U.Porto Journal of Engineering, 8:5 (2022) 68-85
ISSN 2183-6493
DOI: 10.24840/2183-6493_008.005_0008

Received: 17 May, 2022
Accepted: 1 September, 2022
Published: 26 September, 2022

Valorisation of Kiwifruit Residues and their Application in an Anti-ageing Facial Cream

Ana P. S. C. Teixeira[1], Bruna F. M. Coutinho[2], Joana C. Cancela[3], Laura J. R. Cullen[4], Margarida S. C. A. Brito[5]

[1]Department of Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal (up201806097@edu.fe.up.pt) ORCID 0000-0002-1184-6138; [2]Department of Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal (up201806635@edu.fe.up.pt) ORCID 0000-0003-3759-0182; [3]Department of Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal (up201806735@edu.fe.up.pt) ORCID 0000-0001-5404-455X; [4]Department of Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal (up201806139@edu.fe.up.pt) ORCID 0000-0002-5784-2693; [5]LEPABE-Laboratory for Process, Environment, Biotechnology and Energy, Department of Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal; ALiCE-Associate Laboratory in Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal (mbrito@fe.up.pt) ORCID 0000-0003-1134-1743

Abstract

Portugal has a significant production of kiwifruit, from which around 73.8 tons of leaves and branches are generated every year. The composition of these residues shows interesting properties that could be incorporated into a value-added product. In order to create a new product, the steps proposed by the Chemical Product Design procedure were followed: identifying the needs, brainstorming ideas, selecting the best idea, proposing a manufacturing process. The chosen idea was an anti-ageing facial cream since the kiwifruit leaves and branches present interesting properties such as antioxidant, anti-inflammatory and anti-pigmentation effects. In order to obtain this product, a manufacturing plan was designed, and an economic analysis was performed. The proposed circular economy business was found to be profitable and environmentally friendly. This work also includes further innovative steps of the facial cream, such as pigmentation.

Author Keywords. Kiwifruit. Leaves. Stems. Phenolic Compounds. Anti-ageing. Antioxidant. Facial Cream.

Type: Research Article
Open Access Peer Reviewed

1. Introduction

Over the past few years, there has been an increase in the global demand for agricultural products. As a result, Portugal has intensified agricultural production, with an increased productivity of the cultivated area and yield of this sector's activity (CaixaBank Research 2019). A particular industry that has expanded in Portugal is the production of kiwifruit. Due to the favourable climate conditions in the north and centre region, the production of this fruit is predominant in this part of the country (Marketing Agrícola 2019). A particularly interesting species of kiwifruit, *Actinidia Arguta*, has an estimated annual production of 123 tons (Pinto, Delerue-Matos, and Rodrigues 2020). Moreover, the above-mentioned increase in production also results in an increase in the amount of residues generated by this activity. It is estimated that 0.6 tons of residues per ton of kiwis produced are generated by the process of pruning the kiwifruit plant, so annually 73.8 tons of residues are generated (Creto 2018).

Nowadays, many companies, industries and even consumers are driven to invest, create or buy new products that have in mind the concepts of circular economy and sustainability as a response to climate change in order to minimise the environmental impacts associated with it. Therefore, changes have been made in several stages of the life cycle of products, such as the addition of a recycling, reuse, or remanufacturing stage.

Agricultural residues present a significant problem to the environment as residues are often dumped or incinerated, even though they may contain active compounds with interesting properties in different areas of application. This scenario also happens during the pruning process of the kiwifruit plant, as it produces considerable amounts of residues, as previously mentioned. So, the main purpose of this work aims to find and develop a sustainable solution to this problem by adding value to these residues and thus creating a new profitable product that, at the same time, responds to the needs of the market.

2. Raw Material

The main problem related to the pruning of the kiwifruit plant is the amount of residues it produces. As with any other residue, its environmental impacts should be considered. In this case, the leaves and branches that result from this activity are usually disposed of in nature or incinerated. In order to avoid this kind of residue, their composition was analysed to create a new product that takes advantage of the beneficial properties that these residues may provide. It was found that the stems and leaves contain phenolic compounds, such as phenolic acids and flavonoids, vitamins (E and C, for example) and fibres.

On the one hand, regarding the phenolic compounds, the total phenolic content (TPC) in kiwifruit leaves can vary between 140.72 and 440.71 mg GAE/g dw depending on the solvent used to extract these compounds (Almeida et al. 2018), where GAE is Gallic Acid Equivalents. On the other hand, a study found that the total phenolic content in kiwifruit stems is approximately 111.39 mg GAE/g dw (Kim and Choe 2017). Furthermore, depending on the solvent used for the extraction, the total flavonoid content (TFC) present in the leaves varied between 136.72 and 318.11 mg CAE/g dw (Almeida et al. 2018), where CAE is Catechin Equivalents. No information was found regarding the concentration of flavonoids in the stems. However, literature states that the phenolic content in the leaves and stems is similar, so the TFC in the stems was considered the same as the one present in the leaves (Chamorro et al. 2022).

Moreover, research has been done to determine which compounds are present in these residues in larger quantities and which are their most widely known active principles. Firstly, it was verified that the compounds present in the stems and leaves could be divided into three groups: flavanols, flavan-3-ols and phenolic acids. In the first group, the most present compounds are glycosylated kaempferol and glycosylated quercetin. The main compound in the second group is catechin. Finally, the third group is mainly composed of caffeic acid, neochlorogenic acid and chlorogenic acid (Almeida et al. 2018). Furthermore, it was possible to conclude that most phenolic compounds have antioxidant properties that inhibit the oxidation of molecules that may originate free radicals that cause damage to skin cells[1]. In addition, some of these compounds, such as neochlorogenic acid (Navarro-Orcajada et al. 2021), caffeic acid (Cizmarova 2020) or quercetin (Barreca et al. 2021), also have anti-inflammatory properties that reduce redness, swelling or pain in the body by blocking certain

[1]*Pallipedia: The Free Online Palliative Care Dictionary*, s.v. "Antioxidants," accessed December 2021, https://pallipedia.org/antioxidants/.

substances that cause inflammation[2]. Moreover, some compounds also have antibacterial properties, for instance, chlorogenic acid (Jung et al. 1999), caffeic acid (Cizmarova 2020), quercetin (Barreca et al. 2021) or glycosylated kaempferol (Barreca et al. 2021).

Phenolic compounds, which include phenolic acids and flavonoids, were considered one of the most important compounds present in these residues, as they may provide a wide range of noteworthy properties that can be incorporated into different products (Gan et al. 2019).

3. Chemical Product Design (CPD)

In order to create a product that is different and viable in the market, the Chemical Product Design procedure was followed. It proposes the following steps: first, it is necessary to understand the needs of the market and to define the problems that need to be assessed; secondly, brainstorming ideas according to the needs previously settled; then, the best idea should be selected; and, finally, it is necessary to define how the product should be manufactured and how it should be presented to the market. Thus, it is possible to define Chemical Product Design as a set of four steps: 1) Needs, 2) Ideas, 3) Selection and 4) Manufacture (Cussler and Moggridge 2011).

