



Ana Maria Forjaz Morão Dias Coimbra

Licenciatura Bioquímica

A Go- to- Market Strategy for Green Extraction and Impregnation

Dissertação para obtenção do Grau de Mestre em Biotecnologia

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Abstract

The aim of this thesis is to suggest a Go-to-Market Strategy for the Green Extraction and Impregnation (GEI) technology, which uses supercritical carbon dioxide based processes.

The first step of this project consisted in studying deeply all the technical features of the GEI technology and the second in listing several possible applications for the GEI and compare them in terms of innovation and market need. The analysis lead us to conclude that the application of GEI in dental prosthesis is very promising, from the point of view of the market. Two possible applications were considered: i) GEI as a way to remove contaminants after the preparation of the dental prostheses - extraction of methyl methacrylate, which is responsible for allergies, from the acrylic, a material used in dental prostheses - and ii) the use of GEI for the impregnation of dental prostheses with therapeutic active principles. We developed a commercial device under the name GEI dental and submitted it to experimental tests, which allowed the validation of the above mentioned applications. Despite the patent expiration of the GEI technology, there is the possibility to patent a prototype of the GEI dental device.

The business model presupposes the creation of a start-up, Sustainable Solutions (SS) constituted by a team of highly qualified specialists in different areas. It will be responsible for assembling the product and for the sale of the GEI dental to dental laboratories. The target market are the large European laboratories, which are interested in innovation and with a solid financial situation. Portugal is the entry market. About 20% of Portugal's population is dental prostheses users and the number of Portuguese companies, which might be interested in buying the product, is more than 300.

The product should be positioned as a high quality new device, which, at same time, meets a need of orthodontia specialists, adds value to dental prostheses and belongs to a new generation of environmentally friendly products.

The necessary investment to create SS is about 200 000 €.

Keywords: Supercritical carbon dioxide; Green Extraction and Impregnation (GEI); Methyl methacrylate; Dental prosthesis; Dental laboratories; Environmentally friendly products.

Resumo

O objetivo deste trabalho é sugerir uma “Go-to-Market Strategy” para a tecnologia Green Extraction and Impregnation (GEI), que utiliza dióxido de carbono supercrítico.

A primeira etapa deste projecto consistiu em estudar as características técnicas da tecnologia, e segundo passo foi listar várias possíveis aplicações para o GEI e compará-las em termos de inovação e necessidade de mercado. Esta análise levou-nos a concluir que a aplicação da GEI a próteses dentárias é muito promissora do ponto de vista do mercado. Duas possíveis aplicações foram consideradas: i) GEI como via de remoção de contaminantes após a preparação das próteses dentárias-extracção do metil metacrilato, que é responsável por alergias, do acrílico, um material usado em próteses dentárias- e ii) o uso do GEI para a impregnação de próteses dentárias com princípios activos terapêuticos. Um dispositivo comercial designado GEI dental foi desenvolvido e submetido a testes experimentais, que permitiram a validação das aplicações mencionadas acima. Apesar da patente da tecnologia GEI ter expirado, existe a possibilidade de patentear um protótipo do equipamento GEI dental.

O modelo de negócios pressupõe a criação de uma “start-up”, Sustainable Solutions (SS), constituída por uma equipa de especialistas altamente qualificados em diferentes áreas, que será responsável pela montagem e pela venda do GEI dental aos laboratórios de prótese dentária. O mercado alvo são os grandes laboratórios europeus, que estão interessados em inovação e com uma situação financeira sólida. Portugal é o mercado de entrada. Cerca de 20% da população de Portugal usa prótese dentária e o número de empresas portuguesas, que podem vir a estar interessados em comprar o produto, é superior a 300.

O produto deve ser posicionado como um novo dispositivo de alta qualidade, que, ao mesmo tempo, atende a uma necessidade dos especialistas em ortodontia, adiciona valor às próteses dentárias e pertence a uma nova geração de produtos amigos do ambiente.

O investimento necessário para criar a SS é de cerca 200 000€.

Palavras Chave: Dióxido de Carbono supercrítico; Green Extraction and Impregnation (GEI); Metil metacrilato; Próteses dentárias; Laboratórios dentários; Produtos amigos do ambiente.

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List of acronyms and abbreviations

ADDE	Association of Dental Dealers in Europe
BPR	Back Pressure Regulator
B2B	Business to Business
CAGR	Compound annual growth rates
CO ₂	Carbon dioxide
DDSs	Drug Delivery Systems
EMA	European Medicines Agency
EU	European Union
FDA	Food Drug Administrator
FIDE	International Federation of Dentists
GAS	Gas Anti-Solvent
GEI	Green Extraction and Impregnation
GEI dental	Green Extraction and Impregnation dental
GRAS	“Generally recognized as safe”
HPLC	High Performance Liquid Chromatography
IBET	Instituto de Biología Experimental e Tecnológica
IEC	International Electrotechnical Commission
INE	Instituto Nacional de Estadística
ISO	International Organization for Standardization
MMA	Methyl methacrylate
NPV	Net Present Value
PGSS	Particles from Gas Saturated Solutions
PMMA	Poly (methyl methacrylate)
P _c	Critical Pressure
RESS	Rapid Expansion of Supercritical Solutions
SAS	Supercritical Anti-Solvent
SCF	Supercritical Fluid
scCO ₂	Supercritical carbon dioxide

SFE	Supercritical Fluid Extraction
SS	Sustainable Solution
SSI	Supercritical Solvent Impregnation
Tc	Critical Temperature
US	United States

1. Executive Summary

The thesis project “A Go-to-Market Strategy for Green Extraction and Impregnation” was a research line focused on technical innovation and the challenge of taking technologies from the laboratory to the market. The aim of this project was to develop a strategic line to implement a new product in the market with success.

The Green Extraction and Impregnation (GEI) technology comprises the use of the supercritical carbon dioxide (scCO₂) as extract and impregnation solvent. The technical features of the GEI technology are presented in Chapter 2.

After a brainstorming exercise about the possible applications of GEI technology, the choice of the most promising application to develop a deep study was based on two criteria: innovation and market need. The application of GEI in dental laboratories seemed very promising. Two possible applications were considered the most interesting, from the point of view of the market: i) GEI as a way to remove contaminants after the preparation of the dental prostheses - extraction of methyl methacrylate (MMA), which is responsible for allergies, from the acrylic, a material used in dental prostheses, - and ii) the use of GEI for the impregnation of dental prostheses with therapeutic active principles.

The dental prosthesis problems, in which GEI dental may be a solution, are discussed in the Chapter 3.

The product's concept was tested and validated through experimental tests performed in Laboratory Nutraceutal and Delivery, IBET. We developed a commercial device under the name GEI dental and submitted it to experimental tests, which allowed the validation of the above mentioned applications. In this thesis, GEI dental's components are discussed, which include a preliminary design to a future prototype. The description of experimental tests and the preliminary design to a future prototype are presented in Chapter 4.

In Chapter 5 an outlook on potential market was developed focusing on the European dental market. Portugal will be the test market for the implementation of the GEI dental in the market, so the case of Portugal (number of dental laboratories and dental prosthesis users) was studied in detail. Besides consulting surveys and articles about dental sector, interviews were conducted with dental professionals, such as orthodontists, hygienic oral technicians and dental prosthesis technicians. In addition, two online questionnaires about dental prostheses were performed, one directed to the Portuguese population and the other questionnaire was answered by the Portuguese orthodontists. These tools were essential to study and perceive the dental industry.

The potential market was divided into different segments - innovation, size, geographical localization and financial soundness. The target market are the European large dental laboratories which present high interest in innovation and with a solid financial situation.

The product should be positioned as a high quality new device for improving the dental prostheses, which, at same time, meets a need of the orthodontia, adds value to dental prostheses and belongs to a new generation of environmentally friendly products.

Due to the nonexistence of a similar device in dental industry to GEI dental, the competitor analyses were made comparing the features attributed to the acrylic by GEI to the materials most commonly used in orthodontia (acrylic, ceramics and metals).

The market analysis also includes an overview about the dental supply chain and distribution channel, which is based on the current dental European industry.

The concerns about intellectual property and the certifications required by the regulatory authorities are important points to take into account when an idea is turned into a salable product. Chapter 6 is dedicated to discussing these points. Despite the patent expiration of the GEI technology, there is the possibility to patent a prototype of the GEI dental device. Concerning regulation issues, the approval of entities will be necessary, such as the Infarmed, as well as obtaining CE marking.

The business model is discussed in Chapter 7. The business model adopted presupposes the creation of a new start-up, Sustainable Solution (SS) constituted by a team of highly qualified specialists in different areas. The company will be responsible for assembling the device and commercializing it (directly to the customer or through distribution companies).

In Chapter 8 the Marketing Plan to SS is presented which includes the company's vision, mission, objectives, SWOT analyses and the Marketing Mix. The Marketing Mix comprises the Product (principal attributes of GEI dental, SS Logotype and Slogan), Promotion (direct contact and the use of new online platforms), Place (direct distribution in Portugal and distribution through distribution companies to the international market) and Price (mainly based on the costs related to materials that constitute the GEI dental).

Chapter 9 is dedicated to discussing the product's development (the main steps to convert the initial idea into a final product) and the operations plan (equipment and geographical localization).

The SS team, constituted by a team of highly qualified specialists in different areas, is discussed in Chapter 10.

The Chapter 11 is dedicated to the implementation, which comprises the financial plan and the critical risks. The financial plan was supported, whenever it is possible, in real values. The sales were based on estimated values, the most similar as possible to reality, in order to present a financial analysis the most reliable as possible. The critical risks appointed are the high price of components of the product which is reflected on the product's price, idea being recent and there are still several points to be developed and improved, and the possibility of the sales projections fail.

2. Technology

2.1. Description of the technology

A patented technology entitled “Impregnation method of biocompatible polymeric matrices with application in food, cosmetic and/or pharmaceutical industry using a clean technology” is the chosen technology to develop a Technology-Market Transfer Plan. The technology has emerged in the frame of a previous project about contact lenses impregnation, which patent ended up to expire. This project was initiated by PhD. Catarina Duarte and by a Master student, as a result of a Master project about active principles impregnation.

Nowadays, one of the most important global concerns is the waste produced and accumulated from chemical process. There is a growing interest about environmentally friendly technologies, mainly in sensitive issues such as health care and food [1]. Therefore, natural biodegradable materials and cleaner technologies, namely Supercritical Fluid (SCF) based processes, are of growing interest worldwide [2].

The present invention consists of an impregnation method of polymeric matrices using a cleaner technology. In particular, this invention reports to an impregnation method of one or a group of antioxidants or bio active additives in biocompatible polymers that can be either biodegradable or not, by using a Green Extraction and Impregnation (GEI) technology, specifically through the use of compressed fluids. Then technical concepts about SCF based processes applied to polymeric matrices will be exposed in this section.

2.1.1. Supercritical fluids

A pure substance can exist in a solid, liquid or gas phase, which are evidently defined by phase boundaries. The pressure-temperature phase diagram of a pure substance presents a triple point, in which three different phases can be distinguished, solid, liquid, and gas (Figure 2.1). The point on the boundary curve is called the critical point and when the temperature and pressure increase above the critical point, liquid and gas phases coexist [3]. Compressed fluid is a fluid, at high pressures and that can still exist in a liquid state. [2]. A supercritical fluid is a fluid at a pressure and temperature above its thermodynamic critical point.

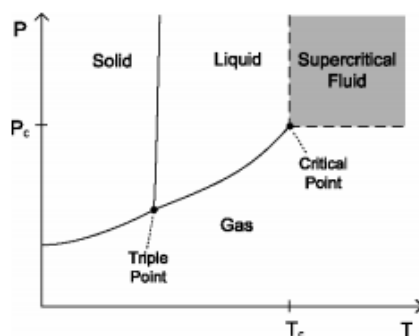


Figure 2.1. Pressure-temperature phase diagram of a pure substance [3].

The supercritical fluids have some similar properties to those of liquids, like their density, and other properties similar to gases, such as low viscosities and large diffusivities [4]. Therefore, this may mean that a supercritical fluid can easily penetrate inside a solid matrix (including polymeric matrices) and extract or precipitate substances from/into them. This can be done through a simple manipulation of pressure or temperature near the critical point, which offers the equivalent of using different solvents, consequently providing selective extraction properties or impregnation capacity. Supercritical fluids usually have excellent plasticizers properties and are able to swell polymeric matrices, thus promoting the diffusion of substances into them and, consequently, allowing the processes of extraction and impregnation to be carried out [2]. The fluids under supercritical media are gases at room temperature and atmospheric pressure. As a result, it is quickly dissipated and can be easily recovered after the process, upon release of pressure leaving no toxic solvent residue behind [5-6].

2.1.2. Carbon dioxide

Supercritical carbon dioxide (scCO₂) “generally recognized as safe” (GRAS) solvent is the most commonly used SCF, because it is abundant and cheap, non-flammable and relatively inert. Besides, it is soluble in aqueous media and it can plasticize and decrease the glass transition temperature of most polymeric materials. Furthermore, it presents low operation temperatures involved in supercritical processes ($T_c = 31^\circ\text{C}$ and $P_c = 73$ bar). This allows working at relatively low temperatures, suitable for thermally labile substances [7-10]. Due to the fact that scCO₂ processes operate at mild conditions, active principals (biologically active or medical ingredients) can be incorporated into polymer substrates without interfering with the performance of the substance [10-11]. The carbon dioxide (CO₂) is used to both dissolve the drug and swell the polymer, thus enabling rapid impregnation. Since it replaces organic solvents, supercritical fluid impregnation is presented as a green process [12]. Compared to the common liquid plasticizers, scCO₂ penetrates deeper into dense polymeric networks and can be easily removed after processing with a simple depressurization [12-18]. The advantages shown by Supercritical Solvent Impregnation (SSI) and Supercritical Fluid Extraction (SFE) using scCO₂ for the development of drug impregnated polymeric materials can be used as Drug Delivery Systems (DDSs) for many biomedical applications [19-20]. In addition, the SSI allows the homogeneous impregnation of polymeric matrices with drugs in a relatively short time. When properly

employed, it does not alter nor damages polymeric matrices physical, chemical, and mechanical properties. Depth of penetration and drug load can be easily controlled by the regulation of several operational conditions [21-24]. The scCO₂ can be also used with the purpose of extracting undesired residual solvents, oligomers or monomers, or any other additives present in polymeric materials [12, 9-10, 14-16, 22, 25].

2.1.3. Polymers

In the last years the behavior of different classes of polymers in supercritical media has been extensively studied. An area that has become a source of interest in polymer science, mainly polymer synthesis and processing, is the manipulation of the physical properties and their selective control [18, 26-27]. Some examples of areas where polymers are usually used are the pharmaceutical and medicinal industries, or even in food packaging [13]. There are many polymeric matrices that might be impregnated by this method and several have already been tested. The polymeric matrices can be polymers, copolymers or mixtures of both. The polymeric matrices can be impregnated with an additive or a group of them, according to the purpose it was intended. The additives should be soluble, in certain degree, in a fluid or in a mixture of fluids and co-solvents, to be used as a plasticizing agent for the polymeric matrix [2]. The CO₂ is susceptible of being dissolved by majority of polymers at high pressure, reaching a concentration up to 10–30 wt% (causing a significant swelling of the polymer). The diffusion rate and penetration of solute molecules into the polymeric matrix is improved by an increase in the free volume of CO₂-swollen polymers [12]. The impregnation results from a balance of interactions between supercritical fluids, drugs and polymers. There is absorption or a physicochemical attachment of drug molecules to the polymeric matrix. So, the CO₂ acts as a temporary plasticizer to assist the adsorption of additives into polymers, as it promotes an increase in the linear dimension of the polymer, thus improving the kinetics of absorption of the diffusing substances [28-30]. The solvent power of the scCO₂ can be abruptly decreased by decompression. As a consequence, the active compound previously dissolved in the supercritical fluid precipitates, as well as it occurs the contraction of the carrier matrix [31].

2.1.4 Conventional impregnation processes

The conventional impregnation processes consists of the immersion of a polymeric matrix into a solution, which can be aqueous or organic, where an additive was previously dissolved. However, this method presents disadvantages, such as the use of toxic organic solvents, the majority of polymers cannot be impregnated by this method due to the additives' low diffusivity which results in low rates of impregnation. In addition, the increase of temperature to enhance the process can degrade the polymer. Also on a posterior stage the system should be submitted to high temperatures to remove the organic solvents, which can also degrade the active principle [1,32-33]. Other common impregnation method is performed during the polymerization reaction. The additives are mixed initially with the monomers and solvents. During polymerization the polymers are formed and the additive is physically

retained inside of the solid polymeric matrix [2]. Due to the specific properties of supercritical fluids described above, they are usually good solvents. Properties as superficial tension being barely zero, low viscosity and high diffusivity, allows that the supercritical impregnation process may be faster and more efficient than the conventional processes [32-34]. Therefore, the present green technology has characteristics that can replace traditional methods of impregnation, such as the immersion of a polymeric matrix into a solution or reactions of polymerization, thereby avoiding typical disadvantages associated with each one of the traditional methods [2].

2.1.5. Summary of the main advantages of GEI

Below it is summarized the main advantages of GEI:

- This method allows an easy control of the amount to be impregnated and the depth of additive impregnation, and in the end the additive is homogeneously dispersed in the polymeric matrix.
- Another very important issue is that the impregnation is made without leaving any residues of dangerous solvent in the polymeric matrix. The recovery of the final product is a simple and easy process, only made by expansion of the system. In the end, the products are recovered dry and free of solvent, without the need of any additional steps of drying/evaporation (and without the energetic costs and the time consuming of an operation associated with this process).
- Generally the polymeric matrix mechanic and physic properties are not changed or damaged, and their constituents, such as additives, polymers and copolymer are also protected from degradation.

The advantages mentioned above are very important in products to human consumption or contact, because the residual presence of organic, dangerous and/or toxic solvents is rigorously established and controlled by international organizations and safety rules. Thus, it is necessary to ensure the complete removal and absence of such substances without exposing the substances to high temperatures, which may eventually lead to thermal degradation [2].

2.2. Possible applications

Below it is discussed several possible applications for the GEI technology.

Food industry

a) The antioxidants are emerging as prophylactic and therapeutic agents. An impregnated gum with an antioxidant could be an option for this technology. The gum would have edible nanoparticles, such as xanthan gum impregnated with antioxidant, so that when it is chewed up the nanoparticles are released. The principles of the new drug delivery systems are a useful tool to significantly improve the performance of the antioxidants. Consequently, this method is a useful alternative to allow a good performance of the antioxidants.

b) An important issue is the conditions of storage of the food in order to avoid the food deterioration. This technology, applied to packages, will enable the increasing of the lifetime, or the quality of products, that are stored. The inside of the package would be coated by a polymeric film of polyethylene and it is impregnated with an antimicrobial agent or an antioxidant which is freed along time. The storage of fresh fish, in order to prevent a quick degradation and the transport of fruit for long distances, are examples of possible situations where this package would be useful.

Pharmaceutical industry

c) Bad breath is a problem which gives social constrains. A buccoadhesive for a good breath can be a solution to the presented problem. In order to prolong the drug residence time in the oral cavity, buccoadhesive drug delivery systems have been created. The referred system is made of mucoadhesive materials which swell upon contact with aqueous media and outer viscous layers [35]. An example of a natural polymer which can be used as a bioadhesive material is chitosan [36]. This technology can allow the impregnation of the mentioned polymer with an antimicrobial solution with a fresh fragrance. The buccoadhesive would be put in the customer's mouth and the solution would be freed throughout the day. So, this technology would allow a healthy mouth and a good breath during the day.

d) The present technology can be very useful in systems of drug delivery that have been developed recently. There is an increasing study and development of drug delivery systems that only releases its payload in specific conditions such as pH or temperature, a feature that could be particularly useful for targeted delivery of cancer treatments. Most of these systems use nanoparticles as drug carriers, so this technology is an option to impregnate the nanoparticles without unnecessary losses and without leaving any dangerous residue of solvent.

e) The mite is the main agent of allergies in a house. Another possible application of this technology is the fabrication of mattress covers anti - dust mites. The mattress cover would have a polymeric matrix impregnated with a solution to kill dust mites. The use of this technology would allow the impregnation of a large amount of the solution in the mattress cover, in order to the effect against the dust mites to last a long period of time. At the same time, the polymeric matrix would be decomposed and the solution would be freed. There are some examples of substances that have been used to kill the dust mites, such as benzyl benzoate, natamycin and others.

f) The infestation by insects, such as ticks and fleas is a major problem for most animals. Besides giving a great discomfort to the animal due to the itching, they are also responsible for the transmission of infectious diseases. An insecticidal collar is a possible device to protect animals from fleas and ticks. The technology would allow the impregnation of the referred collars with enough pesticide to continually kill fleas for a long period of time. The pesticide must be safe and non-toxic because, on the one hand, it has a prolonged skin contact, and on the other hand, the animal may chew the collar. There are various examples of the polymers, which can be form the casing of the collar, such as cellulose plastics, and natural elastomers, such as the rubber. The present green technology allows the collar to have a considerable amount of insecticidal without using high temperatures, unpleasant odors free, and waste of insecticidal.

g) Insect bites are a common problem in many parts of the world and are responsible for the spread of diseases like typhoid or malaria. While in Portugal the diseases transmission by insect bites is very rare, it is uncomfortable and many people are very sensitive to insect bites. Accordingly, an insecticidal bracelet, or a belt similar to the application described above, is another possible application, but for humans. This bracelet would be very useful for people which go to places where the mosquitos are a problem because it is a practical way to keep the mosquitos away. Comparing to traditional methods, such as repellent spray or a head net, the bracelet is more practical and resistant method.

h) A polymer impregnated with an additive can be used in adhesives that will help embed the drug into the skin and provide a controlled drug delivery. The adhesives can be used, for example, by injured athletes during an important competition, in the treatment of burns or back pain. The system consists of two polymer layers: an external, which prevents the loss of the drug and controls the release and the other layer is an adhesive layer responsible for establishing the system into the skin. The polymer matrix impregnated with the drug is sandwiched between the two polymer layers. An example of a polymer most commonly used, in preparing the matrix systems, is cross-linked poly(ethylene glycol) [37].

i) One of the most common complaints of new parents is the difficulty to give medication to their babies. This technology would allow parents to give the medication as their babies suck the pacifier in a simple and practical way. The pacifier would be composed of two parts, a disposable part

containing the drug to be administered and another which would serve as support to the disposable part. The disposable part would be a silicone nipple or a biodegradable polymer so, when the baby sucked, the drug would be freed through the pores of the polymer. The medicine pacifier would be a solution when the parents do not know how to give the medicine to their baby or when the baby is very agitated.

j) Another feature related to the application mentioned above is the difficulty to give medication to pets. Associating the technology to the pet's toy, the toy may be an option for the taking of the medicine. The object would have the flavor or smell of food, so when the pet bit the object the drug would be freed and enter in the organism of the pet. The pet's toy would be composed of successive layers impregnated with medication and coated with a polymeric matrix, such as hydroxypropylcellulose, in order to the medication to be released.

k) The impregnation method can be used in medical devices, such as catheters, the material of which is impregnated with one or more antimicrobial agents to inhibit the growth of bacterial and fungal organisms. There are already various methods that have previously been employed to coat the surface of medical devices with an antibiotic. The medical device may have a polymeric surface such as polyethylene, impregnated with antimicrobial agent, such as rifampin without traces of solvent and with sufficient antimicrobial agent in order to last longer [38].

l) MMA has the potential to provoke inflammation, irritation, and allergic response of the oral mucosa. Acrylic resins used in dental prostheses contain MMA as residual monomer which is released when the patient uses the prostheses. Therefore, residual monomer is undesired as it is capable of producing both stomatitis and an angular cheilitis [39].

The technology can be applied to the dental prostheses, specifically to the acrylic. The application comprises the utilization of supercritical fluids, specifically ScCO_2 , to extract undesired residual monomer, the MMA and to impregnate a polymeric matrix of poly (methyl methacrylate) (PMMA) with an active substance. The referred polymer is used in dental prostheses either removable or fixed. A dental prosthesis that dispenses a useful substance, such as an anti-inflammatory or a solution for a good breath, is going to be released in the oral cavity during the time the patient is using the dental prosthesis.

Agriculture industry

m) One area where this technology may also be useful is agriculture. Nowadays there are already procedures to decrease organic contaminants in groundwater, soils and sediments by using biodegradable polymer-coated nanoparticles into the contaminated area. The method is about introducing polymer coated nanoparticles which would show an enhanced ability to migrate through the soil and would provide a proper treatment in the contaminated area [40]. A biodegradable polymer,

such as alginate biopolymer or ethyl cellulose, could be impregnated by this green technology with substances which react with the contaminants in situ to eliminate them, breaking them down into less harmful substances.

