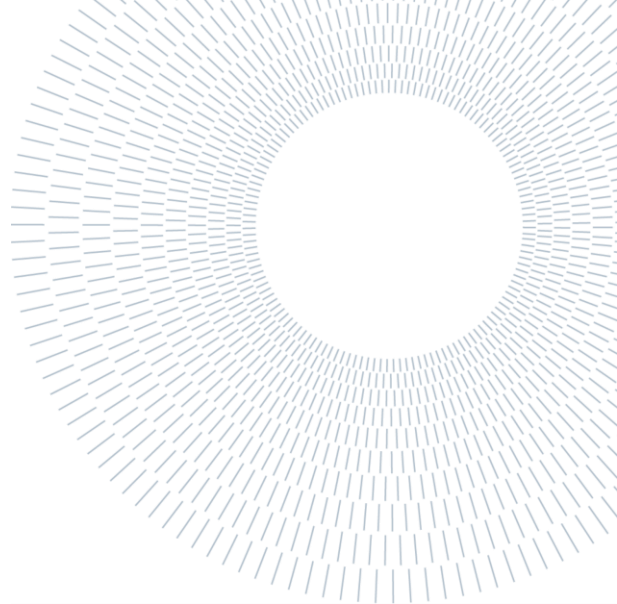**POLITECNICO**
MILANO 1863

SCUOLA DI INGEGNERIA INDUSTRIALE
E DELL'INFORMAZIONE

Oil-based rheological additives substitution with natural biopolymers in skincare leave-on formulations.
Theoretical introduction, laboratorial synthesis and scale-up process towards industrial scale production.

Master of Science in Chemical Engineering – Ingegneria Chimica

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ACADEMIC YEAR: 2022-2023

1. Introduction

In the last twenty to thirty years, the raging and unceasing human industrial activity lead our Planet through several alarming transformations. Such a process has now reached the edge of a tipping point: humankind is called to rethink both its day-to-day life and industrial practice in order to invert this harmful trend.

In particular, over the last few years major concern has grown around the employment of microplastic materials: thanks to their extremely small size, such oil-based particles enjoy an extraordinary versatility of use that allowed them to diffuse in several industrial applications, like in cosmetic products and detergents. However, microplastics are particularly damaging from the environmental point of view[1]: once poured in domestic or industrial sewage, their tiny dimensions make them able to escape wastewater treatment plants, finally reaching seas and their wildlife.

The current thesis project places right inside the ongoing attempt of removing microplastic particles from cosmetic products, by proposing the revamping of two existing leave-on formulations (a moisturizing lotion and a nourishing body cream) and taking their production from the laboratorial to the industrial scale, according to a well-precise scale-up pattern.

The idea is to firstly analyze the type and role of microplastics in the considered emulsions from the physical-chemical point of view, with the goal of finding different biopolymers suited to properly replace the oil-based additives.

The following step deals with a series of laboratory trials aimed at defining, for both formulations, the specific biopolymer blend able to guarantee the same product performances of the original emulsions.

Finally, the synthesis of the revamped novel alternatives is scaled to the pilot (5kg) and industrial (50kg) scale production, taking care of the specific attentiveness demand by scaling an emulsification process.

2.   Raw materials selection

After a detail introduction on emulsions nature, stability and their application in the cosmetic industry[2], the project moves to the analysis of acrylic polymers, namely the microplastic materials to be removed from the original formulations object of the study. They are here applied as rheology modifiers (*thickeners*), thus participating in the final rheology of the emulsion while also enhancing the emulsion stability against gravitational destabilization.

The goal of this analytical portion of the work is to find a variety of natural-based polymers able to replace acrylic polymers as thickening agents, while delivering the same qualitative (smoothness, brightness and skin after-feel) and quantitative (viscosity, physical and chemical stability) performances of the original formulations.

The quest for the most promising biopolymers ranges from well-known substances, already applied in cosmetics production or other similar fields (*i.e.* food industry), to novel substances with small references in the literature; a wide variety of natural-based thickeners is screened to assess their capability of replacing acrylic polymers from the physical point of view[3], together with their chemical compatibility with the considered formulations.

At the end of the above-described analysis, a bench of eight biopolymers is identified as suitable to be tested in the following synthetic part of the project: *Caesalpinia Spinosa* gum, *Xanthan* gum, *Acacia Senegal* gum, *Cellulose* gum, *Cethyl-hydroxyethyl cellulose*, *Dehydroxanthan* gum, *Hydroxypropyl starch phosphate* and *sodium carboxymethyl starch*.

3.   Laboratory scale

The following step of the project deals with the actual synthesis of different revamped formulations, starting from the above-mentioned list of biopolymers and their blends; in order to

ensure replicability, all the emulsions are realized exploiting the same experimental apparatus.

Before starting with the actual experimental work, the study benchmarks are defined and standardized: this is fundamental when it comes to comparing the performances of novel and original formulations object of the study.

3.1. Pre-experimental phase

The benchmarks of the current study are selected in order to guarantee a complete overview of the peculiar features of the original formulations to be replicated.

Starting from the physical-chemical characteristics of the emulsions, viscosity and pH of the final product are considered as key parameters.

For what concern the physical stability, both a typical laboratory centrifuge and a modern stability analyzer exploiting NIR, LuMiFuge® LF 110, are applied to compare the revamped and oil-thickened formulations. Chemical stability of the emulsions is then assessed through a classic stability study, involving samples ripening in different conditions (room temperature, 40°C and 4°C).

Besides these quantitative aspects, some qualitative features about the visual appearance and skin after-feel are considered, being fundamental for the consumer's experience with the cosmetic product.

3.2. Experimental phase

The laboratorial scale synthetic campaigns represent the core of the experimental section of the current project: according to a theoretical based approach, they lead to the definition and further optimization of the novel formulations to be taken to the following production scale.

In particular, for both products the experimental trials are subdivided depending on the specific biopolymer intended as main thickening agent: for each trial, several syntheses are realized using different amount of the considered biopolymer and blending it with other natural-based rheology modifiers.

As anticipated, all the emulsions are synthetized according to the same procedure: the aqueous and oil phase are prepared separately and heated to 75-80 [°C]; at this point, the oil phase is gently poured

in the aqueous base, while the mechanical energy needed for the emulsification process is introduced through a laboratory scale homogenizer (Silverson® L5T turboemulsor).

Once the better performing alternatives are found for both products, these become subject of an economical optimization path aimed at reducing the economic burden associated with polymeric thickeners substitution.

4. Scale-up process

In the last section of the study, the focus moves to the attempt of increasing the production scale of the refined natural-thickened alternatives.

It must be mentioned that scaling up an emulsification process is often extremely challenging, especially when dealing with new or revamped formulations. For this reason, a systematic two-step scale-up procedure is developed:

- The emulsion production is first reproposed in a 5kg turboemulsor, later referred to as "pilot scale";
- Once satisfactory results are obtained in the pilot turboemulsor, the synthesis is repeated in a 50kg industrial vertical turboemulsor, representing the real industrial scale.

Due to the peculiar nature of the experimental apparatus, two different scale-up philosophies are applied when going from the lab to the pilot scale and from the latter to the industrial production.

4.1. Pilot scale

As anticipated above, the pilot scale experimental campaign is realized in a 5kg turboemulsor (AXOMIX 5 by AXOMATIC®), equipped with a pair of counter-rotating blades and a homogenization turbine on the bottom of the vessel.

As a result of the major differences that elapse between the pilot and laboratorial scale apparatus, no mathematical correlation can be derived to realize this first scale-up step; for this reason, an experimental trial-and-error approach is applied. In the specific, each emulsion is synthetized just once, but several samples are taken at regular time intervals from the turbine ignition; in this way, it is possible to assess the homogenization time needed

in the pilot scale to get the desired features in the final bulk. This time interval is referred to as *emulsification time* of the pilot scale.

The results of this empirical procedure are fundamental, as they represent the starting point for the following scale-up step.

4.2. Industrial scale

At this point, the last scaling step is realized: the industrial scale synthesis exploits a 50kg vertical turboemulsor, characterized by a planetary mixing system and a homogenization turbine on the bottom of the mixer.

Thanks to the similarities with the experimental apparatus applied in the pilot scale, the second scale-up step is realized according to a mathematical correlation taken from literature[4] and further modified according to the specific needs of the system.

More in detail, the derived correlation originates from the attempt of computing the emulsification time needed in the industrial turboemulsor to reproduce the performances observed in the pilot scale, by imposing the conservation of the total energy introduced in the system during the emulsification process (*Equation 1*):

$$\tilde{t}_{50kg} = \tilde{t}_{5kg} * \left(\frac{N_{5kg}}{N_{50kg}}\right)^3 * \left(\frac{d_{rotor,5kg}}{d_{rotor,50kg}}\right)^5 * \left(\frac{D_{50kg}}{D_{5kg}}\right)^2 * \left(\frac{H_{50kg}}{H_{5kg}}\right)$$

Equation 1

where N stands for the rotational speed of the turbine and d_{rotor} for the diameter of the turbine rotor, while D and H represent the tank internal diameter and height, respectively.

Since the above-shown procedure is only considering an energetic approach, additional considerations are made to account for the fluid dynamics of the system: this is a crucial point, since emulsification processes are extremely dependent on the mixing patterns that develop in the bulk undergoing processing. In particular, the ratio between the extension of the coalescence and dispersion regions in the starting and arrival scale must be considered, for example by introducing an R_d factor defined as the ratio between the impeller and the tank diameter.

This last care leads to *Equation 2*, a mathematical correlation able to compute the emulsification time to be imposed in the industrial scale ($\tilde{t}_{50kg}^{FD}$) in order

to guarantee the same performances obtained after a precise time interval in the pilot scale ($\tilde{t}_{5kg}$):

$$\tilde{t}_{50kg}^{FD} = \tilde{t}_{50kg} * \left(\frac{R_{d,5kg}}{R_{d,50kg}} \right)$$

Equation 2

where $\tilde{t}_{50kg}$ is obtained from $\tilde{t}_{5kg}$ according to *Equation 1*.

4.3. Results analysis

This last section of the project is intended to analyze the results obtained during the two-step scale-up procedure and consequently assess whether the scaling can be defined as successful or not.

In this sense, it is fundamental to remember that, especially if dealing with emulsions production, succeeding in a scale-up process does not mean that identical results are obtained at different scales, but rather that the obtained results are acceptable and reasonably predictable.

In particular, the capability of *Equation 2* to correctly drive the scale-up process is evaluated through the comparison between the expected values of viscosity (the ones referred to the pilot scale sample, taken at the considered $\tilde{t}_{5kg}$) and the real ones (corresponding to a time interval equal to $\tilde{t}_{50kg}^{FD}$ in the industrial mixer).

Generally speaking, the derived correlation shows great accordance with the expected values of viscosity for both formulations, as it can be observed in *Figure 1* and *Figure 2*, where the percentage error is shown in red for each of the samples considered:
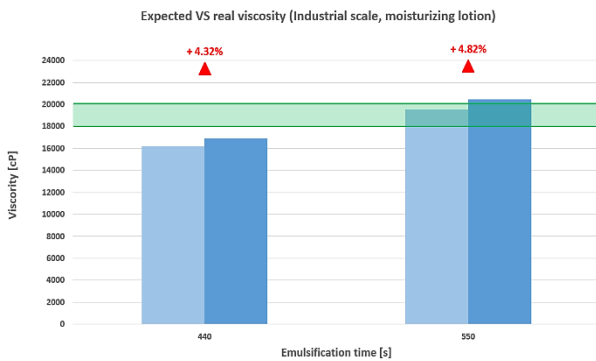

Figure 1. Moisturizing lotion: expected and real viscosity value comparison
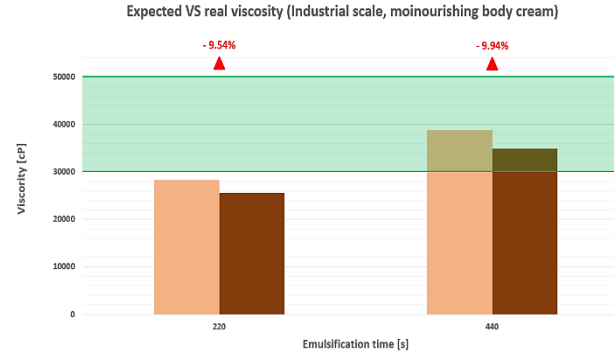

Figure 2. Nourishing body cream: expected and real viscosity value comparison

In both cases, the real viscosity (darker columns) is slightly different from the expected one (lighter columns); more in detail, the percentage error remains below 5% in the case of the moisturizing lotion, while increasing to about 10% for the nourishing body cream.

Such results are suggestive of a pretty successful scale-up process, able to guarantee reasonably predictable quantitative results thanks to a tailor-made mathematical equation accounting for both the energetic peculiarities and fluid dynamics of the system. Note that the residual percentage error could be minimized by refining the considered equation, for example through a properly designed additional experimental campaign.

5. Conclusions

The present thesis work is intended to analyze the main steps of the revamping process of two existing cosmetic formulations, with the aim of removing oil-based thickeners, classified as microplastic materials, in advance of natural rheology modifiers.

Starting from the physico-chemical analysis of the original emulsions considered and the role played inside them by acrylic polymers, a bench of biopolymers with promising thickening and stabilizing qualities is identified.

Several experimental trials are then realized in order to build natural-thickened formulations able to compete with the original ones, both from the quantitative and qualitative point of view.

Each obtained emulsion is tested to assess if the obtained features are able to mime the peculiarities of the original formulations. In particular, special attention is paid to the qualitative characteristics of the final product: smoothness, brightness and

creamy-soft appearance are crucial aspects, being them the first features to be recognized and appreciated by a consumer.

During these trials, *Caesalpinia Spinosa* gum and some modified starches turn out to be the most suitable alternatives for oil-based polymers replacement in the considered emulsions.

After a brief optimization step aimed at reducing the raw materials cost associated with the novel formulations, the project moves forward to the attempt of scaling up their production.

The first passage of scale, from the lab table to a 5kg turboemulsor, is realized according to an empirical procedure based on reiterated sampling of the forming emulsion.

The second scale-up step, leading to the real industrial scale production, proceeds thanks to a mathematical correlation derived from the literature and further corrected to account for the fluid dynamics of the system. Thanks to this expedient, the above-mentioned correlation turned out to be sufficiently reliable when it comes to computing the emulsification time needed to get a precise result in terms of final product viscosity.

The current thesis project shows how it is possible to reduce the environmental impact associated with skincare products, replacing oil-based additives with natural occurring biopolymers already applied in other industrial fields and in cosmetic industry itself. Undoubtedly, such a radical shift will not be easy to achieve: properly designed natural-based formulations well mime the peculiarities of classic cosmetics, but minor qualitative differences are still present and they will not be easily compensated; in addition, biopolymers requested percentage of application is usually five to ten times higher then oil-based polymers one: this aspect, together with the high stock price of natural thickeners, makes green formulations often particularly expensive if compared to the classic ones.

Two are the keys to succeed in such a transformation: a well-focused and oriented research activity and our own will as human beings to reduce the environmental burden associated with our day-to-day life.

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POLITECNICO DI MILANO

Scuola di Ingegneria Industriale e dell'Informazione
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Academic year: 2022-2023

- Every new beginning
comes from some other beginning's end

(Semisonic, Closing Time)

Abstract

Planet Earth is nowadays facing a radical transformation, unparalleled in modern age and driven by human unceasing activities: climate change, rising sea levels, desertification of green areas and overproduction of non-degradable wastes represent only a small allusion on this concerning scenario.
With this in mind, it's easy to understand how humankind is summoned to rapidly force a change of course before reaching the tipping point; such a revolution is possible only by rethinking the core of our day-to-day lifestyle and focusing scientific and technological research on finding and improving novel alternatives to the actual fossil-based industry.

In the middle of the intricate panorama sketched above, places the attempt to reduce the enormous usage of oil-based polymers that today defines both everyday life and industrial practice.
Among polymeric materials, microplastics are particularly widespread: thanks to their tiny dimensions and versatility of use, they can be found in several application. Cosmetics, fertilizers, detergents, coatings and petrochemical products are only a taste of the magnitude of the application potential of these small particles.
On the other hand, the same properties that allowed microplastics to become so diffused make them particularly impacting from the environmental point of view, especially for what concern their capability to escape wastewater treatment plants, finally reaching seas and their wildlife. This scenario is typical of microplastic materials coming from skincare and cleansing products: once the consumer washes his skin after the application of the product, these materials are hopelessly poured in domestic sewage, from which they can easily reach big waterways.
As a result of this, several efforts are in progress at research and development level to substitute microplastic with bio-based polymers both in rinse-off and leave-on cosmetic formulations, without compromising the distinctive peculiarities of the final product.

The present thesis project places right inside this effort, aiming for the revamping of two existing formulation, a moisturizing lotion and a nourishing body cream, interested by the presence of acrylate co-polymers as main rheological agents, and finally taking the revamped models from lab-scale to industrial scale production.
Starting from a general overview on skincare market and a detailed characterization of emulsified products (Chapter 1), the discussion proceeds with the analysis of the acrylic thickeners actually in use and the most promising nature-based alternatives on the market (Chapter 2).
Several laboratory trials were made to identify alternative formulations able to compete, in terms of physicochemical parameters, stability, texture and appearance, with the original formulas; such experimental path is deepened throughout Chapter 3 and Chapter 4.
Once the best natural-thickened alternatives were identified, the project moved to the following section, dealing with the scale-up and industrialization of the process: the production was first taken from the laboratory scale to a 5kg pilot turboemulsor and finally reached the manufacturing scale thanks to a 50kg industrial turboemulsor. Chapter 5 details the scale-up process both from a theoretical and practical point of view, together with the comparison of the result obtained in the different experimental phases and the influence of the scale on the final properties of the emulsions.
Finally, Chapter 6 concludes the thesis project by analysing the entire experimental path from a critical point of view, also considering the most promising feature developments for microplastic substitution in the cosmetic industry.

Sommario

Il Pianeta Terra è oggigiorno sottoposto ad una trasformazione senza precedenti nella storia moderna, sospinta dall'incessante e frenetica attività umana: fenomeni ben noti come il cambiamento climatico, l'innalzamento del livello dei mari, la rapida desertificazione di ampie regioni forestali e la sovrapproduzione di rifiuti non degradabili rappresentano soltanto alcuni dei problemi che caratterizzano il nostro tempo.

In relazione a quanto sopra, è facile comprendere come il genere umano sia chiamato a forzare rapidamente un cambio di rotta, prima di incorrere in danni irreparabili; un tale cambiamento è però possibile soltanto rivoluzionando la nostra quotidianità e concentrando la ricerca tecnico-scientifica sullo sviluppo di un'industria alternativa a quella odierna, tutt'ora basata sull'utilizzo di materie prime di origine fossile.

A giocare un ruolo fondamentale all'interno del complesso scenario appena descritto è il tentativo di ridurre l'utilizzo di polimeri plastici, materiali estremamente diffusi sia a livello industriale che domestico ed ottenuti attraverso complessi processi di trasformazione di materie fossili. All'interno di tale classe di materiali figurano le cosiddette microplastiche, particolarmente diffuse grazie alle loro ridottissime dimensioni ed alla conseguente versatilità di utilizzo in campi come le industrie cosmetica, farmaceutica ed alimentare, nonché nella produzione di fertilizzanti e prodotti petrolchimici.

D'altro canto, quelle stesse proprietà che hanno permesso ai materiali microplastici di permeare svariate aree della produzione industriale, rendono tali particelle particolarmente impattanti a livello ambientale, specialmente a causa della loro capacità di oltrepassare gli impianti di trattamento delle acque reflue, raggiungendo così i principali corsi d'acqua ed infine i mari e la fauna che ivi dimora. Quanto appena descritto è tipico di quei residui microplastici provenienti da prodotti di cosmesi e detergenza personale: nel momento in cui il consumatore risciacqua la pelle dopo l'utilizzo del prodotto in questione, le particelle microplastiche vengono irrimediabilmente sversate nello scarico domestico, dal quale raggiungeranno poi indisturbate i principali corsi d'acqua.

Alla luce di ciò, diversi progetti di ricerca nel mondo cosmetico sono oggi finalizzati alla sostituzione di materiali microplastici con polimeri di originale naturale, al fine di ridurre l'impatto ambientale proveniente dalla produzione e dall'utilizzo di tali prodotti, cercando nel mentre di non alterarne le caratteristiche distintive.

Il presente progetto di tesi punta ad inserirsi proprio all'interno del panorama appena descritto, attraverso il rinnovamento di due emulsioni cosmetiche già in commercio, nello specifico una lozione idratante ed una crema corpo nutriente. Tali formulazioni sono accomunate dalla presenza di co-polimeri acrilici, materiali microplastici utilizzati come principali agenti reologici in entrambi i prodotti: l'obiettivo del progetto è perciò quello di rimpiazzare tali additivi di origine fossile con controparti di origine naturale, per poi portare il processo produttivo sino alla scala industriale.

Partendo dunque da una rapida introduzione sul mercato globale dei prodotti per la cosmesi della pelle, il Capitolo 1 verterà sulla caratterizzazione dettagliata delle emulsioni e del loro utilizzo in ambito cosmetico; procedendo oltre, verrà poi analizzato l'attuale vasto utilizzo di polimeri acrilici come agenti ispessenti nell'industria cosmetica (Capitolo 2) ed i più promettenti sostituti di origine naturale.

A questo punto, una volta analizzate le peculiarità delle due formulazioni in analisi e fissati i parametri di interesse dello studio (Capitolo 3), sarà possibile seguire il percorso sperimentale che, partendo dalla selezione delle materie prime meglio performanti, ha condotto alla sintesi di varianti prive di polimeri acrilici ed alla loro conseguente ottimizzazione (Capitolo 4).

Identificati dunque i campioni adatti al passaggio di scala, il Capitolo 5 sarà dedicato alla descrizione del processo di scale-up, suddiviso in due fasi successive: dapprima saranno presentate le modalità di produzione ed i risultati ottenuti in un turboemulsore da 5kg, considerato in questo caso come "scala pilota" del progetto, per poi spostare l'attenzione sulla scala produttiva successiva, quella industriale (qui rappresentata da un turboemulsore verticale da 50kg). A corredo del capitolo, saranno presentati ed analizzati nel dettaglio tutti i risultati ottenuti, così da comprendere se il passaggio di scala possa effettivamente definirsi riuscito.

Infine, il Capitolo 6 conclude il lavoro di tesi sopra presentato analizzando l'intero progetto da un punto di vista critico e presentando alcuni spunti di particolare rilievo ai fini della rimozione di materie microplastiche da diverse classi di prodotti ad uso cosmetico.

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1. Introduction

Cosmetic and personal care products undergo different regulations and answer several definitions depending on the specific geographical area considered, with non-negligible discrepancies.

In the present work, the definition currently applied in the European Union and stated by the regulation (EC) No 1233/2009 of the European Parliament (Council on cosmetic products of November the 30th, 2009) have been considered, which defines as cosmetic product "*any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours[1]*".

With this definition clear in mind, the following chapter is meant to introduce the reader to the complexity of the modern beauty and cosmetic industry, starting from a quick market overview to later enter deeper in detail into the structure and technical aspects of this industrial field.

1.1 The Beauty & Personal Care market

Since ancient age, cosmetics and personal care products played a fundamental role in our lives: starting from raw mixtures of natural-based ingredients, cosmetic science grew little by little becoming more and more complex over centuries. Today, the formulation of a cosmetic product requires well-defined procedures and deep multidisciplinary knowledge: from chemical to biological aspects, up to industrialization of the manufacturing procedure and marketing strategies, nothing is left to chance.

Thanks to unceasing advancements in ingredient technologies and formulation procedures, cosmetic products have been continuously improving over the last few decades, making it possible to develop highly specialized products tailored for targeted audiences. Nonetheless, the fast economic growth of several developing countries, especially in South America and Asia, made it possible for millions of people to access personal care products as never before.

The combination of technological progress and market expansion led to a real breakthrough in cosmetic industry, with a constant growth of the market value over the last decade and astonishing forecasts for the following one.

1.1.a Market analysis

After a couple of tough years due to the Sars-CoV2 pandemic, distinguished by market contraction as a result of a strong decline in demand in the first half of 2020, the global market is slowly recovering towards pre-pandemic levels.

Among others, beauty and personal care industry has proven stunning promptness in regaining market share: after having lost more than 7.0% of its original pre-pandemic value, the global cosmetic market experienced a rebound that took its value to USD 528.59 billion in 2022, something never reached before. This data was collected accounting for all those products answering to the above-given definition: fragrances, skin and hair care products, deodorants and the whole personal care sector.

As mentioned before, the market is expected to rapidly grow during the following years at a compound annual growth rate (CAGR) of 3.8% between 2023 and 2027, eventually overcoming USD 630 billion[2]. For the sake of completeness, it is useful to precise how the CAGR, an economic indicator widely applied in market analysis and forecasts, is obtained; considering two reference years Z and X, where $N = Z - X$ is the difference between them, the CAGR relative to the highlighted time interval is computed as follows[3]:

$$CAGR_{X \to Z} = (MV_Z - MV_X)^{1/N} - 1$$

Equation 1.1 CAGR quantification

where MV stands for market value; clearly, the highest the CAGR associated to a growing market, the faster its expansion.
Going back to the above-sketched trend, it can be well appreciated in *Figure 1.1*, reporting the value of each segment of the beauty and personal care market starting from 2014 and with the relative forecast until 2027; note that here the term *cosmetics* is mistakenly used only to group make-up and natural products used for decorative purposes.
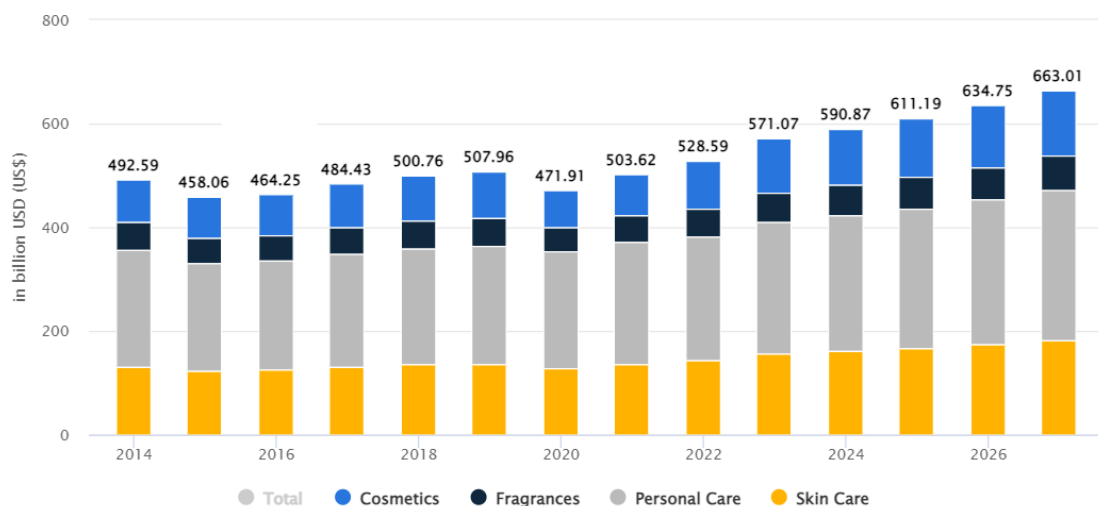
Figure 1.1 Evolution of beauty & personal care market value per segment: cosmetics (face, lips, eyes, nails make-up and natural cosmetics), fragrances, personal care (hair and oral care, shower & bath, deodorants and shaving) and skin care (face and body lotions and creams, baby & child products, sun protection)[2].

From the geographical point of view, China and USA represent the major players worldwide, with a 2022 net revenue of USD 87.13 billion and USD 55.31 billon respectively.
Asiatic market share has rapidly grown over the last ten years, with Japan (38.54 billion) and South Korea (USD 12.10 billion) leading the ride just behind Chinese market: this enabled Asia Pacific (usually referred to as APAC[1]) to generate the major slice of the global beauty and personal care revenue, with about 41% of the total in 2021[2]. This region is meant to completely dominate the market in the following decades.
Other major actors are India and Brazil, accounting for more than USD 20 billion each and both experiencing a net growth with respect to 2019, when the market was not yet affected negatively by the pandemic.

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[1] The set of Asian nations whose coasts are bathed by Pacific Ocean

Figure 1.2 well shows the global situation just described, with USA leading the market in 2022.
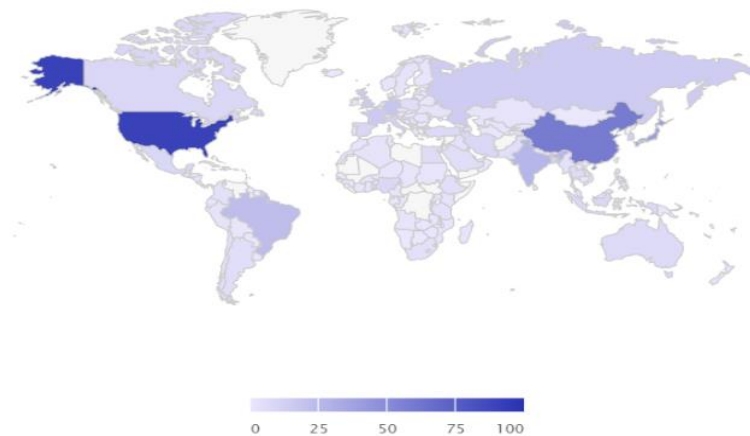
Figure 1.2 Beauty & Personal Care market value global distribution in USD billion, 2022[2].

Despite not being dominant as USA or China, also Europe became a key player in international cosmetic commerce during the last two decades: the actual value of the whole European beauty and personal care market overcame €80 billion in 2022, with a net growth in all countries of the continent.

As always been in the sector, major actors are represented by Germany and France, closely followed by Italy, whose revenue increased over €13 billion in 2022 (+10.7% with respect to 2021 and +8.7% with respect to pre-pandemic value[4]).

Figure 1.3 European cosmetic market: major players and relative shares[4].

1.1.b The skin care segment

Beside personal care products and detergents, skin care covers the majority of beauty market value: in 2022 its share accounted for USD 143.50 billion[5] and it's considered the fastest growing sector in cosmetic industry, with astonishing forecast for the end of the decade (CAGR equal to 6.12% from 2022 to 2029[6]).

This phenomenon is probably driven by the elderly population, a particularly widespread reality in those countries where cosmetic industry scores the highest sales[2] and that calls for growing request of anti-aging solutions. In addition, increasing awareness towards skin health and treatment in new generations is pushing young consumers to enter the market, finally expanding the traditional age range targeted by cosmetic producers.

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[2] Namely, Europe and APAC.

From the product point of view, skin care segment generally includes different types of goods applied by the consumer to smooth, hydrate and provide a touch of brightness to face and body skin, or simply to protect it from sun-induced irritations and hazards, as in the case of sunscreen products. Face masks, moisturizing and nourishing body creams and lotions, serums and exfoliators, products for hand and foot care all belong to this category, together with commodities tailored for babies and child needs.

Being intrinsically connected to people's habits and strongly subjected to public opinion, cosmetic industry undergoes frequent and often unforeseen changes.

A recent trend in skin care segment, emerged right after the Covid-19 biennium, consists of demand for all-in-one and multi-functional products able to ensure an easier but still effective daily skin care routine[7]. This is probably given by the return to pre-pandemic customs: many consumers that approached the world of skin care during lockdown, when more time could be spent in self-care, are now trying to balance the new habit with the reacquired hectic pace of modern life.

Beside this phenomenon, the whole cosmetic industry, and in particular the skin care sector, is experiencing the growing relevance of claims, in particular *free form* ones. Generally speaking, in cosmesis claims are defined as a series of information, indication and adjectives present on the product label, or in the relative marketing material, and aimed in guiding consumers' choice by defining qualities and attributes of the product[8].

In Europe, they are ruled by common criteria stated in Regulation (EU) 655/2013, which defines guidelines for claims justification. Popular claims are designed to catch consumers' attention and approval; usual examples are: "tested under medical control", "hypoallergic" or "Ni-tested", but also "dermatologically tested" and "not tested on animals".

A particular type of claim is represented by *free form* claims: they are specifically meant to underline the complete lack of an ingredient or of a complete family of raw materials[8], and they are frequently applied when dealing with the removal of a controversial ingredient from an existing formulation. In this way, the producer is showing off the elimination of the frowned upon ingredient (usually driven by public opinion rather than real hazardousness thereof), leading the consumer to prefer the revamped product before competitor ones.

Due to their particular nature, these claims are ruled by a dedicated document, the Attachment III to the Technical Document issued by the European Commission (EC) in 2017. Note that free form claims cannot be applied if referring to ingredients forbidden by Regulation (EU) 1223/2013, which cannot be included in any cosmetic formulation by law[8]. Example of typical free form claims refers to allergen or sensitizers, preservatives, parabens, perfumes (for ultra-sensitive consumers' needs) and animal-derived ingredients (to comply with vegan philosophy).

Recently, the most fashionable free form claim is the one regarding microplastics: these are banned by law only in rinse-off[3] products, but their absence is boasted also in leave-on[4] cosmetics to encounter increasing sensibility of consumers towards environmental issues. Being the starting point of this thesis project, microplastic relevance in nowadays cosmetic industry will be later on detailed.

Similarly to what happens with commercial claims, skin care products are currently further and further designed to respect religious and ethical certification that make them appetible for specific submarkets, as happens with Halal certified products for Muslims and Kosher certification for Jews; other examples are vegan and cruelty free certifications.

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[3] Formulations designed to be washed away from the application site, like detergents, shampoos or scrubs.
[4] Formulations meant to be absorbed by the skin, such as moisturizing creams and lotions.

The commercial relevance of these cares is easily understood thinking that, for example, more than 24% of world population belong to the Muslim faith[9] and is therefore buying only Halal certified cosmetics.

Table 1.1 resumes main guidelines for popular religious and ethical certifications for cosmetic products.

Certification	Logo	Fundamental requisites
Halal[10]		• No swine, raptors or domestic donkey derivatives; • Only *Zabiha* ritual butchery animal derivatives; • No insects and their derivatives; • No blood; • No ethylic alcohol; • No narcotics.
Kosher[11]		• No animal derivatives apart from ruminant ones; • Only *Shechita* ritual butchery animal derivatives; • No blood; • No crustaceans and shellfish derivatives.
Vegan OK[12]		• No animal derivatives (neither for packaging purposes); • No animal testing; • No images or user notice incompatible with Vegan philosophy;
Leaping Bunny (Cruelty free)[13],5		• Cruelty-free business policy; • No animal derivatives; • No animal testing; • Constant effort to discourage animal testing of raw materials and finished products.

Table 1.1 Main religious and ethical certification with relative requisites and logo (placed on the product label to indicate the acquired certification).

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5 Note that European Commission repeatedly defined any mention to avoided animal testing as misleading and deceiving, since these practice are already forbidden in cosmetic industry since 2009 (Regulation (EC) 1223/2013)[14].

1.2 Emulsions

Emulsions play a key role in the whole beauty and care industry, especially in skin and hair care segments where, thanks to their extraordinary versatility and peculiarities, they represent most of the finite products put on the market.

Generally speaking, emulsions belongs to the field of colloidal dispersions[6] and are defined as a "*thermodynamically unstable dispersion of two mutually insoluble liquids[15]*", where one component is present as finely distributed droplets (usually spherical) in the bulk of the other liquid; the first is known as *distributed* (or *inner*) *phase*, to distinguish it from the *continuous* (or *outer*) *phase*. Depending on the nature and the mutual interaction of these two phases, together with the dimension of dispersed droplets, different types of emulsion exist, as will be discussed later on in the chapter.

A fundamental aspect to remember when dealing with emulsion is their inherent thermodynamic instability: being formed by mutually insoluble components, an emulsion is not able to last long if not properly stabilized by the addiction of a third component, an emulsifier (oftener a mixture of them), or by electrical or steric expedients. Emulsion stabilization is a complex and wide field of study, better to be detailed in a following dedicated sub-chapter.

1.2.a Classification

As anticipated above, emulsions can be classified depending on the nature of inner and outer phase: this is the simplest and less-detailed way to sort them but enables to rapidly understand the main features of the formulation under analysis.

According to this classification, two type of simple emulsions can be distinguished:

- Oil in water (O/W) emulsions, usually referred to as *direct* ones, where the dispersed phase is represented by oily droplets suspended in the aqueous continuous phase. They are the most common type of formulation in skin care segment, where the aqueous base ensure instantaneous hydration upon application to the skin and refreshing feeling given by water evaporation[16];
- Water in oil (W/O) emulsions, also known as *inverse*, characterized by aqueous droplets inside the oil bulk. These oil-based formulations are particularly appreciated for their occlusive properties and long-lasting soothing action, usually given by the formation of a thin film on skin surface[16].

As can be easily understood, their different nature results in quite opposite properties: O/W emulsions have creamy consistency whereas, being based on oil, W/O ones usually exhibits more greasy and oily texture.

Emulsion type	Component	Percentage
O/W	Continuous phase	65 – 85 %
	Dispersed phase	10 – 30%
	Emulsifiers	~ 5 %
W/O	Continuous phase	30 – 40 %
	Dispersed phase	50 – 65 %
	Emulsifiers	5 – 10 %

Table 1.2 Typical composition range of direct and reverse emulsions[16].

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[6] Heterogeneous systems with intermediate behaviour between homogeneous (or *real*) solutions and heterogeneous ones, with dispersed particles (either solid, liquid or gaseous) ranging from 1 [nm] to 1 [μm] and peculiar turbidity[18].

Beside *simple* ones, it is worth mentioning how *complex* emulsions exist too: these systems are characterized by vesicular structures where internal and external aqueous layers are separated by oil membranes (W/O/W) or vice versa (O/W/O)[17]. Due to their unique properties, multiple emulsions are currently applied in pharmaceutical field for controlled drug delivery and release; nonetheless, several applications are available in cosmetic industry, such as sustained release aerosol fragrances and prolonged skin moisturizers. On the other hand, their large-scale diffusion is still limited as a result of huge manufacturing difficulties when dealing with industrial scale processes.

Figure 1.4 and *figure 1.5* show the place occupied by emulsions in colloidal dispersions world and the structure of each type of emulsion discussed above, respectively:

Figure 1.4 Colloidal systems classification according to Ostwald[19]; note that gas in gas is not defined as a colloidal system, since gases are completely soluble in each other.
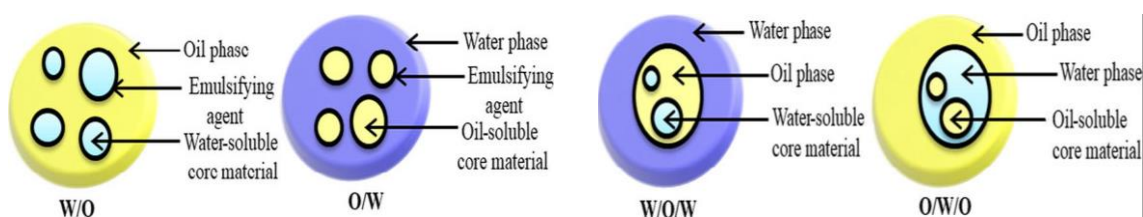
Figure 1.5 Qualitative structure of simple (O/W and W/O) and complex (W/O/W and O/W/O) emulsions[20].

Beside what presented above, emulsions can also be classified according to dispersed particles dimension; in this terms, three types of systems can be recognized[21]:

- Macroemulsions, where dispersed droplets size ranges between 0.1 and 100 [μm], allowing light scattering and thus giving the typical white creamy appearance to the system[22];
- Microemulsions, characterized by droplets ranging from 10 to 100 [nm] and the presence of both emulsifiers and co-emulsifiers. Their peculiarity is to be thermodynamically stable (they form spontaneously) and transparent to the eye[23];
- Nanoemulsions, presenting droplets with mean characteristic dimension between 20 and 200 [nm] and slightly cloudy appearance. They differ from microemulsions because not thermodynamically stable[24] (they are not formed spontaneously).

