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Injectable resorbable polymer shells for soft tissue augmentation

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INTRODUCTION

A biomaterial can be broadly defined as any material (synthetic or natural) that is used as a structural component intended to come into contact with biological systems [1]. This includes medical implants, drug-delivery systems, medical devices and diagnostic equipment.

Biomaterials research is very relevant to developing nations, especially due to the high injury-related burden of disease and congenital defects due to insufficient pre-natal care amongst the poor and disadvantaged. With the rise in human life expectancy, the demand for biomaterials is rapidly growing in the 21st century. Progress in tissue engineering, stem cell research, gene therapy, biotechnology and materials science is believed to largely impact advancements in the field. Worldwide the biomaterials industry is a trillion dollar industry; however, South Africa is a net importer of medical implants and devices.

Our research, therefore, focuses on producing a locally-manufactured resorbable biopolymeric particle system for use in soft tissue augmentation.

APPLICATIONS

Our particle system may be used in a variety of medical conditions ranging from gastroesophageal reflux disease (GERD or heartburn) to minimally invasive cosmetic reconstruction of the face. GERD or severe debilitating heartburn is a very common disease, and apart from the discomfort caused by the symptoms, it leads to an increased risk of oesophageal cancer. Many GERD sufferers have to take expensive medication for the rest of their lives. The main alternative to medication is surgery (laparoscopic fundoplication). Apart from surgery being very invasive, studies have found that more than 62% of the patients return to medication within 10 years of surgery. The GERD treatment market size in the USA is about US$ 10 billion/year [2].

Other conditions that may benefit from the development of our technology include velopharengeal insufficiency. This condition is caused by congenital defects associated with cleft lips and palates. Correcting the velopharengeal muscle through bulking will result in more coherent speech and an increased ability for swallowing food.

Additionally, our technology may be used in facial reconstruction and as a wrinkle filler. Lipoatrophy associated with Aids sufferers may cause hollow and sunken facial features. It would be possible to apply our product in correcting this condition to allow for normal facial features.

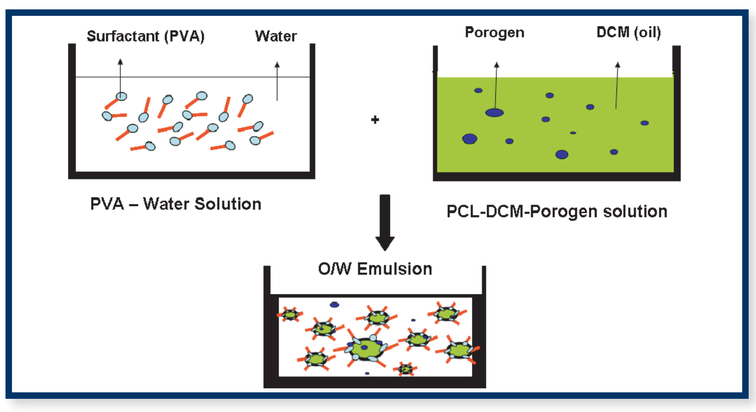
OUR PRODUCT

Our product consists of resorbable biopolymeric particles, in a carrier medium, that provide a protected microenvironment for tissue harbouring while enhancing cell growth and function (Fig.1). Polycaprolactone is the polymer of choice due to its biocompatibility and resorbability in the body. These particles would provide temporary bulking and it is proposed that they will also allow for tissue regeneration in the injected area. Unlike other available products our product has the advantage that it is fully resorbable and not a permanent implant that may have later complications. These ported, resorbable particles have the potential to be used in conjunction with biological additives such as growth factors and adult stem cells to act as cell microcarriers and promote cell growth.

Figure 1. Product in syringe

PREPARATION METHOD

The polycaprolactone micro-porous hemi-spherical micro-particles called 'hemi-shells' are prepared through a porogen-emulsion-solvent evaporation technique (patent pending [3]) as depicted in the schematic below.



This process results in porous single port particles in the 50–200µm range as observed through optical analysis (Fig. 2). The port allows for cell ingrowth into the particle as well as exchange of nutrients and oxygen to the cells.