Cosmetic industry

n) A growing concern of hygiene products is the smell. A diaper with a good smell could be made using this green technology by the coating of a polymeric layer, such as a natural rubber, impregnated with a fragrance. When the customer use the diaper, the polymer would be destroyed and the fragrance would be released. Despite being an option for both baby and adult diapers, probably the second option would have greater acceptance.

o) A cleaning cloth embedded with a detergent or disinfectant can be another option for applying this technology. The cleaning cloth would have a system where nanoparticles carry the detergent or disinfectant. When the customer presses the cleaning cloth, the nanoparticles would be released and broken up, and finally the detergent or disinfectant would be freed. Therefore, two products would be joining into one and in addition the proposed cleaning cloth would be more hygienic compared to the commonly cleaning cloths. This product might have a particularly acceptance in restoration, in which the hygiene rules are increasingly restricted.

p) Sponge impregnated with bath gel is a practical and simple option. Usually, the user purchases separately the sponge and the bath gel. The proposed product would allow the customer to get both products buying a single one. The environmental concern will already be present not only on the technology used but also on the product if all the material used would be biodegradable. The sponge would have a polymeric matrix, such as the alginate impregnated with bath gel.

q) A similar idea is a sponge impregnated with self-tanning. The product would be very useful since not only would allow customers to buy two products into one, but also cleaner and more practical one. The product would answer a customer's need because it would allow a more homogeneous application of the self-tanning. The sponge would have a system where mesoporous poly (acrylic acid) nanoparticles carries self-tanning and, when the customer used the sponge, the nanoparticles would be released and broken, and finally the self-tanning would be freed.

r) An insole that frees a pleasant smell would be another possible application for this technology. The insole would be composed by multiple layers to provide proper support and cushioning to the foot. The superior layer would be a polymer of cellulose impregnated with a perfume or a deodorant. The present technology would allow the impregnation of a considerable amount of perfume, so the fragrance of the insole would be kept over a long period of time. The insole could be used in tennis, shoes or in skates.

The advantages and disadvantages of the different applications of the technology are summarized in Table 2.1.

Table 2.1. A summary of the advantages and disadvantages of technology applications.

Applications	Advantages	Disadvantages
Food Industry		
Antioxidant gum	<ul style="list-style-type: none"> • The product is new • Environmentally friendly • It is a healthier product • Antioxidants are in great demand • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • Possibly there are other simpler and cheaper ways to impregnate a gum with antioxidant
Package	<ul style="list-style-type: none"> • It keeps the properties of the food inside the package for a longer time, which is very interesting in the case of fresh food (fish, fruits, etc.). • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • The use of a drug in food may not be well accepted by the general public
Pharmaceutical Industry		
Buccoadhesive to good breath	<ul style="list-style-type: none"> • The product is new • It allows to maintain the mouth healthy and fresh all day • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • There are other products with the same purposes and probably cheaper
Drug delivery systems	<ul style="list-style-type: none"> • It avoids unnecessary losses • It does not leave any dangerous residue of solvent • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • There are already other methods of impregnation
Anti-dust mites mattress cover	<ul style="list-style-type: none"> • Long term • More efficient • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • There are another products with same purpose
Insecticidal collar	<ul style="list-style-type: none"> • Long term • Resistant • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • Product already widely marketed
Insecticidal bracelet	<ul style="list-style-type: none"> • Practical • Simple • Long term • Resistant • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive
Adhesives	<ul style="list-style-type: none"> • Long term • Resistant • Practical • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • Adhesive may not adhere well to all types of skin

Applications	Advantages	Disadvantages
Medical pacifier	<ul style="list-style-type: none"> • The product is new • Easy way to administer medication to babies • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • Disposable
Pet toy	<ul style="list-style-type: none"> • The product is new • Easy way to administer medication to pets • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • Difficulty controlling the amount of drug that the animal takes
Medical advices	<ul style="list-style-type: none"> • Avoid the contamination of medical advices • Avoid the need to remove and replace of medical advices • The effectiveness of the coating lasts longer • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • There are others method of impregnation which are already used
Dental prosthesis that dispense medicine	<ul style="list-style-type: none"> • The product is new • Solution for many people who have a problem with dentures • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive
Agriculture Industry		
Agriculture	<ul style="list-style-type: none"> • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • There already are other methods of impregnation
Cosmetic Industry		
Smelly diaper	<ul style="list-style-type: none"> • Allows comfort and relaxation for diapers' users 	<ul style="list-style-type: none"> • It is expensive • Disposable
Cleaning cloth with detergent	<ul style="list-style-type: none"> • Two products into one • Cleaner than a simple cloth • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • A simple cloth is already used a long time
Sponge bath shower	<ul style="list-style-type: none"> • Two products into one • Practical to use and carry • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive
Sponge self-tanning	<ul style="list-style-type: none"> • Two products into one • Practical to use and carry • Allows a uniform and clean application (without stains) • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive
Insoles	<ul style="list-style-type: none"> • The product is new • Solution for the bad smell of the feet • Environmentally friendly 	<ul style="list-style-type: none"> • It is expensive • Disposable

Each application for the GEI technology was analyzed in terms of innovation and market need (Table 2.2). The innovation refers to the use of a new idea or method that was not thought of yet, but it does not imply that it is useful. The market need refers to the need and utility about a specific service or product to the customer.

Table 2.2. Analysis of market need and Innovation of technology applications.

	Innovation	No Innovation
Market need	c); i); l); r); s)	d)
No Market need	j)	a); b); e); f); g); h); k); m);n); o); p); q)

Note: a) Antioxidant gum; b)Package; c) Buccoadhesive to good breath; d) Drug delivery systems; e) Anti-dust mites mattress cover; f) Insecticidal collar; g) Insecticidal bracelet; h) Adhesives; i) Medical pacifier; j) Pet toy; k) Medical advices; l) Dental prosthesis that dispense medicine; m) Agriculture; n) Smelly diaper; o) Cleaning cloth with detergent; p) Sponge bath shower; q) Sponge bath shower; r)Sponge self-tanning; s) Insoles

As it is possible to observe in Table 2.2, most applications were classified as having no innovations and no market need. These products are the less interesting to develop a more earnest study. The quadrant related to the axes market need and no innovation has only one application- drug delivery systems. There is an increasing study and development of drug delivery systems and this technology can be a good choice to be applied in these systems but there are already many other viable choices. Such as the previous quadrant, the quadrant referred to the axes no market need and innovation has only one application- the pet toy. Despite this applications being innovative, apparently they do not have a market. The applications in quadrant related to the axes market need and innovation are the most interesting to be developed. The Buccoadhesive to good breath is an interesting product but the present technology is expensive, so probably it will not be the best product for the development of a study. Even though the insoles and the self-tanning sponge are interesting products, they can be impregnated with simple and cheap methods because they do not need to be impregnated with a clean technology. The most interesting applications that deserve a more detailed and earnest study are the medical pacifier and the dental prosthesis that dispenses medicine. The medical pacifier and the dental prosthesis that dispenses medicine are innovative products and probably have market need. They both belong to the health sector, which usually has high safety levels associated. In other words, since healthcare deals with people's health, they must be assured not to be exposed to any risk. The high levels of safety are assured by this new technology because it belongs to a new

generation of green technologies. The characteristics that make this technology safe are previously described above.

2.2.1. Market analysis of medical pacifier and dental prostheses that dispense medicine

In this next section the most promising application of the technology is chosen through the comparison of attributes of each application with its competitors.

2.2.1.1. Medical pacifier

There already exists in the market potential competitors of the medical pacifier that have advantageous characteristics (see Performance Map in Appendix 1). Although there is a pacifier that dispenses medicine in European market, in Portugal there is not a pacifier that dispenses medicine. Probably Portugal may be a good option to patent and market this new product. However, by evaluating the pacifiers available in the market (Appendix 1), it is possible to observe that they have more advantageous characteristics than the impregnated pacifier by GEI. The reasons that support the decision not to go any further with the study of this product are listed below:

- a) Since similar products are being commercialized in other European countries, Portugal is a much too small a country to make the product worth the commercialization;
- b) There are pacifiers with the same characteristics available with good prices;
- c) The available pacifiers present a better dosage control of the medicine.

Therefore, due to the given reasons, the study of the medical pacifier will not be explored any further.

2.2.1.2. Dental prosthesis that dispense medicine

The application of the GEI technology to the dental prostheses was called GEI dental. After a research about whether there are similar devices with the identical features of the GEI dental, no device was found in the dental market. The interviews to the dental professionals (Appendix 2) confirmed the previous assumption. Therefore, it was considered that the application of this GEI technology to dental prostheses is a new idea. The dental industry is a rising sector both on technological development and on the profits it involves. Due to the aspects referred above, it is concluded that applying this technology to dental prostheses may be very promising. So, the development of a study about this new product will be followed with great expectation.

3. Market pain: The value proposition of GEI dental

The following Chapter is dedicated to exposing certain problems of dental prostheses, which may be solved by the application of GEI dental to dental prostheses.

The wearing of removable prostheses can be associated to oral diseases, which can be due to microbial colonization of dental plaque, traumatic irritation by the denture or an allergic response to denture materials. Several studies have been reported that about 25% to 30% of complete denture wearers have problems with their dentures [41].

In odontology, biocompatibility is an essential issue. Biocompatibility refers to the context when tissues are in contact with a determined material and it does not manifest any type of toxic, irritant, inflammatory, allergic response, and severe mutagenic or carcinogenic effects [42]. Concluding, it is the ability to remain biologically inert during its functional period [43].

Allergy

The PMMA is the acrylic resin mostly used in dentistry. The material presents several applications, since removal devices, auxiliaries fixed devices, individual impression trays, orthodontic devices, to artificial crowns [44]. Since the 1960's, there have been reports of hipper-sensibility to acrylic resins. In the majority of the cases, it has been associated to the presence of high content of residual monomer, MMA due to incomplete polymerization. The acrylic resins may cause allergic reactions with local manifestations, such as pain, edema, and erythema. Reactions of systemic order may occur, with a higher or lower intensity, including burn feeling, deglutition difficulty, mouth edema and urticarial [45-47]. Furthermore, according to the dental professionals addressed this problem differs from each patient. There are cases in which patients present a high sensibility to the use of acrylic prostheses and so the patient cannot use the dental prosthesis. In addition, an online questionnaire about dental prostheses was made available to the dentists and the sample comprises 20 dentists (see appendix 3). One of the questions was about whether they considered important the extraction of MMA from dental prostheses, and the answers were unanimous, having all the dentists responded "yes". According to professional addressed the demand of the extraction of MMA from dental prosthesis, in order to reduce the cytotoxicity of the acrylic resins, has been increasing.

The undesired residual monomer, the MMA, can be extracted through the GEI dental.

Malodor

Oral malodor, also known as bad breath, is a common complaint among the population. The bad breath is a severe chronic problem that affects personal relationships and quality of life. According to Tonzetich and Ng, bad breath is a common condition found in approximately 50 % of the adult population [48].

The malodor issue also may be fought through the application of GEI dental to dental prostheses.

Infections

Dental prostheses have been associated to candidiasis, which is a fungi infection. According to Arendorf & Walker, the use of dental prosthesis is a factor that favors the presence and development of various *Candida* specimens [49].

Oral and prostheses hygiene are appointed in many cases, as the main responsible for infections, and dentists should be concerned about these factors [50]. However, the dentist cannot control the hygiene habits of their patients. The application of this technology to dental prostheses may allow dentists to improve the control of oral disorders of their patients. The impregnation of dental prostheses with an anti-inflammatory may allow the dentist to be certain that the patients do the proper treatment.

Portugal's case

A questionnaire (see Appendix 4) has been applied to the Portuguese dental prosthesis users, using an online tool, about the problems they have had with their prosthesis and the kind of benefits they would like their prosthesis to allow. The sample comprises 30 individuals that use dental prosthesis. Among the 30 individuals inquired, about 47% refer having problems with their dental prostheses (Figure 3.1). In Figure 3.2, the most reported problems by the prostheses users are presented. The bad adaptation of dental prostheses and inflammations are the highest percentage problems with about 36% of dental wearers affirming they suffer from the aforementioned problems. The GEI dental may be a solution to the bad adaptation and inflammation problems.

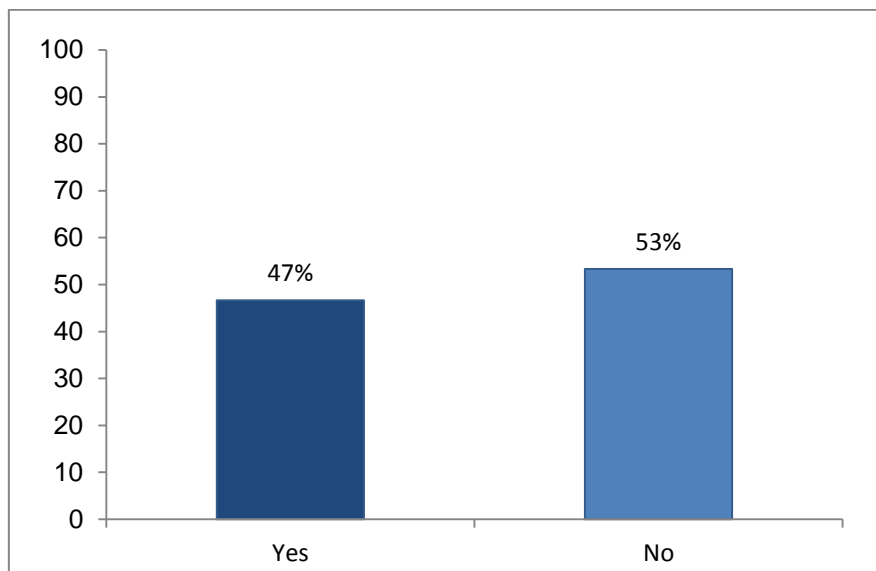


Figure 3.1. Portuguese population with dental prostheses problems (data collected from online questionnaire).

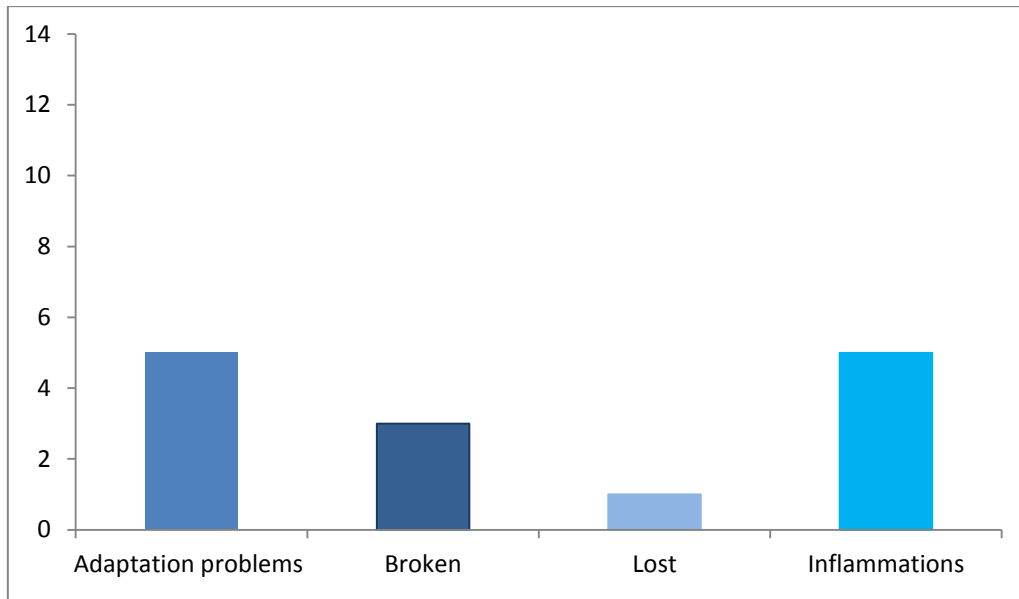


Figure 3.2. Types of problems, which the dental prosthesis users usually have (data collected from online questionnaire).

The GEI dental will appear in the market as a preventive technology, allowing prevention of diseases and infections. If the dentist observed his patient and concluded that he did not have a good oral hygiene, with the purpose of improving it and preventing the development of bacterial or fungi infection, the dentist could order a denture which gradually will release an antimicrobial or other active principle.

In other cases, when the patient was already presenting an infection, the dentist could order the dental prosthesis with the most adequate medicine to the referred case and so the medicine will act locally. As an example, the GEI dental could be useful in the cases mentioned above, such as candidiasis, which will possibility a gradual and local administration of anti-fungi. In this case the technology will act as a treatment technology.

4. Proof GEI dental concept

The application of the technology to dental prostheses is a new and innovative idea, so there is not any experimental test that validates or proves that the technology allows, at sufficient extent, the extraction of MMA from dental prostheses and its impregnation with therapeutic active principles.

In order to verify the effectiveness of using GEI technology, on the one hand, for the extraction of the MMA from the PMMA used in dental prostheses, and, on the other hand, in the impregnation of active principals in PMMA, experimental tests were performed. The experimental tests were divided in two parts. In a first stage, the possibility to extract the residual monomer from the polymer used in dental prostheses was tested. In a second stage, the possibility of impregnating an anti-inflammatory drug was evaluated. The experimental tests were performed in Laboratory of Nutraceuticals and Delivery, IBET. In this Chapter only a summary of the content of the experimental tests is presented, in Appendix 5 the description of the experimental tests is detailed.

The experimental setup and the respective schematic diagram used during the experimental tests is depicted in Figure 4.1 and Figure 4.2 respectively.



Figure 4.1. Image of installation where the tests were performed (1- High-pressure cell; 2- CO₂ pump high pressure liquid; 3-Thermostatized water bath, 4- Pressure manometer).

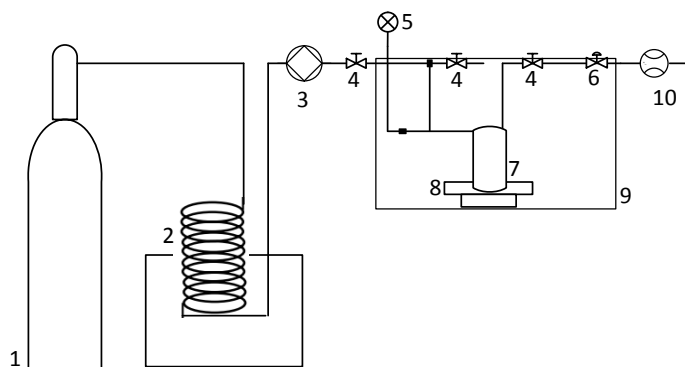


Figure 4.2. Schematic diagram of the installation where the tests were performed (1- CO₂ cylinder; 2- Cooling coil; 3- High pressure liquid CO₂ pump; 4- Valve; 5- Pressure manometer; 6- Micrometer valve; 7- High-pressure cell; 8- Stir plate; 9- Thermostated water bath; 10- Flow meter).

This apparatus consists in a high-pressure cell (made of stainless steel) with an internal volume of 25 cm³, a high pressure liquid CO₂ pump (Haskel Model 29723-71), a water bath and a pressure manometer (Digibar II). During the experiments the cell was placed in a constant-temperature water bath and CO₂ was pressurized with a liquid pump. A system of valves allows the CO₂ to enter the cell. The pressure generator and the cell are provided with an electronic manometer to allow control of the pressure and the inlet and outlet of gas.

The material tested were acrylic samples of the finished material used in dental prostheses, to be used already by patients.

4.1. Extraction Tests

The extraction experiments comprise the study of the effect the several operational conditions in the removal of MMA from PMMA, namely at different pressures, temperatures and contact times with CO₂.

The extraction tests were performed in the installation showed in Figure 4.1. The test consists in immersing the cell with the acrylic samples in the thermostatically bath of water after the desired temperature is reached and consequently pressurizing it with CO₂ until the desired pressure (Appendix 5) and stay in contact with CO₂ for 20 minutes (static period). After the static period, the valves are opened to allow CO₂ pass through the sample continuously for a defined period, named Continuous Period (Appendix 5). Finally, after that period, the depressurization was performed, by slow release of the supercritical fluid.

Table 4.1 Operational conditions and result of the most efficient extraction test.

Test	T (°C)	P (bar)	Static Period (min)	Continuous Period (min)	Continuous Period flow rate (L/min)	ρ_{CO_2} (Kg/m ³)	Efficiency*	Duration of the process (min)
2	25	70	20	30	3	743	68.7	50

*Efficiency = Amount of MMA extracted by scCO₂ / Amount of MMA initially

The most satisfactory result was obtained at 25°C and 70 bar in a process which during about 50 minutes (Table 4.1), these conditions allows a reduction of 68.7% of MMA present in the samples of PMMA. This is a significant reduction of MMA with mild operations conditions in a relatively short time. In addition the samples maintained its circular shape, volume, appearance and weight. However, a slight whitening of the sample on the surface is verified, but it is almost imperceptible. This could be explained by a possible interaction of the CO₂ with the dye. Therefore, the hypothesis that GEI could decrease the amount of MMA of acrylic resins used in dental prostheses was validated. The results obtained are a good starting point to future tests in order to develop and improve the GEI dental features allowing obtain the best efficiency that the technology could.

4.2. Impregnation Tests

In a second stage was tested the impregnation of ibuprofen in the acrylic resin of the dental prostheses. The objective is verified whether the active principle is impregnated in PMMA by the GEI dental. With the purpose to observe if it is possible to fulfill the objective the samples were tested in different conditions of pressure, temperature, CO₂ contact and depressurization period.

The impregnation tests were performed in the equipment presented in Figure 4.1 The tests consist in immersing the cell with the acrylic sample and the ibuprofen in the thermostatically bath of water until the desired temperature is reached and subsequently pressurizing with CO₂ until the desired pressure (Appendix 5). During all tests the samples in the cell were stirred. Inside the cell, the samples were put on a wire support and the ibuprofen inside a metallic network, above it.

The tests were performed in batch during contact period (tCO₂). After the tCO₂, the system was depressurized slowly or fastly, according to the test performed (Appendix 5).

In all test is possible observe that the samples are impregnated with ibuprofen. Different loads were obtained to different temperature and pressure conditions. The tests 11 and 12 present the best loads without changing the samples, operation condition 110 bar and 40°C seems the better condition to impregnate the PMMA with ibuprofen comparing with the operation conditions tested (Appendix 5). However, as mentioned above, in extraction experiments, a slight whitening of the sample on the surface is verified, but it is almost imperceptible. For 30 minutes of tCO₂ the % impregnation is about 7% and to 60 minutes is about 8% (Table 4.2).

Table 4.2. Operational conditions and results of the most successful impregnation tests.

Test	T (°C)	P (bar)	tCO ₂ * (min)	Depressurization Period (min)	ρCO ₂ (Kg/m ³)	Load **	% Impregnation ***	Duration of the process (min)
11	40	110	30	30	684	0,07	7	60
12	40	110	60	30	684	0,08	8	90

* Contact period - Period in which sample, active principle and CO₂ were in contact

**Load = Impregnated ibuprofen/PMMA

***%Impregnation=Impregnated ibuprofen/PMMA x 100

The results allow considering that the GEI dental enables to impregnate the acrylic resins used in dental prostheses. However, only ibuprofen was tested, in other future studies, it is necessary to test other active principles, the required by orthodontists, as well as the respective operational conditions and the drug release profile inside the oral cavity, in order to obtain the maximum efficiency of the process. Therefore, the systems of impregnation with different active principle should be studied with more detail. The solubility of the drug into CO₂, the ability of CO₂ to penetrate the polymer and the partition coefficient of the drug between the dense gas and the polymer phase are important points to take into account during the development of GEI dental.

4.3. Conclusion

The results of the experimental tests allow considering that GEI dental achieves the proposed objectives, both for the extraction of MMA and the impregnation with an active principle in dental prostheses. The GEI enables extracting until 68.7% of MMA present in dental prosthesis in a process which lasts about 50 minutes. In addition, GEI dental allows the impregnation of ibuprofen with a %impregnation of 7% in a process with the duration of 60 minutes. To increase the %impregnation to 8% the duration of the process must also increase to 90 minutes.

The concept of the product was validated, however, it is not yet presented with the best characteristics to introduce into the dental market. Several studies should be done in order to develop the all potentialities of this product. The critical points of the GEI dental based on the experimental tests made are:

- a) The possible interaction of CO₂ with the dye. Nevertheless, there is transparent acrylic without dye used in dental industry and, in addition, the composition of the dye is not the best to human use, probably the dye should be changed in the future, or even this technology could allow the impregnation of a safer dye.

- b) The time of the process is an important point to be improved. The demand of dental care sector is the high efficiency in a shorter period of time possible.
- c) The efficiency of both processes could be improved, it is important to perform future tests in order to improve the processes.

