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Development of a disinfectant and moisturizing hand cream and preliminary design of its manufacturing process

Desenvolupament d'una crema de mans desinfectant i hidratant i disseny preliminar del seu procés de fabricació

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"Ahora es el momento de comprender más, para que podamos temer menos."
Marie Curie

En primer lugar, querría agradecer a mi tutora Alicia Maestro Garriga por su dedicación, ayuda e inspiración a lo largo de todo el proceso.

En segundo lugar, gracias a mi familia, por ser un pilar fundamental en mi vida. Gracias a mis padres por ser ejemplo siempre de esfuerzo, constancia y dedicación. A mis hermanos por el apoyo incondicional y por animarme a alcanzar mis metas.

Para acabar, cierro así una etapa muy importante, llena de esfuerzo y sacrificio.

REPORT

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1 SUMMARY

The current health crisis that society is going through as a result of the COVID-19 pandemic caused by the SARS-CoV-2 virus has led to increased awareness of hand hygiene and cleaning. The products used to prevent the transmission of this, and other viruses are usually alcohol-based hand sanitizers and their frequent use can cause dryness of the skin and alter the integrity and function of the skin barrier. Although many of these products contain glycerin to increase viscosity and reduce dehydration, it may not be enough. Therefore, consumers often combine this product with other moisturizers products to counteract the damage.

The purpose of this project is to develop a hand cream that combines disinfectant and moisturizing action to meet the needs of society. The product must combine the main characteristics of hand disinfectants and creams, so it is necessary to find the balance between disinfecting agents and cosmetic ingredients to create an effective bactericidal, virucidal and fungicidal cream, without irritating the skin.

Disinfectant efficacy, emulsion stability, disinfectant stability, rheology and sensory aspects such as color, fragrance, and moisturizing efficacy have been established as quality factors for the formulated product.

The hand cream has been conceptualized as an O/W emulsion with pseudoplastic behavior, low viscosity when applied to the skin and high viscosity at low shear rates so that it does not spill easily. The emulsion has been conceptualized as whitish and with dispersed phase droplets approximately 20 µm in size. The selection criteria for all ingredients have been based on patents, scientific articles, books, and market trends, considering their efficacy, safety, irritability, and allergenicity. Based on this, peracetic acid has been chosen as the disinfecting agent.

The production process is based on the emulsion and homogenization of the dispersed and continuous phase that forms the formula. It has been designed as a batch process as it is the type of production that is best suited. To carry out the manufacturing process, two stirred vessels have been selected for the premix stages, a coaxial mixing reactor with a high cut stator rotor for the emulsion and homogenization stage, and a storage vessel and filling equipment for the post-treatment stage.

2 INTRODUCTION

COVID-19 is an infectious disease caused by SARS-CoV-2, a recently discovered coronavirus. It was first recognized on December 31, 2019 by the Wuhan Municipal Health and Sanitation Commission (Roujian, et al, 2020). Due to its rapid transmissibility, on March 11, 2020 the World Health Organization was declared a pandemic. According to official data released by the WHO on February 4, 2021, 103 million confirmed cases of COVID-19 have been recorded worldwide.

It affects differently according to each person. The spectrum of symptoms of this respiratory infection can vary greatly. Some of the most common symptoms are fever, dry cough, tiredness, shortness of breath, diarrhea, headache or sore throat, conjunctivitis, and loss of the sense of smell or taste (Fan Yun, et al 2020). Most of the infected have symptoms of mild or moderate intensity and recover without the need for hospitalization. Although can have serious consequences for those who are part of the population at risk. This group includes people over the age of 60, people who have had a previous chronic illness, such as high blood pressure or lung disease, and immunosuppressed people of any age (Fan-Yun, et al 2020).

Transmission of the COVID-19 virus can occur by direct contact with infected people and by indirect contact with surfaces or objects used by an infected person. Direct transmission can occur when a person is in contact with an infected person and, therefore, runs the risk that their mucous membranes or conjunctivae are exposed to potentially infectious respiratory droplets (diameter > 5 μm). Another method of direct infection is due to the inhalation of aerosols (diameter <5 μm) emitted by an infected person (Song Tang, et al 2020). Due to its smaller size, infectivity can be higher as it penetrates deep into the lungs.

The incubation period ranges from 1 to 14 days and the length of time that an individual with COVID-19 is infectious remains uncertain (Lauer, et al, 2020). According to *Lauer, et al* (2020) data report, in 95% of the cases, the median incubation period is 5.1 days.

The global sanitary situation has impacted society behavior and has led people to take more preventive measures regarding personal hygiene maintenance, especially hand hygiene. Hands play an important role in the spread of viruses (Song Tang, et al 2020). The hand-surface contact can transfer a significant proportion of the virus, that could then spread by touching the mucosa of the nose or conjunctiva of the eye.

Organizations such as the *World Health Organization* or the *European Center for Disease Prevention and Control* recommendations emphasize the importance of the correct use of masks and the practice of hand hygiene. They recommend washing the hands with soap and water, or in their absence, rubbing them with a formulation based on a disinfectant agent. This helps to eliminate or minimize the transient flora that inhabits the hands. A good hand hygiene routine helps prevent COVID-19 infection and other infections caused by viruses, bacteria, and fungi.

Viruses are made up of a viral capsid that contains nucleic acid, which serves information for replication (Betty A. Forbes, 2009). The capsid and its associated proteins protect the nucleic acid and serve as bind to host cell receptors. When a virus infects a cell, the genetic information of the virus forces the host cell to synthesize the nucleic acids and proteins of the virus to form new viruses. Viruses without a capsid are unable to replicate and increase in number, until they find a host cell (Qianyu, 2020).

Viruses have a wide diversity of morphologies and sizes. They can be enveloped or non-enveloped (Betty A. Forbes, 2009). The first type is characterized by having a lipid envelope derived from the host cell membrane, whereas the non-enveloped ones lack it. The envelope layer of viruses is made up of lipid bilayers, making the membrane sensitive to chemical and physical conditions. The non-enveloped viruses are more resistant to disinfectants compared to viruses with envelopes. In the case of the SARS-CoV-2, structurally, is a spherical virus of 100-160 nm in diameter, with envelope.

Bacteria are prokaryotic microorganisms with a size ranging from 0.5 to 5 µm. They are generally made up of a cell wall and a displacement system, such as flagella (Betty A. Forbes, 2009). There is a great variety of morphologies, such as cocci, bacilli or spirilla. They are the most abundant organism on the planet and contribute to a wide variety of biological and geological processes. Some pathogenic bacteria are responsible for infectious diseases such as typhus or tuberculosis.

They reproduce asexually by bipartition. In this way, two cells are obtained with identical hereditary information. Under optimal conditions, bacteria can reproduce very quickly, reaching a total of 5 billion new cells in 16 hours. To prevent its proliferation, the formation of the cell wall must be inhibited, thus stopping its life cycle.

Fungi are eukaryotic organisms. There are three main groups: molds, yeasts, and mushrooms (Betty A. Forbes, 2009). They generally reproduce asexually and act as parasites, saprobes or mutualists. Its size is very diverse. They reproduce by spores, which are dispersed in search of optimal conditions for their germination. Inhalation or contact with spores can cause contagion and, therefore, infection. They are usually more dangerous in people with immunodeficiency. It is important to prevent its evolution to protect against the infection. Antifungal agents inhibit cell membrane synthesis thus preventing cell division.

For proper disinfection of the hands, the before mentioned pathogenic microorganisms must be eliminated and eradicated to prevent their growth and proliferation. Although frequent hand disinfection can damage the skin and lead to irritation, itching, stinging, or redness. In the case of hydroalcoholic gels, due to their high alcohol content, their use causes dryness of the skin and the appearance of cracks or inflammation. To protect the hands from the side effects of disinfection, the addition of moisturizing ingredients in disinfectants or, in their absence, the subsequent use of a moisturizing protective cream is recommended.

The *Stratum Corneum* is the outermost layer of the skin and acts as a protective barrier and regulates the permeability of the epidermis thanks to the lipids that form it (Kanerva, et al 2000). According to *Spanish Academy of Dermatology and Venereology,* frequent hand washing, or environmental conditions can cause progressive depletion of surface lipids and lead to dryness. Damage to the skin can also change the flora of the skin, resulting in more frequent colonization by staphylococci and gram-negative bacilli (Larson, 1998).

3 OBJECTIVES

The main objectives of this project are the following:

- Identify the current needs of consumers from bibliographic sources to know their previous background.
- Conceptualize a product that responds to previously defined needs, through the use of patents and scientific articles. Perform an analysis of the product to define its properties and physical characteristics, the mode of application and consumption.
- Define the quality criteria required for that product to ensure its efficacy.
- Formulation of the product selecting the ingredients and their proportion.
- Design of a manufacturing process defining its flow diagram and selecting the unit operations involved and their respective equipment.
- Carry out an preliminary economic study of the manufacturing process.

4 CONCEPTUALIZATION

According to *Ryzhard* (2010), the first step toward developing a product is defining the product itself. The conceptualization of the product is based on consumer needs and market trends. It is necessary to collect information related to what consumers are asking or expecting for, to identify clearly their needs. Some of the typical consumer wants and needs are related to the cost, the size or the safety of the product and legal and environmental issues.

To be successful in developing a product, it is essential to be creative and innovative, as well as studying market trends to understand competing products. It also includes selecting the appropriate form in which the product should be delivered, since it affects consumer perception of the product. Based on this, in this chapter the conceptualization of a hand cream will be executed, including aspects such as researching market trends and defining the functions of the cream and its appearance.

4.1 MARKET TRENDS

It is important to determine the current demand for the product and identify whether the developed product solves a problem and the number of people looking for a solution to that problem. The first step is to identify the market to which the product is aimed and the characteristics of the people who make it up. Companies try to group consumers into segments according to some common characteristics (Aragall, 2012). The cream that is being designed is aimed at consumers who use hydroalcoholic and moisturizing gel, so it does not distinguish between age or gender.

According to the *World Health Organization*, hand sanitizers are antiseptic solutions used as an alternative to traditional hand washing. It is marketed as a foam, gel or spray made with a disinfectant agent. The most common are made by isopropyl alcohol or some form of denatured ethanol, with a concentration of approximately 70%. In the case of the non-alcohol-based, the more common contain either chlorhexidine or hexachlorophene.

