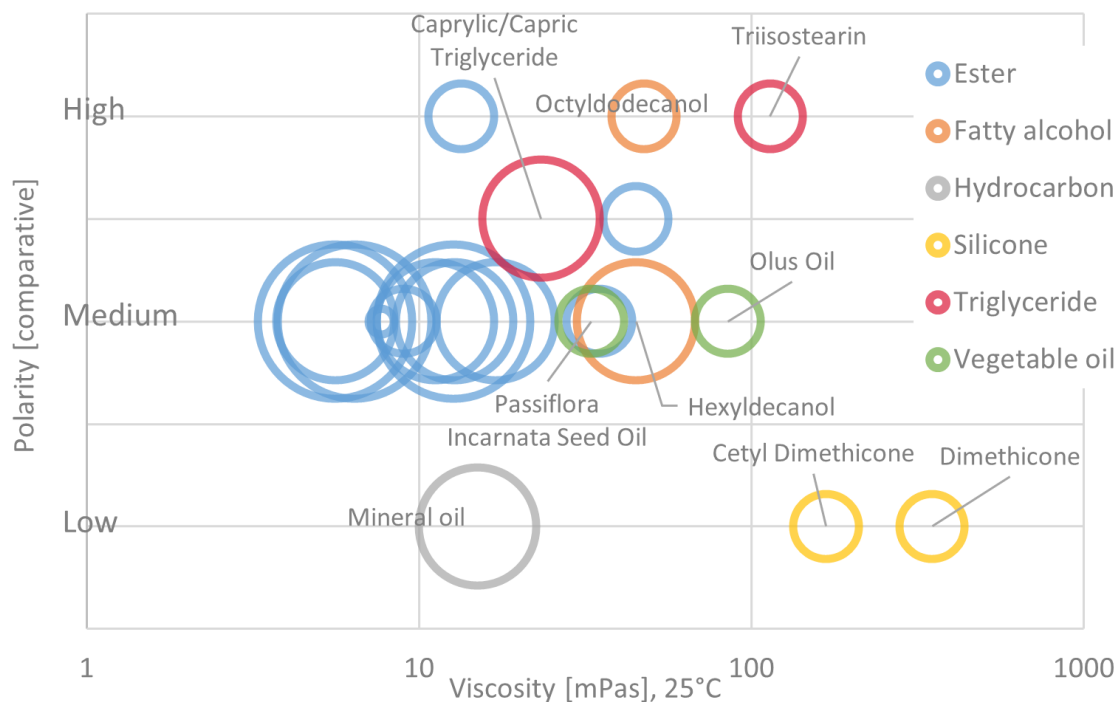


Figure 4. Bubble plot of viscosity and polarity for a sample of 21 emollients from different families. The area of the bubbles represents spreadability (the larger the area, the higher the spreadability).

5.2.Surfactants

Surfactants are used in emulsions for three purposes³⁶: to decrease the energy required during emulsification; to adsorb rapidly at the interface of recently formed droplets; to generate a

barrier, either electrostatic, steric or both, for long-term emulsion stability. They are classified as nonionic and ionic (anionic and cationic). Characteristics that can be considered for surfactant selection include:

- HLB, which is an indicator of how soluble a surfactant or a surfactant mixture is in water or in oil ⁵⁶. Surfactants with low HLB are lipophilic and tend to form W/O emulsions. Surfactants with high HLB are hydrophilic and tend to form O/W emulsions. HLB of surfactant mixtures is calculated with a weighted addition according to the composition of the surfactant system ⁵⁷.
- Surfactant nature, which is mainly ionic or nonionic. Ionic surfactants depend strongly on the electrical characteristics of surfaces, which in turn depend on the electrolyte concentration and pH of the aqueous phase ³⁶. High electrolyte concentrations decrease the range of the electrostatic interactions. pH determines the ionization degree of ionic surfactants, which are effective only when they are dissociated. Additionally, an increase in the temperature or in the polarity of the oily phase favors the stability of O/W emulsions ⁴⁹. Conversely, an increase in electrolyte concentration or surface inactive species concentration is unfavorable for stable O/W emulsions ⁴⁹.
- On their part, nonionic surfactants depend on the specific characteristics of the surfactant molecule and its relation to the emulsion phases. Their effectiveness increases as the interfacial thickness increases and when they are in good solvent conditions. They are less sensible to pH and electrolyte concentration than ionic surfactants ³⁶. However, an increase in temperature or the presence of surface inactive species is unfavorable for O/W

emulsions. For these surfactants, electrolytes may have a positive or negative effect on stability.

- Surfactant solubility in water and in the oily phase, which allows the selection of the phase in which the surfactant is dissolved or pre-dispersed for emulsification.
- Critical micelle concentration (CMC) is the concentration at which the surfactant molecules begin to form micelles in aqueous solution, i.e., an aggregate structure of surfactant molecules ⁵⁸. Below CMC, surface tension is reduced when surfactant concentration increases; above CMC, surface tension remains constant.
- Krafft point is the minimal temperature at which surfactants begin to form micelles. Below this temperature, the solubility of surfactant is low ⁵⁸. Stable emulsions are only formed above this temperature (minimal temperature for stability)
- Cloud point corresponds to the temperature at which the surfactant begins to precipitate when the temperature is increased ⁵⁸. Emulsions are destabilized above this temperature (maximal temperature for stability).
- Sensorial profile
- Environmental and Safety indicators
- Source
- Interactions with other emulsion ingredients
- Stabilization capability. While it is possible to select a surfactant system that favors a type of emulsion (O/W or W/O), to our knowledge, it is still not possible to predict

emulsion stability under real conditions. It is thus necessary to trial the surfactant system experimentally. Heuristics can also be used to select surfactant systems that have already been shown to form stable emulsions ⁵⁷.

For cosmetic use, nonionic surfactants are highly relevant because they are milder on the skin. Nonionic surfactants are subclassified as: alkyl glucosides, glycerol esters, POE alkyl ethers, polyglycerol esters, polyoxyethylene glycerides, sorbitan and sucrose esters. Figure 5 summarize the properties of a list of surfactants commonly used in the cosmetic sector. Figure 6 shows the HLB for a group of different nonionic surfactants in relation to their structures. The HLB increases as the length of the alkyl chain decreases and as the proportion of the hydrophilic part in the molecule increases. Information of both Figures can be used to select possible surfactant categories to be explored for the application of solution strategies responding to the design problem, as for the case of the oils.