4.4. GEI dental components

Since GEI dental will be transferred from the laboratory to the market, a new prototype was designed that should be mounted and tested. Comparing to the installation where the experimental tests were performed, the prototype must be simpler, automatized and with smaller dimensions. A preliminary design has been prepared for a future prototype in order to verify the technical feasibility of the GEI dental process and to estimate the costs associated to its production. The schematic diagram presented in Figure 4.3 was based on the functions of GEI dental, experimental tests performed and on the industry where the products are intended to be commercialized.

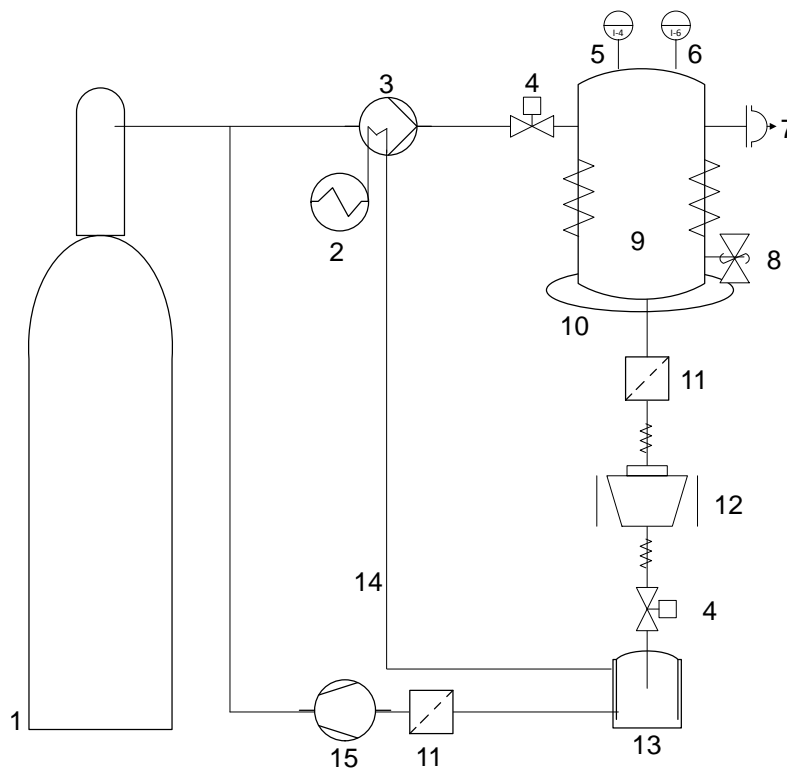


Figure 4.3. Schematic diagram of the GEI dental apparatus (1-CO₂ cylinder; 2- Chiller; 3- CO₂ pump; 4-Valve; 5- Pressure gauge; 6- Temperature gauge; 7- Rupture disk; 8- Relief valve; 9- High pressure vessel with internal stirring and electrically thermostated with a heating jacket; 10- stir plate 11- Filter; 12- Automated Back-pressure regulator (BPR) with a heat exchanger; 13- Trap; 14- Chiller tubing; 15- Compressor).

The entire diagram apparatus is described and discussed next.

Liquid pump and chiller

The apparatus comprises a liquid pump with a chiller to pump the CO₂ into to the system to assure only liquid CO₂ reaches the pump.

Valves

Two automated valves will be necessary, one before the vessel to regulate and control the input of the CO₂ into the high pressure vessel, and other valve to control the output.

High Pressure Vessel

The high pressure vessel is jacketed with a heating mantle and must have the proper dimensions to put the dental prostheses inside without damaging it.

Gauges

The control of the temperature and the pressure will be ensured through controllers and sensors.

Filter

A filter is also required to ensure that the equipment will not clog, particularly BPR. In addition, in the recirculation of CO₂ is also required a filters system.

BPR

The BPR has the function of limiting and precisely controlling the upstream pressure of the gas providing extremely high pressure stability to the system.

Trap

A trap is necessary in order to collect the MMA during the extraction process and to collect the active principle dissolved in the CO₂ during the impregnation process. Chiller tubing allows maintain the trap chilled.

Compressor

The compressor permits the recycle of the CO₂.

As to avoid accidental overpressure, the apparatus proposed includes the installation of a rupture disk and a manual relief valve. All the system will be connected by stainless steel tubings.

The electrical circuit is not presented in Figure 4.3, but the installation will be fitted with an electronic circuit to allow automatic control.

In addition to the necessary equipment to perform the process, a metallic structure will be necessary to hold on the high vessel pressure, the pump with a chiller and the BPR automatized. Concerning the appearance and the design of the device, the entire setup should be coated with metallic plates with a principal open on the top. The mentioned overture corresponds to the opened vessel in order for the customer to put the dental prosthesis, in the case of extraction process, and in the case of the impregnation process, to put the dental prosthesis and the principal active, in the beginning of the process. The schematic apparatus presented in Figure 4.3 is enabled to perform both process extraction and impregnation.

An informative table with the best operation conditions to extract MMA from dental prosthesis and with the best operation conditions to impregnate the dental prostheses with several active principles will be supplied together with equipment.

5. Market Analysis

5.1. Market Outlook

5.1.1. Potential Market Dimension

In North America, Japan and Europe around 6% to 10% of the people are toothless and around 240 million people have lost one or more teeth [51]. The dental market is dominated by Europe, United States (US) and Japan and account for more than 80% of the revenue generated [52]. The markets for dental implants in Europe being in a developing stage, the revenues for the base year were analyzed to be \$0.79 billion and it is estimated to reach \$1.94 billion by 2013 [53].

The tooth replacement has been of greater importance in modern society since it is associated to bone loss as well as to aesthetics [51]. Throughout the past 25 years, the dentistry sector has considerably developed. Most of these changes have occurred in the areas of technology, services made available and patient care. The main factors which were the ignition to the development of new dental materials and equipment were the increasing aging of population, enhanced treatments, improved awareness and high aesthetics [52].

The restorative and preventive dentistry are the largest area of development and the segment in the global dental market that is growing the most is dental implantology. Although the current global economic scenario has impacted the growth of the dental implant market, the implant industry is very strong. Implantology segment is estimated an annual growth rate of 16.3% in the US from 2004 to 2014 and 13.7% in the European Union (EU) from 2003 to 2013 [53-55].

Due to several European countries, particularly Sweden, Switzerland, Italy and Germany, having adopted at an early stage the dental implant technology, Europe is the largest market. Figure 5.1 shows that US, North America (including Canada) represents less than a third of the dollar value of the dental implant market and Europe is the main agent of revenues of dental implant market [53]. Although there had been a recession, the European market has been recovering since 2009 and making considerable improvements in its revenues especially in 2010 [55].

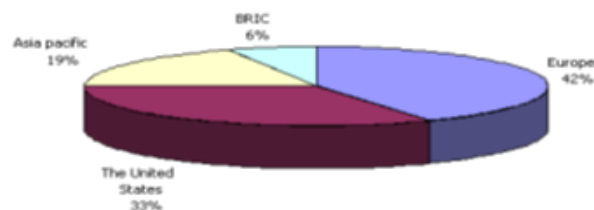


Figure 5.1. Percentages of revenues by geographic region for the global dental implant market for 2010 [53].

In the study of the market outlook it will be focused on European companies due to several reasons:

- a) Europe is the major revenue generator for dental implant manufacturers.
- b) Marketing the new product in European companies may be a less risky bet. The countries are closer geographically to Portugal, so the transportation is simpler and easier.
- c) Countries are more culturally similar and it has an analogous standard of living.

All of the reasons referred above are important when developing a business in the dental industry. On the other hand, more risky and long-term entry strategies are in Brazil and other Latin American countries, US, Asia and Africa. Brazil and other Latin American countries have the disadvantage of being very protective, geographically distant, economically instable, and, last but not least important, the problem with copies and intellectual property. The US, besides being geographically distant, have a very competitive market and it requires large investments given its size. Asia has issues with intellectual property and a different culture. Lastly, Africa is a continent of very poor countries, and besides the underdevelopment of the dental industry, there probably are problems with intellectual property as well.

With the purpose of making a simpler and more objective analysis, it was decided to choose eight European countries, including Portugal, as a representative sample of developed European countries.

The estimative of potential market dimension comprises the observation of two important points: the number of people who use dental prostheses and the number of dental laboratories. The number of people with dentures allows having a global perspective of potential users of this product, in others words, the number of people who will use the product. On the other hand, the dental laboratories will be the companies which will possibly buy the device. So, the number of laboratories gives an estimative of who might be interested in buying the product.

5.1.1.1. The United Kingdom case

There are some essential data to estimate the potential market. Since the United Kingdom was the only country where detailed data were available on several indicators, it will be used to make projections on what is going on in other developed European countries. The United Kingdom seems to be a strong hypothesis to use as a bench mark country, because there are strong correlations of some demographic and health indicators among this country and other European countries.

As it can be observed by tables presented below, there are several data with strong correlations among the United Kingdom and the European countries, such as the life expectancy (Table 5.1), population structure by age group (Table 5.2), and number of dentist/population (Table 5.3). The life expectancy of European countries presented is about 80 years (Table 5.1). The population structure by age group is also very similar among the European countries (Table 5.2). Considering the resemblances of the aforementioned indicators, projections of some essential data are possible to make in order to estimate the potential market.

Table 5.3 presents the number of practicing dentists in eight European countries. The countries can be divided in 3 groups based on the ratio number of dentist /population. One of the groups is represented by Portugal, United Kingdom and Austria which presents about 5 dentist by 10 000 people. Spain, France and Germany represent another group of about 7 dentists by 10 000 people. Finally, a third group is constituted by Italy and Sweden with the biggest proportion of dentist by population comparing to the other two groups of countries. Portugal presents an identical ratio of dentist by population to the United Kingdom which allows establishing strong correlations between the oral health care system of the United Kingdom and the oral health care system of Portugal.

Table 5.1. Life expectancy at birth in Europeans countries [56].

Country	Life expectancy at birth (2009)
Portugal	79.6
United Kingdom	80.5
Spain	81.8
Italy	81.9
France	81.6
Germany	80.3
Austria	80.5
Sweden	81.5

Table 5.2. Population structure by age group in 2010 [57].

Country	0-14 years (%)	15-64 years (%)	>65 years (%)
Portugal	15.2	66.9	17.9
United Kingdom	17.5	66.1	16.5
Spain	14.9	68.2	16.8
Italy	14.1	65.7	20.2
France	18.5	64.8	16.6
Germany	13.5	65.9	20.7
Austria	14.9	67.5	17.6
Sweden	16.6	65.3	18.1

Table 5.3. Number of practicing dentists in Europe [53].

Country	Population (2011)	Number of practicing dentists	Number of Dentists/ Population	Number of Dentists/ Population (per 10 000 habitant)
Portugal	10 636 979	5 000	4.7E-4	4.7
United Kingdom	62 735 000	34 100	5.4E-4	5.4
Spain	47 021 031	30 100	6.4 E-4	6.4
Italy	58 126 212	56 600	9.7 E-4	9.7
France	64 057 792	43 100	6.7 E-4	6.7
Germany	82 329 758	64 000	7.8 E-4	7.8
Austria	8 217 280	4 600	5.6 E-4	5.6
Sweden	9 041 000	8 200	9.1 E-4	9.1

5.1.1.2. Dental prosthesis users

Table 5.4 shows the percentage of people with dental prostheses divided by two age groups of five European countries in 1991. Although the data are of about twenty years ago, they give an idea of the population with dental prostheses in European developed countries. The age group 35-44 shows reduced percentages of people with dental prostheses (less than 1%). On the other hand, the age group >65 is clearly where most of the dental prosthesis users appear in all countries presents. The United Kingdom presents high percentage of people with dental prostheses (67%) compared to other countries (about 20%) in the age group >65.

Table 5.4. Percentage of people by age group with dental prostheses in European countries [58].

Country	Total Population	Percentage of people by age with dental prostheses (1991)	
		35-44	>65
United Kingdom	62 735 000	4.0	67.0
Italy	58 126 212	0.3	18.0
Germany	82 329 758	0.4	27.0
Sweden	9 041 000	1.0	20.0

Table 5.5 shows some data of Dental Health Survey in 2009. Even though the referred survey does not include the population of Scotland, it was considered that the data shown represent United Kingdom. The percentage of women (17%) and men (21%) with dentures is very similar, apparently the use of dentures is regardless of sex. The proportion of adults with natural teeth and dentures varies by the age group. The United Kingdom population with 16-44 years is the age group with natural teeth only (97%) and with a low percentage of people with dentures (3%). Accordingly, the age group 16-44 will use our product less. On the other hand, the age group >75 presents the lowest percentage of natural teeth only (29%) and the highest in users of dentures (70%). Following next, the age group 65-74 presents a percentage of 55% with natural teeth and only 45% are dentures wearers. The age group in which this product will have more users is from 65 up.

Table 5.5. Percentage of people with dentures by age of England, Wales, Northern Ireland (2009) [59].

	Natural teeth only (%)	Natural teeth and dentures (%)	Edentate ¹ with dentures (%)	Edentate, no dentures (%)	With dentures (%)
Age					
16-44	97	3	0	-	3
45-54	88	11	1	0	12
55-64	71	23	5	0	29
65-74	55	30	15	0	45
>75	29	37	33	1	70
All	81	13	6	0	19
Men	83	12	5	0	17
Women	79	14	7	0	21

According to Dental Health Survey, in 2009 about 19% of the population in the United Kingdom is dental prosthesis users (Table 5.5). The strong correlations of some health indicators verified in Tables 5.1, 5.2, and 5.3 allow considering that Portugal and other European countries may have similar numbers of dental prosthesis users. Therefore, it is considered that about 19% of the population of European developed countries uses dental prosthesis and so they will be potential users of the product.

5.1.1.3. Number of dental laboratories

The ratios presented in Table 5.6 allow having an idea about the number of dental laboratories by total Population in developed European countries. Some differences between countries can be observed. In the United Kingdom's case, there is about 5 laboratories per 100 000 habitants, while Germany, Austria and Sweden present about 4 laboratories per 100 000 habitants. Among the countries shown in Table 5.6, the United Kingdom is the country with more laboratories by people. There is a significant

¹ Edentate, that is having no natural teeth.

number of dental laboratories in European developed countries and with a similar proportion of the dental laboratories per capita. So, this technology has a high market size.

Table 5.6. Number of dental laboratories in European countries.

Country	Total Population	Number of dental laboratories	Number of dental laboratories/Total Population	Number of dental laboratories/Total Population (per 100 000 habitants)
Portugal	10 636 979	333 ²	3.1E-5	3.1
United Kingston	62 735 000	2 000 ³	5.3E-5	5.3
Germany	82 329 758	8 600 ⁴	4E-5	4
Austria	8 217 280	657 ⁵	4.1E-5	4,1
Sweden	9 041 000	583 ⁶	3.7E-5	3.7

5.1.1.4. Portugal's Case

The GEI is a Portuguese technology. For this reason, Portugal will be the market test for the implementation of the GEI dental in the market. The following section is intended to discuss about the market size in Portugal.

In Portugal there is not any study about the quantity of Portuguese population that uses dental prostheses. Therefore, it was decided to collect data from a questionnaire applied to the Portuguese population. The questionnaire was conducted online and it is presented in Appendix 4. The sample comprises 143 people randomly chosen. As it is possible to observe in Figure 5.2, about 21% of the Portuguese population uses dental prostheses. The result of the online questionnaire reinforces the previous projection from the United Kingdom's case.

² Number estimated.

³ Source: Dental Laboratories Association of United Kingdom (2011).

⁴ Dental laboratories and companies in Germany in 2000. Source: www.kzbv.de

⁵ Dental laboratories and companies in Austria in 2003. Source: www.kzbv.de

⁶ Source: Malmö University Faculty of Odontology Department of Prosthodontics Sweden (2011).

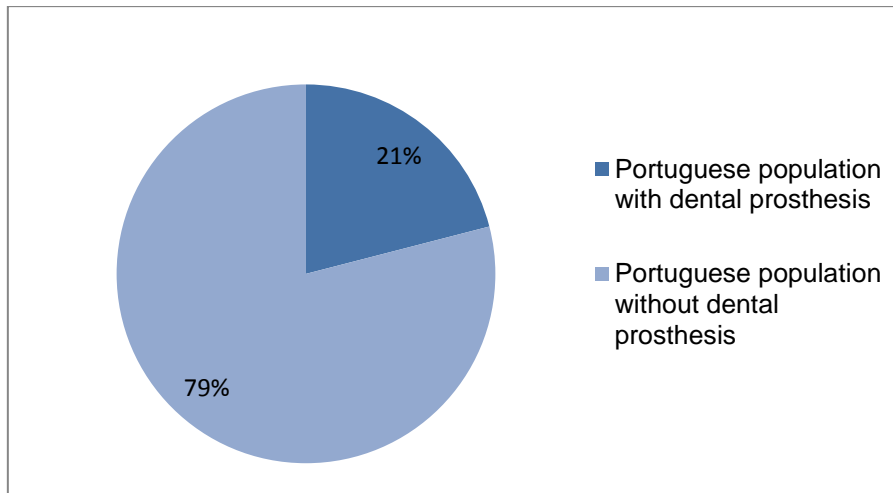


Figure 5.2. Proportion of Portuguese population using dental prosthesis (data collected from online questionnaire).

According to Instituto Nacional de Estatística (INE), the number of enterprises by Economic activity and Employment size class service with activities of dental practice in Portugal are 6 807. This is the unique information about dental industry in Portugal, however it is very limited because activities of dental practice include dentistry, prosthesis technicians, dental clinics and other activities related to the dental industry in general and not only dental laboratories.

Due to the absence of data about the number of dental laboratories in Portugal, a projection of the number of dental laboratories in Portugal was made, considering once more the United Kingdom's case. According to Dental Laboratories Association of the United Kingdom, the number of laboratories in this country is 2 000 (Table 5.6). As it is possible to observe in Table 5.6, the population of Portugal is about 1/6 the population of United Kingdom. The projection is made based on the proportion between the United Kingdom's population and Portugal's population. Therefore, the estimated number of dental laboratories in Portugal is 333.

As a conclusion, about 21 % of Portugal's population possibly is dental prosthesis wearers and they can be potential users of this product. The number of Portuguese companies which might be interested in buying the product is about 333 dental laboratories.

5.1.2. The STP Process

The STP process is the method by which the markets are subdivided into different segments. This process refers to three activities which are segmentation, targeting, and positioning, and the next section is structured around these key elements [60].

5.1.2.1. Segmentation

The market can be divided into distinct groups of customers with different needs, characteristics or behaviors, who can need distinct products or marketing mix [61].

The market is business to business (B2B) in which the client is different to the final customer. Clients are the companies of dental laboratories and the final customer are the dental prosthesis wearers. Although the final customer has the necessity, the dental laboratories are the ones that will buy the product. The company will be a supplier of equipment to the laboratories. The final product are the improved dental prostheses that will be used by the patient, so GEI dental only improves the final product. Therefore, the market is B2B and not Business to customer (B2C) because the company will sell to another company (laboratories) and not to the final customer, the patients.

The study of market segmentation will be based on characteristics of dental laboratories.

Segmentation by interest in the innovation

Innovation is an important feature to segment the market because the product is an innovative technology applied to dental prostheses. So, it is important to segment the market according to the company's interest in innovation.

There are companies with more modern equipment and materials. These companies are equipped with CAD/CAM systems and they are always interested in the latest news. This type of company, besides manufacturing the prostheses, is usually involved in investigation, it has the most modern equipment, and it uses the techniques and materials of the last generation. Other companies are more traditional and use traditional manual techniques, less modern equipment and usually are not involved in research.

Segmentation by the size of dental laboratories

The size of dental laboratories is an important variable to segment the market. It is important to distinguish the companies with a large size from the ones with a small size. The companies with a large dimension are companies with various workers, with a high numbers of dental prostheses manufactured per month, as well as a large number of laboratories. On the other hand, the small companies have a reduced number of laboratories or even none in the European countries, and have a low number of dental prostheses manufactured per month. The companies with large dimensions have the advantage of having a payback in a shorter period of time, since they have more prostheses orders per month. The mentioned advantage shows that the purchase of GEI dental will be more attractive to the companies of a large dimension.

Another important feature to take into account is the number of dental laboratories that each company has in Portugal, since Portugal is the country used as a test market for this product.

Segmentation by location

The market can be segmented according to the geographical location of laboratories. The geographical location is an important feature because, as mentioned above, the characteristics of the markets are different according to their own geographical location.

As it is a Portuguese technology, at the beginning the Portuguese market will be explored, thus Portuguese laboratories are being focused. The next step is entering into the European companies because it is geographically closer, it is culturally similar and it has an analogous standard of living. Besides, Europe has more guarantees concerning intellectual protection compared to other locations, such as Africa or Asia.

One criterion that it is considered important to segment the market is the headquarters/nationality of the companies. This criterion is important because, although the companies can have laboratories in many countries, the headquarters is where most of the important functions of an organization are coordinated and usually is where the innovations are developed.

Segmentation by financial soundness

The financial soundness is another important point to take into account. There are companies with stable and positive financial conditions. On the other hand, there are other companies that do not present the best financial situation. So, it is important to pay attention to this parameter because it helps to evaluate which of the companies have a favorable financial condition to invest in this new product.

The financial soundness may be related to the maturity of the businesses, in other words, the older companies could possibly have a more stable and prosper financial situation. In dental industry there are companies founded about ninety years ago and other for three years. And in some cases the financial condition, the credibility and the confidence that the companies transmit are related to the lifetime of the firm.

5.1.2.2. Targeting

Market segmentation reveals the firm's market segment opportunities. The firm has now to evaluate the various segments and decide how many and which segments can serve the best [61].

The evaluation of marketing target was made by the study of the following features of the companies existing on the market receptivity to innovation, laboratories in European countries especially in Portugal, a large number of laboratories and financial soundness.

An important feature that companies should have is the interest in **innovation**. Usually these companies have most modern techniques and equipment because they have the concern for supplying their customers with the best and more advanced products. On a regular basis, the largest companies are the most involved in research and are those that require the latest technologic advances.

The company having **laboratories** in Europe and especially in **Portugal** is another important required point because Portugal is the market test.

A **large number of laboratories** is another aspect required. Companies which have a large number of laboratories in European countries, and especially in Portugal, are the most interesting to focus on. Companies with a considerable number of laboratories probably require more units of devices.

The financial situation of companies is an important characteristic to pay attention to. A criterion to decide which companies we will focus on is companies' **financial soundness**. The financial soundness can be considered as a guarantee that companies have capital to invest and are in a favorable financial situation. The referred criterion will be evaluated based on the years of the companies in the market, since it was not possible to ascertain the financial situation of the majority of the companies.

A study about dental laboratories worldwide is made with the purpose of having a global view about dental companies of the entire world and how they suit in the targeting criterion. In Appendix 6 a list of several dental companies, evaluated according to the targeting criteria, is presented. Even though most companies are local laboratories with only one laboratory, there are also leading laboratories worldwide with networks of dental laboratories across the world, such as, Nobel Biocare, MDH, Maló Clinic, Precision Dental Studio, Sun Dental Laboratories, among others.

Despite the majority of dental laboratories in Portugal being local, with a small dimension and usually only a single laboratory and not a network of laboratories, it is possible to verify the existence of influential companies in the dental industry in Portugal. Some examples of companies with a strong presence in the Portuguese and European market are MDH and Malo Clinic. The mentioned companies have interest in advanced and innovative technologies. In addition, there are small Portuguese dental laboratories, such as Orallab, which have interest in innovation and to give a high quality service to their customers. Therefore, the mentioned companies are examples of the target market for GEI dental.

5.1.2.3. Positioning

The differentiated value created to the target segments and the product's position must be defined by the company. The product's position can be defined as the way the product occupies in the costumers' minds [61]. Positioning allows distinguishing a product from another and provides to potential clients a reason to buy those [60].

The GEI dental appears in the market as an **innovative device** which uses scCO₂ to improve properties of one of the most used materials in the manufacture of dental prostheses.

The technology does not change the properties of manipulated material, so the **composition of biomaterial** used in the prosthesis is **not altered**. In this way the attributes, such as biocompatibility are not affected after the prostheses are manipulated with GEI dental.

The health care involves a series of restrictions and rules to assure the safety of the patients. Due to the dental prostheses being a medical device, it is important to guarantee that it has not any adverse effect and it does not present any kind of risk to the patients' health. The GEI technology presents the advantages referred in the section of the technology description, which makes the association of this technology to health sector conceivable. Therefore, since the technology does not present any risk to the health, it is considered a **safe product**.

The clean technology belongs to a class of equipments that can **promote sustainable management of resources**. The conditions of operation are mild, in other words, they allow working at relatively low temperatures suitable for thermally labile substances. Nowadays the waste produced and accumulated from the chemical process is a significant global concern. So, for this reason, cleaner technologies are an area of growing interest worldwide.

