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Conceptualization and design of natural throat lozenges bearing active components from olive leaf extract

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Abstract

This work presents the conceptualization and design of throat lozenges bearing active components from olive leaf extract as a means of valorizing olive leaves. This novel product is a vegan alternative to conventional lozenges and its natural formulation avoids the adverse effects of amylmetacresol, 2,4-dichlorobenzyl alcohol, and menthol, which are common ingredients of Strepsils® and Halls® lozenges. A reliable and straightforward methodology for the preparation of natural throat lozenges is herein described. Additionally, this product is compatible with the use of other leaf extracts, allowing the expansion and diversification of the production line. The manufacture process was simulated using Aspen Custom Modeler software and the energy required for the production of the lozenges was determined to be 0.28 kWh per kilogram of product. A preliminary economic analysis revealed that the industrial implementation of this product is viable, and the payback time was estimated at 4 years.

1. Introduction

Seasonal respiratory infections (e.g., the flu) are very frequent during wintertime and widespread around the world (Oxford and Leuwer 2011). The main symptoms result from the inflammation of the throat and include local discomfort with a scratchy sensation, swelling, and pain which causes substantial difficulty in swallowing (Oxford and Leuwer 2011).

Throat soreness is a minor ailment, but patients commonly seek advice and treatment for immediate symptomatic relief (Oxford and Leuwer 2011). Despite the fact that treatment with antibiotics reduces the symptoms of some patients with bacterial infections, the duration of this type of illness is short and often does not require medical attention (Weckmann et al. 2017). Due to the global spread of antibiotic resistances, the unrestrained use of antibiotics for such mild conditions is ill advised by medical professionals (Weckmann et al. 2017).

Many over the counter topical treatments to counter throat soreness are available in the market, including throat sprays, gargles, and lozenges (Oxford and Leuwer 2011). Ideally, these treatments should provide a direct targeting of the inflammatory causes, relief pain rapidly, and be effective against different types of infection (Oxford and Leuwer 2011).

Hard throat lozenges are a type of candy-like medication that is designed to dissolve slowly in the mouth, while releasing the active ingredients continuously in a controlled manner (Choursiya and Andheriya 2018). One of the benefits of hard throat lozenges is their convenience, as they can be consumed without any water or other liquids and can be easily carried anywhere (Choursiya and Andheriya 2018).

The golden standard of throat lozenges available in the market is Strepsils® (Oxford and Leuwer 2011). These round-shaped lozenges are very pleasant and flavourful medicinal product, incorporating amylmetacresol (AMC) and 2,4-dichlorobenzyl alcohol (DCBA) pharmaceuticals as active ingredients (Oxford and Leuwer 2011). AMC and DCBA are typically used in combination and act as mild antiseptics and anaesthetics, being able to kill a large variety of viral and bacterial pathogens while providing pain relief (Oxford and Leuwer 2011; Weckmann et al. 2017). Another reference brand in the international lozenge market is Halls®, that mainly produces over-the-counter lozenges with menthol and eucalyptus oil as active ingredients, which are natural ingredients with antimicrobial and anti-inflammatory properties that aid in the relief of throat soreness (Kamatou et al. 2013; Sabo and Knezevic 2019).

Both Strepsils® and Halls® lozenges are effective antiseptics and pain-reliefers but rely on artificial sweeteners and flavours to construct a candy-like medication far more palatable and easier to take than traditional pills or capsules, for both adults and children (Choursiya and Andheriya 2018; Oxford and Leuwer 2011). Additionally, the active substances used in these lozenges have been reported to cause mild adverse effects on occasion, such as headaches and ulceration of the oral cavity for AMC and DCBA, and airway irritation and shortness of breath in the case of menthol (Gavliakova et al. 2013; Weckmann et al. 2017).

In this work, it is provided the conceptualization and design of natural throat lozenges bearing active components from olive leaf extract. This product poses as a natural and vegan alternative to conventional lozenges. The objective is to utilize the beneficial biological properties of olive leaf extract and enhance them with a carbohydrates-based blend of natural ingredients. The absence of AMC, DCBA, and menthol is expected to yield more sensible lozenges by avoiding the adverse effects of these substances.

Olive trees (*Olea europaea*) are a member of the Oleaceae family (Azbar et al. 2004; Selim et al. 2022). These trees yield greasy fruits (olives) that are rich in monounsaturated vegetable oils and polyphenolic compounds with powerful antioxidant and antimicrobial activity (Azbar et al. 2004; Selim et al. 2022). Olives can be utilized in the production of several food, hygiene, and cosmetic products, or as table olives (Azbar et al. 2004; Selim et al. 2022). Nonetheless, they are rarely consumed as a natural fruit due to their extreme bitterness (Azbar et al. 2004; Selim et al. 2022). Olive oil is one of the oldest known vegetable oils and it is commonly utilized in the mediterranean diet (Kapellakis, Tsagarakis, and Crowther 2008; Selim et al. 2022).

In spite of the economical and nutritional benefits of olive oil, vast quantities of byproducts are produced in the cultivation and processing of olives for olive oil manufacturing (Azbar et al. 2004; Herrero et al. 2011; Kapellakis, Tsagarakis, and Crowther 2008; Khelouf et al. 2023; Selim et al. 2022). The byproducts can be recognized as raw materials for their richness of nutrients and bioactive compounds (Berbel and Posadillo 2018; Selim et al. 2022). Several approaches can be employed for the recovery of bioactive compounds from olive oil byproducts as sustainable alternatives to regular waste treatment procedures (Azbar et al. 2004; Berbel and Posadillo 2018; Selim et al. 2022).

The main byproducts of olive oil production are the pruning biomass (leaves and branches), olive pomace (solid phase remaining after the oil extraction), olive cake (olive residues still containing some oil), olive pits or stones, and wastewater (Fernández-Lobato et al. 2021; Kapellakis, Tsagarakis, and Crowther 2008; Selim et al. 2022). Out of these byproducts, the branches and pits are fibrous materials poor in bioactive compounds, the leaves are fibrous but rich in bioactive compounds, the olive pomace is rich in sugars and bioactive compounds, the olive cake is also rich in bioactive compounds although easily oxidised and thus hard to work with, and the wastewater is also rich is bioactive compounds but very hard to process (Azbar et al. 2004; Kapellakis, Tsagarakis, and Crowther 2008; Selim et al. 2022).

Extensive research confirmed the health benefits of olive consumption, encouraging new markets that use olive oil byproducts to meet the health-related needs of consumers (Berbel and Posadillo 2018; Selim et al. 2022). Valuable compounds present in olive pomace and leaves have biological activity (antioxidant, anticancer, anti-inflammatory, antimicrobial, hypoglycemic, hepatoprotective, neuroprotective, cardiovascular protective), making them relevant for application in the food, pharmaceutical, and cosmetic industries (Azbar et al. 2004; Herrero et al. 2011; Kapellakis, Tsagarakis, and Crowther 2008; Selim et al. 2022).

Olive leaves are one of the most important byproducts of olive farming, constituting around 10% of the olive harvest weight and with an estimated 25 kg produced per tree during pruning, resulting in the acquisition several million tons of olive leaves globally every year (Selim et al. 2022). The olive leaf extract is a dark brown liquid with a bitter flavour and a composition rich in polyphenolic compounds that are responsible for the powerful biological properties of the extract (Khelouf et al. 2023; Selim et al. 2022). For this reason, olive leaf extract is considered one of the most valuable byproducts of olive oil production (Selim et al. 2022). Nevertheless, olive leaves can also be used to make tea, which was historically used as a medicine to cure fever and infections in the mediterranean regions (Azbar et al. 2004; Selim et al. 2022).

Olive leaves are rich in bioactive compounds, but the phenolic content may vary accordingly to their geographic origin (Khelouf et al. 2023). Some of the polyphenols that are commonly found in olive leaves are oleuropein (which provides a major contribution to their bitter taste), oleuroside, vesbascoside, ligstroside, catechol and its derivatives (tyrosol and hydroxytyrosol), phenylpropanoids (e.g., sinapic acid, coumaric acid, ferulic acid), and a large variety of flavonoids (rutin, luteolin, quercetin, myricetin, apigenin, diosmetin), among others (Herrero et al. 2011; Khelouf et al. 2023; Selim et al. 2022).

The mediterranean regions are the centre of olive production and its associated businesses, accounting for over 90% of the worldwide production (Berbel and Posadillo 2018; Kapellakis, Tsagarakis, and Crowther 2008; Khelouf et al. 2023; Selim et al. 2022). In the years 2020 and 2021, Spain was responsible for 46.1% of the global production of olive oil, whereas Portugal produced 3.3% (Selim et al. 2022), concentrating half of the global production of olive oil in the Iberian Peninsula. On average, Spain has produced 1.4 million tons of olive oil per year consistently over the last decade, with the south region of Andalusia producing over 80% of the total Spanish production (Fernández-Lobato et al. 2021). The large production of olive oil in these regions ensures the availability of valuable byproducts, allowing industries to benefit from the readily supply of raw materials.

2. Chemical product design

This study was developed in the context of the Product Engineering course at the Faculty of Engineering of the University of Porto, to pursuit the creation of a new product that can satisfy precise necessities.

Chemical product design (CPD) is very important in the chemical industry since it allows the development of products (pure chemicals or blends) that exhibit desired and specific properties (Moggridge and Cussler 2000; Zhang et al. 2020). Traditionally, chemical products were developed through heuristic and experimental approaches (Zhang et al. 2020). However, this kind of approaches are not practical nor economic (Zhang et al. 2020). As such, rational CPD methods have a major influence on the quality and profit of the products (Moggridge and Cussler 2000; Zhang et al. 2020).

The methodology used in this work is organized in four subsequent steps that aim to optimize the thought process of the CPD (Moggridge and Cussler 2000). The first step consists in the identification of the customers' needs to be satisfied by the chemical product (i.e., business opportunities) (Moggridge and Cussler 2000). Then, several ideas of products with potential to fulfill the customers' needs are laid out and discussed (Moggridge and Cussler 2000). Afterwards, the ideas are organized in different categories and selected according to relevant criteria (Moggridge and Cussler 2000). At last, the main characteristics and composition of the product are defined, as well as a possible manufacturing process (Moggridge and Cussler 2000).

2.1. Needs

This project takes into consideration the principles of sustainable development as societal needs, in addition to customers' needs. Therefore, a contribution to circular economy and waste management is envisioned by taking advantage of the beneficial properties of the byproducts of olive oil production, namely olive pomace or leaves. The identified customers' needs are that of vegetable food and dietetic products rich in healthy nutrients and bioactive compounds to improve health and well-being.

2.2. Ideas and selection

Initially, 24 distinct ideas for products were laid out and discussed (brainstorming). Firstly, the ideas were analyzed and discriminated based on novelty, the maturity of the technology required for production, and the value added to the raw materials. Moreover, pharmaceutical products were excluded from the selection process due to the intense and extensive legislation processes required for their validation, production, and commercialization. Afterwards, a total of 7 ideas were selected for further evaluation.

The selected ideas were then classified as business to consumer (B2C, 4 ideas) or business to business (B2B, 3 ideas), as follows: throat lozenges bearing active components from olive leaf extract (**a**, B2C), toothpaste bearing active components from olive leaf extract (**b**, B2C), olive pomace flour (**c**, B2C), insect repellents bearing active components from olive leaf extract (**d**, B2C), antimicrobial packages bearing active components from olive leaf extract (**e**, B2B), pure bioactive compounds extracted from olive pomace or leaves (**f**, B2B), and olive leaf extracts as conservatives for canned and bottled food (**g**, B2B).

Having identified the most promising ideas, a selection matrix (**Table 1**) was built using six criteria, each having a different ponderation that was attributed subjectively in accordance with their perceived relevance and importance. Points were then attributed for each idea and criterion using a numerical system that varied between 1 and 10. The top three ideas were selected based on the final score obtained (pondered average of the points attributed to each idea), in which the best ideas are the ones with the highest score.

The selection criteria applied, as well as their respective ponderation, are presented as follows: novelty (**I**, 20%), maturity of the technology required for production (**II**, 20%), value added to the raw materials (**III**, 20%), relative quantity of materials required for production and their abundance (**IV**, 20%), risk assessment (**V**, 10%), and environmental impact (**VI**, 10%).

Ideas	**Criteria**						**Total Score**
	I (20%)	**II (20%)**	**III (20%)**	**IV (20%)**	**V (10%)**	**VI (10%)**	
a	8	10	10	10	8	8	9.2
b	6	10	10	10	8	6	8.6
c	5	8	8	3	6	6	6.0
d	8	6	10	7	10	8	8.0
e	10	8	9	10	6	10	9.0
f	7	10	10	8	10	10	9.0
g	6	8	8	7	6	10	7.4

Table 1: Selection matrix presenting the points attributed to the criteria and the total score of each idea.

Upon analysis of the matrix, the top three ideas were identified, them being the ideas **a** (throat lozenges bearing active components from olive leaf extract), **e** (antimicrobial packages bearing active components from olive leaf extract), and **f** (pure bioactive compounds extracted from olive pomace or leaves).

For each of these products, customers' needs were outlined as to define different levels of characteristics that the products are required to have or that make them more appealing. The characteristics are classified as useful, desirable, or essential, and their incorporation is fundamental for the development of successful and competitive products.

In the case of throat lozenges (idea **a**), they should have a pleasant taste (essential), possess anti-inflammatory and antiseptic properties (desirable), and be easy to carry and take anywhere (useful). For the antimicrobial packages (idea **e**), they should be able to preserve food against microorganisms (essential), be a replacement for synthetic food preservatives (desirable), and be practical to assemble (useful). Lastly, the pure bioactive compounds (idea **f**) should be relevant for industrial or research purposes (essential), have high purity (desirable), and be an alternative to arduous synthetic compounds (useful).

After careful appraisal of the ideas, the idea **a** (throat lozenges bearing active components from olive leaf extract) was chosen as the most promising product for appearing to be the most feasible and marketable option overall.

3. Product

The throat lozenges herein described are a unique vegan product made exclusively with natural ingredients infused with active components from olive leaf extract. The product is moulded into round-shaped candy with a pale yellowish colour. Each lozenge weights about 3.5 grams and is composed by glucose as corn syrup (40%), granulated sugar (20%), powdered sugar (20%), water (15%), olive leaf extract (2.4%), pectin (1.6%), citric acid (0.5%), and potassium citrate (0.5%). Citric acid (E330) and potassium citrate (E332) are used as natural additives to regulate the acidity of the product and also as flavouring and preserving agents. A schematic representation of the product, as well as the list of ingredients, can be observed in **Figure 1**.

