Tutora
Dra. M. Esther Santamaría
Departament d'Enginyeria Química i Química Analítica

Grau en Enginyeria Química

Treball Final de Grau

Development of a range of retinoid-based products and preliminary design of its manufacturing process

Aina Planas Muñoz

June 2025

UNIVERSITAT DE BARCELONA

En primer lloc, vull donar les gràcies a la meva tutora Esther per guiar-me, recolzar-me i dedicar-me el seu temps per poder donar forma a la millor versió d'aquest treball.

Seguidament, vull agrair als meus pares, a la meva germana, als meus avis i a la meva parella per acompanyar-me al llarg d'aquests intensos quatre anys. Gràcies per ajudar-me a superar cada nou repte que s'ha anat presentant i per demostrar-me que la constància i l'esforç sempre acaben tenint la seva recompensa.

Aquest treball simbolitza el tancament d'una etapa plena d'aprenentatges, vivències i creixement personal que sempre duré amb mi com a part del camí que m'ha portat a ser qui soc avui dia.

CONTENTS

SUMMARY

In recent years, there has been a change in dermocosmetics towards a more integrated understanding of skin health, emphasizing the balance and internal well-being of the skin microbiome and the prevention of dermatological issues. Since their introduction in dermatology, retinoids have demonstrated their effectiveness in treating acne and the marks it leaves behind, such as post-inflammatory erythema and hyperpigmentation. Moreover, the biologically active forms of retinoids can influence the expression of genes related to cell differentiation and proliferation, thus improving the signs of skin aging.

This project focuses on the development of two products formulated with different retinoids: a retinal-based serum for the topical treatment of acne and post-acne marks, and a retinol-based cream to prevent and treat signs of skin aging. The development stages include product conceptualization, identification of quality factors, formulation in accordance with European regulations, and preliminary design of the manufacturing process, including detailed equipment selection, annual campaign scheduling, and design of the flow process and Gantt diagram.

The formulation of both products consists of oil-in-water (O/W) emulsions, considering the serum a microemulsion, and the cream a macroemulsion. Both feature a combination of active ingredients that act synergistically: the serum includes retinaldehyde, zinc PCA, niacinamide, and a derivative of vitamin B6, while the cream contains a mixture of retinol, hyaluronic acid, and niacinamide. Production is set at 6,000 kg/year for the serum and 10,000 kg/year for the cream, following a batch process on a multiproduct plant with an overlapping production configuration enabling simultaneous processing of different operations and improving time efficiency.

Keywords: product development, production process design, retinal, retinol, skin health, dermocosmetics, acne, post-inflammatory marks, skin aging, formulation.

RESUM

En els darrers anys, ha emergit un canvi en la dermocosmètica cap a una concepció més integral de la salut de la pell, fent èmfasi en l'equilibri i el benestar intern del microbioma cutani i en la prevenció de problemes dermatològics. Els retinoides, des de la seva introducció en la dermatologia, han demostrat la seva efectivitat en el tractament de l'acne i en les marques que deixa aquesta afecció, com la hiperpigmentació i l'eritema post inflamatori. A més, les formes biològiques actives dels retinoides poden influir en l'expressió de gens relacionats amb la diferenciació i proliferació cel·lular, millorant així els signes d'envelliment de la pell.

Aquest projecte se centra en el desenvolupament de dos productes formulats amb diferents retinoides: un sèrum de retinal per al tractament tòpic de l'acne i les marques posteriors a l'acne, i una crema de retinol per prevenir i tractar els signes de l'envelliment cutani. Les etapes del desenvolupament inclouen la conceptualització del producte, la identificació dels factors de qualitat, la formulació segons la normativa europea i el disseny preliminar del procés de producció, incloent-hi la selecció rigorosa d'equips, projectant les campanyes anuals i la seva planificació de fabricació.

La formulació d'ambdós productes consisteix en emulsions oli-en-aigua (O/W), considerant el sèrum una microemulsió i la crema una macroemulsió. Ambdós presenten una combinació d'actius que actuen de forma sinèrgica, essent el retinaldehid, zinc PCA, niacinamida i derivat de la vitamina B6 pel sèrum, mentre que una barreja de retinol, àcid hialurònic i niacinamida per la crema. Es preveu una producció de 6.000 kg/any per al sèrum i 10.000 kg/any per a la crema seguint un procés discontinu basat en una planta multi producte amb una configuració producció superposada, que permet el processament simultani de diferents operacions i millora l'eficiència.

Paraules clau: desenvolupament de producte, disseny de procés productiu, retinal, retinol, salut cutània, dermocosmètica, acne, marques postinflamatòries, envelliment cutani, formulació.

SUSTAINABLE DEVELOPMENT GOALS

The Sustainable Development Goals are a set of global objectives for promoting just and sustainable health at all levels: from the planetary biosphere to the local community. They address the social, economic, and environmental challenges that influence humanity's progress, all under the banner of sustainability (ONU). This project aligns with several of these goals, with relevance in the following areas:

Good Health and Well-being

The development of these products has been carried out with a clear commitment to skin health and consumer safety. The formulations are free from parabens, and synthetic fragrances, and use dermatologically safe, well-tolerated ingredients.

Responsible Consumption and Production

Sustainability has been prioritized throughout the product lifecycle. The packaging is made from recycled polypropylene (PCR-PP), BPA free, while the outer box uses FSC-certified cardboard made from 100% recycled materials. This contributes to minimizing environmental impact and encourages circular use of resources in the cosmetics industry.

Climate Action

The proposed manufacturing process is designed to be energy-efficient, using equipment appropriate to batch size. Shared equipment and overlapping production campaigns enhances efficiency and reduces energy consumption. Additionally, the packaging design consider environmental criteria to reduce carbon footprint.

Gender Equality and Decent Work

The proposed plant is thought to promote inclusive employment practices and workplace safety to foster decent and fair working conditions for all employees.

1. INTRODUCTION

In recent years, emerging social trends have driven significant growth in the use of cosmetic products, thereby consolidating the cosmetics industry as a key sector in the global economy. This dynamism is reflected in market expansion, product diversification, and adaptation to the transformations of daily routines of the population (STANPA, 2024).

According to Regulation (EC) No. 1223/2009 of the European Parliament and of the Council, a cosmetic product is defined as a substance or mixture intended to be applied to the superficial parts of the human body (epidermis, hair system and scalps, nails, lips, and external genital organs) or to teeth and the oral mucosa, with the exclusive or primary purpose of cleansing them, perfuming them, altering their appearance, protecting them, maintaining them in good condition, or correcting body odors. This term does not include medicines, health products, or biocides.

Moreover, cosmetics can be classified according to their function into hygiene products, decorative products, and treatment and maintenance products for skin or hair. This project focuses particularly on the treatment, care, protection, and maintenance of the skin, which falls within the field of dermocosmetics. This discipline addresses mild and non-pathological dermatological conditions with the aim of preserving or improving skin appearance and health.

Currently, there is an emerging change towards a more integral conception of skin health, emphasizing the balance and internal well-being of the skin microbiome and the prevention of dermatological problems over their external appearance. This approach has transformed the skincare market towards products designed to support long-term skin health (Stelmaszczyk, 2024). The media, along with improved dermocosmetic education among dermatologists and pharmacists, have significantly enhanced consumer access to information. As a result, consumers are more knowledgeable about active ingredients and increasingly aware that high-quality products can be found in the national market (Torres H. et al., 2005).

According to Fernández Vozmediano et al. (2003), retinoids have played a fundamental role in dermatology since their introduction in 1943. These molecules, whether natural or synthetic, share the same biological activity as vitamin A. Once assimilated by the body, vitamin A naturally

exists in the form of vitamin A alcohol (retinol), vitamin A aldehyde (retinal), and vitamin A acid (retinoic acid), with the latter being the biologically active form. Hence, innovations in both their structure and formulation have improved their functionality and safety profile in topical and oral formulations. As a result, retinoids have proven effective in treating multiple dermatological conditions, including acne, pigmentation disorders, photoaging, psoriasis, mucosal keratinization disorders, hypertrophic scars, wound healing, rosacea, and others.

Acne is a chronic inflammatory disease of the skin that impacts nearly all teenagers to different extents and can persist into adulthood for some individuals (Zaballos et al., 2000). In addition to the physical blemishes of acne, many people experience post-inflammatory hyperpigmentation or scarring, which can leave lasting marks on the skin even after the acne has cleared. Retinoids offer a promising solution by accelerating skin cell turnover and improving skin texture, thereby aiding in the reduction of scars and dark spots left behind by previous breakouts. Additionally, retinoids are among the most effective substances slowing the skin aging process (Zasada et al., 2019)

The biologically active forms of retinoids can modulate the expression of genes involved in cellular differentiation and proliferation, leading to improvement in signs of skin aging (AsoColDerma, 2024). Moreover, their usage is increasing due to the growing interest in preventive benefits that span all age groups, particularly among young people, where the importance of early prevention is highlighted.

When it comes to product typology, serums have a lighter, water-based formulation with a higher concentration of humectants, so they are particularly suitable for acne-prone skin, offering visible benefits in a short period of time. Creams, on the other hand, have a higher oil content and more emollients, providing a stronger moisturizing and occlusive effect (Nazeer et al., 2023).

Given the growing relevance of retinoids in dermocosmetics and their key role in the development of new treatments tailored to current needs, this project focuses on the development of two chemically formulated products containing two different types of retinoids for topical facial treatment. One product is a serum intended for treatment of acne and post-inflammatory marks, while the other is a cream intended to reduce signs of aging, responding to these specific needs from adolescence to old age.

2. OBJECTIVES

The main objective of this project is to develop a retinal-based serum to treat acne and post-acne marks, and a retinol-based cream to reduce expression lines and signs of aging. The product development process includes the following stages:

Product conceptualization. This initial stage starts off with a market analysis carried out through detailed bibliographic research that includes encyclopedias, scientific articles, patents, and books, among others. The goal is to identify consumer needs and define the target market accurately. This analysis enables the precise definition of the product's characteristics, including its application method and packaging, while ensuring optimal functionality.

Identification of product quality factors. This stage involves determining sensory, rheological, physicochemical and functional factors to maintain consistent performance of products, safety, and consumer satisfaction.

Formulation. Selection of the appropriate ingredients and excipients, as well as their weight percentages, to achieve the efficacy and safety of the products in compliance with European regulations. The formulation process also involves an understanding of how they interact with one another, ensuring that each product can deliver its benefits without causing irritation or adverse reactions.

Preliminary design of the manufacturing process. Includes the description of process operations and the selection of suitable equipment and techniques, considering annual production campaigns, established timelines, the process flow, and the Gantt diagram.

3. PRODUCT CONCEPTUALIZATION

According to Schnarch (2001), product development means creating new products for existing markets to meet changing customer needs and desires, respond to new competitive offerings, or leverage new technologies.

The first step is to conceptualize the product, that is, to define it (Wibowo et al., 2002). This is done by studying current market trends in cosmetics, dermocosmetics, and, specifically, retinoid-based products to detail their functionality and determine the correct application method. Finally, the packaging is selected, ensuring that the container suits the physicochemical properties of the products and that it is as sustainable as possible.

3.1. MARKET TRENDS

As indicated at the beginning of the chapter, conducting a market study is essential to understand the evolution of the sector and the position that skincare occupies within it. Specifically, it is necessary to analyze the status of retinoid-based products and determine the target market for the products to be developed by identifying consumer needs.

In 2023, the global cosmetics market reached an approximate value of USD 570 billion, with a 3.3% growth compared to 2022. The sector is expected to maintain a compound annual growth rate of 2.9% until 2026 (*Figure 1*), driven by the preference for natural ingredients, sustainability, and digital transformation through the adoption of artificial intelligence. These factors will redefine business models and market dynamics in the coming years (Cali Chamber of Commerce, 2024).

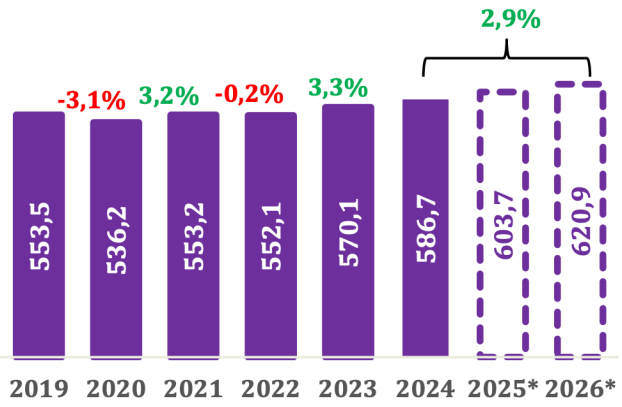

Figure 1. Global cosmetics market value from 2019 to 2026, in billions of USD (Cali Chamber of Commerce, 2024).

The cosmetics, perfumes, and personal care sector in Spain has had a significant impact on private consumption growth, with a 12.1% increase in 2023, four times higher than the average. This positions the sector among the main contributors to economic expansion, alongside industries such as tourism and hospitality. This growth reflects a society that increasingly values well-being and personal care in the profile of Spanish consumers and families. The sector now exceeds €10,400,000 in the market, making it the fourth largest in the EU. The growing awareness of the importance of personal care and well-being has led to a 10% increase in investment in this area. Skincare, as the most relevant category, is growing above the market average, reaching 14.3% and €3,400,000 in consumption (STANPA, 2024).

Global brands such as *L'Oréal, Johnson & Johnson, Estée Lauder Companies, Procter & Gamble, Nivea*, and *Avène* dominate the industry (Statista, 2024), followed by national brands like *ISDIN, Sesderma, Martiderm*, and *Cantabria Labs*.

Regarding product safety, cosmetics should not contain toxic or allergenic ingredients or potentially hazardous chemicals for young children and should include more natural ingredients (Wibowo et al., 2002). Awareness must also be raised about endocrine disruptors, that are chemical substances capable of altering the synthesis, release, transport, metabolism, binding, action, or elimination of natural hormones in the body. These substances can disrupt hormonal balance and the regulation of embryonic development, potentially leading to adverse health

effects on an organism or its offspring. In cosmetics, examples include BPA (bisfenol A), parabens, such as methylparaben, propylparaben, butylparaben, and ethylparaben, among others. Other examples are formaldehyde releasers, phenoxyethanol, certain synthetic fragrances or perfumes, and PEGs (Olea, 2019). Since 2018, the European Commission has required the evaluation and determination of the endocrine-disrupting properties of active substances, preservatives, and synergists. Increasingly, brands are choosing to reduce their use or, ideally, eliminate them entirely from their products, as seen with the company *Freshly Cosmetics*.

Continuing in the context of safety, the legislative framework regulating cosmetic products in the European Union is based on Regulation (EC) No. 1223/2009, recently amended by Regulation (EC) 2024/996 of the European Commission. The purpose of this amendment is to establish stricter limitations on retinol concentrations in cosmetics to reduce the incidence of side effects that this active ingredient may cause, particularly in sensitive skin or individuals with pre-existing dermatological conditions such as atopic dermatitis or rosacea. These skin types are particularly vulnerable to adverse reactions, which can range from redness and flaking to dryness, severe inflammation, and exacerbation of underlying symptoms. According to this regulation, facial cosmetics must not contain more than 0.3% of ER (equivalents of retinol), that is 0.3 % w/w of retinol in their composition to ensure safe use without the need for medical supervision.

This project focuses on the development of retinoid-based products for topical facial application. Currently, a wide range of these products is available on the market, most of which are multifunctional formulations, as they help improve dark spots and hyperpigmentation, acne, and facial photoaging. They come in various forms, such as serums, creams, chemical peels, or toners. To differentiate them, this project will focus on developing a retinal serum and a retinol cream. The vast majority of cosmetics are formulated as emulsions. According to Lui (2009), an emulsion is a heterogeneous system consisting of two immiscible liquids, one of which is dispersed within the other in the form of fine droplets or globules. The dispersed phase is the liquid distributed within the surrounding liquid, which forms the continuous phase. The two main types of emulsions based on the nature of the dispersed phase are:

- **O/W emulsions (Oil-in-Water):** water is the dispersion medium, and oil is the dispersed phase. These emulsions are non-greasy, and water-soluble active ingredients are released more quickly, since they are located in the continuous and

external phase. They have higher electrical conductivity than W/O emulsions because their continuous phase is water, which can conduct electricity if it contains dissolved ions.

- **W/O emulsions (Water-in-Oil):** oil is the dispersion medium, and water is the dispersed phase. These emulsions are greasy, and oil-soluble substances are released more quickly as they are located in the continuous phase. They have very low conductivity because the continuous phase is oil, which does not allow ion movement.

Finally, O/W emulsions are the most common, as they are less greasy and enable faster absorption of water-soluble actives, such as zinc pyrrolidone carboxylic acid also known as zinc PCA (Andrade et al., 2018). Additionally, retinoids are often formulated in O/W systems as they provide better stabilization and a lighter texture, making them more suitable for acne-prone or oily skin. According to Olsen et al. (1997), retinoids can be used from adolescence for acne treatment and later for managing other forms of hyperpigmentation. For this reason, the target market for the products under development includes men and women from adolescence to adulthood, with a middle socioeconomic level and residing in Spain. Within this target market, these products will be of interest to anyone looking to maintain the health of their facial skin or to treat and prevent specific concerns. It is important to note that when using retinoids, personalized guidance and supervision by a professional, whether a pharmacist or dermatologist, are essential.

3.2. PRODUCT FUNCTIONALITY

Before describing each product, it is important to introduce the different forms of retinoids, their mechanism of action on the skin, and the distinction between the most common types. As previously defined, the term retinoids include natural compounds with the biological activity of vitamin A and synthetic analogs, regardless of whether they have biological activity. This family consists of low molecular weight molecules. Vitamin A is a vital dietary element because the body does not synthesize it (Suau, 1987).