3.1. Needs & Ideas

Regarding the Needs, it was defined that the goal of this work was to add value to kiwifruit residues that are usually incinerated or dumped, employing them in a product that takes advantage of the most important active compounds present in these raw materials. Thus the need to create a product that contributes to the valorization of kiwifruit residues is identified in this work as a need. The composition of the kiwifruit leaves and branches was analysed in terms of the advantageous properties that these compounds could provide to a new product.

Then, several ideas were proposed to meet the need mentioned above. Some of the ideas were almost immediately excluded, such as a soothing lipstick, diuretic drinks, bars, bioadhesives or production of cellophane, due to lack of feasibility, high production costs associated with strict product legislation or the fact that the amount of phenolic compounds required would be too high. The four most promising ideas were: an anti-ageing facial cream, an anti-cellulite cream, a burn cream, and an anti-bacterial spray for nebulisers to inhibit the bacteria *P. Aeruginosa*.

The idea of the anti-ageing facial cream came from the several beneficial properties of the phenolic compounds to the skin, especially their antioxidant effect (Silva et al. 2021). The second idea, the anti-cellulite cream, resulted from the anti-inflammatory properties of some phenolic compounds and it was also found that the branch and leaves extracts may provide anti-bacterial activity towards a bacterium that causes cellulite (*S. Pyogenes*) (Basile et al. 1997; Diniz 2018). The idea to produce a cream to treat burns is related to the anti-inflammatory properties of the listed phenolic compounds. Finally, the idea for the anti-bacterial spray for nebulisers emerged from the antibacterial properties of these compounds against the bacteria *A. Aeruginosa* (Basile et al. 1997), as it is one of the pathogenic agents that causes pneumonia in intubated patients (Bush and Vazquez-Pertejo 2020).

3.2. Selection

Table 1 shows a matrix with the four ideas. Different criteria were defined to evaluate each of these ideas, and a weighing factor was attributed to each criterion in order to choose the overall best idea.

---

[2]*Dictionary of Cancer Terms*, s.v. "Anti-inflammatory agent," accessed December 2021, https://www.cancer.gov/publications/dictionaries/cancer-terms/def/anti-inflammatory-agent.

	Innovation	Feasibility	Scientific maturity	Usability	Ease of Licensing	Total
Weighting factor	0.20	0.3	0.20	0.15	0.15	
Anti-ageing facial Cream	4	8	8	10	7	7.4
Anti-cellulite cream	5	6	6	10	7	6.6
Burn cream	5	5	4	10	3	5.3
Anti-bacterial spray for nebulizers	8	2	2	5	2	3.7

Table 1: Selection matrix of ideas for the valorisation of agriculture residues resulting from the kiwifruit production

The chosen criteria were Innovation, Feasibility, Scientific Maturity, Usability and Ease of Licensing. Parameters were selected in accordance with indications presented in the literature (Cussler and Moggridge 2011). A value between 0 and 10 was attributed to each criterion and then a weighted average was calculated for each idea.

The highest weighting factor (0.30 in 1) was attributed to the Feasibility criterion since the main goal of this work was to manufacture a product that could be successfully and easily developed and to add value to residues that are not normally valorised. Scientific Maturity and Innovation criteria were evaluated with a weighting factor of 0.20 due to the research required for its manufacture and the process of innovating. The innovation of a product is not necessarily the best option because the development of a more usual product could be more profitable. Usability and Ease of Licensing were classified with the lowest weighting factor (0.15) because the licensing requirements were not considered a strong factor since it could take a long time for the product to be approved.

Regarding the anti-ageing facial cream, this idea was not considered very innovative since there is already a huge variety of skin creams on the market. Nevertheless, this was also considered an advantage because it means that further advances have been made in this field. Moreover, the production of the facial cream was not deemed too complex and there are already some companies that use natural sources of antioxidant agents to produce anti-ageing creams; the licensing requirements for skincare products are not usually very demanding, and the use of a cream is considered a daily task.

Concerning the anti-cellulite cream, this product was not considered very innovative since there is a great variety of creams on the market. Its production involves more complex processes compared to the production of facial cream due to the fact that it would probably require more in-depth knowledge because this product has a more specific purpose. In addition, the health community states that there is no sufficient scientific proof that anti-cellulite creams are actually effective (Khan et al. 2010). However, the use of this cream is also considered a daily task and its licensing requirements are also not very demanding.

In relation to the cream to treat burns, this idea was considered poor innovation; its execution is not an easy process since pharmaceutical products typically have more complex formulations and it requires demanding standards. Furthermore, there does not appear to be much research regarding the use of natural products to produce burn creams.

Finally, the anti-bacterial spray for nebulizers was considered an innovative idea since it avoids the *P. Aeruginosa* bacteria growth in these devices, which is a pathogenic agent responsible for pneumonia cases in intubated patients (Bush and Vazquez-Pertejo 2020). Nevertheless, the production of this spray was considered a complex process since its formulation would require further research to verify if the concentration of phenolic compounds in the kiwifruit residues could provide an effective antibacterial effect and the licensing requirements for this type of product are usually not flexible.

So, after calculating the total score for all ideas, the idea for the development of facial cream with anti-ageing properties was found to be the one with the highest score. Therefore, the manufacturing process of this product was then outlined.

3.3. Manufacture

3.3.1.Extraction method

The decision on the extraction methods was based on processes found in the literature. Almeida et al. (2018) described this procedure as a solid-liquid extraction method that either uses water, alcohol or a mixture of alcohol and water (50/50 % (v/v)) as extraction solvents (Almeida et al. 2018). After harvesting the kiwifruit, the leaves and branches of the plants are collected, and, to remove the water present in them, they are submitted to a drying process. For this, at a laboratory scale, they are stored at a temperature of -80 °C for subsequent lyophilisation. Afterward, the lyophilised samples are milled and stored in plastic tubes and kept at about 4 °C until the solid-liquid extraction procedure occurs (Almeida et al. 2018). During this process, the phenolic compounds present in 1 g of powdered sample can be extracted with 50 mL of water, ethanol, or water-ethanol solution, for 1 h and at a temperature of 50 °C on a heating plate under constant stirring. Finally, the extract is filtered through a Whatman No. 1 filter paper and, after that, concentrated under vacuum at a temperature of 37 °C (Almeida et al. 2018).

After the extraction, the leaf and stem extracts were analysed to obtain the Total Phenolic Content (TPC) and the Total Flavonoid Content (TFC). The TPC values were obtained through a spectrophotometric method, namely the Folin-Ciocalteu procedure, and the TFC values were obtained through UV-Vis spectroscopy (Almeida et al. 2018). Different extraction solvents have different affinities to the phenolic compounds; since the most effective solvent was the ethanol solution, with a yield regarding the TPC of 440.71 mg GAE/g dw, water was able to extract 189.39 mg GAE/g dw, and, finally, the water-ethanol solution was the least effective solvent, only extracting 140.72 mg GAE/g dw. These results refer to the leaf extracts (Almeida et al. 2018).

3.3.2.Anti-ageing facial cream additional properties related to skincare

In order to study the additional benefits facial creams made from these raw materials could provide to the skin, a more in-depth study of the compounds was performed. Some of the active compounds in the kiwifruit's branches and leaves and their beneficial properties for skincare are summarised in Table 2. It is important to mention that some of these compounds were not mentioned before since they are present in the residues in smaller quantities.

As mentioned before, the most predominant compounds in these residues are neochlorogenic and chlorogenic acids, having both antioxidant activity. It is widely known that age-associated reductions in physiologic functions are caused by the accumulation of oxidative damage to macromolecules (Lin and Beal 2003). Antioxidant compounds help to reduce the consequences of skin oxidation and slow the skin ageing process. Other compounds in these raw materials, namely quercetin, rutin and vitamin C, show this antioxidant activity paired with wrinkle reduction effects (Silva et al. 2021). Therefore, these residues present themselves as a potential ingredient for an anti-ageing facial cream.

Active compound	Skincare property	Reference
Neochlorogenic and chlorogenic acid	Antioxidant and anti-ageing activities	Silva et al. (2021)
Caffeic acid	Protection against UVB radiation; antiwrinkle activity; antimicrobial activity	
Catechin	Depigmentation and anti-inflammatory effects; protection against sunburn inflammation and potentially UV radiation damages	
Quercetin	Anti-ageing and anti-inflammatory effects; stimulation of tissue regeneration and new collagen fibres production	
Rutin	Improvement of skin dermal density and elasticity; reduction of fine wrinkles; antioxidant activity	
p-coumaric acid (only in stems)	Reduction of skin colour and pigmentation attenuation	
Vitamin C	Improvement of the appearance of photo damaged skin regarding firmness, smoothness, and dryness; reduction of small wrinkles; contribution to the maintenance of optimal collagen density; anti-pigmentation effects	
Vitamin E	Reduction of pigmentation; improvement of skin damage caused by UV radiation	
Luteolin	Protection against chemical-induced irritation; improvement of skin hydration; reduction of redness in irritated skin	
Minerals (such as potassium)	Improvement of skin surface hydration	

Table 2: Beneficial properties regarding skincare of some active compounds

The proposed facial cream could also be beneficial in mitigating other problems that concern the beauty industry, such as skin hyperpigmentation and inflammation. Hyperpigmentation happens when there is excessive melanin production that can result from exposure to UV radiation, genetic factors, aging, or as a result of inflammation processes. Some compounds in these residues show activity against pigmentation, specifically p-coumaric acid, vitamin C and vitamin E. Furthermore, inflammation is a response of the immune system to avoid infection and repair affected tissues. However, this process can cause an unaesthetic look on the skin. Both catechin and quercetin have anti-inflammatory properties, and luteolin is able to reduce the redness characteristic of irritated skin (Silva et al. 2021).

Actinidia Arguta leaves are also composed of minerals such as nitrogen, phosphorous, potassium, calcium-magnesium, and sulphur with average concentrations of 2.25%, 0.45 – 0.59%, 1.99 – 2.43%, 5.19 – 5.71%, 0.29 – 0.34%, respectively. Some minerals, such as potassium, may also improve skin surface hydration (Silva et al. 2021).

In conclusion, it was possible to infer that a skin cream using kiwifruit stems and leaves would be a potentially effective anti-ageing cream and could also provide solutions to other skin conditions that consumers wish to attenuate.

3.3.3. Facial cream formulation and preparation

After concluding that the facial cream was the overall best option, it was necessary to determine which type of facial cream and formulation would be most suitable for the application of the properties of the active compounds that can be found in the kiwifruit stems and leaves.

Facial creams, or skin creams, are emulsions composed of a dispersed phase and a dispersion medium. There are two main types of skin creams, namely oil-in-water (O/W) creams, which consist of small droplets of oil dispersed in an aqueous phase, and water-in-oil (W/O) creams, which are composed of droplets of water dispersed in an oil phase. O/W creams are known to be less greasy than W/O creams. Nevertheless, W/O creams have a greater ability to release the active ingredients into the skin and have a more significant moisturising effect, as they create an oily barrier on the skin that highly decreases water losses (Mohiuddin 2019).

Furthermore, facial creams can be classified regarding their purpose. There are cleansing creams, massage creams, night creams, and cold creams, among others. First, cleansing creams are emulsions with the ability to remove dirt, microorganisms, and oil from cosmetic products, etc., and maintain the skin surface moist at the same time. These creams are commonly washed off after being used, so they were not considered to be an ideal option. Massage and night creams are usually water-in-oil emulsions with high oil content, as they are intended to be left on the skin for long periods of time. They have significant moisturising effects and would be able to release the active ingredients into the skin, and their formulations were found to be complex and composed of various ingredients (Mohiuddin 2019). Cold creams are known to be W/O emulsions that provide a cooling sensation when applied to the skin. They can be used for pharmaceutical purposes, to maintain the skin surface moist and avoid rough skin conditions, as a cleansing product, as a carrier for drug substances, etc. Thus, they would be able to release the active ingredients into the skin and, at the same time, contribute to a healthy and moisturised skin. In addition, their formulations were found to be simpler and require less ingredients than those associated with night and massage creams, which would result in lower production costs when compared to night and massage creams (PharmaEducation 2022). Therefore, it was concluded that the production of cold creams was the most suitable option for the application of the properties of the active compounds that can be found in the kiwifruit stems and leaves.

After deciding that producing a cold cream would be the most appropriate choice, it was necessary to determine which formulation should be the basis for developing this cream. There are several formulations that vary depending on the purpose of the cold cream. So, it was decided that using a standard formulation was the most suitable option. The standard formulation's ingredients and their respective quantities and functions are presented in Table 3 (PharmaEducation 2022).

Ingredient	Quantity	Function
White wax/white beeswax	20.00-24.50 g	Stiffening agent
Mineral oil (Liquid paraffin)	50.00-56.00 mL	Emollient, solvent, and vehicles of an oil phase
Sodium Borate USP-NF/Borax BP	0.50-0.70 g	Emulsifying agent
Glycerine USP/ Glycerol BP	4.28 mL	Humectant
Methylparaben	0.20 g	Antimicrobial agent
Propylparaben	0.02 g	Antimicrobial agent
Fragrance	0.50 mL	Flavouring agent
Tween-80/ Polysorbate 80	0.50 mL	Emulsifying agent
Purified water	Up to 100.00 mL	Vehicle and solvent of an aqueous phase

Table 3: The standard cold cream formulation's ingredients and their respective quantities and functions

Based on Table 3, a cold cream should be composed of: a stiffening agent whose purpose is to increase the emulsion's viscosity (Spectrum Chemical Mfg Corp, n.d.); an emollient that soothes and hydrates the skin (NHS, n.d.); a solvent of the oil phase, an emulsifying agent that avoids recoalescence of the droplets (Dickinson 2009); a humectant whose main purpose is to retain moisture without compromising the quality of the cream (Cherney 2019); antimicrobial agents that inhibit the development of microorganisms (Burnett-Boothroyd and McCarthy 2011); a flavouring agent and a solvent of the aqueous phase.