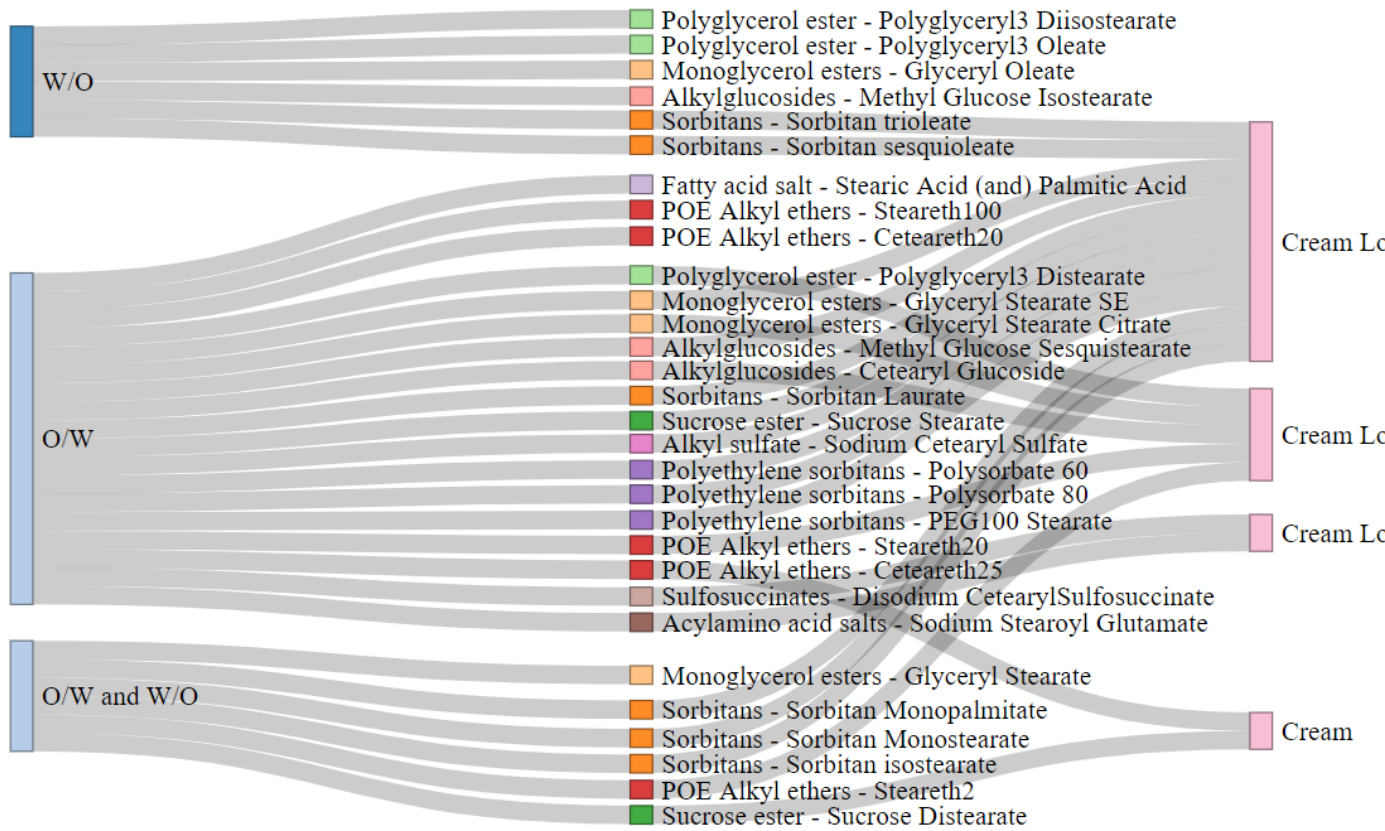
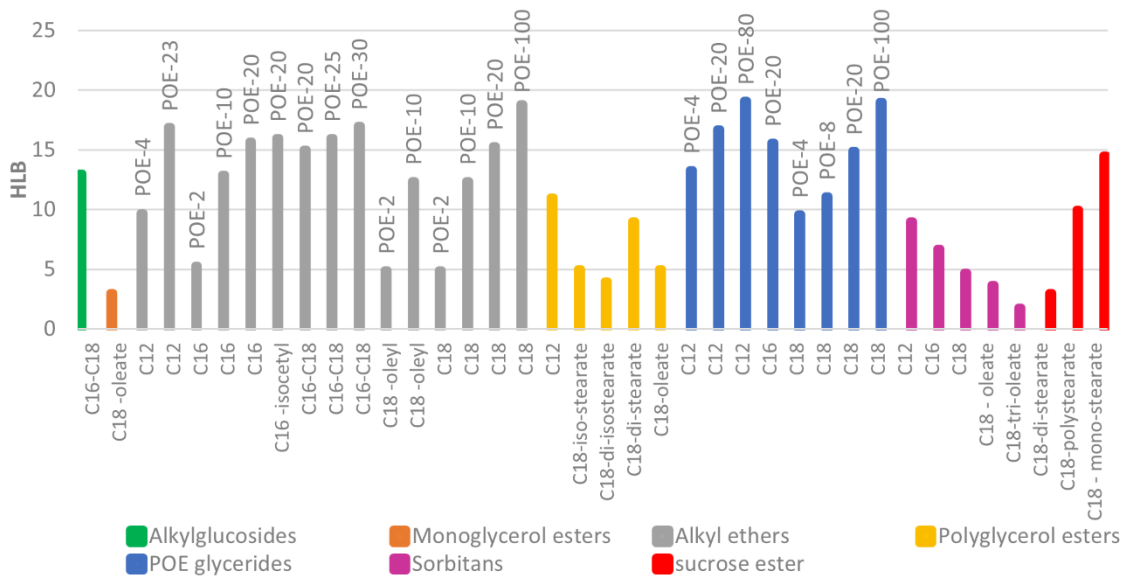


Figure 5. Surfactants commonly used in the cosmetic industry and their application



5.3.Figure 6. HLB of nonionic surfactants commonly used in the cosmetic industry. The

INCI names of the surfactants are presented in Supplementary material Table S4.

Rheological modifiers

Rheological modifiers are added to the formulation for three main purposes⁵⁴: to increase viscosity, to promote a particular rheological behavior (pseudoplastic, thixotropic), and to enhance emulsion stability. Characteristics to be considered for rheological modifier selection include:

- Efficiency, which is the ability to increase viscosity using a certain quantity of the rheological modifier. Efficiency depends on polymer nature, molecular weight, branches and conformation³⁶.
- Stability with other ingredients, because some rheological modifiers may cause the precipitation of other ingredients in the formula⁵⁴.
- Solubility in water: The solubility in water is important to establish how to introduce the rheological modifier to the formula⁵⁴. Some rheological modifiers are soluble in hot but not in cold water and can be pre-dispersed in the latter. Some of them dissolve at low pH and are active at high pH. Some of them can be pre-dispersed in glycols or alcohols before they are dissolved in water.

Rheological modifiers can also be classified according to their ionized nature: anionic, cationic, nonionic or amphoteric. Some of them (mostly cationic) can give a soft texture to the product and work as static control and hair conditioners⁵⁴. Figure 7 presents some rheological modifiers and their properties.

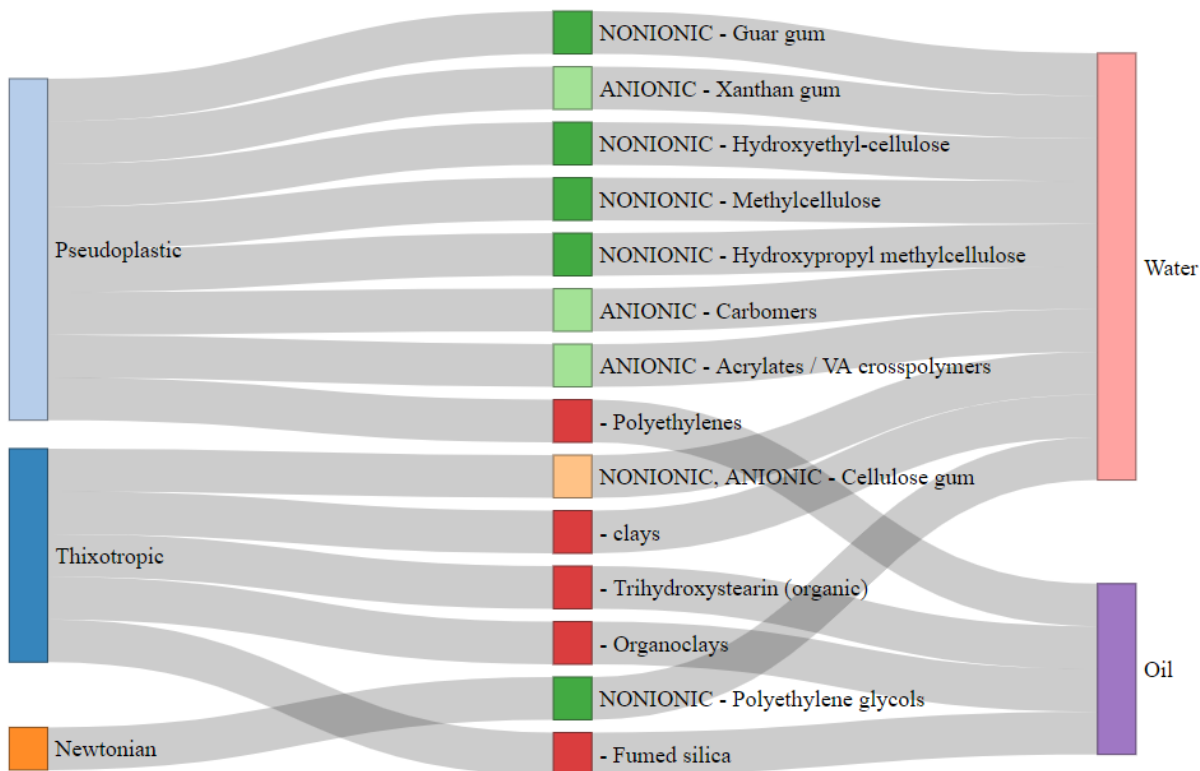


Figure 7. Rheological modifiers commonly used in the cosmetic industry

5.4. Other ingredients

Glycols are chemical compounds containing a certain number of hydroxyl groups. They are water soluble and are widely used in cosmetics due to their moisturizing function⁵⁴. They also work as stabilizer solvents and dispersants of polymers. They have a significant effect on the feel of use⁵⁴.

Preservatives are compounds that prevent products from going off by controlling the growth of microorganisms. Some of them cannot be used for certain product applications and/or they have a maximum allowed concentration in the final product. For their selection, it is important to consider: Efficiency, maximal allowed concentration, toxicity, environmental effect, and possible interactions with other emulsion ingredients.

Other ingredients are chelating agents, antioxidants, colorants, fragrances, solar filters, pH modifiers, special actives. For their selection it is important to consider: their function, efficiency, possible incompatibilities with other emulsion ingredients, toxicity, and environmental effect.

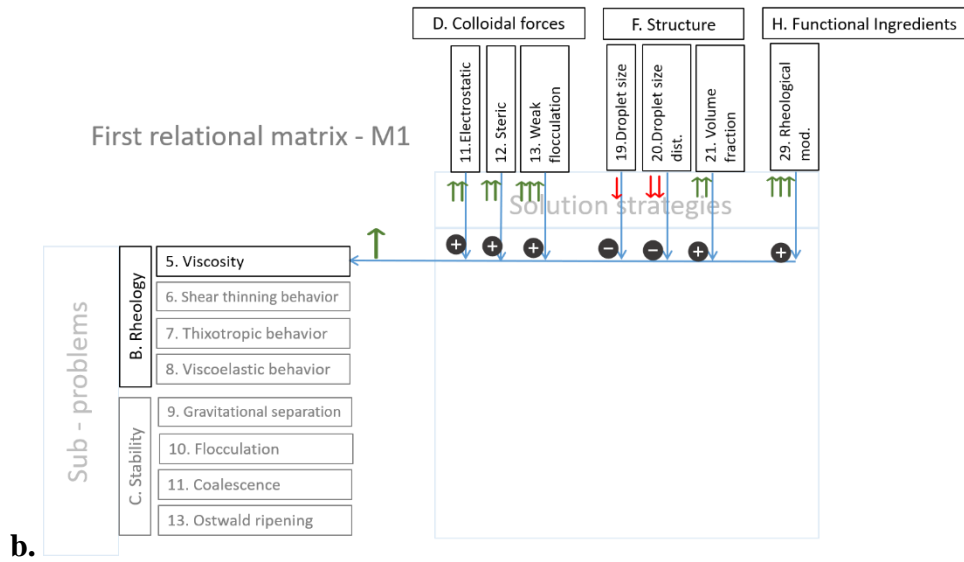
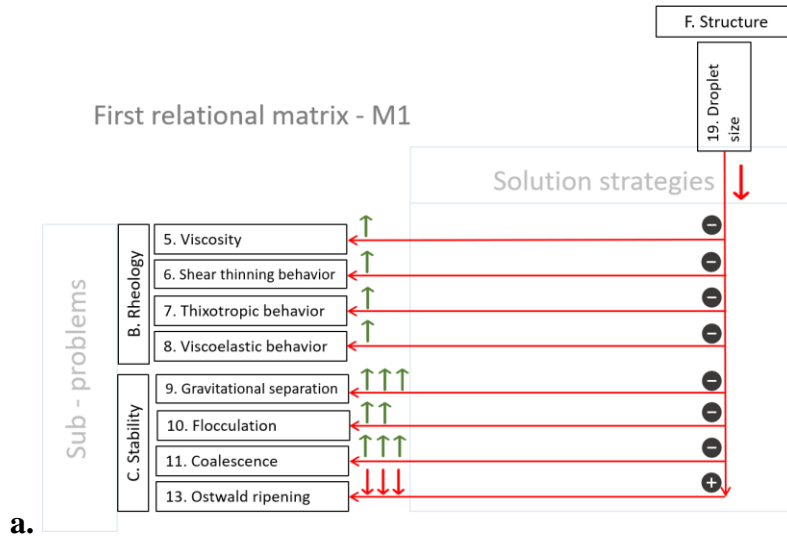
6. The matrix databases

In the methodology the connection between sub-problems and solution strategies is made with the first relational matrix, which is shown in Table 3. It was developed by consulting a group of four experts in emulsion science and rheology from the academy. Experts were interviewed in a Delphi based group discussion to reach a consensus^{59,60}. Within the group, they were asked to agree on the relationship between each sub-problem and each solution strategy relative to the direction (if the sub-problem is enhanced or reduced) and the intensity of the effect (high, intermediate, low and no interrelation). The results were summarized using a seven-point scale: -7, -3, -1, 0, 1, 3, 7, where 7, 3, 1 and 0 correspond to high, intermediate, low and no interrelation, respectively. The negative values correspond to an interrelation sub-problem/solution strategy with an inverse effect. This scale was chosen because it allows a broad segmentation of the data and it identifies positive and negative interrelations. The first relational matrix is applicable to O/W emulsions with low to intermediate concentrations.

For some pairs of sub-problems/solution strategies, the experts were not able to establish a clear and direct link. In these cases, the relationship is represented with a question mark (?), meaning there may be an interrelation between the strategy and the sub-problem, but it is indirect or unknown. For some other pairs, the experts agreed there is an interrelation, that

can be positive or negative, important or not, according to the specific problem conditions. It should be defined later with more information (for example after the pH or some ingredients are already selected). In these cases, the interrelation is represented with an exclamation mark (“!”).

The first relational matrix can help to analyze the effect of a solution strategy on the different sub-problems. For example, droplet size (column F19 in Table 3) is a structural characteristic with multiple effects on emulsion behavior as represented in Figure 8a. It has a negative correlation with the rheology type sub-problems, i.e., an increase in the droplet size tends to reduce viscosity and non-Newtonian rheological behaviors. Correspondingly, a reduction of droplet size tends to increase these rheological behavior(the negative symbol “-” is used to show the relation is inverse). Regarding stability type sub-problems, a reduction in the droplet size tends to increase stability in cases where the gravitational separation, flocculation and coalescence phenomena are prevalent (which is why the symbol is negative, “-”), but to reduce it in cases where the Ostwald ripening phenomenon (row C13) is prevalent (in this case the symbol is positive, “+”). The first relational matrix can also help to identify different solution strategies for a sub-problem as it is shown in Figure 8b, where a set of strategies that can modify emulsion viscosity are highlighted. The exclamation and question marks also give useful information. For example, a change in pH (column A3) can be positive or negative in relation to several sub-problems (Figure 8c), which shows this decision is critical and must be carefully evaluated in relation to all its possible effects.



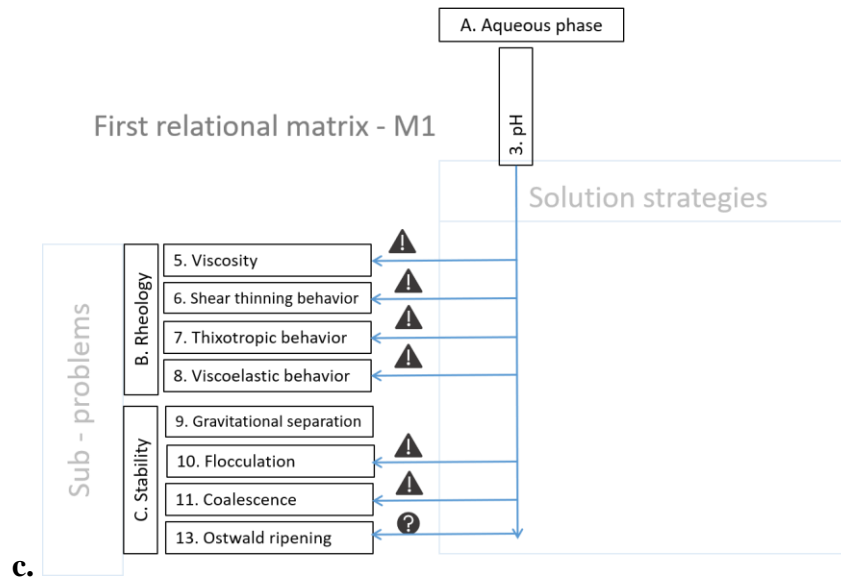


Figure 8. Representation of the type of information given by the first relational matrix M1 in Table 3 a) Effect of the solution strategy droplet size in a group of sub-problems b) Effect of a set of solution strategies in the sub-problem viscosity c) effect of the solution strategy pH in a group of sub-problems

The connection between solution strategies and ingredient categories can be made with the second relational matrix, which is presented in Table 4. It was completed by considering the description of strategies presented in section 4 and the ingredient categories presented in section 5. The interrelation is done with the values 1, -1, 0, !, where 1 indicates the ingredient helps to apply the corresponding strategy, -1 indicates the ingredient reduces its effect, 0 indicates that the ingredient does not apply the strategy and the exclamation mark (!) indicates that the ingredient has an effect which may be positive, negative, significant or not significant, and more information is required to establish it.

For example, to apply the strategy “electrostatic interactions” (column D11 of the second matrix), it is recommended to add a cationic or an anionic surfactant to the formulation as

represented in Figure 9. Additionally, the use of chelating agents can increase this interaction while the presence of electrolytes can reduce it. In this example, the addition of compounds that modified the pH (acids, bases) has an effect which can be negative or positive according to the isoelectric point of the surfactant (and thus additional information about them is required to define the effect). The second matrix has a variable related to the process, the energy input, which has effects on the variables related to the micro-structure of the product (droplet size and droplet size distribution).

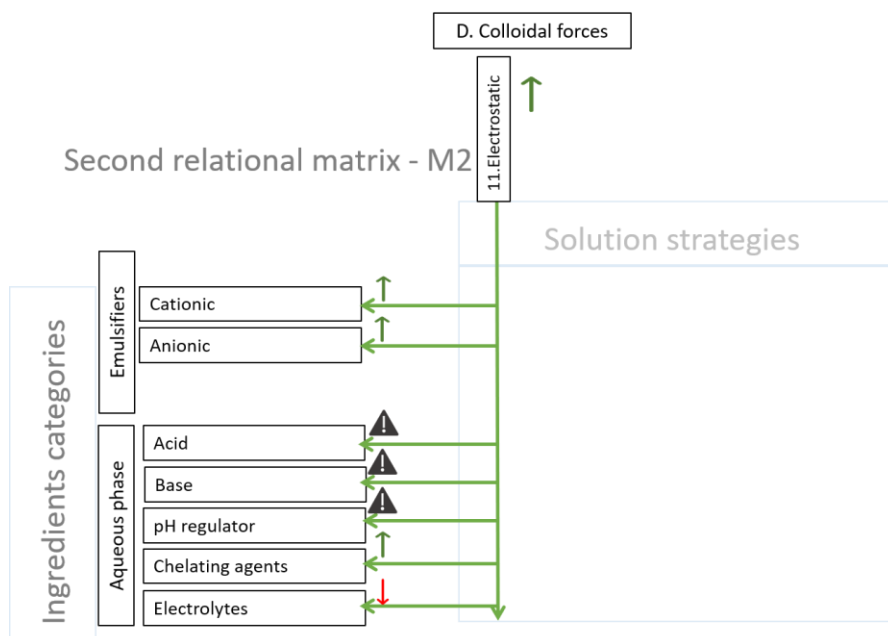


Figure 9. Example of the type of information given by the second relational matrix M2 in Table 4. Ingredients categories that enhance electrostatic interactions

Table 3. First relational matrix M1- Interrelation between sub-problems and solution strategies