According to Ong (1993), vitamin A can be obtained from β-carotenes found in plant-based sources, which act as precursors, and from retinol esters derived from animal tissues, particularly the liver. Once assimilated by the body, it naturally exists in three forms included in *Table 1*:

- **Vitamin A alcohol (retinol).** It's essential for growth, reproduction, vision, and the proliferation and differentiation of epithelial tissue, especially the skin.

- **Vitamin A aldehyde (retinaldehyde or retinal).** Plays a key role in vision by contributing to the formation of rhodopsin, a protein necessary for seeing in low-light conditions.
- **Vitamin A acid (retinoic acid).** The biologically active form. It functions as a signaling molecule that regulates cell growth, differentiation, and the health of the skin and mucous membranes.

Moreover, *Table 1* sets out more common types of retinoids according to Fernández Vozmediano et al. (2003), classified by their chemical structure and how they are formulated.

Table 1. Most common types of retinoids (Adapted from Fernández Vozmediano et al., 2003).

RETINOID	CLASSIFICATION	APPLICATION
Retinol	First generation: non-aromatic	Topical
Retinal	First generation: non-aromatic	Topical
Retinyl palmitate (Retinol ester)	First generation: non-aromatic	Topical
Tretinoin (All-trans-retinoic acid/retinoic acid)	First generation: non-aromatic	Topical/ Oral
Isotretinoin (13-cis-retinoic acid)	First generation: non-aromatic	Oral
Alitretinoin (9-cis-retinoic acid)	First generation: non-aromatic	Topical/ Oral
Acitretin	Second generation: mono-aromatic	Oral
Bexarotene	Third generation: poly-aromatic	Topical/ Oral
Tazarotene	Third generation: poly-aromatic	Topical
Adapalene	Third generation: poly-aromatic	Topical

The biological effects of topical retinoids occur through the activation of specific intranuclear retinoic acid receptors (RAR) and retinoid X nuclear receptors (RXR), regulating gene transcription. Therefore, they penetrate the cell nucleus and act as transcription factors, leading to the activation of various metabolic pathways in the body (Parra-Hernández et al., 2005).

When retinol or retinaldehyde is applied to the skin, these molecules must be converted into retinoic acid within the cytoplasm before they can access the nucleus and bind to the RAR

receptor. In contrast, when retinoic acid is applied directly, it can bind to the RAR in the nucleus without requiring prior conversion. This conversion is illustrated in *Figure 2*.

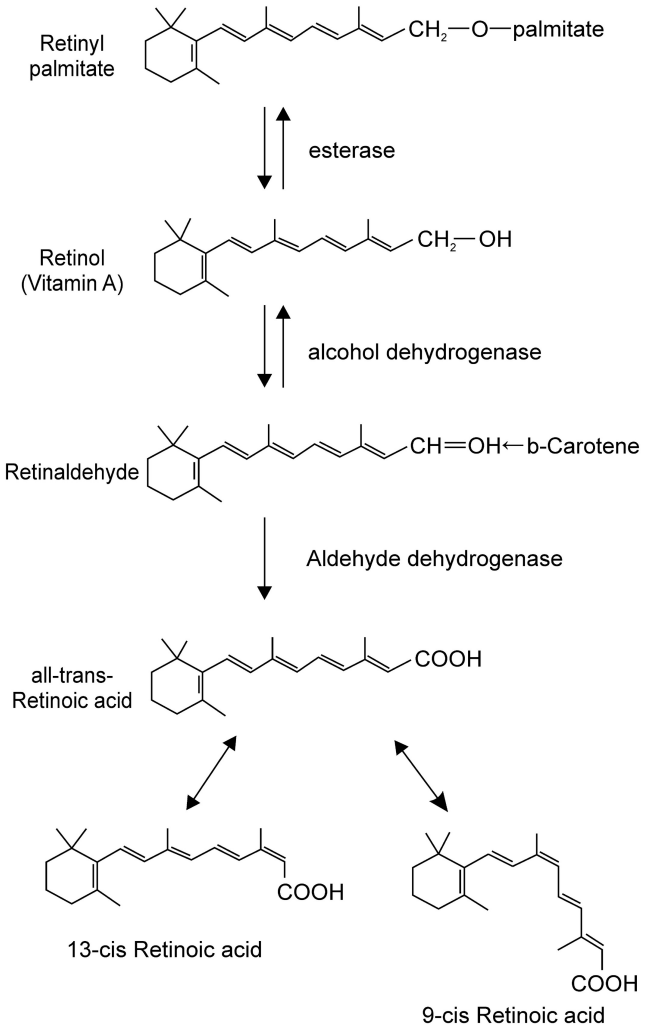

Figure 2. Transformation of retinol and retinal into retinoic acid (Kim et al., 2021).

Retinoids act at both the epidermal and dermal levels *(Figure 3)*. According to Zasada et al. (2019), they are lipophilic molecules capable of penetrating the stratum corneum and reaching the epidermis. They can also penetrate the dermis, effectively repairing the skin barrier and improving softness.

Retinoids influence transcription factors and growth factor secretion, stimulating the proliferation of epidermal cells in the basal layer, enhancing the skin's protective function, and reducing transepidermal water loss. Additionally, retinol promotes the expression of hyaluronic acid in cells, increasing skin elasticity. Furthermore, they exhibit anti-inflammatory mechanisms and boost collagen synthesis, reducing fine lines (Suau, 1987).

According to Sarkar et al. (2013), retinoids also treat various pigmentation disorders such as melasma and post-inflammatory hyperpigmentation, as they cause the dispersion of epidermal melanin. Melanin is the natural pigment responsible for skin and hair color, synthesized by melanocytes, cells located in the basal layer of the epidermis that interact with keratinocytes. Retinoids can also interfere with pigment transfer to keratinocytes and accelerate pigment loss by increasing the shedding rate of the epidermis. Prolonged retinoids use leads to greater stratum corneum compaction and a reduction in melanin content.

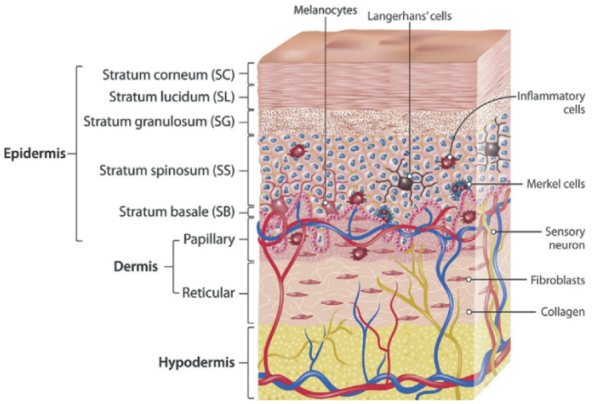

Figure 3. Schematic representation of the multi-layered structure of human skin (Chanda et al., 2023).

In the cosmetics industry, retinoic acid is not commercialized and is only available by medical prescription because this active form of vitamin A can be too harsh on the skin. In contrast, retinal, retinol, and retinol esters are available due to their controlled conversion into retinoic acid, which results in fewer local side effects. Retinol has the longest track record since it was introduced to the market first, whereas retinal is a more recent addition. However, retinal converts into its active form more quickly than retinol, and clinical studies have shown that it is less irritating and better tolerated. Therefore, there is a significant difference in conversion speed: while retinol requires two steps to transform into the active form, retinal only requires one (AsoColderma, 2024).

Retinal-based serum

This product is a retinal serum designed to treat and prevent acne while also reducing post-acne blemishes and improving skin tone uniformity. According to Zaballos et al. (2000), acne vulgaris is a common inflammatory and chronic disease affecting adolescents and young adults. It occurs in the pilosebaceous unit, which consists of the hair follicle and sebaceous gland. Acne is caused by the hyperactivity of sebaceous glands and the blockage of their secretion ducts. Regarding post-acne blemishes, they can be classified as follows:

- **Post-inflammatory erythema (PIE):** This appears as flat red or purple marks on the skin (*Figure 4)*. It results from vascular inflammation following trauma or injury, such as acne (Qazi, 2024).

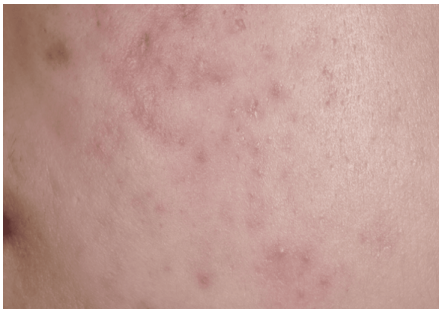

Figure 4. Erythematous marks after inflammatory acne (Barco).

- **Post-inflammatory hyperpigmentation (PIH):** According to Darji et al. (2017), in the case of acne, the lesion triggers melanocytes to release an excess of melanosomes (pigment granules), which darken and discolor the previously affected area. Once the initial blemishes subside, hyperpigmented spots may remain. PIH can appear brown or even black, depending on the individual's skin tone. It is more common in people with higher phototypes, meaning darker skin tones (*Figure 5*). Approximately 1 in 2 people with acne experience both hyperpigmentation and erythema, which can have a significant impact on their psychological well-being.

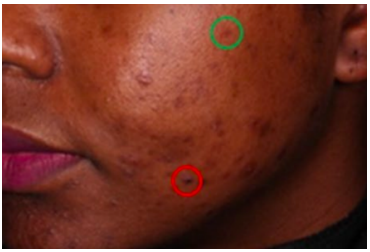

Figure 5. Hyperpigmented acne lesions (Darji et al., 2017).

In skincare, retinal stands out for its lower irritation potential and higher efficacy. This compound converts into retinoic acid in the skin, regulating cell proliferation and differentiation (Zhao, 2024). For this reason, it is suitable for all skin types but especially for sensitive skin with acne tendency. The retinal serum is designed for topical facial application across a wide age range, from adolescence to adulthood, including both women and men with hormonal imbalances. Its serum-like texture not only provides a pleasant consistency but also forms a breathable, thin film that allows the gradual release of active ingredients.

Retinol-based cream

Since the FDA approved retinol for use in anti-aging cosmetics in 1996, it has been widely applied in skincare due to its ability to stimulate fibroblasts to synthesize collagen and inhibit the activity of metalloproteinases, enzymes that break down collagen. As a result, retinol helps prevent collagen fiber degradation, enhancing skin elasticity (Geiger et al., 1996).

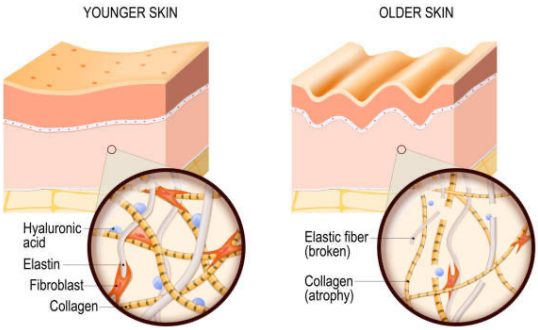

Figure 6. Aging process comparing the structure of young skin with aged skin (FreePik).

Studies have shown that the use of retinol cream effectively improves the appearance of photodamaged skin by reducing fine lines and wrinkles while enhancing skin firmness and elasticity. Long-term research has also found that continuous use of retinol products for one year can lead to a sustained improvement in the signs of skin aging (Zhao, 2024). For this reason, this retinol cream helps reduce expression lines and wrinkles, improving skin firmness and elasticity while also providing skin softness. It is designed for facial application and intended for use in adulthood, including young men and women who wish to prevent skin aging.

Regarding the application method of both products, according to Slade et al. (2009), scientific evidence confirms that topical retinoids are neither phototoxic nor photoallergenic. However, since they can be irritating, their application is recommended at night. It is advisable to introduce retinoids gradually. Initially, apply them every three days for two weeks. If the skin tolerates it well, the frequency can be increased to every other day for another two weeks. After this phase, nightly use can be introduced. A small amount should be applied in a thin layer on clean and completely dry skin, as damp skin becomes more permeable, which may lead to increased irritation (Conejo-Mir et al., 2010). According to Zhao (2024), the use of retinol and its derivatives also presents certain risks and challenges, particularly regarding potential adverse reactions and irritation.

This skin irritation manifests as redness, dryness, peeling, and/or stinging. However, this reaction is dose-dependent, so it is recommended to gradually increase usage until the skin adapts and tolerates topical retinoids.

3.3. PRODUCT PACKAGING

Finally, according to Wibowo et al. (2002), product conceptualization involves packaging. This step must be carefully considered, as the container can significantly influence consumer perception of the product. Firstly, the most critical aspect is ensuring that the packaging is well-suited to the physical and chemical needs of the product, as well as its composition, to prevent oxidation or premature degradation. The choice of packaging depends solely on the overall form of the product, not on the phase of individual ingredients. Additionally, creativity plays a crucial role, reflected in elements such as shape, material, label design, and color, making the product distinctive and recognizable in the market.

However, there is increasing awareness of sustainability, leading to the design of packaging that is as eco-friendly as possible while meeting the specific needs of each chemical product. This includes characteristics such as recyclability or biodegradability. *Table 2* provides examples of commonly used packaging for chemically based consumer products.

Table 2. Most common types of retinoids (Adapted from Wibowo et al., 2002).

Type of Packaging	*Product Form/Delivery System*						
	Composite	*Tablet/caspule*	*Powder/ Granule*	*Cream/ Paste*	*Viscous liquid*	*Dilute liquid*	*Aerosol*
Wrapping							
Carton box	√	√	√				
Paper/Plastic wrap	√	√					
Aluminum foil	√	√					
Bag (Paper/plastic)							
Resealable bag		√	√				
Sealed bag/sachet		√	√	√	√		
Bottle (Glass/Plastic)							
Screw cap		√	√	√	√	√	
Flip cap					√	√	
Slit orifice					√	√	
Pump top					√	√	
Tube (Metal/Plastic)							
Collapsible Tube				√	√		
Squeezable tube					√	√	
Can (Metal)							
Spray can							√

The choice of packaging for the serum will consider its viscous liquid consistency and that the cream is fluid. Therefore, both bottles and tubes can be considered as viable options for both products, with different types of caps available.

It is necessary to analyze the advantages and disadvantages of the possible materials. According to Martínez et al. (2018), glass is transparent, recyclable, resistant to high temperatures and pressures, airtight, impermeable, and does not deform. However, it has the drawbacks of considerable weight, fragility, and the space it occupies when empty. These limitations make it less suitable for products that require lightweight packaging and efficient transport. Metal offers mechanical resistance and lightness, but corrosion can be an issue depending on the packaged product. Finally, plastic stands out for its versatility, lightweight, flexibility, and ease of printing and decoration, adapting to multiple shapes and sizes. These characteristics make it highly attractive for a wide range of products, although its accumulation as waste and environmental impact are important considerations.

The chosen packaging material is recycled polypropylene (PCR-PP), as it facilitates recycling at the end of the product's life and significantly reduces environmental impact.

Compared to traditional polypropylene, using PCR-PP in packaging reduces energy consumption by 50%, water usage by 28%, and CO2 emissions by 30%. These types of containers meet rigorous quality standards, are odorless, and represent a major advancement in the sustainable cosmetics industry (IndustriaCosmética, 2024). Finally, this plastic will be BPA-free, avoiding one of the known endocrine disruptors. The outer box covering the products will be made of 100% recyclable cardboard with FSC-certified paper. Cardboard, as a variant of paper composed of multiple superimposed layers that provide greater rigidity, is an ecological and biodegradable option.

Retinal-based serum

Retinal is chemically unstable and prone to degradation when exposed to light and air, which is why it requires airtight packaging (Zhao, 2024).

The selected packaging is a collapsible tube, as this flexible format allows easy application with light pressure on specific areas requiring treatment while preventing contamination or product deterioration, as shown in *Figure 7*. Finally, the volume selected is 30 mL, because it is intended for sensitive skin, meaning a smaller amount will be used, focusing on breakout-prone areas.

Retinol-based cream

In dermocosmetic development, the shelf life of retinol is extended by selecting appropriate packaging materials, minimizing exposure to air and light, and implementing strict sealing measures during production (Zhao, 2024).

Considering these factors and the fluid consistency of the cream, the same collapsible tube with a pump dispenser and cap has been chosen for both products. However, in this case, the volume is 50 mL, as the cream is meant for full-face application, requiring a more generous amount.

Figure 7. Collapsible tube with airless pump dispenser (El empaque).

3.4. SUMMARY OF PRODUCT CONCEPTUALIZATION

Finally, *Table 3* presents a summary of the most relevant concepts mentioned about both products to develop in this project.

Table 3. Summary of the conceptualization of the retinoid-based products.

	RETINAL SERUM	RETINOL CREAM
Type of product	Topically applied dermocosmetic	
Type of skin	Sensitive and acne-prone skin	All skin types (oily, sensitive, dry, combination)
Age range	From adolescence to adult age	Adult age
Gender	Men and women	
Function	Treats and prevents acne, reduces post-acne marks and improves skin tone uniformity	Reduces expression lines and signs of aging and provides skin softness
Retinoid	Retinal	Retinol
Retinoid characteristics	Newer on the market, less irritating and better skin tolerance. Requires only one step to convert into its active form, acting faster	More experience in its use, but requires two steps to convert into its active form
Type of packaging	Collapsible tube with a pump dispenser (airless and opaque to protect against oxidation), made from recycled polypropylene	
Volume	30 mL	50 mL

4. IDENTIFICATION OF QUALITY FACTORS

After conceptualizing the products based on the study of their functionality, it is necessary to identify the quality factors that ensure their performance.

According to UNIDO (2018), the quality of a product is defined as the degree to which a set of inherent characteristics, such as the raw materials specified in the formula or its stability, meet the defined parameters and satisfy consumer expectations. These studies are carried out at the following stages of a product's life cycle: during conceptualization, after production, and throughout commercialization. Regarding the stability of a dermocosmetic, it is the property that maintains its quality specifications within the range established by the manufacturer during the assigned shelf life and in the selected packaging.

