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Biocomposites based on Polyurethane for Bone Tissue Engineering Applications

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Abstract

The main aim of this work is to develop and characterise biocomposites for tissue engineering applications. The biocomposites are made of a polyurethane polymer and a hydroxyapatite. By combining a polymer and a ceramic material can be formed biocomposites for bone tissue engineering applications, since the structure of bone can be grossly described as a collagen-hydroxyapatite composite. Structural properties and degradation rates in vitro of the composites were determined. The in vitro biodegradation of the composite in the phosphate buffered saline solution increased with incubation time and the rate differed with the coating concentration. The results demonstrate that the scaffold with low hydroxyapatite content will have higher degradation rate than that with high hydroxyapatite content.

Key words: *polyurethane, hydroxyapatite, biocomposites*

Introduction

Polyurethanes represent an important class of synthetic elastomers that have been used extensively as biomaterials over the past decades due to their excellent physical and mechanical properties, good blood compatibility and hydrolytic stability [1,2]. Polyurethanes are not generally biodegradable unless chemically modified [3]. Such modified biodegradable polyurethanes are now being synthesised for use in regenerative medicine. Examples include the fabrication of porous scaffolds for use in soft tissue engineering and cartilage repair. Other medical applications include bone graft substitutes and wound dressings [4,5].

Hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ is an inorganic compound whose chemical composition is comparable to the composition of the bone. It is a very attractive material for biomedical applications such as a bone substitute material in orthopaedics and dentistry due to its excellent biocompatibility, bioactivity and osteoconduction properties [6-9].

Because bone and teeth constitute an organic-inorganic hybrid, a reliable hybrid for implant applications should contain a polymer that possesses high shear strength, appropriate tensile/compressive strength, high hydrolytic stability and good adhesion with the hydroxyapatite. The use of polymer-based composites can provide a combination of good mechanical and tribological properties. Properties of composite materials are influenced by the morphology of the system and the nature of the interface between the phases [10,11].

In this work we selected a polyurethane polymer as support for hydroxyapatite. To improve the physiological response of the implant, the polyurethane prototype was coated with a homogenous layer of hydroxyapatite and the biodegradation of the scaffold *in vitro* was studied.

Experimental

The polyurethane membranes were prepared by solvent casting process using polyurethane and cellulose acetate polymers and N,N-dimethylformamide (DMF) as solvent. A simple Supersaturated Calcification Solution (SCS) with high calcium and phosphate ion concentrations was used for biomimetic coating study. The morphology and properties of the hydroxyapatite/polyurethane composite films were characterized by field emission scanning electron microscopy (Fe-SEM, with Fe-SEM MIRA II LMU CS 01 TESCAN microscope), density and pore sizes measurement. Further details on the materials processing and respective properties of membranes and composites used in this study can be found elsewhere [12-14].

The biodegradation of the scaffold *in vitro* was conducted as: the coated samples, having similar weight (0.5 – 1 g) and dimensions, were immersed in phosphate buffered saline (PBS) solution (1 M) under 37 ^{o}C at pH=7.2 for 1 to 8 weeks. At the end of the period, the samples were rinsed by distilled water for 3 times and dried at room temperature for 24 h for measurement of weight loss at 1 to 8 weeks. The weight ratio was calculated as follows:

$$\text{Weight loss ratio } (\%) = \frac{(w_1 - w_2)}{w_1} \cdot 100\% \qquad (1)$$

where: w_1 and w_2 are the weights of samples before and after degradation *in vitro*, respectively.

Results and discussion

The main aim of this work is to develop and characterise biocomposites for tissue engineering applications. The biocomposites are made of a polyurethane polymer and a hydroxyapatite. All SEM analysis reveals that the composite membrane is structured in a 3D macroporous network that offers a good accessibility to a Supersaturated Calcification Solution and a good adhesion between the hydroxyapatite and the polyurethane [12-14]. By biomimetic method it was possible to induce the growth of the hydroxyapatite films not only at the surface, but also in the bulk of the polyurethane film (Fig. 1).