			SOLUTION STRATEGIES																													
			A. Aqueous phase					B. Oily phase		C. Oily phase - aqueous phase			D. Colloidal forces			E. Interphase				F. Structure			G.	H. Functional ingredients								
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Water activity	Polarity of aqueous phase	pH	Electrolytes concentration	Multivalent electrolytes concentration	Polarity of oily phase	Degree of unsaturation of the oils	Difference in the refractive index between phases	Difference in density between phases	Solubility of the disperse phase in the continuous	Electrostatic interactions	Steric interactions	Weak flocculation	Surface charge density	Surfactant – solvent conditions	Thickness -steric interaction	Interfacial dilatational Gibbs elasticity	Interfacial tension	Droplet size	Droplet size distribution	Volume fraction	Packaging	Antioxidants	Preservatives	Chelating agents	Alcohol, glycol, solvents	Fragrances	Colorants	Rheological modifiers- continuous phase	Rheological modifiers- disperse phase			
SUB-PROBLEMS	A. Appearance	1	Emulsion lightness (opacity)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
		2	Color hue (chromaticity)	0	0	!	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7	0	0
		3	Color intensity	0	0	!	0	0	0	0	-3	0	0	0	0	-1	0	0	0	0	0	-3	!	-3	0	0	0	0	0	7	0	0
		4	Special color features	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7	0	0	
	B.	5	Viscosity	0	0	!	-3	-3	0	0	0	0	0	3	3	7	?	?	3	3	!	-1	-3	3	0	0	0	0	0	0	7	1
		6	Shear thinning behavior	0	0	!	-3	-3	0	0	0	0	0	3	3	7	?	?	3	-1	!	-1	-1	7	0	0	0	0	0	0	7	-?
		7	Thixotropic behavior	0	0	!	-3	-3	0	0	0	0	0	3	3	7	?	?	3	0	!	-1	-1	3	0	0	0	0	0	0	7	0
		8	Viscoelastic behavior	0	0	!	-3	-3	0	0	0	0	0	3	3	7	?	?	1	1	!	-1	-1	7	0	0	0	0	0	0	7	1
	C. Stability against	9	Gravitational separation	0	0	0	0	0	0	0	-7	0	0	0	-3	0	0	0	0	0	-7	-3	3	0	0	0	0	0	0	7	0	
		10	Flocculation	0	0	!	-1	-7	0	0	0	0	3	3	-3	3	3	0	0	-3	-1	-3	0	0	0	3	0	0	0	3	0	
		11	Coalescence	0	0	!	!	-3	0	0	0	0	3	3	-3	3	3	7	7	3	-7	-1	-3	0	0	0	3	0	0	3	?	
		12	Phase inversion	0	0	!	!	!	-7	-1	0	0	0	0	0	0	3	0	0	!	0	0	-7	0	0	0	!	0	0	0	0	
		13	Ostwald ripening	0	0	?	?	?	-7	-1	0	0	-7	0	0	0	?	!	0	-7	7	-7	0	0	0	0	0	-3	!	0	3	1
		14	Lipid oxidation	0	?	!	-1	-1	-3	-7	0	0	-1	0	0	0	0	0	0	0	0	0	0	3	7	?	3	0	0	0	0	
		15	Biological stability	-3	0	3	3	3	0	0	0	0	-1	0	0	0	0	0	0	0	0	0	-1	3	?	7	?	3	!	!	!	0
	D. Transport process and phase	16	Release of a relative nonpolar molecule to a nonpolar medium	?	!	0	?	?	-1	0	0	0	-1	0	0	0	0	0	0	0	0	0	0	0	0	!	0	0	-3	0		
		17	Release of a relative nonpolar molecule to a polar medium	?	?	0	?	?	!	0	0	0	!	0	0	0	0	0	-3	-3	0	-3	?	-3	0	0	0	0	0	0	-3	-3
		18	Release of a relative polar molecule to a nonpolar medium	?	!	0	?	?	-1	0	0	0	-1	0	0	0	0	0	0	0	0	0	0	0	0	!	0	0	-3	0		
		19	Release of a relative polar molecule to a polar medium	0	?	0	?	?	3	0	0	0	!	0	0	0	?	-3	-3	0	-3	?	-3	0	0	0	!	0	0	-3	-3	
		20	Release of a relative polar volatile molecule to the air	?	!	0	?	?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-7	0	0	?	!	7	0	-3	0
		21	Release of a relative nonpolar volatile molecule to the air	0	?	0	?	?	3	0	0	0	!	0	0	0	0	0	-3	-3	0	-3	?	-3	-7	0	0	?	!	7	0	-3

Notes: Symbol (?) In these cases, there may be an interrelation between the strategy and the problem, but it is indirect or unknown. Symbol (!) In these cases, there is an interrelation that can be positive or negative, important, or not according to the specific problem conditions. Specific ingredients used and their nature should be considered

Table 4. Second relational matrix M2- Interrelation between ingredient categories and solution strategies