The sugary matrix of the lozenges masks the bitter flavour of the olive leaves extract. No artificial sweeteners are used in this product, due to their controversial health and metabolic effects (Chattopadhyay, Raychaudhuri, and Chakraborty 2014). In addition, this product contains a small amount of pectin, a water-soluble fibre with a mild sweet taste that acts as an oral demulcent (Roman-Benn et al. 2023). Pectin acquires mucilaginous properties when in contact with water, forming a soothing protective film over mucous membranes (e.g., throat, intestine) that relieves minor pain and inflammation and promotes heath in the digestive tract (Roman-Benn et al. 2023). Moreover, pectin is commonly extracted from citrus fruit peels, thus further contributing to the circular economy and sustainable waste management (Roman-Benn et al. 2023).

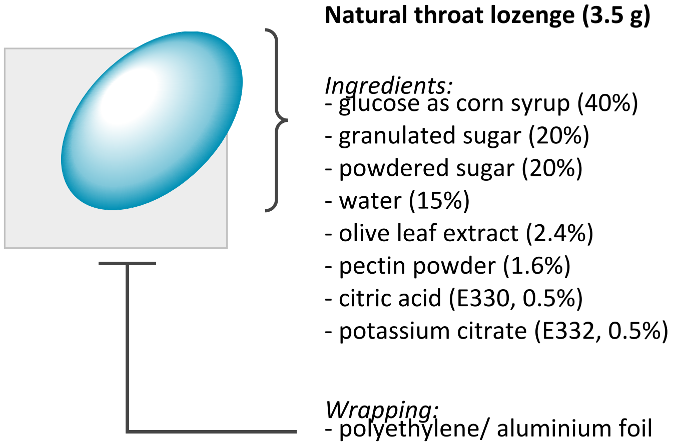

Figure 1: Schematic representation of the product and listing of the ingredients.

4. Manufacture

The manufacture of the throat lozenges (**Figure 2**) is divided into two stages. First, the raw materials (olive leaves), which are purchased from olive farms and associated businesses, need to be properly processed and stored. Then, in the second stage, the olive leaves' bioactive components are extracted and incorporated into the lozenge blend.

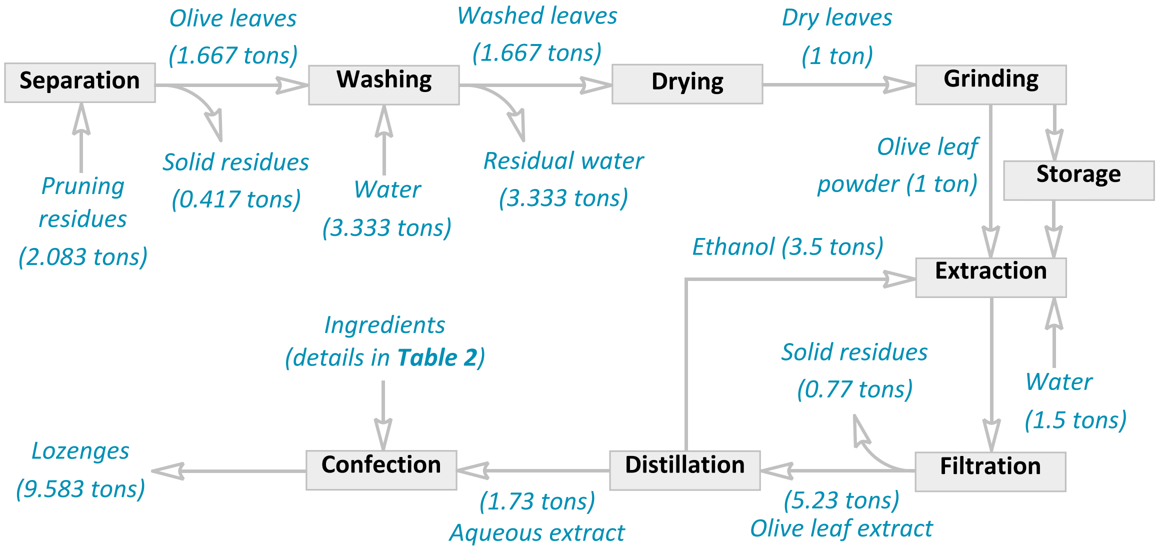

Figure 2: Schematic representation of the manufacture process discerning the main activities and the amount of materials used (relative to 1 ton of dry olive leaves).

The first step of the olive leaves processing consists in the separation of the leaves from other pruning residues (e.g., branches, stones) using a leaf separator. Afterwards, the leaves need to be washed with tap water (approximately double the mass of the olive leaves) to remove dust particles and chemical contaminants, affording clean leaves and wastewater. The clean leaves are then dehydrated in a drying oven at 70 °C for 50 minutes to concentrate the organic matter and extend their storage lifespan (Ahmad-Qasem et al. 2013; Andrejč et al. 2022). Lastly, the dry leaves are grinded into a powder. The leaf powder can be readily used in the next stage on production or stored in appropriate containers without the need to refrigerate, i.e., in sealed stainless steel containers in a dry area without direct exposure to the sun light (Andrejč et al. 2022). The estimated weight loss of olive leaves upon drying is around 40% (Ahmad-Qasem et al. 2013). Therefore, the drying process should reduce the mass of olive leaves to 60% of the initial value (Ahmad-Qasem et al. 2013).

It is important to note that the pruning and harvesting of the olive trees are seasonal procedures. As such, the storage of the olive leaves as powder ensures that the raw material is available all year round. The drying process is required to increase the storage lifespan of the leaves since the enzymatic activity and growth of microorganisms are halted in dehydrated environments, while the leaf grinding improves the subsequent extraction process (stage two of manufacture) and also decreases the space required for the storage of the leaves by allowing a more compact packing (Andrejč et al. 2022). Moreover, these steps only yield the intended product along with water vapor, thus not producing any kind of waste.

The second stage initiates with the extraction of active components from the olive leaf powder. The extraction methodology used is maceration (solid-liquid extraction) and the optimal conditions for this process were defined with basis on the literature (Cifá et al. 2018; Papageorgiou et al. 2022). The conditions were chosen with the aim of improving the recovery of biological components, that is secondary metabolites such as phenolic compounds and flavonoids, but also various minerals and sugars or derivatives (Cifá et al. 2018; Papageorgiou et al. 2022). In particular, the extraction is performed using a 70% ethanol and 30% water solution during 2 hours at 40 °C. The proportion of dry matter to solvent is 1 to 5, that is, for each ton of leaf powder used the process requires 5 tons of the 70% ethanol solution (Cifá et al. 2018; Papageorgiou et al. 2022). After extraction, the solid matter is separated from the liquid by filtration and is latter disposed of as organic residues.

Then, the ethanol is distilled by fractional distillation and recovered to be reused in the manufacturing process. This way, an aqueous solution bearing olive leaf extract is obtained. It is estimated that the total weight of this solution should be around 1.73 tons for each ton of leaf powder processed.

The aqueous solution of leaf extract can be directly used in the confection of the throat lozenge. The extraction yields approximately 23% extract from dry weight (Papageorgiou et al. 2022). This means that 1 ton of leaf powder should afford 0.23 tons of extract in 1.5 tons of water, which is enough extract to produce 9.583 tons of lozenge. In terms of water content, the production of 9.583 tons of lozenge only requires 1.438 tons of water content in the final product. However, the cooking process mandates the use of a larger amount of water to mix all the ingredients, which ends up evaporating until while the blend thickens. As such, to the 1.73 tons of aqueous extract, another 8 tons of water should be added.

Afterwards, the remainder of the ingredients should be added to the aqueous extract, starting with granulated sugar, followed by glucose as corn syrup, and finish with the finest powders (citric acid, potassium citrate, pectin powder and powdered sugar). During this process, the solution should be brought to a boil at 100 °C (Bayline et al. 2018). The boiling point should increase as the water content decreases from evaporation (Bayline et al. 2018). The confection should end when the temperature reaches 115 °C, meaning the water content is 15% (Bayline et al. 2018). However, care is necessary not to caramelize or burn the sugar, which is reported to occur at temperatures above 170 °C (Bayline et al. 2018). At last, the blend is moulded into a round shape at room temperature. The decrease in temperature causes a transition to a glass state (Bayline et al. 2018). As such, the lozenges acquire a tough and glossy texture. To finalize the process, the lozenges are individually wrapped in branded polyethylene/ aluminium foil and packaged in sets of 100 grams. In total, around 0.115 tons of polyethylene/ aluminium foil should be necessary to package 1 ton of lozenges (considering both individual wrappers and 100 grams packages).

There is a large variety of affordable industrial grade equipment available in the market that allows the efficient processing and storage of the olive leaves, as well as the confection of the throat lozenges. It is possible to process several tons of olive leaves yearly depending on the scale of the equipment that is used.

Overall, the production of 1 ton of lozenges requires 0.173 tons of fresh olive leaves (equivalent to 0.104 tons of dry leaves), about 1.3 tons of water, 0.4 tons of glucose as corn syrup, 0.2 tons of granulated sugar, 0.2 tons of powdered sugar, 0.016 tons of pectin powder, 0.005 tons of citric acid, 0.005 tons of potassium citrate, and 0.115 tons of polyethylene/ aluminium foil. This data can be consulted in **Table 2**.

Material	Amount (tons)
Water (total)	1.3
Glucose as corn syrup	0.4
Granulated sugar	0.2
Powdered sugar	0.2
Fresh olive leaves	0.173
(dry olive leaves equivalent)	(0.104)
Polyethylene/ aluminium foil	0.115
Pectin powder	0.016
Citric acid (E330)	0.005
Potassium citrate (E332)	0.005

Table 2: Amount of each material required for the production of 1 ton of lozenges.

Nevertheless, since this work is solely focused of the conceptualization and design of a novel product, no assessments have been made regarding the alleged benefits and safety of the product. As such, the toxicological evaluation of the olive leaf extract and the final product are mandatory. And, if needed, the extract/pectin ratio can be altered to promote the best biological outcomes.

5. Process simulation

The manufacture process was implemented using Aspen Custom Modeler software to provide a comprehensive view of the process. Aspen Custom Modeler enables a high degree of freedom of the complexity of the projected model. The objective of this model is to simulate the mass and energy balances of the manufacture process, thereby determining the flow of materials and other utilities and the energy required to produce the throat lozenges. A schematic representation of the manufacture process can be consulted in **Figure 3**.