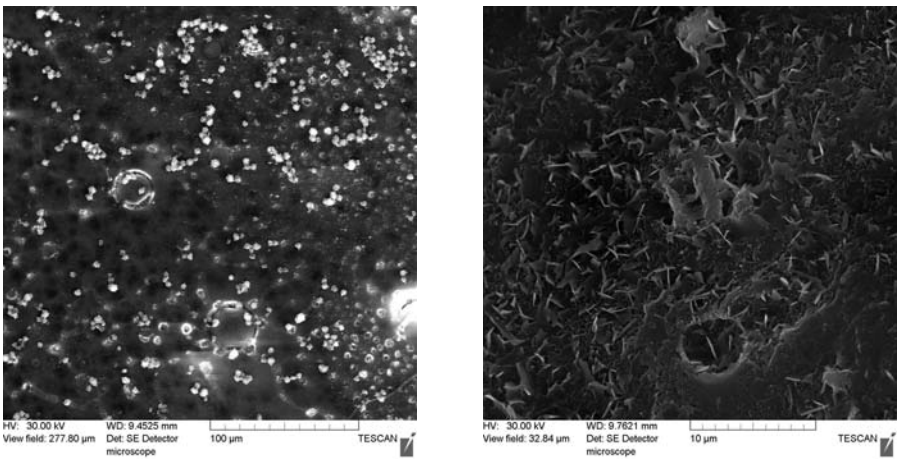

Fig. 1. SEM images of the hydroxyapatite / polyurethane composite films

Therefore, by combining a polymer and a ceramic material can be formed biocomposites for bone tissue engineering applications, since the structure of bone can be grossly described as a collagen-hydroxyapatite composite. The polyurethane polymer is expected to give a highly porous structure and the hydroxyapatite glass particles are expected to reinforce the biological properties of the composites.

The porosities of the scaffolds derived from different chemical compositions were determined by measuring the apparent density of the scaffolds and the densities of the corresponding solid polymeric materials. Based on these density measurements the porosities of the scaffolds were calculated to range between 65 and 80 %.

The *in vitro* biodegradation of the composites was performed on samples with different hydroxyapatite depositions, depending on time of immersion (1, 2 and 3 days) in Supersaturated Calcification Solution (SCS). The total weight loss of the scaffolds after dissolving in a phosphate buffered saline (PBS) solution at 37 ^{o}C for periods up to 8 weeks are represented in Fig. 2 with respect to incubation time.

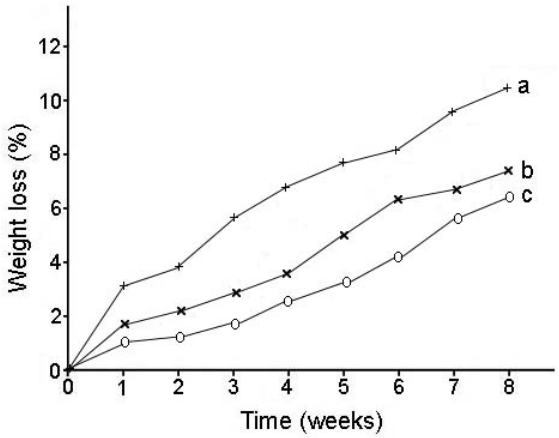

Fig. 2. The weight loss of the hydroxyapatite / polyurethane composite films after *in vitro* biodegradation in a PBS solution at 37 ^{o}C. Samples immersed in SCS for: 1 day (a), 2 days (b) and 3 days (c).

For all the coating scaffolds, the weight loss increased with incubation time. The sample with higher hydroxyapatite coating concentration showed the lowest weight loss (sample c). Moreover, the samples containing low hydroxyapatite amount dissolved more quickly. These results demonstrate that the scaffold with low hydroxyapatite content will have higher degradation rate than that with high hydroxyapatite content. This is attributed to that the increase in hydroxyapatite content in the composite decreases the availability of more polyurethane polymer to degradation.

These results confirm that the porous hydroxyapatite/polyurethane composite may have a good prospect to be used as scaffold for tissue engineering.

Conclusions

The porous hydroxyapatite/polyurethane composite membranes were fabricated via solvent casting process. To improve the physiological response of the implant, the porous polyurethane membranes were coated with a homogenous layer of hydroxyapatite by a coating method. The Supersaturated Calcification Solution was used to investigate hydroxyapatite formation on polyurethane matrix. Bioactivity of the hydroxyapatite coated polyurethane substrates was confirmed by hydroxyapatite formation on the polyurethane substrates after 3 days in Supersaturated Calcification Solution. In addition, the composites exhibited progressive

degradation *in vitro* taken by the mass loss and the degradation rate depended on the hydroxyapatite content in polyurethane matrix. These porous polyurethane composites have good prospects to be used as biodegradable and bioactive scaffolds in bone tissue engineering.

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Biocompozite pe bază de poliuretan cu aplicații în ingineria tisulară osoasă

Rezumat

În lucrarea de față se prezintă un studiu privind caracterizarea unor biocompozite din poliuretan şi hidroxiapatită cu aplicații în ingineria tisulară. Au fost determinate proprietățile structurale şi comportarea la degradare in vitro. Biodegradarea compozitelor în soluție salină tamponată cu fosfat creşte cu timpul de incubare, depinzând de cantitatea de hidroxiapatită de pe suportul polimeric. Rezultatele demonstrează că materialele compozite cu conținut scăzut în hidroxiapatită au o rată de degradare mai mare decât cele cu conținut ridicat în hidroxiapatită.