Recommendations for the use of hand sanitizers and consumer awareness of the importance of hand hygiene for the prevention of contagious diseases, have driven the growth of the sale of hand sanitizers. According to *El Español* (October 26, 2020), since the beginning of 2020, the sales of these gels in Spain have multiplied by 10, going from a turnover of 613,000 euros in January to 6.5 million in September. Only during the first quarter of 2020 in Spain the sale of masks, gloves and hydroalcoholic gels increased by 1,335% compared to the same period of the previous year (*Europa Press,* August 5, 2020). Sales are expected to continue to increase, according to the *Hand Sanitizer Report* made by Statista, the revenue in the hand sanitizer segment amounts to US $5343 million in 2020. The market is expected to grow annually by 6.2% (CAGR 2020-2025).

The problem is that the disinfectant agents can cause excessive drying and be irritating for the skin. Consequently, some people require a supplemental application of a moisturizing hand cream. These types of creams contain ingredients that help protecting, hydrating, and lubricating the skin. That is the reason why the sale of hand creams that help alleviate damage caused by frequent use of sanitizers has increased. According to the market study carried out by *Kantar*, in Spain the personal care category experienced an increase of 11.6% in value during the first quarter of the year.

4.2 FUNCTION OF THE PRODUCT

The product that will be developed in this project is conceptualized as a product that performs complementary functions combined in one product. It is based on the development of a hand cream that incorporates disinfectant and moisturizing action, answering to current market needs. The product will combine the main characteristics of sanitizers and hand creams, so it is necessary to find the balance between disinfecting agents and cosmetic ingredients to create an effective bactericidal, virucidal and fungicidal cream, without being irritating to the skin.

Ingredients that provide disinfection often cause dehydration and irritation of the skin; this is the reason it will be combined with moisturizing ingredients that allow rehydration of the skin. According to *Kanerva, et al* (2000), there are two main types of skin reactions associated with hand hygiene. The first and most common type is irritant contact dermatitis and includes symptoms that are milder, such as dryness, irritation, itching or cracks. The second type is allergic contact dermatitis, which is based on an allergy to some ingredient in a hand hygiene product.

According to the *WHO*, the main strategies to minimize irritant contact dermatitis related to hand hygiene are the selection of less irritating hand hygiene products and the use of moisturizing skin care products after hand cleaning. This is because hand creams often contain moisturizers, fats, and oils that allow skin to rehydrate and replace altered or depleted skin lipids that contribute to the skin's barrier function (Kanerva, et al 2000).

Based on these aspects, the hand cream has been conceptualized as an oil-in-water emulsion, that it will be composed of small oil droplets dispersed in a continuous aqueous phase. This option has been selected because it is one of the most used in cosmetics and it is very comfortable, since the result is less greasy than water-in-oil emulsions. To the emulsion, in addition to the disinfecting agent, typical elements in the formulation of a cream will be added such as humectants, thickeners, emulsifiers or fragrances.

Being a personal care product and aimed at all types of consumers, it is essential that the ingredients of the designed hand cream are safe for people and the environment, without causing any harmful effects. That is why the toxicity, irritability and allergenicity of each of the ingredients will be considered.

4.3 PACKAGING

Consumers often choose cosmetic products based on their perception of the product based on the design or brand of the product (Argall, 2012). This explains why the packaging may greatly affect consumer perception of the product, and therefore should be considered carefully. There are four main purposes to incorporate in the packaging: protection, convenience, image, and sustainability.

As it said before, people can transfer pathogens from one surface to another by touching, or even transfer them to the mouth, nose, or eyes if they touch their face with not disinfected hands. Therefore, it is important for people to perform hand hygiene by using disinfectant agents frequently during the day and the packaging must be small, light and easy to carry.

Flip-cap tube has been selected as the package, recommended for a viscous product, leading to the requirement that the product can flow through the small hole on the cap with ease. According to *Rhyzhard* (2010), this type of tube is convenient for dispensing the cream and reduces the probability of its contamination. It is important to note that the function of the packaging is to protect the cosmetic from light, humidity, and other environmental contaminants.

The size selected for the cream is 50 mL, chosen based on information from market trends and its usefulness. This way it is convenient to carry in pockets, bags, or backpacks, according to the customer requirements. It takes up minimal storage space and fits perfectly into everyday life.

Plastic is one of the most widely used packaging materials due to its low cost. It is also lightweight, flexible, soft, easy to squeeze and durable. Besides that, it is odorless and offers a nice appearance. The most common type of plastic used in cosmetic packaging is polypropylene (Paine, 1991). From an aesthetic perspective, this type of plastic can be made in different colors or tints, according to the brand's decision. In this way it can be customized to make the container more attractive.

The label is a fundamental part of the packaging, it is used to identify, describe and differentiate the product. It includes the name of the product and the brand to which it belongs. It is also used to know the characteristics of the product such as its ingredients, components and weight. It includes indications for its use, conservation and the date of manufacture and expiration. The information it includes depends on the laws and regulations in force or each industry or sector.

In accordance with *Regulation 1223/2009* of the *European Parliament*, the ingredients must be listed in decreasing order of concentration. And if the ingredients have a concentration less than 1%, they can be written regardless of that order after the ingredients with a concentration greater than 1%.

5 QUALITY FACTORS

According to *Ryzhard* (2010), the next step towards the design of a product is to identify the efficacy in terms of quality factors. These factors depend on the product form and the delivery system. The objective of quality control of a product is to verify if all the characteristics of the final product are in accordance with those defined in the conceptualization stage and if they will be maintained during the useful life of the product. In addition to the factors directly related to the main function of the product, aspects such as comfort of use, sensation and durability of the product must be considered.

5.1 DISINFECTION EFFICACY

The two main functions of the developed hand cream are disinfection and hydration. In the case of disinfection, it is necessary to ensure its effectiveness against viruses, fungi, or bacteria. So, the product must be subjected to standardized disinfection tests.

The *UNE 1500: 2013* standard is a European standard that specifies a test method to evaluate the efficacy of a product for the hygienic treatment of hands by friction. It applies to products used in situations where disinfection is indicated for medical reasons, such as in healthcare settings, workplace or at home. It establishes the procedures for the evaluation of the bactericidal activity of the product in the hands of the volunteers including aspects such as the incubation, the counting of the test mix, control, and validation. It is based on the idea of simulating practical conditions to establish whether the disinfectant reduces microbial activity. It consists of the analysis of the evolution of the transient microbial flora of the hands, artificially contaminated, of some volunteers, after using the disinfectant product.

To carry out the study, 18 to 20 people aged 18 years or older are used. The hands of the volunteers are washed, dried, and infected with a suspension of *Escherichia coli K12*. The volunteers are divided into two groups, a control group, and a test group. The hands of the members of the control group are rubbed with 3 mL of 60% propanol-2 solution for 30 seconds. Then an additional 3 mL of propanol is reapplied and rubbed in again for 30 seconds. The procedure is repeated with the test group, but instead of applying propanol-2 the product under analysis is applied.

To measure the disinfection efficiency of the evaluated product, the non-inferiority test of logarithmic reductions is applied. This type of trial focuses on demonstrating that the efficacy of the new disinfectant is not inferior to the standard, in this case 60% propanol.

According to *Qianyu* (2020), the effectiveness of disinfecting agents against viruses depends on the time of contact, the concentration of the disinfecting agent, and the type of virus involved. If disinfection requires a chemical reaction, the effectiveness of the disinfectant will also depend on temperature, pH, or humidity. The effectiveness can be measured by reducing the infectivity of the virus. The disinfection inactivation can be described by the Chick-Watson law:

$$log\frac{N}{No} = -kCT$$

Where: N= Final number of microbes
No= Original number of microbes
C= Disinfectant concentration
T= Contact time
k= Inactivation rate constant that is specific to the microbe

The log unit reduction and percent reduction are used to describe the efficacy of the disinfectant. For example, a 4 log unit correlates to a 99,99% reduction in the viral concentration. The average log reduction of alcohols in the release of test bacteria on artificially contaminated hands is 3.5 log_{10} after a 30 second application and 4 to 5 log10 after a 1minute application (Rotter, 1999). The hand cream is expected to have a 4 logarithmic reduction value, similar to the propanol.

Another way to check the effectiveness of a disinfectant is to use models that simulate the behavior of the skin. This method can be used before testing with volunteers, it consists of testing on substrates that mimic the surface properties of human skin. It is designed to have the same characteristics of the skin, such as pH, topography, or critical surface tension. The effectiveness of the disinfectant can be tested against different microorganisms, such as specific fungus or bacteria.

5.2 EMULSION STABILITY

As mentioned in the conceptualization chapter, the product has been designed as an oil-in-water emulsion. An emulsion is a mixture of two or more liquids that are normally immiscible with each other (Gennaro, 2003). In the case of the developed product, the emulsion is made up of an oil phase that contains mostly moisturizing agents and a water phase that contains the rest of the ingredients related to the disinfectant function.

From a thermodynamic point of view, an emulsion is an unstable system, since there is a natural tendency to separate the phases and reduce the interfacial energy (Casimir, 2008). It is necessary to reduce the interfacial tension to promote a more intimate blending of the two phases and to use one or more additives to stabilize the emulsion.

It is important that during the useful life of the product both phases do not separate; otherwise the product will feel lumpy or grainy when applied to the skin. An emulsion can be considered kinetically stable if the size and number of drops of dispersed phase per unit volume of continuous phase is maintained (Aranberri., 2006). This means that there should be no appreciable changes in the size or size distribution of the droplets in the dispersed phase and that the droplets should remain evenly distributed in the system. According to *Tharwat* (2005), the stability of the emulsion can be affected by the following mechanisms, which are shown in the Figure 1:

- Sedimentation: It is a process created by the action of gravity. It produces a vertical concentration gradient of the drops without changing the distribution of their size.
- Flocculation: It is the process where droplets in an emulsion are attracted to each other forming flocs without merging them. The individual droplets remain separated by a layer of the continuous phase.
- Coalescence: It consists in the fusion of droplets to form larger drops with reduced total surface area. In this case the droplets are not separated by the continuous phase becoming a single unity, unlike the flocculation process.
- Ostwald ripening: In this process there is molecular diffusion transfer from small droplets to the larger ones. The smallest droplets tend to disappear.

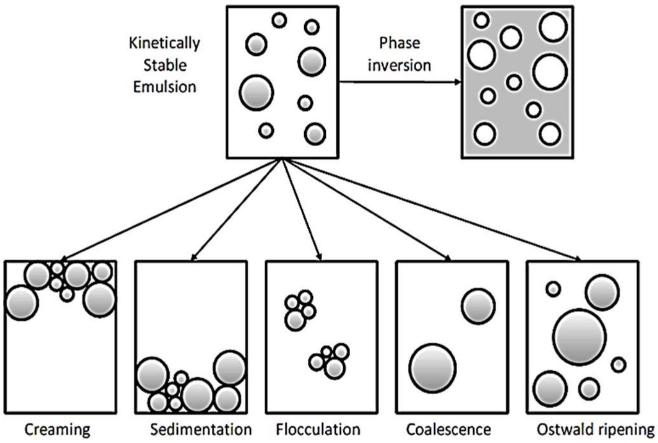

Figure 1: Mechanisms of destabilization of emulsions

A way to emulsify is to use a mechanical device, such as a mixer, to produce a dispersed phase with a droplet size small enough to result in an emulsion. The problem with this method is that the emulsion is stable for a relatively short period of time. To achieve better results, an emulsifying agent is needed.

Emulsifiers are surfactants that migrate to interface making possible the dispersion of a liquid in another immiscible with it, by increasing its kinetic stability. The molecule can adsorb on the interface due to its amphiphilic nature. They can also contribute to skin care by providing benefits such as hydration, nutrition, smoothness, or improvement of the elasticity of the skin. On the other hand, some surfactants can be irritant.

According to Griffin, emulsifiers consist of a molecule that combines a hydrophilic part and a lipophilic part. The balance of the size and strength of these two opposing groups is defined by the concept of hydrophile-lipophile balance number (HLB). The balance of these groups has assigned a numerical value and it is used to classify emulsifiers and facilitates their selection, since it allows predicting their behavior in the emulsion.

To a lipophilic emulsifier a low HLB number is assigned, while a hydrophilic emulsifier is assigned a high number. That is why, according to Griffin, an emulsifier with an HLB lower than 7 dissolves perfectly in the oil phase and favors the formation of a W/O emulsion. Surfactants with an HLB value higher than 8 distribute in favor of the aqueous phase and promote the formation of O/W emulsions type.

The HLB number that corresponds to the maximum stability of an O/W emulsion is called the required HLB number of the oil. This value is a property of the oil. In case of using more than one oil, the required HLB number is calculated by the following expression:

$$HLB_{req} = Z_{O1}HLB_{req,O1} + Z_{O2}HLB_{req,O2} + \ldots + Z_{Oi}HLB_{req,On}$$

Where: Z_{Oi}: Mass fraction of oil in the oily mixture

$HLB_{req,Oi}$: HLB number required by the oil

The HLB value required by the oil phase can be used to find a suitable surfactant mixture for the emulsion formation. The surfactant blend should have a total HLB value equal to the required HLB. The HLB number of the surfactant mixture can be calculated using the following formula:

$$HLB = Z_{A1}HLB_{A1} + Z_{A2}HLB_{A2} + \cdots + Z_{Ai}HLB_{Ai}$$

Where: Z_{Ai}: Mass fraction of the surfactant in the surfactant mixture

HLB_{Ai}: HLB number of the surfactant

In general, it has been observed that the stability of the emulsions is greater if a mixture of surfactants with differentiated HLB values is used, as they can offer a better packing in the interface. Emulsions made with single surfactants or mixtures of them with similar HLB values are less stable.

A way to determine the stability of an emulsion is by analyzing the droplet size distribution of the dispersed phase along the time (Casimir, 2008). In this way it is possible to control whether the average size of the drops grows or not during a long period of time and detect if any of the previously mentioned instability mechanisms is occurring. The smaller the droplet size and the less polydisperse, the more stable the emulsion will be.

The size of the emulsion droplet also influences the physical properties of the cream such as its viscosity, softness, absorption, or ease of application (Casimir, 2008). Depending on the size of the droplet, the emulsion will have an appearance or another according to the following Table 1:

Table 1: Appearance of the emulsion according to its diameter droplet

Droplet diameter (µm)	Appearance
>500	Visible macroglobules
500 - 1	White
1 – 0.1	Bluish white
0.1 - 0.05	Translucent

Hand creams are typically in the 10 -100 µm range. That is why in order to form the emulsion and make it stable, emulsifiers are required. According to *Wibowo* (2001), if it is for cosmetic or pharmaceutical applications, emulsions can be used with drops of a size between 1 and 20 µm that will behave in a smooth and more stable way. For this reason, it was decided to stablish a droplet size around 20 µm.

5. 3 DISINFECTANT STABILITY

It is important to ensure the stability of the disinfectant agent in the cream throughout its shelf life. This is the reason why the amount of disinfectant present in the formulation must be evaluated at specific time intervals. This analysis can be done by titration.

For example, in the case of choosing peracetic acid as the disinfectant agent, obtained from acetic acid and hydrogen peroxide, the titration method can be used to measure the respective concentrations of peracetic acid and H_2O_2 based on the difference in their oxidation capacity. It can be carried out from the titration of H_2O_2 with cerium (IV) permanganate or sulfate and then the peracetic acid can be determined by the formation of iodine from iodide using sodium thiosulfate (Frank, 2014). For this disinfectant, according to the patent *No. US US9044403* (2015), the shelf life is estimated to be 2 years, so it is expected to remain stable during this period.

5.4 RHEOLOGY

The rheological characterization of a material allows to determine how the material will flow under different conditions, during its manufacture, transport, storage, to its use by the consumer (Chhabra, 1999). The developed product requires some rheological testing to characterize and control quality for end user satisfaction.

The rheological behavior of a fluid can be studied from the point of view of the dependence of its viscosity at steady state with the shear rate or the applied shear stress (Vera, et al 2013). Moreover, maintenance of the proper rheological behavior along time is required and it is a measure of stability. To do this, the apparent viscosity can be measured periodically through shear rate or shear stress sweep tests, after exposing the samples to stress conditions, such as high or low temperatures.

Viscosity is defined as the relationship between shear stress and shear rate that characterizes the behavior of fluids, so that it reflects the resistance of the fluid to deformation or flux produced by shear or tensile stressors (Tanja, 2015). Fluids can be distinguished between Newtonians and non-Newtonians. The different type of fluids are shown in the Figure 2 and Figure 3.

- Newtonians: Their viscosity only depends on state variables such as composition, pressure, and temperature.
- Non-Newtonian fluids: They are fluids that have a certain degree of structure. The relationship between shear stress and shear rate is not linear and different behaviors can be observed.
    - Pseudoplastic fluid: Its apparent viscosity decreases with increasing shear stress or shear rate, due to a shear induced destructuring or alignment in the flow direction.
    - Dilating fluid: Its apparent viscosity increases when shear stress or shear rate is reduced.
    - Bingham Plastic: Has a minimum yield stress, below which viscosity is considered infinite. It behaves like a rigid body when it is subjected to small stresses and as a viscous fluid when stress above the yield one is applied.

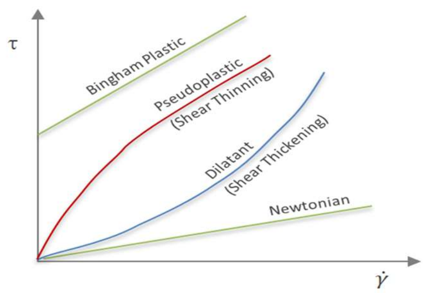

Figure 2: Relationship between shear stress and shear velocity for the different fluids

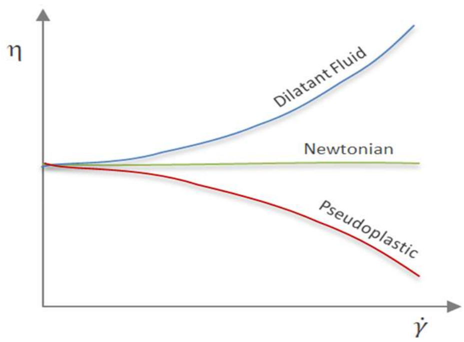

Figure 3: Relationship between viscosity and shear velocity for the different fluids

Each cosmetic product requires a different characteristic rheological behavior (Ming, 2001). A hand cream should have low viscosity at high shear, that allows the cream to form an even thin layer on the skin that will penetrate and absorb more easily. This reduces the greasy or sticky effect. However, it also requires that the viscosity increases at low shear rates, so that it does not spill easily (Wibowo, 2001).

According to these rheological needs, the cream should have a pseudo-plastic rheological behavior, which can be expressed by the Oswald and de Waele power law equation:

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

Where: τ: Shear stress,

K: Consistency index,

$\dot{\gamma}$: Shear rate,

n: Flow behavior index (<1).

According to *Mujica* (2010), the dynamic viscosity of cosmetic creams ranges between 4,000 and 18,000 cP at 25 ºC.

5.5 SENSORIAL ANALYSIS

The success of a cosmetic product in the market depends largely on the consumer's perception of the product. Sensory analysis focuses on the obtention of information about a product in relation to how people feel when they use it, to determine acceptance by the consumer.

ISO 5492: 2008 establishes a guide for sensory analysis. It standardizes the methodology that allows an examination of organoleptic properties, through the senses, of consumer products, such as pharmaceuticals and cosmetics, including the use of adequate techniques to objectify the results with the aid of adequate statistical methods.

Volunteers organized into sensory panels are often used, to provide information about what they experience when using the product in question. They rate the product based on their sensory perceptions, quantifying the products assigning a score on a scale to each perception. Then a statistical tool is used to evaluate the reproducibility and the quality of the collected data. To do this, the scores assigned for the different perceptions and the evaluation carried out by the judges are compared.

5.5.1 Color

Color is an important aspect to consider in cosmetic products as it helps the visual identification of the product (Gisbert, 1999). That is why in cosmetics there is a wide range of colorants that adapts to the wide variety of products in the sector. At the same time, they must be harmless substances.

In the case of the cream developed in this work, it has been decided not to color it and leave it with the characteristic white color of the emulsion. In addition, the choice to use white as a color matches with current market trends. Therefore, the cream is expected to be white, opaque and with some luminosity.

5.5.2 Fragrance

Smell is one of the first senses to be perceived, so it is important that it attracts the attention of the consumers. Fragrances can provide a pleasant smell and make products more recognizable or distinctive, as well as help hide the odor of some ingredients (Knowlton, 1993).

The cream to be developed is characterized by including a disinfectant agent in its formulation. Therefore, the fragrance must help to mask any unpleasant odors derived from the disinfectant used.

5.5.3 Texture

The hand cream is intended to leave a light feel, not too greasy and well distributed on the skin without leaving a sticky feeling or a large amount of residue after its absorption. The absorption of a substance depends on the vehicle used. In the case of O/W emulsions, the oily phase is absorbed into the skin at a higher rate than W/O emulsions. After application, they lose water quickly and do not leave much residue on the skin. The amount of product used, and the condition of the skin are also related to the absorption rate.

5.5.4 Moisturizing efficacy

The hand cream developed is conceptualized as a cream that, in addition to disinfecting, moisturizes the skin. Therefore, it is expected to offer good moisturizing performance. Moisturizers are used to answer a range of skin needs, including protection, healing, as well as moisturization.

Daily exposure to drastic changes in temperature, ultraviolet rays, or harsh and irritating chemicals affects the integrity of the skin (Hachiro, et al 2001). For this reason, it is important to help the skin recover and protect from adverse effects using moisturizing agents. There are different moisturizer agents depending on their mechanism of action.

- Humectants: are characterized by absorbing water from the air or attracting it from the underlying layers of the skin to the surface.
- Occlusives: are oils or waxes characterized by forming a hydrophobic layer on the skin that avoids the transdermal water loss. They also protect the skin by helping prevent irritants, allergens, and other harmful particles from entering through it.
- Emollients: they provide flexibility, softness, and smoothness to the skin. They can also be used to adjust the consistency of creams and lotions.

Dermal tolerance and moisturizing efficacy can be assessed by self-assessment panels or by expert clinical evaluation. These types of evaluation techniques can be well correlated to physiological measures that are difficult to use in clinical settings, such as transepidermal water loss or desquamation.

6. SELECTION OF INGREDIENTS

Now that the functionality of the cream has been conceptualized and quality criteria have been established, it is time to select the ingredients for the final product formulation. Ingredients are selected based on their ability to perform a certain function. In the formulation of multifunctional products, it must be considered that the ingredients must be combined correctly to ensure the effectiveness of all the active principles. It is important to consider the safety of the people during the selection of the ingredients, as it is a product for cutaneous use. Therefore, they must not cause allergies, sensitivity or irritation and must be free of impurities that contain toxic effects.

The selection of the ingredients has been made based on the analysis of different formulas, scientific studies, and patents.

6.1 DISINFECTANT AGENT

Currently on the market there is a wide range of disinfectant agents. The main factors to consider in the selection are the antimicrobial profile, the effects on the skin and the safety. It is important that they can act against viruses, fungi, and bacteria.

To select the disinfecting agent, it is necessary to know the main advantages and disadvantages of the substances on the market. The following Table 2 summarizes some of them (Qianyu, 2020).

Table 2: Advantages and disadvantages of the different disinfectants available on the market

Disinfectant agent	Advantages	Disadvantages
Ethanol	Broad spectrum	Flammable and its effectiveness can be affected by the presence of organic matter
2-Propanol	Broad spectrum	Flammable, and eye and mucous membrane irritant
Peracetic acid	Fast acting, leaves safe residue and still effective in presence of organic matter	Unstable and sour odor
Hydrogen peroxide	Broad spectrum and stable	Slow acting

Sodium hypochlorite	Broad spectrum, no toxic residues and fast-acting	Corrosive to metals at high concentrations and its effectiveness is affected by the presence of organic matter
Formaldehyde	Broad spectrum	Hazardous to health
Benzalkonium chloride	Broad spectrum, odorless and colorless	Activity reduced by the presence of organic matter and slow acting
Metal nanomaterials (Ag or Au salts)	Broad spectrum	Expensive and there is still no evidence of its non-toxicity

Nanomaterials and formaldehyde have been rejected in the present work due to their potential health hazard. Now it is necessary to check the effectiveness of each one of them against the different microorganisms. The following table shows a summary of their disinfectant activity. The Table 3 has been extracted from the *Sterilization Manual for Health Centers* (Acosta-Gnass, 2008).

Table 3: Disinfectant activity of different disinfectants available on the market

Disinfectant agent	Concentration	B	LV	HV	M	F	Mechanism of action
Ethanol	60-95%	+	+	-	+	+	Protein denaturation
Hydrogen peroxide	3-25%	+	+	-	+	+	Oxidant
Quaternary amines	0.4-1.6%	+	+	-	-	+/-	Enzyme inactivation, protein denaturation
Peracetic acid	0.001-0.2%	+	+	+	+	+	Oxidant
Chlorhexidine	0.05%	+	+	+/-	-	+	Cytoplasmic

B: Bacteria, LV: Lipophilic virus, HV: Hydrophilic virus, M: Macrobacteria, F: Fungi, +: Effective against most of them, -: Not effective against most of them, +/- : Depends on the type.

F. Ansaldi, et al (2004) evaluated the virucidal efficacy of six commonly used chemical disinfectants against *SARS-CoV* and other similar airborne viruses, such as *Influenza* and *Respiratory Syncytial Virus* (Acosta-Gnass, 2008). It also gives an idea of the contact time required by each of them to inhibit the virus 4 logarithmic units. The Table 4 shows the results of the study.

Table 4: Contact time required to inhibit Influenza, RSV and SARS-CoV by different disinfectants available on the market against

	Contact time required to inhibit its replication (min)		
Disinfectant	Influenza virus	Respiratory Sincytial virus	SARS-CoV
Peracetic acid 0.035%	<1	<1	<1
Ethanol 70%	2	<1	<1
Sodium hypochlorite 0.01%	30	30	30
Sodium hypochlorite 0.05%	30	1	1
Sodium hypochlorite 0.1%	<1	1	<1
Chlorhexidine digluconate 1%	30	1	<1
Benzalkonium-chloride 1%	30	1	5

The product will be used on the hands, so the disinfectant must act in a broad spectrum and be relatively stable against organic matter. It should require little contact time and avoid the drying effect caused by disinfectants such as ethanol. Finally, it must be not dangerous for people or the environment. According to these criteria, peracetic acid has been chosen as the disinfecting agent.

Peracetic acid (PAA) is an uncolored liquid with a strong sour odor similar to acetic acid. The most common method for its synthesis is through the reaction H_2O_2 and acetic acid.

$$H_2O_2 + CH_3CO_2H \leftrightarrow CH_3CO_3H + H_2O$$

It is used in a lot of industries, including food processing, medical, chemical, pulp and paper, and wastewater disinfection for its high oxidation capacity and antimicrobial activity (Vivek, 2020). It is one of the biocides recommended by the *WHO* to inactivate the coronavirus on surfaces.

According to the *Food and Drug Administration*, it is classified as a high-level disinfectant. PAA disrupts the microorganisms cell membrane via the hydroxyl radical, causing the inactivation or death of a wide range of bacteria, endospores, yeasts, and viruses (Qianyu, 2020). During disinfection, it breaks down, producing water, oxygen, and acetic acid, which are non-toxic and easily soluble in water, which makes it an eco-friendly product. It is more effective in the presence of organic matter than other disinfecting agents such as the sodium hypochlorite, hydrogen peroxide, or chlorhexidine digluconate (Qianyu, 2020).

PAA has been evaluated in accordance with article 16 of *Directive 98/8/EC of the European Parliament* and of the *Council* for its use in different types of products. One of them was the use of PAA as a biocide for topical skin hygiene in humans. It was evaluated for its disinfection capacity and safety of people. For this, 5% PAA was used, diluted in water, in solutions of up to a maximum of 0.2%. Based on the results obtained, PAA was approved as an active substance for use in biocides for hand disinfection in concentrations lower than 0.2% (Official Journal of the European Union, April 29, 2016).

PAA is always sold in solution with acetic acid and hydrogen peroxide to maintain the stability of the substance. The choice of concentration has been made in accordance with *Directive 98/8/EC*, so it has been decided to use a 5% PAA solution to achieve a concentration of 0.2% in the cream. According to a *Report of the Scientific Committee of the Spanish Agency for Food and Nutritional Safety* (March 2, 2020), the product marketed under the name *VigorOx5F&V* contains 25% hydrogen peroxide, 8% acetic acid, and 5% peracetic acid in mass concentration. In this way the cream will contain 0.2% in PAA, 1% in hydrogen peroxide and 0.32% in acetic acid.

According to the patent *US Nº 9044403* (2015), the presence of ethanol in the formulation increases the bactericidal efficacy of the PAA in the hand cream and reduces the time it takes for a total inactivation of the microorganisms. According to the patent *ES Nº 2246076T3* (1998), ethanol acts as a preservative in the solution and has a synergistic germicidal effect with PAA. That is why it has been decided to include ethanol in the formulation. Using PAA the % of ethanol can be drastically decreased. The amount of ethanol in the composition can be from about 10% to 30% (Patent US Nº 9044403, 2015). According to this, 30% ethanol will be added to the formulation. This amount of ethanol is expected to help decrease the required contact time and does not cause dryness.

6.2. MOISTURIZING AGENT

The main objectives of the designed hand cream are disinfection and hydration, so it must offer a moisturizing performance that meets customer expectations. Moisturizing agents must cope with the dryness produced by external conditions and that produced indirectly by the disinfectant. There are many options to enhance moisturization performance in skin. Generally, it is necessary to balance the different categories of moisturizing agents to elicit both a consumer perceived moisturization effect and a clinical enhanced performance.

<u>Emollient</u>

Emollients protect the skin from the dryness and improve the aesthetics of the skin producing softness and smoothness. They also can help to adjust the consistency of the cream. It is very important that they must be non-irritating and non-toxic. They can be classified according to their ease of spreading. The Table 5 shows some examples of emollient agents.

Table 5: Examples of emollient agents and their degree of spread.

Ease of spreading	Emollient agents
Greasy - Poor spreadability	Castor oil, almond oil, oleyl oleate, mineral oil, glyceryl triisostearate, glyceryl ethoxylates…
Creamy - Medium spreadability	Ocryl dodecanol, cetearyl isononanoate, oleyl alcohol, caprylic triglyceride...
Non greasy - Easy spreadability	Isopropyl stearate, octyl stearate, isopropyl myristate, dioctyl cyclohexane, cetostearyl alcohol...

In the case of creams and lotions, consumers expect the spread to be medium. According to *Christine Clark* (2004), the combination of three to four different emollients with various spreading properties can help to obtain better formulations. Therefore, it has been decided to combine three different emollients to offer a result according to the needs.