1.2.b Formulating a stable emulsion

Being thermodynamically unstable, emulsions tend to break as a result of the attempt by the system to reach a stable condition. The reason for this inherent instability is to be sought in the spontaneous tendency of each system to evolve towards equilibrium condition, namely the state of lowest possible energy.

In order to better understand emulsion stability, let's consider the variation of total Gibbs free energy related to the system, given by the surface tension γ, existing between oil and aqueous phase, multiplied times the variation of surface area of contact between the phases (ΔS)[25]:

$$\Delta G = \gamma * \Delta S$$

Equation 1.2 Total Gibbs free energy of the system.

After the emulsion is formed, droplets of the dispersed phase spontaneously tend to get in contact and compenetrate each other to form bigger particles, characterized by lower surface area per unit volume. This phenomenon is known as coalescence and results in the diminution of contact surface between phases, leading to a reduction of Gibbs free energy of the system. For example, considering perfectly spherical particles, the specific surface area per unit of volume can be computed as:

$$a = \frac{S}{V} = \frac{6}{dp}$$

Equation 1.3 Specific surface area of a sphere.

where S stands for the surface area of the dispersed droplet, d_p for the diameter and V for its volume.

As it can be easily seen, the higher the diameter of the particle, the lower the surface area exposed by the particle of dispersed phase towards the continuous one per unit of volume[15].

This phenomenon goes on until reaching the minimum energy state possible, namely the complete separation between the two phases, when the contact surface is minimized because represented by a film (lowest possible surface area per unit of volume).

At this point the emulsion is said to be *broken:* there are no longer internal and external phase, since oil is now floating onto the surface of the aqueous phase. This condition is irreversible.

Emulsion destabilization can happen through different and complex mechanisms, which not always take to complete breaking of the emulsion. These mechanisms will be detailed in the following subchapter.

Figure 1.6[26] well shows the coalescence process, from the aggregation of first oil droplets to the complete breaking of the emulsion:
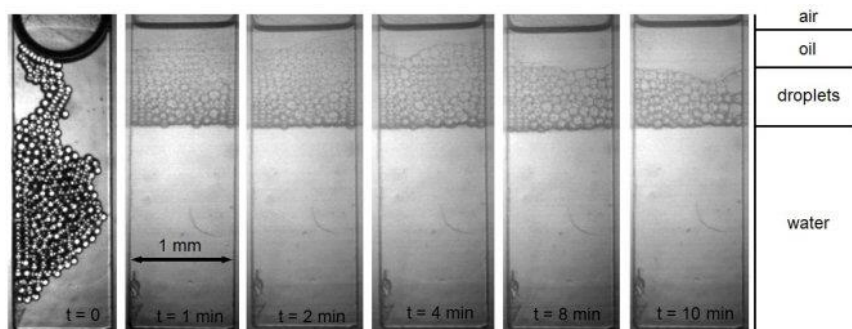
Figure 1.6 Emulsion breaking process due to oil droplets coalescence.

In order to produce a long-lasting technical emulsion, a third component is added: the emulsifier. Emulsifiers belong to the class of *tensides* (or s*urfactants*), surface active molecules able to reduce surface tension between two liquids placing at the interface between them.

From the chemical point of view, tensides are described as amphiphilic molecules: this means that their structure contains both hydrophile (polar heads) and hydrophobic (lipidic chains) groups[27], making them partially soluble both in oil and water phase. When these molecules are present at an oil/water interface, hydrophilic groups dispose towards aqueous phase, while the lipophilic portion of the molecule stretches into the oil phase (or, in the case of water/air interface, towards the latter). Depending on the polarity of hydrophilic group, cationic, anionic, non-ionic[28] and zwitterionic[7] tensides can be distinguished.

Typical examples of tensides are soaps, fatty acids and alkyl sulfonates (cationic), alkyl trimethyl-ammonium chlorides (anionic), N-alkyl betaines (zwitterionic), alcohol ethoxylates and polyethylene oxide alkyl ethers (non-ionic); their molecular structures are shown in Figure 1.7.

$$CH_3\text{-}(CH_2)_n\text{-}COO^- \; Na^+$$

(a)

$$CH_3\text{-}(CH_2)_n\text{-}\overset{CH_3}{\underset{CH_3}{N^+}}\text{-}CH_3 \; Cl^-$$

(b)

$$CH_3\text{-}(CH_2)_n\text{-}\overset{CH_3}{\underset{CH_3}{N^+}}\text{-}CH_2\text{-}COO^-$$

(c)

$$CH_3\text{-}(CH_2)_m\text{-}O\text{-}(C_2H_4\text{-}O)_n H$$

(d)
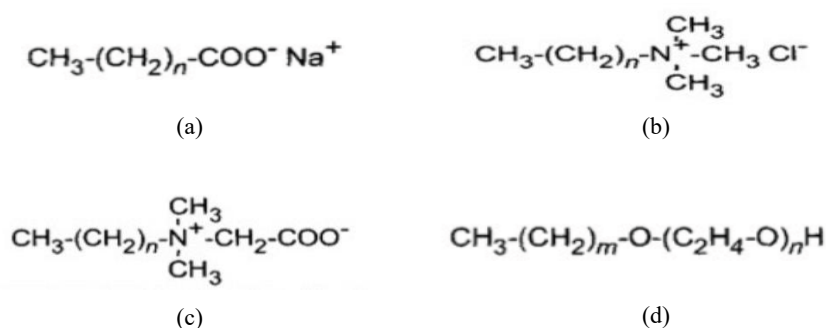
Figure 1.7 Molecular structures of typical tensides: soaps (a), alkyl trimethyl-ammonium chlorides (b), N-alkyl betaines (c) and polyethylene oxide alkyl ethers (d).

Emulsifiers are specific types of tensides, usually of non-ionic nature[28]: thanks to their peculiar characteristics, they are used to build long-lived emulsions. They are able to rapidly migrate towards oil/water interface once added to the formulation, enhancing the emulsification process and minimize the Gibbs free energy associated to the system, thanks to the reduction of the interfacial tension.

In detail, the emulsifier accumulates at the interface and form a protective layer represented by a tough and elastic film, able to prevent droplets to compenetrate each other: when droplets collide, this film is deformed but not broken, avoiding coalescence to take place[15]. At this point, the emulsion is still thermodynamically unstable, but kinetically stabilized by the presence of the emulsifier: in other words, an energy barrier towards coalescence is now present, which slows down recombination of dispersed droplets, and the emulsion is said to be *metastable*.

Generally speaking, the emulsifier system is composed by a mixture of tensides, properly tailored on the specific case under investigation, rather than a single compound; the most suitable mixture of emulsifiers is usually decided depending on the value of the HLB balance[30],[8] of the system to be emulsified. The correct choice of the emulsifier mixture is fundamental to promote the formation of a stable emulsion, with the desired peculiarities.

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[7] Interested by the presence of both positive and negative charges given by anion-cation pairs[29].

[8] Hydrophilic-Lipophilic Balance: index that states the affinity of a surfactant towards a solvent, firstly introduced by Griffin in 1949[31] for the choice of the correct emulsifier; in example, high HLB number indicates high affinity to water and polar solvents in general.

Moreover, it must be considered that the type of emulsifiers used is a decisive factor in the type of emulsion that can be obtained, direct or reverse[15]. In fact, hydrophilic emulsifiers with low molecular weight induce formation of O/W emulsions, while lipophilic emulsifiers favor reverse emulsions[32].

What just told above is usually referred to as Bancroft's rule of thumb, which states how "*the phase in which the emulsifier is more soluble is the outer phase*"; as anticipated above, the study of the correct mixture of emulsifiers is nowadays based on a more quantitative approach, proposed by Griffin in 1949 with the HLB number.

This index can be described as the balance of the size and strength of hydrophilic and lipophilic moieties of a surfactant molecule or a mixture of them[32]. In this way, each emulsifier is identified by a specific HLB value, ranging as follows[15]:

- Oil-soluble hydrophobic emulsifiers show HLB numbers rangin from 0 (fully lipophilic) to 9;
- *Balanced* emulsifiers range between 9 and 11;
- Water-soluble tensides, usually with low molecular weight, are identified by HLB values between 11 and 20;

The following table shows the HLB values for some common tensides[33]:

Surface Active Agents	HLB
Oleic Acid	1.0
Glyceryl Monostearate	2.1
Sorbitan Mono-oleate (SPAN 80)	3.8
Glyceryl Monostearate (Tegin)	4.7
Methyl Cellulose (Methocel 15 cP)	9.8
Triethanolamine Oleate	11.1
Sodium Oleate	16.9
Sodium Lauryl Sulphate	20

Table 1.3 HLB values for some typical emulsifiers.

In the same way, substances to be emulsified also have their own HLB number, referred to as *Required* HLB (RHLB); this index refers to the HLB value that the emulsifier system must provide to ensure the emulsification of the considered substance[34], and it's a specific characteristic of each substance to be emulsified. This value changes depending on the type of emulsion that must be formulated: in general, the same substance presents higher RHLB when dealing with O/W emulsions.

Figure 1.8 displays RHLB values for some frequently emulsified substances[35]:

Oil Phase	HLB w/o	HLB o/w	Oil Phase	HLB w/o	HLB o/w
Acid, Lauric		16	Castor Oil		14
Acid, Linoleic		16	Corn Oil		8
Acid, Oleic		17	Cottonseed Oil		6
Acid, Ricinoleic		16	Dimethyl Silicone		9
Acid, Stearic		17	Isopropyl Myristate		12
Alcohol, Cetyl		16	Lanolin, Anhydrous	8	12
Alcohol, Decyl		15	Methyl Silicone		11
Alcohol, Lauryl		14	Mineral Oil, Aromatic	4	12
Alcohol, Oleyl		13-14	Mineral Oil, Paraffinic	4	10
Alcohol, Stearyl		15-16	Mineral Spirits		14
Beeswax	5	9	Paraffin Wax	4	10
Carnauba Wax		15	Petrolatum	4	7-8
Castor Oil		14	Pine Oil		16
			Polyethylene Wax		15

Figure 1.8 HLB value of some frequently emulsified lipids.

The RHLB of an oil to be emulsified is obtained empirically starting from stable emulsions containing mixtures of pairs of well-known emulsifying agents in defined amount[36]. Once this value is known, the mixture of emulsifiers can be structured according to the following weighted average:

$$HLB_{oil} = HLB_{mix} = \sum_{i=1}^{NC} HLB_i * x_i$$

<div align="right">Equation 1.4 HLB value of a mixture.</div>

where:
- HLB_{oil} is the HLB value for the oil to be emulsified;
- HLB_{mix} is the resulting HLB of the mixture of surfactants;
- HLB_i is the HLB value for each single component[9];
- x_i is the weight fraction of the ith emulsifier in the mixture.

Griffin's HLB method is still nowadays widely applied for the selection of the emulsifier, even if some more accurate and precise methods have been developed recently[30].

Now that it's clear how to correctly choose the most suitable mixture of emulsifiers, it is fundamental to better understand how these molecules act once they are added to the formulation. First of all, the emulsifier quickly migrate towards the interface between the phases to ensure that rapid adsorption lowers the interfacial tension; if the added amount of emulsifier is sufficient, the reduction of interfacial tension is such that dispersed phase separates into small droplets[15]. These divisions cause turbulence into the continuous phase, leading to further formation of droplets and to the spreading of surfactant molecules, which rapidly cover the new born interfaces[15] thanks to diffusion from the bulk of the external medium.

During this process, energy must be supplied to the system to ensure constant formation of droplets; this crucial point will be thoroughly discussed in the following sub-chapter.

It is important to mention how, as they reach the interface between aqueous and oil phases, the molecules of the emulsifier dispose themselves according to a specific pattern that depends on the nature and molecular structure of the surfactant itself, as it can be appreciated in *Figure 1.9[15]*.
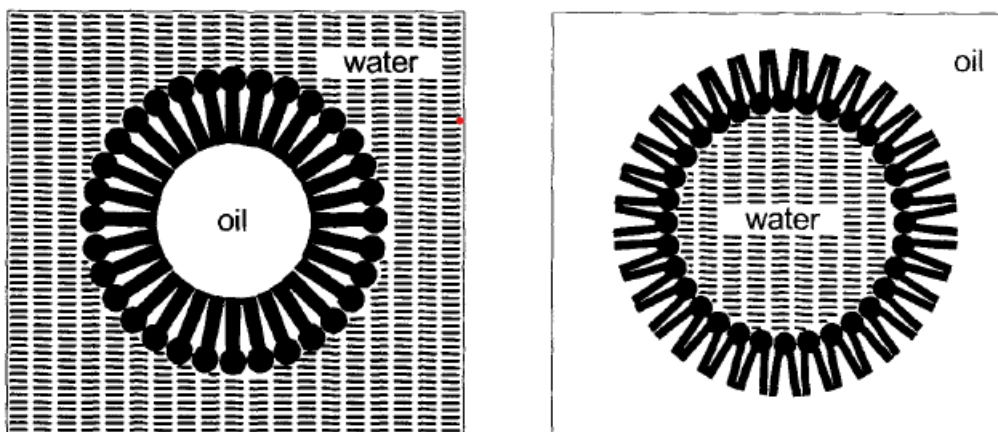
Figure 1.9 Disposition of emulsifier molecules at the interface in a direct (left) and inverse (right) emulsion.

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[9] This value can be computed according to different methods[15]: from the theoretical composition of the emulsifier, using the incremental (or group contribution) method or according to some mathematical relations with the phase inversion temperature (PIT)[36].

This phenomenon is well explained by the so-called *oriented wedge theory*, which states how *"the oil-like or non-polar end of the surfactant turns towards oil, while the polar one toward the water or, in general, the polar liquid[37]"*. In other words, according to the orientation theory, the molecules of surfactants orient themselves at the interface between oil and water with the hydrocarbon radicle, or tail, toward the oil, and the polar head towards water.

Moreover, this theory indicates that *"if the non-polar end of the molecule of the emulsifying agent is the smaller, the emulsion will be one of oil in water (or direct) type, while if the polar end is the smaller, the droplets will be of water (inverse emulsion)[37]"*. This information is crucial, since it suggests how the emulsion type and stability is determined primarily by the nature of the emulsifier, together with the volume fractions of oil and water phases[38].

1.2.c Producing an emulsion

Since macroemulsion are thermodynamically unstable, they are not spontaneously formed when oil and water phases come in contact: an energetic input is needed to get the desired result.

Considering an emulsification process, the energy required to get the dispersion of the inner phase in the form of droplets is defined by the Laplace pressure gradient ($\partial P_L / \partial r$)[39]:

$$\frac{\partial P_L}{\partial r} = \frac{2\gamma}{r^2}$$

Equation 1.5 Laplace pressure gradient.

where γ represents the interfacial tension between oil and water, r stands for the radius of the droplet and P_L is the Laplace pressure, computed as:

$$P_L = \frac{2\gamma}{r}$$

Equation 1.6 Laplace pressure quantification.

According to the above-mentioned equations, if the energy input to the system is sufficient to overcome Laplace pressure gradient, the phase to be dispersed is broken into droplets whose dimension and size distribution depends on several process parameters[40].

This result is usually achieved by the introduction of mechanical energy in the system according to *high-energy emulsification* processes[10], where turbulent flow conditions play a key role in deformation and disruption of big droplets, leading to the formation of smaller ones[39]; nonetheless, also laminar shear contribute is important to get the final result. Such methods exploit *stator-rotor mixers*, high-pressure *homogenization valves*[11] or *cavitation* phenomena[12] to introduce vast amounts of energy in the system: they are the most diffused at industrial level, thanks to their directly controllable process parameters like the quantity of mechanical energy input and the residence time in the equipment[39].

Among these techniques, stator-rotor devices are by far the most diffused equipment: they consist of a rotating disk (*rotor*) inserted into a fixed frame (*stator*) forming a narrow gap (usually between 50 and 1000 [μm]). As the rotor rotates at high rotational speed (1000 to 25000 [rpm]), the fluid is forced to pass through the narrow gap: this promotes the break-up of droplets by

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[10] Also *low-energy emulsification* processes exist, where only laminar flows are present, but they are extremely less diffused at industrial level[39].

[11] Composed of seat, valve and impact ring: the premix fluid passes through the valve, where its velocity increases and turbulence is created, leading to the formation of eddies which in turn break droplets of the dispersed phase[41].

[12] Mechanism in which vapor bubbles (*cavities*) in a fluid grow and collapse due to local pressure fluctuations[42], here usually induced by ultrasound generators.

mechanical impingement against the wall, given by the high fluid acceleration and shear stresses experienced in the turbulent flow between the stator and the rotor[39]. In this case, the controlling process parameters are represented by the residence time, the rotational speed of the rotor and the mechanical design of the latter[43].

More in detail, when mechanical energy is introduced in the fluid by mean of shear stresses induced by the rotor motion, *macro-eddies* are generated. These turbulences in turn decompose into smaller ones, called *micro-eddies*, defined by a specific characteristic length λ, known as *Kolmogorov length* and computed according to the following equation[44]:

$$\lambda = \left(\frac{\nu^3}{\varepsilon}\right)^{1/4}$$

<div align="right">*Equation 1.7 Kolmogorov length.*</div>

where *v* is the dynamic viscosity of the forming emulsion and *ε* is the dissipation rate, namely the power input imposed by the stirrer per unit of fluid mass. Micro-eddies are finally responsible for the energy transfer from the rotor blades to the fluid pockets, resulting in the breakage of the macroscopic phase and the formation of dispersed droplets.

When dealing with emulsions production, high-shear devices are usually referred to as *turboemulsors*.

Typical examples of stator-rotor mixers are reported in *Figure 1.10*; *Figure 1.11* represents the typical fluid velocity distribution obtained with such devices[45].

Figure 1.11 Geometric details of (a and c) the stator and (b and d) the rotor in (a and b) the teethed and (c and d) the blade-screen in-line high-shear mixers[46].
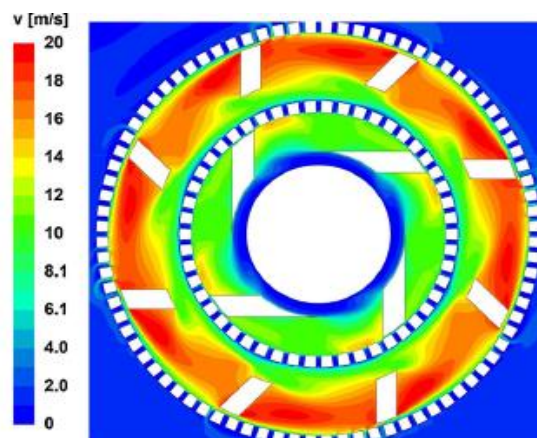
Figure 1.10 Velocity distribution in a Silverston double screen mixer 150/250 MS with rotor speed equal to 6000 [rpm].

In general, the minimum energy required to form an emulsion (*E_min*) can be directly correlated with the increase in Gibbs' free energy, due to the creation of new interfacial area between the phases because of droplets formation, and the dimension of droplets themselves (since, as per Equation 1.3, the lower the diameter, the higher the surface per unit volume and so the related free energy increase):

$$E_{min} = \frac{\Delta G}{V_{droplet}}$$

<div align="right">*Equation 1.8 Minimum energy requirement for emulsion formation[47].*</div>

where ΔG depends on the interfacial tension γ and the increase of interfacial surface area ΔS according to *Equation 1.2*.

At this point, it is possible to better understand the key role played by the emulsifier, which does not only provide long term stability to the emulsion, but it's also able to reduce the energy input needed for its creation by lowering the interfacial tension between aqueous and oil phase. In other words, the surfactant migrates towards the newly born interfacial surface, reducing the free energy content related to the latter and so the effort required to get the emulsion[48].
This means that the surfactants mixture added to the system is able to form a thin film around newly generated droplets of dispersed phase, favoring the formation of the emulsion and leading to a reduction in mechanical energy demand by a factor of 10 or even more, depending on the concentration and nature of the emulsifiers themselves[49]. This is a crucial aspect of emulsions production, especially when dealing with high-intensity methods applied at industrial scale.
Mathematically, the effect of the emulsifier on the interfacial energy can be expressed as follows:

$$\gamma^* = \gamma - \pi$$

Equation 1.9 Interfacial tension in the presence of a tenside.

and so, consequently:

$$\Delta G^* = \gamma^* * \Delta S < \Delta G$$

Equation 1.10 Gibbs' free energy in the presence of a tenside.

where π stands for the surface pressure of the tenside, resulting in the new interfacial tension γ^*, and ΔG^* represents the diminished Gibbs' free energy related to the system.

In any case, the amount of energy introduced in the forming emulsion must be higher than E_{min} computed in *Equation 1.8*, since droplets must be deformed and broken; namely, Laplace pressure (*Equation 1.6*) needs to be overcome.
In this regard, the total amount of energy involved in the emulsification process is usually described as *energy density* (E_v), computed as[50]:

$$E_v = \int P_v(t)\,dt$$

Equation 1.11 Energy density in the emulsification process.

where P_v is known as *power density*, while t is the residence time of the mixture in the equipment.
In a stator-rotor device, E_v is determined depending on the power input to the dispersion volume being treated and the specific features of the mixing device[39].
Considering the minimum energy required to produce the emulsion (E_{min}, *Equation 1.8*) and the total energy input to the system (E_v, just sjown above), the energy efficiency of the emulsification process is usually described as[39]:

$$\eta_{em,\%} = \frac{E_{min}}{E_v} * 100$$

Equation 1.12 Efficiency of emulsification.

Beside the surfactant mixture, other elements are most of the time added to the emulsion to achieve and retain the requisite features and stability[15]:

- *thickeners*, added to increase the viscosity of the outer phase and also able to act as emulsifiers at some extent. They role will be extensively detailed in Chapter 2;
- *plasticizers*, used when the viscosity of the formulation must be decreased, for example to make it sprayable;
- *solubilizers*, which increase solubility of an emulsifier in a phase;
- *protective colloids*, added to the outer phase to hinder coalescence of dispersed droplets by surrounding them without penetrating into the inner phase;
- *preservatives*, widely applied agents able to prevent fungal and bacterial growth in the final product during its whole declared lifetime;
- *defoaming agents*, since emulsions are not usually meant to produce foam, which could result unpleasant for the consumer and detrimental during manufacturing step;
- *additives to be added during the production*, to prevent incrustation on the lid of the container or sticking of oil-based compounds onto the surface of the blades in a stator-rotor equipment.

1.2.d Instability mechanisms

As already detailed above, the addition of the emulsifier makes the emulsion stable from the kinetic point of view, introducing an energetic barrier in the spontaneous tendency of the system to brake, given by the inherent thermodynamic instability of the formulation.

This means that, because of its own peculiar nature, the emulsion is not able to preserve its integrity indefinitely. Coalescence is just the last and irreversible[13] phase of the destabilization path, which can occur according to different mechanism[51]: gravitational separation (*creaming* and *sedimentation*), droplets aggregation (*flocculation*) and *Ostwald ripening*.

They are shown in Figure 1.12.
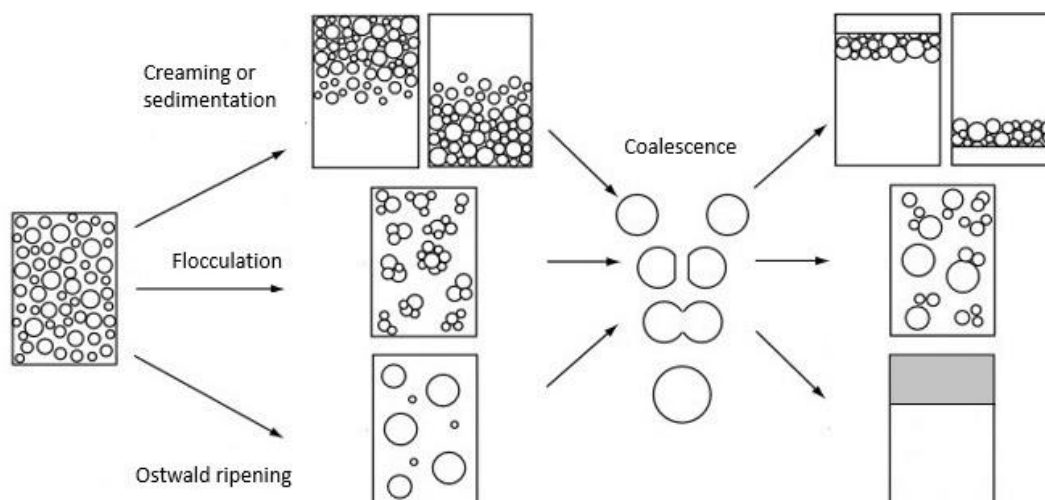
Figure 1.12 Instability mechanisms of emulsions: creaming or sedimentation, flocculation and Ostwald ripening[51].

Each one of them is briefly discussed in the following, together with phase inversion and coalescence phenomena, to better understand how an emulsion can lose its wholeness.

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[13] Coalescence is the only irreversible phenomena among those presented in *Figure 1.12*: this means that the emulsion is not completely loose until this state is reached.

Gravitational separation: *creaming* and *sedimentation*

Gravitational separation is the result of the difference in density between the dispersed and continuous phase forming the emulsion; it is classified as *creaming* when droplets of the dispersed phase drop out onto the free surface of the continuous one, while *sedimentation* occurs when droplets sink down to the bottom of the vessel[51], forming a sort of heavy cake.

Gravitational phase separation can be described according to the velocity of the sinking/emerging droplet travelling into the continuous phase; considering laminar condition, this is mathematically given by Stoke's terminal velocity[52]:

$$v_{dr} = (\rho_d - \rho_c) * g * \frac{d_{dr}^2}{18 * v_c}$$

<div align="right">*Equation 1.13 Stoke's law for particle sedimentation.*</div>

where ρ_d and ρ_c stands for the density of the dispersed and continuous phase, respectively, d_{dr} represents the diameter of the considered droplet and v_c the dynamic viscosity of the continuous phase.

According to the above-shown equation, it is possible to understand how, considering two phases of given density, the diameter of the dispersed droplets and the viscosity of the outer phase play a key role in the determination of the gravitational stability of the final product. In other words, large droplets and low-viscosity of the outer phase make gravitational separation easier.

As a rule of thumb, when d_{dr} overcomes 1 [μm], sedimentation (if $\rho_d > \rho_c$) or creaming (if $\rho_d < \rho_c$) becomes much more likely; on the other hand, as long as the dispersed droplets stay in the submicronic range, Brownian motion [14] tends to keep them suspended and almost evenly distributed if no other forces are acting on the system[51].

Gravitational separation, until not interested by coalescence, is reversible: droplets can be re-dispersed.

Flocculation

Aggregation occurs when two or more droplets of the inner phase attract each other, forming a loosely clamped mass of particles[51] where the single droplet maintain its independence, but shares some contact point with the other droplets constituting the aggregate.

Flocculation process originates from the thermodynamic instability of the system: thanks to reversible aggregation, the system can reach the so-called *secondary minimum*, advantageous situation with respect to the emulsified system from the energetic point of view. At this point, the system can still be ri-dispersed if energy is added from the external environment (from example, through mechanical agitation): otherwise, it will spontaneously evolve towards the *primary minimum*, namely the absolute energetic minimum, coinciding with the coalescence process[52].

This phenomenon can be observed in Figure 1.14, where the *primary minimum* is referred to as *flocculated* state, while the *secondary minimum* coincides with the *unmixed* system.

It is possible to see how each energetic minimum is divided by an energetic barrier (ΔG^a_{floc} and ΔG^a_{coal}), which the system must overcome to evolve towards equilibrium condition, namely the absolute minimum. This is why, even if the emulsified system spontaneously tends to brake, only those impacts with enough energy and the correct orientation can lead to a change in the status of

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[14] Stochastic motion of particles induced by random collision with molecules[53]: it is governed by thermal energy and characterizes colloidal dispersion interested by particles smaller than 1 [μm], where kinetic energy prevails on the gravitational field (weight force is no longer a determining factor).

the system. In other words, aggregation follows a stochastic trend, and the capability to have effective impacts depends on the entity of the energetic barriers dividing the minima.
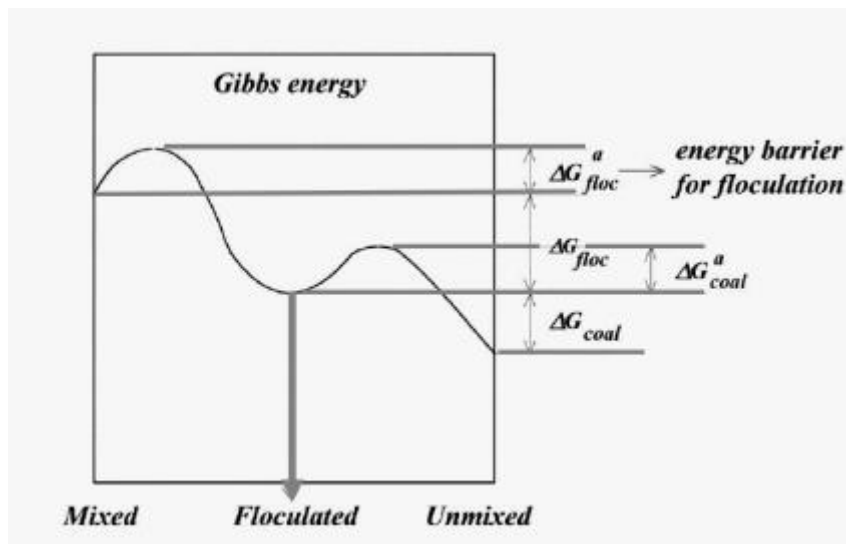
Figure 1.13 Energetic path leading from emulsified system to phase separation[52].

The energetic barriers dividing *mixed*, *flocculated* and *unmixed* conditions can be improved according to electrostatic[15] and steric[16] stabilization methods, which can heavily increase long-term stability of the emulsion. The same result ca be obtained using solid particles[17] to stabilize the formulation.

Anyway, these methods won't be further detailed in this context.

Ostwald ripening

This phenomenon is caused by the difference in pressure inside large and small droplets, resulting in a pressure gradient that leads to a net diffusive mass transfer from the core of smaller droplets to larger ones[51]. In short, large droplets growth at the expense of smaller ones thanks to their lower surface to volume ratio, which ensures higher thermodynamic stability.

Since such instability originates from the polydispersity of the system, it proceeds slower when the droplet size distribution is narrower or when the dispersed phase is very insoluble in the continuous one[51]. As a result of this, the diffusional rate of the process is strictly linked to the solubility of the inner phase in the outer one, which depends on the droplet radius as per the following equation[54]:

$$S(r) = S(\infty) * e^{\left(\frac{2\gamma V_m}{rRT}\right)}$$

Equation 1.14 Dispersed phase solubility as a function of droplet radius.

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[15] Based on electrostatic repulsion between positive and negative charges, thanks to the introduction of ions onto the surface od dispersed droplets.

[16] Based on the presence of steric obstacles (polymeric molecules grafted on the surface of dispersed droplets) that avoid particles to come in contact when they approach each other.

[17] Very finely divided particles, smaller than the droplets dispersed in the continuous phase and properly wetted by the latter, can stabilize an emulsion by placing on the tenside film formed all around the droplets[15].

where $S(\infty)$ stands the solubility of the droplet corresponding to an infinite radius (r), γ represents the interfacial tension, V_m the volume of the single solute and RT the product between the universal gas constant and the absolute temperature of the system.

Due to its high complexity, Ostwald ripening can be considered as a topic in its own right; in addition, it is extremely hard to control at practical level, especially during the first phases of the emulsification process.

Anyway, emulsions can be stabilized against Ostwald ripening by the addition of a third component, a liquid phase preferentially soluble in the dispersed phase rather than in the continuous one[52].

Coalescence

All of the above-mentioned instability mechanisms, if not properly managed, can finally lead to droplet coalescence (*Figure 1.12*)[18], namely the irreversible process of two droplets merging by the disruption of the tenside stabilizing layer forming a larger one[51]. Such a process may eventually lead to the formation of separate oil and water phases: at this point, the emulsion is irreversibly broken.

Analyzing coalescence mechanism more in detail, it is possible to observe how it is not a single stage process, since at least four consecutive elementary steps take place[52]:

- the droplets approach each other, reaching a distance short enough to allow interparticle interactions;
- the continuous phase entrapped between two approaching droplets is completely drained, making it possible for them to directly collide;
- the protective film formed by the emulsifier on the external surface of the droplets is broken;
- the droplets finally collide, compenetrate and merge into a single larger and oblong droplet, which quickly relaxes to a spherical shape[55].

Since coalescence enables the formulation to reach a state of stable thermodynamic equilibrium, represented by the minimum of the Gibb's free energy of the fluid system (*Figure 1.13*), no further spontaneous evolution will verify if the system is left able to freely evolve. Nonetheless, the process cannot be reversed by the introduction of mechanical energy in the system.
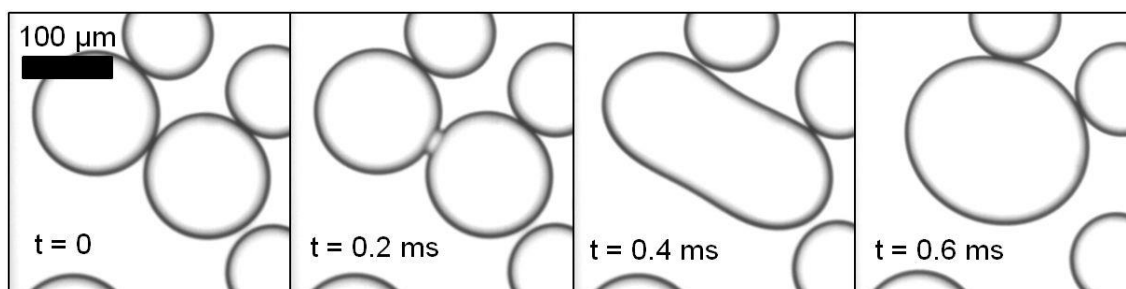
Figure 1.14 Detail of the coalescence process in an emulsion[55].

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[18] It is important to underline how *Figure 1.12* presents only the easiest possible paths leading to emulsion breaking: instability of emulsions is something extremely complex and diversified, hard to explain in a single image; for example, flocculation could take place before creaming or vice versa. In this regard, the purpose of the current sub-chapter is to present guidelines of emulsion instability mechanism, without any claim to deepen the topic in detail.

Phase inversion

Phase inversion makes it possible to change a direct emulsion into a reverse one and vice versa[15], but it also represents an instability mechanism since it can occur undesirably.

In general, the type of emulsion obtained depends on the ratio between the phases, on the manufacture procedure (i.e. the order in which the phases are added and the temperature), on the presence of electrolyte and, especially, on the sort of tenside mixture used[15].

Phase inversion can occur according to:

- temperature increase, able to decrease the polarity of the surfactant and consequently lead, according to Bancroft's rule, to the stabilization of a W/O emulsion starting from an O/W one[52]. This results from the decreasing degree of hydration of the hydrophilic group of the tenside at increasing temperature, and holds in the opposite direction for a decrease in the temperature of the system: if cooled, a W/O emulsion can turn into an direct one. The temperature at which this inversion occurs is known as *phase inversion temperature* (PIT)[15];

- addition of water to an inverse emulsion until it turn into a W/O type. Such a method exploit the variation in the ratio between dispersed and continuous phase: the amount of water needed to invert the emulsion is known as *emulsion inversion point* (EIP), and is usually described in terms of cm^3 of water added to the formulation per cm^3 of oil present[15]. Note that very stable O/W emulsion can be manufactured according to the EIP method and starting from a W/O one.
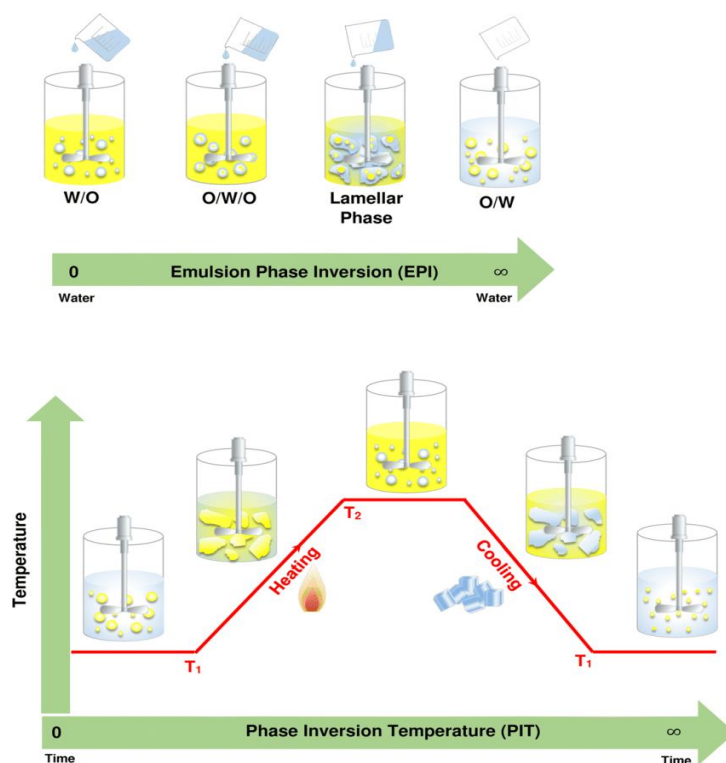
Figure 1.15 Emulsion inversion mechanism according to EIP method (above, starting from a W/O type) and PIT method (below, starting from an O/W type)[56].

1.2.e Rheology of emulsions

Generally speaking, rheology can be defined as the science dedicated to the study of the deformation and flow of a matter[57] considering two fundamental aspects: the viscosity and the flow behaviour, namely the evolution of the shear stress[19] as a function of the shear rate[20] for the body under investigation.

When dealing with fluid cosmetic formulations, as in the interest of the present thesis work, these are key parameters to be considered. This is particularly true when working with emulsions, whose rheological behaviour is usually extremely complex and, clearly, deeply impacting on the final features of the product.

Emulsion viscosity

Dynamic viscosity is usually defined as "*the resistance presented by the material opposing the movement of the system[57]*", and it is strictly connected to the rheological behaviour of the fluid under investigation.

In the case of emulsions, viscosity is strongly influenced by the composition and the characteristics of the outer phase, as described by the so-called *Einstein Formula[15]*:

$$\nu = \nu_0 * (1 + 2.5 * \phi)$$

Equation 1.15 Einstein formula for emulsions viscosity.

where ν_0 represents the dynamic viscosity of the outer phase and ϕ is the inner to outer phase volume ratio.

According to the trend suggested by *Equation 1.15*, it is possible to analyze the evolution of the viscosity of an emulsion as a function of the ratio ϕ, remembering that phase inversion occurs once the EIP is reached, as discussed in 1.2.d.
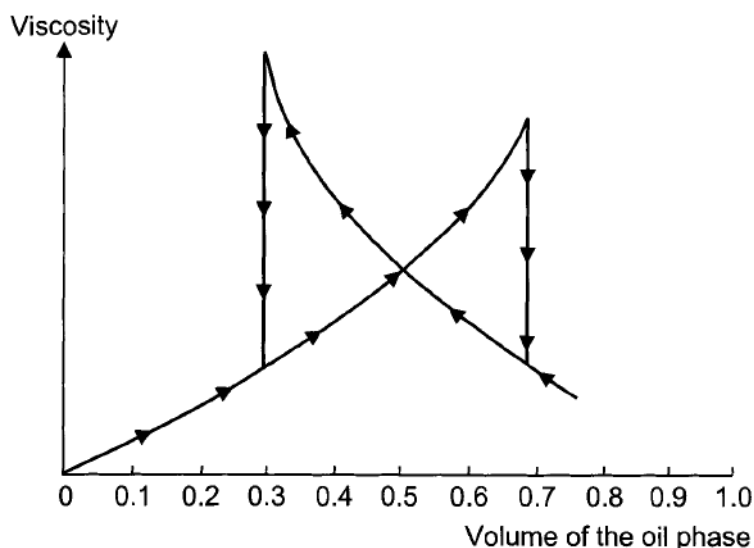
Figure 1.16 Viscosity hysteresis cycle obtained on progressive dilution starting from a concentrated emulsion[15].

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[19] Component of the stress acting on a body coplanar with its cross section.
[20] Rate of change of velocity at which one layer of fluid passes over an adjacent layer[58].

Different phases can be recognized[15] in the evolution shown in *Figure 1.16*:

- when the inner phase occupies less than 30% of the entire volume ($\phi < 0.3$), droplets seldom influence each other: the emulsion viscosity is determined by the external phase viscosity and tends to increase linearly with ϕ;
- once ϕ overcome 0.3, the growth become "more-than-linear" as a result of an increase in dispersed droplets interactions;
- for ϕ values greater than 0.5-0.52, the viscosity starts to increase faster and following a *non-Newtonian* behaviour (see next paragraph for the definition of *Newtonian* behaviour);
- if the emulsion is concentrated over, phase inversion takes place and the viscosity drops to low values. Precisely, emulsions start to become unstable for $\phi > 0.68$, unless a special emulsifier is present, and phase inversion takes place for ϕ greater than 0.74 (when the maximum possible occupation of volume is reached);
- for further addition of water (if originally started from a W/O emulsion), the viscosity versus ϕ profile does not follow the previous path backward but shows a hysteresis cycle[21].

Flow behaviour of the emulsion

The flow behaviour is on of the most important mechanical-rheological characteristic of a fluid formulation, and can be basically defined as the dependence of the fluid viscosity on the shear rate applied to the latter[59]. Different classes of fluids can be distinguished starting from *Figure 1.17*, where the evolution of the shear stress (often τ) is plotted as a function of the shear rate[60]:

- *Newtonian* fluids, in which the viscous stresses arising from their flow is, in every point, proportional to the local shear rate: they represent ideality in the fluid mechanics field, but such a behaviour is rarely found in the cosmetic industry. All those fluids which do not highlight the trend described above, are generally termed as *non-Newtonian*;
- *Pseudoplastic* fluids (also known as *shear-thinning* ones), in which an increasing shear force gives a more-than-linear increase in the shear rate. In other words, they see a diminution in the value of dynamic viscosity as the shear stress acting on them increases;
- *Dilatant* (or *shear-thickening*) fluids, with opposite behaviour with respect to pseudoplastic ones: equal increments in the shear stress give less-than-linear increase in the shear rate, meaning that the dynamic viscosity increase with the shear stress applied to the fluid;
- *Bingham plastic* fluids, characterized by a minimum stress (*yield stress*, usually referred to as τ_0) that must be exceeded before flow begins. When τ_0 is overcome, the behaviour is purely Newtonian;
- *Herschel – Bulkley* (or *Bingham non-plastic*) fluids[58], showing a *non-Newtonian* trend matched with a *yield stress*: they consist of a Bingham fluid with non-linear behaviour.

In other words, when an external force is applied on a fluid, it will flow to a degree which is directly linked with the internal friction forces, derived from internal molecular interactions, and with the magnitude of the external stress exerted on the fluid[60]; from the mathematical point of view, this concept is historically termed by Newton's law of viscous flow:

$$\tau = \nu * \dot{\gamma}$$

Equation 1.16 Newton's law for viscous flow[60].

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[21] Generally, hysteresis is defined as the dependence of the state and evolution of a system on its past history; it's typical of the magnetism field.

where the dynamic viscosity of the fluid undergoing the external stress (v) is the physical constant giving reason of the proportionality between the applied stress τ and the relative shear rate, $\dot{\gamma}$.

In accordance with the section above, *Equation 1.16* is only able to describe the behaviour of Newtonian fluids, in which the dynamic viscosity is completely independent on the shear stress or shear rate applied to the fluid[59].

A general mathematical description of the phenomenon is given by *Herschel - Bulkley equation*[60], able to represent all the flow behaviours presented above:

$$\tau = \tau_0 + K * \dot{\gamma}^n$$

Equation 1.17 Herschel - Bulkley equation.

where:

- τ_0 represents the yield (or *initial*) stress that must be applied to get flow in the case of Bingham plastic or non-plastic fluids. If no initial stress is present, *Equation 1.17* reduces to the so-called *Ostwald – de Waele equation*:

$$\tau = K * \dot{\gamma}^n$$

Equation 1.18 Ostwald – de Waele equation.

- K is known as *consistency coefficient*, constant only in the case of Newtonian and Bingham plastic fluids;
- n is defined as *flow behaviour index*: it is equal to 1 for Newtonian and Bingham-plastic fluids, while ranges between 0 and 1 for shear-thinning fluids (more-than-linear trend) and overcome 1 for shear-thickening media (less-than-linear behaviour);

Note that *Equation 1.17* degenerates into *Newton's law* if no initial stress is present and the index n is unitary; in this case, the consistency factor K coincides with the dynamic viscosity of the fluid[60].
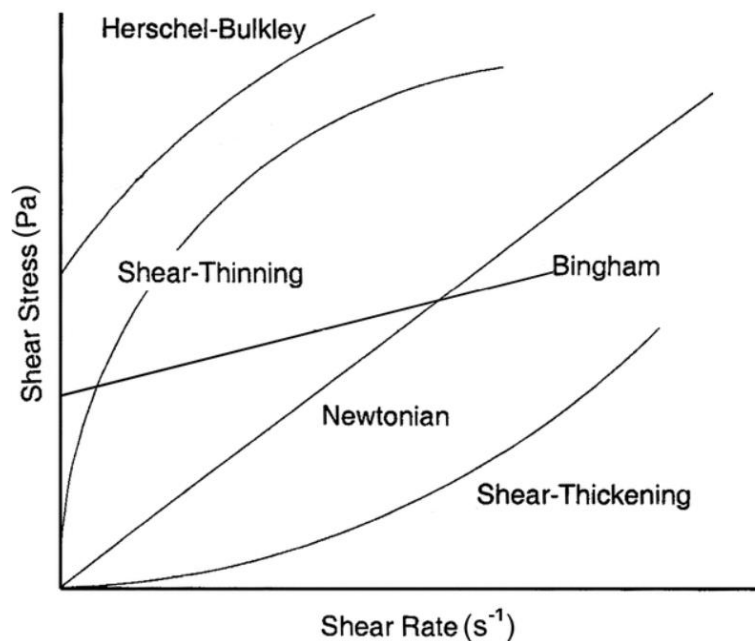
Figure 1.17 Rheograms of Newtonian and typical time-independent non-Newtonian f fluids.

At this point, it is also interesting to mention how the Newtonian idea of viscosity can be applied to non-Newtonian fluids according to the so-called *apparent viscosity* (η_{app}) concept: since no singular and constant value of viscosity can be computed for these media, the idea is to define a variable function of the condition of measurement[60].

The typical evolution of the apparent viscosity of a hydrocolloid as a function of the shear rate applied can be observed in *Figure 1.19*[60], where the shear-thinning behaviour typical of these systems can be identified by the decrease in the apparent viscosity inside the so-called "Power-law region".
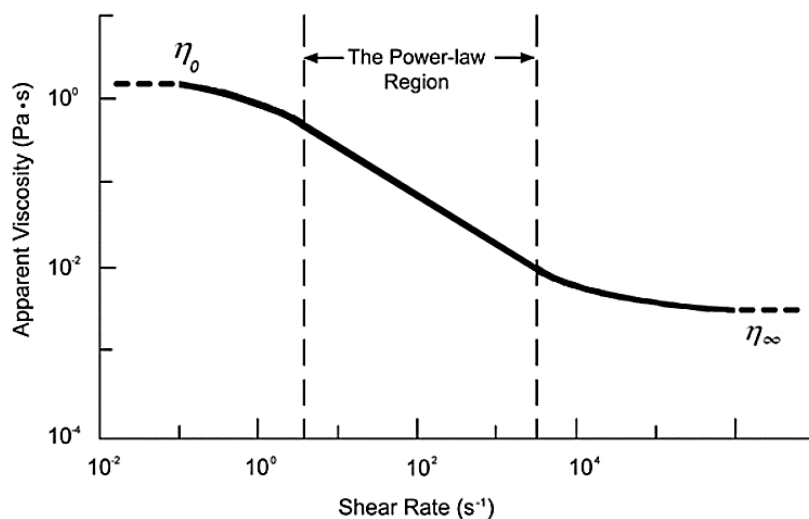
Figure 1.18 Evolution of the apparent viscosity of a hydrocolloid versus the rate of application of the external stress: the apparent viscosity decreases from an initial value η_0 to an asymptotical viscosity η_∞ (shear-thinning trend).

It is fundamental to underline how all the discussion above is meant for isothermal condition and does not account for time-varying behaviours, which would require a different approach and so a distinct treatment. For the sake of completeness, the principal time-dependent flow behaviours are represented in *Figure 1.19*[61] and briefly described in *Table 1.4*.
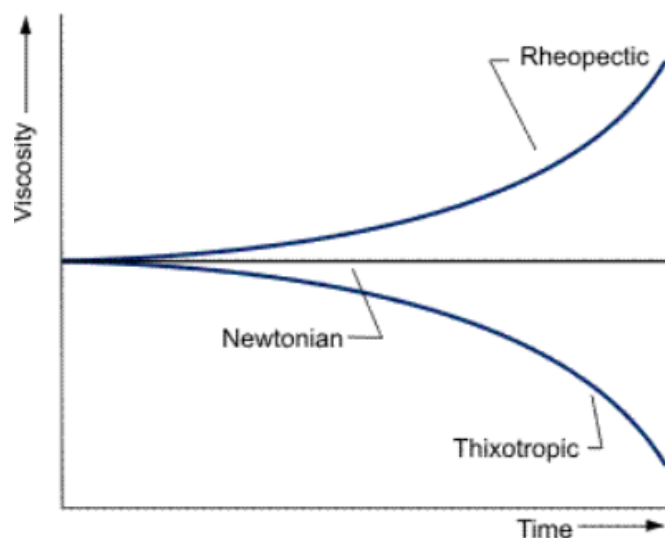
Figure 1.19 Time-dependent flow behaviours.

Time-dependent behaviour	Features
Newtonian	No change in the viscosity with time.
Rheopectic	The apparent viscosity increases during time under a constant shear rate.
Thixotropic	The apparent viscosity decreases during time under a constant shear rate.

Table 1.4 Principal features of time-dependent flow behaviours[59]for fluids undergoing a constant shear rate.

It is possible to notice how *rheopectic* fluids behave in time as dilatant media do with respect to a change in the shear rate, and the same holds for *thixotropic* fluids and pseudoplastic ones. In other words, it can be argued that a strong analogy holds between thixotropy and pseudoplasticity as well as between rheopexy and dilatancy[61].

Finally, it is worth mentioning that the reason behind a time-varying rheology must be sought in those structural changes that interest the fluid under stress at molecular level. More precisely, thixotropic fluid are characterized by disruption of local linkages within the fluid as a result of the strain given by the shear stress kept acting on the fluid body, while rheopectic media experience local alignments in the fluid that lead to an apparent viscosity able to increase as the stress continued to be applied[61].

2. Rheology modifiers in cosmetics

Broadly speaking, the rheology modifiers category includes all those raw materials able to significantly participate in the rheology of the final product, being it a monophasic or biphasic system such a solution, suspension or emulsion[62]. In other words, these substances are added to achieve desirable flow characteristics which would not be possible to obtain in their absence. Rheological modifiers play a key role in different areas, since the final flow behaviour of the formulation is a crucial aspect in several fields like pharmaceutical, food and cosmetic industry. They can be classified depending on various criteria[62], but the most suitable for the purpose of the present thesis project is the one considering their chemical nature together with their origin as raw material. In this case, two different macro-classes of rheological modifiers can be considered:

- *organic rheological modifiers*, further sorted in three categories depending on the substance origin:
    - *natural*, meaning derived from plant, animal or microbial origin and represented by large polymers chemically based on proteins or polysaccharides[63], like gums;
    - *natural-modified*, thus natural polymers treated with specific chemical modifications to enhance their performances in the final product;
    - *synthetic*, like oil-based polymers;
- *inorganic rheological modifiers*, comprising only mineral-based substances like clays and pyrogenic (or fumed) silica[62].
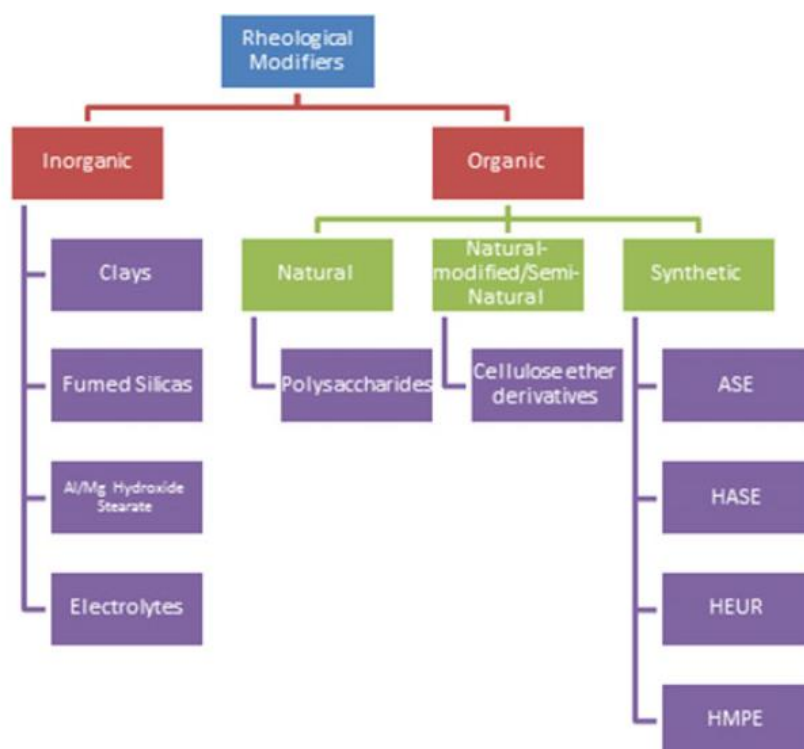
Figure 2.1 Conventional classification of rheology modifiers depending on their chemical nature and origin, with examples of modifiers particularly diffused in personal care products (purple boxes).

As current market trends push for greener, sustainable and non-oil-based raw materials, especially in the cosmetic field, the relevance and diffusion of natural-based ingredients is on the rise in the rheology modifiers field[62].

In fact, starting from the first decade of 2000s, organic cosmetic products recorded a constant revenue increase, finally penetrating in the conventional market segments. Moreover, natural-based cosmetic are still non-mature technologies, meaning that a multitude of opportunities for growth is still available in this developing field.

On the other hand, the substitution of oil-based polymers whit natural and natural-modified additives is only at the beginning in cosmetic industry: in fact, even if this switch has already been accomplished in rinse-off products, leave-on formulations still rely on traditional polymers in most of the cases. The reason behind this delay must be sought in the unique features that oil-based polymers are able to guarantee when added as rheological modifiers: high viscosity, softness, smoothness and white shiny appearance are only some of those peculiarities that consumers require but bio-based polymers struggle to recreate.

Moreover, it must be mentioned that natural polymers often show higher stock prices with respect to the oil-based equivalent and require to be added at higher concentration to get comparable performances, sometimes leading to unsustainable formulation costs. This is particularly problematic considering that, starting from the second half of 2022, raw materials stock costs experienced an unceasing increase, leading to budget cuts and the need for rethinking formulation logics.

Based on the above, it is easy to conclude that the introduction of natural rheological modifiers in skin care product is still a challenge, especially when the idea is to completely substitute oil-based additives, linked with specific and pleasant features of the final product. Fortunately, as shown by the effort of this thesis work, several scientific researchers are currently active on this topic and the most is yet to come, pushed by the increasing demand for all-natural products.

The present chapter analyse in detail the classes of rheological modifiers directly involved in the experimental work further shown, namely oil-based polymers, natural and natural-modified ones, considering their chemical structure, physical properties, field of application and specific implementation in the cosmetic industry.

Special emphasis is placed on those rheological additives directly involved in the experimental phases of the master thesis project.
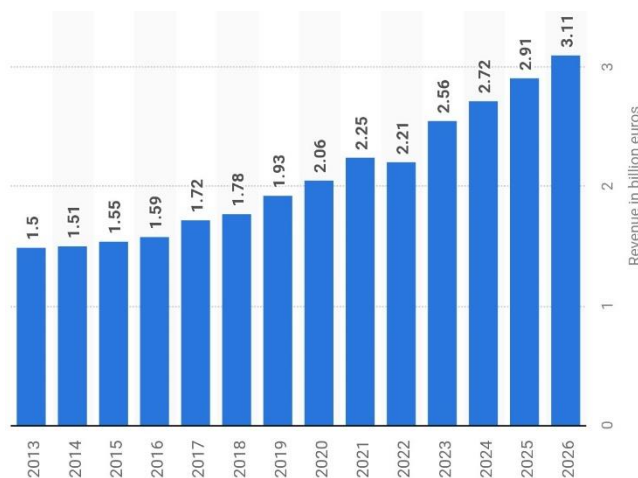
Figure 2.2 European market revenue for natural-based cosmetics in the period 2013-2023, and relative forecast (2023-2026)[64].

2.1 Synthetic polymers

As already mentioned above, rheology modifiers (also known as *thickeners*) are applied in personal care formulations to confer desired delivery characteristics and perceived sensory cues during application, making a product more pleasing for the consumer. Nonetheless, these substances also affect the emulsion stability, creating a crucial additional resistance against gravitational destabilization, extending the shelf-life of the product[65].

Among these essential additives, synthetic polymers represent the dirtiest but still highly common solution in the market: thanks to the unique properties they ensure, oil-based polymers are extremely tricky to be replaced by natural-based ones. When added to an emulsion, these synthetic rheological modifiers provide smooth and creamy texture, ease of application and optimal visual appearance while being fully compatible with the most widespread cosmetic ingredients in the skin-care field[66].

Oil-based polymers are divided into two major groups depending on the polymerization mechanism exploited during their production[67]: *condensation* polymers (produced according by step-growth polymerization[22]) and *additive* polymers (obtained by chain growth mechanism[23]). Nowadays, the majority of synthetic polymers sold as rheological modifiers for cosmetic formulations are addition polymers based on a few building block monomers, such as acrylic acid, acrylamide and acrylic ester derivatives[66]. The reason behind this situation can be found in the availability on global basis of these monomers, which leads to high cost efficiency of the final product: in fact, the same monomers form the basis of other product lines such as dispersing agents, flocculant and super-adsorbents, resulting thus particularly chap with respect to other comparable solutions[66]; moreover, these products can be interested by varying ionic charge and exist in several physical forms, increasing their ease of use.

From the technical point of view, oil-based polymers are used as thickening agents by different mechanisms[67]:

- *chain entanglement* (also referred to as *physical cross-linking*), a simple thickening mechanism in which polymer chains are dissolved into the solvent (usually water) providing soft entanglement that increases with increasing concentration of the polymer, since more chains are occupied in less space. As the concentration of the polymer continue to increase, it become more and more difficult to individually separate the entangled chains for the shear forces acting on the formulation;
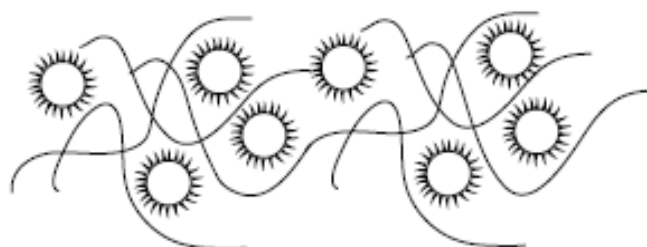
Figure 2.3 Chain entanglement thickening mechanism[68]

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[22] Polymerization process in which the polymer chain increases thanks to the chemical interaction between the functional groups of co-monomers involved in the process.
[23] Polymerization process characterized by the successive addition of monomer molecules to the reactive end of a growing polymer chain.

- *covalent cross-linking*, realized when two polymeric chains attach to each other thanks to the interaction of a bifunctional monomer, which reacts with both the chains forming a covalent bond linking them: this results in a tridimensional network of polymer chains throughout each particle. Cross-linking radically modifies the properties of the original polymer chains involved and represents one of the most important ways to achieve thickening at industrial level[24];
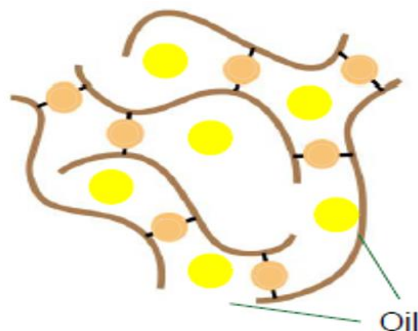
Figure 2.4 Chemical cross-linking of polymeric chains[69].

- *associative mechanism*, characterized by the formation of association network structures leading to viscosity increase as a result of bridge-connections and winding offered by the polymeric agent[68]. This is made possible by the presence of chemically attached hydrophobic groups able of hydrophobic associations similar to those typical of conventional surfactants[65].
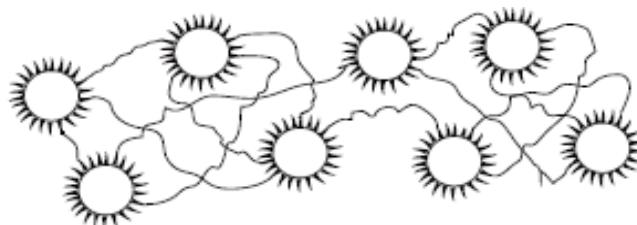
Figure 2.5 Thickening by associative mechanism[68].

Among the most widespread synthetic polymers in cosmetics, it is worth mentioning[67] polyvinylpyrrolidone (PVP), polyvinyl alcohol (PVA), poly-ethylene glycol (PEG) and polyethylene oxide (PEO), usually blended with natural-based polymers.
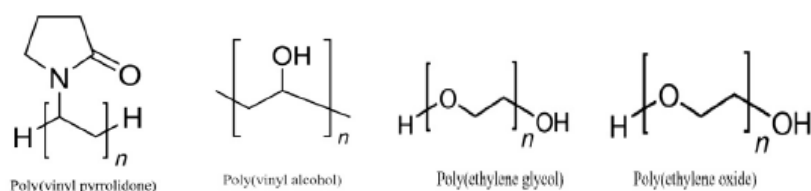
Figure 2.6 Chemical structures of commonly used synthetic polymers in cosmetics[67].

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[24] For example, the vulcanization process, crucial for tires manufacture, is based on covalent cross-linking of natural-based polymeric chains in the presence of sulfur.

By the way, the primary family of synthetic thickeners for cosmetic formulations is represented by acrylic polymers: given their key role in the production of skin-care products, these agents are further detailed in the following dedicated paragraph.

2.1.a Acrylic polymers

Acrylic polymers are considered one of the greatest innovation of modern industrial chemistry: perfected just after World War II, they were first developed to manufacture more versatile and versatile paints[70], later known as *acrylic paints*. Today, these polymers are extremely widespread in several industrial fields, playing a crucial role also in the cosmetics formulations industry.

From the chemical point of view, acrylic polymers are synthetized via chain growth mechanism (usually referred to as *addition polymerization*) starting from acrylic acid, an anionic monomer in turn obtained from ethylene[66] (and so, originally, from oil).
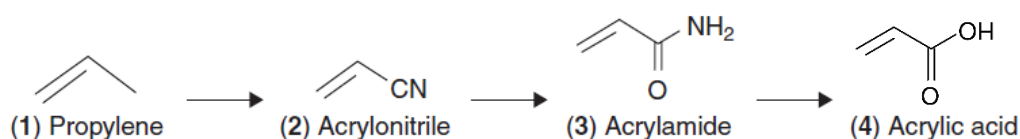
Figure 2.7 Industrial route from propylene to acrylic acid passing through acrylamide[66].

Even if pure acrylic polymers are possible, namely polyacrylic acid or cross-linked polyacrylic acid compounds, most of the acrylic acid is applied to produce acrylic esters like methyl acrylate, ethyl acrylate and butyl acrylate. These are then involved in polymerization processes, resulting in the formation of a wide variety of products: the different ester functionalities of the possible building blocks ensure high versatility and so the possibility to custom the properties of the final product depending on its specific use[70].

Moreover, acrylamide and acrylic acid can be blended at any proportion, allowing the preparation of copolymers in which the ionic content can be chosen by the ratio of acrylamide to acrylic acid (being the latter anionic), as in the case of sodium acrylate-acrylamide copolymer[66].
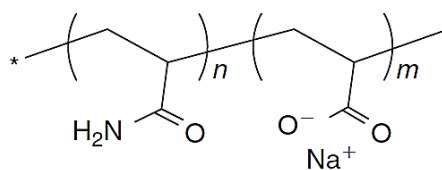
Figure 2.8 Chemical structure of sodium acrylate-acrylamide copolymer[66].

Nonetheless, acrylic polymers also account for polymeric chains obtained starting from the methyl derivative of acrylic acid, the so-called methacrylic acid; even in this case, the starting point for the production of the final polymer is often the methyl or ethyl ester obtained from the acid (namely, methyl methacrylate and ethyl methacrylate).
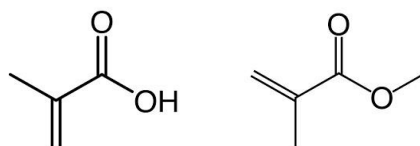
Figure 2.9 Methacrylic acid (left) and its methyl ester, methymethacrylate (right).

The wide diffusion of these rheological additives in cosmetics is mainly attributable to their capability of ensuring high viscosity and pleasant visual appearance of the final product while offering broad range of viscosities, up to extremely high values. Once added to the formulation, acrylic polymers act through swelling or chemical cross-linking depending on their specific nature, thus forming a polymeric tridimensional network able to heavily modify the rheology of the system while offering increased stability towards gravitational destabilization mechanisms.

To better understand the potential of these rheological agents, two common acrylic polymers with INCI[25] name *Carbomer* and *Sodium Polyacrylate* respectively, are studied in detail hereafter; note that this is particularly helpful, since these two compounds will then be the starting point of the experimental work of the present thesis project.

Carbomer 940

Carbomer is the name used to identify a family of synthetic, crosslinked polymers obtained from acrylic acid and polyvinyl ethers, characterized by high molecular weight[72]. They are usually sold in the form of white dried powder to be dispersed in water as thickeners and stabilizers for emulsion, but they also show optimal performance as gelling and suspending agents (in the case of insoluble solids).

Thanks to their exceptional versatility, Carbomers are widely applied in the cosmetic industry: skin, hair, nails cosmetics and make-up are frequently interested by these additives, as well as toothpaste and other personal care products.

Since several compounds belong to the Carbomer series, this label is usually associated with a number representing an indication about the specific components of the polymer and its mean molecular weight. Examples are Carbomer 910, Carbomer 934, Carbomer 940 and Carbomer 941.

In particular, the current work started from emulsions containing Carbomer 940: being its INCI name still simply *Carbomer*, it can be univocally distinguished considering its CAS[26] number (9003-01-04). Again, it is chemically described[27] as: 2-Propenoic acid, polymer with 2,2-bis(hydroxymethyl)propane-1,3-diol 2-propenyl ether)[74].

It is fundamental to mention how all Carbomers requires a neutralization step to act as thickening agent: this process leads to the dissociation of carboxylic acid pendant groups present on the polymeric chain, resulting in electrostatic repulsion, chain relaxation and curing[72]. Sodium or potassium hydroxide are usually applied as neutralizer to reach a final pH ranging between 5 and 12, depending on the specific purpose of the product.

Sodium Polyacrylate

Univocally identified as CAS 9003-01-07, sodium polyacrylate is chemically classified as: 2-Propenoic Acid, homopolymer, sodium salt[74].

Thanks to its optimal thickening and suspending capabilities, sodium polyacrylate its highly diffused in the cosmetic industry: in particular, it is recommended for skin care emulsions to provide glossy white appearance of the final product and a silky-soft after-feel on the skin.

Since it shows good emulsifying properties, sodium polyacrylate can also be applied in emulsifier-free formulations for cosmetic purposes[75].

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[25] International Nomenclature of Cosmetic Ingredients: it is used to systematically recognize and identify cosmetic ingredients on the product label. INCI names are developed by the International Nomenclature Committee (INC) and periodically published in the International Cosmetic Ingredient Dictionary and Handbook[71].

[26] The CAS Registry Number® is a unique numeric identifier with no chemical significance: it provides a direct link to several information about a specific chemical compound[73].

[27] This classification refers to the International Union of Pure and Applied Chemistry (IUPAC) nomenclature.

2.1.b Environmental impact of synthetic polymers

As detailed in the previous section, cosmetic products are nowadays still largely interested by the presence of oil-based polymers. Since a vast portion of these products (namely, rinse-off cosmetics) is intended to be rinsed after the application, it is easy to understand how an enormous amount of polymers reaches the household wastewater every day.

Among these pollutants, microplastics represent a particularly noxious threat to land and maritime environment: for this reason, several institutions all around the world have been evaluating legal means to limit the use and consequent release of polymeric materials with persistency and damaging environmental effects[76].

In order to understand the complex panorama of microplastic pollution, let's first of all consider the definition and guidelines actually in force according to the European Chemical Agency (ECHA). Microplastics are defined as small solid plastic particles composed by polymeric chains and additives: they can originate from the fragmentation of larger plastic during usage (*secondary microplastics*), like wear particles from tires, or they can be intentionally manufactured (*primary microplastics*), as in the case of microbeads in personal care products or industrial abrasives[77]. Only particles of less than 5 mm in any dimension can be considered microplastics, even if some exceptions occur[28].

Thanks to their tiny dimension, microplastics entering a wastewater treatment as part of the influent water can easily overcome all the purification steps, eventually reaching surface water streams; in addition, that portion of microplastic particles adsorbed onto the solid surface in the sludges exiting the wastewater treatment plant, is buried or spread in fields. Once part of the soil, they are washed away by rain and sent back to rivers and ocean[76]. In other words, even if modern wastewater treatment facilities show incredible efficiency, the accumulation on surface water and soil of polymer-based particles coming from cosmetics cannot be avoided.

As it can be easily imagined, once these tiny particles reach oceans and their wildlife, their effect is often extremely harmful: using surface ocean circulations and marine fauna as vectors, microplastics can travel for hundreds of miles, finally reaching high latitudes or accumulation points when different currents meet[78] (like the Great Pacific Garbage Patch, between Hawaii and California).

Figure 2.10 Extension and position of the Great Pacific Garbage Patch (GPGP), the biggest of five garbage packs nowadays existent[79].

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[28] For example, fiber-like synthetic polymers particles with length exceeding 5 mm but lower than 15 mm, are considered as microplastics because particularly persistent[77].

It is important to notice that microplastic noxious effect on wildlife does not interest only oceans: plastic debris washed up on shore can be ingested or further fragmented by the local terrestrial fauna, leading to additional circulation of the polymeric particles. Some detrimental effects of direct interaction between microplastic debris and maritime and land wildlife are shown in *Figure 2.11*[78].

Figure 2.11 Examples of microplastic noxious effect on wildlife: polyurethane microplastics (<53 μm) ingested by brine shrimp nauplii (left) and bear scat containing ingested plastic debris in Alaska (right).

Even if all microplastics are polymer-based, it is fundamental to mention that not all synthetic polymers must be considered microplastics neither are they all persistent[76]. According to ECHA, water-soluble and liquid polymers are not included in the definition of microplastic since do not fulfill the solid-state requirement, and the same holds for biodegradable polymers, which stay out of the definition because not persistent.

On the other hand, most synthetic polymers applied in skin-care formulations are represented by solid particles able to swell once added to the aqueous environment: this is the case of polyacrylates, which remains at the solid state while increasing the viscosity of the emulsion thanks to cross-linking. This means that polyacrylates rightly fall under the name of microplastic particles.

From the normative point of view, starting from 2018 the ECHA started to promote the abandonment of all products answering the above-shown definition, with the aim of reducing microplastics accumulation in the environment.

Italy leads the way in this field, with an ordinance banning microplastic from all rinse-off cosmetic products by 2020[79]; although this normative only hit rinse-off formulations, it is widely believed that the ban will be soon extended to leave-on products, including thus skin-care formulations.

In fact, even if leave-on products are not immediately removed from the skin, they will be sooner or later washed away by the consumer during its personal hygiene routine, leading to polymers accumulation in the household wastewater. In other words, leave-on formulations still contribute to microplastic pollution, even if to a minor extent with respect to rinse-off products, and will be therefore likely interested by restrictions in the near future.

This normative aspect, together with the raising consumers' environmental awareness all over the world, is pushing towards a paradigm shift in the cosmetic industry: the future is represented by a new idea of cosmetics, based on naturalness of the final product and low-impact raw materials coming from organic sources.

2.2 Natural-based polymers

Before the advent of synthetic oil-based polymers during the second half of the last century, natural polymers represented the better alternative to influence the rheological profile of a cosmetic formulation. Actually, the use of these natural compounds in personal care and beauty products can be traced back to Egyptian, Roman and Greek eras[63].

As already mentioned above, natural thickeners are intended as substances obtained from natural sources such as plants, seeds, seaweeds and microorganism[66] with the capability of acting on the viscosity, and in general on the entire rheology, of a product.

From the chemical point of view, natural thickeners applied in the cosmetic industry are represented by polysaccharides, macromolecules formed by the repetition of saccharide[29] units linked together by glycosidic bonds[30] for a minimum of ten monosaccharide molecules[81]. For this reason, they are also known as *hydrocolloids*.

During the past years, they have been widely applied in cosmetic formulations because of their quick availability from natural sources and their exceptional multifunctionality: in fact, they can also serve as suspending agents, moisturizers, co-emulsifiers, emollients and hair-conditioners[63]. Nonetheless, natural polymers show different limitations regarding the texture and visual appearance of the final product when applied as rheological additives in cosmetic emulsions: this aspect, linked with the cost-effectiveness and ease of production of oil-based substances, led to the heavy adoption of synthetic polymers. It must also be mentioned as organic synthetic polymers like polyacrylates are usually able to ensure a desired rheological behaviour at very low percentage, often lower than 0.8%; if the same result has to be obtained applying only natural-based polymers, the total concentration of these additives will easily overcome 1.5%, strongly impacting on the cost balance of the formulation.

In order to better understand the complex panorama of natural thickeners, it is possible to classify and analyze them according to their origin, as in *Figure 2.12[66]*.

Marine	Botanical	Microbial
Carrageenans	Guar gum	Xanthan gum
Agar–agar	Locust bean gum	Gellan gum
Alginates	Gum tragacanth	Pullulan
	Konjac glucomannan	Curdlan
	Tara gum	Dextran
	Cassia gum	Welan gum
	Gum arabic	Rhamsan
	Pectin	Succinoglycan
	Starches	

Figure 2.12 Classification of the most widespread natural thickeners depending on their origin as raw materials.

These classes are further detailed in the following; special care is taken for those natural polymers directly involved in the experimental step of the thesis project.

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[29] Unit structure of carbohydrates consisting of either five or six carbon atoms[81].
[30] Covalent bond holding together a carbohydrate to another group that can either be or not be a carbohydrate[81].

2.2.a Marine polysaccharides

Marine-based natural thickeners include all those polysaccharides directly extracted from seaweed. They are represented by three main families of compounds[66]:

- *Carragenans*, a group of sulphated galactans[31] extracted from different red seaweed (known as *Rhodophyceae*) species, mainly *Eucheuma cottonii*, *Eucheuma spinosum*, *Chondrus crispus* and *Gigartina*. They are in turn split in three different types according to their ester sulphate content, which depends on the specific weed source: the lower the ester sulphate content, the higher the gelling inclination of the considered carrageenan;
- *Alginates*, block copolymers composed of *mannuronic* (M) and *guluronic* (G) *acid* extracted from brown seaweed (*Phaeophyceae*) species like *Macrocystis pyrifera*, *Laminaria hyperborea* and *Ascophylum nodosum*. The M to G ratio depends on the specific type of alginate and governs its final properties in terms of thickening and gelling performance. They are usually commercialized as water-soluble sodium salts, which require the addition of calcium to get the desired thickening effect;
- *Agar*, a general term used to identify a complex mixture of polysaccharides extracted from *Gelidium* and *Gracilaria* species of red seaweed: the major fractions are represented by *agarose*, a neutral polymer, and *agaropectin*, a charged sulphated polymer. When applied as thickener, agar results in the formation of firm and brittle gels.
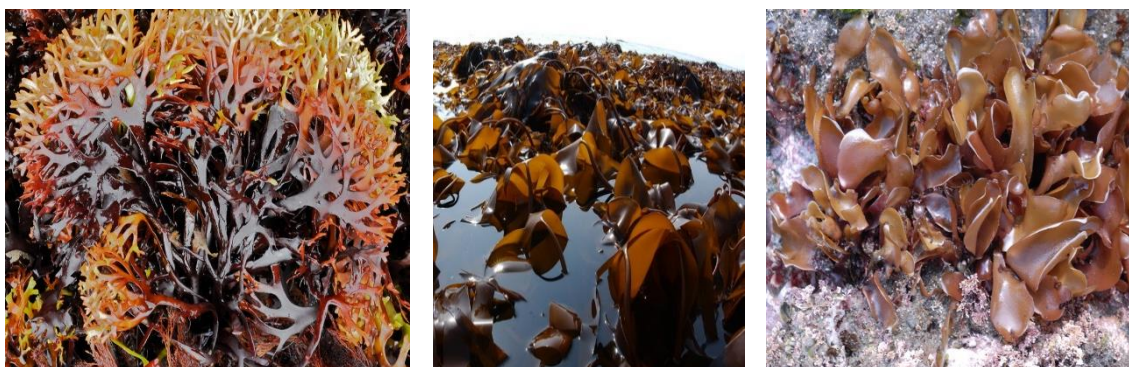
Figure 2.13 Different species of seaweed: from left to right, red seaweed Chondrus crispus, brown seaweed Laminaria hyperborea and red seaweed Gracilaria incurvate[82].

2.2.b Botanical polysaccharides

Being easily achievable and extremely widespread, botanical polysaccharides have been known to man for many centuries. As made for marine-based polymers, they can be classified in different families[66]:

- *Galactomannans* (or *botanical gums*), composed of a C1 to C4 linked mannose[32] backbone with single galactose substituents; they include Guar gum, locust bean gum, Tara gum and cassia gum, which differ in the degree of galactose substitution going from one galactose per every two mannose (Guar gum) to one every four (locust bean gum). They can all be used as thickeners in cosmetic formulations;

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[31] Polysaccharides composed by repeating units of galactose (aldohexose monosaccharide with chemical formula $C_6H_{12}O_6$, isomer of glucose); it can be both branched or unbranched[81].

[32] As galactose, mannose is an aldohexose monosaccharide and an isomer of glucose, obtained from the ash of Fraxinus Ornus and related plants[81].

- *Pectins*, extracted from different vegetal sources like apples and citrus fruits and composed of galacturonic acid residues with occasional rhamnose interruptions. They are usually classified depending on their degree of methyl esterification and not widely applied in the cosmetic field, whereas extremely diffused in the food industry.

Tara gum

Tara gum, namely *Caesalpinia Spinosa Gum*, represents one of the most promising thickening alternatives to polyacrylates in cosmetic formulations. It is obtained by grinding the endosperm of *Caesalpinia Spinosa* (also known as Peruvian carob) seeds, a plant belonging to the *Leguminosae* family and native to the Peruvian and Bolivian Andes[62].

Figure 2.14 Tara gum: from the pod to the flour[62].

It is completely odourless and white to ivory coloured, even if the resulting gel is usually brownish and translucent. Thanks to its long history as thickening agent in the food industry, Tara gum is nowadays internationally recognized as safe for other human applications[62], like cosmetic products.

As anticipated above, its chemical structure is characterized by (1-4)-β-D-mannopyranose linear chains, branched through (1-6) bonds with α-D-galactopyranose units in a 3:1 ratio[62]; the specific mannose to galactose ratio differentiates Tara gum from the others botanical gums presented above and gives it those special features widely appreciated in different fields.

This complex chemical structure can be appreciated in *Figure 2.15[62]*.
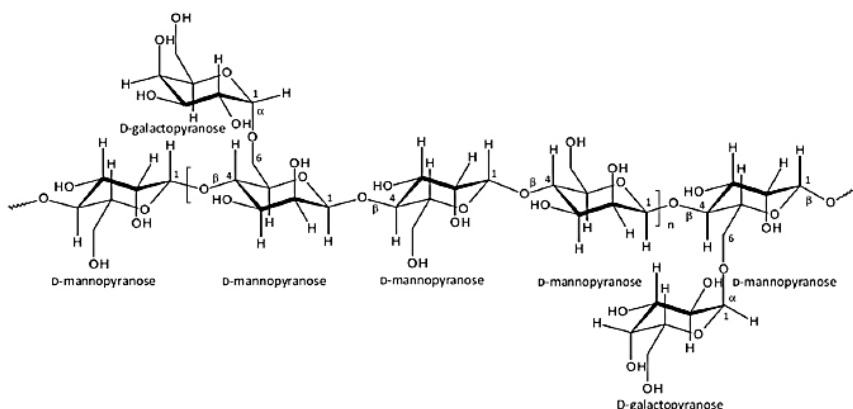
Figure 2.15 Chemical structure of Caesalpinia Spinosa Gum.

For what concern the performance as rheological modifier in cosmetic emulsions, Tara gum shows linear Newtonian behaviour at low concentrations (0.1 to 0.2%), while acquires pseudoplastic features without thixotropy for higher concentrations (0.5to 2%)[62].

The thickening power becomes important over 1.0% concentration, when a dramatic increase in the obtained viscosity can be appreciated, exceeding 50000 [cP] when the concentration approaches 2.0%; moreover, good suspending power is highlighted starting from 0.1% concentration[62].

Finally, Tara gum is stable for a wide range of pH (3 to 12) and tolerates the addition of ethanol up to 10%[62]: in other words, it appears as an optimal potential substitute for polyacrylates in cosmetic emulsion.

2.2.c Microbial polysaccharides

Several microbial polysaccharides have been produced in the last decades, but only a few of them have proved to be as efficient as promised when dealing with the application at industrial manufacturing scale[66].

They are generally produced thanks to controlled and bioengineered fermentation[33] processes of different microorganism: examples are Xanthan gum (secreted by *Xanthomonas campestris*), Succinoglycan (produced during fermentation by *Agrobacterium tumefaciensis*) and Welan and Rhamsan gums (both coming from *Alcaligenes* species)[66]. Among these, only xanthan gum found a stable and fructose application in the cosmetic field.

Xanthan gum

Xanthan gum is a high molecular weight polysaccharide obtained during the fermentation process of the microorganism *Xanthomonas campestris*, commonly found on the leaves of the *Brasica* vegetables, like cabbage[83]. It acts as thickener and stabilizer with optimal performances, and its high solubility in cold water[66] ensure ease of operation both at lab and industrial scale.

Xanthan gum shows an extremely complex chemical formula: its primary structure is a linear (1-4)linked- β-D-glucose backbone with a trisaccharide side chain one every other glucose at C3, containing a glucuronic acid residue linked (1-4) to a terminal mannose unit and (1-2) to a second mannose that connects to the backbone; almost half of the terminal mannose are pyruvylated and the non-terminal residue carries an acetyl group[84].
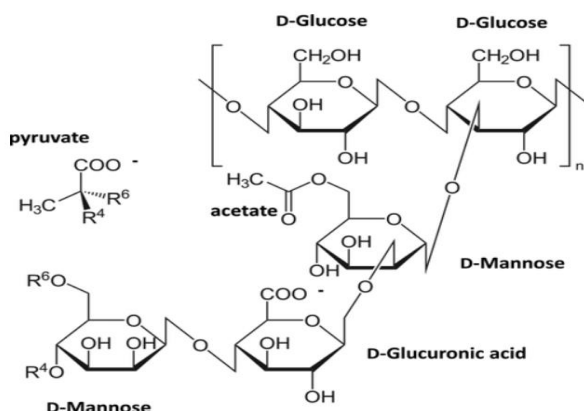
Figure 2.16 Chemical structure of Xanthan gum; note that Na+, K+ and Ca2+ are the most frequent counter-ions[84].

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[33] Biochemical process consisting in the breaking down of sugar molecules into simpler compounds in the absence of oxygen, producing several compounds that can be used in the chemical industry[81].

Moreover, an helical secondary structure can be recognized: this contributes to the high stabilization activity of Xanthan gum when added to an emulsion[83].

From the technical point of view, Xanthan gum solution are highly pseudoplastic: viscosity is progressively reduced when shear stress is applied, but upon its removal the initial value of viscosity is recovered almost instantaneously. This behaviour comes from the capability of xanthan molecules, once in solution, to form intermolecular aggregates thanks to hydrogen bonding and polymeric entanglements: such a phenomenology explain both the high thickening and stabilizing effect offered by Xanthan gum in cosmetic formulations[83]. In addition, the reduction of viscosity following an increasing shear is important to the pouring properties of suspensions and emulsions, as well as to the efficiency of this additive as a processing aid.

For what concern the recommended dosage, Xanthan gum is able to offer good thickening and stabilization properties already for 0.1 to 0.3% concentrations, giving lead to solution with gel-like appearance when increased to 1.0% concentration[83].

However, Xanthan gum is not able to reproduce the smooth and silky texture typical of polyacrylates-containing skin care formulations: emulsions interested by the presence of Xanthan gum often appears jellylike and sticky, something extremely undesired in the skin care segment. For this reason, it is usually blended with botanical gums: this pattern shows synergistic interactions able to provide high viscosity and stability coupled with the pleasant texture and appearance offered by galactomannans[66].

2.3 Natural-modified polymers

Several natural polymers intended to be used as thickeners are subjected to chemical treatments aimed in modifying their chemical structure, with the final goal of magnifying the rheological activity of such polymers. This is the case of chemically modified polysaccharides, which include basically[66]:

- *Modified cellulose* products, interested by chemical modifications to render the basic cellulose backbone soluble. This family of cellulose-based products offers a wide range of functions, from the thickening effect ensured by carboxymethyl cellulose (CMC) to the thermogelation in hydroxyethyl cellulose (HEC);
- *Modified native starches*, consisting of starches interested by chemical transformations to improve their heat and acid resistance and increase processability while reducing tendency to retrogradation[34]. This category includes hydroxyethyl and hydroxypropyl modified starch;
- *Modified alginates*, obtained by esterification with propylene glycol to avoid precipitation at pH lower than 4.0, phenomenon typical of alginates;
- *Modified guar gums*, interested by carboxymethylation to improve alkali compatibility, hydroxyalkylation to improve solubility or phosphatisation to enable cross-linking.

Thanks to their enormous versatility, such modified natural polymers are used in several industrial fields including cosmetics, food, oil drilling, pesticides, textile and many others[66]; even if some of them shows a partial overlap of their properties, each modified hydrocolloid tends to excel in a few specific areas.

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[34] Formation of very strong thermally irreversible gel as a result of association of the polymeric chains through hydrogen bonding[66].

2.3.a Modified cellulose products

Being the major constituent of the majority of land plants, cellulose is the most abundant organic substances existing in nature: it represent the starting material for a wide range of modified natural polymers with several applications in food and cosmetic industry[83]. Well known examples are *cellulose ethers* like methyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose and sodium carboxymethyl cellulose, frequently referred to as *Cellulose gum* (or *Na-CMC*): all these valuable additives come from a specific chemical modification of the same raw material, cellulose.

From the chemical point of view, cellulose shows a polymer chain of two repeating anhydroglucose units, namely β-glucopyranose residues, linked through a 1,4 glycosidic bond; this chain structure can be appreciated in *Figure 2.17*, where n stands for the *degree of polymerization*, here coinciding with the number of anhydroglucose units[83].
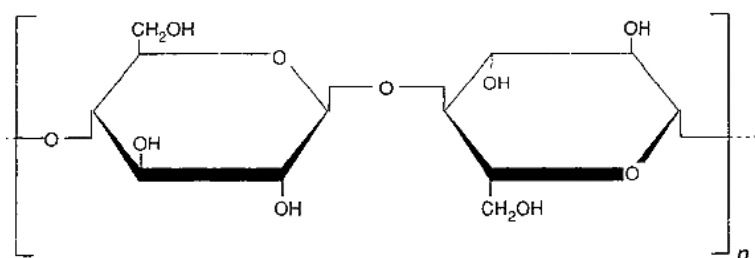
Figure 2.17 Chemical structure of cellulose.

The strong intermolecular hydrogen bonding typical of its structure make natural occurring cellulose highly crystalline and ordered, resulting in insolubility in water; this is the main reason behind cellulose modification to get industrially desirable water soluble rheology modifiers[63].

The abundance of modified cellulose products is made possible by the fact that each anhydroglucose unit contains three hydroxyl groups, which can be in principle substituted giving lead to a various range of possible alternatives. The average amount of hydroxyl groups effectively substituted per unit is referred to as the *degree of substitution* (ds); note that desirable chemical and mechanical properties are usually achieved for a ds much lower than the theoretical maximum[83].

The degree of substitution, together with the polymerization degree and the type of substituents groups introduced in the polymer chain, defines the final set of properties of the modified cellulose product.

Carboxymethyl cellulose is probably the most widespread cellulose derivative in the modern industry: being soluble both in hot and cold water and able to give clear and colourless solutions[83],35, it is particularly appreciated as thickener in food and cosmetic products. In this case, carboxymethyl groups are attached to each glucose unit, with a degree of substitution for industrial application usually ranging between 0.7 and 1.2[63]; considering such a ds, it is possible to produce aqueous solution at 1.0% concentration of cellulose gum with viscosity of 5000 cP at ambient temperature[83].

It is important to mention how the degree of substitution strongly influence the thickening capabilities of CMC: solutions of low-substituted cellulose gum show thixotropic, whereas higher ds lead to pseudoplastic behaviour[83].

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35 Being characterized by a neutral flavour[83] cellulose gum is extremely diffused in food manufacturing, where represents one of the most diffused natural additives.

At a technical level, CMC provides thickening effect upon entanglement of its high molecular weight chains, resulting in stable viscous solutions within the pH range 4 ÷ 7 and at low temperatures[63].
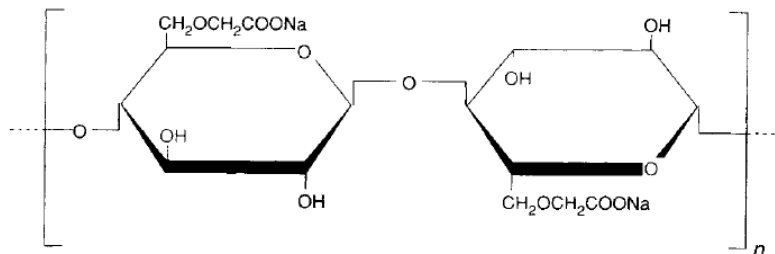
Figure 2.18 Chemical structure of cellulose gum with a degree of substitution of 1.0[83].

Differently from cellulose gum, which shows anionic features, cellulose ethers are cationic semi-natural derivatives of cellulose: thanks to their history of effective and safe use, they represent the main cellulosic alternative in personal care and beauty market[63].

In general, cellulose ethers are able to dissolve in water at room temperature, thanks to hydration of the cellulose backbone: this leads to the development of a sheath of tightly bound water molecules around each polymer chain, allowing them to expand and create the entanglement network needed to build up the desired viscosity[63]. As seen for CMC, high viscosities can be achieved at low concentration thanks to the interactions between the high molecular, rigid cellulose macromolecules.

It is fundamental to state how, once added to whatever emulsion, cellulose ethers are not able to act as suspending agents without the aid of other specific substances showing suspending properties, such as Xanthan gum[63].

The most widespread cellulose ethers are shown in *Figure 2.19*.
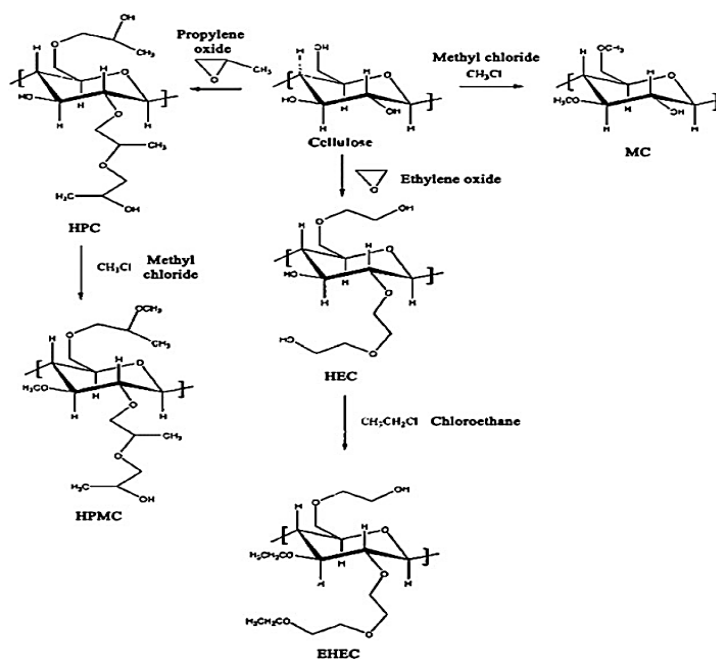
Figure 2.19 Main cellulose ethers and relative synthetic routes[63].

2.3.b Modified starches

Starch is one of the most widespread natural-occurring polysaccharides, stored in all green plants as energy reservoir and commercially isolated starting from several crop plants such as corn, potato, rice, wheat and tapioca[63].

Chemically speaking, natural starch consists of two basic polysaccharides, namely amylopectin[36] and amylose[37]: different starches differentiate one from the other depending on their amylopectin to amylose ratio, on which the final features of the polymer depend; typical molecular weights of amylopectin and amylose are 500 million g/mol and 1 million g/mol, respectively[63].

Being characterized by strong molecular interactions based on hydrogen bonding, starch shows reduced ease of dissolution in water if compared with cellulose[63]: for this reason, it is usually added to hot water to favour the solubilization process.

Starches are popular and well-known thickening agents in food and cosmetic industry, even if the tendence to form hazy and cloudy solutions limits their application in clear formulations manufacture[63].

As mentioned some pages ago, starches are frequently subjected to chemical modifications aiming to maintain their beneficial properties while reducing instability and retrogradation issues[83].

The main modification routes nowadays applied on native starch are shown in *Figure 2.20* together with a simplistic representation of their effect.
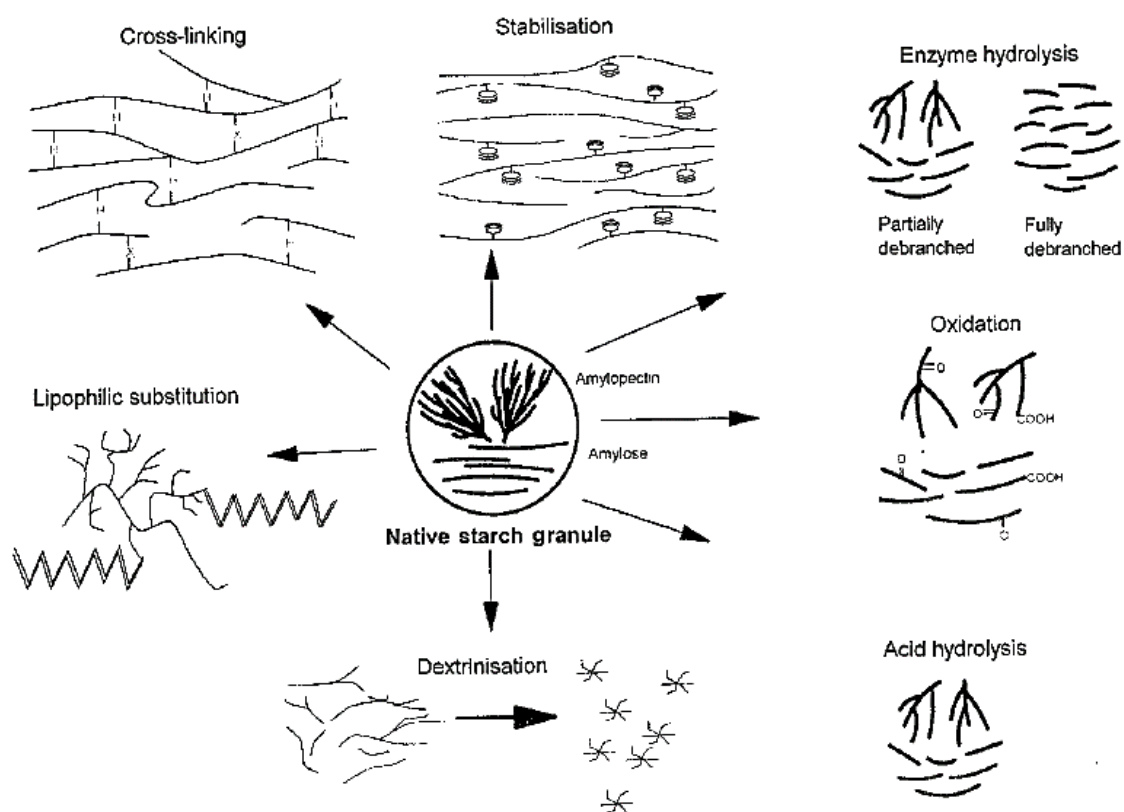
Figure 2.20 Main chemical and biochemical modifications applied on native starch[83].

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[36] Polysaccharide made up of highly-branched chains of α-glucose units[81].
[37] Polysaccharide formed by α-D-glucopyranosyl units linked with α-(1,4) glycosidic bonds[81].

Each chemical manipulation is realized with a specific goal[83]:

- *Cross-linking*, the most frequent chemical transformation applied on starch, consists in the replacement of the hydrogen bonding between starch chains with stronger and more permanent interactions, namely covalent bonds. Such a modification avoid the swelling of the starch granule, preventing so disintegration by chemical attack or imposed shear;
- *Stabilization*, usually applied in conjunction with cross-linking, is another fundamental chemical modification process applied on starch: its aim is to prevent retrogradation by introducing some bulky groups able to create steric hindrance against chains re-alignment;
- *Conversions*, comprising all those transformations occurring by chain-cleavage reactions of starch like *oxidation*, *acidic hydrolysis*, *dextrinization* and *enzymatic hydrolysis*, are able to guarantee various effects on the final properties of starch;
- *Lipophilic substitution* is characterized by the addition of long hydrophobic chains to the starch macromolecules, resulting in higher lipophilicity and increased ability to stabilize interactions between oil and water. An example is given by starch octenylsuccinates, widely applied additives able to rapidly migrate towards an oil-water interface and stabilize it.

3.   Pre–experimental phase

The present chapter provides the starting point of the experimental thesis project herein presented: after a detailed discussion about emulsion nature and rheology, together with some details about synthetic and natural-based rheology modifiers, the focus of the project moves to the practical substitution of polymeric thickeners in the highlighted formulations (chapter 4).

To make it possible, it is first necessary to briefly present the structure of the above-mentioned formulations and the different parameters that will be considered throughout the whole experimental work for the comparison between the performances of oil-based and natural rheology modifiers. These parameters accounts for both chemical and physical stability of the emulsion, measured according to different and innovative methods (i.e. Lumifuge® technology), and investigate also those features regarding the thickening role of polymers (viscosity) and the compatibility with consumers' skin (pH).

After this theoretical phase, referred to as *pre-experimental* one, chapter 4 will extensively present the practical synthesis work conducted at laboratory scale to find the better natural-based alternative to polyacrylate thickeners in the formulations under analysis.

3.1   Investigated formulations

As already mentioned above, two formulations were selected to be revamped by substituting the oil-based rheological additives with natural polymers, with the aim of reducing the environmental impact of the product without sacrificing the distinctive features appreciated by the consumers. Both products represent well-known formulations that have been produced for many years through established procedures and with defined final properties: this is a fundamental aspect, since any change in the processability or in the properties of the final product can be directly blamed on the thickener substitution.

Nonetheless, such emulsions were selected because particularly suitable for the purpose of the current project: in fact, they are characterized by severely different viscosities, and this is extremely helpful to understand how natural-based polymers behave in different viscosity ranges. Moreover, the final purpose of the considered product is quite different, and this too helps in analysing the peculiar behaviour of natural thickeners when required to deliver different textural sensations.

In addition, it is worth mention how, even if a real economic study was not carried out, the total cost of each proposed alternative and its percentage increment with respect to the original formulation were a significant driving force when it came to the selection of the best natural-thickened formulation. This is fundamental, since at industrial level the best solution is not always the theoretical optimal, but the one able to minimize the costs associated to its production while keeping the performances of the product as high as possible; in other words, the correct choice is the techno-economical optimal.

The economical aspect is currently extremely difficult to manage considering the sharp rise in the stock price of raw materials registered in the last two years[38]: each minimum percentage variation

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[38] This increment can be mainly blamed on the SarsCoV2 pandemic, even if the abrupt rise in the cost of energy as a result of Ukraine war further exacerbated it: raw material stock cost reached +45% with respect to pre-pandemic value at the end of 2022[85].

in the concentration of a substance can result in high impact on the global cost of the formulation, with detrimental results when the production volume is in the order of millions of kg per year.

Both formulations are hereinafter briefly presented on a qualitative base, with the purpose of introducing the reader to their main physico-chemical characteristics and targeted use without exposing the industrial secret protecting their quantitative full recipe.

3.1.a Moisturizing lotion

Moisturizing emulsions are applied to the skin in order to hydrate it and make it feel softer and smoother to the touch: they represent a flagship product of the skincare market, and many types of them exist.

The specific formulation under investigation is classified as a moisturizing lotion, meaning that its water (or in general aqueous) content is higher than expected for a generic cream: this ensures optimal hydration and ease of absorption upon application on the skin[86]. More in detail, the aqueous phase of the considered lotion accounts for almost 90% of the total mass of the emulsion, resulting in a soft and fresh sensation combined with an easy application to the skin thanks to the low viscosity (~ 20000 cP).

The main components of the aqueous phase are represented by:

- *water*, the basis of the entire formulation;
- *water-soluble emollients*, which reduce water evaporation from the skin surface thanks to the occlusion of skin pores, resulting thus in hydration via an indirect mechanism[87] (water is trapped, so emollients are not really hydrating the skin, but only reducing water losses from its surface);
- *preservative system*, added with the aim of avoiding microbial contamination and for bacteriostatic and fungistatic purposes[88];
- *pH-controlling agents*, introduced to regulate the pH of the final product in the desired range.

On the other hand, the oil phase is mainly interested by the presence of:

- *emulsifying agents,* needed to make the emulsion formation possible;
- *co-emulsifying agents*, introduced to help the main emulsifier in achieving the formation of the desired emulsion;
- *consistency factors*, namely ceramides and fatty alcohols added to increase the formulation density and stability;
- *carbomer 940*, the synthetic oil-based rheological additive to be substituted by natural thickeners, here added to a concentration equal to 0.2%;
- *antioxidants*, added after cooling to room temperature and fundamental to avoid oxidative processes to take place in the bulk during shelf-life of the product.

For the sake of clarity, the entire formulation is listed in *Table 3.1*; as mentioned above, quantitative references cannot be shown to respect the industrial secret covering these products. Every component is indicated through its INCI name and function, together with the phase of belonging.

Note that, in order to best monitor the influence of each alternative thickener on the properties of the investigated formulations, the concentration of these components will always be clearly shown during the project; in this way, it will be possible to compare the percentage of application of polyacrylic and natural thickeners needed to get the same final performances.

INCI Name	Function	Phase
Aqua	Base	W
Glycerin	Emollient	W
Propylene Glycol	Emollient	W
Allantoin	Moisturizer	W
Sorbitol	Moisturizer	W
Tetrasodium Glutamate Diacetate	Chelating agent[39]	W
Citric Acid	pH adjuster	W
Pentylene Glycol	Emollient	W
Sodium PCA	Humectant[40]	W
Sodium Citrate	pH buffer	W
Aloe Barbadensis Leaf Juice	Humectant	W
Sodium Hyaluronate	Humectant	W
Sodium Benzoate	Preservative	W
Magnesium Aluminium Silicate	Stabilizer	W
Phenoxyethanol	Preservative	-
Ethylhexylglycerin	Preservative (booster)[41]	-
Glyceryl Stearate Citrate	Emulsifier	O
Glyceryl Stearate	Co-emulsifier	O
Cetearyl Alcohol	Consistency factor	O
Caprylic/Capric Triglyceride	Emollient	O
Ethylhexyl Palmitate	Emollient	O
Tocopheryl Acetate	Antioxidant	-
Dimethicone	Emollient	O
Aluminium Starch Octenylsuccinate	Texturizer[42]	-
Prunus Amygdalus Dulcis Oil	Emollient	O
Carbomer	Rheology modifier	O
Parfum	Fragrance	-

Table 3.1 Moisturizing lotion: complete original formulation; W stands for water phase, O for oil phase and – denotes a component not ascribable to any of the two phases.

3.1.b Nourishing body cream

The second formulation object of the present thesis work is a thicker and tacky water-based emulsion, generally indicated as a cream because of its lower aqueous content with respect to the previous lotion. Such a product is intended to be applied on the whole body with a nourishing

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[39] Chelating agents are ingredients that complex with inactive metallic ions to prevent their adverse effects on the stability or appearance of the cosmetic formulation[71]; recently, they have also been proved to boost the effect of the preservative system.
[40] Humectants play the same role as emollients, but through a direct mechanism: thanks to their hygroscopicity, they attract and bind water molecules, forcing it to move from the deeper layers of the skin to the outermost region; they are also able to draw water from the surrounding environment when air humidity overcomes 70%[98].
[41] Preservative boosters are characterize by the capability of strongly increase the effectiveness of the preservative system, even if added at very low concentration (usually lower than 0.1%).
[42] Texturizers are molecules able to influence the final texture and visual appearance of a cosmetic emulsion; such substances are often added after the emulsification have occurred, during the cooling phase.

effect, thus providing those substances needed for the regeneration of the cells of the epidermis responsible for the protection against dehydration and dryness.

In this specific case, the aqueous content of the formulation is near 80%: it is important to notice how a small change in the aqueous phase content with respect to the previous formulation leads to major differences in the final product. In fact, the considered nourishing cream shows a completely different rheology if compared to the moisturizing lotion described above: in the former, viscosity builds up to almost 45000 cP, leading to a quite complete absence of flow even if the recipient undergoes capsizing.

Such creams are usually referred to as "pot creams", because they are generally marketed in small aluminium or glass pots from which the consumer pick up a minor amount of product; on the contrary, thanks to their higher flow capability, lotions are usually marketed in pump bottles or recipients to be squeezed.

Entering more in detail, the main classes of components of the aqueous and oil phase are the same of the moisturizing lotion presented above, even if the single components differ.

Moreover, the rheology modifier is still a polyacrylate, but no longer a carbomer: in this case sodium polyacrylate is applied in the original formulation at 0.75% concentration, resulting in silky after-feel on the skin and white glossy appearance inside the pot.

INCI Name	Function	Phase
Aqua	Base	W
Glycerin	Emollient	W
Xanthan Gum	Rheology modifier/Stabilizer	W
Pentylene Glycol	Emollient	W
Tetrasodium Glutamate Diacetate	Chelating agent	W
Propanediol[43]	Emollient	W
Myristyl Myristate[44]	Emollient	O
Cyclopentasiloxane	Emollient	O
Ethylhexyl Stearate	Emollient	O
Dimethicone	Emollient	O
Cetearyl Alcohol	Consistency factor	O
Glyceryl Stearate	Co-emulsifier	O
Glyceryl Stearate SE	Emulsifier	O
Sodium Polyacrylate	Rheology modifier	O
Isopropyl Myristate	Emollient	O
Phenoxyethanol	Preservative	-
Ethylhexylglycerin	Preservative (booster)	-
Tocopheryl Acetate	Antioxidant	-
Parfum	Fragrance	-

Table 3.2 Nourishing body cream: complete original formulation.

For the sake of completeness, it must be mentioned that the nourishing body cream detailed above faced the removal of a second, important component in addition to the polyacrylic thickener object

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[43] Propanediol is also known to act as booster for the preservative system[75].
[44] Myristyl myristate has a fundamental secondary function: it acts as a whitener[73], a fundamental aspect when dealing with natural polymers resulting in yellowish gels, as in the case of the current project.

of the study: namely, cyclopentasiloxane (D5) was not added to any of the alternative formulation hereinafter investigated. This decision was taken as a result of a European normative limiting cyclopentasiloxane concentration to 0.1% in weight in rinse-off formulations[45]; since the normative will be likely soon extended to leave-on formulations, it seemed wise to take the opportunity offered by this experimental project to start work towards the complete removal of D5 from skincare products.

3.2   Selection of study benchmarks

Remembering that the final aim of the current project is to define whether polyacrylic thickeners can be substituted by natural polymers in the above-detailed formulation without suffering from performance losses, it is necessary to choose some aspect to be compared between original and natural-thickened formulations.

The selection of these parameters is crucial: such benchmarks must be able to ensure a global and accurate comparison between the different formulations, considering both technical details and the final appearance and texture of the product. In fact, the final product must satisfy the consumer needs without showing processing issue or physico-chemical instability, which could result in a shorter shelf-life if compared to the original formulation containing synthetic polymers as thickeners.

In addition, such parameters must be quickly available and easy to be compared to ensure promptness in all the phases of the project; moreover, at least a restricted number of them has to be directly measurable in the production line, thanks to sampling from the bulk undergoing processing and immediate in-field analysis.

Finally, it is worth mentioning how some of the selected criteria, later referred to as *qualitative parameters*, do not come from scientific measurements with appropriate instrumentation, but are rather based on a visual and sensorial perception. This is something not unusual in the cosmetic industry, where the evaluation of some fundamental marketing aspects like the visual appearance of the product, in terms of colour and brightness, or the sensation caused by its application on the skin, is based on a qualitative before quantitative approach[46]. Nonetheless, when it comes to the marketing phase, these parameters are usually examined thanks to standardized panel tests, where volunteer panelists are asked to complete a questionary regarding well-defined qualitative aspects of the product upon trying it.

All the benchmarks considered in the comparison between original and revamped formulations are detailed in the latter, starting from physico-chemical aspects and emulsion stability, finally reaching those qualitative parameters mentioned above.

In addition, each piece of information about measuring devices and procedures is carefully provided with the purpose of making the current study as easy as possible to understand and reproduce, as required for any scientific production.

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[45] Regulation (EU) 2018/35 of the Council of 10th January, 2018, modifying Attachment XVII to the regulation (EC) No. 1907/2006 of the European Parliament and the REACH on octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5).

[46] Note that these parameters, despite being purely qualitative, are the key ones considered by the consumer upon purchasing: this is the reason why various components of cosmetic formulations does not play an active role, but are only added to increase the pleasant appearance of the final product.

3.2.a Physico-chemical parameters

The first aspect to be considered when analysing the result of an experimental synthesis deals with the physical and chemical structure of the product obtained. In the cosmetic research and development field, this results in the evaluation of some parameters regarding the intrinsic nature of the formulation and able to heavily impact on its capability to satisfy consumer needs.
In the present work, two physico-chemical parameters were considered and measured after each experimental trial, namely the viscosity and the pH of the synthetized emulsion. The main reason behind the choice of this specific parameters is found in the ease of measuring, both at laboratorial and manufacturing scale, combined with the ability to describe the potential of the formulation as a cosmetic product.

As extensively discussed in the previous chapters, viscosity deals with flow resistance opposed by a fluid when subjected to an external shear force acting on it.
This aspect is fundamental in the cosmetic industry, since it defines the type of product brought to the market: each formulation must respect a well-defined range of viscosity, which depends on its final application. In example, a generic body lotion is expected to be something easy spreadable and with a fluid-like behaviour: if the product viscosity is too high, the cream would show poor or absent flow, and this may be interpreted as a low-quality index by the consumer.
The range of optimal viscosity for both the investigated formulations is shown in *Table 3.1*, at the end of the current sub-chapter.
For what concern the measuring phase, each viscosity value was collected right after the synthesis at the same temperature (define as *room temperature*, namely 25 °C) and making use of a modern digital rheometer: Brookfield AMETEK DV-1.
The latter is defined as a rotational viscometer, a shear stress-controlled instrument able to measure fluid viscosity by driving a spindle, immersed in the fluid to be tested, through a calibrated spring. The viscous drag force exerted by the fluid against the rotating spindle is measured in terms of spring deflection and returned by the system as a viscosity value in cP[88]. The measurement range of the instrument is extended thanks to the presence of various interchangeable spindles: each rotating head as its own range of application, which can be in turn narrowed depending on the needs of the specific case by acting on the rotational speed, so that to obtain readings as reliable as possible. The detailed set-up selected for each formulation is reported in *Table 3.1*, too.

Figure 3.1 Brookfield viscometer model AMETEK DV-1 and its set of spindles[89].

It is fundamental to underline how each measurement has been conducted just after the synthesis and the following cooling phase: in fact, the viscosity of an emulsion is subjected to non-negligible variation in the days and weeks following its production, as a result of ripening phenomena taking place in the bulk and usually resulting in higher cohesion of the latter. For this reason, collecting the measurement as soon as the emulsion reaches 25 °C is a solution to standardize the procedure and avoid the fluctuation in viscosity given by aging phenomena.

The second parameter collected, that is pH, deals with the chemical nature of the emulsion: as is known, pH is a quantitative measure of the acidity or basicity of a system based on the values of the concentration of hydrogen ions and expressed on a logarithmic base.
The pH value characterizing a cosmetic emulsion is crucial: it defines the possibility for the product to be applied on a specific skin area without compromising the homeostasis of the stratum corneum[47] and the skin permeability.
Recent studies have shown that the pH of the skin ranges between 4.1 and 5.8 depending on the specific body part, with some exceptions of more basic nature (axillae, toe interdigit and others)[90]. Considering the importance of pH in human physiology and pathology, it is easy to understand that the skin, as any other human organ, has to resist acid and alkaline aggression to some extent: this is ensured by a buffer system probably based on free amino acids of the epidermis[90].
It is fundamental for a cosmetic product to not interfere with this pH-maintaining mechanism since various concerns could otherwise arise: for this reason, each formulation has a specific pH range to comply with, depending on the final application area and the desired effect. Aiming in keeping or improving skin appearance and condition, skincare formulations usually have neutral-like pH values, ranging from 5 to 7; the reference values for the investigated formulations are shown in *Table 3.1*.
Concerning the measuring device, the pH value was collected after the cooling phase to 25 °[C] using a laboratorial pH-meter, FiveEasy Plus by Mettler Toledo. Each pH value was then compared with the reference range for the considered formulation and, if necessary, properly adjusted using sodium hydroxide (10% aqueous solution) or lactic acid (80% aqueous solution), added drop by drop.

Formulation	Viscosity [cP] @ 25 °C	pH @ 25 °C
Moisturizing lotion	18000 ÷ 20000 (Spindle S05, 10 rpm)	5.2 ÷ 5.6
Nourishing body cream	35000 ÷ 55000 (Spindle S06, 20 rpm)	6.2 ÷ 6.7

Table 3.3 Reference values for the physico-chemical parameters of the formulations object of the current study..

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[47] The outermost layer of the skin: it consists of keratinocytes that undergo terminal differentiation[90].

3.2.b Physical stability of the emulsion

As already detailed in section 1.2.d, physical instability of emulsions deals with gravity-driven phenomena, like creaming and sedimentation, able to heavily affect the wholeness and probity of the cosmetic product.

For this reason, the research and development stage of cosmetic emulsions always account for methods able to assess the capability of the product to withstand physical instability: this is fundamental to understand if the formulation being developed will exhibit a shelf-life as long as required by consumers' needs. Such methods are often based on centrifugal machines able to impose high centrifugal acceleration on the samples under investigation, thus accelerating any possible phenomena affecting emulsion stability as a result of the gravitational field.

In the current experimental project, two different physical stability analysers were considered: a classical laboratory centrifuge and a modern accelerated stability analyser, namely LUMiFuge®. Both these analytical devices and the related experimental protocols are detailed in the following.

Laboratory centrifuge

Laboratory centrifuges are widely diffused devices applied when dealing with a dispersed system in many scientific fields: they can be both used to impart a desired partitioning (as in the case of blood cells separation from plasma) or to assess the capability of the sample to resist segregation. In the cosmetic field, centrifuges are extensively exploited to investigate emulsions stability with respect to creaming and sedimentation phenomena. This is made possible by the high centrifugal acceleration imposed on the samples: the latter are placed on dedicated cavities, angled at roughly 30° with respect to the horizontal frame and directly hosted on the rotating body of the centrifuge. From the mathematical point of view, the phenomenon can be described starting from the terminal velocity of dispersed particles given by Stoke's law (*Equation 1.13*); since in this case the gravitational force pushing dispersed particles to sedimentation or creaming is enhanced by the presence of the applied centrifugal force, a modified version of the above-mentioned equation must be considered[91]:

$$v_{dr} = (\rho_d - \rho_c) * g * \frac{d_{dr}^2}{18 * v_c} * RCA$$

<div align="right">Equation 3.1 Modified Stoke's law
accounting for centrifugal forces
acting on the sample.</div>

where *RCA*, known as *relative centrifugal acceleration*, is given by the ratio between the applied local gravity, *a*, and the absolute gravitational acceleration *g*; in turn, *a* is computed as in the following[91]:

$$a = (2 * \pi * f)^2 * r = \varpi^2 * r$$

<div align="right">Equation 3.2 Applied local gravity.</div>

where *r* represents the distance between the axis of rotation and the sample, *f* is the frequency of revolution of the centrifuge and ϖ the corresponding angular speed.

As can be easily imagined, the higher the centrifugal force acting on the samples, the faster dispersed particles are forced to move inside the continuous phase, resulting in quicker destabilization of the emulsion.

From the practical point of view, it is fundamental to mention that samples must be properly balanced when loaded on the centrifuge, otherwise the strong centrifugal acceleration applied on them could result in accidental release of the sample during rotation and its consequent disruption. For this reason, samples were always equally filled and loaded pairwise in the centrifuge following a cross pattern, so to ensure stability during operation.

The laboratory centrifuge model adopted in the current thesis work was the MPW-56 by MPW® Med. Instruments, a high-speed rotational centrifuge able to host eight samples simultaneously. Moreover, the specific protocol chosen consisted of three runs of 20 minutes each, conducted at 3000 rpm; after each run, an accurate visual inspection was performed under proper illumination to assess the possible presence of sedimented or surfaced clusters. If all the three inspections came out to be negative, the sample was labelled as stable under centrifugation.
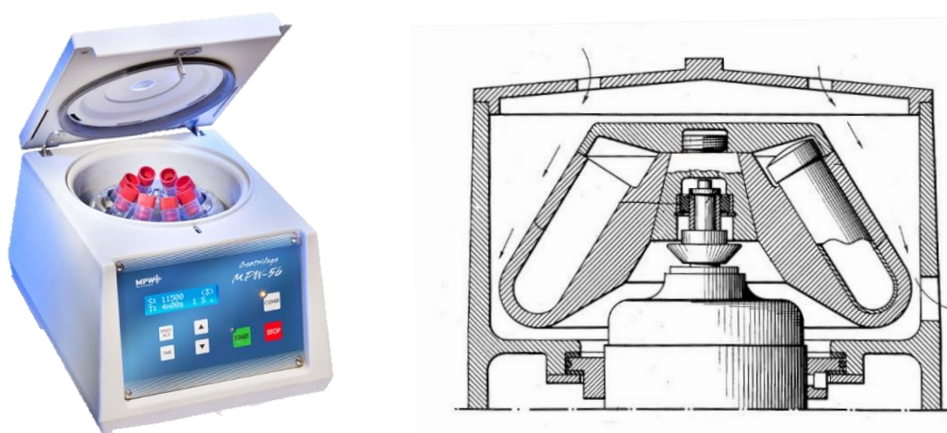
Figure 3.2 Laboratory centrifuge MPW-56 by MPW Med. Instruments[92] (left) and cross-section representation of a typical high speed rotational centrifuge[93] (right).

LUMiFuge® stability analyser

In order to further investigate the physical stability of each synthesized alternative formulation, a second more accurate and modern device was taken into account.

The stability analyser LUMiFuge® LF 110 (L.U.M. GmbH, Berlin, Germany) is a microprocessor controlled analytical photo-centrifuge operating at programmable acceleration profiles[94]. Capable of analysing 8 samples simultaneously at temperatures as high as 60 °C, this modern centrifuge detects droplet migration, imposed by centrifugal forces, and possible changes in size distribution thanks to the alteration of the transmission given by the variation of the local droplet concentration[94]. The transmission profiles change according to the progress of separation: their temporal sequence is displayed and stored in a PC connected to the centrifuge, such that any instability process can be easily observed as a sort of time-lapse motion picture; clearly, each instability mechanism can be recognized because characterized by a precise evolution of the transmission.

At a practical level, samples are placed horizontally on a rotating disk: a NIR[48] light source, hosted just above the samples, emits a signal that hits them; a light sensor is finally mounted on the bottom of the device to receive the portion of light able to cross the sample.

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[48] Near-infrared (NIR) light is defined as an electromagnetic radiation with wavelength ranging from 800 to 2500 nm[95], therefore invisible to naked eyes.

Figure 3.3 shows the initial situation (at time t_0, when no rotation is still occurring) in a LUMiFuge® model able to host 12 samples.
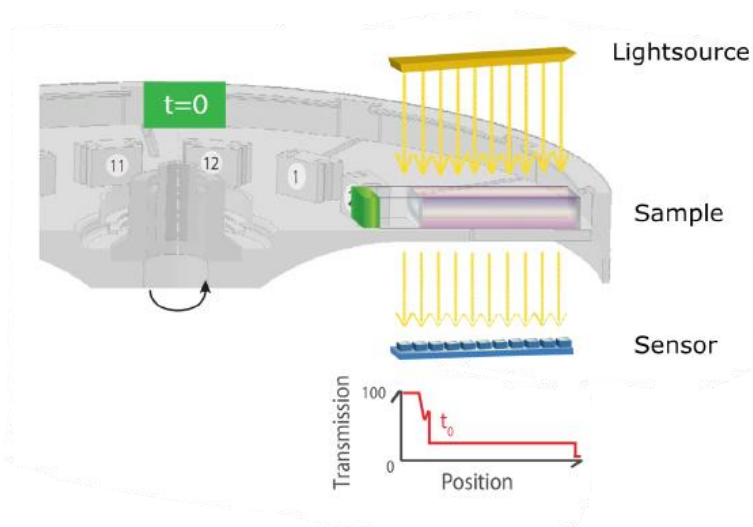
Figure 3.3 Initial situation in a LUMiFuge® stability analyser[96].

As can be easily imagined, the transmission is higher where dispersed droplets concentration is lower: this means that physical instabilities can be detected and distinguished depending on the transmission trend recorded during the analysis. Once the device is activated, the rotating body starts to impose a centrifugal acceleration on the samples, resulting in the acceleration of possible physical instability phenomena (*Figure 3.4[96]*).
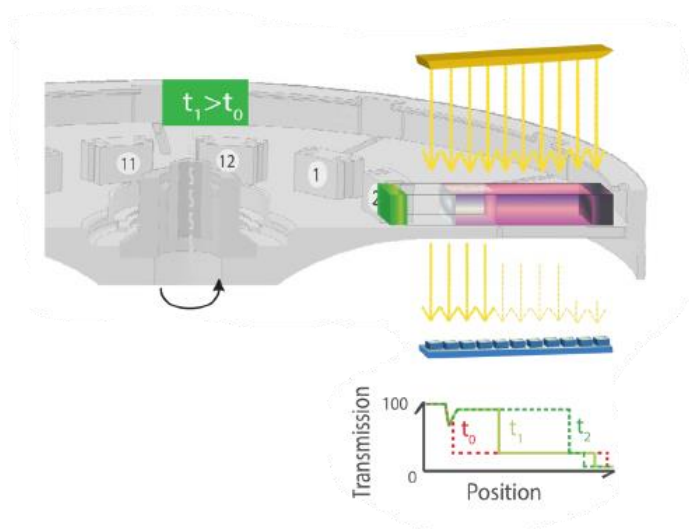
Figure 3.4 Typical evolution of the sample during a stability analysis performed with LUMiFuge®.

As the analysis proceeds, the transmission profiles (expressed as percentage transmission versus the position along the axis of the sample) are collected instant after instant, stored on a pc equipped with a proper software (SEPView®) and superimposed on the same chart. This enables the user to monitor the genesis and evolution of any possible phase separation: in fact, following the transmission profiles from the oldest to the most recent, it is possible to understand how the distributed droplets concentration has changed along the axis of the sample in time.

As anticipated previously, the typical output of the analysis just described is a sort of time-lapse picture, where each type of physical instability can be detected and distinguished.

Figure 3.5 shows the characteristic evolution of the transmission profile for an instable emulsion undergoing sedimentation: as time proceeds, dispersed droplets tend to concentrate towards the bottom of the sample, reducing the transmission capability in this region; on the other hand, the upper portion of the sample experiences a reduction in the concentration of the dispersed phase, resulting thus in increased light transmission. For the sake of clarity, note that green lines refer to the latest profiles, while red ones are the oldest in time.
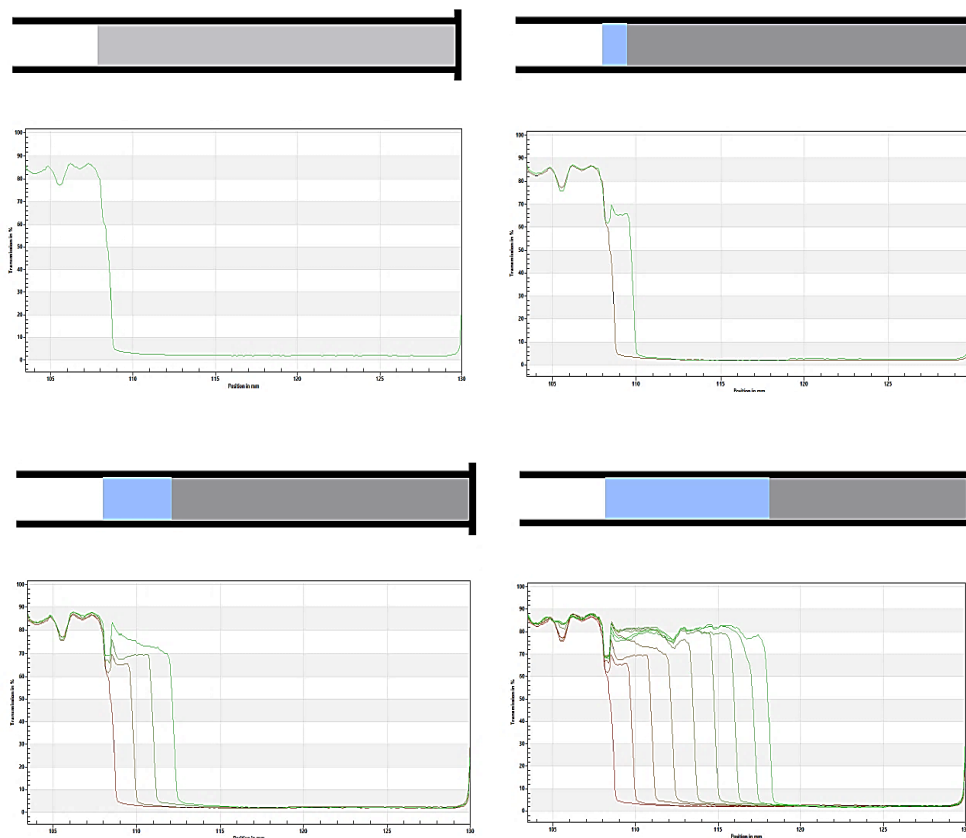
Figure 3.5 Evolution of sample aspect and transmission profiles during sedimentation of dispersed droplets in an emulsion undergoing centrifugation in LUMiFuge®[96].

It is possible to observe how the transmission profile appears to slide rightward during the analysis time in *Figure 3.5*; more in general, the profile moves in the same direction of the dispersed droplets when an instability phenomenon is going on.

In other words, if curves are shifted towards right (coinciding with the bottom of the sample), sedimentation is taking place; on the opposite, creaming can be detected when an apparent leftward movement of the profile is observed. Since the lecture of the obtained time-lapse picture can be sometimes tricky, it is always fundamental to compare the observed profiles evolution with a visual inspection of the sample; for this reason, photos of each sample were collected after every LUMiFuge® run to confirm what inferred from the charts.

The typical final output of a LUMiFuge® analysis can be observed in *Figure 3.6[96]*: consistently with the above description, sedimentation and creaming can be inferred from the left and right chart, respectively.
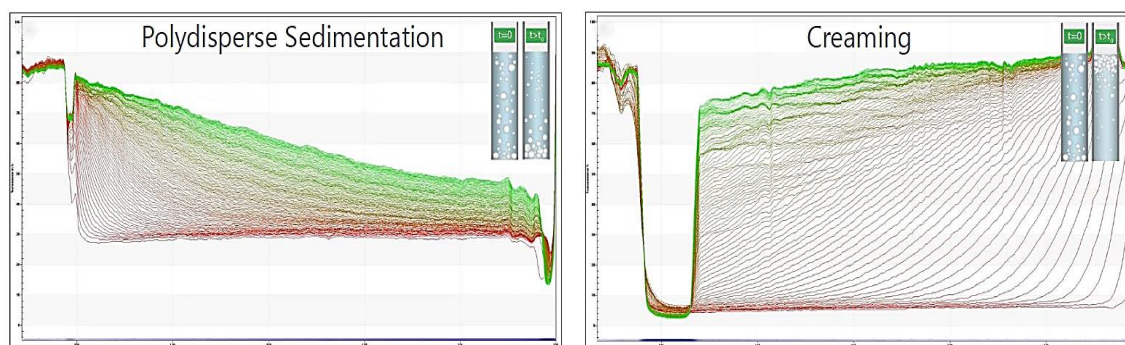
Figure 3.6 Final time-lapse picture of a LUMiFuge® analysis for two different samples undergoing sedimentation and creaming, respectively.

Notice that sensors resolution allows to detect changes in the position of an interface with a resolution as small as 100 μm[94]: this means that the kinetics and degree of phase separation can be traced with high promptness and precision.

During the present thesis project, two different experimental protocols were applied using LUMiFuge® LF 110:

- *Protocol A*, consisting of a 6h run at ambient temperature and 4000 rpm. This procedure was applied to the most interesting formulas able to resist the laboratory centrifugation without showing instability signs;
- *Protocol B*, more severe and applied only to the most promising alternatives in the final phase of the laboratorial step. This procedure included 15h of centrifugation at ambient pressure and 4000 rpm.

In order to determine a reliable scale for the results of the stability test using LUMiFuge® LF110, the samples of the original formulations were analysed too and considered as reference: any sample which proved to be as stable as the benchmark or more stable than the latter in both protocols, was labelled as stable towards physical instabilities.

Additional details regarding the quantitative assessment of formulations stability are supplied in chapter 4, when the analysis of the results obtained at laboratory scale is discussed.

3.2.c Chemical stability of the emulsion

During shelf-life, cosmetic emulsions can experience chemical aging phenomena affecting different aspects of the product: changes of colour, texture and even smell often verify, making the sale product potentially unpleasant for the consumer. In addition, the product can experience several temperature conditions once it exits the manufacturing place, and these further affect the above-mentioned ripening process.

Such instability is not gravity-driven, as in the previous case, but rather based on the chemical nature of the various substances found in the formulation: chemical incompatibilities between ingredients is often figured out only over the days and months following the synthesis of the emulsion. For this reason, cosmetic formulations are generally interested by stability studies aimed at detecting any possible structural and visual change affecting them; these are often performed in parallel under different condition: high temperature storage is used to accelerate aging, while refrigerated samples are useful to investigate if any crystallization phenomenon takes place inside the bulk of the emulsion.

Even if the starting point of the present experimental work is represented by well-established formulations, storage protocols at three different temperatures were defined and followed for each alternative version of the original emulsions.

In the specific, the following procedures were considered and monitored in parallel over a six-month period:

- *Room temperature storage*, at approximately 25 °C;
- *High-temperature storage*, in a laboratory oven kept at 40 °C to accelerate aging phenomena taking place in the bulk;
- *Refrigerated storage*, in a refrigerator at 4°C to investigate whether crystallization takes place.

It is important to remember that a cosmetic emulsion must be both physically and chemically stable: this means that only those alternatives presenting no issues neither in the centrifuges, nor during the storage period, were considered as possible alternatives for the marketing.

3.2.d Qualitative parameters

As hinted previously, visual appearance and texture are key parameters when dealing with cosmetic formulations: they represent the first contact between the product and the consumer, often defining the market success of the former.

Several parameters can be considered in this sense, but some of them are particularly significant for the consumer when it comes to defining whether the cosmetic product meets the expectations. In particular, the following aspects has been considered for the visual and sensorial evaluation of the produced emulsions:

- the *colour* and *brightness* of the emulsion, fundamental for the appearance of the final product. Note that the original formulations are characterized by a particular eye-catcher sparkling white appearance, ensured by the presence of polyacrylic thickeners;
- the so-called *pilling effect*, particularly annoying for the consumer and characterized by the formation of small and sticky clusters on the surface of the skin upon the application of the cosmetic product. Such phenomenon is usually linked with the presence of polymers, both synthetic or bio-based, able to form a thin film on the surface of the skin[49]: when the product is spread on the skin surface, the film is rubbed and clusters are formed;

Figure 3.7 Typical example of pilling effect on the hand skin[97].

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[49] These polymers are known as film-forming ones, and they are crucial in the development of water-resistant formulations, for example in the sun care segment.

- the undesired *whitening effect*, typical of rich formulations like creams and ointments and given by a slow adsorption of the cosmetic onto the surface of the skin.

All the above-mentioned aspects were carefully investigated for each formulation by the author of this project itself, together with three experts with pluriannual experience in the field of skincare formulations.

4. Laboratory scale

Once defined the aim of the project, its starting point and the experimental protocols to be followed throughout the entire deployment of the work, the focus moved into the practical realization of several alternative formulations for the substitution of polyacrylic thickeners in the products under investigation.

Chapter 4 presents in detail this experimental path, starting from the definition of the experimental apparatus and the considered possible bio-based thickeners, to proceed then with an in-depth analysis of the various alternative formulations synthesized and the relative performances. It is important to mention how not all the biopolymers previously presented (sections 2.2 and 2.3) were considered as raw material for the study: in fact, only those alternatives able to potentially give the desired results were taken into account; section 4.1 deals with this crucial aspect.

The final paragraph of the chapter is dedicated to the selection of those alternatives able to better replicate the performances of the original formulations, considering the benchmarks described in section 3.2.

4.1 Materials and methods

Before starting the practical synthesis of different formulations, it was necessary to define the experimental set-up and the synthetic procedure to follow for each of the two products objects of the study.

Since the original formulations have been produced for many years at manufacturing scale without significant issues, the ongoing synthetic methods have been considered as standard for the current discussion. Nonetheless, no information were available for what concerned the addition of some new natural-based polymers: for this reason, the experimental procedures were modified, thanks to information provided in the literature[62],[63],[66],[83],[84], to best assist the introduction of this new substances. Note that these procedures have been kept as simple as possible to facilitate their future application at manufacturing level[50], and so to get a good scalability of the process.

4.1.a Selection of raw materials

As anticipated above, not all the existent biopolymers are able to give the performances, both in terms of thickening effect and texture, required by the project under investigation. This means that a first selection phase was necessary to define those natural-based thickeners potentially capable of substituting polyacrylic molecules.

Such selection was performed starting from literature data about the application of different biomolecules in food and cosmetic emulsions[62],[63],[66],[83],[84]: depending on the results and hints listed in these studies, it was possible to understand which polymers are most suitable to thicken the considered formulations without negatively affect the final texture of the product.

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[50] This is a fundamental aspect when dealing with an industrial reality: every step of the synthetic procedure must be thought remembering that an industrial-scale production must be performed; in other words, what is convenient at laboratory scale, could be difficult or even impossible to realize at manufacturing scale.

In such situations, the following heuristic rule can be considered: when defining an industrial procedure, the fewer steps, the better the result.

In this sense, it must be considered that several biopolymers are known to result in an unpleasant sticky and jelly-like texture of the final product, especially when their percentage in the emulsion becomes significant; an example is Xanthan gum, which percentage of application was never higher than 0.5% to avoid unpleasant gelatinous appearance of the final product.

Nonetheless, various natural-based thickeners show film-forming properties, possibly resulting in massive pilling effect: such polymers, like some modified cellulose[51], have not been considered as main thickeners in the current work to avoid annoying pilling.

Again, several natural thickeners, especially plant-based ones, are not as white as polyacrylic powders: this tends to result in opaque and brownish translucent gels, that in turn give rise to slightly yellowish emulsions, something particularly undesired considering that the sparkling white appearance is a distinctive character of the original product to be replicated. Such aspect was decisive in limiting the percentage of Tara gum to 2%, since this bio-polymer is known to produce off-white to yellowish emulsions for higher concentrations[62].

In addition, marine polysaccharides were not considered as valuable alternatives to polyacrylates in the investigated formulations: in fact, such biopolymers are used to form brittle gels, resulting thus in too high viscosities also for the nourishing pot cream.

Finally, some valuable natural-based thickeners were discarded because of their stock price: this was the case of a sodium carboxymethyl starch, coming from potatoes, particularly promising but economically unbearable for the formulations under investigation. The same was true for other two INCI names: "Cellulose gum, Xanthan gum, microcrystalline Cellulose" and "Xanthan gum, Sclerotium gum, Algin", whose price exceeds 100€/kg.

Thanks to the decision-making process detailed above, a few natural and natural-modified polymers (both pure and in mixture) were selected as raw material for the experimental phase of the project; they are listed in the following considering the INCI name corresponding to the commercial product effectively applied[52]:

- *Caesalpinia Spinosa* (Tara) gum (below 2%);
- *Xanthan* gum (below 0.5%);
- *Acacia Senegal* gum and *Xanthan* gum;
- *Cellulose* gum;
- *Cetyl-hydroxyethyl cellulose*;
- *Dehydroxanthan* gum;
- *Hydroxypropyl starch phosphate*;
- *Sodium carboxymethyl starch.*

Such substances were used both as individual thickeners and in combination, in order to find and exploit any possible synergic effect between them.

It is worth mentioning that when the same compound was available from several producers, all the alternatives were tested and, if no differences were highlighted, the cheapest one was selected as raw material for the present study.

All the alternative formulations created starting from these polymers are listed and detailed in section 4.2.a and 4.2.b for the moisturizing lotion and the nourishing body cream, respectively, together with their physico-chemical and textural characterization.

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[51] In this regard, an exception was made for cetyl-hydroxyethyl cellulose: the latter is recommended to be applied in combination with cellulose gum, to exploit their synergistic effect; since the required percentage of application was extremely low, such polymer was considered as valuable alternative despite being film-forming.

[52] Such decision was taken to identify univocally the applied substances, since the commercial name associated to each INCI name changes depending on the specific provider, while the INCI itself refers to a specific compound or mixture of compounds.

4.1.b Experimental apparatus

All the laboratory trials were carried out exploiting the same experimental set-up, which was designed to be easily replicable and able to minimize raw material wastes associated with the synthesis. In this sense, 0.300 kg was selected as the correct amount of formulation to ensure material for all the after-synthesis analysis while limiting the overproduction of product associated with the early research steps.

The components of the experimental apparatus are hereinafter detailed:

- One 400 ml tempered glass beaker, used to mix the aqueous phase and interested by the addition of the oil phase for the formation of the O/W emulsion. For this reason, it will be referred to as *main beaker* in the following;
- One 300 ml tempered glass beaker, in which the oil phase was mixed and melted before being added to the main beaker;
- One heated magnetic stirrer for the pre-emulsion treatment of the oil phase;
- One heated plate to increase the aqueous phase temperature up to 75 °C, set as reference temperature for both phases to begin the emulsification process. Note that, while being heated, the aqueous phase was kept under mixing thanks to a mechanic stirrer (ARGOlab AM 20-D) equipped with a u-shaped stainless-steel paddle;
- A laboratory turboemulsor, Silverson L5T, needed to finally get the formation of the desired emulsified product. In the specific, the turboemulsor was equipped with a specific perforated stator, able to favour the formation of emulsions[53].

As already mentioned above, all the experimental trials were interested by the specific set-up just detailed, with the aim of minimizing the influence of those external variables possibly affecting the results of each test. In this way, the final performances of the alternative formulations could be easily compared.

Some pieces of the experimental apparatus are shown in hereinafter (*Figure 4.1* and *Figure 4.2*).
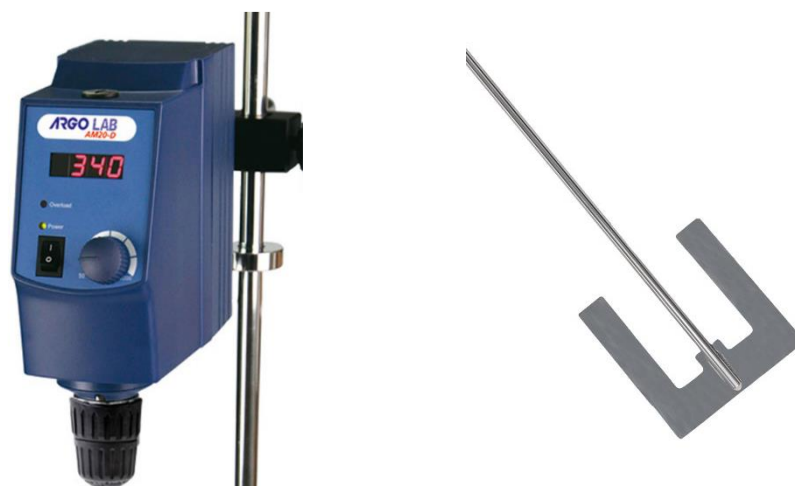
Figure 4.1 Mechanic stirrer ARGOlab AM 20-D (left) and the u-shaped stainless-steel paddle (right) mounted to kept the aqueous phase under mixing.

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[53] The perforated stator is indicated for the synthesis of emulsions since its circular mesh is able to guarantee the formation of micrometric dispersed droplets.
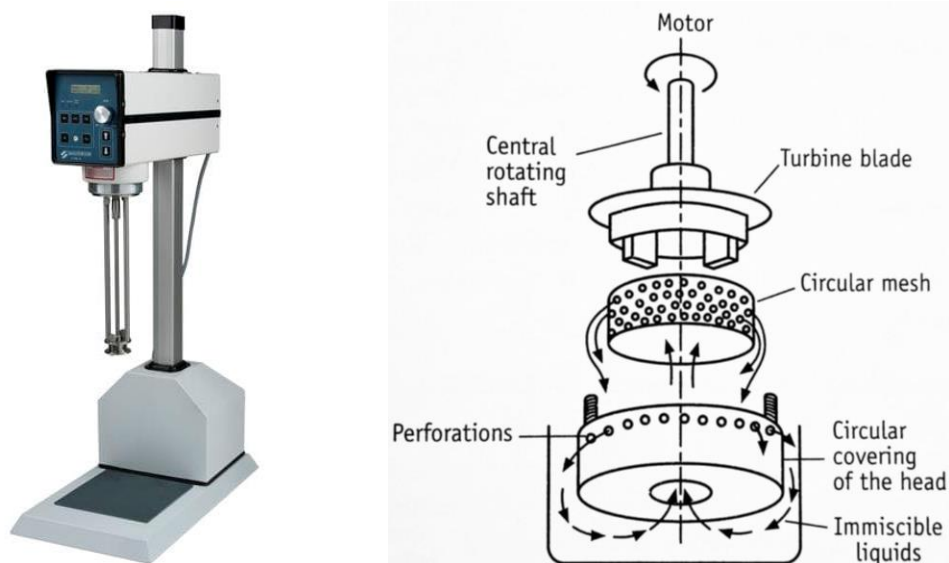
Figure 4.2 Silverson L5T turboemulsor (left) and a particular about its functioning when the perforated stator is applied (right).

4.1.c Experimental procedure

As done for the experimental apparatus, a precise and easily reproducible experimental procedure was defined prior to the beginning of the laboratory trials, for both formulations.

Such procedure has been defined considering the chemical nature of the substances undergoing processing and the desired final result, together with pieces of information coming from literature about the production of similar bio-thickened cosmetic emulsions. Nonetheless, the support and tips given by the experts of the laboratory staff, who developed the original formulations on their own, was fundamental to understand the behaviour of each substance and the best way to process them.

Since both the investigated emulsions are of O/W type, the main idea behind the experimental procedure is the same: the water phase is prepared and heated under continuous stirring in the main beaker, while the oils mixture is melted in a second beaker. When both the mixtures reach the correct temperature for the emulsion process to begin, the oil phase is slowly poured into the main beaker, while the turboemulsor is switched on.

Once the emulsion is formed, the cooling phase begin note that the product is kept under agitation thanks to the mechanical stirrer during this step, so to ensure thermal uniformity in the bulk and avoid the formation of clumps on the internal surface of the beaker. When the temperature falls below 35 °C, thermolabile substances (like fragrances and vitamins) are added.

Even if the experimental procedure is similar for both the emulsions, some differences still exist because of the nature of the specific substances present in each formulation; for this reason, the detailed experimental procedure followed for both products is shown hereinafter.

Note that the procedure will be the same for the 5kg and 50kg turboemulsor (chapter 5), even if some minor adjustment will be made in both cases in order to adapt the protocol to the mechanical reality of these machines.

Moisturizing lotion

The moisturizing lotion was synthetized following step by step the procedure shown hereinafter:

I) Start from the pre-dispersion of hard-to-disperse powders (Tara gum, Xanthan gum, sodium hyaluronate, magnesium aluminium silicate) in the emollients of the aqueous phase, namely glycerine, propylene glycol, pentylene glycol and sorbitol. This pre-dispersion phase, realized in the main beaker, facilitates the dispersion of the above-mentioned powders in water while avoiding the formation of jelly clusters, typical of the direct hydration of natural gums when they are present;

II) Add the totality of water, start heating and keep under vigorous mixing (150-180 rpm) with the mechanical stirrer, thus breaking any possible cluster present in the liquid mixture;

III) When a translucent and brownish gel is observed, hydration is complete: add the rest of ingredients of the aqueous phase and reduce the mixing velocity (90-100 rpm) to avoid massive aeration of the forming gel;

IV) In a second beaker, melt the ingredients of the oil phase, while keeping under agitation[54] using a magnetic stirrer;

V) Add the ingredients of the preservative system to the main beaker;

VI) When the temperature of both phases reaches 75 °C, the emulsification process can take place: drop the turboemulsor in the main beaker, set it to 2700 rpm and slowly pour the oil phase. Keep stirring for 3 minutes: at this point, the emulsion should appear shiny and smooth;

VII) Add the aluminium starch octenylsuccinate and mix vigorously with the mechanical stirrer (180-200 rpm);

VIII) Leave to cool under mixing to avoid the formation of clumps. When the temperature drops below 35 °C, add the thermolabile ingredients;

IX) Once reached 25 °C, perform all the post-synthesis analysis required (centrifuge, pH, viscosity)

Further variation to the procedure can be present when working with specific natural-based thickeners; such details will be discussed case by case in the following chapter.

Nourishing body cream

The procedure is similar to the one just described for the moisturizing lotion:

I) Start from the pre-dispersion of hard-to-disperse powders (Tara gum) in the emollients of the aqueous phase, namely glycerine, pentylene glycol and propanediol with the addition of 10% of the total water;

II) Add the rest of water, start heating and keep under vigorous mixing (180-200 rpm) with the mechanical stirrer, thus breaking any possible cluster present in the liquid mixture. The gel formed in this case is extremely thick: if necessary, use the turboemulsor (1000 rpm) to facilitate its hydration;

III) When a brownish and brittle gel is observed, hydration is complete: add the rest of ingredients of the aqueous phase and reduce the mixing velocity (90-100 rpm) to avoid massive aeration of the forming gel[55];

IV) In a second beaker, melt the ingredients of the oil phase, while keeping under agitation using a magnetic stirrer;

V) When the temperature of both phases reaches 75 °C, the emulsification process can take place: drop the turboemulsor in the main beaker, set it to 2700 rpm and slowly

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[54] Continuous agitation is fundamental during heating and cooling phases, since it guarantee thermal uniformity of the bulk and rapid heating or cooling by increasing mass transfer coefficients.

[55] As a result of the extreme thickness of the gel formed, air is unavoidably incorporated: this is one of the main criticism of this product.

pour the oil phase. Keep stirring for 3 minutes: at this point, the emulsion should appear shiny and smooth;

VI) Leave to cool under mixing to avoid the formation of clumps. When the temperature drops below 35 °C, add the thermolabile ingredients and the preservative system;

VII) Once reached 25 °C, perform all the post-synthesis analysis required.

As in the previous case, further variations come depending on the specific biopolymer applied in the formulation.

4.2 Results: analysis and discussion

The current section is meant to present, analyse and discuss from a critical point of view the results obtained in the laboratorial synthesis conducted.

The idea is to consider all the experimental trials for both formulations, together with the evaluation of their performances and the related cost: in this way, the reader is driven through the scientific process that took from the first trial to the optimal option, thus being able to understand the techno-economic reasons behind each further adjustment.

For the sake of clarity, the different trials are classified depending on the product (moisturizing lotion, F, or nourishing body cream,V) and further subdivided into experimental campaigns depending on the specific biopolymer considered as main rheological modifier in lieu of the polyacrylic additive. Thus, each set of trials has a dedicated sub-section labelled as "*Trial series Fi*" for the lotion and "*Trial series Vj*" for the pot cream. Again, each alternative formulation is presented starting from the percentage composition of the chosen bio-based thickener, and then analysed for what concern the study benchmarks described in chapter 3.

4.2.a Moisturizing lotion

The results regarding all the experimental trials on the moisturizing lotion are shown hereinafter, following the scheme previously detailed.

Trial series F1: Tara gum (alone)

The first experimental trial was realized applying Tara gum as unique rheological additive in turn of Carbopol 940: since no experimental data were found regarding similar test campaigns, the percentage of application of the biopolymer was chosen starting from data about other natural-based thickeners commonly applied in cosmetic, such as Xanthan gum.

Table 4.1 shows the obtained results for the two alternatives of the considered trial series.

Trial	% Tara gum	pH_0[56]	pH	Additions	Viscosity[57] [cP]	Qualitative[58]	Centrifuge		
F1.1	0.50	5.54	5.54	-	2560	✓	✓	✕	-
F1.2	0.70	5.78	5.57	0.16g LA[59]	11420	✓	✓	✓	✓

Table 4.1 Trial series F1: composition and results.

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[56] pH value at the end of the synthesis, before being adjusted to fit the desired range specified in section 3.2.a.
[57] The viscosity was measured as specified in section 3.2.a.
[58] "Qualitative" stands for texture and appearance (qualitative parameters detailed in section 3.2.d.).
[59] LA stands for lactic acid (80% aqueous solution), the chemical compound used in this experimental project to adjust downwards the pH value of the synthetized emulsions.

As it can be easily seen, Tara gum alone has proved unable to meet the desired specification in terms of final viscosity, even if applied in a quite high concentration if compared to Carbopol 940 in the original formulation (0.20%). In addition, no pilling or whitening effect were observed, and the appearance and texture of the product was good, even if not so close to the original one.

Nonetheless, this biopolymer showed a significant more-than-linear increase in the thickening capability going from 0.50% to 0.70% concentration: such behaviour is observed also in literature[62] for concentration higher than 0.6%, and makes Tara gum particularly suitable as rheological additive.

The first trial series was suspended because of the incapability of Tara gum to sharply control the viscosity of the final product: as a result of the exponential behaviour highlighted above, it is extremely difficult to tune the biopolymer content to stay in a viscosity range as sharp as the one of the considered lotion.

In addition, Tara gum shows higher economic impact with respect to Carbopol 940, since the cost of the former is almost five times higher: this aspect strongly limits the application percentage of Tara gum. Nonetheless, such bio-thickener still appeared extremely promising for the purpose of this thesis project: further trials have been conducted using Tara gum in combination with other natural based additives (Trial series F4 and F6), thus exploiting possible synergies while reducing the cost associated to the alternative formulation.

Trial series F2: Xanthan gum

Xanthan gum was selected as natural based biopolymer for the second trial series: despite being commonly applied in the cosmetic industry as rheological additive[84], it is often applied in combination with polyacrylates and never as main rheology modifier. *Table 4.2* resumes the composition of the experimental trials belonging to the investigated series, while *Table 4.3* shows the related performances.

Trial	% Xanthan gum	% Glyceryl stearate citrate[60]	% Cetearyl alcohol
F2.1	0.50	As original	As original
F2.2	0.50	+ 0.50	+ 1.40

Table 4.2 Trial series F2: composition.

Trial	pH_0	pH	Additions	Viscosity [cP]	Qualitative	Centrifuge		
F2.1	5.83	5.50	0.17g LA	4960	✕	✓	✓	✓
F2.2	5.70	5.52	0.10g LA	6680	✕	✓	✓	✓

Table 4.3 Trial series F2: results.

As in the case of Tara gum, Xanthan gum proved to be unable to ensure the desired viscosity, even if added at higher percentage with respect to the polyacrylic thickener. In order to assess if an increased grease content could help in reaching the desired result, the concentration of cetearyl

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[60] Note that the concentration of those ingredients already present in the original formulation is expressed as variation with respect to their original percentage content.

alcohol (consistency factor) and glyceryl stearate citrate (emulsifier) were raised, but no satisfactory results were obtained.

In addition, Xanthan gum turned out to result in unpleasing jelly appearance and sticky behaviour when applied at the considered concentration, making the final product completely different from the emulsion to be reproduced.

For these reasons, trial series F2 was discarded. Anyway, Xanthan gum proved optimal stabilization capabilities, making it particularly suitable to be blended with other biopolymers (trial series F3, F4 and F6).

Trial series F3: Cellulose gum

Cellulose gum was applied in combination with different biopolymers in the attempt of reproducing the performances and skin feel of the original formulation. The composition and performances shown by the resulting emulsions are detailed in *Table 4.4* and *Table 4.5*, respectively.

Trial	% Cellulose gum	% Cetyl-hydroxyethyl cellulose	% Xanthan gum	% Glyceryl stearate
F3.1	0.40	0.30	0.00	As original
F3.2	0.60	0.00	0.40	+ 2.00
F3.3	0.50	0.00	0.30	+ 1.60
F3.4	0.50	0.00	0.30	+ 2.00

Table 4.4 Trial series F3: composition.

Trial	pH_0	pH	Additions	Viscosity [cP]	Qualitative	Centrifuge		
F3.1	5.81	5.57	0.16g LA	10800	✕	✓	✓	✓
F3.2	5.81	5.56	0.17g LA	22960	✕	✓	✓	✓
F3.3	5.64	5.57	0.03g LA	12600	✓	✓	✓	✓
F3.4	5.60	5.60	-	13200	✓	✓	✓	✓

Table 4.5 Trial series F3: results.

As it can be observed in *Table 4.5*, neither formulation F3.1, nor formulation F3.2, were found adequate from the qualitative point of view: the former was interested by massive pilling effect, probably due to the presence of cetyl-hydroxyethyl cellulose (film-forming agent), while the latter showed jelly-like behaviour as a result of the high percentage of Xanthan gum.

Anyway, the combination between Cellulose gum and Xanthan gum turned out to be adequate in terms of thickening performance, leading thus to additional experimental trials based on this biopolymers blending. Formulations F3.3 and F3.4 were interested by further adjustment to the oil phase, but neither of the two was able to guarantee a viscosity value inside the desired range. As a result of this, the current trial was interrupted.

Nonetheless, since the above-described formulations showed quantitative features quite close to the desired ones, formulation F3.4, the most pleasant of the series from a qualitative point of view, was selected to undergo further stability analysis using LUMiFuge® LF110.

Such analysis was first performed according to protocol A (section 3.2.b – LUMiFuge® stability analyser), to which the sample resist without showing any instability sign; at this point, the analysis was performed again according to protocol B, more stressful and able to highlight even the smallest instability tendency.

The results of this second analysis are reported in *Figure 4.3*.
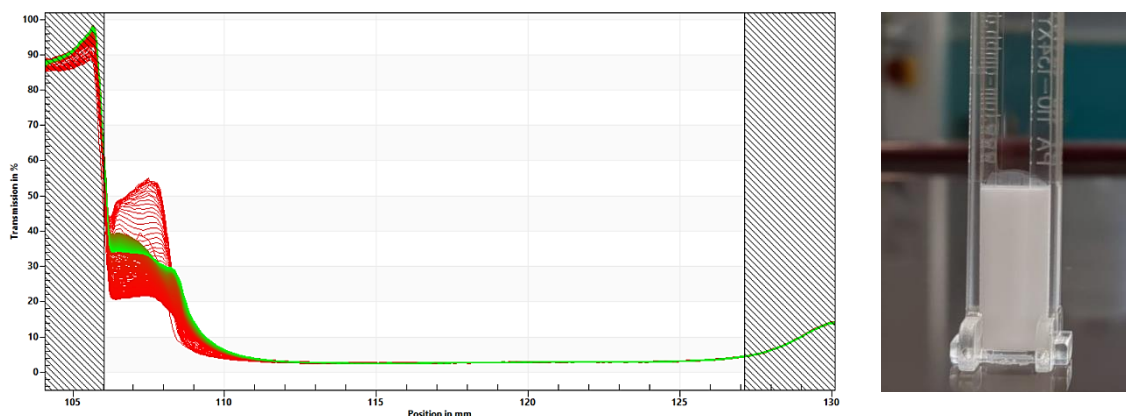
Figure 4.3 Results of the stability analysis conducted on formulation F3.4 using LUMiFuge® LF110: the left image shows the typical output chart of the analysis, while on the right a photo of the sample, taken just after the centrifuge cycle, can be observed.

It is possible to notice how a minor instability can be observed in the upper section of the sample: in fact, after an initial decrease in the percentage light transmission due to the meniscus accommodation (rarefied red curves), the trend shift upwards again. This means that a small portion of oil was able to separate and migrate towards the upper section of the sample, thanks to its lower density with respect to the emulsion.

Anyway, the instability index[61] associated to the investigated formulation (0.013) turned out to be even smaller than the one referring to a sample of the original formulation (0.017) taken from a pack ready to be marketed. Since no problem regarding the stability of the original product were notified during the last five years, formulation F3.4 was labelled as stable, with an estimated life[62] span of twelve months after opening.

In addition, it is fundamental to underline that no sign of the above-mentioned instability could be detected from a visual inspection of the sample, as can be observed in *Figure 4.3*: this clarify the accuracy and resolution of LUMiFuge® stability analyser. In any case, the direct visual inspection of the sample remains a fundamental step to validate the results of the analysis, especially for what concern the initial stance of the meniscus.