The manufacture was simulated as a continuous process and any pumping operation was neglected for the energy input, that is, the electrical energy required to operate the pumps was neglected. However, the process should be a batch process for the second stage of the process (extraction, distillation and recovery of ethanol, and cooking).

Considering an annual production of 30 tons of lozenges and a total of 4000 working hours (14 hours, 285 days, 2 daily shifts) the resulting mass flow is 7.5 kilograms per hour. And the raw material pruning residues with a mass flow of 0.96 kilograms per hour. The employment expenses are included in the Supporting Information data sheet.

The branches of the pruning residues are separated from the leaves in a separator. It is assumed that the raw material contains of 80% leaves and that the separation process is ideal. To calculate the required energy the technical data of an ALVAN BLANCH brushing leaf separator were used leading to an energy input of 0.018 kWh per kilogram of leaves.

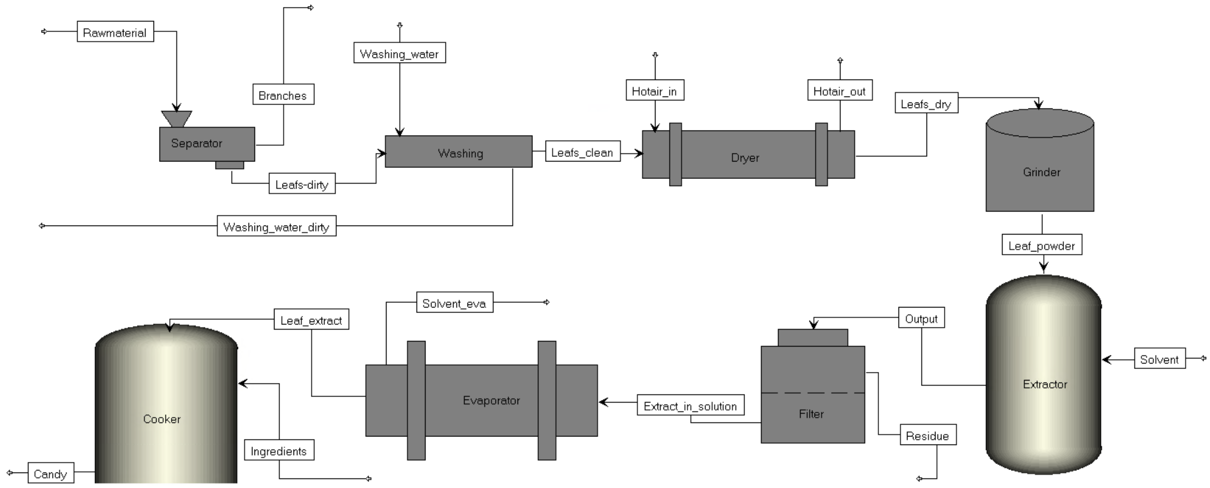

Figure 3: Schematic representation of the manufacture process discerning the main activities and (by)products – built using Aspen Custom Modeler software.

Afterwards, the leaves are washed using approximately 2 litres of tap water per each kilogram of leaves. The amount of dirt and other residues was neglected in the simulation as well as the energy input for the washing operation. Then, the leaves are dried using hot air, which was modelled as an ideal gas. To prevent condensation of water vapor in the oven, the double of the minimum hot air mass flow required is used for the simulation. The required energy input is 0.0016 kWh per kilogram of dry leaves.

The dried leaves are converted into a powder by grinding. The grinder is assumed to have similar technical data to a BRABENDER® quadrumat senior, requiring 0.1375 kWh per kilogram of leaf powder. An extraction is then performed under the conditions previously mentioned, and the energy to maintain the temperature of the extractor is neglected, only considering the energy required for the initial heating. The content of the extractor was modelled as an ideal liquid. An average and constant heat capacity is used to compute an energy input of 0.0125 kWh per kilogram of solution. After the extraction, the grinded olive leaves' suspension is removed by filtration. The energy required for this step was neglected.

Following, the ethanol is removed using an evaporator. Despite being described in the project, the recovery of the ethanol was not considered in the simulation. To calculate the energy input, the enthalpy of evaporation of water and ethanol are used. The required energy for this procedure is 0.33 kWh per kilogram of solution.

For the candy confection, the same assumptions as the extraction were made. The heat capacity of the candy used was consulted at *The Engineering ToolBox* website and is 3.89 kilojoule per kilogram per °C, leading to an energy input of 0.097 kWh per kilogram of candy.

To sum up, the energy input for the whole manufacture process is 0.28 kWh per kilogram of candy.

6. Economic analysis

An economic analysis was performed to assess the viability of producing and commercializing the novel throat lozenges. The analysis begins with the plan of the activities to be performed during the first six years of business, which is presented as a Gantt's chart in **Figure 4**.

