The Effect of Adding a Hydrogel Porogen into a Poly(lactic-co-glycolic acid) Scaffold

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Introduction

Poly(lactic-co-glycolic acid) (PLGA) has been shown to be biocompatible and biodegradable, and is therefore commonly used as a biomaterial. A novel hybrid scaffold combining PLGA and hydrogel builds upon the success of PLGA scaffolds by adding the possibility of a multidrug delivery system. Drug-loaded hydrogel porogen allows for an initial drug release (for example, an anti-inflammatory or antibacterial drug) followed by prolonged release of an addition drug or growth factor from the PGLA matrix. Changing the weight ratio of PLGA to hydrogel will allow for system tuning of the drug delivery rate, the overall amount of drug delivered, and the mechanical properties. Each of these factors will dictate the overall feasibility of using the scaffold in a range of applications, such as bone or cartilage implants, that can benefit from a synergistic effect resulting from a potentially dual releasing scaffold in conjunction with mechanical support.

Methods

PLGA microspheres (<250 μm) were fabricated using a water/oil/water ($W_1/O/W_2$) double emulsion technique.

Hydrogel particles (<500 μm) were made of a poly(β amino ester) (PBAE) biodegradable system through a step-wise reaction to make a H6 hydrogel (J Adv Mater, 2006, 18, 2614-2618) followed by free radical polymerization. A fixed mass of microspheres was mixed with increasing amounts of hydrogel particles at weight of ratios of 40:60, 50:50 and 60:40 (microspheres:hydrogel) to yield samples having overall weights of 70, 84 and 105 mg. The mixture was ground together, consolidated, and sintered for 2 days at the glass transition temperature to allow for the microspheres to fuse together.

To measure degradation, samples were shaken at 37 °C in 4 mL PBS. At each time point, scaffolds were removed, lyophilized, and the remaining mass measured. A Bose ELF 3300 mechanical testing system was used to measure the compressive modulus of dry samples as well as samples that had been incubated in PBS for 5 days.

Results and Discussion

All of the scaffolds experienced a plateau in mass loss after 6 days from the degradation of the hydrogel particles (Figure 1). The 40:60 scaffolds showed the greatest mass loss up to day 20, which was expected because the hydrogel particles made up the largest portion of the overall mass. The 50:50 and 60:40 scaffolds had similar trends, even though the 60:40 scaffolds had almost 20 mg more hydrogel particles. This could be because the hydrogel particles made up such a large portion of the 60:40 scaffold that the hydrogels may have encapsulated some of the microspheres and carried them out during the initial degradation.

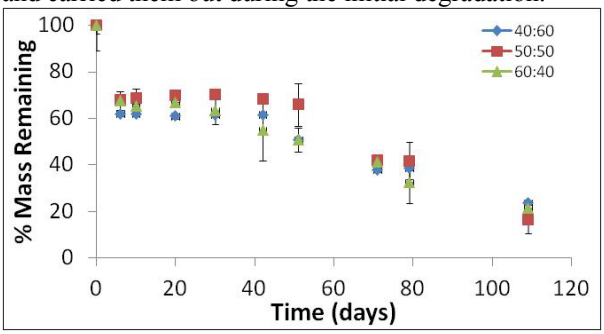

Fig 1. Degradation of scaffolds over time.

For the dry scaffolds, larger amounts hydrogel particles reduced the compressive modulus (Figure 2). This is to be expected since the amount of fused microspheres would decrease as more hydrogel is added, acting as a barrier between microspheres. After 5 days, the 50:50 scaffolds had a higher compressive modulus than did the 60:40scaffolds, which can be attributed to the overall mass loss of the 60:40 exceeding that of the other scaffolds. Additionally, the compressive modulus of the 60:40 scaffolds would be lower since fewer microspheres would have fused together. The 40:60 and 50:50 scaffolds had 28 and 42 mg of hydrogel particles, but by day 6 both had lost approximately 26 mg. Even though the hydrogel particles decreased the initial modulus, after 5 days the added mass of remaining particles helped contribute to the modulus of the 50:50.

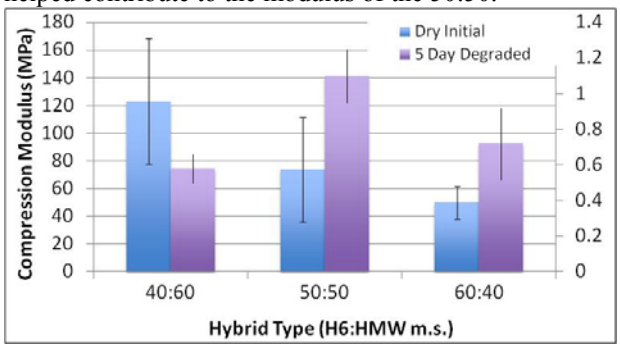

Fig 2. