

Time-Dependent Development of Porosity in a Hybrid Polymeric Scaffold

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Introduction

The overall goal of this research was to develop and characterize a hybrid polymeric scaffold in which pores are formed as a function of time of incubation in solution.

The system combining poly(lactic-co-glycolic acid) (PLGA), poly(β -amino ester) (PBAE) hydrogel, and salt particles. By adjusting the time course over which porosity develops, the scaffolds might be useful for different tissue engineering applications. In the present study, different weight ratios of PLGA to hydrogel to salt were examined to determine the compositional relationship to increasing porosity and mass loss.

Materials and Methods

PLGA (50:50, IV: 0.55-0.75 dL/g, acid-terminated; Durect Corporation) microspheres were fabricated by using a water/oil/water double emulsion technique. The first emulsion sonicated 10% v/v PBS into a solution of 13wt/v% PLGA dissolved in dichloromethane (DCM), while the second emulsion homogenized the above solution into a 1% poly(vinyl alcohol) in deionized water. The resultant microspheres were stirred overnight, then washed, lyophilized and sieved to <250 μ m.

The hydrogel macromer was synthesized through a step-wise reaction between a poly(ethylene glycol) diacrylate (PEGDA; Polyscience) and diethylene glycol diacrylate (DEGDA) (molar ratio of 3:1, DEGDA:PEGDA) and isobutylamine (Sigma-Aldrich) and 2,2-dimethoxy-2-phenylacetophenone (DMPA; Sigma Aldrich) to make a single macromer system. Hydrogels then underwent chemical initiated free radical polymerization via UV photopolymerization. The hydrogel slab was mixed with PLGA microspheres and grounded using a mortar and pestle where different salt particles were added to the mixture.

A fixed mass of microspheres was mixed with different amounts of hydrogel and salt particles at percentage of 40:40:20 (150 μ m), 30:40:30 (250 μ m) and 30:40:30 (150 μ m, salt particle size) (hydrogel %: microsphere %: salt %) to yield samples having an overall mass of 105 mg. The mixture was combined into a mold having sample dimensions of 2.4 mm height and 6 mm diameter. The mold was placed in an oven at 42°C for 2 days to sinter allowing the PLGA microspheres to fuse together around the hydrogel and salt particles. The samples were then taken out the mold and placed in stirred water overnight for salt particles to leach out and then dried vacuumed for two days. The samples were then placed in 4 mL phosphate buffered saline (PBS), pH 7.4, on a plate shaker at 37°C for two weeks. The samples were lyophilized and the scaffolds analyzed using microcomputed tomography (microCT;) to monitor porogen degradation and determine scaffold morphology.

Results and Discussion

The initial state of all the pre-salt leached scaffolds was a solid mass with negligible porosity (Figure 1, top). After salt leaching (Figure 1, middle), there was an overall

porosity of 20, 30 and 35% for the 40:40:20 (150 μ m), 30:40:30 (250 μ m) and 30:40:30 (150 μ m), (hydrogel:microsphere:salt) scaffolds, respectively, which was expected from the theoretical salt volume calculations. After 2 weeks in PBS, an overall porosity of 69, 80 and 74% for the 40:40:20 (150 μ m), 30:40:30 (250 μ m) and 30:40:30 (150 μ m) was seen (Figure 2). Once samples were placed in PBS, the PBAE hydrogel porogen began to degrade and the porosity increased. The difference in porosity between the scaffolds was due to the different amount and size of salt particles, and the amount of hydrogel porogen. The porogen particles started degrading as the PBS infiltrated the scaffold from the outer circumference inward, and after the porogen is degraded, the residual PLGA matrix degrades at a much slower rate (Figure 1, bottom).

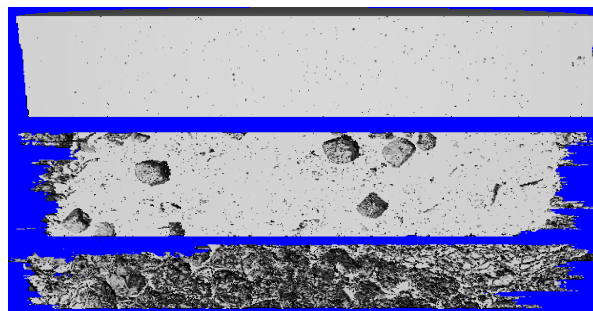


Figure 1: MicroCT images illustrating architecture of scaffolds before salt leaching, after leaching and after 2 weeks incubation in PBS.

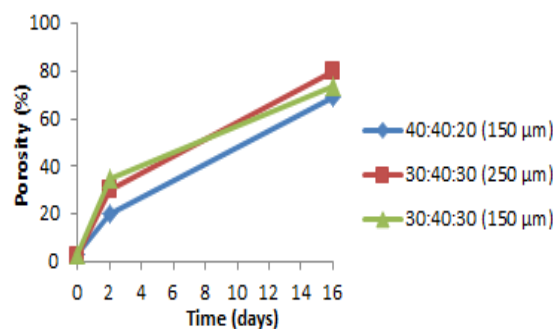


Figure 2: Increase in porosity before salt leaching, after leaching, and after 2 weeks incubation in PBS (days 0, 2, and 16, respectively).

Conclusions

This study demonstrated the effect of combining a porous scaffold with a quick-degrading porogen to further develop porosity as PBS infiltration occurs. The time-dependent development porosity may be also useful for drug delivery as cells migrate into the scaffold.