The GEI dental is presented as a **versatility product**, besides having two distinct functions. On the one hand, it allows the **extraction** of residual monomers, the MMA, and, secondly, it allows **impregnating** the prosthesis with an active principle. The versatility can be related also to the fact that it can be **impregnated with different active principles** which gives different properties to the dental prostheses. The active principles present a variable range of possible utilizations, such as anti-inflammatory or a substance to good breath

The product will be positioned as a device that **adds value** to the dental prostheses and it will also **respond to a necessity** of dental prostheses. The extraction of MMA was suggested by the dental professionals addressed, as being a problem of acrylic resins used in orthodontia, so the GEI dental responds to a necessity of dentistry industry. On the other hand, the possibility to impregnate dental prostheses with an active principal confers an additional value to dental prostheses. A big concern of oral health care are the infections, which are a common problem. The GEI dental can be considered as a device aimed at the **prevention of dental diseases or in other cases as a treatment**.

Another aspect to take into account is the equipment design. The device will be manufactured in order to have a **practical** and **simple manipulation**, because it will not be used by a supercritical fluids' specialist.

The product is clearly noticeable and it will be requested by its possible customers due to the follows aspects:

- Innovative product
- It does not interfere with the dental prostheses characteristics, including biocompatibility
- It is safe

- It is environmentally friendly
- It presents versatility
- It meets a need of the orthodontia
- It adds value to the dental prostheses
- The manipulation is practical and simple

All the characteristics mentioned above allow the product to be presented to the dental market as a high quality new device for improving the dental prostheses.

5.2. Competitors

Although there are several researches to improve the properties of acrylic, there is not yet any device in the market to change it or add the attributes that the GEI dental proposes.

Dental industry presents a wide scope of materials used in dentistry, which may be used, for example, in the production of dental bases, restorations, impressions and prostheses [52]. However, it is possible to divide them into three main groups: acrylic (polymers), ceramics and metals.

The dental prostheses should be prepared for a long period contact with oral tissues and fluids. Some key elements must be taken into account in its fabrication, its components must have characteristics that assure a safety profile and should not be either allergenic or carcinogenic [62].

Polymers

Since acrylic polymers are the mostly used in prosthodontics, the acrylic was considered a representative of polymers. The main attributes of acrylic resins are their easy processing, low cost, lightweight, and color matching ability. On the other hand, the material is low in strength, brittle, low in thermal conductivity and it has been shown to be cytotoxic [63]. In the field of dentistry, the use of acrylic has a very wide range of applications. These include the use in dental impressions, the use as a veneer in crowns, in temporary procedures, such as bridges, the use in dentures, in implants and in mouthpieces.

Ceramics

The ceramics has many positive characteristics, such as high biocompatibility, the color and translucencies are similar to natural tooth, and it is suitable to work in dental bridges and implants [54]. However, this material also presents a low impact resistance, properties difficult to reproduce and difficulties in processing and fabrication [64]. Ceramics is mainly used for inlays, crowns, fixed bridges and aesthetic veneers.

Metals

Prostheses are often constructed using metals, due to their characteristics, such as hardness, strength, stiffness, durability, corrosion resistance, and bio-compatibility [62]. The referred group of materials comprises a large variety of options and the type of metals most commonly used in dentistry

is the amalgam, gold alloys and base metal alloys. Nevertheless, the color of these materials is not similar to natural tooth color. The metals are used in primarily for crowns, fixed bridges, and partial dentures [52]

The materials described above represent a general view of the dental materials. There is a demand in the improvement and innovation of dental materials. The mentioned materials are available in the market throughout supply companies of dental laboratories. There are companies which are dedicated exclusively to the sale of metal to dental implants. On the other hand, there are companies that sale all types of consumable materials to dental laboratories including acrylic and ceramics.

5.2.1. Performance Map

As mentioned above, it is possible to divide dental materials in three main groups: acrylic (polymer), ceramics and metals. GEI dental is a technology applied to the acrylic, so in Table 5.7 the performance of GEI dental refers to the acrylic after being manipulated with the technology. The following map compares the performance of dental materials according to some attributes.

Table 5.7. Performance Map: Attributes vs Competitors.

	GEI dental (Acrylic)	Acrylic	Ceramic	Metal alloys
Avoid infections	✓	⊖	⊖	⊖
Avoid allergic reactions	✓	⊖	✓	✓
Avoid malodor	✓	⊖	⊖	⊖
Esthetic	✓	✓	✓	✗
Easy manipulation	✓	✓	⊖	✗
Several applications	✓	✓	⊖	⊖
Resistance	✗	✗	⊖	✓
Price	⊖	✓	⊖	⊖

Legend: Green ✓ : High performance; yellow ⊖ : Medium performance; Red ✗ : Low performance

Avoid infections: The risk of infection is an important feature to take into account in this type of devices. The GEI dental will be allowed to reduce risks of infection, as well as its treatment.

Avoid allergic reactions: The material which presents a biggest risk of allergic reactions is the acrylic. The GEI dental can decrease the referred risk, since it allows the extraction of the MMA.

Avoid malodor: The malodor is associated to acrylic prosthesis. The GEI dental is a good option to end the problem and it will allow the acrylic to become more competitive against the other competitors.

Esthetic: The esthetic is another important feature and metals are a less esthetic material compared to others.

Easy of manipulation: One of the advantages of acrylic is the ease and simplicity of its manufacture. On the other hand, the ceramics and metals require a complex manipulation, especially the metals. The GEI dental does not change this attribute of acrylic.

Possibility to use in many applications: The acrylic is one of the most used materials in dentistry with a high range of possible applications. Therefore, the acrylic presents more possibilities of use compared to the metal and ceramics.

Resistance: The resistance of material refers to the facility of material break. Metal presents high tensile and fatigue strength compared to ceramics and acrylic resins. However, ceramics presents also a high resistance capacity, so acrylic is the most susceptible material to be broken.

Price: The acrylic is the cheapest material comparing to metal and ceramic. Although the GEI technology will turn acrylic more expensive, the technology will bring other important benefits.

Although the acrylic has some limitations, it presents important attributes which made it one of the most used materials in dental prostheses' manufacture. As a consequence, there is a significant research about it with the purpose of improving its properties. The GEI dental allows improving some disadvantageous characteristics of acrylic without changing the advantageous ones. In conclusion, the technology could permit **less risks of infection, less risks of allergy**, as well as a **good breath**. Therefore, the acrylic then manipulated by GEI dental is a stronger product compared to its competitors, because it provides important features to the dental prostheses, which will allow high comfort and safety to the patient.

5.3. Supply chain

5.3.1. Value chain

The value chain of the dental industry is presented next in Figure 5.3 and comprises suppliers, distribution companies, dental laboratories and dental clinics.

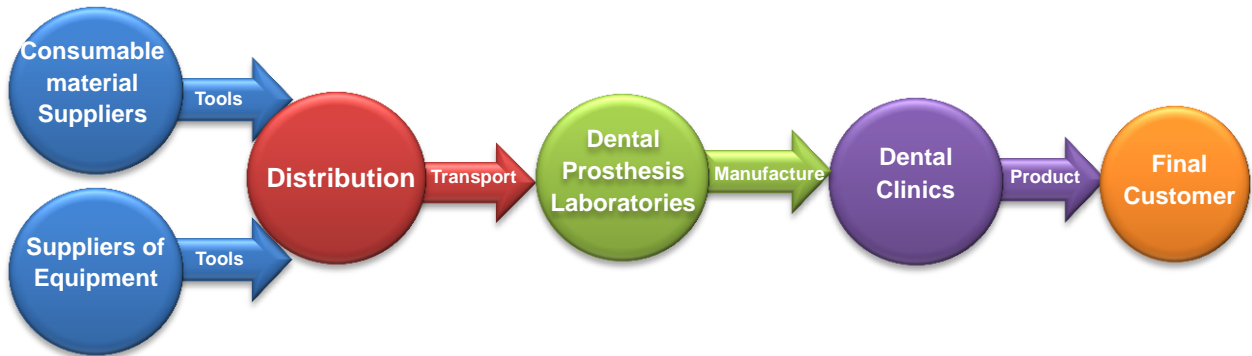


Figure 5.3. Value chain of dental industry.

Suppliers

There are two types of products which the laboratories order to the companies that manufacture the dental prostheses, the consumable materials and equipment. The dental consumables refer to all materials and consumables used by the dental professionals in their daily work, such as acrylic, metallic alloys, ceramics and others. The companies which supply laboratories with acrylic and ceramics are companies specialized in these products and there are a considerable number in Portugal. Although the companies which supply laboratories with metallic alloys are big metal manufacturing companies, they have a small department directed to dental laboratories. The dental equipment comprises large and small equipment. As an example of large equipment, there are autoclaves, sterilizer and digital imaging system. Considering small equipment, there are amalgam removal systems, handpiece cleaner, and ultrasonic cleaners.

Distribution

In this point the value chain can be different, in other words, it can have a distribution company only responsible for transportation and marketing the product (Figure 5.3) or, on the other hand, it can present supply companies doing their own transportation and marketing (without a distribution company in the value chain). Distribution will be analyzed in detail in section 5.3.3. Distribution channels

Laboratory

The laboratories are responsible for manufacturing the dental prosthesis from the mold of the patient provided by dentists. Each prosthesis is made specifically for each patient from the mold, and the techniques of dental laboratories make the shape with the appropriate materials and the all esthetic part of the prosthesis, until its complete fabrication, which will be used for the final customer.

Clinic

In the dentist clinic, the dentists are responsible for choosing the most appropriate type of prosthesis to the patient and make the mold. After the prosthesis being made by laboratories, the dentists are responsible for putting the dental prosthesis in the patients' mouth and make the final adjustments, in order to the prosthesis to be well adapted.

5.3.2. Potential suppliers

The potential suppliers will be the companies which will sell the necessary components to assemble the GEI dental device.

The GEI dental will be constituted by a high range of materials, from valves, high pressure vessels to electronic material. This kind of material is all of high pressure, so it is important that it presents high levels of quality in order to GEI dental to execute its functions without any problem. The majority of materials can be ordered through companies that commercialize supercritical fluid equipment. Each supplier is selected according to the meeting of following criteria: quality of materials, price and trust.

Besides, the company only being responsible for the proper assemblage of devices presents a high external dependence level, so the choice of suppliers and the connections created are very important to the good functioning of the company. The purpose is to make advantageous partnerships with the companies which sell the aforementioned products in order for the company to honor its commitment without unnecessary spending.

5.3.3. Distribution channels

As previously mentioned, the company will focus on the European market, so this section will take into account the European distribution channels.

An essential point to consider is how the product gets to the client. According to the CBI Market Information Database, it is possible to define two main trade channels through which dental products are distributed. The different trade channels are direct distribution and distribution through an intermediary [65].

Direct distribution

If the product is delivered to an end-user, such as dental laboratory is considered direct distribution. The purchases for healthcare professional's facilities are increasingly made through websites, such as the Global Health Exchange (<http://www.ghx.com>), which were developed by the major players in the market. Likewise, the Association of Dental Dealers in Europe (ADDE) and International Federation of Dentists (FIDE) started an initiative to develop an e-commerce site for the industry.

Distribution through an intermediary

Distribution through an intermediary is when distributors intervene as middle-men. In terms of product knowledge, the dental distributors are highly specialized and usually have a large network given its development and experience in dental industry. Among distributors and dental specialist, user groups, and technicians responsible for maintaining the equipment, there is a high level of communication and cooperation. CBI Market Information Database recommends for developing countries suppliers that distribute through an intermediary. They consider that direct distribution is very difficult for newcomers to the market for various reasons, such as company size, service, personal relationship, reputation and activities. The sites known as dental depots are used in many of the European markets to sell dental equipment to dental practitioners via distributors. Dental depots stock has a wide range of products and sells their products directly to the public and private dental practices [65].

5.4. Market trend, Growth potential

5.4.1. Potential value of market

The final customer of GEI dental are the dental prosthesis users. Following next, a global view of dental wearers in the last 12 years and projections until 2020 is presented.

According to the U.S. CENSUS Bureau International Database and GSK Incidence Data, in the last twelve years there was a growth about 15% of dental wearers (Figure 5.4). In addition, it is expected that in the next eight years dental wearers will grow about 20%. This growth of dental wearers through time and the prediction that it may continue to increase can be explained by several reasons. They include a demographic shift towards an aging population, along the desire to retain tooth structure later in life, an increased desire for aesthetics and the growing concern and consciousness about oral health [66].

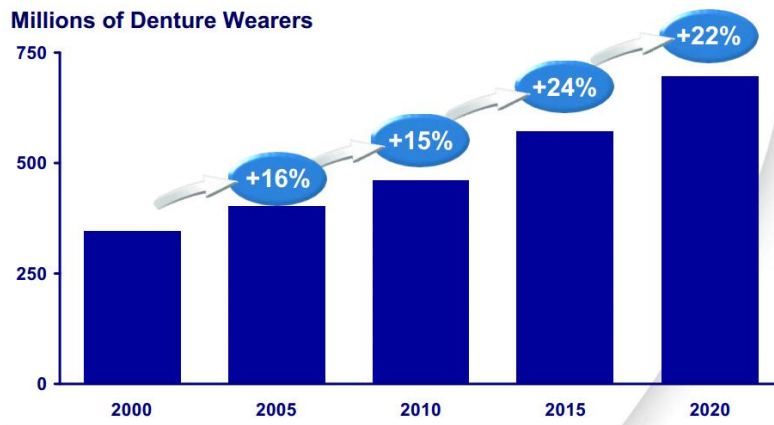


Figure 5.4. Evolution of global dentures wearers over the years [67].

5.4.2. Growth rate of industry

The fast growing of the dental industry sector is presented in Figure 5.5. From 2006 to 2013 the compound annual growth rates (CAGR) for the dental implants market in Europe is estimated to be 13.7 per cent [55].

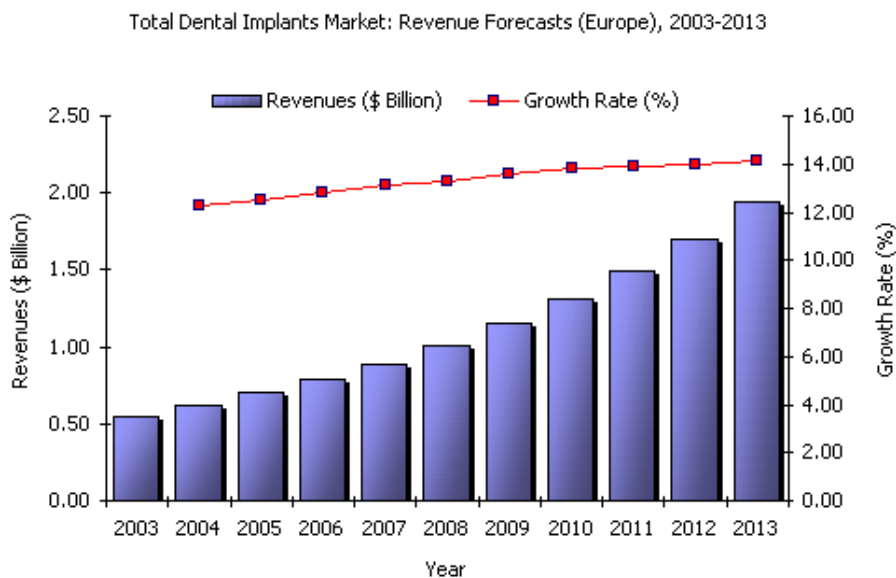


Figure 5.5. Revenue forecasts for the total European dental implants market from 2003 to 2013 [53].

The Figure 5.6 presents a global dental consumables market analysis by product segment, 2008-2015. The restorative and cosmetic supplies, materials, and prosthetics is the product segment with the largest revenues, in 2010 was valued at \$9 billion and in 2015 is expected to reach \$11.7 billion. In 2010 the global dental consumables and prosthesis market was valued at \$15.9 billion, while in 2015 the market is expected to reach \$18.5 billion [68].

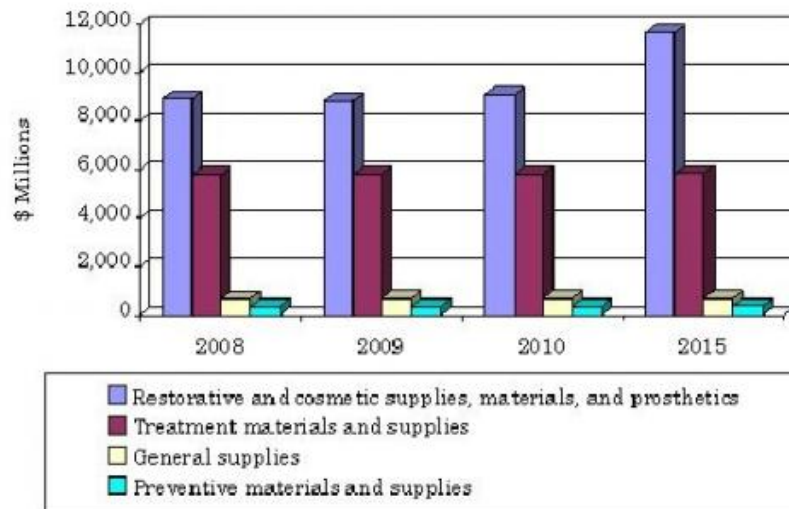


Figure 5.6. Global dental consumables market analysis by product segment, 2008-2015 [68].

The dental market presents a solid growth determined by a number of factors. Some of them are already mentioned above when the growth of dental prostheses wearers is explained, because the growth of both dental prostheses wearers and dental market are related. In addition to these factors, there are others, which include the growth of available profits, a desire to meet dentists and patients' needs, a bigger concern for oral preventive care, including the durability of natural teeth, and an interest in technological development [65-66]. This last item, technological development, represents a great benefit to global dental market, since it is an important tool for the dentists to offer a higher quality treatment to their patients. The technological innovation of the dental market has been growing considerably compared to the dental market in general, which is still expected to continue in the future [66].

5.5. Key Stakeholders

Regulatory authorities

The commercialization of the product can be influenced by the product's certification and approval of certain authorities. The accreditation of Infarmed in Portugal is crucial to marketing any health product in Portugal, moreover it is important to obtain the CE marking.

The suppliers and distribution companies

The suppliers and distributors are essential partners in order to deliver a high quality product to the customer. Establishing good partnerships with suppliers is crucial to guarantee the components which

constitute GEI dental, to assembly the device on time, in order to meet deadlines. The choice of the distribution company which will represent the GEI dental is another significant point to take into account because it is important to have a trust, efficient and quality transportation and divulgation service of this new product to the international dental market.

6. Commercial strategy- Legal aspects

6.1. Intellectual property

The product came up from the application of the technology with the following patent-PT 103360 A. The main features of the patent are presented in Table 6.1 and the main steps of the patenting process are presented in Table 6.2. The patent PT 103360 A has only a Portuguese protection.

Table 6.1. Patent features.

Publication number	PT 103360 A
International classification	B29B 15/10 (2006.01) C08J 3/20 (2006.01)
Coordinator	IBET (Instituto de Biologia Experimental e Tecnológica)
Inventors	Catarina Maria Martins Duarte Ana Rita Cruz Duarte Ana Vital Morgado Marque Nunes Carlos Tiago Baioneta Soares Cravo

Table 6.2. Steps followed in patenting process.

Filing date for National Patent with Instituto Nacional de Propriedade Intelectual (INPI)	2005.09.28
Publication of filing National Patent PT 103360 A	2007. 03.30

Current situation

Due to the high cost of the patent's maintenance, the payment was cancelled and as a consequence the patent expired. Although the current project had started based on this patent, it presents substantial differences from the idea described in the patent. As a result, the GEI dental will require a new patent.

Possibility of a new patent

The protection of an idea is important to avoid copies, however the patenting involves a high cost initially and also for maintenance of the patent. In addition to the process of patenting being expensive, the compliance of restricted criteria is necessary. Licensing an idea is a complex and not always successful process. The three main criteria to consider patenting an idea are the following:

New: the idea should never be mentioned in patents, scientific articles or oral presentations.

Inventive activity: It is not obvious to an expert in the area.

Industry application: it should be reproducible.

Firstly, in order to guarantee the novelty of the idea, an intense search was made related to the patents or scientific articles which can be compromised at the possibility of patenting our idea.

Impregnations and extracting methods using $scCO_2$ have already been described in various patents and articles. The possibility of patenting the idea appears in the application given to the technology, and not in the technology itself, because the novelty is the application and not the process. In addition, a new and sophisticated prototype should be created. The results of the survey about extraction of MMA by $scCO_2$ from dental prostheses or the impregnation with active principle are positive because no scientific article was found nor any patent reporting to it specifically. However, there are studies that have reported the use of $scCO_2$ in the extraction of MMA from PMMA used in other products and not used in dental prostheses, and there are even more scientific articles reporting $scCO_2$ as polymerization of the PMMA medium. Therefore the first criterion, the novelty of the idea, may have some difficulties to be fulfilled.

Concerning the second criterion, some barriers may be found. There is a scientific article, "Process design for the removal of residual monomer from latex products using supercritical carbon dioxide" which can question the performance of the second criterion. The article describes the use of $scCO_2$ to extract MMA from the latex [69]. While the article refers to latex products, experts would consider it logical that the process can be adapted to dental prostheses, since the polymer (PMMA) is the same. The same happens with the impregnation of dental prostheses, because there are already scientific articles which report impregnation of PMMA using $scCO_2$. Even though no patent or scientific article specifically reports the extraction and the impregnation of dental prostheses, there are already articles about MMA extraction from PMMA and about impregnation of PMMA using $scCO_2$ but in different products that are made of PMMA. So, an expert would be considering it logical that the process could be adapted to dental prosthesis, since the polymer is the same.

Finally, reproducibility is also assured since it is possible to improve the prototype in a way as to turn technology into a more easily manipulated and more automated system in order to commercialization to be possible. Therefore, the invention will have industrial applicability.

In conclusion, besides the high cost of the patenting process, there is a high probability of the criteria not being achieved. Furthermore, by the scenario presented it might be difficult to patent the idea. However, there will be the possibility to patent the final product, since its characteristics are completely new. Nowadays there is not any device enabled to remove MMA, after the preparation of the dental prostheses, from the acrylic or impregnate dental prostheses with therapeutic active principles. So, after the development of the GEI dental, which includes obtaining the best operation conditions' for both the processes and having different impregnation systems of active principles, it is expected to have a new product which can fulfill all the criteria referred above in order for the GEI dental patent to be possible. Therefore, it is expected that it may be possible to patent a prototype of the GEI dental device enabled to extract MMA from the acrylic used in dental prostheses and to impregnate dental prostheses with different active principles and the respective drug release profile well known.

6.2. Regulatory concerns

The GEI dental is a device by which dental prostheses are manipulated, in other words, the device will change in a certain way some dental prostheses' characteristics. Dental prostheses are a class IIa medical device (medium-risk devices), consequently it is exposed to several restricted rules and norms. In addition, this product is considered a medical device because it involves active drug administration systems which will be used for human beings for the purpose of the prevention and the treatment of diseases. The manufacturing of GEI dental should be done in a way as to guarantee that these restricted rules are maintained.

In order to offer a proper treatment to the patients, it is crucial to consider the safety of the medical devices. So, there are entities responsible for checking and assuring the safety features of several medical devices and for guaranteeing that the untested or the inadequately tested devices do not enter the market [70]. The certificates and rules which GEI dental should achieve to be commercialized will be presented next.

EMEA

All the information that will be mentioned following can be found at the European Medicines Agency (EMA) homepage. The evaluation and supervision of medical products for human or animal use is the responsibility of the EMA which is a decentralized body of the EU. The aim of this agency is protecting human and animal health. In order to enter in the EU market, medical devices must obey the Directive 93/42/EEG and have the CE marking. The producers of drugs and medical devices who want to commercialize their products in the EU must only submit one single marketing authorization application to the EMA, in which the documentation should be written in English, French or German. An enterpriser who does not have the company registered in an EU country should designate a single authorized representative in the EU [71].

ISO

A standard for quality management system for medical devices called ISO 13485 was developed by the International Organization for Standardization (ISO). This standard is founded on ISO 9001:2000 and provides guidelines to the companies to implement and maintain a quality management system. In many countries this standard is considered as a way of achieving Good Manufacturing Practice [71]. In deciding to deploy ISO, the company must hire a company that will conduct a certificated audit, to verify if the company meets the requirements of the standard. This certificated company is an independent entity and authorized to conduct audits.

IEC

Furthermore, there is also regulation related to electrical equipment. The international organization responsible for the preparation and publication of International Standards for all electrical, electronic and related technologies is the International Electrotechnical Commission (IEC). The IEC 61293 is an international standard, which establishes minimum requirements and general rules to electrical equipment and other characteristics allowing the appropriate and safe installation of electrical equipment [72].

