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Dynamic mechanical behavior of starch-based scaffolds in dry and physiologically simulated conditions: Effect of porosity and pore size

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Abstract

The three-dimensional scaffolds of a blend of starch and poly(L-lactic) acid, SPLA70, were produced using compression molding of polymer/salt mixture followed by leaching of salt. One series of scaffolds were prepared with varying polymer-to-salt ratio while keeping the salt size constant, and the other series of scaffolds were prepared with varying salt sizes while keeping the polymer-to-salt ratio constant. The X-ray microcomputed tomography and scanning electron microscopy assay were used to analyze the porous morphologies, porosity and distribution of porosity of the porous scaffolds. Salt-free and integrated SPLA70 scaffolds with porosities ranging from 74% to 82% and pore sizes of 125–250 to 500–1000 μm can be fabricated using the present fabrication technique. The water uptake of the SPLA70 scaffolds increases with increasing porosities and also with increasing pore size. In dry state, the storage modulus decreases with increasing porosity and also with increasing pore size. The normalized modulus values are related to normalized density of the scaffolds by a power-law function with an exponent between 2 and 3. For the immersed scaffolds under physiological conditions, the storage modulus was less dependent on porosity and pore size. However, the loss factor increased significantly compared with dry state measurements. The present study clearly shows that the mechanical performance of porous polymeric constructs in dry and in immersed state is completely different, and for comparison with biomechanical performance of tissues, the tests should ideally be performed in immersed state.

Keywords: Dynamic mechanical properties; Porosity; Pore size; Dry and immersed state; Starch blend

1. Introduction

Tissue engineering approaches have great potential in the biological and functional regeneration of tissues, allowing for overcoming the lack of donor tissue and to promote a biologically and mechanically functional tissue. An important step to engineer tissues is the development of porous three-dimensional scaffolds for different anatomical locations in the body. Generally, the materials of scaffolds are either of natural origin or synthetic biodegradable polymers [1–4]. Synthetic polymers have design flexibilities in terms of materials composition, processability, control over macro- and microstructures, and mechanical properties [4]. These properties can be tuned for specific applications. However, natural polymers are also used in biomedical applications for their excellent biocompatibility and biodegradability [3,5].

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Poly(α-hydroxy acids) including poly(lactic acid) (PLA), poly(glycolic acid) (PGA) and their co-polymers (PLGA) are the widely accepted polymers for most of the tissue engineering applications [6]. These thermoplastic polyesters have reasonable biocompatibility, biodegradability, mechanical strength and easy processability. Blends of PLLA and starch (SPLA) have also been proposed in our group to be used in the biomedical field, and were found from cell adhesion and proliferation tests, to interact positively with cells [7].

The fabrication of porous scaffolds from a polymer melt allows fast production of scaffolds with different shape and sizes in an efficient way. The most straightforward way is to melt a polymer of a polymer/salt mixture, cool it and subsequently remove the salt particles, thus producing the porous scaffolds. The desired porosity and pore sizes could be independently controlled by the fractions and sizes of salt particles, respectively [8,9].

The mismatch between the mechanical properties of scaffolds and the tissue intended to be regenerated may compromise the clinical success of the tissue engineering construct. In this regard, stiffness is a relevant mechanical property of scaffolds as it will determine the deformability of the structure upon implantation. The modulus of elasticity describes the slope of the stress–strain relationship for a given material under load. Such property depends strongly on the porosity in the case of a porous system, and may also be influenced by pore size [10]. In the case of polymeric-based materials, one should also consider their viscoelastic properties as they will determine the capability of the device to dissipate mechanical energy and are responsible for the time-dependent nature of its mechanical performance. Moreover, living tissue also exhibits a clear viscoelastic behavior and, ideally, the implantable scaffold should present similar properties in order to maintain the contact with the surrounding tissue during all the physiological stress–strain history. Of course, this would be difficult to achieve using polymer-based materials intended to be used in the replacement or regeneration of hard tissues. Although some rheological properties could be similar in biomaterial and tissue (e.g. damping), stiffness-related properties are more difficult to achieve.

Dynamic mechanical analysis, DMA, is a non-destructive technique widely used in the characterization of the viscoelastic properties polymer-based systems including biomaterials covering wide temperature and frequency ranges [11]. Such studies are particularly relevant if the tests are performed at physiologically meaningful conditions, i.e., with the specimens completely incubated in solutions at 37 °C. Similar procedure was previously implemented to study starch-based biomaterials [12,13]. However, such dynamic tests performed at conditions close to the in vivo situation are not yet sufficiently established among the community. This work intends to strengthen the importance of such kinds of experiments.

In this study, the biodegradable polymeric scaffolds were prepared using compression molding technique with the melting of the polymer in a polymer/salt mixture followed by the dissolution of salt in water. One series of scaffolds was prepared by varying the polymer-to-salt ratio while keeping the salt size constant, and the other series of scaffolds was prepared by varying the sizes of the salt particles while keeping the polymer-to-salt ratio constant. The morphology of the scaffolds was assessed by X-ray microcomputed tomography analysis and scanning electron microscopy. The accessibility of internal pores or hydraulic conductivity of the scaffolds prepared with different pore sizes and porosities was determined by relative water uptake of the scaffolds. Moreover, the dynamic mechanical properties of the scaffolds were assessed in both dry and incubated state at physiological temperature of 37 °C. The relationship between mechanical properties, pore sizes and porosities were then established.

2. Materials and methods

2.1. Materials and scaffold processing

A 30/70 (wt.%) blend of starch and PLLA (SPLA70) was used in this study. The SPLA70 was obtained by melt blending of 70 wt.% PLLA and 30 wt.% of corn starch. The PLLA of SPLA70 had L-lactide content of 94%.

2.1.1. Powder preparation and compounding

SPLA70 pellets were dried at 50 °C in a vacuum oven and cryogenically milled in an ultra-centrifugal mill (Retsch, ZM-100) with liquid nitrogen at 14,000 rpm. The selected NaCl particle sizes were hand-sieved with the stacked stainless steel sieves (ISO3310, Endecotts Ltd., England).

2.1.2. Compression molding

The compression-molded disks of around 5 mm thickness and 80 mm diameter were prepared on a steel mold using a Moore hydraulic press (UK), with 50 ton capacity. Prior to compression molding, the powdered SPLA70 was dried in a vacuum oven. The polymer/salt mixtures were put in between Teflon release papers in the mold. The mold was then placed in between the hot plates of the hydraulic press at top and bottom platen temperature of 180 °C. To remove the trapped air in bulk powder, the pressure was slowly raised around 20 MPa and released, and this process was repeated five times. The polymer/salt mixture was then allowed to melt for 6 min at constant pressure of 151 kPa, the weight of top half of the mold. The mold was then cooled to room temperature. The initial compositions of the constituents that were used to prepare the studied scaffolds are shown in Table 1.

2.1.3. Porogen leaching

The molded disks were sliced to $\sim 5 \times 5 \times 5\ mm^3$ cuboids and put into water. The leaching was performed in beakers filled with de-ionized water at 37 °C. Water was replaced every 4 h. The presence of NaCl content

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