Furthermore, the quality factors of products are crucial for consumer satisfaction. The most common ones for creams and serums are functional, rheological, physical, and sensorial factors (Wibowo et al., 2001). Most of the already mentioned quality factors are qualitative; therefore, product performance is measured using a set of indices. Examples of these indices include stability, hygroscopicity, visual appearance, odor, application feel, ability to flow under gravity, ease of spreading when rubbing the product, and the capacity to provide uniform coverage when applied to a surface (Wibowo et al., 2002).

4.1. FUNCTIONAL QUALITY FACTORS

Referring to Wibowo et al. (2001), functional quality factors refer to those that ensure the correct functionality and effectiveness of products over time. Therefore, it is essential to consider the purpose behind the development of the products and from there, analyze all elements that contribute to fulfilling this purpose. As previously mentioned, the main function of the retinal serum is to treat acne and the post-acne marks it leaves behind, helping to even out skin tone and improve texture. Besides, the retinol cream is designed to address signs of skin aging, such as fine lines and wrinkles, by promoting firmness and elasticity.

In both cases, the core functional quality factor is dermofacial treatment, meaning the product's ability to deliver active ingredients that have beneficial effects on skin health. To ensure that this function is carried out effectively, the active ingredients must be able to penetrate the skin barrier and reach the specific layers where they exert their targeted action. This process depends not only on the chemical nature of the active ingredients but also on the delivery system used to carry them, as well as their compatibility with the other components in the formulation. In the formulation stage, it is also important to preserve the stability of these actives, which may require combining them with antioxidant agents and soothing ingredients to minimize irritation. Additionally, product effectiveness is influenced by how it is applied. For optimal results, the product should be applied to clean skin, avoiding excessive rubbing, which could cause irritation or hinder the penetration of active ingredients. It should also be allowed to absorb completely before applying any other products.

4.2. PHYSICOCHEMICAL QUALITY FACTORS

Stability studies of dermocosmetic products help to understand and document the potential physical and chemical changes that may occur when the products are exposed to various environmental factors such as temperature, humidity, vibration, and light, among others.

Both retinol and retinal degrade over time and are particularly sensitive to light, temperature, heavy metals, and acids (Zhao, 2024). For this reason, enhancing their stability and maintaining their bioactivity remains a key focus in skincare formulation research.

As outlined in the previous chapter, the products being developed are emulsions. According to Tadros (2013), emulsions are a class of disperse systems consisting of two immiscible liquids. Liquid droplets (the disperse phase) are dispersed in a liquid medium (the continuous phase).

During the product development stages, the following laboratory-scale studies are carried out to ensure the stability of emulsions (UNIDO, 2018):

- **Centrifugation tests**. Emulsions are subjected to stress conditions such as centrifugation or enhanced gravitational force in order to evaluate potential flocculation, sedimentation, and phase separation. One common method involves spinning the formulation at 3000 rpm for 30 minutes.

- **Temperature tests.** Products are exposed to various temperature conditions using ovens or refrigerators. In ovens, typical test temperatures include 37 °C, 40 °C, 45 °C, and 50 °C ± 2 °C. In refrigerators, commonly used temperatures are 5 °C, –5 °C, and –10 °C ± 2 °C. Additionally, the products' response to sudden changes in temperature and humidity is assessed.
- **Photostability tests.** The effects of light exposure are evaluated, especially changes in color, odor, and the degradation of active ingredients. Light sources for this study may include natural sunlight filtered through glass windows or xenon lamps.
- **Vibration tests.** These tests examine the potential changes that might occur under conditions like those during product distribution, such as whether emulsions could separate or collapse during transport. Typically, these are performed using a vibrator with controlled frequency and amplitude for a defined period.

Other parameters that will be studied include pH and density according to the selected formulation in the next chapter of this project. An example of a cosmetic product stability testing protocol is provided in *Appendix 1*. The main outcomes expected from these physicochemical tests include the identification of critical parameters to control along with tentative specification ranges, the behavioral trend of the formulation, the approval or rejection of certain ingredients, and the definition of properties that should be monitored in further stability studies.

Quality changes may also occur during the transport, storage, or handling of the final product, leading to emulsion destabilization. According to Tadros (2013), in the case of emulsions, multiple breakdown processes may occur during storage, depending on the particle size distribution and the density difference between the droplets and the medium, as illustrated in *Figure 8*.

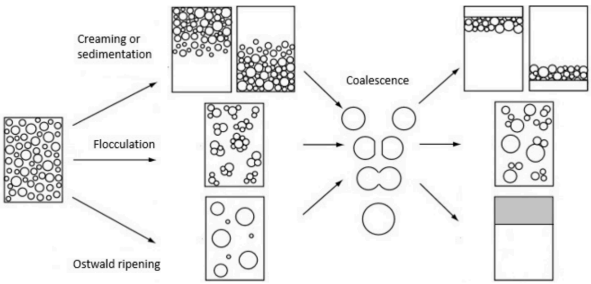

Figure 8. Breakdown mechanisms of emulsions (Costa et al., 2019).

Creaming and sedimentation are forms of gravitational separation that arise from density differences between the dispersed and continuous phases. Creaming occurs when lighter droplets rise to the top, while sedimentation happens when heavier droplets sink to the bottom (Costa et al., 2019).

Flocculation is the aggregation of dispersed phase droplets into loosely bound clumps or flocs. During this process, droplets maintain their individual integrity but adhere to each other (Panagiotou et al., 2012).

Ostwald ripening is caused by the difference in pressure inside large and small droplets, which leads to a mass diffusion from the smaller to the larger droplets. It proceeds slower when the size distribution of the drops becomes narrower or when the dispersed phase is very insoluble in the continuous phase (Costa et al., 2019).

Coalescence refers to the thinning and rupture of the liquid film between droplets, resulting in the fusion of two or more droplets into larger ones. In the extreme case, coalescence leads to the complete separation of the emulsion into two distinct liquid phases, a process known as phase separation (Tadros, 2013).

Referring to UNIDO (2018), shelf life is defined as the period during which the product continues to meet its designated quality specifications. These studies are essential to define the product's shelf life and determine any necessary adjustments to the formulation, as stability is influenced by each individual ingredient.

According to Regulation (EC) No 1223/2009 on cosmetic products, those with a shelf life exceeding 30 months are not required to display an expiration date. However, the packaging must indicate the Period After Opening (PAO), which specifies the safe usage duration of the product (Madurga, 2009). If the manufacturer considers it appropriate to ensure the product's safety, both an expiration date and the PAO can be included. Based on global and detailed market research, it is determined that, in this project, the retinoid-based cream and the serum have a shelf life of 36 months and a PAO of 3 months approximately, indicated as 3M. In this case, it is not necessary to indicate the expiration date because the shelf life is longer than 30 months.

The droplet size of emulsions is another physicochemical quality factor that directly affects the stability, bioavailability, and appearance of the active ingredients in the formulation. Within this classification, there are macroemulsions and nanoemulsions. Macroemulsions are thermodynamically unstable and consist of droplets with diameter of 1 to 100 μm (Johns et al.,

2007). Nanoemulsions are also thermodynamically unstable and have a droplet size of 20 to 200 nm in diameter (Chavda et al., 2019).

Generally, conventional emulsions have a droplet size of 1 to 20 μm. Furthermore, microemulsions exist as well. They are thermodynamically stable systems, with droplet sizes typically ranging from 10 to 200 nm. Moreover, the fact that microemulsions are thermodynamically stable implies that they form spontaneously, while macroemulsions and nanoemulsions are only kinetically stable. A microemulsion is an optically isotropic system in which two immiscible liquids, water and oil, are blended to form a single phase using an appropriate surfactant or a combination of surfactants. In other words, when light passes through them, they behave as a homogeneous phase that is either transparent or slightly opalescent. These types of systems constantly evolve between different structures, ranging from swollen micelles to bicontinuous structures (Grampurohit et al., 2011).

According to Scriven (1976), it is more appropriate to visualize microemulsions not as a dispersion of small droplets but as a bicontinuous structure. Microemulsions offer the advantage of enabling sustained or controlled drug release for percutaneous, topical, and transdermal administration. Additionally, they are easy to manufacture because of their spontaneous formation, and they enhance the cutaneous absorption of lipophilic drugs such as retinoids compared to conventional formulations.

It has been decided that the retinal serum will be formulated as a microemulsion while the retinol cream will be formulated as a macroemulsions, so their compositions will differ. The cream will have a richer oily phase and the presence of more emollients and thickening excipients. Therefore, the serum will have more humectants. This difference will also be noticeable in color, with the serum appearing more transparent and the cream slightly opaquer.

4.3. RHEOLOGICAL QUALITY FACTORS

To begin with, it is necessary to translate the requirements related to perception of the products into rheological requirements. Rheology, in the context of cosmetic product design, is the area of study and understanding of the flow behavior of liquids, dispersions, and stable phases with different structures. Rheological behavior describes attributes in cosmetic formulations related to the tactile sensation and the movement of ingredients through the product matrix over

time, which are influenced by parameters such as temperature and texture. Flow properties serve as indicators of extensibility on the skin and ease of application (Gräbner et al., 2017). Furthermore, Sanches et al. (2023) put forth that the equipment used in rheological analyses is not complex to use. For instance, the rotational rheometer, which works by applying a force while one part moves in relation to another under rotational motion.

Several factors can influence the rheological properties of an emulsion. Among these, viscosity is one of the most measured properties in rheological studies and is defined as a fluid's resistance to flow. According to Newton's law of viscosity, shear stress is proportional to shear rate in Newtonian fluids (Akbari et al., 2018).

García Quesada (2008) states that a Newtonian fluid is defined as one whose viscosity remains constant for any shear rate, at a given pressure and temperature, and is independent of the duration of the applied shear. The variation in viscosity with shear rate must be considered for fluids that do not follow Newton's law, known as non-Newtonian fluids. In such cases, viscosity is dependent on the shear rate. Among this group, the pseudoplastic (shear thinning) behavior is seen in fluids, to varying degrees, whose viscosity decreases as the shear rate increases, such as in emulsions, suspensions, and dispersions. Conversely, in dilatant behavior, fluids exhibit an increase in viscosity with an increase in applied shear rate, caused by reorganizations in their microstructure. Another classification is Bingham plastics, where the material behaves like a rigid body under low shear stress, and a certain threshold shear stress must be exceeded for the system to begin flowing as a viscous fluid. These different behaviors are illustrated in *Figure 9*.

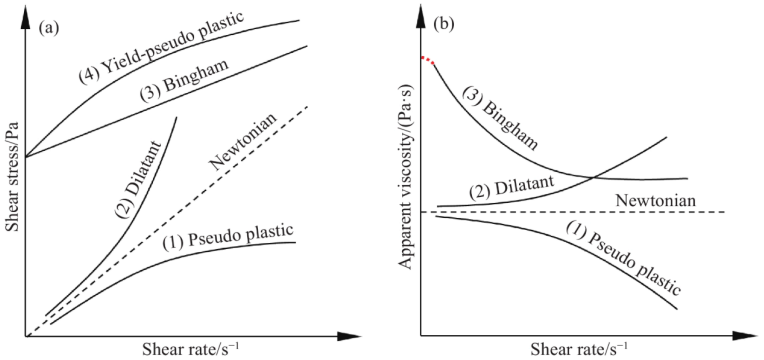

Figure 9. Graphical representation of the variation of shear stress with shear rate (a) and apparent viscosity with shear rate (b) (Chinese Journal of Engineering, 2020).

In the case of emulsions, having a high viscosity at low shear helps prevent spillage, as there is resistance to flow, which contributes to maintaining shape and avoiding dripping or spilling when handling the container (Ali et al., 2022).

Dhawan et al. (2020) point out that low viscosity facilitates product application, improving distribution and increasing penetration. Regarding emulsions, as indicated by Gräbner et al (2017), the O/W type has lower viscosity and greater elasticity compared to W/O emulsions, which can be attributed to the molecular structure and the interaction between the dispersed and continuous phases.

Therefore, the retinol cream and retinal serum should have low viscosity at high shear rates, so that they flow easily when rubbed on the skin, and at low shear rates, their viscosity should increase significantly to prevent easy spillage. This describes a pseudoplastic fluid behavior (Wibowo et al., 2001).

To describe the flow properties, many models have been proposed throughout history to process experimental data. However, a single model may not satisfactorily correlate the behavior of a particular substance over a wide range of shear rates. The power law, as known as Ostwald-de-Waele model (1), is one of the most used for non-Newtonian fluids, and it can explain Newtonian, dilatant, and pseudoplastic behaviors depending on the value of n. In this rheological equation, the inverse of n, often called the pseudoplasticity index, is commonly used as an indicator of a substance's pseudoplasticity. One of the drawbacks of this model is the prediction of very high viscosities at low shear rates, which could lead to a drastic overestimation in flow situations where the shear rate is very low (García Quesada, 2008).

$$\tau = m\,\gamma^{n} \tag{1}$$

τ: shear stress. [Pa]
γ: shear rate. [s^{-1}]
m: flow consistency index. [$Pa \cdot s^{n}$]
n: flow behavior index/pseudoplasticity index [dimensionless].

- n < 1 pseudoplastic non-Newtonian fluid.
- n > 1 dilatant non-Newtonian fluid.
- n = 1 Newtonian fluid.

Moreover, *Table 4* presents the typical shear rate ranges for creams and pastes. Attention should be given to the action of active ingredients, tube extrusion, and topical application.

Table 4. Typical shear rates in processing and application of creams and serums (Wibowo et al., 2001).

Action	Shear rate, γ[s^{-1}]
Suspending pigment or active ingredients	10^{-3}-10^{-1}
Pouring from a bottle	5×10^{1}-10^{2}
Extrusion from a bottle or tube	10^{1}-10^{3}
Topical application of lotions/creams	10^{2} - 10^{4}
Forcing through homogenizing valve	10^{3} - 10^{5}
Colloid milling	10^{5} - 10^{6}

To quantify these flow properties, it has been found that emulsions often have a low viscosity around 0.025 Pa·s when applied to the skin at a high shear rate of 5,000 s^{-1} for creams. At very low shear rates, the viscosity can be as high as 1,000 Pa·s (Brummer et al., 1999).

4.4. SENSORIAL QUALITY FACTORS

The sensory experience of a product focuses on evaluating consumer needs based on sensory factors such as aromas, textures, visual stimuli, and sensations during application. Consumers are considered multisensory individuals who adapt and respond to various stimuli. Therefore, these factors must be creatively and innovatively satisfied, as they significantly influence the final purchasing decision of products (Benson et al., 2019). The sensory process begins with the initial interaction of the consumer with the dermocosmetic, and this information reaches sensory receptors, converges at the neural level, and is processed and integrated by the brain, creating a perception of the product. These perceptible categories to the senses are called organoleptic, and they determine the product's acceptance parameters since they are the first impressions the consumer perceives. As mentioned by to Wibowo et al. (2001), by nature, sensory quality factors are perceptions that can only be quantified using an arbitrary scale. An index is assigned based on the structural and material properties through psychophysical models to reflect the level of satisfaction with the product's use. An example of a protocol for sensory quality factors is shown in *Appendix 2*.

Fragrances

Aroma is the stimulus that conveys and adds value to a concept and experience. There are natural fragrances, such as essential oils, and synthetic fragrances, which are typically aromatic molecules formulated to avoid allergens. However, the absence of fragrance significantly reduces the risk of adverse reactions and aligns with a safe formulation, dermatologically responsible, and free from endocrine disruptors (Olea, 2019).

Therefore, the final products will be presented as fragrance-free, even though they may retain a mild scent from the active ingredients like retinoids, which is of low to moderate intensity.

Sensation upon application

The tactile sensation can lead to either positive or negative feelings, thus having a significant impact on the product's overall perception (Malfitano, 2007). From the point of view of Wibowo et al. (2001), the sensory quality factors that make a cream competent include the absence of irritation when applied to the skin, a slightly opaque appearance, a refreshing sensation, and a smooth, non-greasy feel. Therefore, the cream will have a slightly denser texture due to the addition of a thicker excipient. In contrast, the serum will be lighter but will maintain qualities like smoothness, a refreshing feel, and no irritation. Finally, the aim is to achieve moisturizing and comforting effect after application in both products.

Color. Visual appearance

In terms of quality, the color of the formula and the packaging must be considered not only for aesthetic purposes but also because colors trigger specific signals in the central nervous system and cerebral cortex (Proyectacolor, 2025). According to Sporn et al. (1994), retinoids are compounds related to vitamin A and, due to their chemical structure, are characterized by a yellow color. Moreover, macroemulsions are opaquer and microemulsions are either transparent or semitransparent to visible light (Robb, 1982). Considering the differences in ingredients and textures of the two products, both formulas should be yellowish, with the retinal serum being more transparent, while the retinol cream being slightly more whitish and opaquer. This variation in color appearance can influence not only visual appeal but also the perception of efficacy and quality, indicating that if the color is maintained, the product is well-concentrated.

4.5. SUMMARY OF IDENTIFICATION OF QUALITY FACTORS

To sum up, *Table 5* presents the functional, physicochemical, rheological and sensorial quality factors established for the development of the retinal-based serum and retinol-based cream.

Table 5. Summary of quality factors for the retinal-based serum and retinol-based cream.