CE marking

The requirements to obtain CE marking for all medical devices are mainly a technical documentation, a risk analysis, a proof of compliance with the essential requirements of the directive and a product related declaration of conformity issued by the manufacturer. The non-sterile class I devices without measuring function are the only ones that do not need the involvement of a Notified Body. The mentioned devices are marked by the producer's only responsibility with the CE marking without a number. On the other hand, all the other devices need the certification by a Notified Body before the manufacturer can put the CE marking in combination with the number of the Notified Body on the device. The manufacture can choose different certification routes, depending on the device class [73]. In addition, due to the equipment being electrical, CE marking is required to electrical equipment.

Infarmed

Infarmed is the regulating entity in Portugal. According to the official Infarmed website, the entities holding facilities engaged in the manufacturing of medicine and health products are under the industrial licensing in accordance with the applicable law- Decree-Law nº 209/2008 of 29 October, Decree nº 8/2003, 11 April, Ordinance nº 464/2003, 6 June. The entity coordinating the industrial license is the Ministry of Economy and Innovation with Infarmed participating as a consulted entity in the field of manufacturing medicine and health products.

7. Business Model

The business model describes the way a company generates revenues by specifying its position in the value chain [74].

7.1. Value Proposition

The acrylic resins are one of the materials mostly used in dentistry. However, it presents certain limitations, and as consequence the referred material has been widely studied in recent years with the purpose of improving it. The mentioned material is a polymer PMMA and its monomer is MMA. One of the main features of the material is releasing MMA when the patient is using the dental prosthesis, which has adverse effects (Chapter 3 Market Pain). This feature is a dental professional's concern about the use of acrylic in dentistry, and it was even referred by one of the dental professional addressed (Appendix 2). Another important feature in oral health care are the infections. Very often dental prosthesis users suffer infections and other characteristic diseases associated to dental prostheses use. In addition, malodor is another problem associated to the denture users and a good breath is a characteristic which everyone desires.

The GEI dental is presented as a solution to solve the above problems in dentistry. The technology provides both an improvement of acrylic properties and adds favorable characteristics to dental prostheses. In addition, this product belongs to a new generation of green products, which is a very important aspect, allowing the association of dental industry with supercritical technology or even presenting supercritical technology to the dental industry.

7.2. Entry in the market: Value chain

The GEI dental will enter in the market through the creation of a start-up, Sustainable Solutions (SS). The company will be responsible for manufacturing the product and for maintaining the equipment after the acquisition by dental laboratories.

The various components for GEI dental come from outside suppliers (see Chapter 5, section 5.5.2. Potential suppliers) and the SS is responsible for the manufacturing of the GEI dental device. The manufacturing consists in assembling and testing. SS team is responsible for properly assembling all components in order to obtain a high quality product. Afterwards, the product is tested in our installations, because if any kind of problem occurs it can be repaired before it is delivered to end-users.

The product, after being manufactured, will be commercialized by two ways: either directly to the dental laboratories or through distribution companies. The direct sales to the dental laboratories will be

performed by SS team directly to the dental laboratories. On the other hand, the GEI dental can also be sold by companies specialized on the sales of dental equipment which usually supply the dental laboratories. As mentioned in Chapter 5, this type of companies has a high level of involvement and knowledge about dental industry and as consequence it is a great option to commercialize and spread the product. In addition, the distribution company will be responsible by the maintenance of GEI dental after being sold. Therefore, the SS presents a positioning in the dental industry value chain as a dental laboratory supply (Figure 7.1).

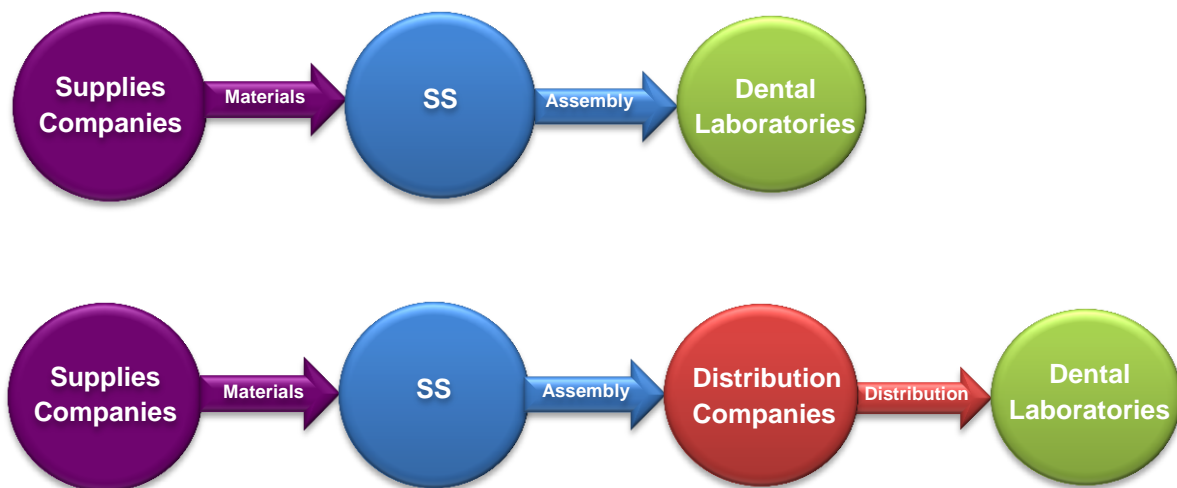


Figure 7.1. GEI dental value chain.

The steps to increase the value capture to GEI dental are presented next:

1. Since the product is very recent, it will be essential to develop, improve and test it.
2. GEI dental will be mainly presented to the dental market as an innovative, useful and necessary product which will improve dental prostheses.
3. Besides the product's improvement, dental prostheses stand forward by the use of supercritical fluids which become a friendly environmentally product. GEI dental appears as an emergent technology targeted to sustainable development.
4. Participation in competitions of entrepreneurship and innovative technologies, in order to obtain financial means to support the company in a first stage.
5. Directing sales to the dental laboratories or selling through dental suppliers according to what becomes more advantageous. In the beginning of the commercialization of the product in Portugal, directing sales to the dental laboratories seems to be the better option.
6. Personalized and high quality service, including availability of monitoring and clarifying the customer when necessary. In addition, the responsibility to saving the equipment maintenance which will be an additional paid service.

7. The participation in dental fairs in which the product will be presented to potential customers.
8. Create a solid network in the dental industry.
9. The possibility of partnership or associations with dental companies interested in new products, which makes the product more competitive and allows a bigger acceptance in the dental industry.
10. In addition, the acrylic is used in many other areas besides dentistry. As a consequence, the commercialization of the equipment may be extended to other areas.
11. The company will always be involved in research with the purpose of enhancing and developing new applications to GEI dental, increasing its market.

7.3. Revenue model

Generating revenue allows companies sustaining themselves and that is an important issue in any business.

The mainly source of revenues of SS comes from the sales of the device. Besides the profits related to the sales of the GEI dental device, the profits will come from the maintenance of the device which includes periodic cleans and checkups. Therefore, the company will be generating its revenue sales both by selling the GEI device and by maintenance services.

The sale will be directly to customers with a practical demonstration or through an intermediary as mentioned above. The device and the other services will have a fixed cost which will be presented to the customer in the beginning of the contract.

8. Marketing Plan

8.1. Vision, Mission and Objectives

Vision

Sustainable Solutions wants to be recognized as a high quality company which contributes to technological progress.

Mission

Sustainable Solutions aim to make available safe and environment friendly technologies to improve dental care.

Objectives

The company's objectives are the following:

1. Attracting potential customers: the main goal of the company is to enter into the dental industry, so the acquisition of first clients is primordial.
2. Acceptance of the dental sector as an important product to lead the dental prosthesis to another level.
3. Partnerships with components suppliers' as well as influent dental companies: the establishing of partnerships with distribution companies and suppliers guarantees an efficient delivery service. On the other hand, the partnership with dental companies can be important to implement GEI dental in the market.
4. Company proposes effective solutions to create innovative and high performance oral care products using a sustainable technology.

8.2. SWOT Analysis

Strength <ul style="list-style-type: none">• Innovative technology• Product environmentally friendly• Increase of dental prostheses value making the process more successful and less painful• Improvement of PMMA, reduction of the cytotoxicity.• Slowing infections and rejections of dental prostheses wearers• Introduction of supercritical technology on health care market	Weakness <ul style="list-style-type: none">• Duration of extraction and impregnation processes• Alternative materials to the acrylic have been used in dentistry• High costs of the components that constitutes the product• The high product price• Time needed to optimize the product• High development cost• New company with an innovative product
Opportunities <ul style="list-style-type: none">• Aging people• Increase of dental prosthesis wearers• Huge market potential• Patients' concerns for quality treatment• Increase patients' demand for more• Growth of dental industry - intensive needs for more dental equipment, material and technologies• Partnerships with influent companies• Need/demand for new technologies• Demand for environmental technologies• Concern with future generations (development sustainable)	Threats <ul style="list-style-type: none">• Development of competing materials• Patent expired

8.3. Marketing Mix

8.3.1. Product

In the development of a product, it is necessary to define the benefits that the product can offer to the client [63]. Following next, the attributes of the product will be exposed.

Features

GEI dental is a device with two distinct functions:

- Extraction of residual monomers MMA which has been related as responsible for allergies (Chapter 3 Market Pain).
- Impregnation of acrylic (material used in dental prostheses) with an antimicrobial, anti-inflammatory, fluor or even a substance against malodor

The main feature of the device is the use of SCF, particularly the $scCO_2$. The equipment, which was intended to marketing, is evolving to sustainable development. The market trends are going in the direction of this new approach, which replaces old and pollute organic solvents. Therefore, the product, besides improving the properties on most of the used materials in dentistry, and also in others areas, helps the future, which is essential to preserving the world for future generations.

Quality

Quality is essential in our product because the equipment will be used with the purpose of improving a medical device. The trust in the product is crucial to attract the customer's confidence, as to ensure that the equipment respects the strict rules associated to medical devices and does not to change any important property of dental prostheses. The quality is ensured by competent regulatory entities and the product has all required certificates as described in Chapter 6 in section Regulatory Concerns.

Design

The product's design takes into account two main aspects presented next:

- **Simplicity** – The equipment will be all automatized so that any person is capable of using it, because it is essential take into account that the device will be used by dental technicians without any knowledge about supercritical fluids.
- **Size** – Dental laboratories do not usually have large areas, so it is important that the device does not occupy a large space.

- **Appearance-** The outside part of equipment is another feature to be considered because the appearance also conveys a message. The product should look sophisticated, modern and simple.

Logotype



Figure 8.1. SS logotype.

The colors, image and letters' type have been taken into account in the logotype. The use of green is on purpose, in order to transmit the concern and commitment to developing sustainability. Blue is associated to health care sector. The global image is clean and sophisticated as the company itself.

Slogan: Dental care moves to a sustainable future free from diseases.

Packaging

The device should be well packaged as to guarantee quality and avoid damaging during transportation, in order to arrive to the customer in perfect conditions. In addition to the importance of a well packaging, the logo will be presented in the package.

Guarantee

The company ensures solving any problem in a two year period after acquiring the product. The period of guarantee was chosen based in the guarantee periods considered by dental companies.

8.3.2. Place

In this section the best and most advantageous way of delivering the product to the customer is discussed.

Firstly, it is important to define how transportation is being done to the customer to commercialize GEI dental. Due to high logistic costs related to transportation, usually only companies with a large dimension, with both great volume sales and market penetration, have their own transportation department.

The business will initially be only in Portugal, including the company's office. There are already several Portuguese companies responsible for dental products' distribution. However, Portugal is a small country, as well as the dimension of the market, and so this is one of the reasons why it is our market test. Therefore, in the early stage of the company, low amounts of orders are expected and, as a consequence, it is predictable that the process of transportation will be simple. Although it is considered that the companies in an early stage should be delegate the distribution to specialized firms be a better option, the direct distribution may probably be a better option during the first stage of commercialization in Portugal, and the SS team could be responsible for publicizing and commercializing the product.

After the product is implemented in the Portuguese dental market, it is expected to be expanded to the European dental market. The European market requires a quite complex network distribution because of its large scale. As mentioned in Chapter 5, there are already well-defined networks of dental products distributing across Europe. Using the referred distribution companies seems the best option to GEI dental. An important feature is looking for dental distribution and making partnerships with them to guarantee a delivery service of quality to our customers. These companies present professionals with a good knowledge of this sector and usually have a high range of clients, which assures facilitating the access to them. In conclusion, the option of distribution through an intermediary could be a good choice in a first stage of the product's presentation in international dental market, in order to provide an extensive and easier promotion of the product. There are several trade channels responsible for the dental equipment distribution, however, it is important to choose a company interested in publicizing and marketing our product. One of the options is creating an exclusively contract with a company.

8.3.3. Promotion

The communication of company value propositions to customer is an essential point to consider on establishing and maintaining any kind of relationship with customers [55]. In launching a new product, its disclosure is extremely important. Therefore, the outlining of the product's promotion is one of the most important actions which deserve the maximum of attention and effort. A successful promotional campaign is crucial to the product's introduction in the market.

Personal selling

In the healthcare sector, where trust is essential, direct contact is the strategy that has been used the most. GEI dental will be adopted as a personal selling tool in order to establish a relationship with customers based on trust and proximity.

In the case of GEI dental, this tool is highly important because it allows this innovative product to expose its features and benefits. In addition, this tool also allows explaining how the device operates by a practical demonstration and receive the customers' feedback by perceiving their reluctance and needs.

The company will have a department specialized in this kind of sales in order to guarantee that the promotional actions convey the right message to the potential customer and with the purpose of improving through time.

Public relations

The presentation of the product in dental industry is important to launch both the product and the company itself. There is a high range of events in this area, such as conferences and dental fairs. The company's presence in that type of events is essential to begin to build a solid network.

The company will select some of the most important events based on geography and presence of potential customer targets, in which the company will promote their message and product.

Advertising and sales promotion

Besides divulgating the product in dental laboratories, it is important to publicize it among dental prostheses wearers and dentists. The product's publicity oriented to dental prostheses wearers is a tool to become popular among final customers. Thereby, the patients will start asking to their dentistry about this product and, as consequence, the dentist will require to laboratories this innovation in the dental prostheses ordered.

Nowadays there is already a high range of platforms through which the publicity of the product is easy and does not involve high costs. In addition, these platforms allow promoting the product to a large number of people, including not only dental laboratories but also the potential users of dental prostheses manipulated by GEI dental. This is extremely important to access and approve the product.

Examples of platforms are presented next.

The website is the simplest and cheapest way to present our company and products to the potential customers. Nowadays all companies have a website where they expose their values and what they intend to offer to their customer, therefore it is an important tool to promote not only the products but also the company's message. The website should be conveying a proper image of the company and products. In our case, the website should be presenting a green message, in other words, it must be

showing to website viewers that GEI dental is meeting the sustainable development and concern needs about future generations. In addition, another purpose of the website is to show the needs of dental prostheses wearers and how this high quality technology can solve them.

The email is an important and easy tool to establish the first contact with potential customers. This platform allows promoting GEI dental more directly to dental companies.

In addition, this tool is also useful to promote the existence of this product to dentists because the dentists could start to require this technology on the dental prostheses ordered to laboratories.

Social networks are another useful platform especially to present the product to the general public. By presenting the product on social networks, it may allow the public to question why their dental prosthesis do not already have this innovation and eventually ask their dentistry, in the next appointment, why that is so. Therefore, this platform basically allows promotion to a high and global range. This tool is also relevant to another important purpose of the company-the concern for sustainable development. Social networks play an important role in public opinion turning out to be a great means of demonstrating the importance of these companies which commercialize green products replacing old and damaging technologies, such as organic solvents.

8.3.4. Price

The definition of the price of the product is always a complex process, and so several aspects need to be considered.

Product costs

Firstly, it is important to take into account how much will be spent to manufacture the device, including all the materials and workforce.

The company should determine its fixed costs and variable costs associated to the manufacturing of the product. The required materials to compose the device have high costs, as well as the workforce, which should be specialized technicians, also requiring high costs. Therefore the price of the equipment will have high costs of manufacturing, and the product will become uneconomic.

Price of similar equipment

The use of supercritical fluids in dental industry is a novelty, so in fact there is not any similar equipment. However, both the prices of the other equipment presented in dental laboratories and the prices of the devices associated to supercritical technology with other purposes were considered. The price of supercritical technology is much higher than the prices of the equipments used in dental laboratories.

Product price

The expenses associated to the components' costs will determine the final price of the GEI dental. The price that the GEI dental will have is 45 000€. The price is very high comparing to the common dental equipment because the high cost of the components that are required to assemble GEI dental lead to the mention value.

Value created to the client

Another important feature that is important to define is payback, in other words, the time that a client delay to recover the money invested in the GEI dental device. The parameter considered was the number of dental prostheses sales during a month by dental prosthesis. Therefore, by an estimated number of dental prostheses sales and by adding an extra value in the price of dental prostheses, a payback is possible to predict. The knowledge of this value by the customer is important because it is a parameter that will be present in the purchase decision.

Then, after consulting some dental professional of target customer, it is possible to define a credible add value created to the client by GEI dental. The add value that the dental laboratories could perform to each dental prosthesis manufactured is about 50 €. Considering that a dental laboratory does not make less than 30 dental prostheses per month, the payback will be in less than 3 years. In the case of large laboratories, for example Maló Clinics which was a dental laboratory address, and according to the dental professionals addressed, they produce 600 or more dental prostheses per month. Looking at both scenarios, the large and the small dental laboratories, a 2 year payback was considered, which is very positive.

Customer perception of pricing

In order to obtain a considerable profit of the product, it will be presented to the dental market as a product of high quality and that reflects on the price. The product which is intended to be commercialized is innovative, made by green process and technologically complex. Therefore, the features of the product above mentioned justify the high price.

Although the initial perception of future customers about the price could not be the best, since they could be considering it too high, the payback is about 2 years, which is a reasonable time to make the investment worth.

9. Product Development and operations plan

9.1. Prototype to finished product

GEI dental still needs to be developed in certain aspects to convert the prototype to a finished product available for marketing. The idea of this product has recently emerged and as a consequence there are still several parameters to be developed. Probably a year will be at least necessary to develop and test the product before reaching the market. The main points to take into account are discussed and listed below.

The only tests made were to inquire and verify whether this technology could be applied to dental prostheses. So, the product needs to be developed and tested. Firstly, a primordial issue is defining the optimal conditions of operation, which will require a significant time and commitment. The main objective is to define the operation conditions (temperature and pressure) in the shortest operation time possible, obtaining an efficiency process. In addition, it is necessary to test the impregnation of different active principles. The active principles usually used in dental care will be tested in order to offer a high range of viable and efficient options to the customer. In conclusion, in a first stage, to convert the prototype into a finished product, it is essential to define a better process of extraction and impregnation, in order to take the maximum advantage of technology and guarantee a high quality to the product.

After the product being optimized in order to guarantee the maximum efficiency of processes, the equipment being completely automatized is other aspect to take into account in the prototype conversion into a finished product. So, the device should have an electrical component. Afterwards, due to the dental laboratories usually not presenting large dimensions, the device should have a relatively small size. Therefore, converting the initial prototype in a product with these parameters is essential in order to turn this technology saleable and easy to use.

9.2. Equipment

The equipment required will be simple, only the common office equipment and the equipment necessary to manufacturing the product. Concerning the common office equipment, tables, computers and chairs will be necessary. Communication tools, such as cell phones and portable computers are also required equipment by the team.

In manufacturing the device, the necessary equipment will be protection eye glasses and a box tool, which brings all the necessary material to assemble the GEI dental.

As mentioned above the main components that constitute the GEI dental are:

5. Liquid pump
6. Valves
7. High pressure vessel
8. Back Pressure Regulator (BPR)
9. Compressor
10. Temperature and Pressure gauges
11. Filters

9.3. Geographical Location

Besides the SS being an assembly company, the better location for the company is a warehouse in an industrial area. The space does not need to be very large, which is an advantage considering cost.

10. Team

The SS team is a crucial issue because the success of the company depends also on a good and adequate team that will maximize the chances of success. The company requires a high specialized teamwork in different areas with high motivation in order to create a successful company.

The SS organization there will be two stages. Initially, having a workforce with knowledge about supercritical fluids is primordial, in order to develop, improve and test the product. Another essential requirement is a specialized team in electronics to help the conversion of the prototype into a finish product. A team with the referred skills of about three people is required initially in the first year, when the product is still being developed.

On a second stage, when the product starts to be commercialized, the team can be increased and divided in specific departments following described.

Research and Production

Two elements of the first team referred above are maintained in the production and research department. The technicians with electronic and supercritical knowledge are responsible for manufacturing the device. They will be charged for the development and research of the product. In addition, to the technical skills, it is important to show passion about what they are doing and dedication because they need focus in the project.

Marketing and Sales

The marketing and sales department will be given to one person with the proper profile. This person will be responsible for the divulgation, promotion, product sales of the company and its products. Therefore, having people with both communication skills and a deep knowledge of the product, including the technology and dental area, is important.

Finances

The company's finances should be given to a person with proper skills and knowledge about finance management. An accountant is essential because it is important the company present a stable and positive financial situation. The referred person could be a freelancer accountant who treats the company's accounts monthly.

Project Management

Coordination and organization are vital to the good functioning of any company. This department is responsible for taking important and crucial decisions, concerning both human resources management and production issues. The organization must have someone who keeps people focused on a daily basis. This person should be able to lead the group and ensure that all aspects of the project are covered and this function will be played by the CEO.

According to the departments division mentioned below a SS organogram is presented.

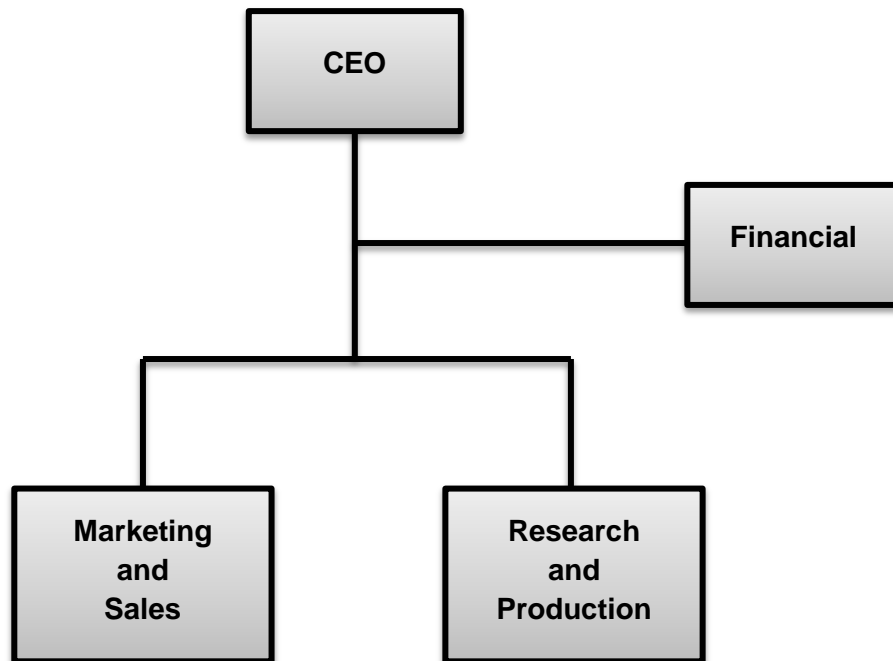


Figure 10.1. SS Organogram.

11. Implementation

11.1. Financial Plan

The financial plan was made to five years of SS activity and it starts in 2013. The product's development is performed during the first two years and the commercialization will start in 2014. The studies with the purpose of developing the product will continue to take place in IBET. The projections made during the implementation of this financial plan are only estimated values and not precise values.

11.1.1. Revenues

Sales' projection will be presented next in Table 11.1. The estimated values are supported by the conversations with the dental professionals addressed, on the development of dental industry over the last twelve years and the next eight years and on the market size (Chapter 5). These values are uncertain due to being very difficult to predict who will indeed buy GEI dental.

The revenues will come from the sales of the device and by the maintenance of the device (only the devices sold in Portugal) which includes periodic cleans and checkups. The selling price stipulated to each GEI dental will be 45 000 € and the price of each maintenance services will be 100€. The GEI dental should need maintenance at least two times a year.

Table 11.1 Sales projection for the first five years of SS activity.

	2013	2014	2015	2016	2017
Sales in Portugal	-	6	15	30	30
Spain	-	-	4	15	30
Other European countries	-	-	-	30	60
Number of sales	0	6	19	75	120

Table 11.2. Revenues projection for the first five years of SS activity

	2013	2014	2015	2016	2017
GEI dental sales Revenues (€)		270 000	855 000	3 375 000	5 400 000
Maintenance sales Revenues (€)		1 200	3 000	6 000	6 000

Sales Projection

In 2013 the SS will advance only on the development of the product, consequently it will not be sold any device this year. In this first year, it is expected to develop the product until obtaining the best possible extraction process of MMA (in terms of efficiency and time). On the other hand, in terms of the impregnation process, it is expected unless one active principle to be impregnated in dental

prostheses with the maximum efficiency possible and with the proper parameters required by the dentists (short time of process, amount of active principle to impregnate well study, including drugs release profile well known).