Glycereth-18 ethylhexanoate (Hest G-18-O) is a polyethylene glycol ether of glycerin and contains an average of 18 units of ethylene oxide. Therefore, it has the benefits of glycerin and glyceryl ethoxylates without the negatives like slow absorption, greasiness, or stickiness. It helps to maintain a soft, smooth feel and a more moisturized appearance. It also has humectant properties. It also has antimicrobial properties effective against a wide range of microorganisms. According to the patent *WO Nº 103441 A2* (2007), thanks to its structure, it has the advantage of being very water soluble and non-irritating. Its HLB value is 15.

According to the manufacturer *Global Seven Inc* the recommended usage levels vary with the uses but are generally 0.5 - 10%. According to the recommendations of the manufacturer and the patent *WO Nº 103441 A2* (2007), a concentration of 5.5% will be used.

To counteract the greasy effect of glycereth-18, two lighter emulsifiers have been selected. The first is isopropyl myristate which is an ester derived from isopropyl alcohol and myristic acid. It is widely used in cosmetic products where good skin absorption is desired. It is a colorless and odorless liquid and has an HLB value of 11.5. According to the manufacturer *Ecosmeticos*, the recommended concentration for cosmetic formulation is between 0.25 and 10%. A concentration of 3% will be used.

Cetostearyl alcohol is widely used in the formulation of cosmetic products due to its great versatility. It will counteract the stickiness caused by the first emollient, glycereth-18. It is a mixture of alcohols made up mainly of cetyl and stearyl, called fatty alcohols. It has an HLB value of 15.5. Usage rates depend on the end use of the product. According to the *European Institute of Dermostetics*, in the case of creams or lotions, a concentration of 1-15% is recommended. A concentration of 5% will be used.

According to *Wibowo* (2001), the amount of emollient must be between 5-15%. In this case, it is going to be 13.5%.

<u>Occlusive</u>

Occlusive agents are another type of skin conditioning agent, they cover the skin with a protective film that prevents transepidermal water loss. There is a wide range of occlusive agents on the market. Therefore, it is necessary to find which is the one that best suits the needs of the formulation to be developed. Natural ingredients are used more and more in today's cosmetics. Based on this aspect, it has been decided to opt for beeswax.

Beeswax is a natural wax with occlusive and anti-inflammatory properties. Therefore, it will be able to counteract the damage caused to the skin by the disinfectant. It is a non-toxic agent and has a low comedogenic index, that is, it does not clog pores as much as other occlusive agents. It contains vitamin A that exerts a stimulating action on the skin's metabolism, promoting collagen synthesis, which contributes to firmer skin. It has a required HLB value of 12. According to the *Lu & Jo* distributor, the amount of beeswax used in lotions is between 5-15%. The selected concentration is 5%.

6.3. THICKENER

According to *Karsheva* (2006), thickener agents are substances which increase the viscosity of the formulated product. A high viscosity of the continuous phase can reduce the movement of the particles avoiding their tendency to coalesce and settle, thus offering greater stability of the emulsion (Wibowo, 2001). According to *Vera, et al* (2013), the addition of polymers, such as xanthan gum or carbomer, can increase the viscosity of cosmetics, influence physical stability and even affect consumer acceptance of emulsified systems.

Xanthan gum is the most used natural gum in cosmetics, due its properties, affordable price, and ease to use. It has a highly pseudoplastic behavior, it exhibits high viscosity at low shear rates and lower viscosity at high shear rates, with Newtonian behavior at very low shear rates (Khan, 2018). Figure 2 shows the steady state viscosity of several solutions of xanthan gum.

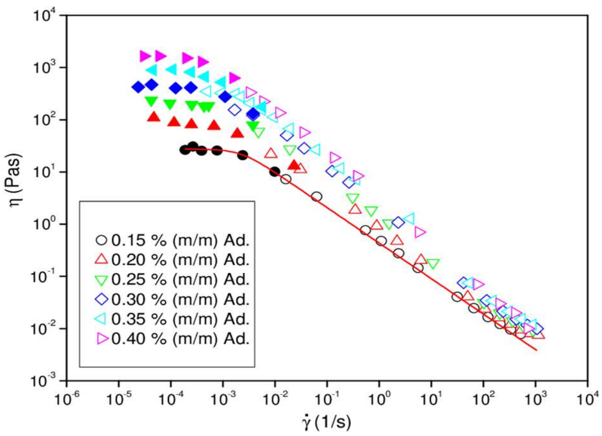

Figure 2: Relationship between viscosity and shear rate of solutions of different concentrations of xanthan gum (Carmona, 2015)

Manufacturers recommend a concentration between 0.2-0.5% for the formulation of creams. It has been decided to use a concentration of 0.25%, according to the recommendations of the patent *No. US9044403* (2015).

6.4 FRAGRANCE

A fragrance is required to mask the strong characteristic smell of peracetic acid. Not all fragrances can mask the strong odor of PAA, according to *US patent No. 9044403 B2*, some fragrances available from the *Wellington Fragrance* company have been found to be suitable for use with PAA. To test their effectiveness, volunteers were offered formulations with some of these fragrances. Not all of them were accepted, for example, the *Blackberry Sage Tea* fragrance, was not attractive to the volunteers during the sensitivity analysis.

Salvia and Chamomile fragrance has been selected because it does not affect the stability of the emulsion or the stability of PAA. It also fits with market trends since it is a floral scent. According to *Fragrance Science*, due it is a skin care product, the fragrance content should be between 0.01-0.5%. According to the patent *US No. 9044403 B2,* a concentration of 0.11% will be used.

6.5 PRESERVATIVE

PAA is unstable, so a way to improve its stability is to maintain it in the presence of an excess of acetic acid and hydrogen peroxide relative to equilibrium, in order to reverse the balance towards the formation of the PAA (Patent ES Nº 2246076T3, 1998). According to the patent *US Nº 4051058A* (1976), the addition of a metal ion sequestering agent, helps to increase the stability of the solution. These stabilizers are designed to remove traces of metal ions, which would accelerate the decomposition of peroxides. This category of stabilizing agents includes phosphonic acid or its acid salts (Patent ES Nº 2246076T3, 1998).

Etidronic acid (1-hydroxyethane-1,1-diphosphonic acid) or HEDP, is a bisphosphonate that acts as a chelator. It can also be used as a dispersant, corrosion inhibitor or calcification inhibitor. According to the *Zschimmer & Schwarz* manufacturer, it is especially recommended for the stabilization of peroxides. It is often used to stabilize peracetic acid. For this reason, it has been decided to use it for the stabilization of the emulsion. Based on data collected by the *Safety Assessment of Etidronic Acid and Its Simple Salts* (2016), the maximum etidronic acid concentration reported for leave-in skin products was 0.12%. So, the concentration selected is 0.1%.

6.6 EMULSIFYING AGENTS

The selection of the emulsifying agent plays a fundamental role in the preparation of an emulsion formulation since its stability depends on it. It must be able to form a layer around the droplets of the dispersed phase that gives stability to the emulsion and prevents its coalescence (Aranberri, 2006). Emulsifiers adsorb on the water-oil interface, reducing the energy required to break the interface.

Bancroft's rule states that the phase in which the emulsifying agent is most soluble constitutes the continuous phase. That means that what makes an emulsion O/W or W/O is not the relative percentages of oil or water in the emulsion. According to this rule, O/W emulsions require an emulsifying agent that is more soluble in water than in oil (Gennaro, 2003). Surfactants can be classified based on the nature of their hydrophilic group. There are 4 main groups: anionic, cationic, non-ionic, and amphoteric. Non-ionic surfactants are the most used in cosmetic formulation. They can act as emulsifiers, humectants or solubilizers. Some of the most widely used nonionic surfactants in industry are fatty alcohol ethoxylates, castor oil ethoxylates, and fatty acid ethoxylate.

When the formulations contain many compounds, like in a hand cream case, it is very difficult to find a single emulsifier that has all the properties necessary to stabilize the emulsion. For this reason, mixtures of more than one emulsifier are going to be used. It has been decided to opt for fatty alcohol ethoxylates and castor oil ethoxylates as emulsifying agents for the hand cream.

Polyethylene glycol monoethyl ether, known as Oleth 35 or Hetoxol Oa-35 is an ethoxylated alcohol and has been selected because it is often used in cosmetics formulation and the patent *No. US9044403* (2015) recommends it. It has an HLB value of 16.9. The manufacturer *Global Seven*® suggests a usage concentration of 0.5 to 5%.

To ensure the stability of the emulsion, it has decided to add one more emulsifier. In accordance with the recommendations of patent *No. US9044403* (2015), it has been decided to opt for PEG-30 castor oil. It is a non-ionic emulsifier obtained by reacting castor oil with ethylene oxide in a 1:30 molar ratio. It is commonly used in cosmetics as an emulsifier, especially with perfumes and fragrances. According to the manufacturers, the use concentration can be between 0.1-20%. It has an HLB value of 11.

To select the concentrations of the surfactants, the required HLB value of the oily mixture is calculated, which corresponds to the maximum stability of an O/W emulsion.

$$HLB_{req} = Z_{O1}HLB_{req,O1} + Z_{O2}HLB_{req,O2} + \ldots + Z_{On}HLB_{req,On}$$

Beeswax (5%), $HLB_{req,O1}$ = 12, $Z_{O1} = \frac{5}{13} = 0.38$

Isopropyl myristate (3%), $HLB_{req,O2}$ = 11.5 , $Z_{O2} = \frac{3}{13} = 0.23$

Cetostearyl alcohol (5%), $HLB_{req,O3}$ = 15.5 , $Z_{O3} = \frac{5}{13} = 0.38$

Using the formula, a value of 13.23 has been obtained. The required HLB value conforms to that expected in an O/W emulsion. The surfactant should have a total HLB value equal to the required HLB.

$$HLB = Z_A HLB_A + Z_B HLB_B = Z_A HLB_A + (1 - Z_A) HLB_B$$

Polyethylene glycol monoethyl ether, HLB_A = 16.9

PEG-30 Castor oil, HLB_B = 11

Using the above formula, a concentration of 38% and 62% has been obtained for olyethylene glycol monoethyl ether and PEG-30 castor oil respectively. *Wibowo* (2001) suggests that in a hand cream the total emulsifiers concentration should be between 0.1-3%. A total surfactant concentration of 3% has been assumed. Accordingly, a concentration of 1.87% of PEG-30 Castor Oil and 1.13 of Polyethylene glycol monoethyl ether has been obtained.