A new formulation was developed to produce a sustainable cream that uses as many natural and safe ingredients with lower environmental impacts. Regarding the stiffening agent, it was found that white beeswax is made from honeycomb from bees and is safe to be applied directly on the skin (WebMD Medical Team 2020), so this ingredient was kept in the new formulation. For the oil phase solvent, it was necessary to find an alternative to the liquid paraffin, as it is a by-product of crude oil distillation that can cause pulmonary diseases, and long-term exposure of the skin to this product may lead to skin irritation problems or even dermatitis (Speight 2020). A safe alternative to liquid paraffin is coconut oil, which is obtained from dried coconut meat (copra)[3], and it is known to have high moisturing effects due to its organoleptic characteristics (Neto, Silva, and Neto 2020). Furthermore, borax, used as an emulsifying agent in the formulation shown above, although it occurs naturally, is known for being associated with several health issues, such as irritation of the skin and eyes, hormone problems, organ damage, poisoning, among others (Cirino 2018). Glyceryl oleate was considered an alternative to borax since it can be extracted from natural sources, such as olive oil, peanut oil, pecan oil, or tea seed oil, is not normally associated with irritation problems and is deemed safe to be applied in cosmetics (Puracy, n.d.). In addition, concerning the humectant, glycerine was kept in the new formulation because it is a natural compound that can be obtained from vegetable oils and does not have significant side effects associated with it (Frothingham 2019). Moreover, methylparaben and propylparaben were not considered safe as antimicrobial agents due to the fact that some studies have linked parabens to the development of breast cancer (Lebreux 2017). Phenoxyethanol was chosen as a substitute for these compounds based on the fact that it can be extracted from green tea or chicory (Guthrie 2019) and is deemed safe by the European Commission on Health and Food Safety when present in the cream up to a concentration of 1% (Pedroja 2018). Regarding the emulsifier, polysorbate 80, this ingredient was kept in the new formulation as it is classified as a chemical of low concern on the United States Environmental Protection Agency's Safer Chemical Ingredients List (EPA 2021). Finally, the use of a flavouring agent was not considered necessary as it would only imply additional production costs and is not a mandatory feature in a facial cream, and the use of purified water was also maintained.

After the selection of alternative ingredients for the cold cream, a new formulation, which is shown in Table 4, was created. It is important to note that the quantities of the equivalent ingredients in the standard formulation were kept invariant because the substituted compounds have the same function as their respective alternatives. This formulation enables the production of 183.4 g of cream. The quantity of stiffening agent was defined as the lowest (20.00 g) to avoid the unpleasantness associated with very thick creams, and the quantity of glyceryl oleate, one of the emulsifying agents, was defined as the highest (0.70 g) to guarantee an efficient mixture of both phases, and the quantity of coconut oil, which also presents emollient properties, was likewise defined as the highest (56.00 mL) to maximise the cream's moisturising effects.

[3]*Encyclopaedia Britannica Online*, s.v. "Coconut oil," last modified June 7, 2021, https://www.britannica.com/topic/coconut-oil.

Ingredient	Quantity	Function
White beeswax	20.00 g	Stiffening agent
Coconut oil	56.00 mL	Emollient, solvent, and vehicles of an oil phase
Glyceryl Oleate	0.70 g	Emulsifying agent
Glycerine	4.28 mL	Humectant
Phenoxyethanol	0.22 g	Antimicrobial agent
Polysorbate 80	0.50 mL	Emulsifying agent
Distilled water with kiwifruit residues extract	100.00 mL	Vehicle and solvent of an aqueous phase

Table 4: Formulation with alternative ingredients for the cold cream

At laboratory scale, the cold cream is firstly prepared by melting the white beeswax and the coconut oil in a glass beaker at 75 °C and mixing both compounds to prepare the oil phase. Then, in another beaker, the phenoxyethanol, polysorbate 80, glyceryl oleate, and glycerine are dissolved in water at a temperate of 75 °C in order to prepare the aqueous phase. After this, the oil phase is added to the aqueous phase under continuous stirring until a homogenous emulsion is formed and it cools down to room temperature (PharmaEducation 2022).

As the preparation of the cream requires the use of water, it was decided that the extraction process would be a hydrodistillation since this would enable the direct incorporation of the extract (water + phenolic compounds) in the aqueous phase and an additional step to eliminate other solvents (such as in the extraction method that uses a water-ethanol solution) would not be needed. Moreover, the hydrodistillation process can extract 189.39 mg GAE/g dw (Almeida et al. 2018) and keeping in mind the TPC value found for the kiwifruit stems (111.39 mg GAE/g dw) (Kim and Choe 2017), an average quantity of phenolic compounds present in the water extract was considered to be 150.40 mg GAE/g dw. It is important to outline that it was decided that, during the production of the cream, the residue samples for the hydrodistillation would contain a mixture of leaves and stems. The natural green color of leaves and streams is not a problem for the final product because the color will remain in the mixture of leaves and stems and not in the extract composed of the phenolic compounds.

In order to verify if the above-mentioned concentration of phenolic compounds would be safe to be applied directly on the skin, a study of the market was done to determine the average concentration of phenolic compounds in facial creams. It was found that in Thailand's market, the average concentration varies between 0.46 and 47.92 mg GAE/30 g cream (Mapoung et al. 2021). Considering the significant properties of these compounds, it was decided to produce creams with a concentration of 45 mg GAE/30 g cream. It was also decided that the amount of cream per package would be 39 g, which is the average size of smaller creams present in the market. Thus, the concentration of phenolic compounds in a cream would be 58.5 mg GAE/39 g cream. It was also verified that the hydrodistillation process can provide this concentration of phenolic compounds.

Nonetheless, it was also necessary to take into account that this extraction method is also able to extract 136.72 mg CAE/g dw of flavonoids (Almeida et al. 2018), so it means that a cream could contain approximately 58.16 mg CAE of these compounds. No information was found stating the maximum concentration of flavonoids a cream must contain. However, it was found that an adult should not ingest more than 120 mg of flavonoids per day (European Commission 2015), and since cosmetic regulations are usually less strict than food regulations, it was possible to infer that the quantity of flavonoids present in the cream would not be harmful to the consumers' health.

It is also important to mention that it was not possible to test the proposed formulation in the laboratory, so, in the future, it would be necessary to carry out some experiments in order to verify if the above-mentioned ingredients and their respective quantities form a stable emulsion, and, if not, adjustments to the formulation would have to be made. Additionally, analyses would have to be carried out in order to confirm the total phenolic content present in the kiwifruit stems and leaves when the solid-liquid extraction is performed using water as the solvent since this step in the production of the cream was also not performed in the laboratory. The quality of the extract in the scale-up of the facial cream production is ensured by the operating conditions defined at lab scale, such as temperature, pressure and time.