In 2014 the development of the product continues and more systems of impregnation will be developed in order to obtain a more versatile product to meet orthodontia needs. After obtaining the final product, the next step is to patent the final product and the accreditation and validation by regulatory authorities in order to have a high quality product to be commercialized. In this year, it was assumed to sell about 6 devices to the biggest and more developed dental laboratories in Portugal, which are the Portuguese laboratories interested and receptive to new technologies

In 2015, it is expected to have the final product more complete with a high range of impregnation systems with different active principles well studied and explored. The product should be prepared to be presented to international market, so the international patent of the product will be required. The first international dental market to which GEI dental will be presented is the Spanish due to being the closest country geographically.

In 2016 a jump on the product sales' is assumed, because the product is expected to present a sound position in the European dental market. In the next two years, the continuing growth of the sales is predicted because it is believed that, due to GEI dental being a high quality product and meeting orthodontia needs, after be divulgated in European market, it will be required by most of the dental laboratories. The main factor which could bring caution to the projection sales or that could lead to the failure of the projection sales is the high price of the device, which can induce the laboratories not to acquire GEI dental.

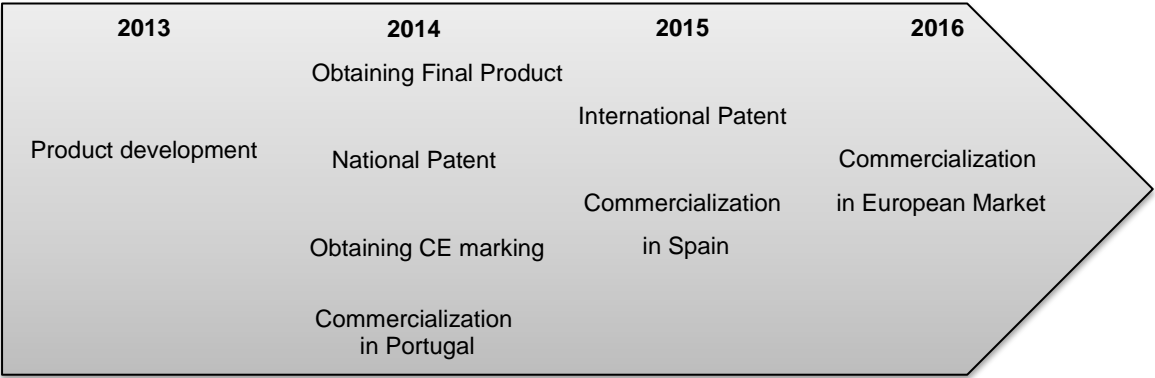


Figure 11.1. Activities timeline for the five years of the SS company.

11.1.2. Expenses

Several costs must be taken into account, such as marketing costs, human resources costs, research costs, among others.

Table 11.3. Expenses related to the first five years of SS company activity.

Expenses (€)	2013	2014	2015	2016	2017
Research and product development	5 000	5 000	–	–	–
Equipment	60 000	–	–	–	–
Certifications	–	30 000	–	–	–
Industrial Property	–	2 000	6 000	–	–
Office Rent	2 400	2 400	2 400	2 400	2 400
Total	67 400	39 400	8 400	2 400	2 400

Research and Product development

The product will be developed during the first two years. Although the product initially will be developed in installations of IBET, there will be costs associated with the necessary experiments to develop the product. Current material of laboratory will be necessary, samples of active principles and CO₂ cylinders. In addition, it will be necessary buy protection equipment, such as eye glasses protection and to buy material necessary to assembly the GEI dental, such as a tool box.

Equipment

The expenses associated to the equipment include the triple of the costs associated to the acquisition of a similar device of the product expected to commercialize, in order to perform the experimental and prototype tests, the cost of each equipment is around 20 000€.

Certifications

The estimated value to certification expenses is based on the official website of CE marking.

Industrial Property

The industrial property strategy will comprise two steps: in 2014 the national patent of the final product will be required and in the next year the international patent.

Office rent

The value considering to office rent is real and includes all the office equipment.

Table 11.4. Marketing expenses in the next five years of SS activity.

Marketing expenses (€)	2013	2014	2015	2016	2017
Website design	500	-	-	-	-
Trade shows	-	9 000	9 000	9 000	9 000
Other costs	500	2 000	2 000	2 000	2 000
Total Cost	1 000	11 000	11 000	11 000	11 000

Website design

The Website is an important tool to divulge the company and the product (Chapter 8). There are several companies specialized in the creation of a website according to the image and message that the company intends to show.

Trade shows

Trade shows are important events to publicize the GEI dental and it is expected that SS will annually go to at least three trade shows. The value includes the cost with the travels, accommodation and other fairs' expenses.

Other costs

Other costs refer to expenses with transportation and promotional actions associated to the publicized product, which include visit cards, leaflets, screens and others. The value is only an over supposition and does not have any real support.

Table 11.5. Human resource costs.

Annual salaries* (€)	2013	2014	2015	2016	2017
CEO	8 400	14 000	21 000	21 000	21 000
2 Specialized Technicians	14 000	22 400	28 000	28 000	28 000
Accountant	2 400	2 400	2 400	2 400	2 400
Marketing Manager	-	12 600	14 000	14 000	14 000
Total costs	24 800	51 400	65 400	21 000	37 400

*14 months are taken into account

Table 11.5 presents the salaries of SS's team for the first five years of activity. The salaries were based on the current salaries practiced in Portugal, including the value attributed to pay annually to the freelancer accountant who deals with the company's accounts annually.

Table 11.6. Variable costs during for the first five years of SS's existence.

Variable expenses (€)	2013	2014	2015	2016	2017
Components	–	120 000	380 000	1 500 000	2 400 000
Royalties	–	2 712	8 580	33 810	54 060
Transportation	–	3 600	3 600	3 600	3 600
Distribution	–	–	63 000	708 750	1 417 500
Total	–	6 300	75 150	746 100	1 475 100

Components

The components are the necessary components to assemble the GEI.

The variable costs are the cost that will depend on the unit of the devices sold. The costs entailed by SS with the components that constitute the product depend on the unit sales, the materials will be ordered according to the devices ordered by dental laboratories. The price of each material necessary to the GEI dental assemblage was based on real values performed by the suppliers' companies. The materials will have a cost of 20 000 € per unit sold, this value is the soma of the price of the each component that constitutes the GEI dental device. The price of each component is based on real values practiced by supply companies.

Royalties

Since all the research and one of the patent owners is IBET, it has the right to royalties on the devices' commercialization. Royalties in the field usually range from 1% to 5% for each unit sold. This value will be negotiated before starting the commercialization, but in the financial plan it was considered 1% because usually the start-ups get good accords.

Transportation

Transportation costs are related to expenses to move across Portuguese territory, which includes the transportation of the product to the customer.

Distribution

Distribution companies are used to international commercialization, and to the financial plan a margin of 35% of the product sales' was considered to the respective companies, in other words, 35% of the revenues by the sales of the product in the international market will be to the distribution company. The margin considered was based on the commonly margin practiced by the distribution companies.

In Appendix 7 is presented financial plan in detail. Looking to Free Cash Flow is possible to verify that an investment of 200 000 € will be necessary to founded SS company. The Net Present Value (NPV)(15%) to the first five years of activity is 35 501 € and the payback period is 3 years. Finally, the Net Profit after tax of the last year is 1 059 926€.

11.2. Critical risks

The high cost of the components that constitute GEI dental are reflected on the price of product to the customer. Probably it is the highest risk to overcome. The components which compose the device have a high cost and the technicians required must be specialized. Therefore, the product will be presented to the dental market with a high price which could be a barrier in the acceptance by dental laboratories.

Furthermore, a concern about the product is the possibility of the optimal conditions achieved not being the best to the dental professionals. In order to obtain the final product, there are several conditions and points which will have to be tested, developed and enhanced. So, there is the possibility that the product has not the exactly characteristics required by dental professionals. Another risk related to the aspects referred above is the possibility that important active principals may not be associated to this technology. This risk is associated to the product being a new idea and the active principles appointed by the orthodontists not being yet tested.

There is the possibility of not obtaining enough financial support in a first stage of research and the product's development, because interested investors could appear only when the final product was already. Probably, in a first stage of development, the financial support will only come through funds and prizes, which has an associated risk because there is the possibility of not obtaining any funds or these funds not being enough.

The projections sales fail can be another risk. Despite the initial sales being supported in the interviews by potential customers, there is not a guarantee that the referred customers will buy the product and for a long period the sales projections will only be supported based on the market size and in the growth of the dental industry. Therefore, the value given to sales projection is very uncertain and there is a high error margin.

12. Conclusion

There are several possible applications to the GEI technology. The extraction of MMA from the acrylic used in dental prosthesis and the dental prostheses impregnation with active principles was the application considered most interesting to taking GEI technology from the laboratory to the market .

Due to the GEI dental being a new idea, it was necessary to test the effectiveness of the technology applied to dental prostheses. The extraction and impregnation concept applied to dental prostheses was validated through the results of the experimental tests performed. According to experimental tests, GEI dental is able to extract about 68.7% of MMA present in dental prostheses through a process, which lasts about 50 minutes. In addition, GEI dental allows the impregnation of ibuprofen with a %impregnation of about 7% in a process about 60 minutes long, in order to increase the %impregnation to 8% the duration of the process must also increase. The experimental tests results were very promising which strengthens and increases the potential of this product. Other additional experimental test should be done to develop and improve this new idea in order to obtain a final product with a high quality and useful characteristics.

The next steps are enhancing the extraction process and develop new impregnation systems with the required active principles by the orthodontists. The impregnations systems should be developed taking into account the amount of active principle recommended by the orthodontists, and the drug release profile well known and approved by the orthodontists. Therefore, the impregnation systems should have developed together with the orthodontists.

The potential customers of this product are the dental laboratories, and the final users are the dental prosthesis wearers. The target market of this technology are the large European dental laboratories which are interested in innovation and with a solid financial situation. Portugal was the country chosen as the market test for this product. Malo Clinics is one of the target customers, and some professionals of the referred company were addressed. The feedback was very positive, which supports the importance and the need of the GEI dental. During the development of this master thesis, it was possible to verify how important a product with these characteristics could be in dental market.

The GEI dental should be in costumers' mind as an innovative, hi-tech, sustainable, useful product, in which meets a need of the orthodontia.

Analyzing the GEI dental characteristics related to its competitors, it is possible to mention the following advantages – decrease of the risk of allergies due to the extraction of residual monomer, reducing the acrylic resins cytotoxicity, giving dental prostheses new functions, such as allowing dental prostheses users to have a fresh breath and take diary medicine. Furthermore, GEI dental could allow the prevention and treatment of infections.

Due to the patent of the technology having expired, it will be important to submit a new patent. However, the process of patenting is complex because it is necessary to fulfill all the criteria required and achieving some criteria could be difficult. On the other hand, the final product is absolutely new, there is not any device with similar functions in the dental market, and so patenting the final product could be an option to obtain intellectual protection. Concerning regulation issues, no problems are expected, since it is a safe technology without any risk to people's health. So, GEI dental should fulfill all the required criteria by CE marking.

The business strategy will be based on the creation of a start-up, SS, which, in an early stage, will be focusing on the product's development until a final product will be obtained with the desired characteristics. Afterwards, the company will be responsible for assembling, testing and commercializing the GEI dental.

The marketing plan aim is to present the GEI dental as a hi-tech, sustainable and useful product in order to have great acceptance by the orthodontia sector and make important partnerships.

The product is in an initial stage and so several points should be taken into account to convert the prototype into a finished product ready to be commercialized. After obtaining efficient process of extraction and impregnation, size, design and simplicity of the manipulation of the device are other aspects to take into account in the prototype conversion into a finished product. The final product must have a small size, with a modern and sophisticated appearance and completely automatized.

The financial plan was made to first five years of SS activity appoint to an initial investment of 200 000€ with a payback of 3 years. The NPV (15%) to the first 5 years of activity is 35 501 € and the Net Profit after tax of the last year is 1 059 926€.

The main critical point is the high price of the GEI dental, which can lead to difficulties in selling the product to the dental laboratories. The product price is much higher comparing with to the prices of the equipment used in dental laboratories. Despite this, the time that a client delay to recover the money invested in the GEI dental device, the client payback, is less than 3 years, which is a reasonable time to make the investment worth. So, although the initial perception of future customers about the price could not be the best, since they could be considering it expensive, the payback can balance the initial perception of the high price.

Analyzing the entire Technology – Market Transfer Plan, it is possible to verify that, by attributing an innovative application and with a market need, it is possible to bring a technology, until now in the laboratory, to the market and with a potential to be commercialized. The application of this supercritical technology to dental prostheses was a successful choice, because according to the gathered opinions, the dental industry is receptive to this product and there is a considerable market size to commercialize the GEI dental.

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Appendix 1: Performance Map of Medical Pacifier

Table 1.1. Comparative analysis of main competitors of pacifier impregnated with a medicine.

	Portugal GEI	USA Safety 1st pacifier	UK Mothercare	USA TYKES	USA Munchkina	USA Wyoming	USA Dr. Brown's	USA Kidz-Med®
								
Price (€)		2,18	6,85	14,53	2,15	4,63	4,63	7,24
	⊖	✓	✓	✗	✓	✓	✓	⊖
Control of dosage	⊖	⊖	⊖	✓	⊖	⊖	⊖	⊖
Easy dispense medicine	✓	✓	✓	⊖	✓	✓	✓	✓
Easy to clean	✓	✓	✓	✓	✓	✓	✓	✓
Possibility to use various times	✓	✓	✓	✓	✓	✓	✓	✓
Size	✓	✓	✓	⊖	⊖	✓	✓	✓

Appendix 2: Summary of the dental professionals' interviews

In order to have a feedback about what dental professionals think about this product, several dental professionals were addressed. The summary with the main questions made during the direct contact with dental professional is present in table 2.1.

Table 2.1. Summary of the interviews made during the direct contact with dental professional.

Professionals addressed		Is it interesting to associate this technology to dental prostheses?	Dental prostheses disadvantages and pathologies	What substance or medicine are interesting to be released ?	Observations about the product (*)
João Carlos Roque	Representing Nobel Biocare and Professor of Faculdade de Medicina Dentária de Lisboa (FMDUL)	Yes	–	-Promote the Healing -Anti- fungi -Daily medicines	“An interesting idea” “It is interesting and new to the dental industry”
Luis Loureiro	Orthodontist	Yes	Negative charge of the removable prostheses	-Fluor -Antibiotics -Amoxicillin -Anti-fungi	“Interesting application”
Sandra Ribeiro	Professor of FMDUL and Oral Hygienist	Yes	Bacterial and fungi colonization; Candidiases, Allergies to the acrylic resins	-Anti-fungi -hygienic products -Chlorhexidine	“It will be useful”

Professionals addressed		Is it interesting to associate this technology to dental prostheses?	Dental prostheses disadvantages and pathologies	What substance or medicine are interesting to be released ?	Observations about the product (*)
Henrique Luis	Professor of FMDUL and Oral Hygienist	Yes	–	-Anti-fungi -Hygienic products	–
Luis Jardim	Dentist	Yes	–	-Anti-inflammatory	–
Jaime Portugal	Dentist, Professor of FMDUL and President of the Sociedade Portuguesa de Estomatologia Dentária	Yes	MMA release inside the mouth (allergies focus)	-Anti-inflammatory -Anti-fungi -Chlorhexidine	“Important to know the period of time that the active principle is released” “Interesting product”
António Silva	Maló Clinics Ceramics Dental Laboratory Coordinator	Yes		-Chlorhexidine -Hyaluronic acid	“There are several patients who react negatively to the acrylic, this technology could be a solution” “Interesting product”

Professionals addressed	Is it interesting to associate this technology to dental prostheses?	Dental prostheses disadvantages and pathologies	What substance or medicine are interesting to be released ?	Observations about the product (*)
Miguel Nobre	Maló Clinic	Yes	-	<p>-Chlorhexidine</p> <p>-Hyaluronic acid</p> <p>“I am very interested in a product with these characteristics”</p> <p>“you have an interesting project in hands”</p>
Bruno Seabra	Orthodontist Maló Clinic	Yes	-	<p>- Chlorhexidine</p> <p>-Hyaluronic acid</p> <p>“It is an interesting product”</p> <p>“The product’s features are interesting”</p> <p>“The MMA extraction is a great idea, with a huge interest”</p>
Filipa Brás	Dental Prosthesis technician and CEO of the Highland Factory	Yes	-	<p>-</p> <p>-</p> <p>“Product with useful characteristics”</p> <p>“since it is a new company, It may be an add value to the company because it could help to demark from my competitors”</p>

*The product was presented to dental professionals before the experimental tests, so the product presented to the dental professionals was the product which is intended to obtain.

Appendix 3: Online questionnaire performed to the Portuguese dentists

In order to inquire the opinion and acceptance of the dental professionals, particularly the dentists, an online questionnaire about dental prostheses was performed to the dentists. The sample was of 20 Portuguese orthodontists.

1. Which type of dental prosthesis is more used by your patients?

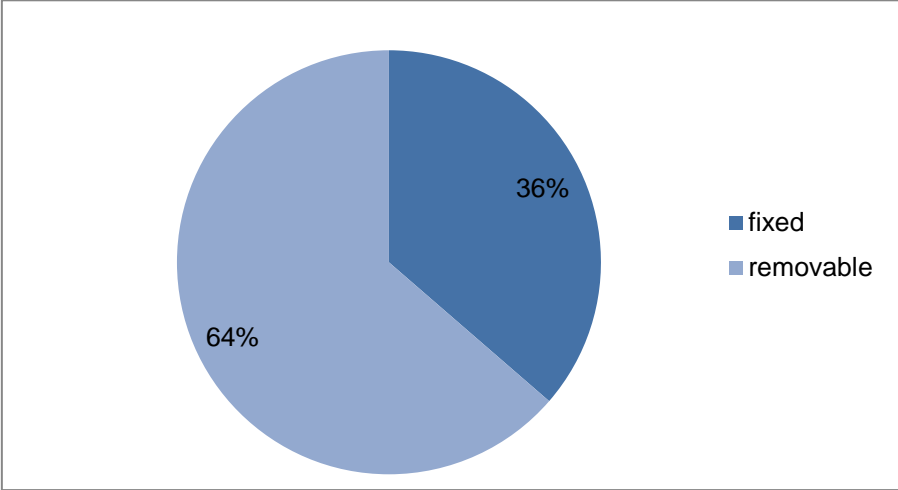


Figure 3.1. Proportion of the type of dental prosthesis more used (question 1).

2. Which age is more common to put/use dental prosthesis?

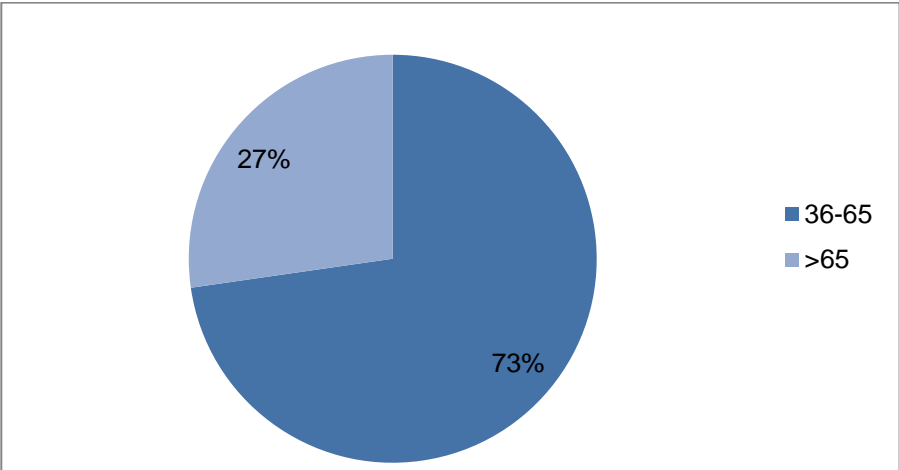


Figure 3.2. Age group which more often uses dental prostheses (question 2).

3. The percentage of patients with problems due to dental prosthesis use

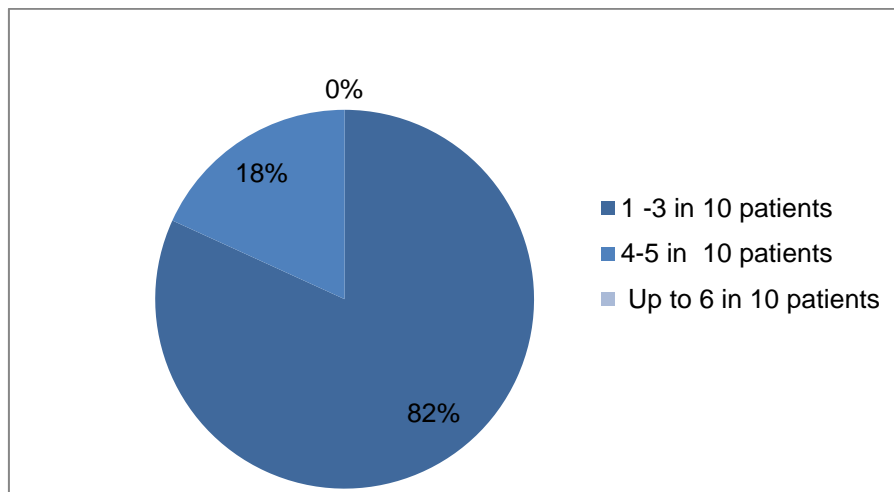


Figure 3.3. Patients with problems due to dental prostheses use (question 3).

4. The relevance to impregnate dental prostheses with an active principle which would be gradually released inside the mouth (1-no relevant, 5- very relevant):

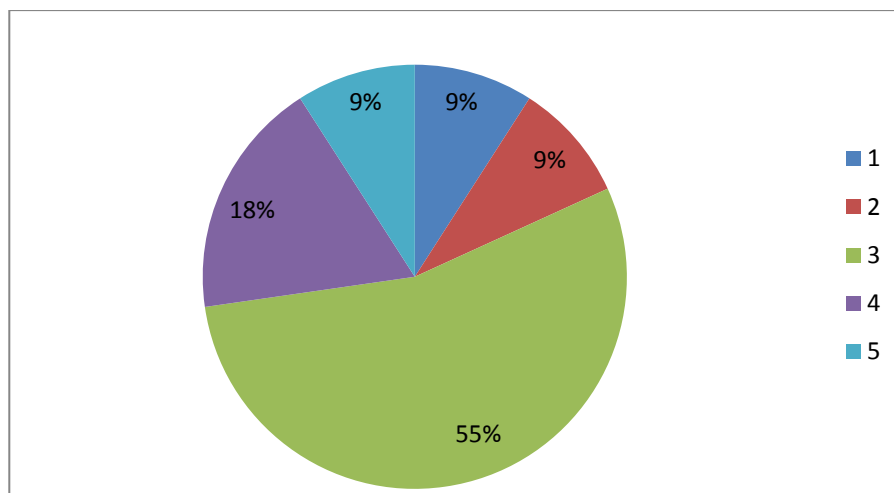


Figure 3.4. Relevance of the dental prostheses impregnation (Question 4).

5. Relevance of the antibiotic impregnation (1-no relevant, 5- very relevant).

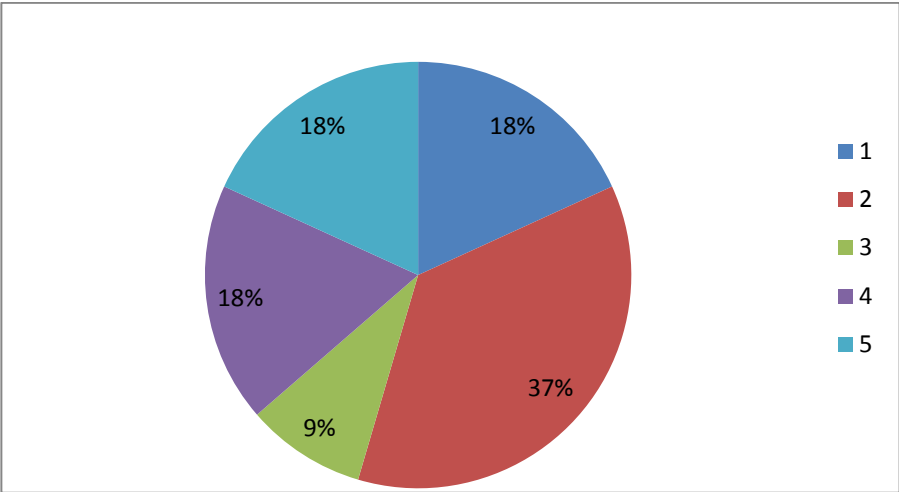


Figure 3.5. Relevance of the dental prostheses impregnation with an antibiotic (Question 5).