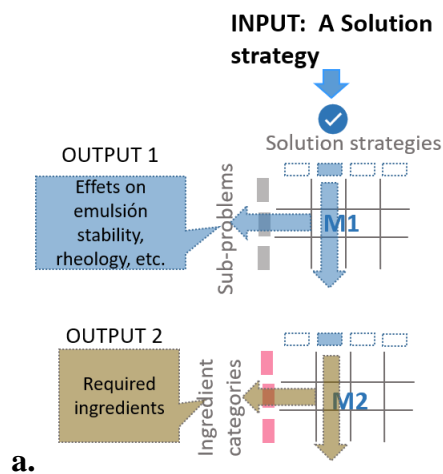
			A. Aqueous phase					B. Oily phase		C. Oily- aqueous phase			D. Colloidal forces			E. Interface				F. Structure			G	H. Functional ingredients									
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
			Water activity	Polarity of aqueous phase	pH	Electrolytes concentration	Multivalent electrolytes concentration	Polarity of oily phase	Degree of unsaturation of the oils	Difference in the refractive index between phases	Difference in density between phases	Solubility of the disperse phase in the continuous phase	Electrostatic interactions	Steric interactions	Weak flocculation	Surface charge density	Surfactant – solvent conditions	Thickness -steric interaction	Interfacial dilatational Gibbs elasticity	Interfacial tension	Droplet size	Droplet size distribution	Volume fraction	Packaging	Antioxidants	Preservatives	Chelating agents	Alcohol- glycol, solvents	Fragrances	Colorants	Rheological modifiers- continuous phase	Rheological modifiers- disperse phase	
OILY PHASE	EMOLLIENTS	Hydrocarbons					-1	(!)(d)	(!)(e)	(!)(f)	-1							(!)	(!)(m)	(!)(m)	1												
		Waxes					(!)	(!)(d)	(!)(e)	-1	(!)								(!)	(!)(m)	(!)(m)	1											
		Esters					1	(!)(d)	(!)(e)	(!)(f)	1								(!)	(!)(m)	(!)(m)	1											
		Vegetable oils					1	(!)(d)	(!)(e)	-1	1								(!)	(!)(m)	(!)(m)	1											
		Higher alcohols					1	(!)(d)	(!)(e)	(!)(f)	1								(!)	(!)(m)	(!)(m)	1											
		Fatty acids					1	(!)(d)	(!)(e)	(!)(f)	1								(!)	(!)(m)	(!)(m)	1											
		Silicons					-1		(!)(e)	(!)(f)	-1								(!)	(!)(m)	(!)(m)	1											
	RHEOLOGICAL MODIFIER OILY PHASE																		1	(!)(m)											1		
	FRAGRANCES					1	(!)(d)	(!)(e)	(!)(f)	1												1						1					
	SUN FILTER OILY PHASE					1	(!)(d)	(!)(e)	(!)(f)	1													1										
COLORANTS OIL PHASE					1	(!)(d)	(!)(e)	(!)(f)	1													1											
COMPOUNDS SOLUBLE - OILY PHASE					(!)	(!)(d)	(!)(e)	(!)(f)	(!)												1												
AQUEOUS PHASE	SURFACTANTS	Cationic	-1	(!)		1	(!)(e)			(!)(f)	1	1			1				-1	-1	(!)												
		Anionic	-1	(!)		1	(!)(e)			(!)(f)	1	1			1					-1	-1	(!)											
		Nonionic	-1	(!)						(!)(f)	1			1		(!)(i)	(!)(j)	(!)(j)		-1	-1	(!)											
	RHEOLOGICAL MODIFIER AQUEOUS PHASE	Cationic	-1	(!)		1	(!)(e)								(!)						(!)(n)	(!)									1		
		Anionic	-1	(!)		1	(!)(e)								(!)							(!)(n)	(!)								1		
		nonionic	-1	(!)											(!)							(!)(n)	(!)								1		
	ACIDS	-1	(!)	(!)	(!)	(!)						(!)	(!)(g)	(!)	(!)	(!)(i)														(!)			
	BASE	-1	(!)	(!)	(!)	(!)						(!)	(!)(g)	(!)	(!)	(!)(i)														(!)			
	PH REGULATOR (BUFFER)	-1	(!)	(!)	(!)	(!)						(!)	(!)(g)	(!)	(!)	(!)(i)														(!)			
	POLYSACCHARIDES AND PROTEINS	-1	(!)	(!)	(!)(b)	(!)(c)						(!)	(!)(g)	1	(!)	(!)(i)	(!)(j)	(!)(j)	(!)														
	GLYCOLS	-1	(!)	(!)	(!)(b)						1		(!)(g)		(!)(i)																		
	PRESERVATIVES	(!)(a)	(!)		(!)(b)	(!)(c)						(!)(k)	(!)(g)			(!)(i)														1			
	CHELATING AGENTS	-1	(!)		-1	-1						1	(!)(g)	-1	1	(!)(i)														1			
	ANTIOXIDANTS	(!)(a)	(!)		(!)(b)	(!)(c)						(!)(k)	(!)(g)			(!)(i)														1			
	COLORANTS	(!)(a)	(!)		(!)(b)	(!)(c)						(!)(k)	(!)(g)			(!)(i)															1		
	SUNFILTERS	(!)(a)	(!)		(!)(b)	(!)(c)						(!)(k)	(!)(g)			(!)(i)																	
	COMPOUNDS SOLUBLE IN WATER	-1	(!)		(!)(b)	(!)(c)						(!)(k)	(!)(g)	(!)(h)		(!)(i)																	
SOLID DISPERSABLES IN WATER														(!)																			
PRESENCE OF SOLVENTS	-1	(!)		(!)(b)	(!)(c)							(!)(g)			(!)(i)															1			

	ELECTROLYTES - Compounds that dissociate in water	-1	(!)		1	(!) (c)								-1																		
INTER- FACE	COMPOUNDS THAT ADSORB AT THE INTERFACE													(!)	1	(!)	(!)															
	PROCESS	Energy input																		-1	(!)(o)											

Notes: (!) the effect of the ingredient depends on its specific characteristics (a) -1 if the compound is soluble in water. (b) 1 if the compound dissociates in water (c) 1 if the compound can dissociate in multivalent ions (d) Attention should be paid to iodine number of the oily compounds. (e) Refractive index of the oily face depends on its composition (f) 1 if the oil component has a low density (g) 1 if the component favors good solvation conditions of the surfactant. (h) 1 for polymeric no absorbed molecules. (i) Agents present in water may affect solvent conditions of the surfactant (j) Use of polymeric and biopolymeric surfactants increase interfacial thickness and may increase Gibbs elasticity. (k) -1 if the compound dissociates in water (l) -1 if the polymeric compound adsorbs at the interface (m) Attention should be paid to viscosity of the dispersed phase. As it increases, droplet size and droplet size distribution may increase (n) a change in the viscosity ratio of the dispersed and continuous phase may affect the droplet size. During homogenization under turbulence conditions experimental evidence have shown a minimum in droplet size when viscosity ratio is between 0.05 and 0.5^{36,61} (o)The effect of the energy in droplet size distribution depends on the homogenization system

7. Use of the matrix databases in the design process

The matrices from Tables 3 and 4 are very rich in information, and they can be used in multiple forms to support the decision-making process during design. They can be used to analyze solution strategies as indicated in Figure 10a. In that case, if one solution strategy is applied (columns in first and second matrix), the first matrix gives information of its effects on emulsion characteristics/sub-problems (stability, rheology, appearance, transport process and phase behavior), while the second matrix describes how to apply it (ingredient type to be added to the formulation). Moreover, the matrices can be used to check the effect of an ingredient on emulsion characteristics/sub-problems, which is useful for reformulation or ingredient substitution problems (Figure 10b). In that case, if an ingredient category is selected (raw in the second matrix), using the matrices it is possible to identify the strategies it implies (second matrix) and the emulsion characteristics/sub-problems it changes (first matrix).



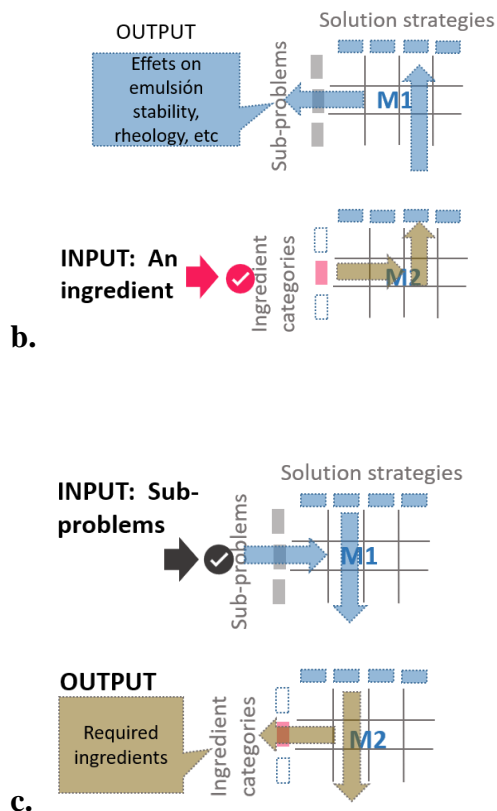


Figure 10. Representation of the multiple possible uses of the matrices: a) analysis of a solution strategies and its effects, b) support in decision-making during reformulation or ingredient substitution, c) design of a new emulsified product. The symbol M1 corresponds to the first relational matrix in Table 3 and M2 to the second relational matrix in Table 4

In this article, the matrices are proposed as a support to the decision-making during the design of new products (Figure 10c). For this purpose, it is recommended to follow the next steps (also shown in Figure 1):

Step 0 - Definition of the design problem

Before the ingredients and process conditions can be selected, it is necessary to set product specifications, i.e., quantifiable product properties and characteristics, defined based on

customer needs, which are used to guide the design.^{62,63} This is a fundamental task that may require an interdisciplinary collaboration between several experts (marketing, design, formulation), consultation of experts and interviewing customers. This publication focuses on the steps following the problem definition.