QUALITY FACTORS SUMMARY		
Type	**RETINAL SERUM**	**RETINOL CREAM**
Functional	Treats acne and reduces post-acne marks	Treats expression lines and signs of aging
	Penetration of retinoides in the skin barriers and reach of the specific layer	
	Minimization of irritation and excessive rubbing	
	Complete absorption of products, remaining on the skin to enhance efficacy	
Physicochemical	Stability of emulsions is ensured by laboratory tests	
	Shelf life: 36 months 	
	PAO: 3 months (3M) 	
	Microemulsion (O/W)	Macroemulsion (O/W)
	Lighter texture because the presence of more humectants	Heavier texture because the presence of a richer oily phase, more emollients and thickeners
Rheological	Pseudoplastic behaviour	
	Easy to flow when rubbed on the skin	
	Easy to dispense from packaging and avoiding spilling and dripping	
Sensorial	Transparent yellowish	Yellowish and opaquer
	Smooth, fresh, non-sticky and non-greasy sensation	
	Moisturizing and comforting effect after application	
	Fragrance-free	

5. PRODUCT FORMULATION

This chapter addresses the selection of ingredients and excipients after conceptualizing the two products and identifying their quality factors. As illustrated by Wibowo et al. (2001), there are no exact formulas regarding which ingredients to select and in what proportions they should be combined. However, based on patents, scientific articles, and other product formulations, it is possible to identify a suitable formulation for the developed products, as well as to establish the most appropriate percentages by weight. Additionally, whenever possible, it is advisable to choose multifunctional ingredients.

Therefore, given that the main retinoid in each product is different, and that they differ in functionality and physicochemical properties a characteristic formulation will be developed for each product. These topical formulations will include ingredients and excipients that are non-toxic, non-comedogenic (does not clog pores), non-sensitizing, physiologically compatible, and highly biocompatible, with a particular focus on ensuring that ingredients combined with retinoids are not too harsh on the skin and do not cause irritation.

Specifically, to prevent skin peeling and adverse reactions, the combination of retinoids with benzoyl peroxide, exfoliating alpha hydroxy acids (AHAs) such as glycolic acid, beta hydroxy acids (BHAs) like salicylic acid, and high concentrations of vitamin C should be avoided (Hernández Navarro, 2024).

Moreover, this is the key chapter to distinguish between a serum and a cream. According to Nazeer et al., (2023), a serum is lightweight with a concentrated formula and a fine texture that allows for rapid absorption and deep penetration into the inner layers of the skin. In contrast, creams have a higher oil content and more emollients. Serums contain more humectants than creams, and their texture can be adjusted depending on the combination of these moisturizing agents. Thanks to their high concentration of active ingredients and light formulation, they are particularly suitable for sensitive, oily, or acne-prone skin, offering visible benefits in a short period of time. The aim of the formulation is to achieve a serum that is fluid, hydrating, lightweight, and watery, and a cream more oily but still easy to spread without heaviness.

5.1. SELECTION OF INGREDIENTS

Active ingredients are the chemical substances responsible for the desired effect (Ismail et al., 1998). The main actives are retinoids, and they were already defined from the beginning of the project. However, the formulation of this products needs to be complemented.

Excipients are inert substances that are mixed with active ingredients to give formulations consistency and other properties that facilitate their dosing and use. These components can be of various types, for instance preservatives, emollients, thickeners, emulsifiers, humectants, and pH regulators (Agencia Española de Medicamentos y Productos Sanitarios, 2021).

According to Regulation (EC) No. 1223/2009, the ingredients of cosmetic products must be listed on the packaging using the INCI (International Nomenclature of Cosmetic Ingredients), an international nomenclature required for all cosmetics marketed in the European Union. In this list, the components must appear in descending order of their percentage amount, from the highest to the lowest concentration.

5.1.1. ACTIVE INGREDIENTS

5.1.1.1. RETINAL-BASED SERUM

Treatment for acne and post-acne marks

The main function of this product is the treatment of acne and post-acne marks. According to patent ES2692188T3, in cosmetic formulations, the concentration of retinaldehyde is typically in the range of 0.05% to 0.1% by weight relative to the total weight of the composition. However, in patent EP0751764B1, a more precise and optimized concentration of retinal in a stabilized O/W emulsion is proposed, preferably 0.05% retinal. Furthermore, it states that retinal is present in the oil phase due to its lipophilic nature, which helps protect it from oxygen and hydrolysis. As a consequence, a concentration of 0.05% retinal has been selected for the serum formulation.

As stated by Andrade et al. (2018), zinc PCA is a common ingredient in anti-acne formulations due to its antimicrobial and anti-inflammatory properties, as well as its ability to regulate sebum production. In addition, its combination with niacinamide enhances its effectiveness on acne-prone and oily skin, with good results in reducing inflammatory lesions. Niacinamide has anti-inflammatory activity, reduces sebum content, improves ceramide synthesis, inhibits melanin

transfer, improves hydration, and decreases inflammation without compromising the skin barrier. For example, the *Acniben Night Concentrate* retinal serum by *ISDIN* combines retinal, zinc PCA, and niacinamide. The full formulation is studied in *Appendix 3*.

Another ingredient is the liposoluble derivative of Vitamin B6 (pyridoxine tris-hexyldecanoate), which strengthens the skin barrier and reduces transepidermal water loss (TEWL), creating an effective synergy with zinc PCA and niacinamide. For these reasons, zinc PCA, niacinamide, and a derivative of vitamin B6 have been selected for the retinal serum formulation. In the study by Andrade et al. (2018), it was shown that for acne treatment, the combination of 1% zinc PCA, 4% niacinamide, and 3% vitamin B6 derivative is a non-comedogenic, effective, and well-tolerated option that does not cause irritation when used to treat inflammatory acne. Applied twice a day for six weeks, it reduced inflammatory acne lesions by an average of 60%.

Accordingly, 0.05% retinaldehyde, 1% zinc PCA, 4% niacinamide and 3% vitamin B6 derivative have been added to the formulation of the serum for the treatment of acne and marks.

Surfactants

Surfactants, also known as emulsifiers, are substances that exhibit surface activity, reduce surface or interfacial tension, and have autoaggregation capacity *(*Ande et al., 2022).

According to Robb (1982), in the formation of emulsions, since the interfacial tension between two immiscible pure liquids is always greater than zero, the dispersion of the inner liquid increases the system's free energy. Emulsifying agents stabilize this inherently unstable system for a sufficient time by forming oriented film at the liquid/liquid interface that performs a few functions:

- Reduces the interfacial tension and consequently the thermodynamic instability.
- Decreases the rate of coalescence of the dispersed liquid particles by forming mechanical, steric, and/or electrical barriers around them. The steric and electrical barriers inhibit the close approach of one particle to another. The mechanical barrier increases the resistance of the dispersed particles to mechanical shock. In the formation of macroemulsions, the reduction of interfacial tension reduces the amount of mechanical work required to break the inner phase into dispersed particles; in the case of microemulsions, the interfacial tension is reduced at least temporarily to a value of zero so that emulsification occurs spontaneously.

Surfactants have an amphiphilic structure, with a hydrophilic part (polar head) and a hydrophobic part (non-polar tail). Moreover, can require co-surfactants, especially single-chain ones, to reduce the toxicity of the formulations. Surfactants can be classified into four categories based on the charge of the water-soluble part of the surfactant, as shown in *Table 6 (*Ande et al., 2022).

Table 6. Classification of surfactants. Adapted from Ande et al., 2022.

CLASS	EXAMPLES
Anionic (negative charge)	Na stearate, Na dodecyl sulfate (SDS), Na dodecyl benzene sulfonate
Cationic (positive charge)	Laurylamilne hydrochloride, Trimethyldodecylammonium chloride, Cetyltriammonium bromide
Nonionic (no charge)	Polyoxyethylene alcohol, propylene oxide-modified polymethylsiloxane, alkylphenolethoxylate, Tween 20, Span 20, polyglyceryl-3 Methylglucose Distearate
Amphoteric (containing a positive and a negative)	Dodecyl betaine, lauramidopropyl betaine, cocoamido-2-hydroxypropyl sulfobetaine

However, it is essential to consider the hydrophilic–lipophilic balance (HLB). The HLB considers the relative contribution of the hydrophilic and hydrophobic components of the surfactant molecule, being HLB = 0 for a totally hidrophobic molecule and HLB = 20 for a molecule composed by only hydrophilic groups. Oil-in-water systems tend to need high HLB values (8 - 18) of the surfactant or surfactant mixtures. Consequently, the selected mixtures will maintain the HLB value within this range. In general, O/W emulsions are produced by emulsifying agents that are more soluble in the water than in the oil-phase (Robb, 1982).

In line with Tadros et al. (2013), nonionic surfactants are efficient, and can be used to emulsify both O/W and W/O systems. Moreover, these surfactants can stabilize the emulsion against flocculation and coalescence. On the other hand, ionic surfactants, such as sodium dodecyl sulfate (SDS), can also be employed as emulsifiers for O/W systems; however, the formulation becomes more sensitive to the presence of electrolytes. Thus, mixtures of surfactants, specifically blends of nonionic surfactants, can be more effective in both emulsifications.

Grampurohit et al. (2011) also highlight that nonionic surfactants are preferred for microemulsions due to their excellent skin compatibility, lower irritation potential, and reduced toxicity. Therefore, a combination of nonionic surfactants has been selected for the serum, considered as a microemulsion. After reviewing the most used surfactants available on the market, a blend of two nonionic surfactants have been chosen, specifically:

- Sorbitan Laurate (Span 20), which serves as the primary surfactant due to its insolubility and its harder viscosity (WO2010054495A2). Its role is to assist in the dispersion or dissolution of retinal in the non-aqueous phase while stabilizing the formulation. This can be combined with Tween 20, as shown in the example in *Appendix 4* from the *Neutrogena* formulation.
- Polysorbate 20 (Tween 20), which acts as a secondary surfactant (co-surfactant), is known for its mild properties, solubilizing effect, and irritation-reducing capabilities. Notably, it does not significantly increase the viscosity of emulsions, making it ideal for use in serums (WO2010054495A2). A study by Malhotra et al. (2004) specifically reports that the viscosity of samples containing Tween 20 remains low, in contrast to surfactants such as SDS, which do increase viscosity.

In accordance with Patent US5856355A based on a pharmaceutical emulsion gel analog to a serum, a combination of 1 % Span 20 and 5 % Tween 20 is effective for this type of composition, hence its inclusion in the formulation.

5.1.1.2. RETINOL-BASED CREAM

Anti-aging treatment

As outlined in the product conceptualization chapter, according to Regulation (EC) No. 1223/2009, recently amended by Regulation (EC) 2024/996 of the European Commission, facial cosmetics must not contain more than 0.3% w/w of retinol in the composition to ensure safe use without the need for medical supervision.

Studies have shown that the use of a 0.1% retinol cream effectively improves the appearance of photo-damaged skin, reducing fine lines and wrinkles while enhancing skin firmness and elasticity (Zhao et al., 2024). A market study confirms that the combination of retinol with hyaluronic acid (HA) is effective and widely used in anti-aging treatments, as it generates a

synergistic effect that enhances the benefits of retinol. According to Li et al. (2017), hyaluronic acid retains water, providing hydration and thus preventing irritation associated with retinol on the skin. Therefore, hyaluronic acid also acts as a humectant. An example is the *Rapid Wrinkle Repair Regenerating* retinol cream from *Neutrogena*, studied in *Appendix 4*, which also combines retinol and hyaluronic acid.

Bukhari et al. (2018) suggest that formulations that include HA have been shown to improve skin elasticity, stimulate collagen production, and reduce facial wrinkles. In anti-aging creams, typical concentrations of HA are around 0.1%. The molecular weight of HA should also be considered, as low molecular weight molecules penetrate the skin more effectively, producing faster results.

Moreover, the Patent US20110158922A1 also combines retinol and hyaluronic acid for an anti-aging composition.

As it has been exposed, niacinamide improves ceramide synthesis and improves hydration (Andrade et al., 2018). According to Boo (2021), there is clinical evidence supporting the anti-aging effects of niacinamide, as it promotes collagen synthesis and helps prevent its degradation. The study also highlights that niacinamide combines well with retinol. A 5% concentration of niacinamide was found to be well tolerated by the skin and effective in improving various aspects of skin appearance, including fine lines and wrinkles, texture, hyperpigmentation spots, redness, sallowness, and elasticity. For this reason, retinol at 0,1%, low molecular weight hyaluronic acid at 0.1% and 5% of niacinamide have been selected for the formulation.

Surfactants

For the cream, a mixture of non-ionic surfactants is again selected to stabilize it. After researching the most used surfactants in retinol creams, the following have been chosen:

- Polyglyceryl-3 methylglucose distearate. According to the Patent KR20050097587A, it is a non-ionic emulsifier. For this reason, it's a good option for light effective creams, providing stability to the emulsion. The patent describes typical O/W emulsions using it as the main emulsifier and ensures that this compound allows the emulsion to be stable without the need for additional emulsifiers. It improves the skin's moisture retention capacity, prolonging the hydrating effect and providing skin softness. A study by Bîrsan et al. (2022) confirmed its effectiveness at a concentration of 3.5%.

- In creams, Span 20 is also added at 1%. This combination of these two emulsifiers is used in the *Retinol Revitalift Laser* cream by *L'Oréal*, found in *Appendix 4.*

5.1.2. EXCIPIENTS

Emulsions can be presented in various topical cosmetic forms, where the presence of ingredients such as emollients and humectants help achieve objectives like softening the skin, improving the absorption of hydrophobic functional ingredients, facilitating application, and enhancing the product's texture (Ali et al., 2022).

5.1.2.1. RETINAL-BASED SERUM

Emollients

Svarc et al. (2012) hint at the idea that emollients are substances that help the stratum corneum retain its water content, thus counteracting the symptoms of dry skin. These ingredients are usually lipids and oils and are directly related to the sensory perceptions of the product.

As defined at the beginning of this chapter, serums are lighter, more aqueous formulations with fewer emollients and oils than creams. This allows them to be absorbed more quickly and deliver active ingredients to deeper layers, penetrating more than a cream. Lipids and oils make up the oily phase, acting as emollients, emulsifiers, and co-solvents. A significant number of retinal serums on the market use caprylic triglyceride because it is a non-comedogenic, emollient derived from coconut oil and glycerin, commonly used in cosmetic formulations for its lightweight, non-greasy feel, and low risk of clogging pores. It is safe for use in facial products, even for acne-prone skin, and also acts as an occlusive ingredient (Fowler, 1982).

The patent WO2011159439A2 describes a facial cosmetic composition with a caprylic triglyceride range of 1-3%. More specifically, the Patent ES2639464T3 establishes 3% caprylic triglyceride, as emollient and occlusive, on the preparation of a facial cosmetic serum, which is the selected amount for the retinal serum. In this patent, also it is combined with a 3% of triethylhexanoin, an ester that acts as an emollient. Both ingredients have been selected for the retinal serum with the corresponding concentrations mentioned.

Humectants

Conforming to Patent T0999/01, humectants help maintain and increase the water content in the stratum corneum while reducing transepidermal water loss. Glycerin, also known as glycerol, and butylene glycol are particularly noteworthy as effective humectants. Glycerin is an alcohol that has been included for many years in topical dermatological preparations and plays a significant role in skin hydration, elasticity, epidermal barrier repair, protection against irritant stimuli, and even exhibits antimicrobial properties (Fluhr et al., 2008). In facial cosmetic formulations, glycerin is commonly used at concentrations ranging from 1% to 5% (Saigu, 2020). The Patent ES2639464T3, concerning a facial serum, incorporates 2% butylene glycol, which also functions as an emollient. Therefore, the final formulation includes 2.5% glycerin and 2% butylene glycol. Additionally, zinc PCA, one of the active ingredients selected for this formulation, is included at a concentration of 1%, and also acts as a humectant (Andrade et al., 2018).

To achieve the desired texture for the serum, ensuring it remains lighter than a cream while still providing hydration without increasing density, an additional humectant is required. Sodium PCA has been selected for this purpose, as it is a widely used humectant in cosmetics. The typical usage range in leave-on products is between 0.2% and 2.5%, concretely 0.75% is the maximum established for facial products (Fiume, 2015). As consequence, a 0.2% of sodium PCA has been chosen.

Furthermore, humectant ingredients provide hydration by releasing water into the formulation or drawing it from the dermis, and they are often combined with occlusive agents that minimize water evaporation (Hernández-Barrera et al., 2011).

Occlusives

Referring to Hernández-Barrera et al. (2011), occlusive ingredients form an impermeable lipid barrier that reduces water evaporation and are combined with humectants to support epidermal hydration. However, this effect can produce a greasy sensation to the touch, which is why lower concentrations should be added to the serum for acne and hyperpigmentation compared to the cream intended for aging skin.

An appropriate occlusive to combine with retinoids is dimethicone, a silicone that provides smoothness to rough skin textures by forming a protective barrier and reducing potential skin irritation (Eurolab).

The Patent WO2011159439A2 states that dimethicone is typically used in concentrations ranging from 0.01% to 10% in the composition. To start testing the formulation, a concentration of 2% of dimethicone has been chosen for the retinal-based serum.

Solvents

Zasada et al. (2019) state that retinoids are lipophilic molecules and therefore poorly soluble in water, requiring an appropriate solvent since they are soluble in fats and alcohols. Butylene glycol is one of the humectants selected for this formulation and, in addition to functioning as a humectant, also acts as a solvent.

Furthermore, based on Patent ES2639464T3 for a facial serum, a 10% concentration of propanediol is also included as a solvent, and this choice is supported by the serums reviewed in *Appendix 3*, which confirm that propanediol serves as a solvent for retinal.

Thickeners

According to Santos et al. (2019), thickeners, also known as rheological modifiers, stabilize products and enhance their physical and sensory properties, such as texture and ease of application. Although they may have additional functions as humectants or emulsifiers, their primary role is to adjust the viscosity of aqueous solutions by means of polymer entanglement. Thickeners with pseudoplastic behavior are preferred, as they allow for smooth application on the skin. Based on their origin, thickeners are classified as natural, semisynthetic, or synthetic. Natural thickeners, such as plant, microorganism, or algae-derived gums, are valued for their cost-effectiveness and alignment with the growing demand for sustainable cosmetic products. Xanthan gum has been selected as the thickener for this formulation.