7. FORMULATION

The following table (Table 6) contains the formulation for the elaboration of the designed cream:

Table 6: Final formulation of the developed hand cream

Ingredient	Concentration (%) by weight
Water	46.52
Ethanol	30
Glycereth-18 ethylhexanoate	5.5
Cetostearyl alcohol	5
Beeswax	5
Isopropyl myristate	3
PEG-30 Castor oil	1.87
Polyethylene glycol monoethyl ether	1.13
Hydrogen peroxide	1
Acetic acid	0.32
Xanthan gum	0.25
Peracetic acid	0.2
Fragrance	0.11
Etidronic acid - HEDP	0.1

8. PRELIMINARY DESIGN OF THE MANUFACTURE PROCESS

The conceptualization of the product, the quality criteria, and the ingredients, according to the needs of consumers, are have been already defined. Now it is necessary to design a process for the manufacture of the product and choose the set of steps by which raw materials are transformed into the final product. This chapter will define the flowsheet process and the selection of the necessary equipment.

The selection of the type of process affects the energy required, the duration of the process and the size of equipment needed in the production process. Production processes can be classified in continuous or batch, according to how the raw material input is made and how the product is obtained from it.

For the preparation of the hand cream, batch production has been chosen since it has been the option that best fits. It offers flexibility in the processes, since unlike the continuous processes, it allows to produce a great variety of different products in the same equipment. The operations are carried out sequentially, so that more than one operation can be performed in the same equipment, resulting in savings on equipment. The capital required for this type of production is less than that required by the continuous processes. Another advantage of processing in batch is that if there is a batch with problems, it is easier to detect it. It helps the traceability of batches, which is why it is usually used in the pharmaceutical and food industry.

8.1 BATCH SIZE

According to the business data platform *Statista*, in 2019 around 5.8 million people in Spain were medium users, consumers who use hand cream once a week. Due to the current situation caused by COVID 19, it has been estimated that in 2020 the use of cream has increased to counteract the damage caused by frequent hand disinfection. Consumers who used to use it once a week in 2019 are now using it daily. Moreover, it must be added that this cream will be used not only as a moisturizer but also as a disinfectant product. Based on *Neutrogena® Perfumed Concentrated Hand Cream*, each cream is considered to allow around 200 applications. According to this, it has been estimated that hand cream consumers will consume 4 creams per year.

The estimated production is 1.16 million tube creams per year, which corresponds to 5% of the total demand. The composition of the cream is mostly water and alcohol, so it has been estimated that the density of the cream is 1 kg/L. Taking into account that the cream container has been designed for a capacity of 50 mL, approximately 60,000 kg/year will be produced. It has been decided that 120 batches will be produced per year of 500 kg each.

The production scheme has been carried out based on a specific production, although it is estimated that once it is underway there may be variations depending on the demand for the product, being able to product more or less. So, the production or the number of batches may vary according to demand. Generally, the capacity of the plant is greater than that required to produce a single product. It is common to dedicate the entire plant or some equipment to the production of more than one product. Therefore, plants can be dedicated to the production of a single product or more than one. In this case, the plant will be free for production of other creams for some periods of time along the year.

8.2 PROCESS FLOWSHEET

Generally, there are basically five major processing steps in the manufacturing process of chemical-based products: pre-treatment, mixing, structure formation, post-treatment, and packaging (Ryzhard, 2010). In the case developed in this project, the sequence of processes will be similar. The flow chart of the designed manufacturing process is attached in Figure 3:

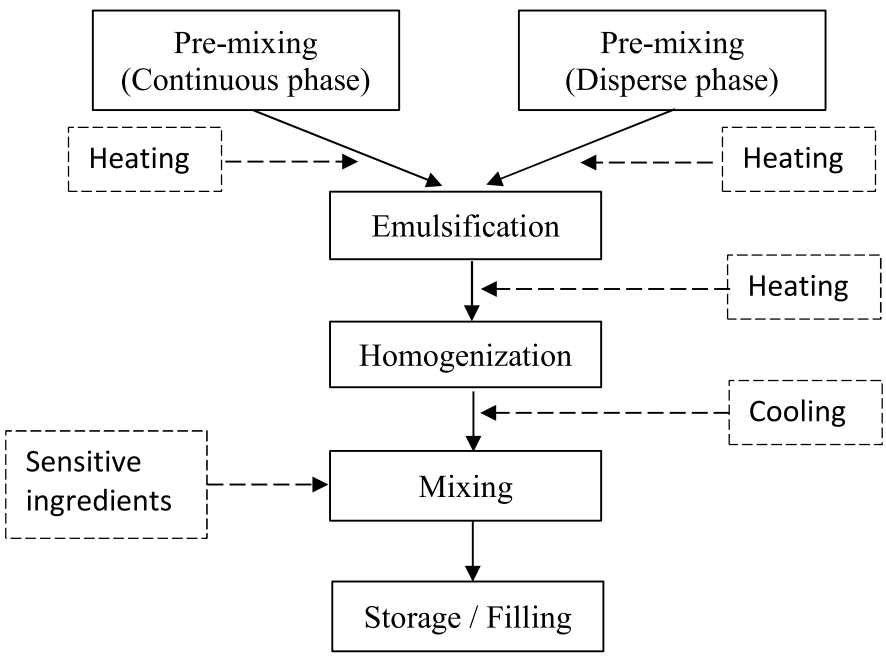

Figure 3: Process flowsheet of the product developed

Pre-mixing

As previously mentioned, the cream has been conceptualized as an O/W emulsion, so the formulation is made up of an aqueous phase and an oily phase. So, there are two types of ingredients: water soluble or oily. That is why it is necessary to find which ingredients are most compatible with each other to be premixed.

The continuous phase consists mainly of water and, water soluble ingredients. The emulsifiers must be incorporated into the continuous phase since it is an O/W emulsion and their HLB number is relatively high. The thickening ingredients are also incorporated into the continuous phase, as they thus increase the viscosity of this phase and produce more resistance to the movement of the oily phase (Wibowo, 2001). This can improve the stability of the emulsion by preventing instability phenomena such as coalescence or phase inversion (Wibowo, 2001). To ensure the homogeneity of the phase, the mixture must be mixed and heated to a temperature between 70-80ºC.

In the dispersed phase all ingredients are not in a liquid state at room temperature, so it is necessary to heat them to dissolve them and improve their mixing. This phase will be stirred and heated to a temperature between 70-80ºC to guarantee that all the ingredients are liquid. Table 7 shows where the ingredients are incorporated.

Table 7: List of ingredients that make up the continuous phase and the dispersed phase

Continuous phase ingredients	Dispersed phase ingredients
Water	Cetostearyl alcohol
Glycereth-18 ethylhexanoate	Beeswax
Polyethylene glycol monoethyl ether	Isopropyl myristate
PEG-30 Castor oil	
Xanthan gum	

Emulsification

This stage is based on the pre-emulsion of the cream. To do this, one liquid is dispersed in the other, thus increasing the interfacial region (Di Scipio, 2008). Agitation is used to help to homogenize the reactor contents so that the concentration and temperature are the same throughout the reactor volume.

The oil phase must be transferred from the equipment where it was to the main mix equipment, where the continuous phase is first transferred. It should be done slowly without stopping stirring. The oily phase is dispersed as droplets in the continuous phase to form a pre-emulsion with relatively large droplet size and polydispersity. The droplets are estimated to have a diameter of approximately 100 µm. At the end of this stage, the transfer of the dispersed phase is completed, and the mixture begins to be macroscopically homogeneous. This step will be carried out heating the emulsion between 70-80ºC.

Homogenization.

The product of the pre-emulsion may not have the desired microstructure (Ryzhard, et al 2010), so now is subjected to further processing to obtain the desired droplet size (1-20 µm). The main objective of this step is to produce droplets as small as possible to increase the shelf life of the hand cream.

This step will be carried out keeping the same temperature as the previous stages, i.e. between 70-80ºC. Carrying out the emulsion at the right temperature is essential to obtain emulsions with stable droplets and prolong the conservation of the product.

Mixing

After homogenization, stirring is maintained while the emulsion cools. Ingredients that can break down if subjected to harsh processing conditions, such as fragrances, active agents, or preservatives, can be added in the post-treatment step (Ryzhard, et al 2010). This is the case for fragrance, the HEDP and the disinfectant agent. In the case of the PAA it is important that the temperature does not reach values higher than 60 ºC as it can degrade, ignite, or explode. According to *Wibowo* (2001), heat sensitive ingredients should be added after the temperature drops to approximately 40-50ºC.

After finishing adding the ingredients, it is necessary to continue stirring but at a slower rate. The manufacturing process of the hand cream will be considered finished when the temperature of the emulsion reaches room temperature, approximately 25-30ºC.

Storage step / Filling

When the cream is considered finished, it must be stored or refilled in its container. In the case of storage, the emulsion must continue to be stirred, although the mixing rate must be only to maintain the macroscopic homogeneity of the cream. The temperature of the product will be controlled so that the room temperature is maintained, approximately 30ºC or lower. If the filling stage is chosen, the cream is transferred to a filling and closing machine. The result is the cream already prepared for distribution in 50 ml bottles.

8.3 EQUIPMENT

Pre-treatment equipment

As mentioned above, in the premix stage the phases are mixed and heated separately to prepare them for the emulsification step. Therefore, equipment capable of providing agitation and heat to the solutions will be needed. It has been decided to opt for stirred vessels because they are some of the most used operating units in chemical processes due to their versatility.

To provide the necessary heat and to unify the temperature, vessel jackets will be used. They are designed to control the temperature of vessel content, surrounding the container through which a cooling or heating fluid circulates. It allows a uniform heat exchange through the walls.

The goal of agitation in this step is to improve the homogeneity of fluid properties. The type of stirring depends on the characteristics of the fluid to be stirred. Propeller and turbine agitators are typically used for low and medium viscosity solutions, while agitators capable of scraping the vessel walls are essential for high viscosity emulsions (Tharwat, 2016). During the premix stage, since the continuous and dispersed phases are processed separately, the viscosities are not expected to be very high. So, the first group of agitators mentioned has been chosen.