Step 1 - Division into sub-problems

In this step, product specifications are classified according to the sub-problems presented in Figure 2. It is possible to associate one specification to more than one sub-problem and/or to classify it as a special function, i.e., it may require the inclusion of specific functional ingredients (U.V. filters, moisturizers, antioxidants, etc.). For example, the specification of the product odor is related to a special ingredient, a specific fragrance, and its intensity is related to the sub-problem – “Release of a relative nonpolar volatile molecule to the air”. All product specifications are analyzed and translated into a list of sub-problems and/or special functions during this step.

Step 2 - Connection to solution strategies

In this step, sets of solution strategies to solve the identified sub-problems are selected using the first relational matrix M1 (Table 3). It is possible to form more than one combination of solution strategies (sets). Their formation can be guided by answering the following key questions regarding the specific design problem:

- What kind of surfactant best meets the specifications of the problem?

If the answer is ionic, the solution set should include the solution strategies D11-electrostatic interaction and E14- surface charge. In that case, aqueous

phase composition also has an important effect on emulsion performance, thus, attention should be paid to the solution strategies A3- pH, A4 – electrolyte concentration and A5 – multivalent electrolyte concentration.

If the answer is nonionic, the solution set should include the solution strategies D12 – steric interaction, E15- quality of solvent, E16- interphase thickness, E17- Gibbs elasticity.

The use of a mixture of ionic and nonionic surfactants implies the combination of all the previous mentioned strategies.

The selection of a surfactant type depends highly on the product application. For example, for products where high detergency is required, ionic surfactants are preferred (for example in shampoos). For products that are supposed to be gentle on the skin, nonionic surfactants are preferred. Heuristics can be also applied to define the most convenient surfactant type. Availability must also be taken into account.

- It the answer is yes, one or more solution strategies of the category H - Functional ingredient should be selected. For example, if among the product specifications aroma is relevant, the solution strategy H27-fragrance should be included within the solution set.
- What is the nature of oils that best meets the specification of the problem? The answer implies the solution strategies connected to the oily phase (B6 and B7) and to the relation oily -aqueous phase (C8, C9, C10). For example, if it is required to use only natural oils (due to availability or user preferences), the solution strategy “B6 – high polarity of oily phase” should be included in the

solution set because natural oils tend to be more polar than petroleum derivatives.

- What is the effect of the micro-structure in the solution of the design problem?
The question is related to the possibility of modifying process variables to vary emulsion characteristics. For example, if it is possible to explore different homogenization speeds and operating regimes, solution strategies related to the micro-structure, F19, F20 and F21 should be included in the solution set.

Once a set of solution strategies responding to the design specifications is created, it is possible to check whether all sub-problems have been treated by summarizing the effect of all the implemented solution strategies (j) on each sub-problem (i), using the information contained in the first relational matrix (Table 3) and equation 1. A positive value of sP_i means the set favors the solution of the sub-problem i .

$$sP_i = \sum_j^n x_{ij} \quad (1)$$

where $sP(i)$ is the score for sub-problem (i), x_{ij} is the value in the cell ij of the first matrix in Table 3 multiplied by 1 if the strategy is applied as an increase and by -1 if the strategy is applied as a reduction, j is one of the selected solution strategies and n is the quantity of selected solution strategies.

Selected sets can be more integrated (more than one problem is addressed with the same strategies due to a synergy) or more decoupled (each sub-problem has an independent solution strategy to resolve it). It is recommended to decouple key sub-problems related to specifications that are very important in the design problem or those that have narrow target intervals and require more control. For example, if a

design case considers two sub-problems: to enhance stability against gravitational separation and to increase viscosity, both can be treated with the solution strategy droplet size reduction. In the case, a precise viscosity value is required, it is better to apply an additional solution strategy, for example, the use of a rheological modifier, for a precisely control of the requirement. The degree of integration of a set can be calculated with equation 2. If it is higher than 1, it indicates a certain degree of coupling.

$$Set_{Integration} = \frac{I}{J} \quad (2)$$

where, I is the total number of sub-problems of the design and J is the total number of solution strategies of the set.

Step 3. Creation of design possibilities

Solution strategies are connected to ingredient categories using the second matrix (Table 4). More than one ingredient category can be selected to apply a strategy, i.e., more than one product possibility corresponding to the same solution set can be generated. For example, electrostatic interactions can be enhanced by using one, either an anionic or cationic surfactant. In both cases the solution strategy is the same, but the result can be either a shampoo or a conditioner. Thus, in this step, it is possible to select specific ingredients using databases such as those proposed in Figures 4 to 7 or implementing heuristics as shown in ⁵⁵

30.

8. Example of the use of databases

In this section an example of the design of a mineral sunscreen is presented. A more complete example is presented in the second part of the article.

The main specification of a sunscreen is the Solar Protection Factor (SPF). The SPF is normally generated by the presence of molecules that either block or absorb the UVA and UVB light ¹². Additionally, it has been found that the SPF increases when the product forms a uniform film on the user's skin, because it enables the protection of the entire exposed area ⁶⁴. Uniform films can be enhanced by a certain degree of rheological thixotropic behavior ⁶⁴. Applying the methodology as shown in Figure 11, it turns out that:

Step 0: The specification of a SPF higher than 30 is set. The specification thixotropic behavior is set.

Step 1: These specifications are classified into two sub-problems. Special ingredient properties – UV protection (Sub-problem category E) and rheology – thixotropic behavior (Sub-problem B7).

Step 2: According to the first relation matrix in Table 3, the following sets of strategies can be applied to solve the two considered sub-problems.

- a. Use of a specific functional ingredient – UV filter and increase weak flocculation (Solution strategy D13). This set is difficult to implement because it can destabilize the emulsion (see stability sub-problem)
- b. Use of a specific functional ingredient – UV filter and decrease droplet size (Solution strategy F19).

- c. Use of a specific functional ingredient – UV filter and increase of volume fraction of the dispersed phase (Solution strategy F21). This implies an increase in the oil phase or the addition of particulate matter and consequently an increase in the costs of the emulsion
- d. Use of a specific functional ingredient – UV filter and use of a rheological modifier (Solution strategy H29). The advantage of this set is that it also increases the stability of the emulsion (see stability sub-problem in Table 3).
- e. Use of a specific functional ingredient – UV filter, decrease droplet size (Solution strategy F19) and use of rheological modifier (Solution strategy H29). This solution set is the combination of sets b and d.

Different or more sets are also possible by applying other strategies from Table 3 (as shown in Figure 11). Here, it is decided to apply sets d, and e, because they consider not only the functionality but also the stability of the emulsion.