Xanthan gum is a polysaccharide soluble in both hot and cold water, known for its high viscosity. Solutions containing xanthan gum exhibit pseudoplastic behavior, and their viscosity increases with higher concentrations. This gum offers various properties, including a versatile texture characterized by firmness, elasticity, and hardness (D'Agostino Garcia et al., 2019).

According to Zurita Acosta et al. (2021), concentrations between 0.5% and 1.5% show satisfactory rheological performance. However, temperature must be considered, as higher temperatures increase the viscosity.

Since viscosity rises with concentration, 0.5% xanthan gum is added to the serum to achieve a lighter consistency, while 1.5% will be incorporated into the cream to provide a thicker texture.

Preservatives

Preservatives can be classified as antioxidants and antimicrobials. To ensure the stability of retinal against oxidation, the Patent EP0751764B1 specifies that it must be combined with one or more liposoluble antioxidants, commonly including tocopherol (vitamin E), butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA). Patent WO1995025507A1 confirms that tocopherol should be present in a range of approximately 0.01–0.5%. Therefore, 0.05% tocopherol is added to start testing the formulation.

On the other hand, microbiological quality is a fundamental requirement. The microbiological specifications of raw materials and finished cosmetic products, along with the results of control tests, are mandatory elements of the cosmetic product safety report, in accordance with European legislation (Flanagan, 2011).

Zurita Acosta et al. (2021) declare that both natural and synthetic antimicrobial preservatives exist, although natural ones tend to be less effective at low concentrations. Non-natural preservatives are the most used, provided they are proven to be safe. It has been chosen that this product must be paraben-free. One such preservative is caprylyl glycol, which also functions as an emulsifier, humectant and emollient. In a study conducted on an O/W emulsion, the addition of 0.3% caprylyl glycol significantly improved microbial growth control. Therefore, 0.3% caprylyl glycol is included in the serum's formulation (*Table 7*).

pH Adjuster

Following Orlandi (2004), the pH of the skin's acid mantle ranges between 4.5 and 5.9 at the surface. When the surface pH becomes more alkaline, it can lead to itching and nonspecific dermatitis. For this reason, it is essential that cosmetic products maintain a pH that preserves the skin's natural physiological balance. Maintaining this pH is key to preventing irritation, dryness, and skin disorders.

To adjust the pH, citric acid is selected, as non-irritating AHA commonly found in formulations containing retinoids, keeping a stable value of pH.

The Patent ES2149037T5 states that citric acid may be included in a cosmetic emulsion in amounts ranging from 0.1% to 5% of total weight, with a specific example of 1% citric acid.

To sum up, all selected active ingredients and excipients are included in *Table 7* for the retinal serum and in *Table 8* for the retinol cream.

Table 7. Formulation selected for retinal-based serum.

Ingredient INCI	Function	Concentration [%]
Aqua	Vehicle	61.4
Propanediol	Solvent	10
Tween 20	Surfactant, emulsifier	5
Niacinamide	Active	4
Caprylic triglycerid	Emollient, occlusive	3
Triethylhexanoin	Emollient	3
Vitamin B6 derivative	Active	3
Glycerin	Humectant	2.5
Dimethicone	Occlusive	2
Butylene glycol	Solvent, humectant	2
Citric acid	pH adjuster	1
Zinc PCA	Active, humectant	1
Span 20	Surfactant, emulsifier	1
Xanthan gum	Thickener	0.5
Caprylyl Glycol	Preservative (antimicrobial), emollient, emulsifier, humectant	0.3
Sodium PCA	Humectant	0.2
Retinaldehyde	Active	0.05
Tocopherol	Preservative (antioxidant)	0.05

5.1.2.2. RETINOL-BASED CREAM

Emollients

Firstly, caprylic triglyceride has been selected again as an emollient ingredient, but in this case combined with other emollients. In agreement with Patent ES2639464T3, which describes the preparation of a cosmetic cream, a concentration of 3% caprylic triglyceride is specified.

In the case of the cream, which aims for a lightweight, non-greasy texture, cetyl alcohol is particularly suitable. It acts multifunctionally as an emollient and thickener. For example, in a cream formulation, a concentration range of 1–3% cetyl alcohol is used, more specifically 2%, according to Patent WO2011159439A2.

Lastly, glycine soja oil, referred to as soybean oil, is also incorporated. This vegetable oil is rich in essential fatty acids, particularly linoleic acid (omega-6), which helps restore the skin's barrier function. It is widely used in cosmetics due to its ability to improve skin hydration, softness, and elasticity, as well as for its compatibility with liposoluble actives like retinol. The Patent US7625575B2 describes dermatological compositions containing glycine soja oil at concentrations ranging from 1% to 4% by weight, in combination with other emollient ingredients. To achieve the desired textural results, 4% glycine soja oil is added to the formulation.

Humectants

As in the serum formulation, glycerin and butylene glycol have been selected as the main humectants in the cream, since, as reported by the products studied in *Appendix 4*, these ingredients are commonly found in both serums and creams due to their efficacy in retaining moisture and improving skin feel. In this case, 5% of glycerin is added to ensure the expected results.

However, in the specific case of the retinol cream, there is no need to include zinc PCA or sodium PCA, as their sebum-regulating function is not a priority. Nevertheless, hyaluronic acid (HA), already selected as an active ingredient, also serves a significant humectant function, as outlined in patent T0999/01 on facial cosmetics, which validates its use in hydration and skincare treatments.

Solvents

As previously explained for retinal, retinoids are lipophilic compounds, meaning they are highly soluble in fats and certain types of alcohols (Zasada et al., 2019). This factor influences solvent selection in formulations containing retinoids, as ensuring their stability and bioavailability is essential. In this context, butylene glycol not only acts as an effective humectant but also exhibits good solvent properties, especially in mixed systems that include both aqueous and lipid phases. It therefore serves a dual function: enhancing the solubility of lipophilic actives and contributing to the sensory profile and stability of the final product. As a consequence, 2% of butylene glycol is also added to the retinol cream. Additionally, as illustrated in the formulation example from Patent ES2639464T3 for a facial cream with retinoids, 10% propanediol is included as a co-solvent.

Occlusives

For the retinol cream, the selected occlusive ingredient is also dimethicone, whose concentration in cosmetic formulations may vary between 0.01% and 10%, depending on the type of product and the desired effect (WO2011159439A2). As in the serum, it has been included 2% of dimethicone in the cream. This difference allows for the evaluation of how occlusivity varies between both products, as discussed at the beginning of the chapter.

Thickeners

Given that the viscosity of a formulation increases proportionally with the concentration of thickening agents (Santos et al., 2019), 0.5% xanthan gum has been incorporated into the serum to achieve a more fluid and lightweight texture. In contrast, 1.5% xanthan gum has been used in the cream to obtain higher viscosity and a richer, more substantial skin feel. This differentiation allows the rheological properties of each product to be tailored to their respective modes of application and desired user experience.

Preservatives

The Patent T0999/01, which refers to a stabilized retinol skin care composition, specifies the combined use of two antioxidants to preserve the stability of the active ingredient.

In particular, to protect retinol from oxidation, BHT, which is a liposoluble antioxidant, is used at 0.1%, acting synergistically with ascorbic acid, a water-soluble antioxidant, at 0.1%. It has been chosen that this product must be paraben-free. As in the serum formulation, caprylyl glycol is also included as a preservative at a concentration of 0.3%, taking advantage of its antimicrobial properties and compatibility with sensitive systems such as those containing vitamin A derivatives.

pH Adjuster

To maintain the desired pH value between 4.5 and 5.9, citric acid has also been selected as a pH-regulating agent. In this context, Patent ES2149037T5 specifically states that in a cosmetic cream, citric acid may be present at concentrations of up to 1 %, thus ensuring the stability of the formulation and its compatibility with the skin.

Table 8. Formulation selected for retinol-based cream.

Ingredient INCI	Function	Concentration [%]
Aqua	Vehicle	59.3
Propanediol	Solvent	10
Glycerin	Humectant	5
Niacinamide	Active	5
Soybean Oil	Emollient	4
Polyglyceryl-3 methylglucose diestearate	Surfactant, emulsifier	3.5
Caprylic triglycerid	Emollient, occlusive	3
Cetyl Alcohol	Emollient, thickener	2
Butylene glycol	Solvent, humectant	2
Dimethicone	Occlusive	2
Xanthan gum	Thickener	1.5
Citric acid	pH adjuster	1
Span 20	Surfactant, emulsifier	1
Caprylyl Glycol	Preservative (antimicrobial), emollient, humectant, emulsifier	0.3
Retinol	Active	0.1
Hyaluronic acid	Active, humectant	0.1
Ascorbic acid	Preservative (antioxidant)	0.1
BHT	Preservative (antioxidant)	0.1

6. PRELIMINARY DESIGN OF THE MANUFACTURING PROCESS

Once the products are conceptualized, the quality factors identified, and the formulation established, the final step is to design the preliminary manufacturing process. This stage begins with determining the annual production quantity for each product, considering the batch size for each production unit, and then proceeds with a detailed design of the process. According to Wibowo et al. (2001), this step involves developing a summarized process diagram capable of producing the target product, selecting the most suitable operating equipment, defining both the sequence of ingredient addition and the equipment's operating conditions. Finally, the manufacturing is scheduled and distributed into production campaigns.

6.1. ANNUAL PRODUCTION

It is assumed that the retinal serum and the retinol cream are intended for a target group of approximately 100,000 end consumers. The estimated annual consumption per person is 2 units of each type. During the product conceptualization, the packaging volumes were established at 30 mL for the serum and 50 mL for the cream. Therefore, it is required to produce 6,000 L of serum and 10,000 L of cream. Based on the weight percentages of each component in the formulation, the total product density can be calculated from the values shown in *Appendix 5*. Both the serum and the cream have a density of 1.05 kg/L, and since this value is close to 1 kg/L, it is adopted for both cases. As a result, the required annual production of the serum is 6,000 kg and that of the cream will be 10,000 kg. Depending on the nature of the operations, production processes can be continuous (flow), discontinuous (batch), or semi-continuous (semi-batch).

According to Tomazi et al. (2005), in the cosmetics industry, batch processing is commonly used, as it offers several advantages over continuous processes, particularly for small-scale productions (typically less than 500,000 kg/year), especially in terms of cost-effectiveness. Batch processing is more suitable for products with variable demand over time and in situations where equipment needs to be reused for producing different formulations, in multiproduct operations.

Additionally, when there is demand variability, batch processing provides the necessary flexibility to adapt and respond to consumer needs, whereas continuous processes are much more limited in terms of adaptability. For these reasons, a batch process has been chosen for both the cream and the serum. This type of process is defined as one in which raw materials are processed over a set period of time in fixed quantities (batches), in a sequential manner.

In cosmetic manufacturing, facilities are often designed to accommodate more than one processing line within a single plant. These are known as multi-process or multiproduct plants (Torres N et al., 2005). Therefore, in order to use the same equipment and reduce operating costs, it has been established that the initial annual production will be carried out in 400 kg batches for both products. However, production volumes may vary in the future depending on consumer demand. Consequently, 15 batches per year of the retinal serum and 25 batches per year of the retinol cream will be produced. A summary of all these specifications can be found in *Table 11*.

6.2. SYNTHESIS OF THE PRODUCTION PROCESS: OPERATIONS AND CONDITIONS

In agreement with Wibowo et al. (2002), the manufacturing process of chemical-based consumer products basically consists of five-unit operations: pretreatment, mixing, homogenization, post-treatment, and packaging or filling. The general flow sheet of the batch process for both products developed in this project is represented in *Figure 10*.

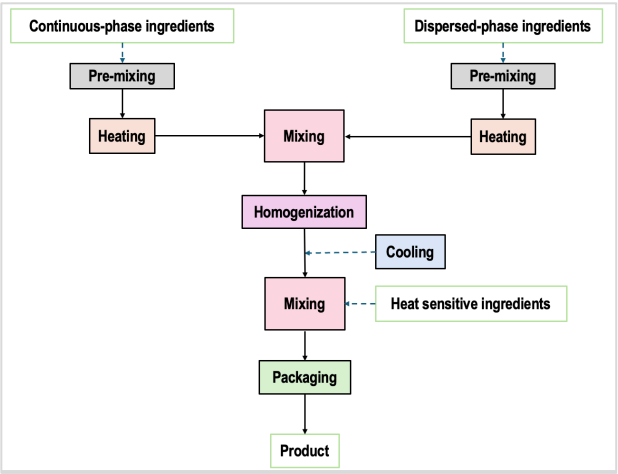

Figure 10. Synthesized flow sheet of the manufacturing process of both products developed.

PRE-MIXING AND HEATING

As it can be seen in *Figure 10*, the first unit operation is pre-mixing, in which the continuous-phase ingredients, which are water-soluble, and dispersed-phase ingredients, which are oil-soluble, are mixed separately in the pre-mixing units. If there are insoluble solid ingredients, they could require further pre-treatment operation such as particle size reduction (Wibowo et al. 2001). However, there are no insoluble ingredients in either of the two formulations developed.

To ensure the desired viscosity, it is necessary to define the order in which ingredients are added. According to Clark (2013), the correct procedure is to introduce the surfactants in the continuous phase. The Patent WO2018206904A2 also states that an O/W emulsion is prepared by forming the aqueous phase comprising the surfactants.

After considering the solubility of each ingredient, the formulation components have been classified into the two phases. This classification is detailed in *Table 9* for the retinal serum and in *Table 10* for the retinol cream. In accord with the Patent ES2120417T5, based on stabilized retinoid-containing facial compositions, retinoids are thermolabile and must be incorporated at controlled temperatures once the emulsion is formed and cooled to avoid thermal degradation and guarantee its physical-chemical stability within the cosmetic formulation. Moreover, preservatives are usually heat-sensitive ingredients, so they must be incorporated after cooling.

Table 9. Classification of the serum ingredients in the two phases.

Continuous-phase ingredients (water)	Dispersed-phase ingredients (oil)	Heat-sensitive ingredients
Aqua	Caprylic triglycerid	Retinaldehyde
Propanediol	Dimethicone	Caprylyl Glycol
Glycerin	Triethylhexanoin	Tocopherol
Niacinamide	Vitamin B6 derivative	
Butylene glycol		
Citric acid		
Zinc PCA		
Sodium PCA		
Xanthan gum		
Tween 20		
Span 20		

Table 10. Classification of the cream ingredients in the two phases.

Continuous-phase ingredients (water)	Dispersed-phase ingredients (oil)	Heat-sensitive ingredients
Aqua	Glycine Soja Oil	Retinol
Propanediol	Caprylic triglycerid	Caprylyl Glycol
Glycerin	Cetyl Alcohol	Ascorbic acid
Butylene glycol	Dimethicone	BHT
Citric acid	Polyglyceryl 3 methylglucose diestearate	
Xanthan gum		
Hyaluronic acid		
Niacinamide		
Span 20		

Before starting mixing, both phase units are heated to facilitate the mixing and to minimize viscosity at elevated temperatures between 70-80ºC. Heating ensures that emulsifiers are activated and compatible with the systems (Wibowo et al., 2002).

An example of operating conditions is the Patent WO2005097059A1, based on methods for the preparation of O/W cosmetic formulations suitable for topical dermatological products and with examples of formulations containing vitamin A. Taking this Patent into account, it has been selected that mixing and heating be carried out at 80 ºC over a 30-minute period. According to Ramírez González (2020), in a cosmetic emulsion production plant with similar temperature conditions and similar batch size, an agitation speed of 2000 rpm is used, which has been selected for this project. These conditions are initially established for the manufacturing process of the retinal serum and the retinol cream, considering that the formulation is not exactly the same.

MIXING

After pre-mixing and heating, the following operation is mixing, forming a pre-emulsion, in which the oil phase is dispersed into the aqueous phase. The procedure involves adding the continuous phase to the main vessel first, followed by the gradual addition of the dispersed phase with vigorous agitation (Clark, 2013). Agitator type and mixing speed are critical to prevent air entrapment, phase inversion and coalescence. Moreover, they are key in achieving proper dispersion (Wibowo et al., 2001). At this stage, the mixture typically contains relatively large-sized

droplets and lacks the final emulsion structure. Therefore, a high shear mixing, or homogenization step is required immediately afterward to obtain the desired texture and product stability.

Considering Patent ES2720130T3 of a basic formulation for cosmetic products, the mixing operation is carried out at elevated temperatures of up to 90 ºC between 20 and 60 min. A temperature of 80 ºC and a time of 60 minutes have been selected.

HOMOGENIZATION

According to Wibowo et al. (2001), in homogenization, larger droplets are broken down into smaller ones. This step is typically conducted at elevated temperatures ranging from 70–80 °C to reduce viscosity and facilitate dispersion. The resulting product should exhibit a fine and uniform internal structure. According to Rosdi et al. (2016), the results of their study outlined the optimum homogenization parameters for an emulsion are 80 °C and a homogenization time of 30 min. The remaining homogenization operation conditions will be defined upon selection of the equipment.

COOLING AND MIXING

Once homogenization is completed, the mixture is cooled down to 40–50 °C, at which point heat-sensitive ingredients, as listed in *Table 9* and *Table 10*, are added (Wibowo et al., 2001). According to Patent ES2120417T5, retinoids and preservatives must be added once the emulsion has cooled down to 50 ºC. Patent WO2005097059A1 related to cosmetic preparations, specifies that the emulsion should be cooled gradually under vigorous stirring.

Considering Patent ES2720130T3 of a basic formulation for cosmetic products, the mixing time may range from 20 to 60 minutes. Additionally, according to Patent CN107496267A for an acne removing emulsion, the cooling is carried out with stirring at a cooling rate of 2 ºC/min. In this process, 30 minutes have been established to complete the emulsion mixing, followed by approximately 15 minutes for the cooling step from 80 ºC to 50 ºC.

PACKAGING

The final products are filled under controlled conditions into the collapsible tubes with airless pump dispensers made from recycled polypropylene. In accordance with Patent ES2120417T5, once sealed, the tubes are set aside to determine retinol stability after storage for various periods of time at different temperatures. Both retinol and retinal degrade upon exposure to ultraviolet light; therefore, precautions must be taken throughout the entire emulsion preparation process to protect them from UV radiation. This can be achieved by turning off the lights in the work area or

by conducting all handling and processing steps under yellow light. As defined during the product conceptualization, the serum packaging has a volume of 30 mL, and the cream packaging is 50 mL. Considering the annual production unit manufactured and the number of batches per year, it can be packaged as 13,300 units per batch for the serum and 8,000 units per batch for the cream.

6.3. SELECTION OF EQUIPMENT

Equipment selection is carried out for each unit operation, bearing in mind a wide range of capacity and low energy consumption.

PREMIXING AND MIXING

For pre-mixing, pre-emulsification, and dispersion of solids in liquids, an agitated vessel under turbulent shear is the most commonly used (Wibowo et al., 2001). According to Jaszczur et al. (2020), the suitability of the mixing system can be assessed by the characterization of the flow behaviour and flow pattern within the agitation vessel. These are influenced by a combination of factors, including:

- Internal vessel geometry or configuration (baffle plates, heating jacket)

- Fluid properties (density, number of phases, viscosity)

- The location and mode of operation of the turbulent impellers that create the flow pattern (flow-pumping direction, clearance). *Figure 11* shows the different flow patterns generated by radial, axial, and mixed-flow impellers.

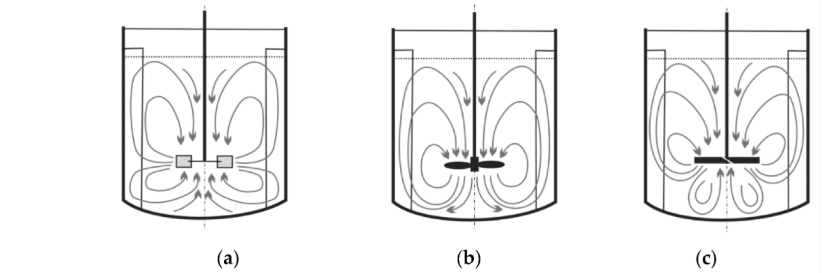

Figure 11. Flow motion generated by different types of impellers: (a) radial; (b) axial (c) mixed (Jaszczur et al., 2020).

Axial impellers such as the A310 generate smooth circulation patterns that promote bulk homogeneity while minimizing high-shear zones, which can be detrimental to active compounds (Fernandes del Pozo et al., 2020). These flow patterns are particularly well-suited for viscous, non-Newtonian systems like cosmetic creams or serums, where uniform distribution and controlled mixing intensity are critical. Moreover, they can be combined with baffles, which are vertical plates that stick out from the inside wall of the vessel. The presence of baffles reduces vortex formation, enhances axial mixing, and improves mass transfer in agitated vessels (Jaszczur et al., 2020). Furthermore, it has been decided to equip these vessels with a heating jacket. The agitation of the fluid increases heat transfer between the fluid and the jacket along the vessel wall.

Agitated vessels from the company ACE Tank (*Figure 12*) have been selected because they can be equipped with axial impellers, heating jackets, and baffles. Moreover, they are used in the cosmetics industry (ACE Mixers). The batches of both products are 400 kg, which is equivalent to 400 L. For pre-mixing, the volumes are 350 L for the continuous-phase and 40 L for the dispersed-phase in the case of the serum, and 340 L and 60 L, respectively, for the cream. Since the process occurs in a multi-product plant, it is necessary to leave a margin for adjustments; therefore, the selected equipment volumes are 500 L for the continuous-phase premixing and combined-phases mixing, and 80 L for the dispersed-phase pre-mixing.

Figure 12. Agitated vessel (V-01, V-02, V-03 and V-04).

HOMOGENIZATION

The homogenization operation is necessary to achieve uniform, consistent and high-quality consumer products. The most common types of homogenizers are high-pressure homogenizers, ultrasonic homogenizers and mechanical homogenizers, such as a colloid mill (Zwirner Equipment).

Juttulapa et al. (2017) pointed out that high-pressure homogenizers are particularly effective at reducing droplet size and improving physical stability. For this reason, this technology has been selected for both products developed in this project. The system includes a pump that draws in and pressurizes the pre-emulsion, an inlet valve to regulate flow, and a pressure intensifier that increases pressure before the fluid enters the homogenizing valve. These mechanical forces reduce particle size, resulting in finer and more stable emulsions.

The SEHH750 model from SeFluid (*Figure 13*) has been selected for this application due to its widespread use in the cosmetic industry, with a rated pressure of 25 MPa and a wide range of rated flow rate between 500 L/h and 5000 L/h. A piston pump draws in and pressurizes the pre-emulsion into the homogenization chamber. Inside, high-pressure pumps create a significant pressure increase. The high-pressure substance passes through a narrow homogenization valve. This valve creates a high-pressure zone, and a sudden pressure drop. As the substance passes through the valve, intense turbulence and shear forces cause larger particles, droplets, or aggregates to be broken down into smaller particles, resulting in a more uniform mixture. The pressure is then released, and the homogenized substance exits the high-pressure homogenizer for further processing (SeFluid).

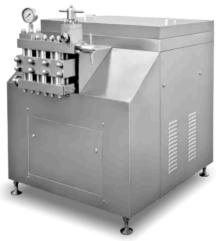

Figure 13. High pressure homogenizer (PH-01 and VH-01).

COOLING

After homogenization, the mixture is cooled to 50 ºC using a heat exchanger for subsequent incorporation of heat-sensitive ingredients. When selecting this equipment, it is necessary to prioritize efficient heat transfer to avoid product degradation, as well as to maintain hygiene and prevent cross-contamination of products intended for dermofacial treatment.

A scraped surface heat exchanger has been selected. Specifically, the model Alfa Laval CS from Contherm (*Figure 14*) is particularly suited for processing viscous, heat-sensitive products and containing-particulates products that are to be pumped. The product enters the cylinder

through the lower product head and flows upwards through the cylinder. At the same time, the cooling medium travels in counter-current flow through the narrow annular channel between the heat transfer wall and the insulated jacket. Rotating blades continuously remove product from the cylinder wall to ensure uniform heat transfer between the medium and the product. The working temperature can range from -35 ºC to 170 ºC, and water has been selected as the cooling fluid. Moreover, the equipment is designed to comply with the most stringent hygienic standards, making it ideal for cosmetic applications (Alfa Laval).

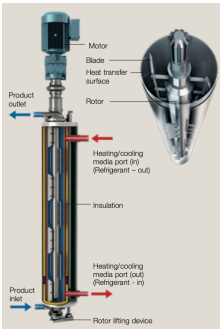

Figure 14. Scraped surface heat exchanger (H-01).

PACKAGING

For packaging the products into collapsible tubes, an automatic filling and sealing machine has been selected. Specifically, the model NTT-400A from NEWECO (*Figure 15*) is compatible with this type of PP tubes and airless pump dispensers. It also offers adaptable capacity, making it perfect for the cosmetics industry. The machine has an output of 40 tubes per minute. Consequently, this operation has a filling and sealing time of 1.5 seconds per unit (NEWECO). Considering an additional 120 minutes for in-plant operations or adjustments, the estimated packaging time per batch is approximately 450 minutes for the retinal serum and 320 minutes for the retinol cream.

Figure 15. Automatic filling and sealing machine (PK-01).

At this stage, the total batch time of each product must be determined. All previously mentioned process times are considered, along with additional time for filling and possible unforeseen events. To summarize, *Figure 16* illustrates the process diagram, highlighting all the equipment, temperatures and volumes. In addition, *Table 11* below provides a comprehensive overview of all the previously mentioned specifications.

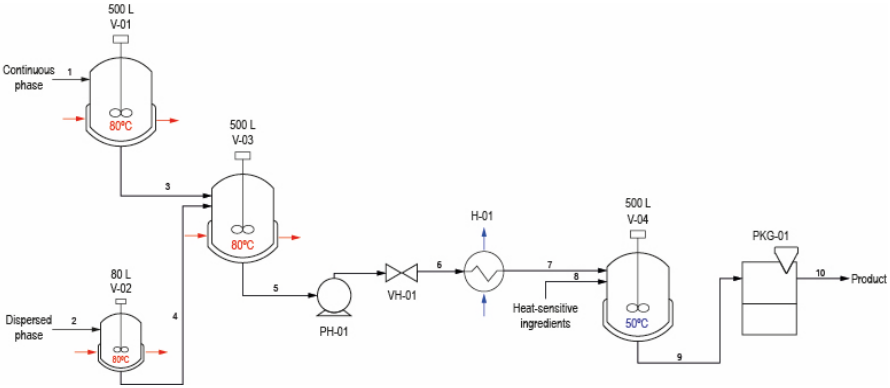

Figure 16. Process flow diagram for both products.

Table 11. Specifications of manufacturing.

	RETINAL SERUM	RETINOL CREAM
Estimated number of consumers [consumers/year]	100,000	100
Average annual units consumed per consumer [units/consumer·year]	2	2
Total annual product units manufactured [units/year]	200,000	200,000
Product volume per unit [mL/unit]	30	50
Total annual mass production [kg/year]	6,000	10,000
Batch size [kg]	400	400
Number of batches per year [batches/year]	15	25
Tubes packaged per batch [units/batch]	13,300	8,000

6.4. SCHEDULING AND CAMPAIGNS

In order to optimize overall plant performance, scheduling must be strategically planned to maximize efficiency. For each equipment involved, a cleaning stage must be considered.

The CIP (Clean In Place) system has been chosen due to its built-in safety, automation and ease of use, as it operates without requiring disassembly of the production machinery. The cleaning cycle consists of an initial wash of 5 minutes with hot water above 60°C, a 20 min alkali solution wash at a temperature of 60-80°C, an intermediate wash of 10 min with clear water below 60°C and a final wash of 5 minutes with clear water, totaling a complete cycle of 40 min (ACE Machinery, 2022). *Table 12* shows the operation time study of each operation including cleaning time. It can be seen that the time required to complete a batch (batch time) for the serum is 655 min and for the cream, it is 525 min.

Table 12. Operation time (OT) and time schedule for each operation.

		SERUM			CREAM		
		OT [min]	Start [min]	End [min]	OT [min]	Start [min]	End [min]
V-01/V-02	PREMIXING	30	**0**	30	30	**0**	30
	Cleaning	40	30	70	40	30	70
V-03	MIXING	60	30	90	60	30	90
	Cleaning	40	90	130	40	90	130
PH-01 + VH-01	HOMOGENIZATION	30	90	120	30	90	120
	Cleaning	40	120	160	40	120	160
H-01	COOLING	15	120	135	15	120	135
	Cleaning	40	135	175	40	135	175
V-04	MIXING	30	135	165	30	135	165
	Cleaning	40	165	205	40	165	205
PKG-01	PACKAGING	450	165	615	320	165	485
	Cleaning	40	615	**655**	40	485	**525**

A batch process with overlapping configuration has been implemented to improve the efficiency of the plant. This means that a new batch begins before the previous one has ended, and the start of the next batch is determined by the longest stage, considered the bottleneck of the process (cycle time).

Therefore, as shown in *Table 13*, for the serum, the cycle time is 490 minutes, and for the cream it is 360 minutes. This means that a new batch can start every 490 minutes (*Figure 17*), considering the packaging and cleaning stages. Similarly, for the cream, a new batch can start every 360 minutes (*Figure 18*).

Table 13. Time study indicating the cycle time.

	SERUM	**CREAM**
	OT Total [min]	OT Total [min]
V-01/V-02	70	70
V-03	100	100
PH-01 + VH-01	70	70
H-01	55	55
V-04	70	70
PKG-01	490	360

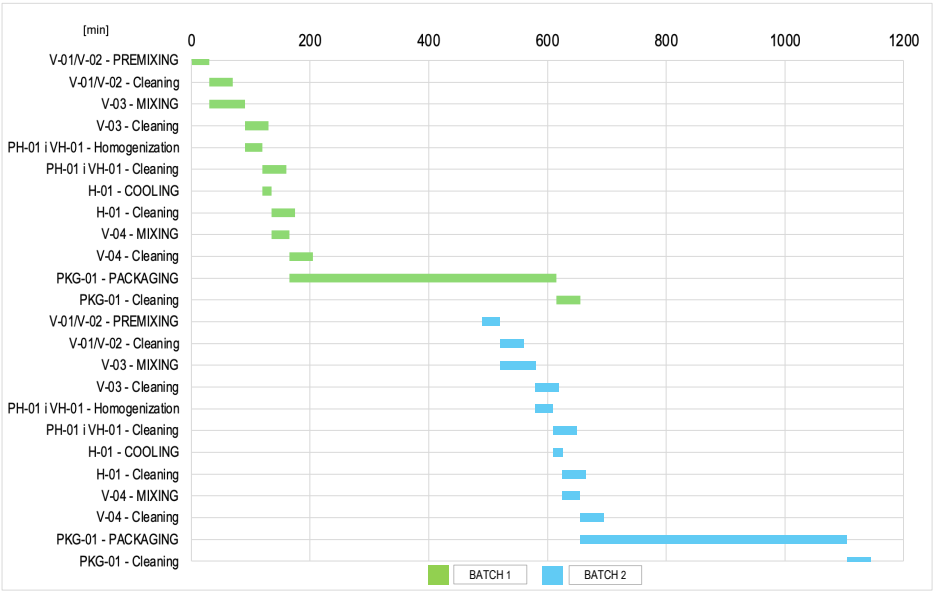

Figure 17. Gantt diagram of overlapping configuration for the serum manufacturing process.

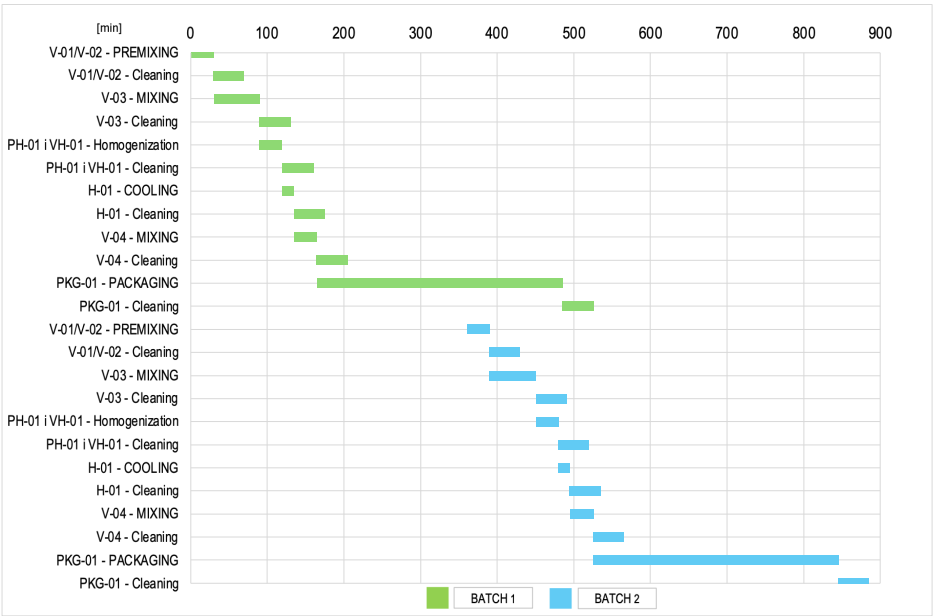

Figure 18. Gantt diagram of overlapping configuration for the cream manufacturing process.

This overlapping process is organized into various campaigns. Since it is a multiproduct plant, it will remain operational throughout the entire year, covering all 52 weeks, working 5 days from Monday to Friday, and operating with three 8-hour shifts per day (24 hours/day). To meet annual demand, based on 15 batches of serum and 25 batches of cream, the manufacturing schedule is organized into two production campaigns per year, each campaign dedicated to one product. To achieve the desired production of the serum, 1 week and 1 day per year are required. For the cream, 1 week and 2 days per year are needed.

For instance, the serum and the cream can be produced in January. This approach allows the remaining weeks of the year to be allocated to manufacturing other products. Given that the serum and the cream are intended for night-time use, the rest of the year could be strategically dedicated to manufacturing complementary products within the same dermocosmetic range. These could include facial cleansers, day creams, sunscreen formulations, or eye contour products, among others. This diversification not only maximizes equipment utilization and production efficiency but also enhances the brand's product range, creating a complete routine that covers both day and night needs. Additionally, producing these complementary products during the remaining weeks ensures flexibility in adapting to market demand and supports product launches or seasonal campaigns. Moreover, in case of increased sales of these products, their production could be expanded accordingly.

7. CONCLUSIONS

The development of a retinal-based serum and a retinol-based cream has been achieved through extended bibliographic research. The project has encompassed all stages of product development, from conceptualization and identification of quality factors to ingredient and excipient selection, ending with a preliminary process design.

In the context of functionality, the retinal-based serum has been developed to treat and prevent acne while reducing post-acne marks (post-inflammatory erythema and post-inflammatory hyperpigmentation) and improving overall skin tone, while the retinol cream has been developed to reduce expression lines and signs of aging, enhancing firmness and elasticity. Note that both products help improve acne and signs of aging at the same time, with niacinamide and a retinoid as common actives ingredients. Furthermore, these products are intended for topical facial use at night. The serum targets a broad age, from adolescence to adulthood, including both women and men with hormonal imbalances. The cream is intended for use in adulthood, including young men and women who wish to prevent skin aging. Since retinoids are prone to degradation when exposed to light and air, a collapsible tube with an airless pump dispenser has been selected as a sustainable packaging solution to protect them.