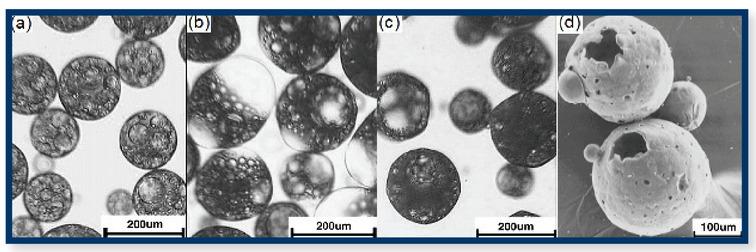


Figure 2. Optical photomicrographs of the hemi-shell morphological development with time: (a) 10 min, (b) 20 min, (c) 30 min, and (d) SEM micrograph of the final morphology of the polycaprolactone particle.

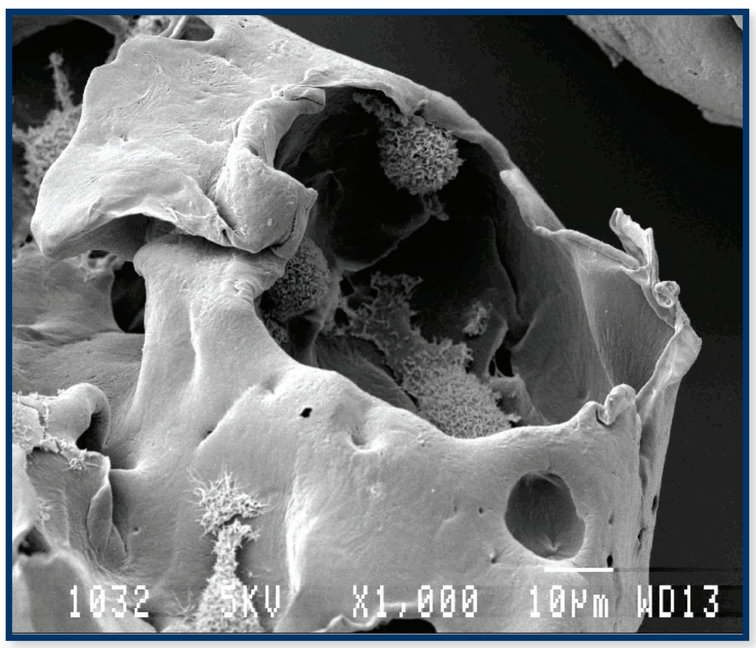


Figure 3: Cell growth on a hemi-shell

In order to assess the biocompatibility of our product, studies on cell lines were conducted. After five days cells showed spindle-shaped morphologies, closely following the internal and external contours of the microspheres, indicative of high focal adhesion. In the scanning electron microscope (SEM) image in Fig. 3, SKUT (leiomyosarcoma tumour cell line) cells are located on the external surface of the particle, but also surrounding the port and inside the internal cavity. It is proposed that our particles create a void space when injected in human tissue and that cells will locate inside the particle. This should lead to long term bulking after the particle has resorbed in 9-24 months.

CONCLUSIONS

The particle manufacturing process developed by CSIR researchers resulted in biocompatible particles that can be used in soft tissue augmentation applications. These particles are specifically tailored to provide a tissue harbour in which new tissue will be able to develop to allow long term bulking once the particle has resorbed into the body. This research had resulted in a patent application that has received a positive international preliminary report on patentability that will facilitate the eventual commercialisation of this unique product.

FUTURE DEVELOPMENT

Due to the product's classification as a class III medical device by the US Food and Drug Administration (FDA), a full pre-clinical study and subsequent clinical study is planned. As a first application we will be targeting the minimally-invasive cosmetic surgery market. This market is fast growing and our product has a possible niche application in longer term soft tissue augmentation. Our product will be formulated to be an injectable wrinkle filler that provides medium to longer term bulking. Further development work is planned in order to apply our product to other applications in the longer term.

REFERENCES

1. http://www.pharmaceutical-technology.com/glossary/biomaterials.html
2. Ollyo JB, Monnier P, Fontolliet C, Savary M. 1993. The natural history, prevalence and incidence of reflux oesophagitis. Gullet 3(suppl):1-10
3. WO 2007/113762 A2

CSIR researchers have developed an injectable, resorbable soft tissue bulking product that has potential applications in fields ranging from heartburn and reconstructive surgery, to minimally invasive cosmetic surgery.