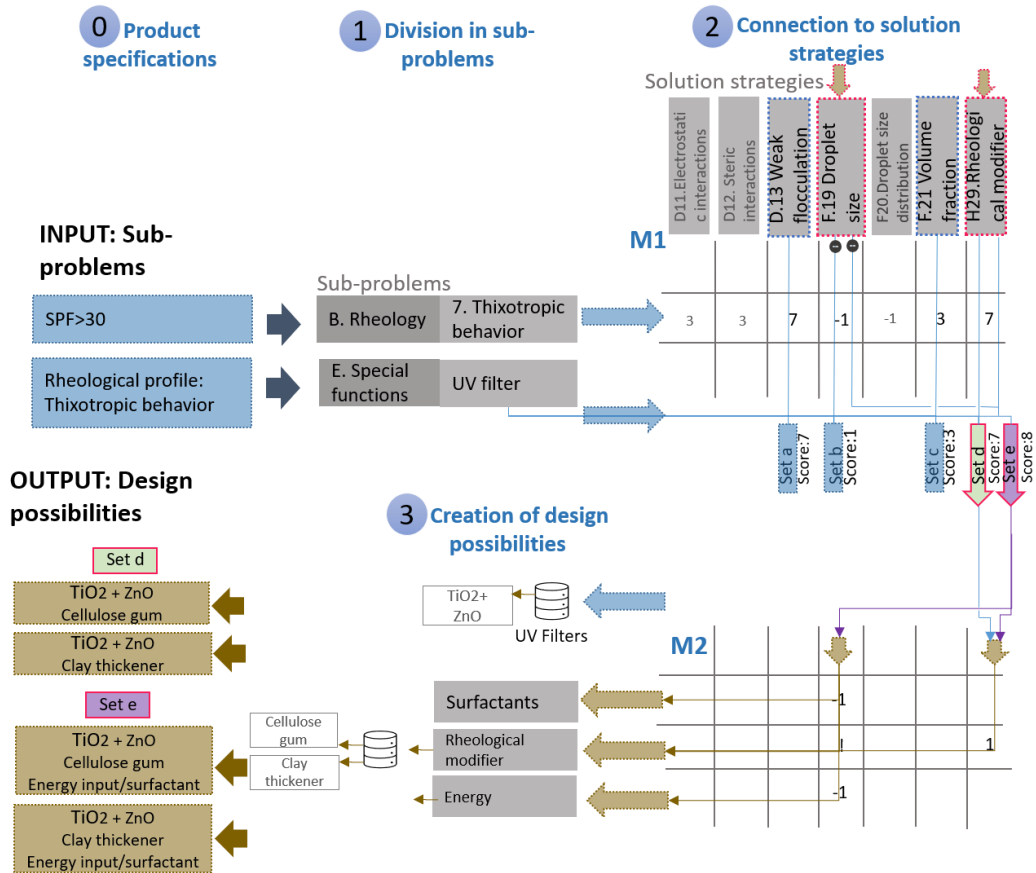


Figure 11. Representation of the methodology applied to the example. Formation of solution sets d (UV filter + rheological modifier) and e (UV filter + rheological modifier + reduction of the droplet size) using the two relational matrix (Table 3 and 4)

Step 3. In this step, ingredients and process conditions that enable the application of identified solution sets are selected using the second relational matrix. Searching in the UV filters database, it is possible to select the mineral U.V. filters titanium dioxide and/or zinc dioxide to achieve a desired SPF (Table S6 in supplementary information). They have a low toxicity. From both, only zinc oxide gives a broad-spectrum protection. Searching in the thickeners database, two thickeners with thixotropic behavior are selected: clays and cellulose gum

(Figure 7 and Table S5 in supplementary material). Based on this, the following design concepts are generated:

Design concept 1: Solution set d with cellulose gum – Formulation of an emulsion containing titanium dioxide, zinc oxide and cellulose gum

Design concept 2: Solution set d with clay thickener – Formulation of an emulsion containing titanium dioxide, zinc oxide and a clay thickener

Design concept 3: Solution set e with cellulose gum and decreasing droplet size- Formulation of an emulsion containing titanium dioxide, zinc oxide and cellulose gum under process conditions/ surfactant concentration favoring droplet sized reduction.

Design concept 4: Solution set e with clay thickener and decreasing droplet size - Formulation of an emulsion containing titanium dioxide, zinc oxide and clay thickener under process conditions/ surfactant concentration favoring droplet sized reduction.

An experimental design varying the thickener agent and concentration, the energy, and the surfactant quantity is required to compare the four design concepts experimentally. The previous reflection serves to plan this experimental design meaningfully to fulfil the specifications of the problem.

9. Conclusions and perspectives

Micro-structured chemical products such as emulsions and colloidal products have multiple applications in different product sectors such as foods and cosmetics. These products are

difficult to design because of their intrinsic complexity: An ingredient affects not only a phenomenon, but also the assembly of the whole emulsion (e.g., a rheological modifier changes the viscosity but also the stability of the product). Likewise, the change in the structure of the emulsion affects its entire functioning (e.g., the particle size may affect the appearance, rheology, stability, and release of actives). Thus, the design process cannot be applied straightforwardly. To contribute to the development of a functional and robust methodology for the design of micro-structural chemical products, this article presents a design methodology focused on O/W emulsions and applicable to early design stages. The novelty of this proposal is that it considers the complexity and interrelations between different design decisions.

The methodology is applied in the following steps: 0) problem definition, 1) selection of sub-problems representing the design problem, 2) selection of solution strategies responding to sub-problems and 3) creation of design possibilities - selection of ingredients. It proposes two databases enabling progress in the design process. The first database enables the classification of product specifications into sub-problems and the connection of these latter with sets of solution strategies. The second database enables the correlation of solution strategies to ingredient categories and ingredient information. The databases were compiled based on emulsion science knowledge and expert information. The methodology presented here is systematic because it enables a coherent and organized decision-making process, and it is holistic because it views an emulsion as a system with multiple interrelations and not just as a set of ingredients. Moreover, as the first relational matrix was built based on emulsion science principles, it can be used for the design of any non-concentrated emulsion

regardless of the application. The second relational matrix and ingredient database is sector specific.

The proposed approach is a decision aid methodology that should be continuously enriched by expert knowledge and experience. The first and the second relational matrices can be completed by considering synergies between their elements, which has not been covered in the presented proposal.

The extension of to other product types and product sectors is possible but it requires knowledge and expert consultation. Thus, its applicability to all product types is highly dependent on the expert's availability to assess the matrices.

Despite that limitation, the two relational matrices proposed here can be extended in many directions. It is possible to add more components and more phenomena to them and adapt them to other product sectors different than cosmetics. Moreover, it is also possible to adapt them with more details and a greater degree of accuracy to specific design problems. The latter may be interesting for companies working in specific sectors and/or with a specific group of products. In the case, there are enough data available, it may be possible to define interrelation between elements not with a categorical variable (as we did in the matrix that we filled with values) but with continuous functions and quantitative data. The approach can also be completed considering process variables since in this article only the energy and its qualitative effect on product microstructure was considered.

Currently, we are working on the digitalization of the tools and the databases proposed. This will allow us to apply the approach in more and complex cases.

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Supporting information

A file containing:

- Table S1 articles proposing methodologies for formulated products
- Extended explanation of sub-problems and solution strategies
- Table S2 Commonly used cosmetic oils
- Table S3 List of some surfactants frequently used in cosmetic emulsions
- Table S4 INCI names of surfactants used in Figure 6
- Table S5. List of some rheological modifiers frequently used in cosmetic emulsions
- Table S6. List of UV filters approved by the FDA

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