In general, agitators usually have a central shaft driven by a motor that supports one or more agitators. This shaft can be added to the top or bottom of the reactor. The main types of agitator are as follows (Tharwat, 2016):

- Axial flow agitators: They pull the flow 45º, making the fluid follow a round path parallel to the axis of rotation. They are set up to create effective top to bottom motion in the tank.
- Radial flow agitators: They can generate radial flow for any Reynolds and provide high tangential velocity but low thrust capacity. The radial flow impacts on the wall of the container, causing one part of the fluid to be propelled upward and another downward.
- Tangential flow agitators: These types of agitators operate close to the tank wall and are very effective for high viscosity fluids.

When mixing, the push capacity is sought to be as high as possible, to ensure greater homogenization of the mixture. For this reason, the axial flow agitators are more used than radial ones. In addition, according to *Bridges* (2020), axial flow impellers provide more flexibility in choosing shaft lengths than radial flow impellers. For this reason and because it is estimated that the fluid is not very viscous, it has been decided to use axial agitators.

Some of the most common types of axial flow impellers are (Tharwat, 2016):

- Pitched axial flow blades: They produce a good balance between shear and fluid flow, making them suitable for a wide variety of applications.
- Marine propeller: They generate less shear stress compared to pitched blades but produce a good pumping rate.
- Hydrofoils: They generate the least amount of shear stress in fluids compared to others.

It has been decided to use a pitched axial impeller turbine due to its characteristics and because it adjusts to the volume and viscosity of both the continuous and dispersed phases. According to *Dickey* (2004), typical axial mixers have diameters from ⅓ to ½ of the diameter of the tank. So, the size of the container used determines the diameter of the impeller. The Figure 4 shows an example of pitched axial impeller turbine.

Figure 4:Pitched axial impeller turbine

To prevent formation of vortex on the vessel, baffles are normally installed. They cause top-to-bottom mixing and prevent mixing-ineffective swirling motion (Perry, 1992). According to *Bridges* (2020), round tanks should have with 4 baffles located 90º from each other with a thickness of 1/12 of the tank diameter.

Agitator impellers and vessels are typically made of stainless steel because it is an easy-to-clean and corrosion-resistant material. There are different grades of stainless steel for different applications. It has been chosen to use 304 stainless steel, since according to the manufacturer *Caframo LabSolutions* it is widely used in industries such as dairy, food and chemical.

Considering that the batches are 500 kg, the content of the aqueous phase and the oily will be respectively 402 kg and 65 kg. Based on these values, the capacity of the containers to be used has been selected. The volume chosen for the oil phase and aqueous phase vessel is respectively 80 L and 500 L. *De Dietrich Process Systems* offers a range of reactors to meet estimated needs. Specifically, the *CE* design of the *DIN Range*. The jacket of the selected vessel offers the possibility of working at a maximum temperature of 200 ºC, so it can manage the required 70 ºC. The Figure 5 shows the DIN Range reactor.

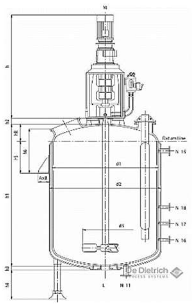

Figure 5: Mixing vessel CE design Din Range froml De Dietrich Process Systems

Emulsification and homogenization equipment

A proper mixing for emulsification requires sufficient agitation to produce a turbulent flow to break the dispersed phase into small droplets. Various parameters must be controlled, such as flow rate, turbulence, or type of impellers (Tharwat, 2016). Particle size reduction is a key process in the synthesis of high-quality stable products such as emulsions, suspensions, and dispersions.

The choice of homogenizer depends on factors such as batch volume, desired throughput, energy requirement, final required droplet size distribution, or cost. If the required droplet size is less than 1 µm, it is necessary to use colloid mill, ultrasonic or high-pressure homogenizers. If not, it is more common to use a high-speed mixer. Since the hand cream has been conceptualized as an emulsion with a droplet size of 1 to 20 µm, a high-speed mixer will be used.

As mentioned above, axial mixers can handle low to moderate viscous fluids, so if the flow is very viscous, a tangential impeller is required. This type of impeller can have different structures, but the most common varieties are helical and anchor (Dickey, 2004). This type of impeller typically has diameters equivalent to 85 to 95% of the tank diameter (Dickey, 2004). Some of them even have flexible scrapers, which are 100% of the diameter of the tank. This type of mixers requires low speed and high torque to remove viscous fluids. The tank should be round, and the shaft should be centered so that the clearance between the impeller and the wall remains nearly constant.

A coaxial mixer has been chosen, which is based on the association of different agitators that rotate at different speeds, combining the capacity of each one. In the end, a dynamic and very efficient mixer is obtained that adapts to the required process (Foucault, 2006). This type of equipment is used in the manufacture of gels, creams, ointments, and other complex rheological products. The most common configuration combines a dispersion turbine and a wall-breaking anchor. The turbine rotates at high speed producing a distributive and dispersive effect throughout the container, while the anchor rotates at low speed to scrap the container walls (Foucault, 2006). An example of coaxial mixer available in Bachiller Barcelona is attached in Figure 6:

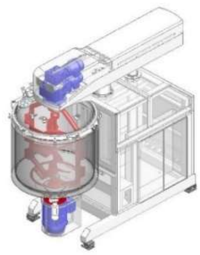

Figure 6: Example of a coaxial stirrer from the manufacturer Bachiller Barcelona

These types of reactors typically include a high cut stator rotor, which acts as a turbo emulsifier. The rotor produces a powerful suction that sucks the fluid towards its center and then propels it radially. As the fluid passes through the stator openings, mechanical shear cuts the drops at a speed greater than 20 m/s. In this way it reduces the droplet size of the dispersed phase. The rotor can be installed at the bottom of the reactor, like in the Figure 5, or in line with the reactor.

The Bachiller Barcelona company markets a reactor called the *Bachmix Multifunction* that meets the required characteristics. It includes a jacket that helps to provide the necessary utilities. It has been decided to work with a 600L reactor, 20% larger than the batch size, to provide safety and to have the opportunity to increase the capacity of the batch. The agitator and the reactor are made of 304 stainless steel. The equipment offers the possibility of independently controlling each agitator. That is why it has been decided to use the same equipment to carry out the emulsion and homogenization. For this, the continuous and dispersed phases will be incorporated into the reactor with the coaxial stirring activated to form the pre-emulsion. Once pre-emulsified, the emulsion will be made by activating the cut stator rotor and coaxial stirring (1-20 μm).

The cooling and mixing stage are carried out in this equipment as well. When the mixture begins to have a homogeneous appearance, the cooling system is started until the temperature of the emulsion is 50 ºC. The rest of the ingredients are incorporated through the loading hole located in the lid of the reactor. The emulsion continues to cool until it reaches room temperature (25-30ºC). Coaxial stirring continues to operate but at reduced speed. Then the hand cream process is considered finished.

Storage equipment

To store the finished product, it has been decided to use a vessel with characteristics similar to those used in the premixing stage. In this case, the impeller will serve to supply a low speed that guarantees the maintenance of the homogeneity of the cream. The jacket has to keep the temperature of the cream at room temperature, to guarantee its correct condition. The volume that has been selected is 600L.

Filling and closing equipment

Once the hand cream manufacturing process is finished, it's time to bottle it. The container is the one selected in the conceptualization stage (50 mL bottle). The empty bottle is made up of a cylinder open at the top and closed at the bottom by the cap. The empty cylinder is introduced into a bottling machine and there it is filled with the hand cream. Then it would only be necessary to hook the label on the bottle.

JM Filling Solutions has an automatic tube filling and closing machine that adapts to the needs of the cream. It has a dose capacity of 3-300mL and a kinematic speed of 80u/min. It will allow to make the batch of 500kg - 10,000 bottles in 125 min. It has an automatic tube loading warehouse and a mobile control screen. The equipment is shown in the Figure 7:

Figure 7: Tube filling and closing Machine from JM Filling Solutions.

8.4 PRODUCTION PLANNING

Now that the equipment units have been chosen and the tasks have been defined, production planning will take place. The production of the hand cream can be carried out by alternating batches of only this product or combining it with another product that is produced in the same manufacture. To get an idea of the planning of the production process, the activities or tasks carried out in each equipment have been determined. A time has been estimated for the fulfillment of the different tasks, as shown in Table 8.

Based on the estimated times, it has been concluded that the limiting stage is the emulsion step. The time required for a batch (Bt) is 10.2 h. The cycle time (Ct) that corresponds to the time occupied by the limit stage is 5.9 h. Based on the total production initially estimated, it is expected to manufacture 120 batches per year, distributed in 10 batches per month. To determine the time required to produce 10 batches per month, the Makespan time (Mt) has been used. Taking as a reference that the factory operates 18 hours a day, it has been obtained that two complete batches are manufactured per day ($Mk_{n=2}$ = 17.1h). Therefore, the manufacture of 10 batches will take 5 days.

$$Mt_N = Bt + (N-1)Ct$$

Table 8: Production planning of the process

		Start (h)	End (h)	Duration (h)	Ot (h)
Aqueous vessel	Load aqueous phase	0.0	0.5	0.5	2.5
	Mix and heat aqueous phase (70º)	0.5	1.5	1.0	
	Pump to the reactor aqueous phase	1.5	2.0	0.5	
	Cleaning	2.0	2.5	0.5	
Oily vessel	Load oily phase	1.0	1.3	0.3	1.5
	Mix and heat oily phase (70º)	1.3	1.8	0.5	
	Pump to the reactor oily phase	1.8	2.0	0.3	
	Cleaning	2.0	2.5	0.5	
Emulsion	Load aqueous phase	2.0	2.5	0.5	5.9
	Load oily phase	2.5	2.8	0.3	
	Mix and heat (70º)	2.5	4.0	1.5	
	Mix and cool (50ºC)	4.0	5.0	1.0	
	Load other ingredients	5.0	5.2	0.2	
	Mix and cool (30ºC)	5.2	6.2	1.0	
	Pump to the storage vessel	6.2	6.7	0.5	
	Cleaning	6.7	7.7	1.0	
Filing	Load	6.7	7.2	0.5	3.5
	Filling of bottles	7.2	9.2	2.0	
	Cleaning	9.2	10.2	1.0	

8.5 PRODUCTION-RELATED COSTS

The sales volume is estimated at 1.16 million tubes of cream per year, which corresponds to what is determined in the Batch Size section. The final product will be sold to shopping centers, pharmacies, and other distributors. Based on this, a sale price of 1.25€/u has been estimated.