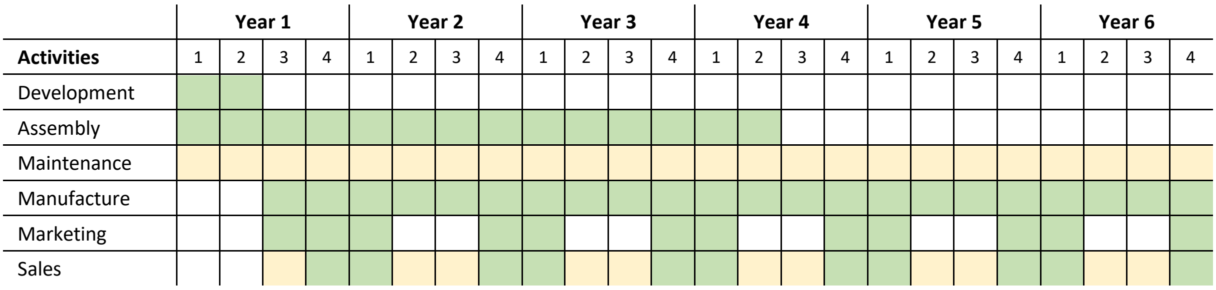

Figure 4: Gantt's chart of planned activities – green cells represent periods of intense activity, while yellow cells represent periods of lesser activity.

The first activity is the development and consists of the fine tuning of the production process at industrial scale with the proper infrastructure and in preparation of the manufacture. It also includes test runs of the equipment as the lines are assembled. Both the development and the assembly of the equipment and infrastructures initiate at the beginning of the project. Although only two trimesters are planned for the development, while the assembly extends for fourteen trimesters to ensure the growth of production until it reaches the desired volume. Maintenance is planned to occur continuously during the whole project.

The manufacture is planned to start at the end of the development and extend for the remainder of the project, reaching its peak after the assembly is completed. The marketing campaigns initiate simultaneously with the manufacture but are planned in discontinuous and regular phases, with more intensity in the trimesters with higher predictable sales volume. As for the sales, they also initiate after the development. The periods predicted to provide higher sales volume are the winter seasons, which comprise two trimesters each year.

The product is to be sold in packages of 100 grams with an average price of 30 euros per kilogram, equivalent to 3 euros per package. The price stipulated is well above the regular market value, which rounds 20 euros per kilogram, and sets the product as premium grade. The alleged quality and health benefits of the vegan throat lozenges made 100% from natural ingredients and with no expected adverse effects is sure to be a determinant factor to justify its price. The product is idealized to be commercialized in Europe and eastern Asia.

Due to the abundance of olive leaves, it should be possible to produce over 4 million tons of product annually, but the project herein described operates at a much smaller scale. In the first year of the project, there are only two trimesters of manufacture that were set to a production of 120000 packages (12 tons of product). In the following three years, a stable 8% increase in production is estimated each year until 2027 when the maximum production level of 302331 packages per year is reached (approximately 30 tons of product annually). The production is meant to be constant throughout the project, with four trimesters of production every year. The storage system will ensure that the production remains constant even in the seasons where the uptake of olive leaves is lower.

The estimated cost of the materials (olive leaves, other ingredients, wrappers) for manufacture is approximately 3000 euros per ton of product and the revenue provided by the sale of 1 ton of throat lozenges is 30000 euros. The cost was determined based on market prices of food-grade ingredients for industrial use and the cost of olive leaves was estimated at 1 euro per kilogram based on the literature (Baptista et al. 2022). As such, the cost of materials for production is 10% of the sales.

Further expansion of production is possible due to the large availability of olive leaves in the Iberian Peninsula. Nevertheless, the manufacture and composition of the lozenges is compatible with different types of leaves and extracts, such as eucalyptus, lemon, rosemary, and others, that can either be used individually or in combination with each other. This strategy could allow the throat lozenges manufacture to expand beyond what is herein assessed and provide a larger variety of lozenge flavours to suit the preferences of customers.

The financial analysis of the project was performed using a tool for evaluation of investment projects provided by IAPMEI – *Agência para a Competitividade e Inovação*. All of the expenses can be consulted in the Supporting Information data sheet. It was assumed that all sales are performed immediately after production. In **Figure 5**, it can be consulted the difference between the operational costs and sales revenue for the first six years of business.

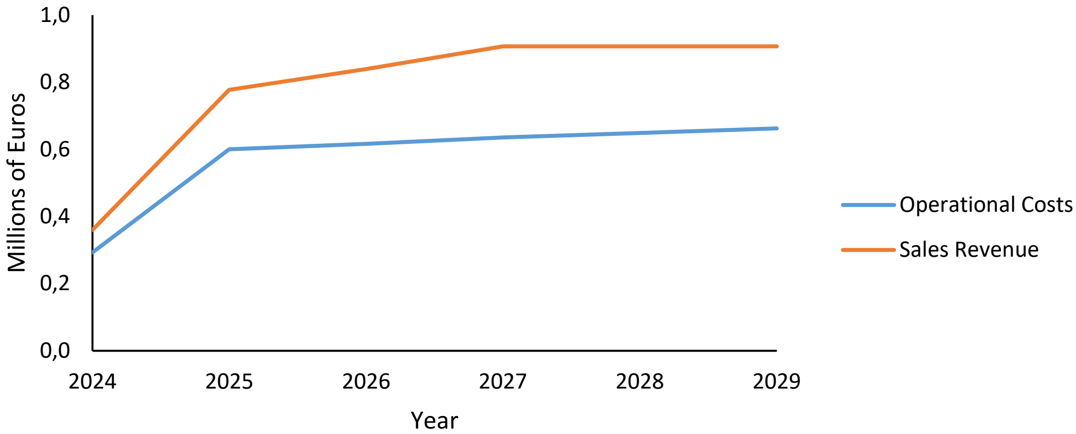

Figure 5: Graphical representation of the operational costs and sales revenue for the first six years of business.