For this reason, each sample was subjected to accurate inspection to the naked eye; in the following, the result of every stability analysis will come with the photograph of the investigated sample just after the centrifuge cycle.

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[61] Parameter, ranging between 0 and 1, able to describe the tendency towards the formation of physical instabilities during the entire length of the analysis; usually, values of the instability index lower than 0.025 are considered as referring to noise floor, not suggestive of real instabilities.

[62] Being more stable than the original product, the investigated formulation is considered able to resist instabilities at least for the same period of time as the former.

Trial series F4: Tara gum (blended)

Trial series F4 began with the idea of developing the huge potential exhibited by Tara gum in the first experimental series: the aim was to discover possible synergies resulting from the application of such gum with other biopolymers with promising features, possibly leading to the fulfilment of the desired quantitative and qualitative specification.

All the alternatives tested are detailed in *Table 4.6*: as it can be seen, differently from trial series F2 and F3, the oil phase was left unaltered during the current experimental campaign; *Table 4.7* resumes the performances of each alternative formulation.

Trial	% Tara gum	% Xanthan gum	% Acacia Senegal gum
F4.1	0.15	0.00	0.45
F4.2	0.80	0.20	0.00
F4.3	0.50	0.10	0.00

Table 4.6 Trial series F4: composition.

Trial	pH_0	pH	Additions	Viscosity [cP]	Qualitative	Centrifuge		
F4.1	5.71	5.52	0.12g LA	5080	✓	✓	✓	✓
F4.2	5.70	5.59	0.04g LA	27400	✗	✓	✓	✓
F4.3	5.80	5.59	0.13g LA	12520	✓	✓	✓	✓

Table 4.7 Trial series F4: results.

Acacia Senegal gum, applied in formulation F4.1, proved unable to boost the performances of Tara gum, even if the two biopolymers were blended according to the optimal ratio recommended by the raw material supplier. This result in highly low viscosity, extremely far from the desired rheological behaviour.

Better results were obtained adding a small percentage of Xanthan gum, which turned out to act synergically with Tara gum for what concern the thickening performances of the biopolymer; nevertheless, formulation F4.2 was characterized by unpleasing clumpy consistency, something not acceptable for the consumer.

The percentage of application of Xanthan gum was further adjusted in formulation F4.3, resulting in a pleasant touch and soft skin feel, even if the viscosity of the product was still below the lower bound of the goal range.

It is important to mention that each of the three alternatives proved optimal stability under centrifugation, also when subjected to LUMiFuge@ stability analyser according to protocol A only.

In general, the considered trial series confirmed the huge potential of Tara gum as replacement for polyacrylic thickeners; in addition, the synergic effect of Xanthan gum and Tara gum was noticed, and it was further exploited in a successive experimental campaign (trial series F6).

Trial series F5: Dehydroxanthan gum

The aim of the current trial series was to investigate the performances of Dehydroxanthan gum, a natural-modified biopolymer sold as able to guarantee the same benefits of Xanthan gum (thickening capability and emulsion stabilization) without the annoying sticky and jelly consistency typically coming from the application of the latter. From the chemical point of view, Dehydroxanthan gum is obtained by the dehydration of the corresponding natural occurring gum. The characteristics and results of the single formulation belonging to the considered experimental campaign are reported in *Table 4.8* and *Table 4.9*.

Trial	% Dehydroxanthan gum	% Glyceryl stearate
F5.1	0.30	+ 1.60

Table 4.8 Trial series F5: composition.

Trial	pH_0	pH	Additions	Viscosity [cP]	Qualitative	Centrifuge		
F5.1	5.61	5.49	0.03g LA	14800	✓	✓	✓	✓

Table 4.9 Trial series F5: results.

Formulation F5.1 showed good qualitative characteristics, namely soft and smooth skin feel and white appearance, together with a rheology similar to the one of the original formulation and a viscosity value close to the desired range. On the other hand, even if interested by the application of Dehydroxanthan gum alone and at low percentage, the high stock price of this biopolymer made the considered alternative quite heavy from the economic point of view, with an overall formulation cost almost 42% higher if compared to the base case.

Anyway, due to its great performances, formulation F5.1 was subjected to stability analysis according to both protocol A and protocol B using LUMiFuge® LF110; the results of protocol B analysis cycle are reported in *Figure 4.4*.
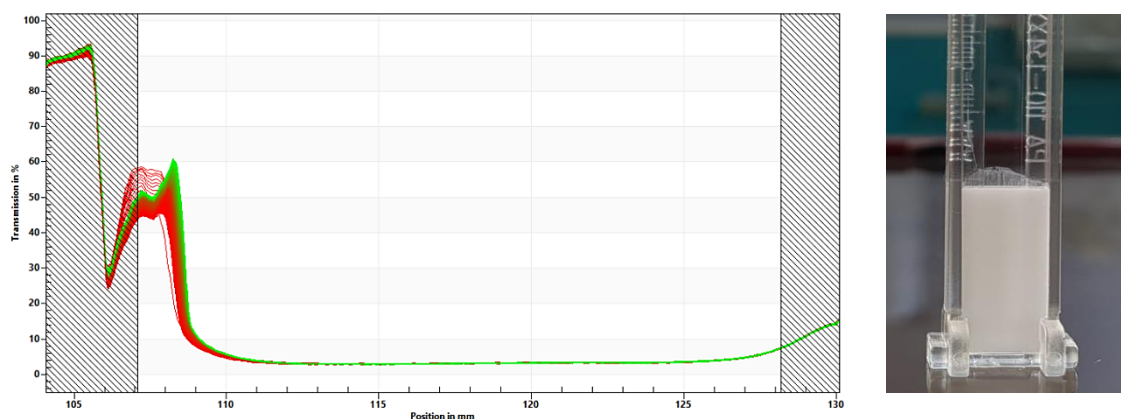
Figure 4.4 Results of the stability analysis (LUMiFuge® LF110, protocol B) conducted on formulation F5.1: time-lapse evolution of light transmission (right) and sample after the centrifuge cycle (left).

No sign of instability was highlighted during the analysis, as confirmed by the instability index associated to the investigated sample (0.018); again, the estimated life of the formulation can be supposed equal to the one of the original product (twelve month after opening).

Trial series F6: Hydroxypropyl starch phosphate

As detailed in section 2.3.b, chemically transformed starches are already known as rheology modifiers for emulsion, especially in the food industry. Trial series F6 started with the idea of testing such natural-modified polymers, in order to assess whether they are able to successfully replace traditional acrylic thickeners in cosmetic emulsions.

In the specific, a modified starch with INCI name Hydroxypropyl starch phosphate was considered as starting point for the current experimental series: composition and results related to each trial of the series are shown in *Table 4.10* and *Table 4.11*, respectively.

Trial	% Hydroxypropyl starch phosphate	% Tara gum	% Xanthan gum	% Glyceryl stearate
F6.1	1.50	0.00	0.00	As original
F6.2	1.50	0.40	0.10	As original
F6.3	1.00	0.40	0.10	+ 1.00
F6.4	0.70	0.30	0.10	+ 1.30

Table 4.10 Trial series F6: composition.

Trial	pH_0	pH	Additions	Viscosity [cP]	Qualitative	Centrifuge		
F6.1	5.74	5.59	0.11g LA	8300	✓	✓	✓	✓
F6.2	5.88	5.54	0.25g LA	19120	✓	✓	✓	✓
F6.3	5.88	5.50	0.24g LA	17800	✗	✓	✓	✓
F6.4	6.07	5.56	0.31g LA	18680	✗	✓	✓	✓

Table 4.11 Trial series F6: results.

The experimental campaign started testing the modified starch alone (formulation F6.1): the latter showed optimal characteristic from the qualitative point of view, being able to confer pleasant smoothness and a silky touch to the final product, but it was not able to guarantee the desired thickening performances.

Relying on the experience gained during the previous experimental series and on the optimal qualitative performances of the modified starch, the following formulation, F6.2, was interested by the addition of Tara gum and Xanthan gum, which proved optimal thickening and stabilizing capability. Such blend of natural polymers turned out to guarantee the desired features in the final product: in fact, the viscosity value of the investigated alternative (19120 cP) fits perfectly in the goal range (18000 ÷ 20000 cP), while the presence of the starch ensures the pleasant appearance and texture described above.

In addition, no pilling or whitening effects were observed, with a global skin feel extremely similar to the one of the original product and a comparable white colouring.

Such excellent characteristics suggested the need to deeper analyse formulation F6.2: both LUMiFuge® LF110 protocols were imposed to the sample, with promising results; the output of protocol B analysis are reported in Figure 4.5.
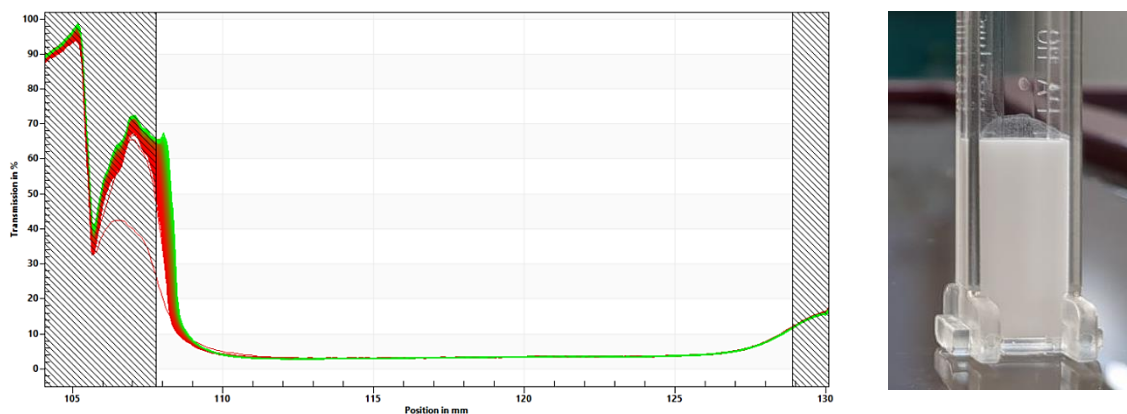
Figure 4.5 Time-lapse evolution of light transmission (right) and sample after the centrifuge cycle (left) using protocol B on LUMiFuge® LF110, formulation F6.2.

No signs of instability could be detected neither from the inspection of the light transmission trend, nor from the visual analysis of the sample; with an instability index of 0.018, also formulation F6.2 can be therefore considered as stable as the original product, with an expected life of at least twelve month after opening.

Despite the optimal performances and the proven stability, formulation F6.2 proved to be quite troublesome from the economic point of view: the biopolymers blend applied resulted in a global formulation cost 55% higher than the original product. For this reason, additional trials were made, with the aim of reducing the economic burden coming from the substitution of polyacrylates with natural-based thickeners.

This attempt of economic optimization resulted in formulation F6.3 and formulation F6.4, in which the biopolymer content was reduced in connection with the percentage increase of glyceryl stearate, a consistency factor belonging to the oil phase and much cheaper than the considered rheology modifiers. Even if both alternatives proved great from the rheological point of view, they were not perceived as pleasant on the skin[63]: formulation F6.3 resulted in massive whitening effect, while formulation F6.4 showed unpleasant clumpy consistency.

As a result of what described above, either of the attempt of economic optimization proved adequate to compete with formulation F6.2: at this point, the latter was selected as the best solution to reproduce the original product without the presence of polyacrylic thickeners.

The chosen alternative was therefore part of the scale-up phase of the project, first in the 5kg turboemulsor (section 5.1) and finally in the industrial 50kg turboemulsor (section 5.2).

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[63] The unpleasant texture of formulations F4.3 and F4.4 was mainly due to the increase in the oil phase percentage, which lead to a completely different behaviour with respect to the desired silky touch and fresh skin after-feel; for this reason, the economic optimization attempt was not successful.

4.2.b Nourishing body cream

The results related to the experimental trials on the nourishing body cream are detailed in the following, as previously done for the moisturizing lotion.

Note that the applied biopolymers are the same seen in the case of the hydrating lotion, since they proved great performances in skin care emulsions; clearly, their percentage of application will be higher, since the desired viscosity is more than doubled with respect to the previous case.

Trial series V1: Dehydroxanthan gum

Dehydroxanthan gum showed great thickening capabilities at low percentage of application when applied in the moisturizing lotion experimental campaign (trial series F5): for this reason, it was selected as first candidate for the replacement of sodium polyacrylate in the pot cream formulation.

The composition and performances of the only trial belonging to this series are reported below (*Table 4.12* and *Table 4.13*, respectively).

Trial	% Dehydroxanthan gum	% Isopropyl Myristate[64]
V1.1	1.00	+ 0.50

Table 4.12 Trial series V1: composition.

Trial	pH_0[65]	pH	Additions	Viscosity[66] [cP]	Qualitative[67]	Centrifuge		
V1.1	7.23	6.67	0.15g LA	23700	✓	✓	✓	✓

Table 4.13 Trial series V1: results.

As seen in the case of the moisturizing lotion, Dehydroxanthan gum highlighted good performances from the qualitative point of view, but its thickening capabilities were not sufficient to reach the desired viscosity range. More in general, the rheology of the obtained emulsion was far from the desired one: in the specific, flow was observed as the recipient was subjected to oscillation, and this is something undesired when dealing with pot creams.

Since the obtained viscosity value was significantly smaller than the lower bound of the goal range, the experimental trial was abandoned: in fact, the percentage of biopolymer required to reach the correct rheology would have led to an unbearable economic burden, since the stock price of Dehydroxanthan gum is almost three times higher than the one of the original synthetic thickener, sodium polyacrylate.

Thus, the project moved further, towards the testing of others natural-based polymers as main thickeners for the investigated pot cream.

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[64] As done for the moisturizing lotion, all the substances already present in the original formulation are treated in terms of percentage variation with respect to their original content in the base case.
[65] See section 3.2.a for details on the measuring procedure.
[66] See section 3.2.a for details on the measuring procedure.
[67] See section 3.2.d for details on the qualitative parameters considered.

Trial series V2: Hydroxypropyl starch phosphate

Trial series V2 started with the aim of analysing whether hydroxypropyl starch phosphate, already proved optimal in the case of the moisturizing lotion, could act as main rheological modifier also in the case of the nourishing body cream.

As it can be observed in *Table 4.14*, the considered modified starch was applied both as single thickener and in combination with other biopolymers; the performances of each trial are shown in *Table 4.15*.

Trial	% Hydroxypropyl starch phosphate	% Dehydroxanthan gum	% Tara gum	% Dimethicone[68]	% Xanthan gum
V2.1	3.00	0.00	0.00	+ 0.50	As original
V2.2	3.00	0.30	0.00	+ 0.50	As original
V2.3	3.00	0.00	0.60	+ 0.50	+ 0.10

Table 4.14 Trial series V2: composition.

Trial	pH_0	pH	Additions	Viscosity [cP]	Qualitative	Centrifuge		
V2.1	7.67	6.64	0.21g LA	16200	✓	✓	✓	✓
V2.2	7.61	6.56	0.21g LA	24200	✓	✓	✓	✓
V2.3	7.82	6.35	0.38g LA 0.40g SH[69]	45800	✓	✓	✓	✓

Table 4.15 Trial series V2: results.

The application of hydroxypropyl starch phosphate alone (formulation V2.1) didn't work as desired, since the obtained viscosity value remained below 20000 cP, extremely far from the target range (35000 ÷ 55000 cP). Neither the addition of a small percentage of Dehydroxanthan gum, in formulation V2.2, was able to guarantee the desired rheology.

On the other hand, the synergic combination of hydroxypropyl starch phosphate, Tara gum and Xanthan gum, already investigated in the case of the moisturizing lotion, proved to be extremely valuable also in the case of the pot cream. In fact, formulation V2.3 showed the desired rheology, with a viscosity value perfectly falling in the goal range, together with a pleasant texture and delicate skin after-feel; if subjected to capsizing, no flow is observed as required for pot creams. Nonetheless, its visual appearance revealed not completely adequate, since a slight yellowish colouring was observed in the synthetised bulk; in addition, the global formulation cost associated to this alternative appeared extremely high, almost 62% higher than the one referring to the original product.

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[68] The percentage value of dimethicone was increased in most of the experimental trials, since it helps to get the desired silky-soft touch.

[69] SH stands for Sodium Hydroxide (10% aqueous solution), used as pH adjuster in the current study.

Nonetheless, formulation V2.3 respected the quantitative constrain on the viscosity value, and it was therefore subjected to detailed stability analysis using LUMiFuge® LF 110; the results of protocol B can be observed hereinafter (*Figure 4.6*).
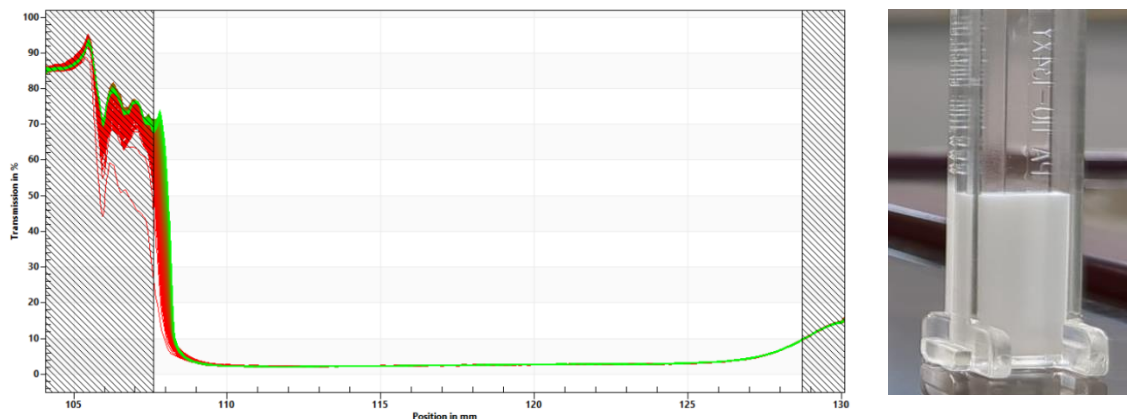
Figure 4.6 Results of protocol B analysis using LUMiFuge® LF110 on formulation V2.3: time-lapse chart (right) and sample after the centrifuge cycle (left).

The light transmission profile along the axis of the sample is nearly constant over time, meaning that no instability phenomena, like creaming or sedimentation, is taking place; such behaviour is confirmed by the visual inspection of the sample, fully integer.

The instability index associated to the investigated sample turned out to be equal to 0.017, almost equal to the one related to the marketed sample of the same product (0.0169; anyway, such values stand below the above-mentioned threshold for instability detection (0.025). As a result of this, the sample was considered as stable as the original product, able to last twelve month after the opening data.

The capability of formulation V2.3 to replicate the rheology of the original product, together with its optimal stability towards gravity-driven phenomena, made this alternative particularly interesting even if not advantageous from the economic point of view. For this reason, the investigated formulation was considered as a valuable candidate for the scale-up phase of the project, but the experimental campaigns moved forward with the aim of finding a cheaper, but equally performing, natural-based alternative.

Trial series V3: Sodium carboxymethyl starch

The following experimental campaign was based on another modified starch, namely sodium carboxymethyl starch, originally derived from potatoes and chemically transformed to ensure the desired properties as rheology modifier.

The information and results regarding the investigated trial are provided in *Table 4.16* and *Table 4.17*.

Trial	% Sodium carboxymethyl starch	% Dimethicone
V3.1	1.00	+ 0.50

Table 4.16 Trial series V3: composition.

Trial	pH_0	pH	Additions	Viscosity [cP]	Qualitative	Centrifuge		
V3.1	7.30	6.65	0.31g LA	4500	✕	✓	✓	✓

Table 4.17 Trial series V3: results.

As it can be inferred from *Table 4.17*, the considered modified starch wasn't able to guarantee the desired performances: both the rheology and the qualitative aspect of the final product strongly differed from the original one. In fact, formulation V3.1 appeared more like a liquid rather than a pot cream.

Since the obtained results proved to be extremely far from the required set of properties, no further effort to use sodium carboxymethyl starch as main rheological additive were made, and the former was labelled as inadequate for the substitution of polyacrylic thickeners in the considered formulation.

Trial series V4: Tara gum

During the experimental campaigns conducted on the moisturizing body lotion, Tara gum proved optimal thickening properties and the ability to confer a pleasant texture to the final product. For this reason, it was considered as possible rheological additive also in the case of the pot cream, giving birth to trial series V4, whose specifications and results are listed hereinafter (*Table 4.18* and *Table 4.19*).

Trial	% Tara gum	% Xanthan gum	% Cetearyl alcohol	% Dimethicone	% Glyceryl stearate[70]
V4.1	1.60	As original	As original	+ 0.50	0.00
V4.2	1.20	- 0.10	As original	+ 0.50	0.00
V4.3	1.30	- 0.10	As original	+ 0.50	0.00
V4.4	1.40	- 0.10	As original	+ 0.50	0.00
V4.5	1.00	- 0.10	+ 1.30	+ 0.50	0.00
V4.6	1.00	- 0.10	+ 1.30	+ 0.50	1.00
V4.7	1.10	- 0.10	+ 1.30	+ 0.50	2.00
V4.8	1.25	- 0.10	As original	+ 0.50	1.00

Table 4.18 Trial series V4: composition.

The first attempt of the series considered only Tara gum itself as rheology modifier, but the chosen percentage composition proved to be excessively high: the resulting viscosity exceeded 85000 cP, producing an unpleasant pasty behaviour not adequate for the product to be reproduced.

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[70] Note that glyceryl stearate is an oily consistency factor, not present in the original formulation; such product was considered after the optimal results obtained in the moisturizing lotion campaign, where glyceryl stearate made it possible to reach the desired viscosity range without changing the delicate touch of the lotion.

In the following trials (formulation V4.2, V4.3 and V4.4), the content of Xanthan gum was zeroed and the percentage composition of Tara gum was adjusted in order to meet the desired specification; optimal results were reached with formulation V4.4, characterized by a viscosity value fully fitting the goal range and a pleasant smooth and delicate touch on the skin. On the other hand, the high content of Tara gum led to a slightly yellowish colouring, quite far from the sparkling white appearance of the original product.

Trial	pH_0	pH	Additions	Viscosity [cP]	Qualitative	Centrifuge		
V4.1	7.79	6.60	0.27g LA	88000	✗	✓	✓	✓
V4.2	7.77	6.66	0.26g LA	28300	✓	✓	✓	✓
V4.3	7.75	6.55	0.28g LA	32500	✓	✓	✓	✓
V4.4	7.74	6.38	0.29g LA	38900	✓	✓	✓	✓
V4.5	7.74	6.27	0.30g LA	26050	✓	✓	✓	✓
V4.6	7.70	6.36	0.24g LA	29350	✗	✓	✓	✓
V4.7	7.43	6.24	0.27g LA	34550	✗	✓	✓	✓
V4.8	7.50	6.27	0.25g LA	35200	✓	✓	✓	✓

Table 4.19 Trial series V4: results.

Formulation V4.4 was subjected to detailed stability analysis using LUMiFuge® LF110, and the obtained results for protocol B are reported below (*Figure 4.7*).
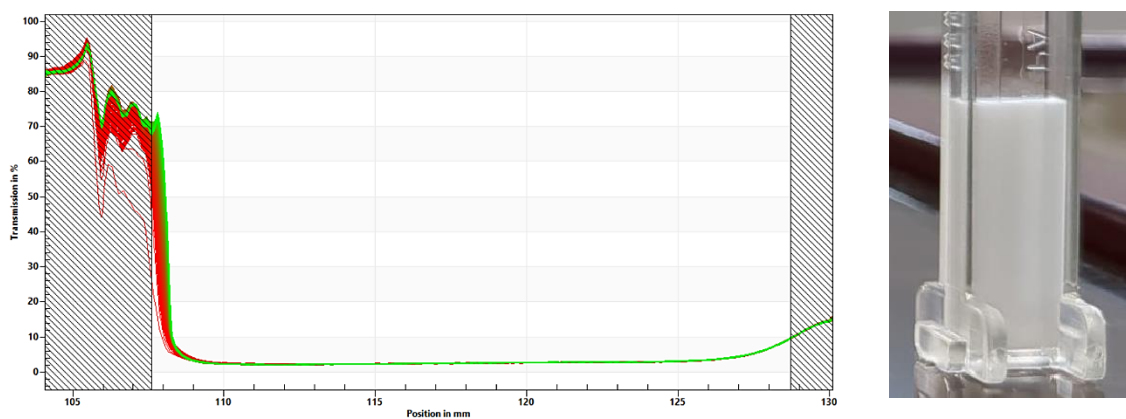
Figure 4.7 Formulation V4.4: results of protocol B using LUMiFuge® LF110 stability analyser (light-transmission evolution over time and sample after the centrifuge cycle).

As for the case of formulation V2.3, the instability index associated to the current sample amounted to 0.018, meaning that formulation V4.4 can be considered as stable as the original product; in addition, no instability sign could be detected neither from the light transmission time-lapse, nor from the visual inspection of the sample itself.

Even if the results obtained with the alternative under investigation were quite close to the desired ones, both the visual appearance and the economic burden associated to the emulsion (+ 44% with respect to the original product), were considered inadequate, leading to the need of extra trials using Tara gum.

The additional formulations were realized by adding an oily consistency factor, glyceryl stearate, able to act as a whitening agent too: this made it possible to reach the desired viscosity value while lowering the Tara gum content in the emulsion, with positive results both on the colouring and on the global cost associated to the formulation (- 5% with respect to formulation V4.4).

The last trial of the series (formulation V4.8) was able to meet the goal standards, ensuring rheological and qualitative properties extremely close to the original pot cream.

Since glyceryl stearate was extensively used in the experimental campaigns regarding the moisturizing lotion without causing any stability issue, formulation V4.8 was labelled as stable as the original product without being subjected to detailed analysis using LUMiFuge® LF110. This assumption seems quite reasonable, as formulation V4.8 differs from formulation V4.4 (stable under LUMiFuge analysis) only for what concern the percentage content of Tara gum (which is anyway quite similar) and the addition of glyceryl stearate, not influencing the stability of the emulsion. For this reason, the optimal stability proved during the classic centrifuge analysis was considered sufficient to define the emulsion as stable, considering the results regarding all the previous similar samples.

At this point, the series of experimental campaigns on the replacement of polyacrylic thickeners in the nourishing body cream was stopped: formulation V4.8 was able to respect all the given constrains, both from a physical and qualitative point of view, offering pleasant qualities combined with an easy and natural-based set of rheology modifiers. As a result of the above, formulation V4.8 was preferred to formulation V4.3, and the former was considered as the optimal candidate for the scale-up phase of the pot cream.

At this point, the laboratorial phase of the project was concluded: thanks to several experimental trials, a valuable polyacrylates-free alternative able to ensure the desired performances was found for both products, namely formulation F6.2 for the moisturizing lotion and formulation V4.8 for the pot cream. The detailed description of the production of the identified alternatives in the 5kg and 50 kg turboemulsors is presented in the following chapter.

The application of LUMiFuge@ stability analyser made it possible to detect even the slightest instabilities, ensuring that those alternatives elected for the scale-up phase of the project exhibit a shelf-life comparable with the one of the original product. Note that the results of all the analysis conducted using LUMiFuge® LF110, in terms of light-transmission profile over time and picture of the sample after the centrifuge cycle, can be visualized in the appendix (*Appendix A*).

Finally, for what concern the chemical stability of the emulsions, both alternatives proved to resist the three-month period analysis described in section 3.2.c in all the considered conditions; in the interest of time, such results were verified only after the scale-up phase described in the following, thus avoiding the temporal extension of the project to become excessive.

5. Scale-up: towards the industrial scale

The present chapter deals with the description of the scale-up phase for the production of the two formulation under investigation, moving from the laboratory scale, just described in Chapter 4, to the industrial manufacture through an intermediate step, represented by a 5kg turboemulsor.
It is fundamental to underline that such scale-up approach was adopted to describe a step-by-step path from the few hundred grams produced in the laboratory to the 50 kg obtained in the industrial turboemulsor, as usual when dealing with the industrial scale-up of emulsions[71] and, more in general, as good practice of any scale-up process. In addition, the major differences between the laboratorial apparatus and the batch turboemulsors made the first phase of the scale-up process extremely challenging; for this reason, as detailed in the following, the transition from the laboratory scale to the 5 kg turboemulsor was based on an experimental approach, while the final scale-up step leading to the 50 kg industrial turboemulsor comes with a mathematical correlation adjusted *ad hoc* for this specific case.

Before presenting the two phases of the scale-up process, both the 5 kg and 50 kg turboemulsors are described with the aim of guiding the reader through the decision-making process of this fundamental part of the project.
In addition, the end of the chapter is interested by a detailed comparison between the three different scales to assess whether the natural-thickened alternatives highlighted in Chapter 4 can be reproduced with the desired performance also at industrial scale. Those physico-chemical and qualitative parameters already described in the previous chapters represent the starting point of this final comparison between scales.
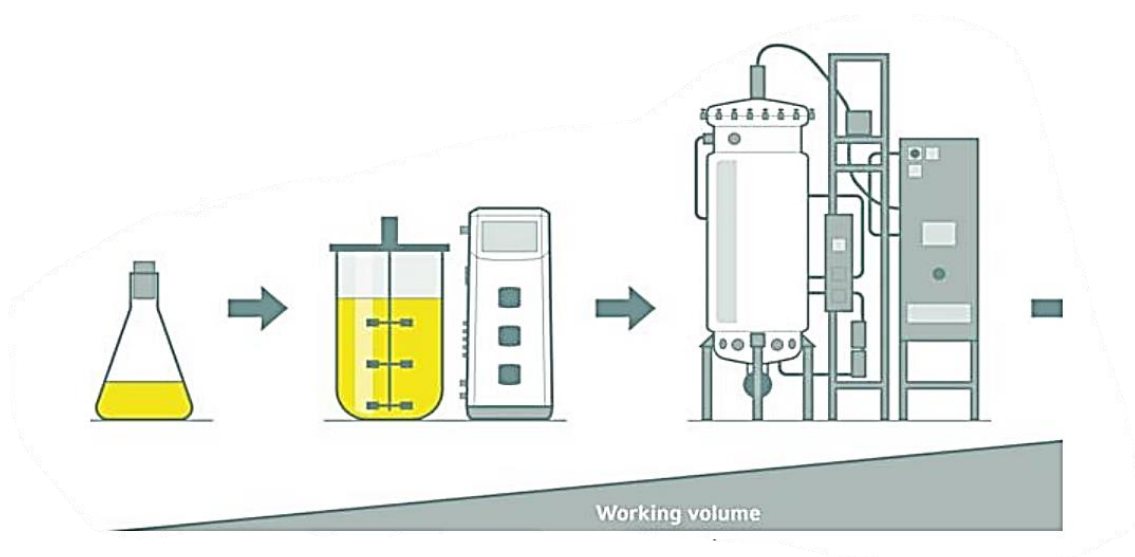
Figure 5.1 Typical layout of a scale-up path[99]: starting from the laboratory scale, where some hundreds gams are usually produced, the production moves towards the industrial manufacturing scale through the kilo-scale.

[71] More in general, all the scale-up processes in the chemical industry usually require different steps to ensure good results in the final manufacturing scale: this is particularly true when dealing with processes interested by complex mass and energy transfer phenomena, as in the case of synthetic procedures or, for example, emulsions formation.

5.1 Pilot turboemulsor (5 kg)

The first phase of the scale-up process dealt with the transition from the laboratory scale to the so-called *kilo-scale*, in this case represented by a 5 kg turboemulsor equipped with a stator-rotor mixer placed on the bottom of the cylindrical mixer and able to operate under deep vacuum condition.

As briefly anticipated above, this part of the project was extremely challenging: in fact, the experimental apparatus applied in these two scales was completely different, and this made it impossible to apply a mathematical relation for this scale-up phase. This point will be further stressed in the following, through a detailed description of the pilot turboemulsor thought to introduce the mechanical features of the kilo-scale and highlight the main differences with respect to the laboratory apparatus.

5.1.a Experimental apparatus: AXOMIX 5 (AXOMATIC®)

The specific piece of equipment applied for the transition to the kilo-scale in the current experimental work is represented by AXOMIX 5, a 5 litres mixer by AXIOMATIC® Group equipped with a homogenization turbine on the bottom of the vessel.

More in detail, AXOMIX 5 is characterized by a vertical cylindrical body, flanged and tilting to ensure ease of application during loading and unloading phases; the whole body is made of stainless steel, namely AISI316L, a special alloy applied in the chemical industry based on nickel and chromium, with a low carbon content and the addition of molybdenum[100] to guarantee optimal resistance towards corrosion and mechanical stress.

Externally, the mixer is interested by a metallic jacket covering the entire lateral and bottom surface of the vessel, enabling easy and fast cooling and heating operation thanks to cold or hot water circulating in the hollow space; in this regard, the temperature control is ensured by a contact sensor and a programmable thermostat.

Figure 5.2 External layout of AXOMIX 5 (left) and particular of the counter-rotating blades equipped with Teflon scrapers[101](right).

Moreover, AXOMIX 5 is equipped with a flanged tight lid, characterized by a silicone interlocked gasket to avoid air infiltration during vacuum operation. This aspect is particularly important, since such mixer was designed to deal with emulsions and pastes: the capability to operate under vacuum make it possible to avoid the formation of aerated bulks, something extremely annoying[72] if not intentionally sought (as in the case of cosmetic mousse, for example). In this case, vacuum is guaranteed by a liquid ring vacuum pump.

The core of the pilot turboemulsor is represented by the mixing system, designed to obtain optimal heat and mass transfer: two counter-rotating blades (*Figure 5.2*), equipped with Teflon scrapers and able to reach 120 rpm, keep the bulk under continuous agitation while the turbine on the bottom of the vessel provides the mixing energy required for the emulsion formation.
In the specific, the homogenization turbine is characterized by a stator-rotor system where the rotor, powered by a 1.1 kW electric motor and equipped with 3 hourglass-shaped tines, force the fluid pockets through the 16 vertical slits of the stator, fixed to the bottom of the mixer.
The mechanical details of the stator-rotor equipment just described can be appreciated in the following technical draws, obtained directly from the AXIOMIX Series user manual (*Figure 5.3[101]*):
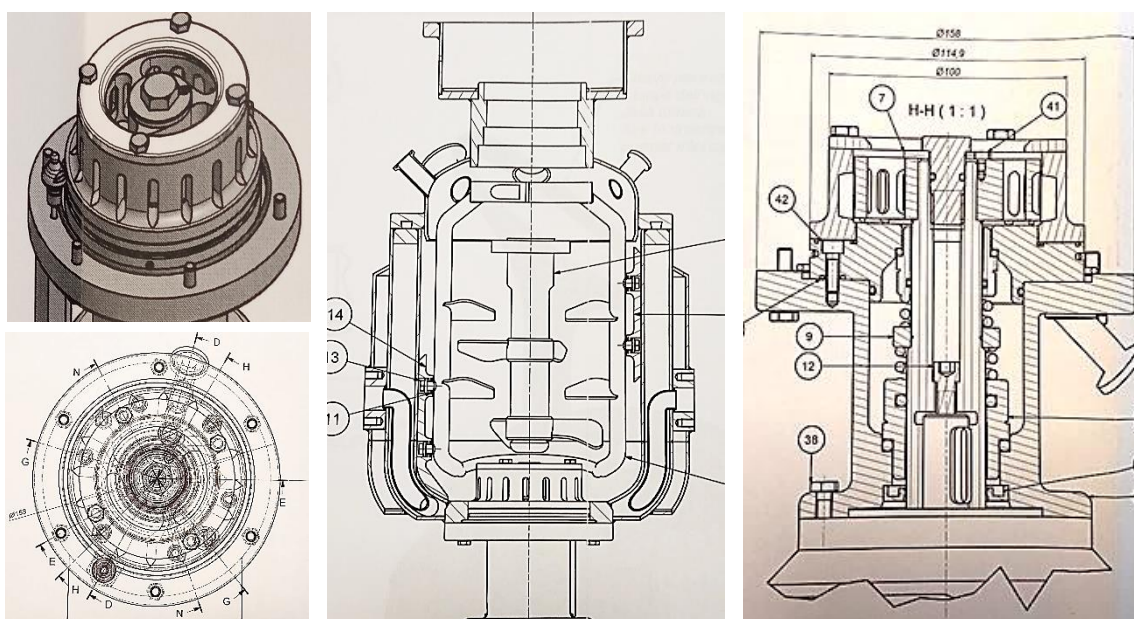
Figure 5.3 From left to right: stator-rotor equipment isolated from the rest of the body (upper left corner) and top view of the turbine once mounted on the bottom of the mixer (lower left corner); particular of the whole mixing system (counter-rotating blades, scrapers and stator-rotor mixer; front view of the lower section of the AXIOMIX 5 mixer.

As it can be observed from the particular of the top view in *Figure 5.3*, the turbine is interested by a lateral duct to enable the injection of raw materials and additives while the rotor is spinning. In addition, it is possible to appreciate how the distance between the rotor blades and the stator body is extremely narrow, as typical for high-shear stator-rotor homogeneisers applied in emulsion fabrication.
Again, it is worth noting that the considered turbine can overcome 2500 rpm, ensuring exceptional mixing properties that overcome the needs of the current experimental project; as discussed in the

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[72] In the case of emulsions, aerated bulks show distorted viscosity and skin-feel, and must therefore be treated to release the air content entrapped in the structure of the product: this requires a vacuum treatment, resulting in time and money losses.

following, the rotational speed of the rotor was kept much lower than this value during the whole kilo-scale experimental procedure.

5.1.b Scale-up protocol

As already anticipated in the opening lines of the current chapter, the major differences between the laboratory apparatus and the pilot turboemulsor made this first phase of the scale-up process particularly difficult: in fact, no mathematical correlation suitable for the desired purpose was found in literature, since the scaling up is made too unpredictable by several aspects, hereinafter detailed.

The most impacting factor is given by the difference between the mixing systems of the two configurations: even if the geometry of the vessels where the emulsification process takes place is similar (both the baker and the mixer are characterized by a vertical cylindrical shape), the specific mixing equipment strongly differs from one case to the other.
In fact, the AXOMIX 5 can guarantee a continuous agitation during the emulsion formation fostered by the turboemulsor on the bottom of the mixer, while in the laboratory scale the emulsification process is conducted by the submersible turboemulsor alone, with no other stirring devices contemporary acting on the bulk. As a result of these, two different flow patterns are originated in the systems: in the laboratory scale, the Silverson L5T turboemulsor generates a localized recirculation of fluid pockets between the rotor and the mashed stator, while in the pilot turboemulsor the action of the counter-rotating blades ensure wider fluid recirculation that interest the whole bulk undergoing processing, leading to better mixing and improved mass transfer phenomena. Such difference can be partially compensated by moving the Silverson turboemulsor all around the beaker during the emulsification process, as an attempt to reproduce the flow pattern typical of an industrial turboemulsor like AXOMIX 5; by the way, the two scenarios still remain not comparable.
In addition, the fluid dynamic of the two systems is made further divergent by the position of the stator-rotor device: in the laboratory baker the turbine is dipped into the bulk from the top, while in the pilot mixer the stator-rotor device is fixed to the barrelled end of the cylindrical body.
Figure 5.4 shows the differences between the two flow patterns originated by the mixing systems described above:
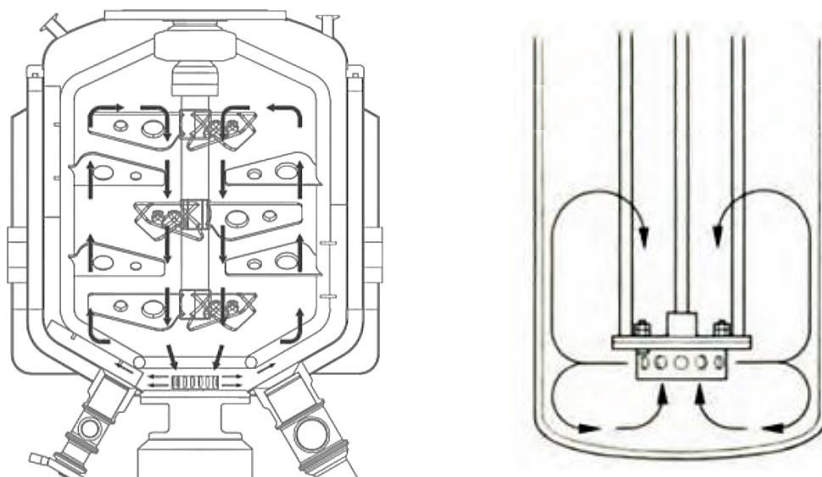

Figure 5.4 Flow patterns originated during the emulsification process in the AXOMIX 5 turboemulsor[101] (left) and in a laboratory baker with Silverson L5T submersible turboemulsor[102] (right).