Both products have been formulated as O/W emulsions, considering the serum a microemulsion and the cream as a macroemulsion. Their estimated shelf life is 36 months, and the PAO is set to 3 months. Moreover, in terms of rheology, these emulsions describe a pseudoplastic fluid behavior. Physicochemical studies have ensured that the formulations have been designed considering efficacy, stability, and consumer satisfaction. This thorough analysis guarantees product performance and safety over time and enhances user experience through optimized textures and skin compatibility.

The selection of formulation has been guided by rigorous criteria for ingredients and excipients, prioritizing skin tolerances, scientific evidence, patents, current market products, and compliance with European Regulation (EC) Nº 1223/2009 and Regulation (EU) 2024/996. Regarding the active ingredients, a combination of retinaldehyde, zinc PCA, niacinamide, and a vitamin B6 derivative has been added to the serum, acting synergistically at safe concentrations

to treat acne and related marks. Similarly, the cream includes a mix of retinol, hyaluronic acid, and niacinamide for an anti-aging treatment.

A batch process has been designed for a multiproduct plant with overlapping production scheduling. The manufacturing process consists of the same equipment and operations for both products: agitated vessels for pre-mixing and mixing operations (V-01, V-02, V-03), a high-pressure homogenizer (PH-01, VH-01) for the homogenization stage, a scraped surface heat exchanger for cooling (HE-01), and an automatic tube filling and sealing machine (PKG-01). Manufacturing is planned in 400 kg batches, with a total production of 6,000 kg per year for the serum and 10,000 kg per year for the cream. To meet this annual demand, the schedule is organized into two production campaigns per year, each campaign dedicated to one product. Finally, this planned configuration provides flexibility for adjusting production according to consumer demand.

REFERENCES AND NOTES

Abd Sisak, M. A., Daik, R., & Ramli, S. (2017). Study on the effect of oil phase and co-surfactant on microemulsion systems. *Malaysian Journal of Analytical Science, 21*(6), 1409–1416. https://doi.org/10.17576/mjas-2017-2106-23

ACE Machinery. (2022). *CIP (Clean in Place)*. Retrieved May 2025, from: http://es.ace-chn.com/knowledge/cip_clean_in_place.html

ACE Mixer. (n.d.). *Mixing tanks with agitator*. Retrieved May 2025, from: https://acemixer.com/product/mixing-tanks-with-agitator

Afriat, I., & Chanvin, F. (2004). *Emulsión que contiene ácido ascórbico y sus utilizaciones en los ámbitos cosmético y dermatológico* (ES2149037T5). Oficina Española de Patentes y Marcas.

Agencia Española de Medicamentos y Productos Sanitarios. (2021). Excipientes de medicamentos. Retrieved April 2025, from https://www.aemps.gob.es/industria-farmaceutica/etiquetado-y-prospectos/excipientes-de-medicamentos/

Akbari, S., & Nour, A. H. (2018). Emulsion types, stability mechanisms and rheology: A review. *International Journal of Innovative Research and Scientific Studies, 1*(1), 1–9.

Alfa Laval. (n.d.). Contherm® scraped-surface heat exchangers. Retrieved May 2025, from: https://www.alfalaval.com/products/heat-transfer/scraped-surface-heat-exchangers/scraped-surface-heat-exchangers/contherm-scraped-surface-heat-exchangers/

Ali, A., Khan, N. R., Iqbal, Z., Abbas, M., Khan, A., & Shah, K. U. (2022). Relationship between sensorial and physical characteristics of topical creams: A comparative study on effects of excipients. *International Journal of Pharmaceutics, 613*, 121370. https://doi.org/10.1016/j.ijpharm.2021.121370

Ande, S. N., Sonone, K. B., Bakal, R. L., Ajmire, P. V., & Sawarkar, H. S. (2022). Role of surfactant and co-surfactant in microemulsion: A review. *Research Journal of Pharmacy and Technology*, *15*(10). https://doi.org/10.52711/0974-360X.2022.00811

Andrade, J. P., Wagemaker, T. A. L., Mercurio, D. G., & Maia Campos, P. M. B. G. (2018). Benefits of a dermocosmetic formulation with vitamins B3 and a B6 derivative combined with zinc-PCA for mild inflammatory acne and acne-prone skin. *JBPR*, *15*, 214-223.

Barco, D. (n.d.). *Types of scars and acne marks*. Retrieved March 2025, from https://dbdermatologiabarcelona.com/cicatrices-marcas-de-acne/

Benson, H. A. E., Leite-Silva, V. R., Roberts, M. S., & Walters, K. A. (2019). *Cosmetic formulation: Principles and practice*. CRC Press.

Boo, Y. C. (2021). Mechanistic basis and clinical evidence for the applications of nicotinamide (niacinamide) to control skin aging and pigmentation. Antioxidants, 10(8), 1315.

Brummer, R., & Godersky, S. (1999). Rheological studies to objectify sensations occurring when cosmetic emulsions are applied to the skin. *Colloids and Surfaces A: Physicochemical and Engineering Aspects, 152*(1–2), 89–94. https://doi.org/10.1016/S0927-7757(98)00627-3

Bukhari, S. N. A., Roswandi, N. L., Waqas, M., Habib, H., Hussain, F., Khan, S., Sohail, M., Ramli, N. A., Thu, H. E., & Hussain, Z. (2018). Hyaluronic acid, a promising skin rejuvenating biomedicine: A review of recent updates and pre-clinical and clinical investigations on cosmetic and nutricosmetic effects. *International journal of biological macromolecules*, *120*(Pt B), 1682–1695. https://doi.org/10.1016/j.ijbiomac.2018.09.188

Bîrsan, M., Gore, E., Stan, C. D., Cristofor, A. C., Palimarciuc, M., Scripcariu, Ş.-I., Antonoaea, P., Vlad, R. A., Todoran, N., & Ciurba, A. (2022). Development and evaluation of hydrophilic cream bases suitable for custom cosmetic skincare or compounding pharmaceutical dermal products. *Farmacia*, *70*(5). https://doi.org/10.31925/farmacia.2022.5.13

Cali Chamber of Commerce. (2024). *Beauty and personal care: Challenges and growth perspectives* (Report No. 43). Retrieved March 2025, from https://www.ccc.org.co/inc/uploads/2024/12/Informe-Econo%CC%81mico-Belleza-2024-43.pdf

Chanda, A., & Singh, G. (2023). Skin. *Mechanical Properties of Human Tissues. Materials Horizons: From Nature to Nanomaterials.* Springer, Singapore. https://doi.org/10.1007/978-981-99-2225-3_2

Chavda, V. P. (2019). Chapter 4 – Nanobased nano drug delivery: A comprehensive review. In Micro and Nano Technologies (pp. 69–92). Elsevier. https://doi.org/10.1016/B978-0-12-814029-1.00004-1

Chen, X. (2017). *Acne-removing cosmetic and preparation method thereof* (CN107496267A).

Chinese Journal of Engineering. (2020). Current status and prospects of rheological research on full tailings paste (Part 1): Concepts, characteristics, and models. *Chinese Journal of Engineering, 42*(7), 803–813.

Clark, J. P. (2013). Emulsions: When oil and water do mix. *Food Technology, 67(8)*, 80–82. Institute of Food Technologists.

Clum, C. E., & Wang, J. C. T. (2003). *Composiciones estabilizantes de tratamiento para la piel, conteniendo retinoides* (ES2120417T5).

Colombian Association of Dermatology (Asocolderma). (2024). *Skincare tips: Differences between retinol and retinal.* Retrieved February 2025, from https://asocolderma.org.co/tips-del-dermatologo/cuidados-de-la-piel/skincare-tips-diferencias-entre-retinol-y-retinal

Conde, J. A. N. (2019). Basic formulation for cosmetic products (ES2720130T3).

Conejo-Mir, J., Camacho, F., & Moreno Giménez, J. C. (2010). *Manual of dermatology*. Madrid: Aula Médica.

Costa, C., Medronho, B., Filipe, A., Mira, I., Lindman, B., Edlund, H., & Norgren, M. (2019). Emulsion Formation and Stabilization by Biomolecules: The Leading Role of Cellulose. *Polymers*, *11*(10), 1570. https://doi.org/10.3390/polym11101570

Couval, E., Peyrot, N., Firmino, N., Jammes, H., & Clairand, V. (2001). *Retinal-containing composition* (EP0751764B1).

Craige, S., Miles, J. V., Selse, D., & Krigsman, J. (2018). Oil-in-water emulsions (WO2018206904A2).

Darji, K., Varade, R., West, D., Armbrecht, E. S., & Guo, M. A. (2017). Psychosocial Impact of Postinflammatory Hyperpigmentation in Patients with Acne Vulgaris. *The Journal of Clinical and Aesthetic Dermatology, 10(5),* 18–23.

Dhawan, S., Sharma, P., & Nanda, S. (2020). Cosmetic nanoformulations and their intended use. In *Nanocosmetics: Fundamentals, Applications and Toxicity* (pp. 141–169). Elsevier. https://doi.org/10.1016/B978-0-12-822286-7.00017-6

Dupont, E., Samson, M., & Galderisi, A. (2011). Skin care compositions and method of use thereof (US20110158922A1).

D'Agostino Garcia, R., O'Lenick, A., & Rodrigues Leite-Silva, V. (2019). Thickening Agents. In H. A. E

Eurolab (n.d.). *Dimethicone analysis*. Retrieved May 2025, from https://www.eurolab.net/ca/testler/kozmetik-testleri/dimetikon-analizi/.

European Patent Office. (2006). T0999/01 (Skin care composition/JOHNSON & JOHNSON), 26-04-2006. Boards of Appeal.

Fernandes del Pozo, D., Liné, A., Van Geem, K. M., Le Men, C., & Nopens, I. (2020). Hydrodynamic analysis of an axial impeller in a non-Newtonian fluid through particle image velocimetry. *AIChE Journal*, *66*(6), e16939.

Fernández Vozmediano, J., & Armario Hita, J. (2003). Retinoids in dermatology. *Medicina Cutánea Ibero-Latino-Americana*, *31*(3), 271–294.

Ferrer Montiel, A. V., Almiñana Doménech, N., Cebrián Puche, J., Van Den Nest, W., Carreño Serraïma, C., & Delgado González, R. (2017). *Compuestos útiles para el tratamiento y/o cuidado de la piel y sus composiciones cosméticas o farmacéuticas* (ES2639464T3).

Flanagan, J. (2011). Preserving Cosmetics with Natural Preservatives and Preserving Natural Cosmetics. Formulating, Packaging, and Marketing of Natural Cosmetic Products, 169–178. https://doi.org/10.1002/9781118056806.ch10

Fiume, M. M. (2015, January 13). *Safety assessment of PCA (2-pyrrolidone-5-carboxylic acid) and its salts as used in cosmetics: Final amended report*. Cosmetic Ingredient Review.

Fluhr, J. W., Darlenski, R., & Lachmann, N. (2008). Glycerol and the skin: Holistic approach to its origin and functions. *British Journal of Dermatology*, *159*(1), 23–34.

Fowler, J. (1982). Noncomedogenic ingredients in cosmetic formulations. *Journal of the American Academy of Dermatology*, *6*(6), 1048–1051.

García Quesada, J. C. (2008). *Tema 2: Fluidos viscosos*. Universidad de Alicante, Departamento de Ingeniería Química.

Geiger, J. M., Hommel, L., Harms, M., & [otros si hay más, hasta 20]. (1996). Oral 13-cis retinoic acid is superior to 9-cis retinoic acid in sebum suppression in humans. *Journal of the American Academy of Dermatology*, *34*(3), 513–515.

Go, Y. M., & Kim, Y. J. (2005). O/W type cosmetic composition prepared using polyglyceryl-3 methylglucose distearate (KR20050097587A).

Grampurohit, N., Ravikumar, P., & Mallya, R. (2011). Microemulsions for topical use: A review. *Indian Journal of Pharmaceutical Education and Research*, *45*(1), 100–107.

Gräbner, D., & Hoffmann, H. (2017). Rheology of cosmetic formulations. In *Cosmetic Science and Technology: Theoretical Principles and Applications* (pp. 471–488). Elsevier. https://doi.org/10.1016/B978-0-12-802005-0.00027-6

Guth, J., & Lentner, V. (2005). *Method for the preparation of cosmetic emulsions* (WO2005097059A1).

Hernández Navarro, E. (2024). Prima evidencia científica de los activos escogidos para formular. IM Farmacias.

Hernández-Barrera, N. R., Moncada, B., Navarrete-Solís, J., Fuentes-Ahumada, C., Torres-Álvarez, B., Castanedo-Cázares, J. P., & Cano-Ríos, P. (2011). Assessment of moisturizing creams available in México. *Gaceta Médica de México*, *147*(3), 270–274.

IndustriaCosmética. (2024). *Recycled polypropylene revolutionizes the cosmetic sector.* Retrieved March 2025, from https://www.industriacosmetica.net/noticias/el-polipropileno-reciclado-revoluciona-el-sector-cosmetico-OLpHG

Ismail, A. R., Dzolkifli, O., Ooi, T. L., & Ahmad, S. (1998). Oleoquimicos a base de palma, como ingredientes inertes en formulaciones de plaguicidas. *Palmas*, *19*(2), 59-65.

Jaszczur, M., & Młynarczykowska, A. (2020). A general review of the current development of mechanically agitated vessels. *Processes*, *8*(8), 982.

Johns, M. L., & Hollingsworth, K. G. (2007). Characterisation of emulsion systems using NMR and MRI. *Progress in Nuclear Magnetic Resonance Spectroscopy*, *50*(2-3), 51-70.

Juttulapa, M., Piriyaprasarth, S., Takeuchi, H., & Sriamornsak, P. (2017). Effect of high-pressure homogenization on stability of emulsions containing zein and pectin. *Asian Journal of Pharmaceutical Sciences, 12*(1), 21–27. https://doi.org/10.1016/j.ajps.2016.09.004

Kim, J., Lee, Y. I., Suk, J., Lee, D., & Lee, J. H. (2021). *A pilot study evaluating the efficacy and safety of retinaldehyde-loaded niosomes against mild-to-moderate acne. Journal of Cosmetic Dermatology, 20(11),* 3586-3592. https://doi.org/10.1111/jocd.14478

L'Oréal. (nd). *What is BHT?* Retrieved May 2025, from: https://interior-productos.loreal.es/ingredients/bht

Li, W.-H., Wong, H.-K., Serrano, J., Randhawa, M., Kaur, S., Southall, M. D., & Parsa, R. (2017). Topical stabilized retinol treatment induces the expression of HAS genes and HA production in human skin in vitro and in vivo. *Archives of Dermatological Research, 309*(4), 275-283. https://doi.org/10.1007/s00403-017-1723-6

Lui, D. (2009). *Emulsions*. Department of Pharmaceutics and Pharmaceutical Administration (DAFAF), UNMSM.

Madurga Sanz, M. (2009). El papel de la cosmética: excipientes y conservantes. *Pediatría Atención Primaria, 11*(41), 81–100.

Malfitano, O. (2007). *Neuromarketing: Cerebrando negocios y servicios*. Ediciones Granica.

Malhotra, A., & Coupland, J. N. (2004). The effect of surfactants on the solubility, zeta potential, and viscosity of soy protein isolates. *Food Hydrocolloids, 18*(1), 101-108. https://doi.org/10.1016/S0268-005X(03)00047-X

Martínez, D. C. R., González, D. G., Montañez, A. M. F., & Domínguez, O. F. C. (2018). *Sector de envases plásticos para cosméticos: Rutas para el fortalecimiento de la competitividad sectorial* (p. 359).

Nazeer, F., Sivas, S., Anvar, S., Souparnika, D., Philip, F., Senthila, S., & Prasanth, V. V. (2023). Current insights into the formulation and delivery of therapeutic and cosmeceutical agents for fairness serum. *Mount Zion College of Pharmaceutical Sciences and Research*, 22(6).

NEWECO. (n.d.). *Llenadora selladora automática de tubos plásticos NTT-400A*. Retrieved May 2025, from: https://www.neweco.biz/es/maquinas/llenadora-selladora-automatica-de-tubos-plasticos-ntt-400a/

Olea, N. (2019). *Libérate de tóxicos: guía para evitar los disruptores endocrinos.* RBA Books.

Olsen, E. A., Katz, H. I., Levine, N., Nigra, T. P., Pochi, P. E., Savin, R. C., Shupack, J., Weinstein, G. D.,

Ong, D. E. (1993). Retinoid metabolism during intestinal absorption. *The Journal of Nutrition, 123,* 351-355.

ONU. (n.d.). Take action for the sustainable development goals. Retrieved June 2025, from: https://www.un.org/sustainabledevelopment/sustainable-development-goals/

Orlandi, M. C. (2004). Healthy skin and acid mantle. *Folia Dermatológica Peruana*, *15*(2), 121–124.

Panagiotou, T., & Fisher, R. (2012). Improving product quality with entrapped stable emulsions: From theory to industrial application. *Challenges*, *3*(2), 84–113. https://doi.org/10.3390/challe3020084

Parra-Hernández, E., Nava-Reyes, H., & Zamudio-Cortés, P. (2005). *Retinoic acid and lung function. Journal of the National Institute of Respiratory Diseases, 18(1),* 59-69.

Perry, J. M., Deaver, D. R., Hickey, M. B., Remenar, J. F., Vandiver, J., Palmieri, M. J., Jr., & Pan, Z. (2020). *Pharmaceutical compositions having improved storage stability* (US10639376B2).