In terms of manufacture operations, the expected sales overgrow the operational costs, building a reasonable profit margin when the maximum production is achieved in 2027. However, this chart does not reflect the return of investment. As such, the operational cash flow was determined for each year and can be consulted in **Figure 6**.

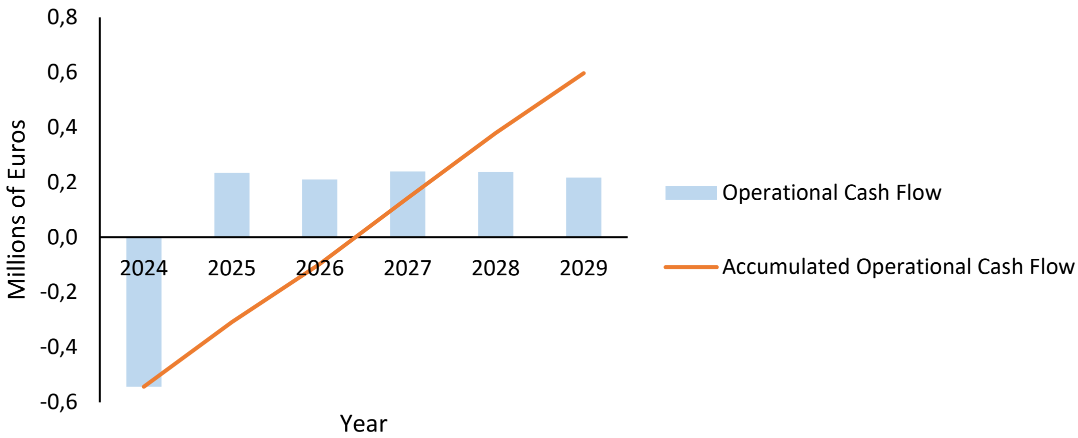

Figure 6: Graphical representation of the yearly and accumulated operational cash flow for the first six years of business.

It can be observed in **Figure 6** that the operational cash flow increases rapidly in the second year of business due to the significant increase in production that occurs. This is due to the fact that in 2024 there are only six months of production, while in the remainder of the years, 12 months are envisioned. There is a steady growth of the sales revenue until 2027, after which the production remains constantly at maximum capacity. It has also been determined that the payback period for this project is 4 years, that is, it is the expected time that the business requires to recover its investment costs. The payback period was determined by the forecast of the cash flow using the weighted average capital cost (3.85 years) and by the forecast of the cash flow using the capital asset pricing model (4.09 years). According to both methods, the expected payback period is approximately 4 years.

7. Conclusions

In this work, it is provided the conceptualization and design of natural throat lozenges bearing active components from olive leaf extract. This project is meant to valorise olive leaves, a major byproduct of the olive oil industry that has corroborated medicinal properties. Additionally, the lozenges also contain pectin as a secondary active ingredient, which is obtained from the valorisation fruit peels and promotes the health of the intestinal tract.

This product is a vegan alternative to conventional lozenges and is composed solely of natural ingredients. The absence of AMC, DCBA, menthol, and artificial sweeteners or flavours should bear more sensible lozenges that avoid the adverse effects of these substances.

A detailed manufacture plan is provided for the preparation of these novel lozenges starting with pruning residues as raw materials. The manufacture plan was built to minimize waste and optimize the rentability of the olive leaves through careful processing and storage. However, the preparation of the lozenges has yet to be performed, and the effectiveness of the scale-up process for commercialization has not been confirmed. It is estimated that up to 40 tons of lozenges can be produced annually due to the abundance of the raw materials. The economic analysis provided useful insight on the business potential of this project and the payback period was determined to be 4 years, accounting with a maximum production of 30 tons of lozenges from the year 2027 forward. Further expansion of production is possible due to the large availability of olive leaves. However, the manufacture and composition of the lozenges is also compatible with other types of leaves and extracts, which could allow the providence of a larger variety of lozenge flavours.

The successful preparation of the throat lozenges herein conceptualized would certainly prove significant for the food industry as the search for natural and vegan products in the market increases, posing as a competitive alternative to conventional lozenges. However, more research is needed to ensure the feasibility, quality, and safety of this product, namely, the validation of the production procedures, a complete chemical characterization of the extract and the final product, the toxicological and biological evaluation of the olive leaf extract and the final product, and the determination of the product's shelf life are required.

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