Fabrication and Characterization of Hybrid Polymeric Scaffolds

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Introduction

The ultimate goal of this research was to fabricate and characterize hybrid polymeric scaffolds composed of at least two components to mimic natural tissue structure at specific defect sites. Using salt particles and degradable hydrogel particles as a porogens allows for controlled pore opening after implantation as well as the potential for drug release during degradation. The controlled pore opening also allows the scaffolds to withstand the necessary mechanical properties at the implant site while degrading at a rate consistent with tissue regeneration. The system comprised poly(lactic-co-glycolic acid) (PLGA), poly(β-amino ester) (PBAE), and salt particles. In the present study, homogenous and layered scaffolds were examined to determine the compositional relationship, mass loss, pore size and pattern of porosity development to design application-based scaffolds.

Materials and Methods

PLGA (50:50, IV: 0.55-0.75 dL/g, acid-terminated; Durect Corporation) microspheres (MS) were fabricated using a water/oil/water double emulsion technique. The resultant microspheres were sieved to <250 µm. The hydrogel (HG) macromer was synthesized through a step-wise reaction between poly(ethylene glycol) diacrylate (PEGDA; Polysciences), diethylene glycol diacrylate (DEGDA; Polysciences) and isobutylamine (Sigma-Aldrich) with DEGDA:PEGDA molar ratios of 3:1, 2:1, 1:1, where the ratio of amine to total diacrylate was 1:1.2. The macromer was combined with initiator and solvent before UV photopolymerization. For homogeneous scaffolds, MS, HG and salt were mixed using cryomill at weight percentages of 50:30:20 (MS:HG:salt) to yield samples having an overall mass of 105 mg. The mixture was poured in a mold device and exposed to 49ºC for 2 days to sinter, allowing the MS to fuse together around the porogens. Samples were then salt leached, vacuum dried and placed in 4 mL phosphate-buffered saline (PBS), pH 7.4, on a plate shaker at 37°C for almost 60 days. Samples were lyophilized and analyzed using microcomputed tomography (microCT) to monitor porogen degradation and scaffold morphology. Two-layered scaffolds were fabricated using the same material ratios as the homogenous samples. The cryomill process for the bottom layer consisted of HG and MS, and the top layer consisted of MS and salt particles both sieved to <250 µm. The mixture then went through the same mold process as homogenous scaffolds.

Results and Discussion

All pre-salt leached scaffolds showed negligible porosity. Once leached, there was an overall porosity of 20% as expected from theoretical salt volume calculations. Once samples were placed in PBS, the 30 wt% HG porogen began to degrade consistent with their degradation rate to increase the overall porosity of the samples. An average pore opening of 100-130 µm was measured. The difference in time dependent development of porosity between the scaffolds was due to the three different HG porogens. As expected, samples with higher PEGDA content had faster degradation rates (Figure 1). This accelerated degradation is due to the increased hydrophilicity of the PEGDA as compared to the DEGDA, thus allowing more water into the network structure to accelerate hydrolysis. Once the hydrogel porogen was degraded, the residual PLGA matrix degraded at a much slower rate (Figure 2). The two-layered samples went through the same degradation process, leaving the top layer with pores ranging from 250 to 300 µm, while the bottom layer consisted of pores ranging from ~100-130 µm (Figure 3).

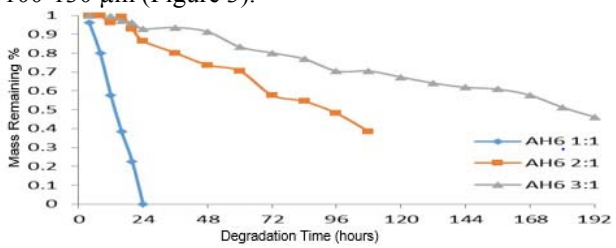

Figure 1. Degradation of PBAE porogens, where A: DEGDA, H: PEGDA and 6: isobutylamine.

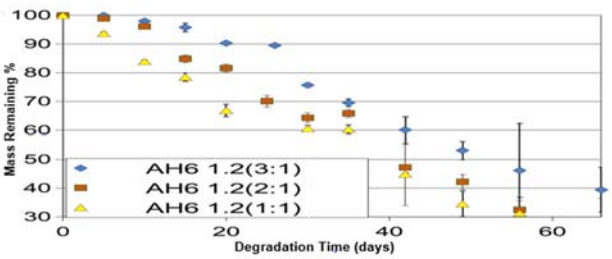

Figure 2. Degradation of 50:30:20 (wt%) MS:HG:NaCl scaffolds containing HG porogen having different degradation rates (Figure 1).

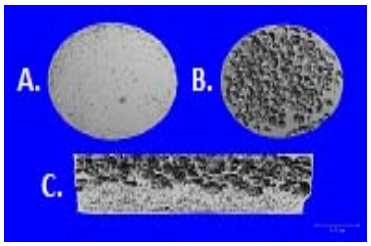

Figure 3. MicroCT images illustrating architecture of the two layered scaffold. A) Prior salt leaching, B) post leaching, and C) cross section after 2 weeks degradation.

Conclusions

This study demonstrated controlled pore opening with degradation as a function of time through different HG porogens. Spatiotemporal modulation of hybrid scaffold properties, e.g., pore opening, pore size, and mechanical and structural characteristics, can be used to design scaffolds for specific applications.

Acknowledgement

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