Apart from the mixing system, other minor differences between the two experimental apparatus made the scale-up process so tricky.

For example, in the laboratory approach the emulsification process was realized into an open beaker, while the pilot turboemulsor was operated under vacuum condition: this led to big differences in the aeration degree of the final products, making them hardly comparable.

Again, thanks to the external jacket, heating and cooling phases were much quicker in the case of the pilot turboemulsor, ensuring higher control on the final properties of the product.

In light of the above, the scaling-up from the laboratory to the kilo-scale was realized according to an experimental procedure based on a sort of trial-and-error approach: after the definition of an appropriate rotational speed for the stator-rotor device, each of the two formulations was synthetized just once, but several samples were taken at regular time intervals starting from the moment when the turbine was turned on. At this point, the samples were analysed as described in the previous chapters, and the optimal solution was elected as the one able to link the desired final performances with the lowest time of utilization of the turbine.

In other words, the impossibility of defining a proper mathematical relationship for the scale-up process towards the kilo-scale was circumvented by defining the emulsification time needed to get the desired performances of the product according to an empirical approach, having previously fixed the rotational speed of the impeller.

Even if the above-mentioned procedure differs from the classical scale-up protocols based on the conservation of adimensional quantities or on the application of empirical correlations (as in the case of the second scale-up phase, presented in section 5.2), optimal results were obtained and both emulsions proved to be completely suitable for the kilo-scale production. Such results are detailed in the following section, together with the accurate description of the experimental procedures applied for both formulations in the AXOMIX 5 pilot turboemulsor.

5.1.c Experimental procedures and results

In the abstract, the experimental procedure to be followed when dealing with the production of the desired emulsion in the pilot turboemulsor should be identical to the laboratorial production method seen in section 4.1.c. Actually, even if the backbone of the synthetic procedures was kept equal to the one applied in the laboratory scale, some minor adjustments were made to enable a simpler and efficient utilization of the AXOMIX 5 mixer.

Generally speaking, when dealing with the different phases of a scale-up process, several corrections are made on the original production method on a case-by-case basis: in this way, each scale is managed with a proper synthetic procedure tailored on its specific needs, so to maximize the ease of use and the proficiency of every phase of the scaling process.

The need for such adjustments come from the increasing challenges linked with the processing of larger and larger quantities of raw materials: for instance, the dispersion of several kilograms of a generic granulated solid, is more likely to cause clamps and accumulation on the internal surface of the mixer if compared with the dissolution of few grams of the same solid in a laboratory beaker, even if the ratio between the solute and the solvent stays the same. In addition, when dealing with hundreds of kilograms of raw materials, their management on the production site is much more complicated with respect to the laboratory case: in example, forklifts and other mechanical devices are required to move such tonnage, even if briefly.

Such practical issues become more and more impactful as the destination scale increases: for this reason, the experimental procedure applied in the kilo-scale is still close to the one designed from the laboratory scale, while the 50 kilograms turboemulsor required a little extra attention to be handled properly (as explained in section 5.2.c).

The procedures followed for the synthesis of the moisturizing lotion and the nourishing body cream in the 5kg turboemulsor are briefly discussed hereinafter, together with the results obtained in terms of study benchmarks. Mind that all the experimental trials presented from this point on refers only to those formulations elected as most promising natural-thickened alternatives in the previous chapter, namely formulation F6.2 and formulation V4.8.

Note that both formulations were treated with 1250 [rpm] as fixed rotational speed for the impeller of the stator-rotor device, with counter-rotating blades kept at 120 [rpm] to favour vigorous mixing of the forming emulsion and, consequently, optimal homogeneity of the bulk.

Moisturizing lotion

As anticipated above, the backbone of the synthetic procedure is the same analysed in section 4.1.c, with some minor adjustments:

- The aqueous phase was directly prepared into the body of the pilot turboemulsor, but a portion of water was saved to clean the internal surface of the vessel used to mix and pre-heat the oil phase, so to limit the loss of oily products (much greater than the one observed in laboratory scale, since the internal surface of the backer, and so the extension of the oil film formed on the glass surface, is wider in this case).

  It is worth noting that the formed aqueous gel was extremely viscous and coherent, leading to several trouble for what concern the initial stages of the homogenization process;

- Since the pilot turboemulsor AMOMIX 5 cannot be interested by rainfall addition of additives (the rotating blades are coherent with the tight lid, making it impossible to keep the bulk under agitation when adding a component; in addition, for safety reason, the turbine is automatically blocked when the lid is not completely closed, leaving the mass completely staring), the aluminium starch octenylsuccinate was added to the aqueous phase prior to the emulsification process.

  Such aspect revealed particularly tricky, since the above-mentioned component caused the formation of strong clumps on the surface of the rotating blades once the lid was resealed; as a result of this, a manual intervention was needed to disaggregate such clamps before adding the oil phase;

- Before starting the emulsification process, vacuum was made inside the mixer (-0.4 [barg]) by activating the equipped vacuum pump: this enabled to limit the ingestion of air inside the forming emulsion,

- As detailed in the previous section, several samples were collected during the emulsification process: namely, four withdrawals were made at regular intervals of two minutes from the activation of the turbine at the fixed rotational speed.

  The results obtained from the analysis of each sample are shown in *Table 5.1*.

Sample	Emulsification time [min]	pH_0	Viscosity [cP]	Qualitative	Centrifuge		
F.A	2.00	5.88	14500	✗	✓	✓	✓
F.B	4.00	5.92	16200	✓	✓	✓	✓
F.C	6.00	5.92	22820	✓	✓	✓	✓
F.D	8.00	5.93	23250	✗	✓	✓	✓

Table 5.1 Results coming from the analysis of the moisturizing lotion samples withdrawn after 2,4,6 and 8 minutes from the activation of the turbine homogenizer in the 5 kilograms pilot turboemulsor.

As it can be observed, none of the collected samples was able to fulfil the specification regarding the viscosity range of the final product; anyway, sample F.C scored a viscosity value quite close to the upper boundary of the optimal range (20000 [cP]). In addition, the considered sample also proved optimal qualitative features, extremely close to the ones characterizing the original product, and great stability under centrifuge.

As a result of the above, sample F.C was elected as the best candidate among the four withdrawn: since the viscosity of the final product proved to increase for increasing emulsification time, the surplus viscosity of sample F.C with respect to the desired range was corrected by considering 5 minutes as optimal time for the emulsification process. Such time extent, known as *emulsification time*, will be later on exploited as starting point for the final phase of the scale-up process, the one leading to the industrial manufacturing scale.

For the sake of completeness, it is worth mentioning that sample C required the addition of 3.62 g of AL to get a pH value inside the desired range: this result is perfectly compliant with the one got at laboratory scale, since the relative addition of AL is around 0.075 % of the total mass of the bulk either way (and the final pH value is equal to 5.54 for both products).

Nourishing body cream

Similarly to what seen for the case of the moisturizing lotion, the production protocol for the nourishing body cream stayed close to the one adopted at laboratory scale, even if a few special cares were taken also based on the experience made with the kilo-scale synthesis just described above.

In the specific:

- Given the particularly high content of Tara gum, a greater portion of the total amount of water (approximately 25%, against the 10% used in the laboratory scale) was added to the pre-mix of aqueous emollients used to disperse the natural polymer, so to avoid those mixing issues experienced during the production of the moisturizing lotion in the pilot turboemulsor.

  Such caution proved particularly helpful and was therefore applied also when dealing with the 50 kg turboemulsor, as it will be detailed in the following section.

- The vacuum was pushed further in this case (-0.6 [barg]), since some air bubbles was still detected in the bulk of the moisturizing lotion produced as described above (limiting the vacuum to -0.4 [barg]).

  Thanks to this additional care, the air content of the produced emulsion was indeed lower.

- Three samples were collected during the emulsification process at regular intervals of two minutes from the activation of the turbine at 1250 [rpm].

  The results obtained from the analysis of such samples can be observed in *Table 5.2*.

Sample	Emulsification time [min]	pH_0	Viscosity [cP]	Qualitative	Centrifuge		
V.A	2.00	7.71	28300	✓	✓	✓	✓
V.B	4.00	7.80	38750	✓	✓	✓	✓
V.C	6.00	7.82	42500	✗	✓	✓	✓

Table 5.2 Quantitative and qualitative analysis of the pot cream samples withdrawn after 2,4 and 6 minutes from the activation of the turbine in the 5 kilograms pilot turboemulsor.

Differently from the previous case, one of the three samples was able to ideally fit all the qualitative and quantitative request of the study benchmarks: in fact, sample V.B showed incredibly similar appearance and texture with respect to the original product, coupled with a viscosity value perfectly falling into the desired range (35000 – 55000 [cP]).

For this reason, the *emulsification time* for the nourishing body cream was set at 4 minutes; as hinted previously, this parameter will be fundamental in the mathematical apparatus of the scale-up phase towards the 50 kilograms turboemulsor.

Again, the datum regarding the pH correction was in great accordance with the laboratory scale result: 4.32 g of AL (~ 0.086% of the total mass) were poured in the bulk to lower the pH to 6.21, while 0.25 g (~ 0.083% of the total mass) were used in the laboratory trial to reach a final pH value of 6.27.

5.2 Industrial turboemulsor (50 kg)

As anticipated in the previous section, the second and last phase of the scale-up process dealt with the passage from the kilo-scale, coinciding with the 5 kg pilot turboemulsor AXOMIX 5, to a 50 kg industrial turboemulsor, representing the manufacturing scale of the current work.

Actually, the capacity of the latter mixer is still small if compared to the typical sizes of industrial turboemulsors applied in the cosmetic industry, namely 1000, 2000 or even 5000 kg and beyond; nonetheless, the considered size is often taken into account at industrial level for the production of particular products with small tonnage and, primarily, during the industrialization process[73] of a new bulk. In other words, the scale-up procedure presented below could be applied to further increase the production scale up to reaching the typical sizes cited above, but this goes beyond the interest of this thesis project, deliberately limited to the first size relevant for industrial purposes.

Differently from what seen in section 5.1, the geometrical and mechanical similarities holding between the pilot turboemulsor and the 50kg mixer, made it possible to structure a mathematical-based procedure for the change of scale, starting from a literature research. Such procedure is deepened in section 5.2.b, right after the detailed description of the turboemulsor (section 5.2.a).

5.2.a Experimental apparatus: 50kg vertical turboemulsor (CO.M.ER.)

The specific device applied in this phase of the project was represented by a 50kg vertical turboemulsor designed by Costruzioni Meccaniche Erba (CO.M.ER.) S.R.L., equipped with a homogenization turbine on the bottom of the vessel and a pair of counter-rotating blades with a single Teflon scraper.

As it can be figured out from the above, the mixing system just described is quite similar to the one seen in the case of the pilot turboemulsor, even if some minor differences still exist. In particular, the design of the mixing blades is here different from the typical rotating shaft equipped with alternate paddles: the blade is subdivided into two different sections that work differently on the fluid undergoing mixing; again, the drive shaft moving the scraper in the opposite direction with respect to the composite blade is completely detached from the crankshaft of the latter, differently from what happened in the pilot turboemulsor, where the two rotating shafts were, as often happens, concentrical. Such details can be observed in *Figure 5.5*.

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[73] This term is usually applied to describe the totality of the scale-up steps leading from the laboratory production to the standardized industrial scale production of a new product.

Figure 5.5 Details of the mixing system: structure of the counter-rotating blade and scraper (left) and their detached crankshafts (right); personal processing (directly taken on the field by the author).

It is important to notice that the above-described mixing system is based on a planetary motion[74], which combines the rotational motion of each crankshaft around its own axis with the revolution motion given by the rotation of the upper plate holding both shafts. The main advantage of planetary mixers with respect to traditional ones, like the pilot turboemulsor based only on the rotation of the two concentric crankshafts around their common axis, is given by the reduced amount of air retained in the bulk in the first case.

For what concern the homogenization turbine placed on the bottom of the cylindrical vessel, its layout is extremely close to the one applied in the 5kg turboemulsor: in this case the rotor is characterized by 6 vertical straight tines, able to push the fluid through the 16 vertical slits carved out of the stator metallic body. *Figure 5.6* shows a photograph of the above-mentioned stator-rotor mixer, together with the schematic representation of the 50kg mixer mechanical layout:
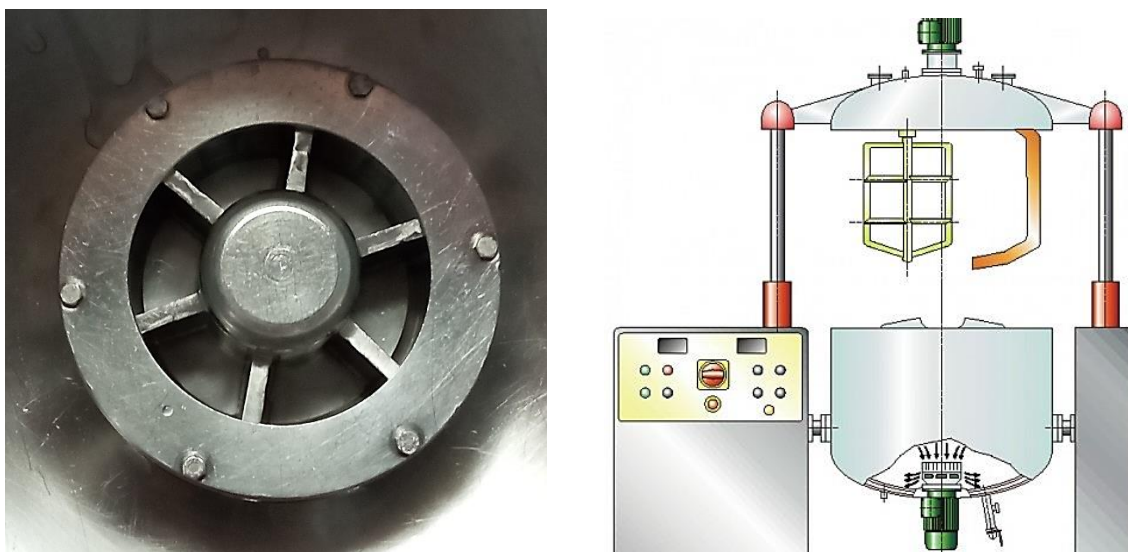
Figure 5.6 Homogenization turbine on the bottom of the mixer (left, personal processing) and its mechanical layout (right[103]); note that the electrical motor powering the turbine is hanging below the mixer itself.

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[74] Mixing devices based on planetary motion are not rare to be found in the cosmetic, food and pharmaceutical industry, even if their prevalence is limited by the increased complexity and the higher need for maintenance.

It is worth mentioning that the equipped turbine is not able to overcome 1500 [rpm] as maximum rotational speed: this aspect will be crucial during the design of the scale-up relationship to be applied, as detailed in the following.

Apart from the mixing system, the considered turboemulsor is equipped with an external jacket, ensuring rapid heating and cooling transients, and a vacuum pump to enable deep vacuum operation.

The construction material is AISI316, the same stainless steel described above for the pilot turboemulsor and extremely widespread in cosmetics manufacturing.

5.2.b Scale-up protocol

In accordance with what anticipated in the introduction to the current chapter, the geometrical and mechanical similarities holding between the 5kg and the 50 kg turboemulsors made it possible to base the second step of the scale-up process on a mathematical relationship.

In particular, the mixing systems under investigation are highly comparable: even if the layout of the rotating blades is different, as detailed above, both mixers are mainly interested by tangential flux of the fluid inside the vessel, with little vertical motions limited to secondary circulation with low impact on the global fluid dynamics of the system. In other words, a pair of counter-rotating blades and scrapers is applied to guarantee continuous renewal of the fluid on the internal surface and bottom of the vessel, so to keep the bulk homogeneous and to limit the formation of *dead zones*[75]; in addition, the stator-rotor turbine applied to introduce the energy needed for the emulsification process in the two cases is extremely similar.

Several approaches exist in literature for the scale-up procedure of emulsification processes, even if no accurate solutions still exist: this is a direct consequence of the complexity of such processes, influenced by an enormous number of variables. For example, the determination of the precise amount of energy given by the mixing system to the forming emulsion it's still extremely challenging; beside this energetic issue, the fluid dynamics of the system is quite complex to be determined, since usually (as it happens in the case under investigation) the bulk is interested by the contemporary action of a homogenization turbine and some rotating blades.

In general, such difficulties are overcome thanks to some scale-up rules that are applied as starting point when it comes to translate a process from smaller to larger scales; in the specific, one of the following rules is usually considered[104]:

- Constant impeller speed:

$$N = constant$$

Equation 5.1 Constant impeller speed.

- Constant impeller tip speed:

$$N * d_{rotor} = constant$$

Equation 5.2 Constant impeller tip speed.

- Constant circulation time (t_c), namely the time interval employed by a fluid pocket to come back in the original point as a result of mixing occurring in the system, and mathematically defined by the following relationship:

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[75] In fluid dynamics, dead zones are stagnant regions were little or no exchange of material with the well-mixed (homogeneous) regions of the vessel occur; in the case of emulsification processes, they can result in the formation of greasy clumps in the final product.

$$t_c = \frac{V_{bulk}}{N_C * d_{rotor}^3 * N}$$

Equation 5.3 Circulation time definition.

where V_{bulk} is the total volume of the mixture undergoing emulsification, N_c is the so-called circulation number, an adimensional quantity of empirical nature.

- Constant Reynolds number (referred to the rotor of the turbine):

$$Re = \frac{\rho_{bulk} * N * d_{rotor}^2}{\mu_{bulk}} = constant$$

Equation 5.4 Constant Reynolds number.

- Constant power input offered to the system, with:

$$P = N_p * \rho_{bulk} * N^3 * d_{rotor}^5$$

Equation 5.5 Power input in the system.

- Constant mean energy dissipation (ε_{av}), that is the average power input per unit of mass, computed as follows:

$$\varepsilon_{av} = \frac{P}{m_{bulk}} = \frac{N_p * \rho_{bulk} * N^3 * d_{rotor}^5}{\pi * \frac{D^2}{4} * H * \rho_{bulk}}$$

Equation 5.6 Mean energy dissipation in the bulk.

where N_p is the power number, a dimensionless quantity widely applied in the fluid dynamics field and depending on the tank configuration, flow pattern, impeller type and speed and the physical properties of the mixture involved in the process.

In the current study, the last rule among the ones presented above was considered as starting point for the scale-up step towards the industrial scale: in fact, working imposing the conservation of the power input per unit of mass makes it possible to maintain the process virtually equivalent from the energetic point of view, even if the production scale increases.

On the other hand, such procedure was not completely suitable for the case under investigation: in fact, the conservation of ε_{av} is conventionally used to compute the rotational speed of the rotor to be applied in the destination scale (N_{to}), as in the following:

$$N_{to} = N_{from} * \left(\frac{N_{p,from}}{N_{p,to}}\right)^{1/3} * \left(\frac{d_{rotor,from}}{d_{rotor,to}}\right)^{5/3} * \left(\frac{D_{to}}{D_{from}}\right)^{2/3} * \left(\frac{H_{to}}{H_{from}}\right)^{1/3}$$

Equation 5.7 Rotational speed in the destination scale according to ε_{av} conservation.

In this specific case, since the two mixers applied in the pilot and industrial scale showed similar features in terms of flow pattern and impeller features, the ratio between their power numbers was considered equal to one, leading to:

$$N_{50kg} = N_{5kg} * \left(\frac{d_{rotor,5kg}}{d_{rotor,50kg}}\right)^{5/3} * \left(\frac{D_{50kg}}{D_{5kg}}\right)^{2/3} * \left(\frac{H_{50kg}}{H_{5kg}}\right)^{1/3}$$

Equation 5.8 Rotor speed needed to keep ε_{av}
unchanged during the scaling.

Turning to numbers, the rotational speed to be applied in the industrial turboemulsor according to *Equation 5.8* resulted $N_{50kg} = 1557.04 \approx 1560 \ [rpm]$. Unfortunately, as detailed in section 5.2.a, the maximum rotational speed allowed for the stator-rotor device equipped on the industrial mixer was 1500 [rpm].

For this reason, the above-mentioned procedure was rethought to better suits the need of the case under investigation. In the specific, the rotational speed of the homogenization turbine of the destination scale was fixed in advance to an acceptable value, namely 1450 [rpm]; in addition, the concept of mean energy dissipation was replaced by the conservation of the total amount of energy introduced in the system per unit of mass, simply given by the product between ε_{av} itself and the emulsification time, intended as the time interval in which the turbine is kept running.

Doing so, the sought parameter became the emulsification time of the destination scale ($\tilde{t}_{50kg}$), namely the time needed for the turbine, moving at 1450 [rpm], to offer the same energy per unit of mass experienced in the pilot turboemulsor; mathematically:

$$\tilde{t}_{50kg} = \tilde{t}_{5kg} * \left(\frac{N_{5kg}}{N_{50kg}}\right)^3 * \left(\frac{d_{rotor,5kg}}{d_{rotor,50kg}}\right)^5 * \left(\frac{D_{50kg}}{D_{5kg}}\right)^2 * \left(\frac{H_{50kg}}{H_{5kg}}\right)$$

Equation 5.9 Emulsification time in the
industrial mixer.

Anyway, *Equation 5.9* was still not adequate to fully describe the reality of the system: in order to get a reliable prevision of the emulsification time in the destination scale, some additional parameters had to be considered.

In fact, the criterion applied to perform the scale-up calculations presented above (the conservation of mean energy dissipation, *Equation 5.6*) is only considering an energetic approach based on an average value of the power per unit mass introduced in the system, without considering the fluid dynamics of the latter. Energetic-based scale-up correlations often use ε_{av} rather than its local value since the data for the latter are not readily available; anyway, many literature sources determined that the ratio between the maximum and mean energy dissipation hovers around 40[105].

Such big differences in the value of the power density introduced in the system originates as a result of the fluid dynamics of the mass undergoing mixing: those areas closest to the impeller are interested by a direct power input, resulting in high dispersion rates; conversely, the more quiescent regions, placed well away from the rotating blades of the impeller, show lower power input and result in favoured coalescence rather than dispersion. In this sense, the mixer volume can be subdivided in different regions[105]:

- A *dispersion region*, where the ratio between the local and mean value of the power density introduced in the system (R_ε) is ≥ 3.0, and dispersion phenomena dominate;
- A *coalescence region*, interested by $R_\varepsilon \leq 0.1$ and characterized by coalescence phenomena;
- An intermediate *transition region*, where both coalescence and dispersion occur without clear predominance.

Note that in a properly designed emulsification process coalescence is prevented by the number of surfactants add to the formulation, and the coalescence region can be described as a still portion of the system were little or no dispersion is occurring.

The distinction between the above-mentioned regions is all the more apparent when the mixer is interested by the presence of a high-power stator-rotor mixer, as in the case under investigation, and is strongly influenced by the ratio between the rotor diameter (d_{rotor}) and the tank diameter (D). Also the clearance between the bottom of the impeller and the bottom of the tank (C) plays a key role.

In light of what discussed above, the following considerations were made to properly include the fluid dynamics of the system in the mathematical apparatus of the scale-up protocol towards the industrial scale:

- Generally speaking, the ratio between the clearance C and the rotor diameter, here named R_C, must be considered; in this specific case, since both the pilot and the industrial turboemulsor are characterized by a homogenization turbine fixed on the bottom of the vessel, R_C had no impact being null in both cases;
- On the other hand, the different ratio between the extension of coalescence and dispersion regions in the starting and arrival mixers was considered by introducing the ratio between the impeller diameter and the tank internal diameter:

$$R_d = \frac{d_{rotor}}{D}$$

Equation 5.10 R_d definition.

Such aspect was introduced in *Equation 5.9* as the ratio between the R_d values of the two scales, resulting in something like a fluid-dynamic correction factor refining the emulsification time of the arrival scale:

$$\tilde{t}_{50kg}^{FD} = \tilde{t}_{50kg} * \left(\frac{R_{d,5kg}}{R_{d,50kg}} \right)$$

Equation 5.11 Final scale-up correlation.

As it can be observed from *Equation 5.11*, the introduction of the above-described correction factor modifies the emulsification time previously computed depending on the variation of the rotor diameter to tank diameter ratio between the two scales.

In other words, if R_d decreases moving from the pilot to the industrial scale, the volume fraction occupied by the coalescence region in the industrial mixer will be higher than in the pilot turboemulsor, resulting in slower dispersion phenomena and longer time to complete the emulsification process. Conversely, if R_d increases, the volume fraction dominated by dispersion phenomena does the same, and the emulsification time is adjusted downwards by *Equation 5.11* (since dispersion, and therefore the emulsification process, is fastened with respect to the departure scale).

In short, *Equation 5.11* combines the conservation of the specific power input per unit of mass (Equation 5.9) with a gross consideration on the fluid dynamics of the mixing system (R_d), resulting in a complete and reasoned correlation for the scaling-up, something extremely different from the experimental-based approach seen in the first phase of the scale-up process (section 5.1.b). As it will be briefly discussed in Chapter 6, Equation 5.11 should be fixed by assessing the correlation between the fluid-dynamic correction introduced (ratio between the R_d values of the

two scales) and the refined emulsification time, here considered as linear for the sake of simplicity; anyway, this goes beyond the purpose of the current thesis project.

However, it is important to remember that, especially when dealing with emulsions, a successful scale-up does not mean that identical parameters are obtained at different scales, but rather that the scale-up results are acceptable and reasonably predictable. The final aim is to avoid losses in capacity, quality, safety and profits that can arise from scale-up errors and the relative need for time consuming, costly and sometimes impossible corrections at large scale.

To conclude, it is fundamental to underline how the above-described scale-up protocol holds for both formulations, since no specific parameter has been considered while deriving the mathematical apparatus that led to *Equation 5.11*.

5.2.c Experimental procedures and results

As anticipated in section 5.1.c, the experimental procedure was slightly modified to better meet the needs and peculiarities of the industrial scale turboemulsor; in addition, it must be kept in mind that industrial procedures must be as easy and reproducible as possible, in order to be able to face several in series productive cycles.

Generally speaking, the synthetic procedures of both emulsions stayed close to the ones applied at pilot scale, with two big differences imposed by the specific layout of the mixing system and by the increased tonnage:

- Differently from what seen in the case of the pilot scale, the 50kg turboemulsor can be interested by rainfall addition of powdered additives through a metallic mesh, while maintaining the turbine in rotation.
  This made it possible to easily avoid the formation of troublesome clumps and aggregates typical of fine powders like Xanthan gum and the other biopolymers considered in the current work; moreover, rainfall addition results particularly convenient for workers at industrial level and help them proceeding faster during the synthesis.
  For these reasons, the turbine was kept at 750 [rpm] during the addition of powdered compounds in the aqueous phase and switched-off during the heating phase of the latter.

- Since the mass of the oil phase overcame 5kg in both cases, the pre-mixing step of greasy substances was achieved thanks to an auxiliary 20 litres fuser kept under agitation and heated by hot water circulating in its external jacket.
  When the time came for the emulsification process to begin, the fuser was connected to the bottom of the industrial mixer by a 1.5 inches diameter pipe: at this point, vacuum was made in the 50kg turboemulsor. By opening the manual ball valve placed on the junction between the pipe and the mixer, the oil phase was sucked into the latter thanks to the imposed pressure gradient.
  The homogenization turbine was re-activated only once the whole oil phase had reached the mixer, just as did in the pilot scale experimental procedure.

As already stated before, the turbine was set to 1450 [rpm] for both productions and kept rotating for a time interval equal to $\tilde{t}^{FD}_{50kg,j}$ (where j stands for the specific formulation being considered), as for *Equation 5.11*. The planetary mixing apparatus was maintained in rotation throughout the entire duration of the process (including the preparation of the aqueous phase and the cooling step of the produced emulsion), at a constant rotational speed of 120 [rpm], as did in the pilot scale.

Deep vacuum was applied to the turboemulsor throughout the entire emulsification process in order to minimize the amount of air retained in the bulk; this is particularly important at industrial scale, since air bubbles entrapped in the bulk can both cause quality issues to the final product and make the packaging phase particularly challenging.

Moisturizing lotion

Apart from the synthetic procedure already described for the 5kg production in the plot turboemulsor, the following cares were adopted when dealing with the moisturizing lotion at industrial scale:

- A small portion of water (roughly 5% of the total) was used to remove the oil deposits from the internal surface of the auxiliary fuser used to prepare the oil phase, with the aim of minimizing those losses that can alter the final result of the emulsification process.
  Such aspect is fundamental when considering an industrial scale production process: water washing helps in ensuring a quite constant composition of the final product by recovering the majority of the greasy substances from the auxiliary mixers, ensuring thus greater uniformity in the quality of different production batches;
- As anticipated above, due to the characteristics of the 50kg turboemulsor, rainfall addition of powder additives (i.e. Xanthan gum, Caesalpinia Spinosa gum, citric acid and others) was performed: this helped in reducing the formation of clumps and aggregates in the aqueous phase, leading to a smooth and bright yellowish aqueous gel.
- Particular attention was made for what concern aluminium starch octenylsuccinate: since the latter additive caused several issues during the pilot scale synthesis (namely the formation of resistant and sticky clumps on the surface of the rotating blades), rainfall addition was considered not sufficient to protect the quality of the final product.
  For this reason, the above-mentioned powder was added to the oil pre-mix: being an hydrophobically-modified starch, its dissolution in the oil phase is easier and avoid the formation of hard to dissolve clumps in the main mixer. On the other hand, such procedure made the oily mixture particularly jelly and viscous, increasing thus the complexity associated to its transportation from the auxiliary mixer to the principal one, when emulsification took place.

According to what previously described, when both the aqueous and oil phase were complete and heated to approximately 75-80 [°C], deep vacuum was made in the 50kg turboemulsor: once the whole oil phase was sucked in the principal mixer, followed by washing water, the turbine was switched on to begin the emulsification process.

The emulsification time to be imposed ($\tilde{t}^{FD}_{50kg}$) was computed as detailed in the previous section, considering 5 minutes as emulsification time of the starting scale ($\tilde{t}_{5kg}$, as specified in the result analysis for the moisturizing lotion in the pilot scale); the following table lists the mechanical and process parameters used to perform the scale-up calculations for the considered formulation:

Parameter	Shortcut	Value	Unit of measure
Rotor speed, pilot	N_{5kg}	1250	[rpm]
Rotor speed, industrial	N_{50kg}	1450	[rpm]
Rotor diameter, pilot	$d_{rotor,5kg}$	0.094	[m]
Rotor diameter, industrial	$d_{rotor,50kg}$	0.132	[m]
Tank diameter, pilot	D_{5kg}	0.215	[m]
Tank diameter, industrial	D_{50kg}	0.450	[m]
Tank height, pilot	H_{5kg}	0.220	[m]
Tank height, industrial	H_{50kg}	0.530	[m]

Table 5.3 Moisturizing lotion industrial synthesis: parameters for scale-up calculations.

Using the above-shown parameters, the resulting emulsification time for the industrial scale synthesis (according to *Equation 5.11*) of the moisturizing lotion resulted 9 minutes and 13 seconds, later approximated to 9 minutes and 10 seconds. For the sake of completeness, the resulting emulsion was also sampled after a homogenization time corresponding to 4 minutes in the pilot scale (namely, 7 minutes and 20 seconds from the turbine ignition), so to investigate the quality of the adopted correlation[76].

Table 5.4 shows the obtained results:

Sample	Sampling time [min.sec]	pH_0	Viscosity [cP]	Qualitative	Centrifuge		
F50.A	7.20	5.89	16900	✓	✓	✓	✓
F50	9.10	5.96	20500	✓	✓	✓	✓

Table 5.4 Moisturizing lotion industrial synthesis: results.

As it can be noticed, the results obtained in terms of emulsion viscosity are compliant with the one observed in the pilot scale: starting from 5 minutes as emulsification time in the departure scale, a value of 20500 [cP] was measured for the final product of the industrial scale. Such value is slightly above (~ 4%) the desired range for the considered benchmark in the case of the moisturizing lotion, and completely in line with the results obtained through the experimental procedure described in section 5.1c for the pilot scale.

In addition, sample F50.A showed a viscosity value very close to the expected one, namely 16900 [cP] versus 16200 [cP], enhancing the reliability of the considered scale-up procedure for the specific system under investigation.

From the qualitative point of view, the obtained product fulfilled all the requirements: no clumps or aggregates were detected in the bulk, which appeared particularly smooth, bright and globally very similar to the original formulation. In other words, the scale-up procedure was defined successful in the case of the moisturizing lotion, since no particular problems arose during the synthetic procedure at industrial scale and the obtained results were in good accordance with the expected ones.

Nourishing body cream

As seen for the moisturizing lotion, also the synthetic procedure of the nourishing body cream required some adjustments to be carried out at industrial scale, in the 50 kg vertical turboemulsor. In the specific:

- Given the high concentration of *Caesalpinia Spinosa gum* in the aqueous phase prepared in the main tank, rainfall addition of the considered additive was performed to reduce the likelihood of aggregates formation.
  Moreover, since the gel obtained in the pilot turboemulsor was extremely thick and hard to manage, a specific path for the addition of water to the pre-dispersion of aqueous emollients was followed: in particular, the alternate addition of 50 g of Tara gum and 1 kg of water was performed, making it possible to keep the gel well hydrated and homogeneous.

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[76] Note that, in order to make the comparison reliable, the sample was interested by the same treatment of the main bulk (cooling phase to room temperature and addition of volatile and thermolabile additives) before being analysed.

Such procedure turned out to be fundamental to avoid the retention of big quantity of air in the final bulk, while reducing the turbine fatigue originating from the reiterated treatment of high viscosity fluids at high rotational speed;

- As made for the previous formulation, a portion of water (approximately 10% of the entire amount) was saved to clean the internal surface of the auxiliary mixer from the greasy substances composing the oily pre-mix to be sucked in the main tank.

Once both phases reached the desired temperature, the oil phase was transferred into the main mixer and the emulsification process started to take place.

The emulsification time for the industrial scale was computed using the same mechanical parameters adopted for the moisturizing lotion and summarized in *Table 5.3* but considering 4 minutes as emulsification time of the pilot scale (as detailed in section 5.1.c). According to *Equation 5.11*, 7 minutes and 22 (approximated to 7 minutes and 20 seconds) was identified as the time needed to obtain similar results to trial V.B of the pilot scale synthetic campaign. Also in this case, a second sample of the forming emulsion was taken to assess the reliability of the adopted scale-up correlation.

The following table reports the results associated with the industrial scale production of the considered nourishing body cream:

Sample	Sampling time [min.sec]	pH_0	Viscosity [cP]	Qualitative	Centrifuge		
V50.A	3.40	7.46	25600	✓	✓	✓	✓
V50	7.20	7.59	34900	✓	✓	✓	✓

Table 5.5 Nourishing body cream industrial synthesis: results.

According to what observed for the previous formulation, also in this case the results obtained in the 50kg turboemulsor matched quite well the expected ones: the final bulk showed a viscosity of 34900 [cP], ending thus in the desired range even if slightly misaligned if compared to the corresponding result in the pilot scale (38750 [cP]). The same holds for sample V50.A, whose viscosity value was somewhat lower than the expected one.

Qualitatively speaking, both samples were compliant with the desired features and not far from the global appearance and texture of the original formulation to be revamped.

In short, the scale-up procedure towards the industrial scale production of the considered nourishing cream can be considered as successful, even if some minor difficulties arose during the synthetic procedure, especially when dealing with the formation and mixing of the thick aqueous gel in the main mixer; moreover, the obtained results are in good accordance with the expected ones, but less precise (~ 10% error) if compared to the moisturizing lotion case.

All the quantitative and qualitative results presented during the whole scale-up procedure are recapped and deepened in the following section, intended as the last analytical portion of the current thesis project.

In any case, the results just shown are suggestive of a successful scale-up process able to guarantee acceptable and reasonably predictable outcomes.

5.3   Scale influence on physical-chemical parameters

In order to analyse the capacity of *Equation 5.11* of predicting with reasonably precision the result of the scaling between the pilot scale (5kg turboemulsor) and the considered industrial scale (50kg turboemulsor), let's first of all review the output of the pilot scale synthesis.

As extensively detailed in section 5.1.b, an experimental approach was preferred to the construction of a mathematical correlation as a result of the core differences between the laboratorial apparatus described in chapter 4 and the pilot turboemulsor.
The following chart (*Figure 5.7*) shows the output of the experimental sampling conducted at regular time interval of two minutes, as described in section 5.1.c. The blue line refers to the moisturizing lotion, while the brown one represents the nourishing body cream; the upper and lower green regions represent the optimal viscosity range for the two formulations (see *Table 3.3*) under investigation:
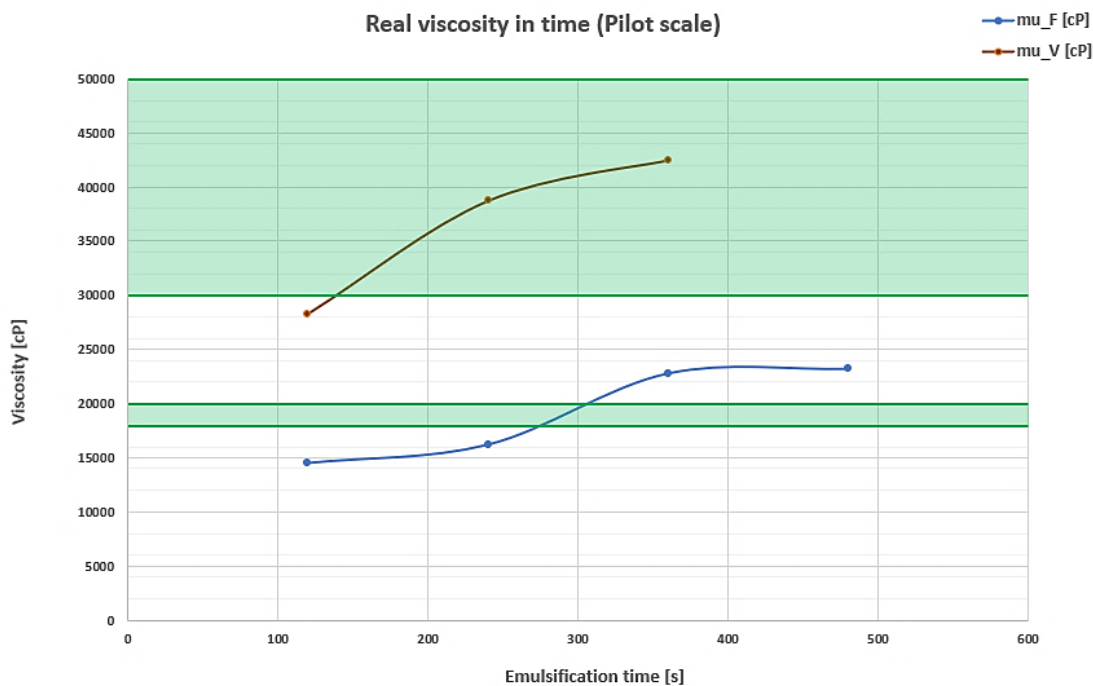

Figure 5.7 Real viscosity versus emulsification time for the moisturizing lotion (blue curve) and the nourishing body cream (brown profile); personal processing.