Proyectacolor. (2018). *Fisiología del color*. Retrieved March 2025, from http://proyectacolor.cl/teoria-de-los-colores/fisiologia-del-color/

Qazi, N. (2024). *Differences between PIE and PIH.* Retrieved March 2025, from https://qaziclinic.com/es/resources/diferencias-entre-pie-y-pih/

Ramírez González, V., Durán Becerra, G., & González, C. (2020). *Planta de preparación de emulsiones cosméticas*. University of Santiago Chile.

Richter, F., & Steiger, M. (1997). Pharmaceutical composition (US5856355A). Novartis AG.

Regulation (EC) Nº 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products.

Regulation (EU) 2024/996 of 3 April 2024 amending Regulation (EC) No 1223/2009 of the European Parliament and of the Council as regards the use of vitamin A, Alpha-Arbutin and Arbutin and certain substances with potential endocrine disrupting properties in cosmetic products.

Robb, I. D. (Ed.). (1982). Microemulsions (1st ed.). Springer. ISBN 978-0306408342

Rosdi, M. R. H., Ariffin, A., & Ishak, Z. A. M. (2016). Optimizing homogenization parameters for improving ethylene vinyl acetate emulsion stability in pour point depressant application. *Egyptian Journal of Petroleum, 25*(3), 445–452. https://doi.org/10.1016/j.ejpe.2016.01.002

Saigu. (2020). *Leer etiquetas de cosméticos.* Saigu Cosmetics. Retrieved May 2025, from https://saigucosmetics.com/blogs/articulos/leer-etiquetas-cosmeticos.

Sanches, S. C. da C., Ré, M. I., Silva-Júnior, J. O. C., & Ribeiro-Costa, R. M. (2023). Organogel of Acai oil in cosmetics: Microstructure, stability, rheology and mechanical properties. *Gels*, *9*(2), 150. https://doi.org/10.3390/gels9020150

Santos, M. B., dos Santos, C. H. C., de Carvalho, M. G., de Carvalho, C. W. P., & Garcia-Rojas, E. E. (2019). Physicochemical, thermal and rheological properties of synthesized carboxymethyl tara gum (Caesalpinia spinosa). International Journal of Biological Macromolecules, 134, 595–603. https://doi.org/https://doi.org/10.1016/j.ijbiomac.2019.05.025

Sarkar, R., Arora, P., & Garg, K. V. (2013). *Cosmeceuticals for Hyperpigmentation: What is Available? Journal of Cutaneous and Aesthetic Surgery, 6(1),* 4–11. https://doi.org/10.4103/0974-2077.110089

Schnarch, A. (2001). *New Product: Creativity, Innovation, and Marketing* (3rd ed.). Colombia: Nomos SA.

Scriven, L. (1976). Equilibrium bicontinuous structure. *Nature, 263*(5576), 123–125. https://doi.org/10.1038/263123a0

SeFluid. (n.d.). *Homogeneizador de alta presión*. Retrieved May 2025, from: https://www.sefluid.com/es/productos/homogeneizador-de-alta-presion/

Slade, H. B., Shroot, B., Feldman, S. R., Cargill, D. I., & Stanfield, J. W. (2009). *Reappraising the phototoxicity of tretinoin: a report of four controlled clinical trials. Photodermatology, 25.*

Sporn, M. B., Roberts, A. B., & Goodman, D. S. (Eds.). (1994). *The retinoids: Biology, chemistry, and medicine* (2nd ed.). Raven Press.

STANPA. (2024). Overview of the cosmetics and perfumery sector in Spain.

Statista. (2024). *Leading companies in perfume and cosmetic manufacturing in Spain*. Retrieved February 2025, from https://es.statista.com/estadisticas/514820/empresas-lideres-en-la-fabricacion-de-perfumes-y-cosmeticos-espana/

Stelmaszczyk, O. (2024). Skincare brands are racing to join the dermocosmetic movement. *Euromonitor International.*

Suau, A. M. (1987). Retinoids. *Balearic Medicine, 2(2),* 31-39.

Svarc, F. E., Arnejo, N. A., Carballo, O., & Argentina, F. S. B. A. (2012). Emulsionantes, emolientes, HLB, parámetros de solubilidad y teroia de las emulsiones. Análisis comparativo.

Tadros, T. F. (2013). *Emulsion formation and stability*. Wiley-VCH. https://doi.org/10.1002/9783527647941

Tomazi, K. G., Linninger, A. A., & Daniel, J. R. (2005). Batch processing industries. In Batch Processes (pp. 19-54). CRC Press.

Torres, H., & Torres, X. (2005). Situation of cosmetology and aesthetics within dermatology: Evolution of dermocosmetics in the last 30 years. *Ibero-Latin American Cutaneous Medicine*, *33*(1), 1–5.

Torres, N., Rivera, J., Salamanca, A., & Luque, D. (2005). Estudio descriptivo del sector productor y comercializador de cosméticos en Bogotá DC Colombia. *Revista Colombiana de Ciencias Químico Farmacéuticas*.

Umbert Millet, I. (2018). *Composición cosmética para el rejuvenecimiento de la piel* (ES2692188T3).

United Nations Industrial Development Organization (UNIDO). (2018). *Recommendations for the development of stability studies of cosmetic products (Safe+ Program)*.

Velkoborsky, V., & Ghosh, S. (2010). *Non-aqueous colloidal formulation* (WO2010054495A2).

Wagoneer, B. K. (2009). Dermatological composition (US7625575B2).

Walke, B. (2011). Skin moisturizer (WO2011159439A2).

Wibowo, C., & Ng, K. M. (2001). Product-oriented process synthesis and development: creams and pastes. AIChE Journal, 47(12), 2746-2767. https://doi-org.sire.ub.edu/10.1002/aic.690471214

Wibowo, C., & Ng, K. M. (2002). Product-centered processing: Manufacture of chemical-based consumer products. *AIChE Journal, 48(6),* 1212–1230. https://doi.org/10.1002/aic.690480609

Zaballos, P., Echevarría, V., Rodero, J., & Garrido, A. (2000). Dermatosis eritematosas faciales agudas. Revista Médica, 36(7), 245–252.

Zasada, M., & Budzisz, E. (2019). *Retinoids: Active molecules influencing skin structure formation in cosmetic and dermatological treatments. Advances in Dermatology and Allergology, 36(4),* 392-397.

Zhao, B. (2024). Retinol (Vitamin A) and Its Derivatives: Synthesis and Applications. *Highlights in Science, Engineering and Technology*, *116*, 336-342. https://doi.org/10.54097/fyk88356

Zurita Acosta, N., & López Pérez, A. M. (2021). Elaboración de Emulsiones Cosméticas con Ingredientes de Origen Natural.

Zwirner Equipment Company. (n.d.). *Homogenizer types and applications*. Retrieved May 2025, from: https://www.zwirnerequipment.com/blog/homogenizer-types-and-applications/

ACRONYMS

AHA: Alpha Hydroxy Acid

BHA: Butylated Hydroxyanisole / Beta Hydroxy Acid

BHT: Butylated Hydroxytoluene

BPA: Bisphenol A

CLP: Clean In Place

EC: European Commission

EU: European Union

FDA: Food and Drug Administration

FSC: Forest Stewardship Council

HA: Hyaluronic Acid

HLB: Hydrophilic-Lipophilic Balance

INCI: International Nomenclature of Cosmetic Ingredients

ISO: International Organization for Standardization

O/W: Oil-in-Water Emulsion

PAO: Period After Opening

PCA: Pyrrolidone Carboxylic Acid

PCR: Post-Consumer Recycled

PEG / PEGs: Polyethylene Glycol(s)

PP: Polypropylene

RAR: Retinoic Acid Receptor

RXR: Retinoid X Receptor

SDS: Sodium Dodecyl Sulfate

TEWL: Transepidermal Water Loss

USD: United States Dollar

UV: Ultraviolet

W/O: Water-in-Oil Emulsion

APPENDICES

APPENDIX 1: EXAMPLE OF STABILITY TESTING PROTOCOL

QUALITY PHYSICOCHEMICAL FACTORS			
STABILITY STUDY PROTOCOL		**Document code**	**Company Logo**
Product Name			
Page X/X			
General information			
Product	**Active Substances**		
Commercial Presentation			
Packaging Material			
Responsible for Marketing			
Lot Number			
Study Start Date			
Study Completion Date			
Objective of the Study			
Study Conditions			
Batch	**Batch Type**	**Fabrication date**	**Batch size**
Storage condition 1	Temperature: X °C	Relative Humidity: X %	
Storage condition 2	Temperature: X °C	Relative Humidity: X %	

Sampling Time (weeks, months)	Storage Condition 1	Storage Condition 2	
0	X		
1	X		
2		X	
3		X	
4	X		
6			

Parameter	Sampling Frequency	Method Used	Result
Organoleptic Parameter	0, 1, 2, 3, 4, and 6 months		
Physico-chemical Parameter			

Prepared by:	X
Reviewed:	X
Approved:	X

APPENDIX 2: EXAMPLE OF QUALITY SENSORIAL FACTORS

QUALITY SENSORIAL FACTORS			
SENSORY EVALUATION PROTOCOL		**Document code**	**Company Logo**
Product Name			
Page X/X			
Date			
Reviewed:	X		
Approved:	X		
AROMA (Fragrance)			
Criteria	**Scale (1 to 5)**		
Odor intensity	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5		
Perceived naturalness	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5		
Pleasantness	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5		
Lack of unpleasant scent	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5		
Comments			
VISUAL APPEARANCE			
Criteria	**Scale (1 to 5)**		
Cream color	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5		
Homogeneity	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5		
Color-container match	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5		
Visual appeal	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5		
Comments			

TEXTURE AND TOUCH (Application feel)	
Criteria	**Scale (1 to 5)**
Ease of application	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5
Absorption (speed/residue)	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5
Refreshing sensation	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5
Softness to the touch	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5
Non-oily feel	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5
Perceived irritation	☐ None ☐ Mild ☐ Moderate ☐ Strong
Comments	
OVERALL RATING	
Criteria	**Scale (1 to 5)**
Overall satisfaction	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5
Purchase intent	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5
Additional comments (optional):	

APPENDIX 3: CURRENT MARKET FORMULATIONS OF RETINAL SERUMS

	**PRODUCT:**	Acniben Night Concentrate
	BRAND:	ISDIN
INGREDIENT INCI		**FUNCTION**
Aqua (Water)		Vehicle
Dimethicone		Occlusive
Niacinamide		Active
Lauryl PEG/PPG-18/18 Methicone		Emulsifier, surfactant
Propanediol		Solvent
Dibutyl Adipate		Emollient, skin softener
Alcohol Denat.		Solvent, astringent
Zinc PCA		Active, humectant
Pentylene Glycol		Humectant, preservative booster
Caprylyl Glycol		Preservative (antimicrobial), emollient, humectant, emulsifier
Xylitol		Humectant, skin-conditioning agent
Caprylic Acid		Emollient, antimicrobial agent
Tocopheryl Acetate		Antioxidant (Vitamin E derivative)
Caprylic/Capric Triglyceride		Emollient, skin-conditioning agent
Glycerin		Humectant
Hydroxyacetophenone		Antioxidant, preservative booster
Tocopherol		Antioxidant (Vitamin E)
Retinal (Retinaldehyde)		Anti-aging and skin-renewing active
Sodium Hydroxide		pH adjuster
T-Butyl Alcohol		Solvent and stabilizer
Citral		Fragrance with antioxidant
Ascorbic Acid		Preservative (antioxidant)

	**PRODUCT:**	Pro Retinal Dual Treatment
	BRAND:	Paula's Choice Skincare

INGREDIENT	**FUNCTION**
Water (Aqua/Eau)	Vehicle
Caprylic/Capric Triglyceride	Emollient
Dimethicone	Occlusive
Polyglyceryl-2 Stearate	Emulsifier
Propanediol	Solvent
Polyglyceryl-3 Diisostearate	Emulsifier and stabilizer
Sodium Stearoyl Glutamate	Emulsifier
Retinal	Active
Tocopherol	Vitamin E, antioxidant
Saccharomyces Ferment Filtrate	Hydration booster
Albatrellus Confluens (Mushroom) Extract	Plant extract with antioxidant properties
Punica Granatum Pericarp Extract	Plant extract with antioxidant properties
Oleyl Adapalenate	Antioxidant and retinoid derivative
Glyceryl Stearate	Texture enhancer
Stearyl Alcohol	Texture enhancer
Butylene Glycol	Humectant
Cetyl Glyceryl Ether	Emollient
Ricinus Communis (Castor) Seed Oil	Emollient plant oil
Sodium Polyacrylate	Film-forming agent
Isopropyl Myristate	Emollient and texture enhancer
Hydroxyacetophenone	Humectant
Caprylhydroxamic Acid	Chelating agent
Sodium Phytate	Chelating agent and stabilizer
Xanthan Gum	Thickener
Glycerine	Humectant
1,2-Hexanediol	Preservative
Sorbitan Oleate	Emulsifier
Citric Acid	pH adjuster
Titanium Dioxide (CI 77891)	Occlusive and opacifying agent

APPENDIX 4: CURRENT MARKET FORMULATIONS OF RETINOL CREAMS

	**PRODUCT:**	Rapid Wrinkle Repair Regenerating Retinol Cream, Fragrance-Free + Hyaluronic Acid
	BRAND:	NEUTROGENA
INGREDIENT		**FUNCTION**
Water		Vehicle
Glycerin		Humectant
Dimethicone		Emollient, skin conditioner
Stearyl Alcohol		Emollient, co-emulsifier
Cetearyl Alcohol		Emollient, co-emulsifier
Butylene Glycol		Solvent, humectant
Ceteareth-20		Emulsifier
Dimethicone		Occlusive
Sodium Polyacrylate		Thickener, stabilizer
Caprylyl Glycol		Preservative (antimicrobial), emollient, humectant, emulsifier
Sodium Acrylate/Sodium Acryloyldimethyl Taurate Copolymer		Emulsion stabilizer
Polyacrylamide		Gel former, thickener
Polysorbate 20		Emulsifier, surfactant
Retinol		Active
BHT		Preservative (antioxidant)
HA		Active, humectant
Sodium Hydroxide		pH adjuster
Ascorbic Acid		Preservative (antioxidant)

	**PRODUCT:**	Laser Pressed Cream Noche con Retinol + Niacinamida
	BRAND:	L'Óreal

INGREDIENT	**FUNCTION**
Aqua / Water	Vehicle
Butylene Glycol	Solvent, humectant
Glycerin	Humectant
Niacinamide	Active (brightening, anti-inflammatory)
Glycine Soja Oil / Soybean Oil	Emollient
Aluminum Starch Octenylsuccinate	Oil absorbent, mattifying agent
Caprylic/Capric Triglyceride	Emollient
Acetyl Dipeptide-1 Cetyl Ester	Peptide, soothing agent
Sodium Hyaluronate	Humectant, moisturizer
Trisodium Ethylenediamine Disuccinate	Chelating agent
Panthenol	Humectant, pro-vitamin B5
Retinol	Active
Hydroxyethylcellulose	Thickener
Polyglyceryl-3 Methylglucose Distearate	Surfactant, emulsifier
Sodium Polyacrylate	Thickener, stabilizer
Sorbitan Laurate	Emulsifier, surfactant
Tocopherol	Antioxidant (Vitamin E)
Dimethicone	Occlusive
Benzyl Alcohol	Preservative, solvent
Citronellol	Fragrance component
Limonene	Fragrance component
Linalool	Fragrance component
Caprylyl Glycol	Preservative (antimicrobial), emollient, humectant, emulsifier
Chlorphenesin	Preservative
Phenoxyethanol	Preservative
Parfum / Fragrance	Fragrance

APPENDIX 5: DENSITY VALUES OF BOTH FORMULATIONS

RETINAL-BASED SERUM

Ingredient INCI	Function	Density [kg/L]
Aqua	Vehicle	1
Propanediol	Solvent	1.05
Niacinamide	Active	1.4
Caprylic triglycerid	Emollient, occlusive	0.95
Triethylhexanoin	Emollient	0.95
Vitamin B6 derivative	Active	1.1
Glycerin	Humectant	1.26
Dimethicone	Occlusive	0.97
Butylene glycol	Solvent, humectant	1
Citric acid	pH adjuster	1.66
Zinc PCA	Active, humectant	1.35
Xanthan gum	Thickener	1.5
Span 20	Surfactant, emulsifier	1.02
Caprylyl Glycol	Preservative (antimicrobial), emollient, emulsifier, humectant	0.96
Tween 20	Surfactant, emulsifier	1.1
Sodium PCA	Humectant	1.33
Retinaldehyde	Active	0.95
Tocopherol	Preservative (antioxidant)	0.95

RETINOL-BASED CREAM

Ingredient INCI	Function	Density [kg/L]
Aqua	Vehicle	1
Propanediol	Solvent	1.05
Glycerin	Humectant	1.26
Niacinamide	Active	1.4
Caprylic triglycerid	Emollient, occlusive	0.95
Soybean Oil	Emollient	0.93
Polyglyceryl-3 methylglucose diestearate	Surfactant, emulsifier	1.05
Cetyl Alcohol	Emollient, thickener	0.82
Butylene glycol	Solvent, humectant	1
Dimethicone	Occlusive	0.97
Xanthan gum	Thickener	1.5
Citric acid	pH adjuster	1.66
Span 20	Surfactant, emulsifier	1.02
Caprylyl Glycol	Preservative (antimicrobial), emollient, humectant, emulsifier	0.96
Retinol	Active	0.94
Hyaluronic acid	Active, humectant	1.1
Ascorbic acid	Preservative (antioxidant)	1.65
BHT	Preservative (antioxidant)	1.05