3.3.4. Scale-up of the facial cream production

After planning and designing the selected product, it was necessary to decide the quantity of creams that would be produced per year. In order to achieve this, a study of the target audience was performed, considering that this type of product is mainly bought by women with ages above 30. In 2020, the Portuguese female population above this age was approximately 3.5 million individuals (Pordata 2020). Considering that the estimated duration for this type of cream (that can be used in the morning and in the evening) is approximately four months, there is a sales opportunity of nearly 11 million creams per year. In addition, considering the competition, insertion in the market and the fact that not every woman has the same skincare routine and taste in skincare products, the number of creams produced in the third year since the formation of the company was set to be around 1.5 million. In the first year, the number of creams produced would be 500 thousand and, in the second year, would be 1 million, because in the first two years, the consumer community would still be getting to know and trust the brand and the sales of 1.5 million were deemed difficult to achieve.

In order to produce 500 thousand, 1 million and 1.5 million creams, it is necessary 1297, 2593 and 3890 kg of wet raw material, including branches and leaves, which is much less than the available amount of residues produced in Portugal every year (73.8 tons). These quantities were calculated from the amount of dry raw material needed to produce one cream and considering that the humidity of kiwifruit leaves and branches is stated to be 85.3% (Sanz et al. 2021). The amount of dry raw material necessary to produce a cream was calculated, bearing in mind that 1 g of dried residues and 50 mL of water is necessary to obtain an extract with a concentration of 150.4 mg GAE/50 mL of water. As previously mentioned, this concentration was obtained by calculating the average between the TPC values reported for the branches and leaves since different articles obtained slightly different quantities for these active ingredients.

The production line of the facial cream was divided into two main sections: 1) the extraction of the active compounds and 2) the production of the cream.

For the first section and as mentioned before, equipment to dry, mill, store, extract the phenolic compounds and filter the extract would be necessary. Regarding the drying process, it was decided that a dryer could deliver this function since the main goal is simply to remove the water present in the raw material, and lyophilisation is known to be an expensive procedure. It would also be necessary for a mill to grind the dried leaves and branches. In order to conserve the raw material's properties, the product that would not be immediately used for extraction would then be cooled to a temperature of 4 °C in a cooling division (Almeida et al. 2018). Regarding the extraction process, a mixing and heating tank of 50 L was chosen as the best option. This volume was considered appropriate for the desired quantity of creams. After the extraction process, the product obtained would need to be filtered. Thus, a vacuum filter machine and a vacuum pump were chosen for this process. After the extraction section, the solution of water with the active ingredients dissolved in it would be transferred to the cream machine using a pump. For this process, a water pump was chosen since the fluid is mainly water.

For the production of the cream, it would be necessary equipment for the production of the emulsion and then for subsequent packaging and labeling. For the facial cream production, a cream mixer-making machine with water phase and oil phase tanks with a capacity of 50 L each, an emulsifying tank with the capacity of 100 L and with an incorporated vacuum pump was chosen. After this, the emulsion will be packed and labeled, and so filling, capping and labeling machines will be required. In order to transport the cream to this next section, a volumetric pump would be needed, as the viscosity of emulsions is considerably high. Since the cream would be at a temperature of around 75 °C after being finalised, it would be necessary to cool it down using the cooling system incorporated in the emulsifying tank before it leaves the mixer in order to avoid the formation of microorganisms in the cream after closing the jars.

It was decided that the two main machines, the extractor and the mixer to produce the emulsion, would have maximum capacities of 50 L and 100 L, respectively, as explained before. Considering the desired number of creams and the working hours each day, the annual production would require less days than the average number of working days per year (253 days). If the volume of cream produced annually were to be increased in the future, it would be necessary to extend the days of manufacture or eventually implement night shifts.

Regarding the extraction, it was necessary to calculate the quantity of extract needed to produce the desired number of creams. It was concluded that the concentration of phenolic compounds in the extract was higher than the established concentration for the cream, so the extract would have to be diluted. Furthermore, from the formulation ingredients' proportions in the aqueous phase of the cream, it was also concluded that the amount of water per batch on the cream-making machine would be 47.3 L, with 43.3 L coming from the extractor and 4.0 L of distilled water added for the dilution. The required amount of raw material for this extraction would be 0.87 kg per 43.3 L of water. Considering that the extraction time and the time to make the cream was estimated to be of 2 hours each, and considering 8 h working days, it was decided to make three batches of cream per day, which corresponds to a total of 2224 creams per batch, thus 6672 creams per day. Therefore, 75 days are required to produce 500 thousand creams, 150 days to produce 1 million creams and 225 days to produce 1.5 million creams.

The flowsheet for the cream manufacturing process is present in Figure 1.

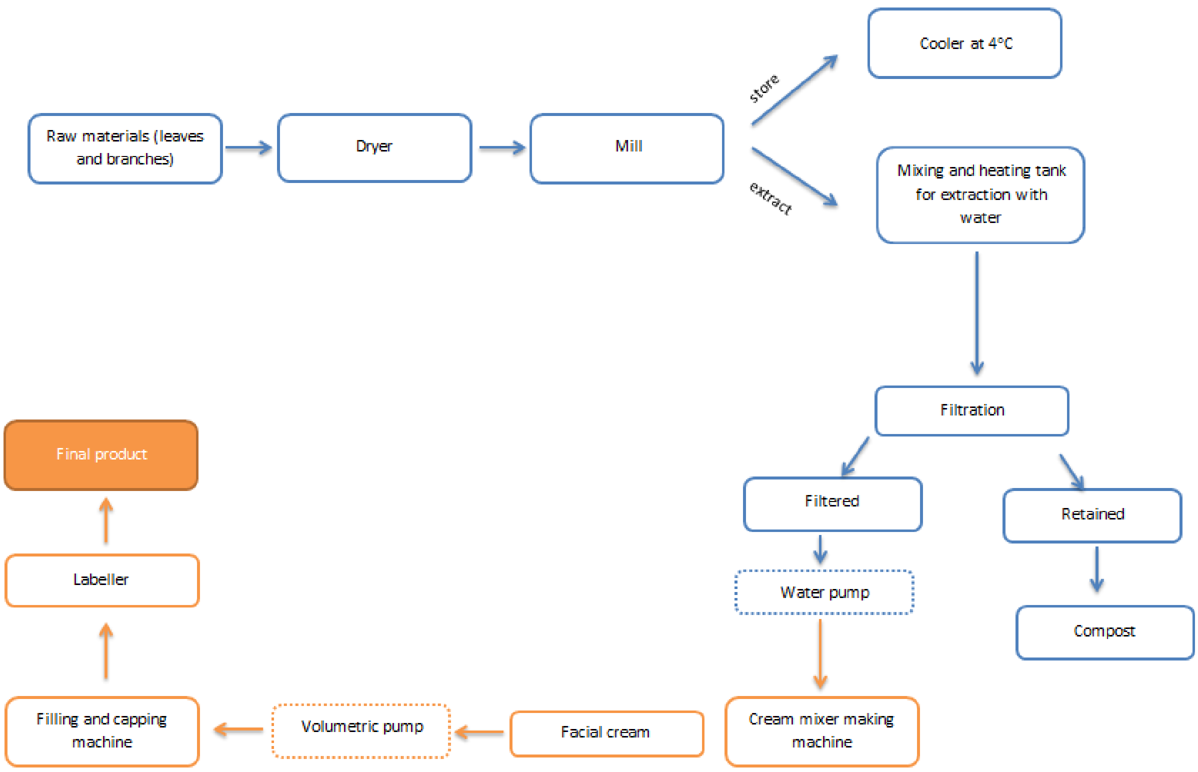

Figure 1: Cream manufacturing process flowsheet

4. Economic Analysis

In order to decide the final price of the facial cream and the costs associated with its production, it was necessary to perform an economic analysis to assess the viability of this product.