It is possible to observe how both profiles show an increasing viscosity as the emulsification time (time from the ignition of the homogenization turbine) proceeds.
This is the typical behaviour of a forming emulsion: as the microscopical structure of the emulsion starts to take shape thanks to the mechanical energy introduced in the system by the rotating blades of the turbine, the viscosity increases and the visual aspect of the bulk turns from clumpy and inhomogeneous to smooth and creamy. In this sense, the blue line (moisturizing lotion) perfectly mimes the above-described evolution: after an initial low-slope period, the viscosity starts to increase at higher rate, finally reaching a sort of plateau. At this point, further introduction of mechanical energy in the system could result in emulsion breaking, with the consequent irreversible impairment of the whole bulk.

Keeping the focus on the moisturizing lotion curve, it is important to notice how the desired viscosity range coincides with the region of the curve at higher slope: this is a common challenge when manufacturing cosmetic emulsions, those a small error in the emulsification time could result in a final product with a rheology quite distant from the desired one.

For what concern the nourishing body cream (brown curve), the behaviour seems to be quite similar to the one described for the moisturizing lotion, even if anticipated in time; in any case, additional samples should have been done to confirm such hypothesis (i.e. one sample after one minute from the ignition of the turbine and a conclusive one at t = 8 minutes). Note how the acceptability region for the viscosity of this second product is extremely higher than in the previous case, making the productive goal easier to be pursued.

At this point, it is useful to consider the last productive scale of the current project, represented by the 50kg vertical turboemulsor, and compare the real values of viscosity obtained from the experimental sampling of the produced bulk with the expected ones, namely the viscosity values observed in the pilot scale production.

As described in the previous section, two samples per formulation were taken during the industrial scale production: they were withdrawn after a time interval computed through *Equation 5.11*, starting from the sampling time applied in the pilot scale. The following table shows the peculiarities of each sample for both formulations:

Formulation	Sample	$\tilde{t}_{5kg}$ [s]	$\tilde{t}_{50kg}^{FD}$ [s]	Expected visc. [cP]	Real visc. [cP]	% Error
F	F50.A	240	440	16200	16900	+ 4.32%
	F50	300	550	?	20450	?
V	V50.A	120	220	28300	25600	- 9.54%
	V50	240	440	38750	34900	- 9.94%

Table 5.6 Industrial scale samples.

Note that:

- *F* stands for the moisturizing lotion, while *V* refers to the nourishing body cream;
- The considered samples are the same presented in section 5.2.c;
- $\tilde{t}_{50kg}^{FD}$ represents the emulsification time computed according to *Equation 5.11* and starting from $\tilde{t}_{5kg}$, the corresponding sampling time in the pilot scale;
- The expected viscosity is the one measured in the pilot scale: the more the real viscosity approximates the expected one, the more reliable *Equation 5.11* can be considered;
- The percentage error[77] is computed as follows:

$$\varepsilon_\% = \frac{(\mu_{real} - \mu_{expected})}{\mu_{expected}}$$

Equation 5.12 Expected versus real viscosity error.

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[77] Note that, in order to consider the actual entity of the real viscosity in comparison with the expected one, the error is not defined as an absolute one: in this way it is easy to understand if the applied correlation is underestimating or overestimating the emulsification time needed to reach the desired product features.

As it can be easily observed from *Table 5.6*, no experimental data is available for the moisturizing lotion after 300 [s] in the pilot scale. In fact, as detailed in section 5.1.c, samples were withdrawn after four and six minutes from the ignition of the turbine; then, depending on the characteristics of such samples, five minutes was identified as optimal emulsification time, even if no experimental measure was taken after the considered time interval.

In order to bridge this gap and proceed with the results analysis, it is possible to grossly estimate the viscosity value of the considered formulation by linearizing the behaviour shown in *Figure 5.7* between 200 and 400 seconds from the ignition of the homogenization turbine; *Figure 5.8* shows a graphical representation of what just described:
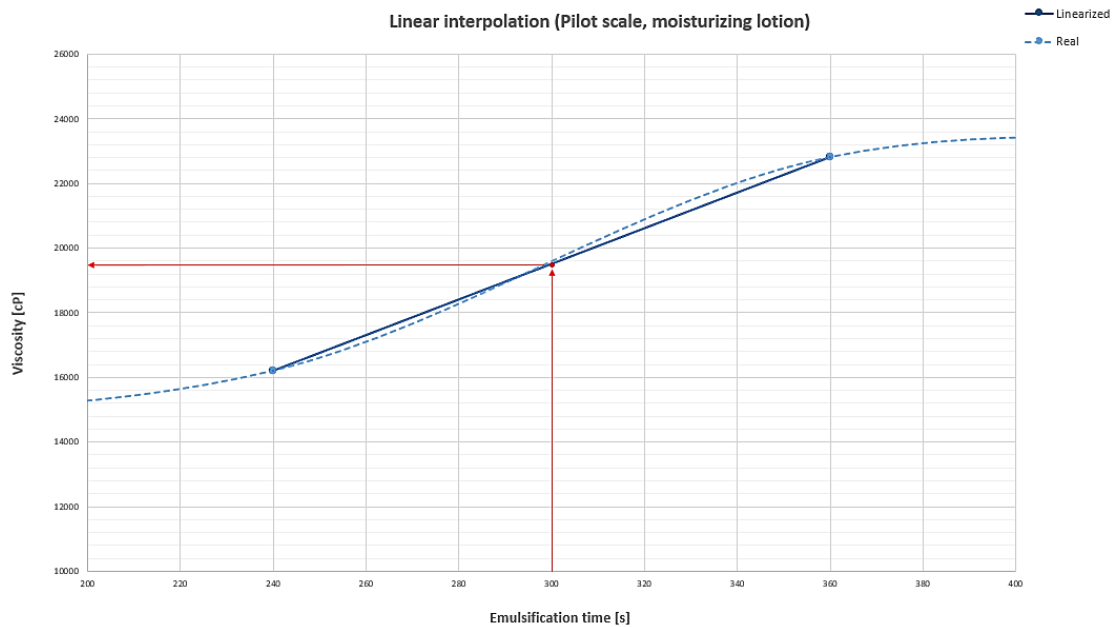
Figure 5.8 Viscosity profile linearization between 200 and 400 seconds from the beginning of the emulsification process (moisturizing lotion); personal processing.

The desired viscosity value can now be inferred graphically, as shown in the chart above, or either by computing the equation of the straight line through the two experimental points at 200 and 400 seconds, namely:

$$\mu^F_{expected} = 55.167 * \tilde{t}_{5kg} + 2960 \ [cP]$$

Equation 5.13 Linear model for the moisturizing lotion viscosity in the pilot scale (between 200 and 400 seconds).

At this point, the desired value can be obtained by introducing the corresponding time in the above shown equation, resulting in $\mu^F_{expected,300} = 19510 \ [cP]$; the associated percentage error, according to *Equation 5.12* and considering the relative value of real viscosity measured in the 50kg turboemulsor (*Table 5.6*), equals to $\varepsilon^F_{\%,300} = + 4.82\%$.

Clearly, the obtained value is just a gross estimation of the real one, computed according to a linearized model built starting from only two experimental points and made with the sole purpose of examining the reliability of the scaling correlation in the small experimental region considered. Nonetheless, in the specific time interval taken into account, the linear model fits quite well the evolution of the original curve, as it can be observed in *Figure 5.8*.

Now that all the entries of *Table 5.6* have been completed, it is possible to investigate the discrepancies between the expected viscosity values and the ones obtained in the 50kg turboemulsor; *Figure 5.9* and *Figure 5.10* show such comparison for the moisturizing lotion and the nourishing body cream, respectively:
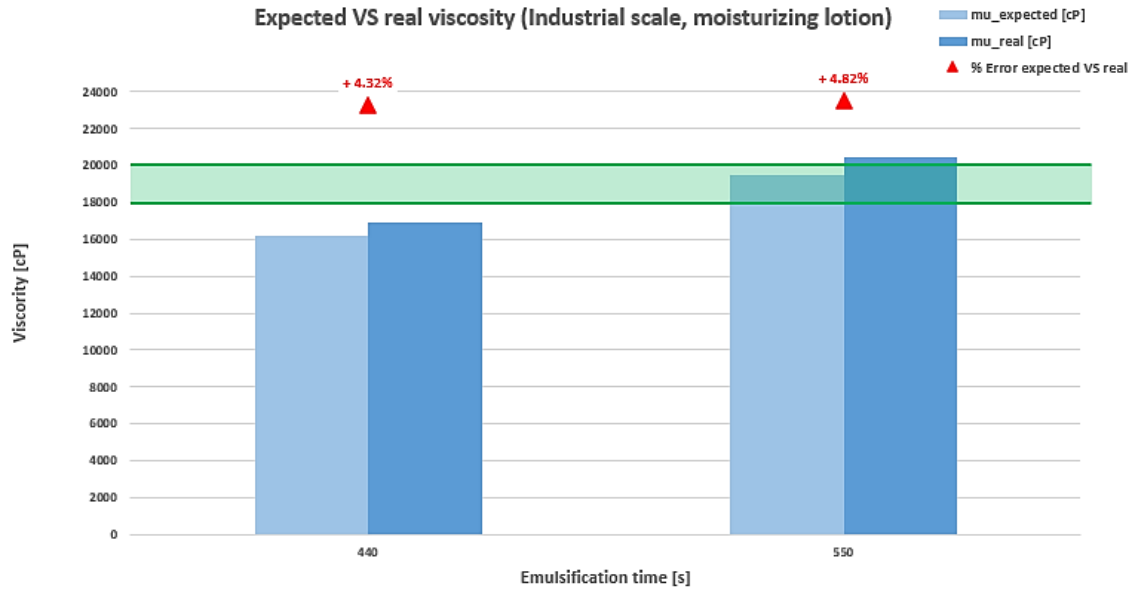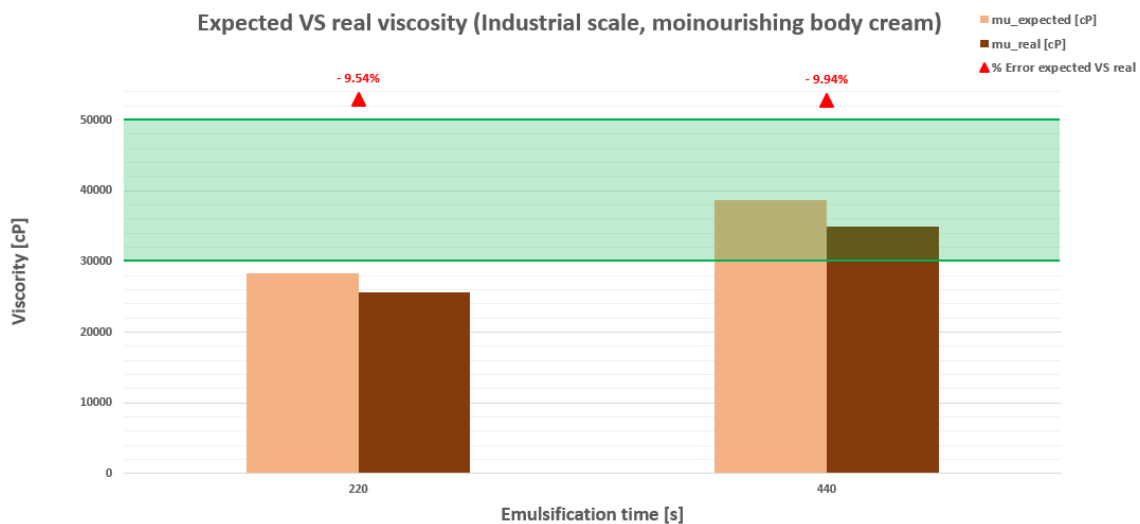

Figure 5.9 Moisturizing lotion: expected viscosity, real viscosity and percentage error at 440 and 550 seconds from the ignition of the homogenization turbine; personal processing.

Figure 5.10 Nourishing body cream: expected viscosity, real viscosity and percentage error at 440 and 550 seconds from the ignition of the homogenization turbine; personal processing.

Generally speaking, it is possible to observe how the applied correlation works quite well in both cases, even if the results show greater accordance in the case of the moisturizing lotion, with a positive percentage error lower than + 5% for the analysed samples. This means that *Equation 5.11* is slightly overestimating the time needed to complete the emulsification process for this specific formulation.

On the opposite, if considering the nourishing body cream, both samples reveal a negative percentage error of around – 10%, meaning that *Equation 5.11* is here underestimating the correct emulsification time, while also resulting less precise with respect to what seen for the previous formulation.

In light of the above, as already anticipated in section 5.1.c, the scale up process can be considered successful since, even if a minor percentage error is present for both formulations, the derived mathematical correlation (*Equation 5.11*) is able to provide reasonable results in great accordance with the expected ones.

In this regard, it is important to remember that scaling an emulsification process towards the industrial scale production is a tough challenge, often still faced through a trial-and-error approach. This is particularly true for several of those small and medium size enterprises that make up today's cosmetic industrial sector, leading to time, money and raw materials waste when it comes to increase the scale of a new or already known production process.

For this reason, the analysed discrepancies between the expected and real viscosity are considered acceptable, in particular for what concern the moisturizing lotion (percentage error lower than 5% for both samples). Nonetheless, the current thesis work is only laying the foundation for some fancier project: time and money constraints made it impossible to implement wider and more complex experimental campaigns in the pilot and industrial scale, which could result in a more robust mathematical correlation and, probably, in lower deviations between the expected and measured values of viscosity.

6. Conclusion and feature developments

Having come to the conclusion of the present thesis project, in light of what discussed throughout the previous chapters, it is possible to argue that a valuable bio-thickened alternative was found for both the formulations object of the study.

In fact, starting with a theoretical approach aimed at understanding how to substitute acrylic polymers as thickening agent in cosmetic emulsions without compromising their distinctive features, several laboratorial trials were made to identify the best biopolymers blends able to successfully complete the task. In the specific, *Caesalpinia Spinosa* gum (also known as Tara gum) was found to be particularly suitable for acrylic thickeners substitution, both as unique additive (as in the case of the nourishing body cream) and in blend with other biopolymers (as seen for the moisturizing lotion, where hydroxypropyl starch phosphate and Xanthan gum were added, too). The novel green alternatives revealed particularly satisfying, since optimal results were obtained both from the quantitative (viscosity, pH) and qualitative (smoothness, brightness and silky-soft touch on the skin) point of view, with a good global capacity of reproducing the cosmetic experience offered by the original version of both products.

As a result of biopolymers significant stock price and the contemporary need for higher percentage of use with respect to Carbomers, several attempt were made to optimize the new green formulations in order to make them affordable in the optic of an industrial production. Such optimizations were based on the manipulation of the oil phase, mainly acting on the application percentage of greasy consistency factors like Glyceryl stearate; unfortunately, the aforementioned procedure revealed effective only in the case of the nourishing body cream, while no reduction in the economic impact was achieved for the moisturizing lotion. Because of time constraints, no other optimization trials were carried out.

Nonetheless, further studies could be designed to assess if the manipulation of either the aqueous or oil phase would result in additional economic benefit while not compromising the peculiarities of the cosmetic emulsion being manufactured.

Once all the laboratorial activities were completed, the project moved to the following part, namely the attempt of build a two-step scale-up procedure with the aim of synthesizing emulsion in a real industrial turboemulsor.

Due to the core differences between the lab and pilot scale experimental apparatus, the first scale-up step was conducted via an empirical procedure realized through a systematic sampling activity on the bulk undergoing emulsification in a 5kg turboemulsor.

The results obtained in the pilot equipment were used as starting point for the main part of the scale-up process, the one leading to the industrial scale, here represented by a 50kg vertical turboemulsor. In this case, a proper mathematical correlation obtained from literature[104] was further modified to consider the specific system under investigation, leading to the scaling correlation (*Equation 5.11*) used to compute the emulsification time to be imposed in the industrial turboemulsor.

For both emulsions, the applied equation turned out to be in good accordance with the expected results, leading to an error of about 5% in the case of the moisturizing lotion and slightly less than 10% for what concern the nourishing body cream. As already anticipated in the final chapter of the current work, additional experimental campaigns at pilot and industrial scale would be needed to build a proper base of experimental data, from which it would be possible to further refine *Equation 5.11* and consequently reduce the correlated forecast bias.

In addition, it is worth mentioning that this thesis work was thought to develop and scale the revamped version of two existing formulation, without considering the rest of the production chain. Nonetheless, the pouring and packaging phases are fundamental steps of any cosmetic production at industrial level: in particular, pouring trials would have to be conducted to assess whether the new formulations require specific cares in terms of filling operations and temperature, for example.

Going back to a general level, as anticipated in the opening section of the current project, microplastics substitution with bio-based polymers will continue to be a dominant trend in the near future, also considering the increasing awareness between worldwide consumers and the consequent pressure from public opinion. Fortunately, several biopolymers are showing great capabilities in terms of oil-based additives replacement, and hundreds of bio-based solutions have yet to be tested.

On the other hand, even if this wide variety of biopolymers is able to well mime the performances of oil-based additives in terms of rheological performances and texture, a slight difference will probably be always present if compared to the original formulations, especially for what concern the visual appearance and that extreme silky-soft after-feel typical of polymeric additives. In addition, it must be remembered that biopolymers are often expensive solutions, and their percentage of use in a typical cosmetic emulsion is far higher than the one related to conventional polymeric substances.

This means that microplastics and polymer removal will represent a real change of paradigm in the modern cosmetic industry, leading to a new idea of cosmesis, more environmentally friendly but, probably, less comfortable in some extent. Such a change will represent a real challenge both at industrial level and in our everyday lives: we are asked to give breath to our planet, but giving up on comforts is always unpleasant.

Will we be able to put Planet Earth's needs ahead of our own ease? Only time will tell.

A| Appendix

The following section is designed to help the reader in better understanding the use of LUMiFuge® stability analyzer made in the current work, thanks to the results of all the stability analysis not detailed throughout the previous sections.

Protocol A

Let's start with the results of protocol A, the quickest type of analysis. Such test was performed on the original products (both synthetized by the author and taken from a market sample, named "F/V original" and "F/V factory" respectively) and on the following formulations: F3.1, F3.4, F4.3, F5.1, F6.1, F6.2 and V2.2, V2.3, V4.4.

F original

Instability index: 0.063.
Result: NOT STABLE (~ 1 mm H_2O ring on the bottom of the sample).
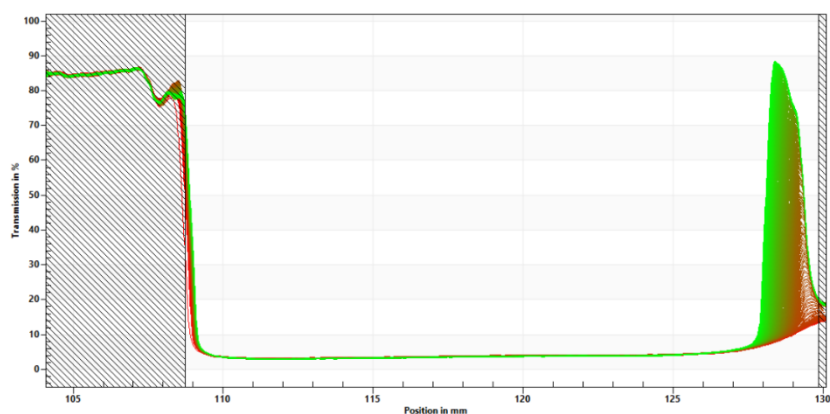
F factory

Instability index: 0.013.
Result: STABLE (no instability signs).
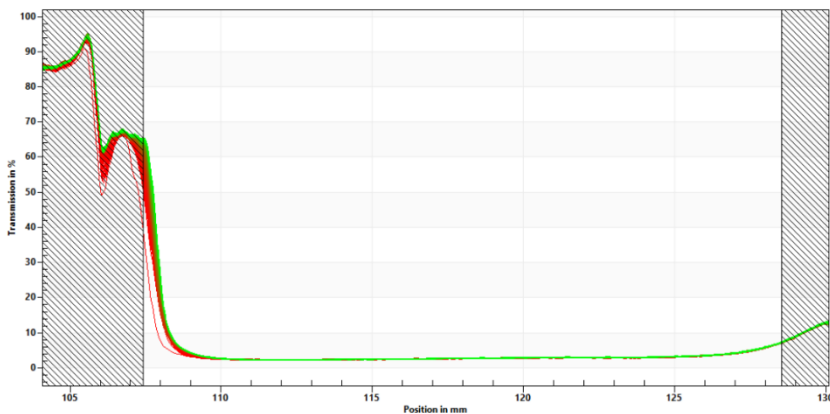
<u>F3.1</u>

Instability index: 0.016.
Result: STABLE (no instability signs).
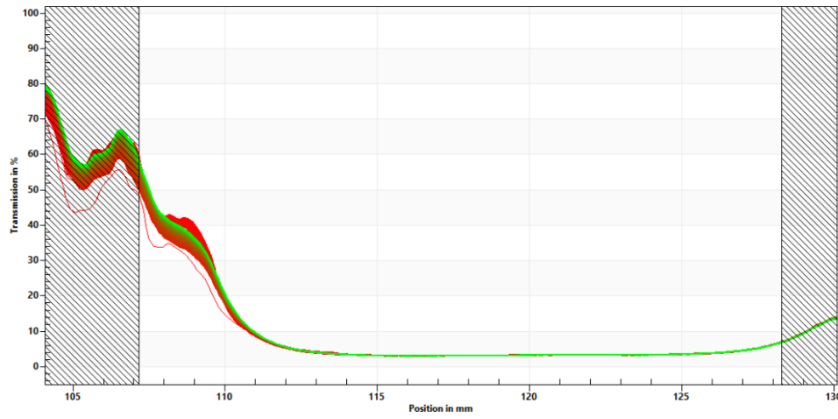
<u>F3.4</u>

Instability index: 0.008.
Result: STABLE (no instability signs).
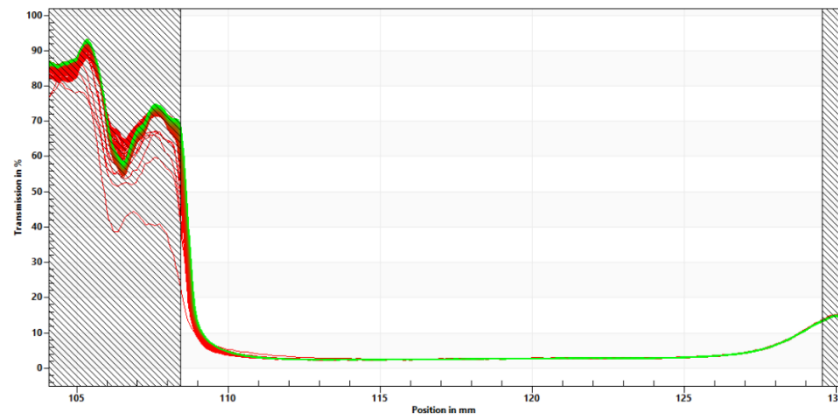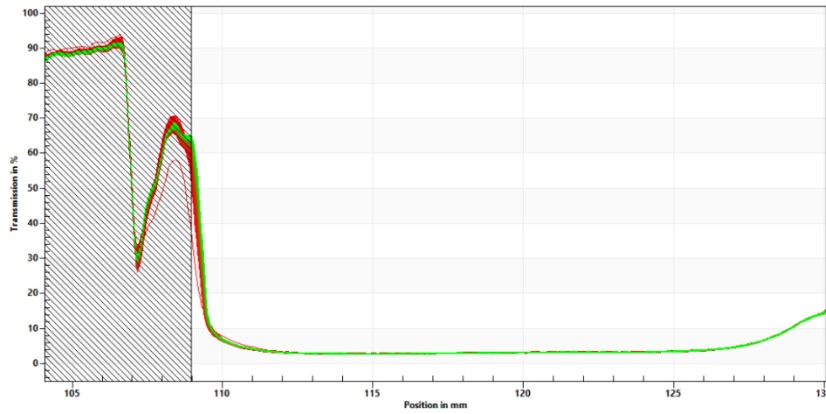

<u>F4.3</u>

Instability index: 0.185.
Result: NOT STABLE (~ 0.5 mm H_2O ring on the bottom of the sample).
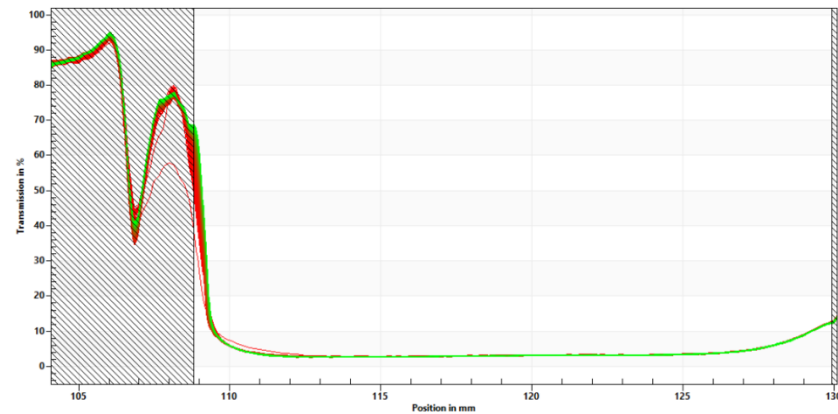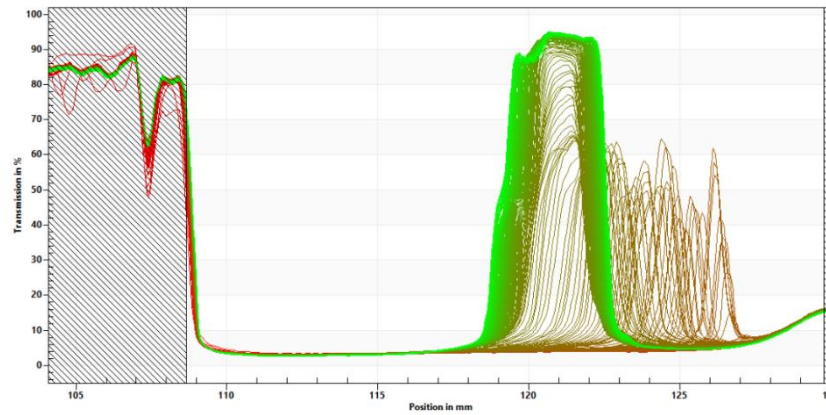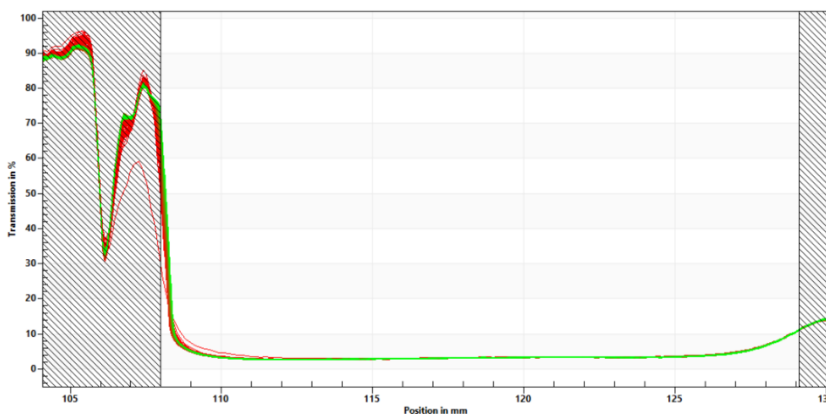
F5.1

Instability index: 0.007.
Result: STABLE (no instability signs).

F6.1

Instability index: 0.185
Result: NOT STABLE (rupture of the emulsion continuity).
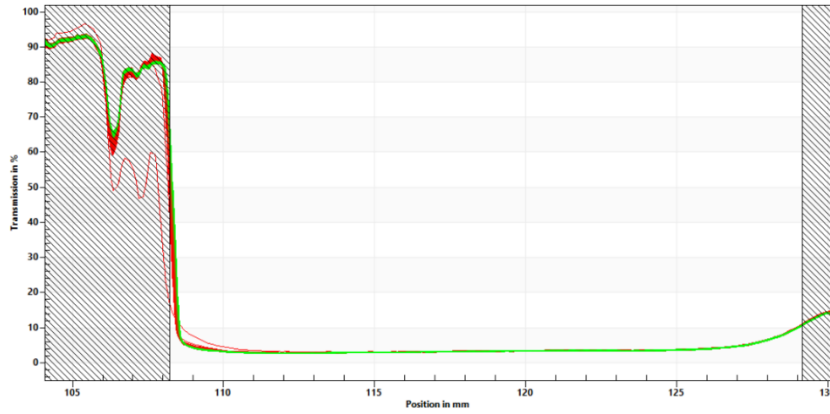

F6.2

Instability index:0.006.
Result: STABLE (no instability signs).

V original

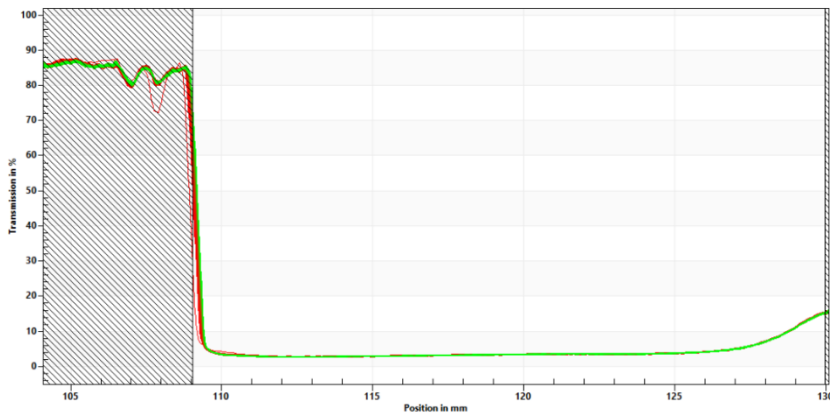Instability index: 0.005.
Result: STABLE (no instability signs).

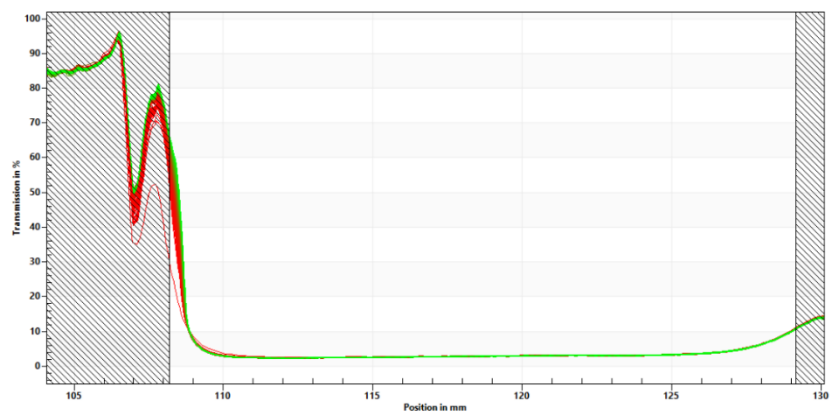

V factory

Instability index: 0.007.
Result: STABLE (no instability signs).

V2.2
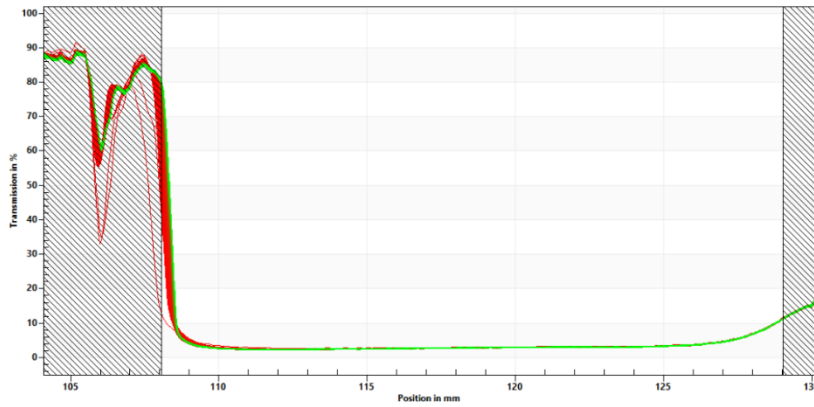
Instability index: 0.009.
Result: STABLE (no instability signs).
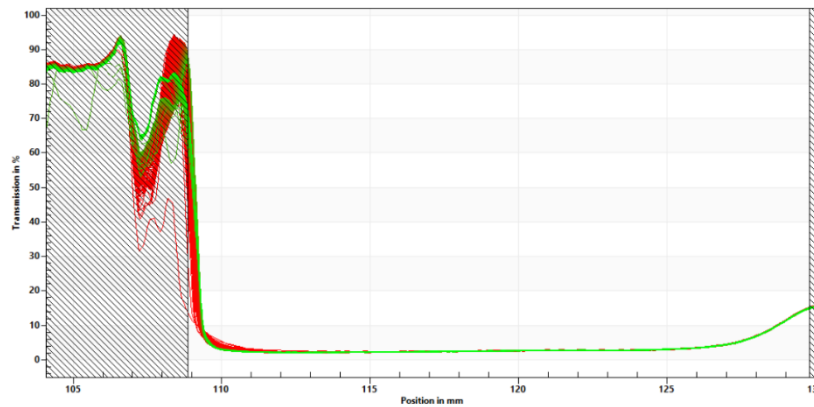
V2.3

Instability index: 0.011.
Result: STABLE (no instability signs).

V4.4

Instability index: 0.010.
Result: STABLE (no instability signs).

Protocol B

The second type of analysis was applied on the following samples: F3.4, F5.1, F6.2, F6.3, F6.4, F factory and V2.3, V4.4, V4.6, V factory.

F3.4

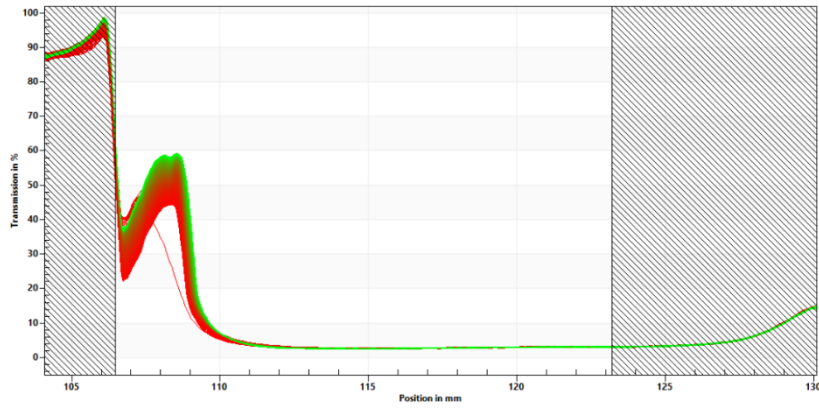See section 4.2.a.

F5.1

See section 4.2.a.

F6.2

See section 4.2.a.

F6.3

Instability index: 0.044.
Result: SLIGHTLY NOT STABLE (minor instability signs).

F6.4

Instability index: 0.036.
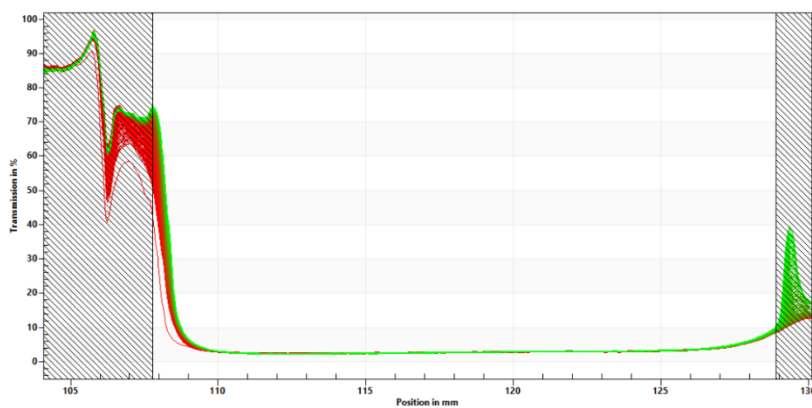Result: SLIGHTLY NOT STABLE (minor instability signs).
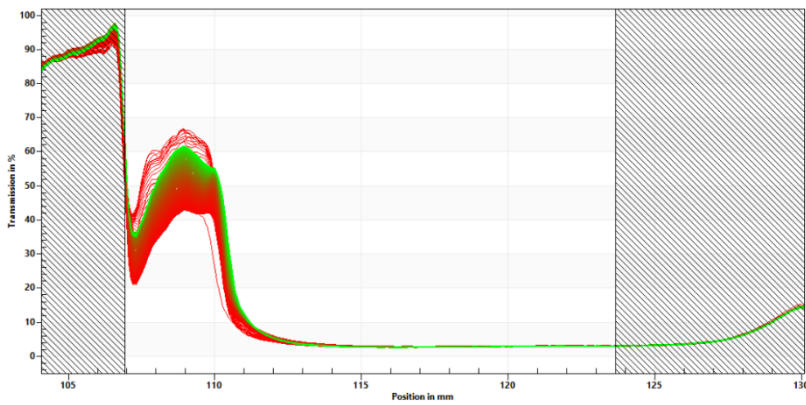
F factory

Instability index: 0.017.
Result: SLIGHTLY NOT STABLE (incipient formation of water sediment).

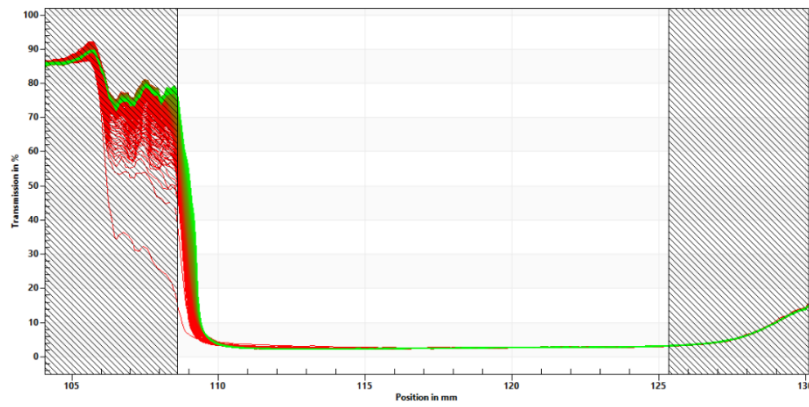### V2.3

See section 4.2.b.

V4.4

See section 4.2.b.

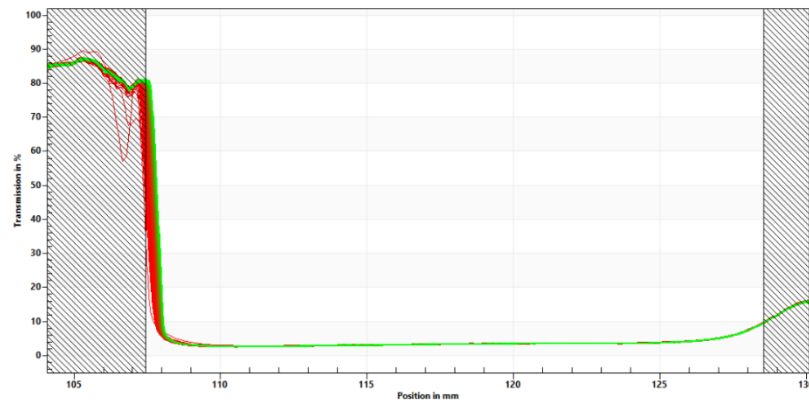### V4.6

Instability index: 0.024.
Result: STABLE (no instability signs).

V factory

Instability index: 0.016.
Result: STABLE (no instability signs).

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