6. Relevance of the anti-inflammatory impregnation (1-no relevant, 5- very relevant).

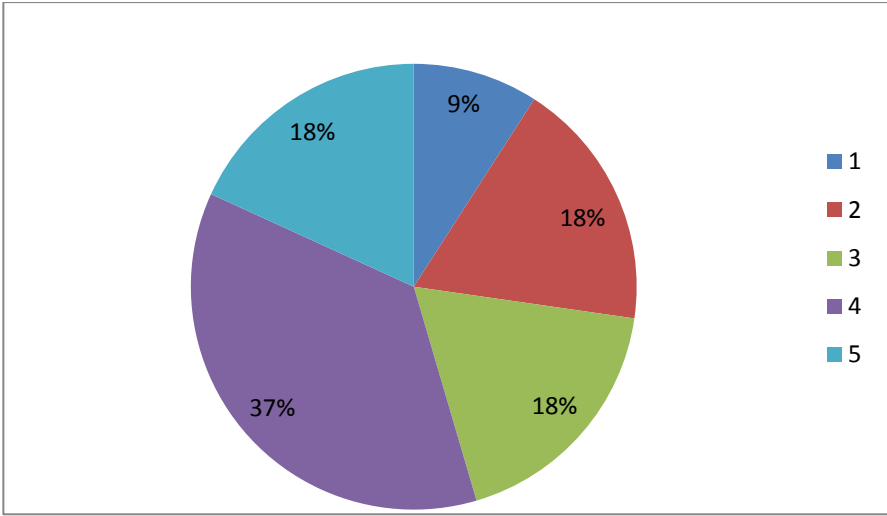


Figure 3.6. Relevance of the dental prostheses impregnation with an anti-inflammatory (Question 6).

7. Relevance of the healing impregnation (1-no relevant, 5- very relevant).

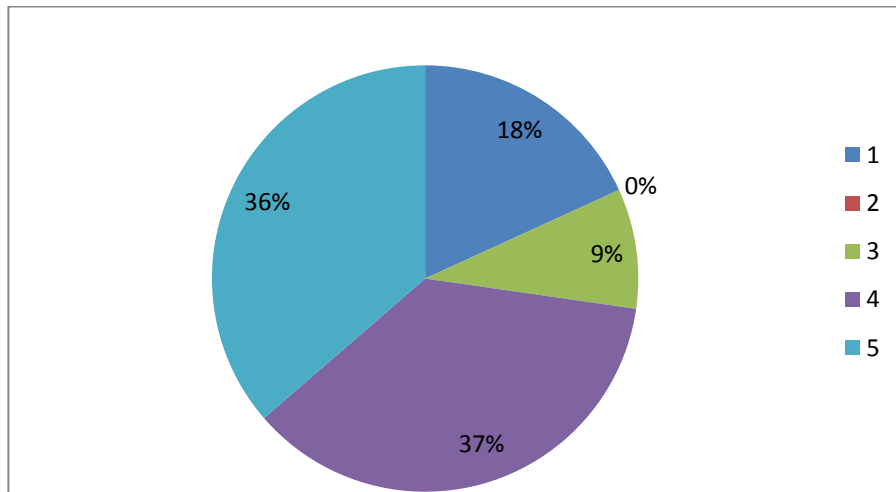


Figure 3.7. Relevance of the dental prostheses impregnation with a healing (Question 7).

8. Relevance of the antibacterial impregnation (1-no relevant, 5- very relevant).

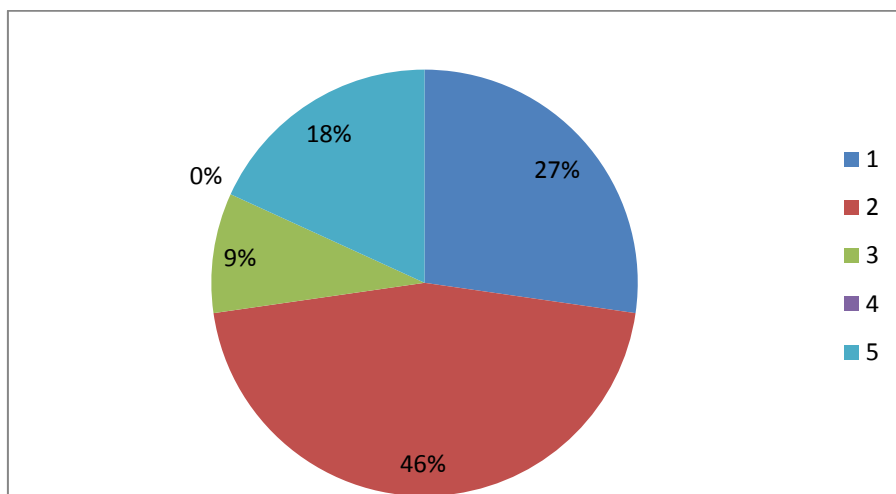


Figure 3.8. Relevance of the dental prostheses impregnation with an antibacterial (Question 8).

9. Is it important to remove the monomer (MMA) from acrylic prostheses?

The answers to this question was unanimous, all the orthodontists answered yes-**100% Yes**

Appendix 4: Questionnaire performed to the Portuguese population

A questionnaire about dental prostheses was performed online through the platform “Google Docs”. The sample was of 143 Portuguese population and their respective characteristics are presented below:

1. Sex:

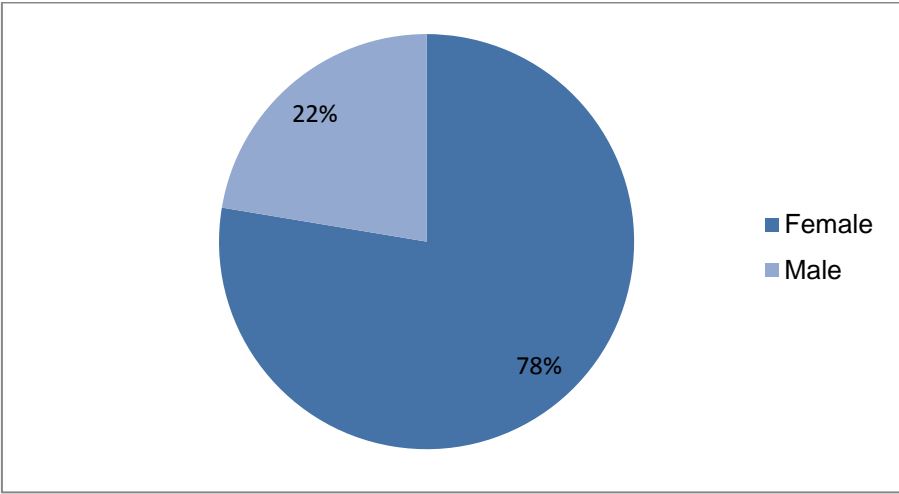


Figure 4.1. People who answered to the questionnaire by sex (question 1).

2. Age:

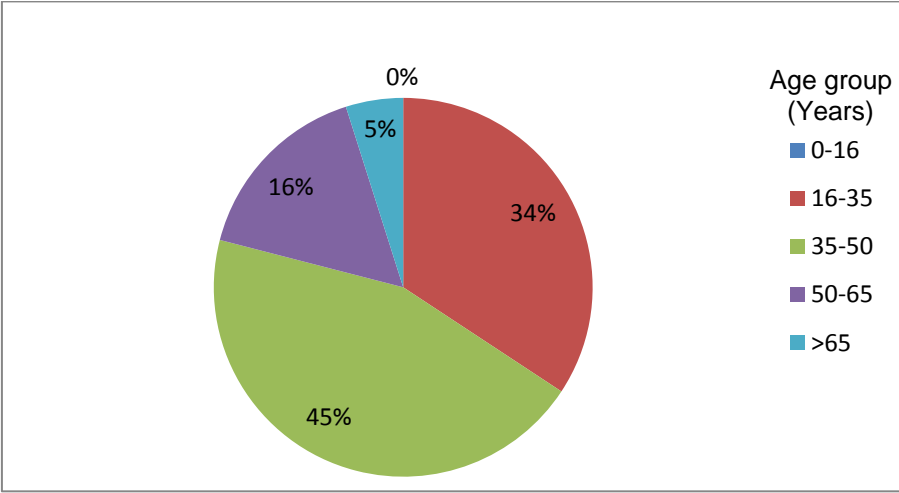


Figure 4.2. Population by age group (question 2).

3. Profession

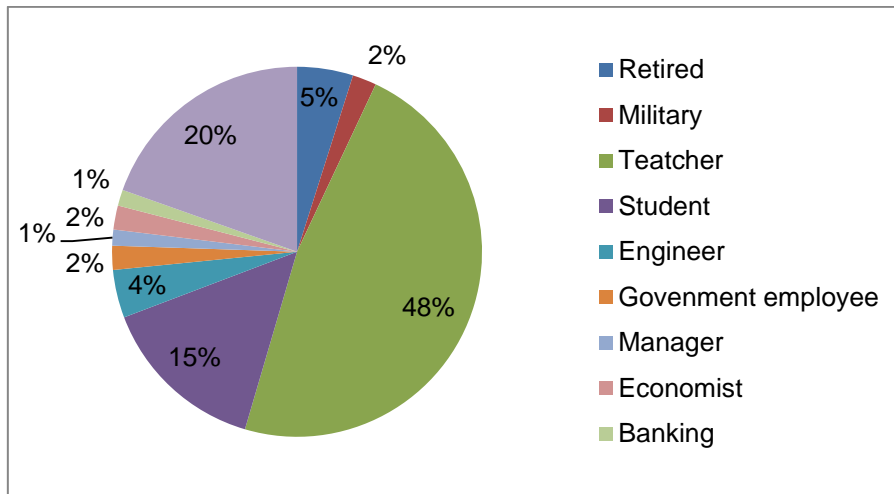


Figure 4.3. Population by profession (question 3).

4. What importance does oral hygiene have for you? (1- No importance, 5 – Very important):

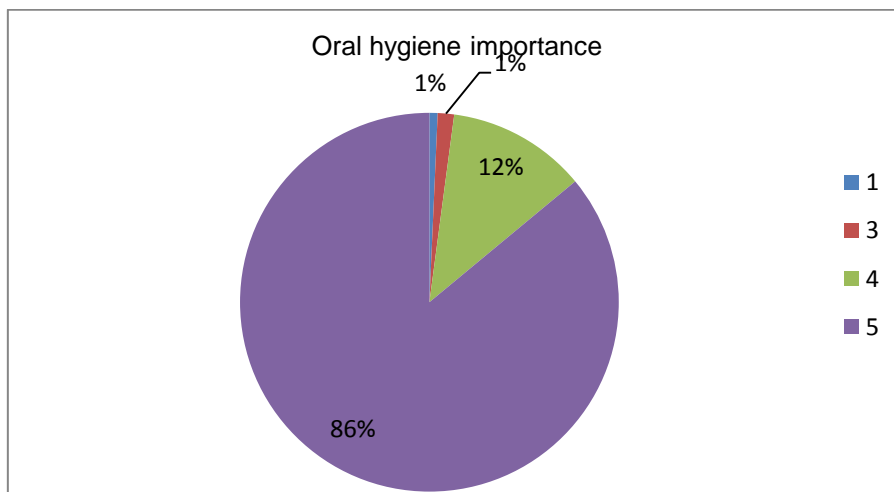


Figure 4.4. Oral hygiene importance (question 4).

5. Do you use dental prosthesis?

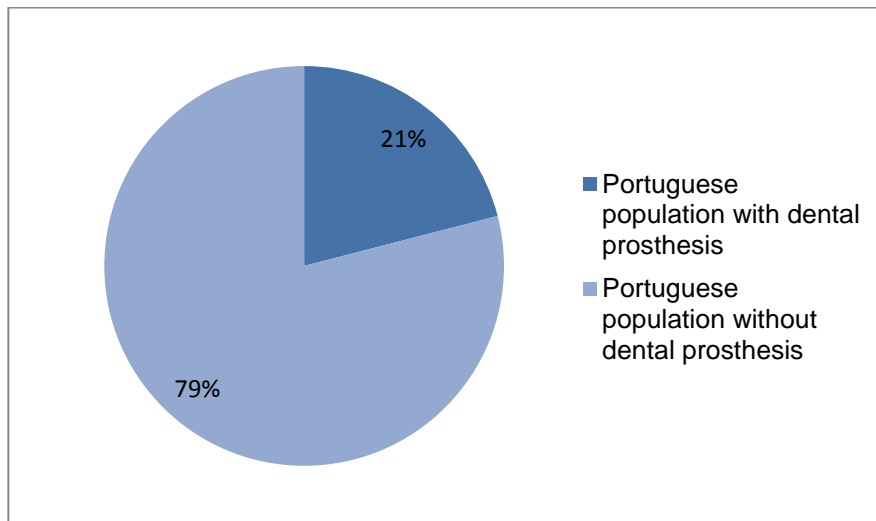


Figure 4.5. Proportion of dental prosthesis users in the Portuguese population questioned (question 5).

The number of people who responded “yes” to question 5 is 30, so the following questions were answered by them (sample of 30 people), since only dental prosthesis users responded to the following questions.

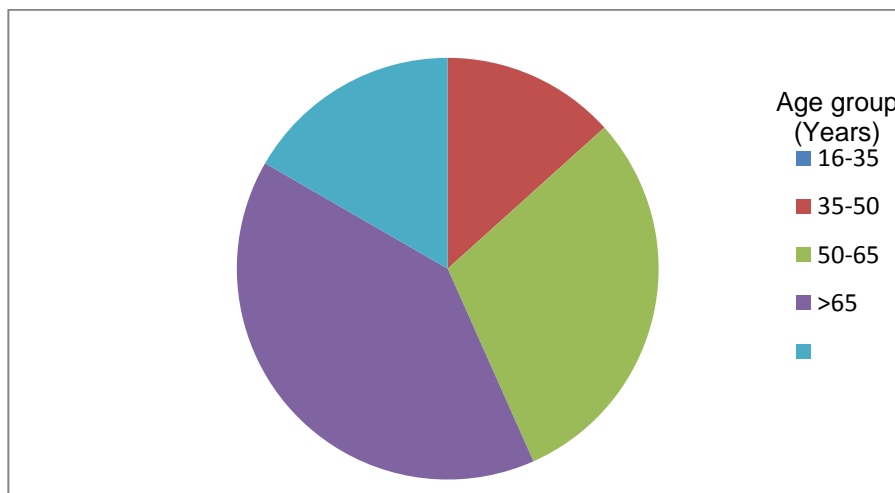


Figure 4.6. Dental prosthesis users by age group (question 2)

6. Type of dental prosthesis:

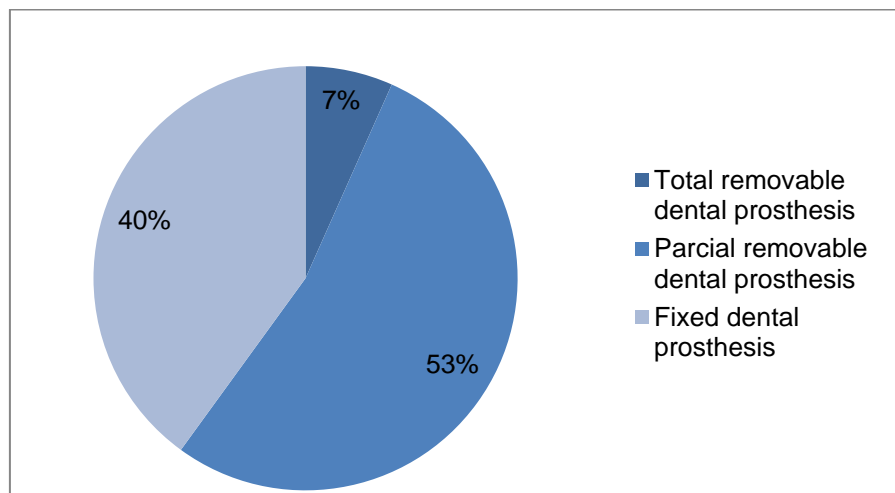


Figure 4.7. Proportion of the type of dental prosthesis used by the Portuguese population (question 6).

7. If you use fixed prostheses the process was:

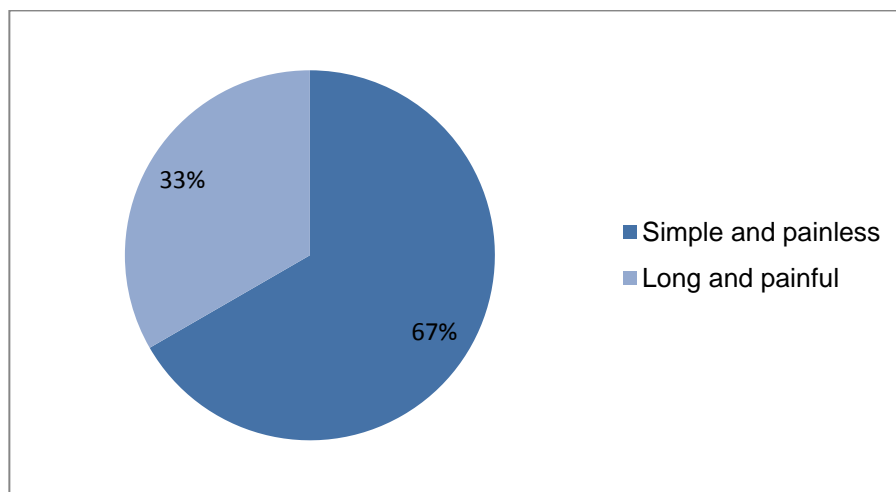


Figure 4-8. Process of putting and adaptation of fixed dental prostheses (question 7).

8. Do you have problems with your dental prosthesis (removable or fixed)?

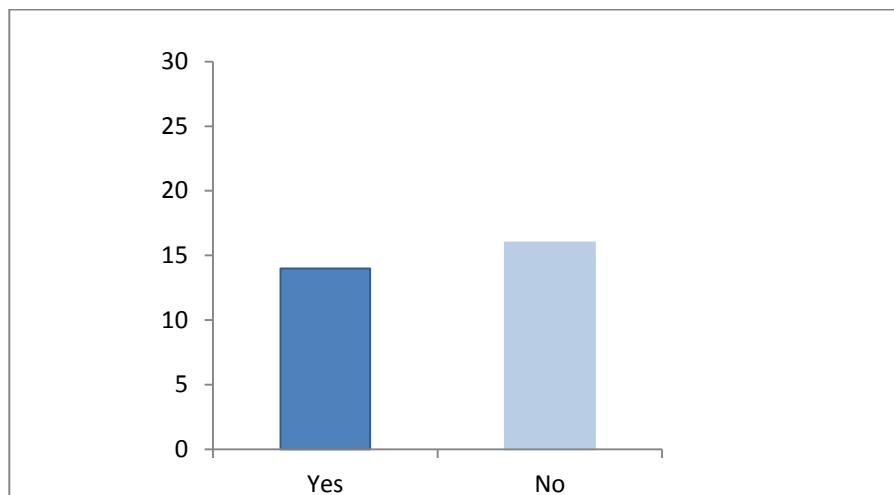


Figure 4.9. Problems with dental prostheses (question 8).

9. If you answer yes, which problem have do you have with your dental prosthesis?

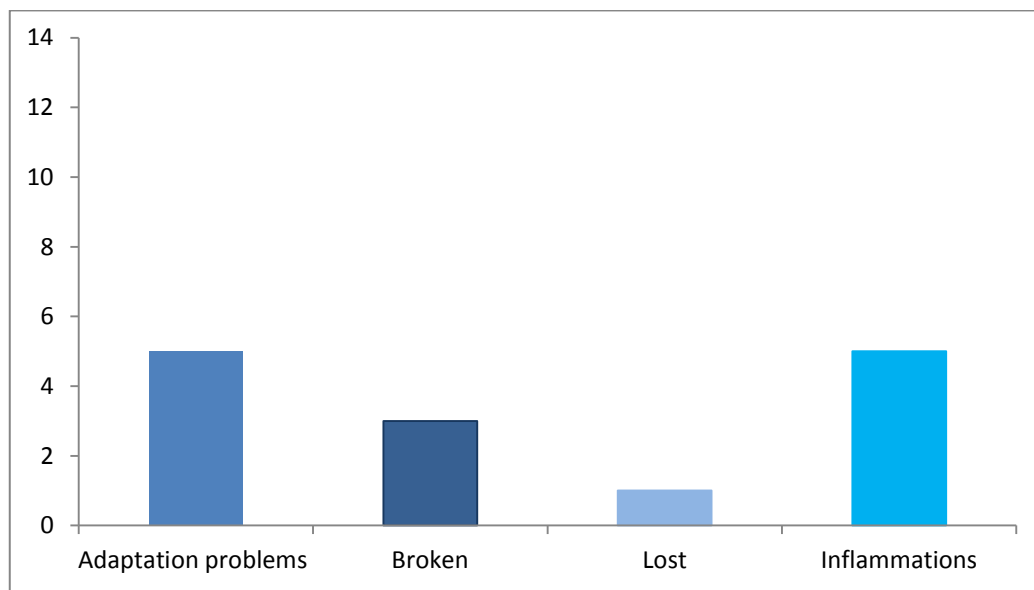


Figure 4.10. Type of problems with dental prostheses (question 9).

10. What would you like your dental prosthesis to offer:

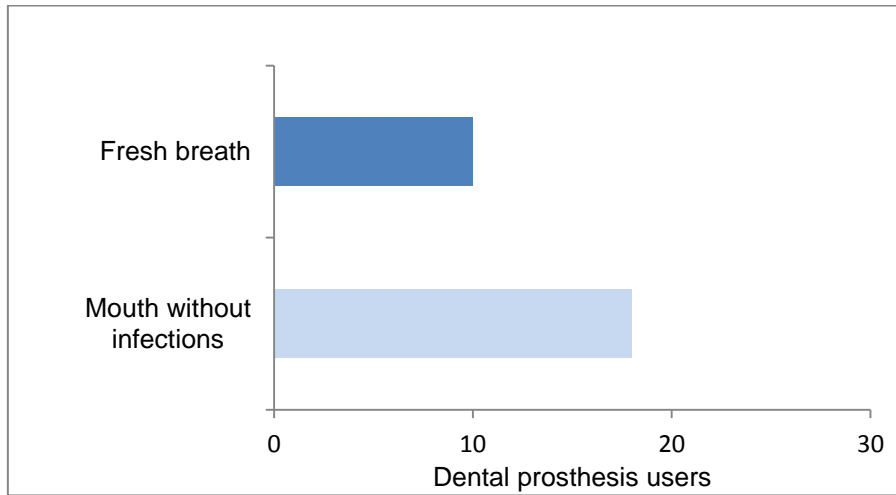


Figure 4.11. What dental prosthesis users would like their prosthesis could offer (question 10).

Appendix 5: Proof GEI dental concept

In order to verify the effectiveness of the use of the using supercritical technology for the extraction of the MMA from the PMMA used in dental prostheses and in the impregnation of active principals in PMMA, experimental test were performed, which are described next. The experimental tests were divided in two parts. In a first stage, the possibility to extract the residual monomer from the acrylic used in dental prostheses was tested. In a second stage, the possibility of impregnating an anti-inflammatory drug was evaluated.

5.1. Reagents and standards

Table 5.1. Characteristics and manufacturers of the reagents.

Reagent	Formula	Molar mass (g/mol)	Purity (%)	Manufacturer
Acetone	$(\text{CH}_3)_2\text{CO}$	58.08	>99.5	CarloERBA Reagents
Acetonitrile	CH_3CN	41.05	≥ 99.8	LiChrosolv – Merck (Darmstadt, Alemanha)
Carbon Dioxide	CO_2	48	99.99	Alphagaz
Phosphoric acid	H_3PO	98	85.0	Panreac Química S.A.U. (Barcelona, Espanha)
Ibuprofen	$\text{C}_{13}\text{H}_{18}\text{O}_2$	206.28	–	–
Methanol	CH_3OH	32.04	99.8	LiChrosolv – Merck (Darmstadt, Alemanha)
Methyl methacrylate	$\text{CH}_2=\text{C}(\text{CH}_3)\text{COOCH}_3$	100.12	95	Self Curing Vertex
Poly(methyl methacrylate)	$(\text{CH}_2=\text{C}(\text{CH}_3)\text{COOCH}_3)_n$	–	–	Probase Hot Cold (Pink)
➤ The water used during detection by HPLC was obtained through a system Milli-Q (Milli-Q Millipore Integral 15, Millipore Corp., France)				

The acrylic samples used to manufacture dental prostheses and standard of MMA, which were used in the experimental tests were given by Professora Catarina Cortes Martins professor of Faculdade de Medicina Dentária de Lisboa. The samples are examples of the same material used in dental prostheses, in other words, the samples, which were performed in the tests, were acrylic samples of the finished material, already to be used by patients. The technology will act after the dental prostheses were manufactured. The acrylic samples characteristics and polymerization conditions are presented next.