Capital Expenditure (CAPEX) is the cost associated with the plant which include aspects such as cost of equipment, control instrumentation, pipes, valves, and installation. It has been calculated based on factor estimates by *S. Peters*, *et al* (2003). The method is based on the use of ratio factors to estimate capital investment items based on the cost of the equipment. It has been assumed that the site is already available for the installation. The cost of the equipment is in the Table 9 and the CAPEX in Table 10 of the Appendix.

The variable costs, which depend on the volume of production, and the fixed costs, which are independent of it, have been calculated. In the case of variable costs, the cost of raw materials and utilities has been considered. In the case of fixed costs, aspects such as the payroll of workers, maintenance or advertising have been considered.

The profit and loss statement of the process has been made (Table 12-Appendix). For its calculation, it has been assumed that all the manufactured product is sold, that the Operating Expense (OPEX) is invariable and is set at 8% of sales and the 25% profit tax is applied in accordance with Spanish legislation. The amortization of the investment is considered in 10 years and at a fixed rate (22839€/year).

The Cost of Goods Sold (COGS) shown in Table 11-Appendix, have been calculated, which refers to the direct cost attributable to the final product and includes fixed and variable costs. Then, the factor of Earnings Before Interest and Taxes (EBIT) has been calculated by subtracting COGS and OPEX from net sales. The tax reduction is applied to this value and the Net Profit is obtained. The results are the same in each year since it has been estimated that the plant will operate at full capacity and the annual production will not vary over the years. These results are shown in Table 12-Appendix.

Then the working capital (WC) is calculated. It has been estimated that the inventory turnover is 30 days and the collection and payment to customers and suppliers is 60 days. The cost of inventories, accounts receivable, and accounts payable has been calculated using the following formulas. The WC is calculated from the sum of the stocks and the customers and the subtraction of the suppliers. Then the variation of WC has been calculated (ΔWC). The results are shown in the Table 13-Appendix

$$Inventories = \frac{COGS}{365} \cdot days \quad Receivables = \frac{COGS}{365} \cdot days \quad Payables = \frac{Net\ sales}{365}\ days$$

Cash flow CF is the net accumulation of assets in a period and can be used to analyze the liquidity and viability of an inversion project. It is calculated by the sum of net profit and amortization and the subtraction of investments and working capital. To calculate the accumulated cash flow (CFD), the following formula, and a discount rate of 8% have been used. The results are shown in the Table 14-Appendix. Between 0 and 1st year the value changes from negative to positive. It means that the initial investment is recovered within this period, specifically from the eighth month. This corresponds to the Pay Back value which is represented in Figure 8-Appendix.

$$CFD = \frac{CF}{(1+0.08)^i}, \quad i = year$$

9. CONCLUSIONS

In the context of the current health situation caused by the COVID-19 pandemic, the need to develop a hand cream with disinfectant and moisturizing properties has been identified to minimize or eliminate skin problems derived from frequent disinfection. Based on this, a hand cream has been developed establishing its quality criteria, selecting the ingredients that best adapt and their proportion, and the production process has been preliminary designed.

The hand cream has been conceptualized as an O/W emulsion with a droplet size of 20µm. It has been established to exhibit pseudoplastic behavior, with low viscosity when applied to the skin and high viscosity at low shear rates so that it does not spill easily. The emulsion contains active ingredients, surfactants, and additives such as thickeners, fragrances, and preservatives. When selecting the ingredients, their multifunctionality, efficacy, non-irritability or non-dangerousness have been considered.

The selected disinfectant has been peracetic acid for its effective action against viruses, bacteria, and fungi. It requires little contact time and low concentration, and its residues are safe. It is effective against SARS-CoV. It has been recommended as a disinfectant by organizations such as the WHO and endorsed by the European Parliament.

The manufacturing process has been designed as a batch process as it is the type of production that is best suited. An approximate annual production of 60,000 kg has been estimated based on the current market trend and future forecasts. To carry out the manufacturing process, two stirred vessels for the premix stages, a coaxial mixing reactor with a high cut stator rotor for the emulsion and homogenization stage, a storage vessel and, a filling equipment have been selected.

The planning process has been estimated to determine batch time, cycle time, and Makespan time, and it has been concluded that the planned production of 10 batches per month will require five days. The profit and loss statement, the working capital and the cash flow results have concluded that the inversion will be profitable. The initial investment is recovered within the first eight months.

10. NOTATION

Bt: Batch time [h]

CAGR: Compound Annual Growth Rate

CAPEX: Capital Expenditure

CF: Cash Flow

COGS: Cost of Goods Sold

Ct: Cycle time [h]

EBIT: Earnings Before Interest and Taxes

HEDP: 1-hidroxietano-1,1-difosfónico acid, etindronic acid

HLB: Hydrophilic-Lipophilic Balance

ISO: International Organization for Standardization

K: Consistency index, [Pa·s^n]

MCR: Counter Rotating Mixer

Mt: Makespan time, time needed to produce N batches [h]

OPEX: Operating Expense

Ot: Occupancy time of an equipment

O/W: Oil in water emulsion

PAA: Peracetic Acid

SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus

UNE: Spanish Association for Standardization

WHO: World Health Organization

W/O: Water in oil emulsion

WC: Working Capital

Za: Mass fraction

τ: Shear stress, [Pa·s]

$\dot{\gamma}$: Shear rate, [1/s]

n: Flow behavior index

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12. APPENDIX

Table 9: Equipment costs results

Equipment	Company	Equipment cost (€)	Total (€)
Pre-mix equipment 80 L	KEAN	2,000	99,300
Pre-mix equipment 500 L	ZHONGHAO	8,000	
Storage equipment 600 L	KEAN	8,000	
Emulsifier-hom 600 L	Inoxpa	48,000	
Filling equipment	LTPM China	30,000	
Vacuum pump	Zhonghao	1,500	
Lobe pump	WenZhou Leno	1,800	

Table 10: Capital Expenditure - CAPEX results

	Factor	Cost (€)
Equipment cost	Ec	99,300
Installation of the equipment	0.4·Ec	39,720
Pipes and valves	0.3·Ec	29,790
Instrumentation and control	0.1·Ec	9,930
Structure and building	0.1·Ec	9,930
Electrical installation	0.1·Ec	9,930
Total Direct Costs (Dc)		198,600
Constractor's fee	0.05·Ec	4,965
Contingency	0.2·Ec	24,825
Total Indirect Costs (Ic)		24,825
Fixed Capital, CAPEX (Dc+Ic)		223,425

Table 11: Cost of Goods Sold - COGS results

COGS (€/year)	713,943
Variable costs (€/year)	517,101
Raw materials (€/year)	486,794
Utilities (€/year)	30,307
Fixed costs (€/year)	196,842
Workers (€/year)	94,500
Advertising (€/year)	60,000
Maintenance material (€/year)	20,000
Amortization 10 years (€/year)	22,343

Table 12: Profit and loss statement results of the process

k€/year	0	1	2	3	4	5	6	7	8	9	10
Sells volume	0	1,160	1,160	1,160	1,160	1,160	1,160	1,160	1,160	1,160	1,160
Net sales	0	1,450	1,450	1,450	1,450	1,450	1,450	1,450	1,450	1,450	1,450
Variable costs	0	517	517	517	517	517	517	517	517	517	517
Fixed costs	0	197	197	197	197	197	197	197	197	197	197
COGS	0	714	714	714	714	714	714	714	714	714	714
OPEX	0	116	116	116	116	116	116	116	116	116	116
Total expenses	0	830	830	830	830	830	830	830	830	830	830
EBIT	0	620	620	620	620	620	620	620	620	620	620
Tax	0	155	155	155	155	155	155	155	155	155	155
Net profit	0	465	465	465	465	465	465	465	465	465	465

Table 13: Working capital - WC results of the process

k€/year	0	1	2	3	4	5	6	7	8	9	10
Stock	0	59	39	39	39	39	39	39	39	39	39
Clients	0	191	191	191	191	191	191	191	191	191	191
Supplier	0	117	117	117	117	117	117	117	117	117	117
WC	0	132	112	112	112	112	112	112	112	112	112
ΔWC	0	132	-20	0	0	0	0	0	0	0	0

Table 14: Cash flow - CF results of the process

k€/year	0	1	2	3	4	5	6	7	8	9	10
Net profit	0	465	465	465	465	465	465	465	465	465	465
+ Amortization	0	22	22	22	22	22	22	22	22	22	22
- Investment	223	0	0	0	0	0	0	0	0	0	0
- ΔWC	0	132	-20	0	0	0	0	0	0	0	0
CF	-223	355	507	487	487	487	487	487	487	487	487
CFD	-223	329	435	387	358	332	307	284	263	244	226
ΣFCD	-223	106	540	927	1,285	1,617	1,924	2,209	2,472	2,716	2,942

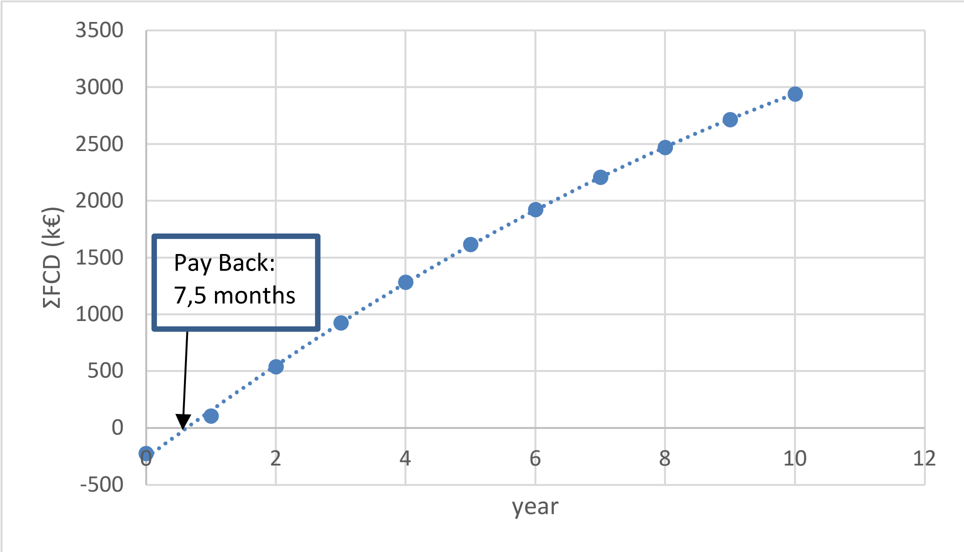

Figure 8: Graphical representation of the Pay Back value