4.1. Warehouse and transportation

The potential warehouse for the production equipment would be situated in the north of Portugal, being relatively close to the Kiwi Greensun company (Fortis Consulting 2018). The price to rent a place in this region was estimated to be around 600 € per month; thus, the final value would be 7200 € per year. Moreover, it would be necessary to use the services of a transport company to take the raw materials from the Kiwi Greensun producer to the warehouse. This transportation would only occur once a year since most of the residues come from the pruning of kiwifruit trees during wintertime, and this would imply a cost of 109.2 € per year (Dore 2019).

4.2. Equipment and energy

The estimated investment for the above-mentioned equipment would be approximately €100 thousand. These devices carry energy costs related to their respective power consumptions. The annual operating time for each processing unit was calculated considering the number of creams produced and taking into account each device's operating time and their average energy consumption, the annual use of energy was determined. From these values and considering the average energy price and an estimate of expenses resulting from the energy supplied to other devices, the electricity costs of the equipment were then determined for each year. These values were approximately €7 thousand, €13 thousand, and €20 thousand for the first, second and third years (and onwards).

4.3. Cream formulation and packaging

In order to estimate the costs of the ingredients for the cream production, it was essential to calculate the quantity of each ingredient per cream and its final price. These values were €290 thousand, €580 thousand, and €870 thousand for the first, second and third years (and onwards), respectively.

The cream packaging includes one jar, a label, and a small cardboard container to store the jar. The prices regarding the labels, jars and cardboard containers were €250 thousand, €510 thousand, and €760 thousand for the first, second and third years (and onwards), respectively, and also include the logotype of the company, which is in Figure 2.

Figure 2: Logotype of the company

4.4. Salaries

In an initial phase, the company would be employing six equipment operators, two for the extraction section, two for the cream production section and two for the packing and labeling section. It would also employ two engineers, one for production and another for Research and Development (R&D). Finally, two persons would be included in the administration department, and so they would be responsible for the bureaucratic and accounting work. Career progress was also considered, so salaries would be increased by ten percent every two years and also by the contributive taxes of the Portuguese legislation. These values would be €170 thousand in the first and second year and €190 thousand in the third year and onwards.

4.5. Sales and marketing

The price for producing one cream and its packaging would be approximately 1.08 €.

It was planned that the product would be sold in an online store and in physical stores. For the online sales, the price of the facial cream to the final consumer would be 3.99 €. Regarding the sales in physical stores, the price to the final consumer would still be 3.99 € but 2 € would be paid to the store for the shelf space and the remaining 1.99 € would be part of the profit. In addition, it was decided that in the first year, 50% of sales would be online and 50% in physical stores. In the second year, 65% of sales would be online, and 35% would be in physical stores. From the third year onwards, 77% of sales would be online, and 23% would be in physical stores. The percentage of sales online would increase with time because the customer would get to know the product, and it would be more convenient to buy online.

Furthermore, the marketing would be adding €500 thousand in the first year and €250 thousand to the costs from the second year onwards since the target audience needs to get to know the product to gain trust and invest in it. The expenses for marketing in the first year are higher since it is related to its first impact on the audience. This investment would be divided between adverts on social media, such as Facebook and Instagram, on social events in physical stores to promote the product and by means of people with high social media coverage.

4.6. R&D department

It was decided that in the first year and so on, 15% of the estimated profit would go towards the R&D department. In the future, the cream could feature new properties, such as pigmentation, and this could be achieved with the aid of this department.

4.7. Overall analysis

From the economic analysis, it was verified that in the sixth trimester, the accumulated costs would equal the accumulated profits, as shown in Figure 3, so the proposed business would witness a payback time in the sixth trimester, considering that all creams produced per year would be sold. Furthermore, the Net Present Value (NPV) was calculated for each trimester, as shown in Figure 4, and it was verified that it becomes positive in the sixth trimester and the initial investment for this business would be €930 thousand. Also, the Internal Rate of Return (IRR) was determined, and it was found to be 32.3%. Thus, in conclusion, this business was deemed profitable.

Finally, it is important to outline that the prices and costs stated above only consisted in a preliminary study and, in the future, a more in-depth economic analysis would have to be performed in order to take into account certain factors that were not considered in this work.

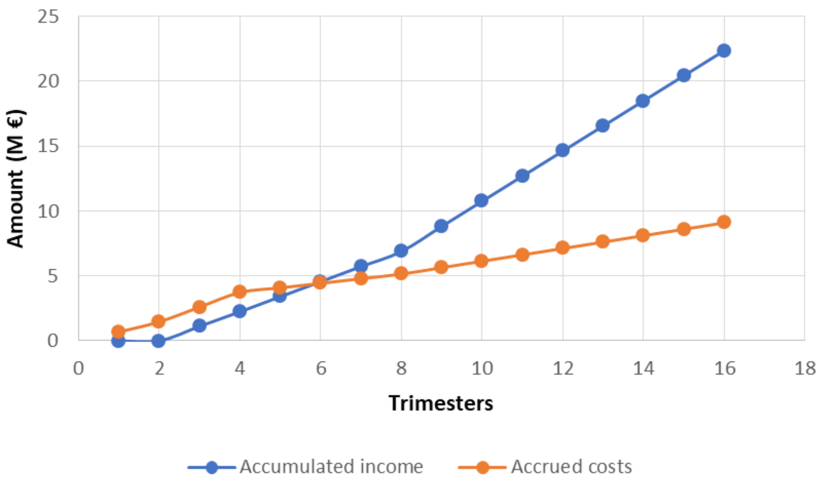

Figure 3: Variation of the accumulated income and accrued costs throughout the trimesters

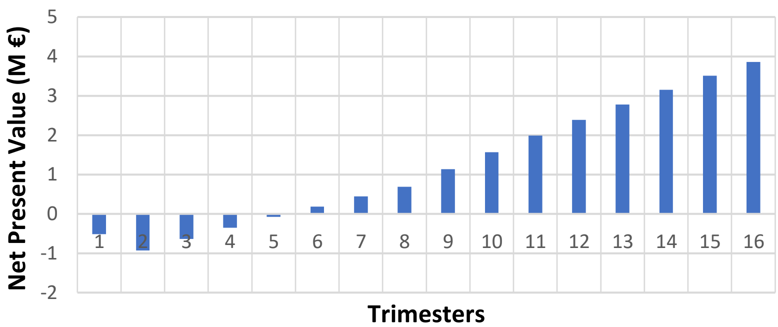

Figure 4: Variation of the Net Present Value throughout the trimesters

5. Conclusions

Portugal is a country with significant production of kiwifruit, particularly of the species *Actinidia Arguta.* As a result of pruning, about 73.8 tons of leaves and branches are discarded in nature or even incinerated every year, which is not environmentally sustainable. In order to avoid such impacts and, considering the advantageous properties of these residues, a product was designed to satisfy the needs of the market while contributing to a circular economy model.