Table 5.2. Samples characteristics and Conditions of polymerization.

PMMA samples characteristics	Probase Hot Cold (Pink)		
	Type 2 Classe 1 ISO 1567 AOA12		
Polymerization reaction	Batch 023891		
	Time (min)	Temperature (°C)	Pressure (bar)
	15	55	2,5

Table 5.3. Characteristics of standard of MMA.

Standard of MMA characteristics	Self curing Vertex
	Type 2 Class 1 ISO 20795-1
	Batch XX131L03
	Validity: 2016/09

5.2. Experimental setup

The experimental setup used during the test (both extraction and impregnation) is depicted in Figure 5.1.



Figure 5.1. Image of installation where the tests were performed (1- High-pressure cell; 2- CO₂ pump high pressure liquid; 3- Thermostated water bath, 4- Pressure manometer).

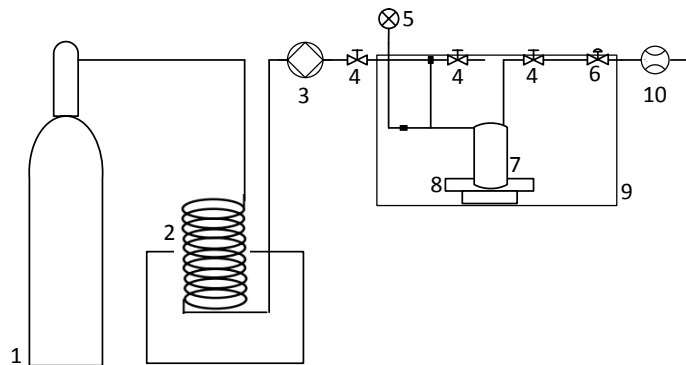


Figure 5.2. Schematic diagram of the installation where the tests were performed (1- CO₂ cylinder; 2- Cooling coil; 3- High pressure liquid CO₂ pump; 4- Valve; 5- Pressure manometer; 6- Micrometer valve; 7- High-pressure cell; 8- Stir plate; 9- Thermostated water bath; 10- Flow meter).



Figure 5.3. High-pressure cell and components used during impregnation tests (1- High-pressure cell; 1a- basket; 1b- metallic net; 1c- wire support).

This apparatus consists in a high-pressure cell (made of stainless steel) with an internal volume of 25 cm³, a high pressure liquid CO₂ pump (Haskel Model 29723-71), a water bath and a pressure manometer (Digibar II). During the experiments the cell was placed in a thermostated water bath and CO₂ was pressurized with a liquid pump. A system of valves allows the CO₂ to enter the cell. The pressure generator and the cell are provided with an electronic manometer to allow control of the pressure and the inlet and outlet of gas.

5.3. Detection method

The High Performance Liquid Chromatography (HPLC) was used to quantify both the residual MMA content in the sample after the extraction procedures as well as the ibuprofen impregnated.

Chromatography is a physic and chemical method of components separation of a given mixture, performed throughout the distribution of these components by two phases, which are in contact. During the passage of the mobile phase to the stationary phase, the components of the mixture are distributed by the two phases, each one being selectively retained by the stationary phase, which results in different migrations of these components [75-76]. The stationary phase can be solid or liquid, put on a solid support with big superficial area. The mobile phase can be a gas, a liquid or even a supercritical fluid, which passes through a stationary phase and carries the different mixture components. HPLC is the analytical tool most used in the pharmaceutical industry, the name of liquid chromatography is related due to its mobile phase being in a liquid [77]. The HPLC system is constituted by a pump, an injector, a column and a detector.

5.4. Extration Tests

5.4.1. Method

5.4.1.1. Extract tests

The tests were performed in the equipment showed above in Figure 5.1. The operations' conditions of the test presented in Table 5.4 are in accordance with Kemmere and Hwang [69, 78]. All tests were made in duplicate.

The test consists in immersing the cell with the sample in the thermostated bath of water after the desired temperature is reached and subsequently pressurizing it with CO₂ until the desired pressure (Table 5.4) and stay in contact with CO₂ for 20 minutes (static period). After the static period, the valves are opened to CO₂ pass by the sample continuously for the period presented in Table 5.4, namely Continuous Period. Finally, after Continuous Period, the depressurization, the release of SCF, was performed at the same flow rate of the Continuous Period.

Table.5.4. Operation conditions of extraction tests.

Tests	Sample's Weight (mg)	T (°C)	P bar)	Static Period (min)	Continuous		ρ_{CO_2} (Kg/m ³)
					Period (min)	Period Flow Rate (L/min)	
1	265	25	70	20	15	3	743
2	313	25	70	20	30	3	743
3	315	40	130	20	30	3	743
4	298	60	80	20	30	3	191

5.4.1.2. Quantification of MMA extracted

The quantification of MMA was made by the calibration curve method. A range of standard MMA solutions was prepared in methanol in a range of concentrations 10^{-4} - 10^{-6} mL/mL.

The protocol to sample destruction to extract the MMA present in each sample is according to Ohyama and it is presented below [79]:

1. The samples after the tests were dissolved in 2 mL of acetone during about 24h.
2. After 200 μ L of previous solution and 800 μ L of methanol were put in an 1 mL eppendorf to precipitate the polymer (white precipitated is observed).
3. Centrifugation at 13000 rpm during 3 min and the supernatant was put in a vial in order to be detected in the HPLC.

Table 5.5. HPLC conditions used in the analysis of residual monomer.

Analytical column	Phenomenex Gemini-NX 5 μ C18 110A (150 X 4,60 mm) 435814-4	
Oven program	Temperature	Rate
	40°C	1.0 mL/min

After the performance of the protocol that led to sample destruction, HPLC analysis was performed using the conditions summarized in Table 5.5 which was performed according to Ohyama [79]. The separation was made in an isocratic way with a mobile phase composed by 50:50 (%v/v) acetonitrile: water, with a flow of 1,0 mL.min⁻¹. The analytic column of reverse phase used was a Phenomenex/Gemini-NX-C18 (150 mm x 4,6 mm, particles size: 5 μ m, pore size: 110 Å), coupled to a

pre-column of reverse phase, thermostated at 40°C. The detection was made at 205 nm. The injection of each sample was replicated two times, and it was previously filtrated through a 0,45 µm filter.

5.4.2. Results

The first stage of experimental test had the objective of verifying if the technology allows the extraction of MMA from acrylic resins used in dental prostheses. In order to evaluate this possibility, several tests were made at different operational conditions of temperature, pressure and extraction time.

As observed in Table 5.6, different operational conditions led to different extraction efficiencies, in addition, it was observed that in some conditions (test 3 and 4) the samples after the tests presented a noticeable white color, probably due to the CO₂ interaction with the dye. The circular shape, the volume and the weight of the samples are maintained after the tests. Assay 2, corresponding to T= 25°C and P= 70 bar, presents the best efficiency, about 68.7% of MMA removal, which is a significant reduction of MMA with mild operational conditions in a relatively short time and allowed the sample to maintain its volume, shape and color after the test. However, a slight whitening of the sample on the surface is verified, but it is almost imperceptible. This can be explained by a possible interaction of the CO₂ with the dye.

Table 5.6. Extraction process efficiency.

Tests	Sample's Weight (mg)	Concentration initial* (mL/mL)	Concentration** (mL/mL)	Efficiency*** (%)	Duration of the process (min)
Control	316	0,0045	-	-	-
1	265	-	0,004	7.6	35
2	313	-	0,001	68.7	50
3	315	-	0,003	39.2	50
4	298	-	0,003	33.5	50

* Concentration of MMA present in the sample before the tests.

** Concentration of MMA remained in the samples after the tests.

***Efficiency = Amount of MMA extracted by scCO₂ / Amount of MMA initially in PMMA

The result obtained in test 2 validates the use of this technology to remove the MMA from dental prostheses, and in addition, they are a good starting point for future tests. Therefore, the hypothesis that GEI could decrease the amount of MMA in acrylic used in dental prostheses was tested and validated.

Vanessa Urban has reported a method to extract the residual monomer after polymerization of acrylic resins used in prosthodontics [80]. The referred study reports the water-bath (stored in water at 37°C for 48 h) and microwave irradiation (placing them in an adjustable microwave oven (Sensor Crisp 38, Brastemp, Manaus, AM, Brazil) and irradiating with: 550 W/3 min) post-polymerization procedure to reduce the residual monomer content in acrylic resins. The reduction of MMA from PMMA by these methods does not present successful results: “the residual monomer level of the denture base resin specimens polymerized (...) was not affected by any of the post-polymerization treatments” [80]. The referred methods are not usually dental laboratories procedures. Although this extraction is important as previously described in Market Pain chapter, nowadays the extraction of MMA post-polymerization is not performed during the dental prosthesis manufacturing in dental laboratories. The test performed allows the verification that the GEI dental permits the extraction of MMA from PMMA used in dental prostheses. Comparing with the method described by Vanessa Urban it is possible to observe several advantages:

- a) The efficiency is superior: GEI dental allows a significant decrease on the MMA level.
- b) Process duration is shorter than the water bath method reported by Vanessa Urban.
- c) GEI dental is a clean and safe technology

5.5. Impregnation Tests

5.5.1. Method

5.5.1.1. Supercritical Impregnation

The method comprises three steps:

1. Solubilization of active principle (solute) in the supercritical fluid (solvent). During the impregnation tests, the active principal used was Ibuprofen and the supercritical fluid was CO₂.
2. Contact of the matrix impregnated with the supercritical phase, which includes the active principal and the supercritical fluid.
3. Depressurization of the system, which consists in the release of the supercritical fluid [81].

The efficiency of the process results of a complex mechanism which involves interactions among the solute, solvent and the matrix [82]. The operational parameters that influence the supercritical impregnation rate are the CO₂ pressure, temperature, impregnation time and the depressurization period [81,83].

5.1.2. Active Principle

The active principle chosen was ibuprofen because it is an anti-inflammatory drug, which is soluble in CO₂. Ibuprofen is a non-steroid anti-inflammatory, it belongs to the sub-group of the derived of propionic acid [84-86]. Like the other non-steroid anti-inflammatories, it acts inhibiting the production of prostaglandins, chemicals produced by the organism which cause inflammation and contribute to the pain perception by the brain [83]. This medicine is a white crystalline powder or colorless crystals, practically insoluble in water, easily soluble in acetone, methylene chloride, ether and methanol. Ibuprofen dissolves in dilute solutions of hydroxides and carbonates of alkali metals (USP 26, 2003).

Table 5.7. Ibuprofen characteristics.

Ibuprofen	
Molecular formula	C ₁₃ H ₁₈ O ₂
Molecular weight	206,28 g/mol
IUPAC Name	(RS)-2-[4-(2-methylpropyl)phenyl]propanoic acid
Melting point	75-78°C

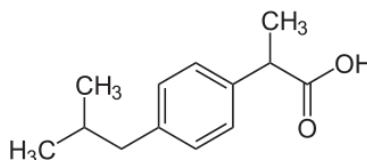


Figure 5.4. Ibuprofen structure.

1.5.1.3. Conditions of impregnation tests

The conditions of impregnation were based in the solubility of ibuprofen in scCO₂ to ensure the solubilization of ibuprofen in scCO₂ [87]. The impregnation tests were performed in the equipment presented in Figure 5.1 and the conditions used for the impregnation are presented in Table 5.8. The tests consist in immersing the cell with acrylic samples and the ibuprofen in the thermostatically bath of water until the desired temperature is reached and subsequently pressurizing with CO₂ until the desired pressure (Table 5.8). During all tests the samples in the cell were stirred. Inside the cell, the acrylic samples were put on a wire support and the ibuprofen inside a metallic network, above it. The tests were performed in batch during the tCO₂ presented in the Table 5.8. After the tCO₂, the system was depressurized slowly or fastly, according to the test (Table 5.8).

Table 5.8. Conditions of impregnation tests.

Tests	Sample's weight (mg)	Initial Ibuprofen (mg)	T (°C)	P (bar)	tCO ₂ * (min)	Depressurization Period (min)	ρCO ₂ (Kg/m ³)
5	302	123	50	138	60	30	665
6	288	119	50	138	60	Fast	665
7	267	90	35	130	60	30	786
8	284	90	35	130	30	30	786
9	122	130	40	130	30	30	743
10	123	130	40	130	60	30	743
11	97	100	40	110	30	30	684
12	113	100	40	110	60	30	684
13	108	120	40	120	60	30	718

*Contact period - Period in which sample, active principle and CO₂ were in contact.

5.5.2. Quantification of impregnated ibuprofen

The protocol to sample destruction to extract the ibuprofen present in each sample is according to Ohyama and it is presented below [79]:

1. The samples after the essays were cleaned with ethanol to remove the ibuprofen which could be in the superficies of the samples.
2. Then the samples were dissolved in 2 or 4 mL (according to the weight samples') of acetone during about 24h.
3. After 200 μL of previous solution and 800 μL of methanol were put in a 1 mL eppendorf to precipitate the polymer (white precipitated is observed).
4. Centrifugation at 13000 rpm during 3 min and the supernatant was put in a vial in order to be detected in the HPLC.

Table 5.9. Conditions used in analysis of sample content with ibuprofen.

Analytical column	Phenomenex Gemini-NX 5 μ C18 110A (150 X 4,60 mm) 435814-4	
Oven program	Temperature	Rate
	40°C	2.0 mL/min

The separation was made in an isocratic way with a mobile phase composed by 60:40 (%v/v) acetonitrile: acidificated water with phosphoric acid (pH 2,5), with a flow of 2,0 mL.min⁻¹. The analytic column of reverse phase used was a Phenomenex/Gemini-NX-C18 (150 mm x 4,6 mm, particles size: 5 μ m, pore size: 110 Å), coupled to a pre-column of reverse phase, thermostated to 40°C. The detection was made to 221 nm. The injection of each sample was replicated two times, that was previously filtrated through 0,45 μ m filter. The quantification of Ibuprofen was made by curve calibration method.

5.5.3. Results

In this second stage of tests, the impregnation of ibuprofen in the acrylic resin used in dental prostheses was tested. The objective was to verify whether the active principle is impregnated in PMMA by the GEI dental. With the purpose of observing if it is possible to fulfill the objectives, the effect of pressure, temperature, CO₂ contact and depressurization period were tested.

Table 5.10 presents the results of impregnation tests which were performed in different operational conditions. To validate the use of this technology to impregnate dental prostheses is necessary to observe the existence of ibuprofen in the sample. The test 6 was not considered because after the test, ibuprofen was only in the surfaces of the sample, so this result allows the verification that slow depressurization is a better option than the fast one. In all tests, it is possible to observe that the samples are impregnated with ibuprofen, so the technology allows the impregnation of ibuprofen in PMMA used in dental prostheses. Different loads were obtained with different temperature and pressure conditions, and for some operational conditions, the samples, after the tests, presented a different appearance, more translucent with a white color and swelled. This was verified in the tests with high pressures and temperatures (tests 5, 6, 9,10 and 13). On the other hand, tests 11 and 12 present the best loads without changing the samples. After the mentioned tests, the samples maintained their circular shape, color and volume. As mentioned above, in extraction experiments, only a slight whitening of the sample on the surface is verified, but it is almost imperceptible.

The operation condition 110 bar and 40°C seems to be the best conditions to impregnate the PMMA with ibuprofen comparing to all the operational conditions tested. The only difference between test 11 and 12 was the tCO₂, it seems to have influence on the loads. For 30 minutes of contact the

%impregnation is about 7% and to 60 minutes is about 8%. The time of the process is an important point to take into account. In order to obtain the best process for impregnation to present to the dental industry, it is important to evaluate time and efficiency, to have the best combination.

Table 5.10. Results of impregnation tests.

Tests	Depressurization period (min)	Load*	% Impregnation**	% Efficiency***	Duration of the process (min)
5	30	0.03	3	8.3	90
6	Fast	–	–	–	–
7	30	0.01	1	2.5	90
8	30	0.01	1	3.8	60
9	30	0,02	2	1.7	60
10	30	0.02	2	2.0	90
11	30	0.07	7	6.8	60
12	30	0.08	8	8.9	90
13	30	0.09	9	8.0	90

*Load = impregnated ibuprofen/PMMA

**%Impregnation = impregnated ibuprofen/PMMA x100

***Efficiency = impregnated ibuprofen/initial ibuprofen

The results allow considering that the GEI dental enables to impregnate the acrylic resins used in dental prostheses. However, only ibuprofen was tested, in other future studies, it is necessary to test other active principles, the required by orthodontists, as well as the respective operational conditions and the drugs release profile inside the oral cavity, in order to obtain the maximum efficiency of the process. The systems of impregnation with different active principle should be studied with more detail. The solubility of the drug into CO₂, the ability of CO₂ to penetrate the polymer and the partition coefficient of the drug between the dense gas and the polymer phase are important points to take into account during the development of GEI dental.

5.6. Conclusion

The results of the experimental tests allow considering that GEI dental achieves the proposed objectives, both for the extraction of MMA and the impregnation with an active principle in dental prostheses. The GEI dental enables extracting until 68,7% of MMA present in dental prosthesis in a process with that lasts about 50 minutes. In addition GEI dental allows the impregnation of ibuprofen with a %impregnation of 7% in a process with the duration of 60 minutes. To increase the %impregnation to 8% the duration of the process must also increase to 90 minutes.

The concept of the product was validated, however it is not yet presented with the best characteristics to introduce into the dental market. Several studies should be done in order to develop the all potentialities of this product. The critical points of the GEI dental based on the experimental tests made are:

- d) The possible interaction of CO₂ with the dye. Nevertheless, there is transparent acrylic without dye used in dental industry and, in addition, the composition of the dye is not the best to human use, probably the dye should be changed in the future, or even this technology could allow the impregnation of a safer dye.
- e) The time of the process is an important point to be improved. The demand of dental care sector is the high efficiency in a shorter period of time possible.
- f) The efficiency of both processes could be improved, it is important to perform future tests in order to improve the processes.

Appendix 6: Targeting criteria applied to the dental laboratories worldwide

With the purpose of evaluating the companies which have the required characteristic mentioned in Chapter 5, section 5.1.2.2, Table 6.2 is presented next, with a list of several dental companies which shows an evaluation in the targeting criteria. Each one will be classified according to what is presented in Table 6.1.

Table 6.1. Targeting criteria classification.

Evaluation	Innovation	Laboratories in Portugal	Number of laboratories in Europe	Financial soundness
0	Nothing	Do not have	Do not have	0-5 years
1	Little	1 laboratory	1-4 laboratories	5-10 years
2	Medium	2 laboratories	5-10 laboratories	10-30 years
3	Very	More than 3 laboratories	More than 10 laboratories	More than 30 years

Table 6.2. Targeting variables evaluation.

Companies	Innovation	Laboratories in Portugal	Country	Number of laboratories in Europe	Financial soundness	Total
Albilab	0	1	Portugal	1	0	2
Attenborou gh Dental	2	0	UK	1	3	6
Babichenko Dental Laboratory	2	0	USA	0	2	4
Bien-Air	3	0	Switzerla nd	1	3	7
Bright Dental Lab	1	0	China	0	1	2
Coroadent	0	1	Portugal	1	2	4
1st Dental	1	0	UK	3	2	6
Diagnodent	0	1	Portugal	1	0	2

Companies	Innovation	Laboratories in Portugal	Country	Number of laboratories in Europe	Financial soundness	Total
Dental Services Group	2	0	USA	0	3	5
Dental Union Laboratory	3	0	Poland	1	2	6
Excel Dental Lab	1	0	Thailand	0	3	4
Glidewell Laboratories	2	0	USA	0	3	5
Hi-TECH	0	1	Portugal	1	0	2
Incisal	0	1	Portugal	1	0	2
Malo Clinic	2	1	Portugal	1	2	6
MDH	2	1	Germany	1	1	5
Mimetik	0	1	Portugal	1	1	3
National Dentex Corporation	2	0	USA	0	2	4
Nobel Biocare	3	1	Swiss	3	3	10
Orallab	2	1	Portugal	1	2	5
PraticDent	0	1	Portugal	1	2	4
Proincisal	0	1	Portugal	1	1	3
Precision Dental Studio	3	0	United Kingdom	1	3	
Sun Dental Laboratories	2	0	USA	2	2	6
Southern Cross Dental Laboratories	1	0	Australia	1	2	4

Companies	Innovation	Laboratories in Portugal	Country	Number of laboratories in Europe	Financial soundness	Total
Swift Dental Group	2	0	UK	1	2	5
Trident	2	0	USA	0	2	4
TOKUSHINK AI	1	0	Japan	1	2	4
Vita Zahnfabrik (Vita Masterlabs)	2	0	Swiss	3	3	8
Williams dental lab	2	0	USA	0	3	5
32Dent	0	1	Portugal	1	1	3

The choice of the dental companies presented in Table 6.2 consisted in a random search of the existing companies worldwide and mainly in Portugal. The only criterion of choosing the dental companies was the companies' dental prostheses manufacture and not only dental implants which are only made of metal. There are companies which manufacture exclusively metal to dental implants. Due to the GEI dental being applied to acrylic, the companies which only sell dental implants are not potential customers.

Table 6.2 presents the dental companies evaluated according to the criterion of Table 6.1. Despite the majority of dental laboratories in Portugal being local, with a small dimension and usually only a single laboratory and not a network of laboratories, it is possible to verify the existence of influential companies in the dental industry in Portugal. Some examples of companies with a strong presence in the Portuguese and European market are MDH and Malo Clinic. The above companies have interest in advanced and innovative technologies. In addition there are Portuguese dental laboratories, such as Orallab, that have interest in innovation and to give a high quality service to their customers. Therefore, the mentioned companies are examples of the target customer for GEI dental. The Table 6.2 gives a global view about some dental companies of the entire world and how they suit in the targeting criterion.

Appendix 7: SS Financial Plan

SS Financial Plan					
	2013	2014	2015	2016	2017
Investment					
Intangible Assets					
Research and development	5.000	5.000	0	0	0
CE marking	0	30.000	0	0	0
Industrial Property	0	2.000	6.000	0	0
Tagible Assets					
Equipment	60.000	0	0	0	0
Total investment	65.000	37.000	6.000	0	0
Revenues and Expenses	2013	2014	2015	2016	2017
Sales Revenues					
Units (Portugal)	0	6	15	30	30
Units (Other European countries)	0	0	4	45	90
Unit Price(€)	0	45.000	45.000	45.000	45.000
Annual Maintenance Service	0	1.200	3.000	6.000	6.000
Total Revenues	0	271.200	858.000	3.381.000	5.406.000
Costs (€)					
Components	0	120.000	380.000	1.500.000	2.400.000
Office rent	2.400	2.400	2.400	2.400	2.400
Marketing	1.000	11.000	11.000	11.000	11.000
Transport (National)	0	3.600	3.600	3.600	3.600
Distribution Companies (35%)	0	0	63.000	708.750	1.417.500
Royalties (1%)	0	2.712	8.580	33.810	54.060
Total Costs	3.400	139.712	468.580	2.259.560	3.888.560
Human Resources Costs (annual)					
CEO	8.400	14.000	21.000	21.000	21.000
2 Specialized Technician	14.000	22.400	28.000	28.000	28.000
Accountant	2.400	2.400	2.400	2.400	2.400
Marketing and Sales director	0	12.600	14.000	14.000	14.000
Food subsidy (120 € per work)	360	480	480	480	480
Social Security (34,75% of the salary)	6.672	14.595	18.765	18.765	18.765
Income Tax (12% of the salary)	2.976	5.880	7.560	7.560	7.560
Total Costs	34.808	72.355	92.205	92.205	92.205
Total Expenses	38.208	212.067	560.785	2.351.765	3.980.765
Financial Analysis	2013	2014	2015	2016	2017
Gross Profit	0	151.200	478.000	1.881.000	3.006.000
EBITDA	-38.208	59.133	297.215	1.029.235	1.425.235
Depreciation and Amortization	12.000	12.000	12.000	12.000	12.000
Earnings before Tax	-50.208	47.133	285.215	1.017.235	1.413.235
Tax losses	-50.208	-50.208	-3.075	0	0
Income Before Taxes	0	-3.075	282.140	1.017.235	1.413.235
Corporate Tax (25%)	0	0	70.535	254.309	353.309
Net Profit after tax	-50.208	47.133	214.680	762.926	1.059.926
Cash Flow from Operations	-38.208	59.133	226.680	774.926	1.071.926
Working capital requirement	-13.000	-57.800	-160.533	-627.000	-1.002.000
Investment	-65.000	-37.000	-6.000	0	0
Free Cash Flow	-116.208	-35.667	60.147	147.926	69.926
Net Present Value (NPV) (15%)			35.501 €		
Internal Rate of Return (IRR)			24,41%		
Payback Period			3 years		