Both kiwifruit branches and leaves are rich in certain phenolic compounds that have interesting properties such as antioxidant, anti-inflammatory and antibacterial effects. In order to develop a product, it was necessary to follow the Chemical Product Design procedure. First, brainstorming of ideas was performed based on the needs of the market. Then, the best idea was chosen from a selection matrix. The chosen product was an anti-ageing facial cream since kiwifruit branches and leaves have compounds that provide interesting skincare properties. Finally, it was defined how the product should be manufactured and how it should be presented to the market.

Some extraction methods were analysed, and the one that showed more advantages was the hydrodistillation process, as it would not require an additional step to purify the extract and its yield of extraction was deemed satisfactory. A formulation for the facial cream was then created, considering it would be a cold cream and the use of natural ingredients with low impacts on the consumer's health and the environment was prioritized. After making these decisions, it was necessary to scale up the production of the facial cream from laboratory to industrial scale and choose the appropriate equipment for this process. The production line was divided into two sections: the first section would require equipment to dry, mill, store, extract the phenolic compounds and filter the extract; the second section would require equipment for the production of the emulsion and then for subsequent packaging and labeling.

An economic analysis was then performed to evaluate if this business proposal would be economically viable. To this end, the costs associated with the warehouse rent, transportation of the kiwifruit residues, purchase of equipment, energy consumption, cream formulation and packaging, employee salaries, sales and marketing and the R&D department were calculated. Thereby, it was verified that by the sixth trimester, the business would witness a payback time, considering that all creams produced per year would be sold. Moreover, the NPV would become positive in the sixth trimester, the initial investment for this business would be €930 thousand and the IRR was estimated at 32.3%.

In conclusion, the proposed product satisfied the aim of this work which was to propose a circular economy business and the creation of a value-added product that could take advantage of the beneficial properties of the compounds present in kiwifruit residues.

In the future, studies would have to be made in order to verify the stability and effectiveness of the facial cream; analyses should be conducted to determine the exact quantity of phenolic compounds present in the kiwifruit residues and a more in-depth economic analysis should be performed to obtain a more realistic scenario regarding the profits of the proposed business.

References

Almeida, D., D. Pinto, J. Santos, A. F. Vinha, J. Palmeira, H. N. Ferreira, F. Rodrigues, and M. B. P. P. Oliveira. 2018. "Hardy kiwifruit leaves (Actinidia arguta): An extraordinary source of value-added compounds for food industry". *Food Chemistry* 259: 113-21. https://doi.org/10.1016/j.foodchem.2018.03.113.

Barreca, D., D. Trombetta, A. Smeriglio, G. Mandalari, O. Romeo, M. R. Felice, G. Gattuso, and S. M. Nabavi. 2021. "Food flavonols: Nutraceuticals with complex health benefits and functionalities". *Trends in Food Science and Technology* 117: 194-204. https://doi.org/10.1016/j.tifs.2021.03.030.

Basile, A., M. L. Vuotto, U. Violante, S. Sorbo, G. Martone, and R. Castaldo-Cobianchi. 1997. "Antibacterial activity in Actinidia chinensis, Feijoa sellowiana and Aberia caffra". *International Journal of Antimicrobial Agents* 8, no. 3: 199-203. https://doi.org/10.1016/S0924-8579(97)00376-2.

Burnett-Boothroyd, S. C., and B. J. McCarthy. 2011. "Antimicrobial treatments of textiles for hygiene and infection control applications: an industrial perspective". In *Textiles for Hygiene and Infection Control*, edited by B. J. McCarthy, 196-209. Woodhead Publishing.

Bush, L. M., and M. T. Vazquez-Pertejo. 2020. "Pseudomonas e infecções relacionadas". *Manual MDS*. https://www.msdmanuals.com/pt-pt/profissional/doencas-infecciosas/bacilos-gram-negativos/pseudomonas-e-infeccoes-relacionadas.

CaixaBank Research. 2019. *Portugal's agriculture sector: still dual, but promising*. https://www.caixabankresearch.com/en/sector-analysis/agrifood/portugals-agriculture-sector-still-dual-promising.

Chamorro, F., M. Carpena, M. Fraga-Corral, J. Echave, M. S. Riaz Rajoka, F. J. Barba, H. Cao, J. Xiao, M. A. Prieto, and J. Simal-Gandara. 2022. "Valorization of kiwi agricultural waste and industry by-products by recovering bioactive compounds and applications as food additives: A circular economy model". *Food Chemistry* 370: Article number 131315. https://doi.org/10.1016/j.foodchem.2021.131315.

Cherney, K. 2019. "How humectants keep hair and skin moisturized". HealthLine Media. https://www.healthline.com/health/humectant.

Cirino, E. 2018. "Is borax toxic?". HealthLine Media. https://www.healthline.com/health/is-borax-safe.

Cizmarova, B., B. Hubkova, B. Bolerazska, M. Marekova, and A. Birkova. 2020. "Caffeic acid: A brief overview of its presence, metabolism, and bioactivity". *Bioactive Compounds in Health and Disease* 3, no. 4: 74-81. https://doi.org/10.31989/bchd.v3i4.692.

Creto, A. R. S. 2018. "O potencial nacional para a produção de biocombustíveis a partir de resíduos agroindustriais". Master's thesis, Faculty of Sciences, University of Lisbon. https://repositorio.ul.pt/handle/10451/35264.

Cussler, E. L., and G. D. Moggridge. 2011. *Chemical Product Design*. 2nd ed. Cambridge Series in Chemical Engineering. Cambridge: Cambridge University Press. https://doi.org/10.1017/CBO9781139035132.

Dickinson, E. 2009. "Hydrocolloids and emulsion stability". In *Handbook of Hydrocolloids (Second Edition)*, edited by G. O. Phillips and P. A. Williams, 23-49. Woodhead Publishing. https://doi.org/10.1533/9781845695873.23.

Diniz, C. G. 2018. "Infecções de pele e de tecidos moles". Powerpoint slides from Bacteriologia, Universidade Federal de Juiz Fora. Accessed December 2021. https://www.ufjf.br/microbiologia/files/2013/05/Infeccoes-de-pele-e-tecidos-moles-claudio-2018.pdf.

Dore, E. 2019. "Como calcular custo de transporte de cargas na prática?". *Maplink* (blog). August 22, 2019. Updated October 4, 2021. https://maplink.global/blog/como-calcular-custo-transporte-carga/.

EPA (Environmental Protection Agency). 2021. "Safer chemical ingredients list". Updated August 11, 2022. https://www.epa.gov/saferchoice/safer-ingredients#searchList.

European Commission. 2015. "Commission implementing decision (EU) 2015/1213 of 22 July 2015 authorising extension of uses of flavonoids from Glycyrrhiza glabra L. as a novel food ingredient under Regulation (EC) No 258/97 of the European Parliament and of the Council". *Official Journal of the European Union*. http://data.europa.eu/eli/dec_impl/2015/1213/oj.

Fortis Consulting, Atos Innovation Consulting, Lda. 2018. *Minho Export - Capacitar para Internacionalizar: Estudos de caso*. In.Cubo - Incubadora de Iniciativas Empresariais Inovadoras. https://fortis.pt/estudos/.

Frothingham, S. 2019. "Is glycerin good for your face and skin?". HealthLine Media. https://www.healthline.com/health/glycerin-for-face#glycerin-benefits.

Gan, R.-Y., C.-L. Chan, Q.-Q. Yang, H.-B. Li, D. Zhang, Y.-Y. Ge, A. Gunaratne, J. Ge, and H. Corke. 2019. "Bioactive compounds and beneficial functions of sprouted grains". In *Sprouted Grains*, edited by H. Feng, B. Nemzer and J. W. DeVries, 191-246. AACC International Press. https://doi.org/10.1016/B978-0-12-811525-1.00009-9.

Guthrie, S. 2019. "Phenoxyethanol in skin care: A natural preservative?". https://theodermaskincare.com/blogs/news/phenoxyethanol-in-skin-care-a-natural-preservative-theoderma.

Jung, H. A., J. C. Park, H. Y. Chung, J. Kim, and J. S. Choi. 1999. "Antioxidant flavonoids and chlorogenic acid from the leaves of Eriobotrya japonica". *Archives of Pharmacal Research* 22, no. 2: 213-18. https://doi.org/10.1007/BF02976549.

Khan, M. H., F. Victor, B. Rao, and N. S. Sadick. 2010. "Treatment of cellulite. Part II. Advances and controversies". *Journal of the American Academy of Dermatology* 62, no. 3: 373-84. https://doi.org/10.1016/j.jaad.2009.10.041.

Kim, J., and E. Choe. 2017. "Improvement of the lipid oxidative stability of soybean oil-inwater emulsion by addition of daraesoon (shoot of Actinidia arguta) and samnamul (shoot of Aruncus dioicus) extract". *Food Science and Biotechnology* 26, no. 1: 113-19. https://doi.org/10.1007/s10068-017-0015-4.

Lebreux, F. 2017. "Preservative deep dive: Parabens and their alternatives". https://knowledge.ulprospector.com/6776/pcc-preservative-deep-dive-parabens-alternatives/.

Lin, M. T., and M. F. Beal. 2003. "The oxidative damage theory of aging". *Clinical Neuroscience Research* 2, no. 5-6: 305-15. https://doi.org/10.1016/S1566-2772(03)00007-0.

Mapoung, S., W. Semmarath, P. Arjsri, S. Umsumarng, K. Srisawad, P. Thippraphan, S. Yodkeeree, and P. Limtrakul. 2021. "Determination of phenolic content, antioxidant activity, and tyrosinase inhibitory effects of functional cosmetic creams available on the Thailand market". *Plants* 10, no. 7: Article number 1383. https://doi.org/10.3390/plants10071383.

Marketing Agrícola. 2019. "Produção e comercialização de kiwi". https://marketingagricola.pt/producao-e-comercializacao-de-kiwi/.

Mohiuddin, A. K. 2019. "Skin care creams: Formulation and use". *Dermatology Clinics & Research* 5, no. 1: 238-71.

Navarro-Orcajada, S., A. Matencio, C. Vicente-Herrero, F. García-Carmona, and J. M. López-Nicolás. 2021. "Study of the fluorescence and interaction between cyclodextrins and neochlorogenic acid, in comparison with chlorogenic acid". *Scientific Reports* 11, no. 1: Article number 3275. https://doi.org/10.1038/s41598-021-82915-9.

Neto, A. S. da S., L. M. S. Silva, and B. Melo Neto. 2020. "Use of coconut oil in the production of cosmetics: A bibliographic review". *Research, Society and Development* 9, no. 11: e75491110397. https://doi.org/10.33448/rsd-v9i11.10397.

NHS (National Health Service). n.d. "Emollients". Updated September 14, 2020. https://www.nhs.uk/conditions/emollients/.

Pedroja, C. 2018. "Is Phenoxyethanol in Cosmetics Safe?". HealthLine Media. https://www.healthline.com/health/phenoxyethanol.

PharmaEducation. 2022. "Cold cream: Uses, formulation, preparation, tests". https://pharmaeducation.net/cold-cream-uses/.

Pinto, D., C. Delerue-Matos, and F. Rodrigues. 2020. "Bioactivity, phytochemical profile and pro-healthy properties of Actinidia arguta: A review". *Food Research International* 136. https://doi.org/10.1016/j.foodres.2020.109449.

Pordata. 2020. "População residente do sexo feminino, média anual: total e por grupo etário". Accessed December 2021. https://www.pordata.pt/Portugal/Populacao+residente+do+sexo+feminino++media+anual+total+e+por+grupo+etario-11.

Puracy. n.d. "Glyceryl oleate". Accessed December 2021. https://puracy.com/blogs/ingredients/glyceryl-oleate.

Sanz, V., L. López-Hortas, M. D. Torres, and H. Domínguez. 2021. "Trends in kiwifruit and byproducts valorization". *Trends in Food Science and Technology* 107: 401-14. https://doi.org/10.1016/j.tifs.2020.11.010.

Silva, A. M., P. C. Costa, C. Delerue-Matos, P. Latocha, and F. Rodrigues. 2021. "Extraordinary composition of Actinidia arguta by-products as skin ingredients: A new challenge for cosmetic and medical skincare industries". *Trends in Food Science and Technology* 116: 842-53. https://doi.org/10.1016/j.tifs.2021.08.031.

Spectrum Chemical Mfg Corp. n.d. "Stiffening agent excipients". Accessed January 2022. https://www.spectrumchemical.com/chemical/stiffening-agent-excipients.

Speight, J. G. 2020. "Pharmaceuticals". In *Handbook of Industrial Hydrocarbon Processes (Second Edition)*, 553-95. Boston: Gulf Professional Publishing. https://doi.org/10.1016/B978-0-12-809923-0.00013-8.

WebMD Medical Team. 2020. "Beeswax - Uses, side effects, and more". https://www.webmd.com/vitamins/ai/ingredientmono-305/beeswax.

Acknowledgments

This work was developed under the scope of the course unit of Product Engineering of the Master in Chemical Engineering at the Faculty of Engineering of the University of Porto during the 1st semester of the 2021/2022 academic year. This work was also financially supported by: LA/P/0045/2020 (ALiCE), UIDB/00511/2020 and UIDP/5011/2020 (LEPABE), UIDB/50020/2020 and UIDP/5020/2020 (LSRE-LCM), funded by national funds through FCT/MCTES (PIDDAC).

The authors of this work would like to acknowledge the help and guidance provided by Professors Yaidelin Manrique, Margarida Brito, Ricardo Santos, and Cláudia Silva. They also wish to thank the Associate Laboratory of Chemical Engineering ALiCE and the Associate Laboratory LSRE-LCM.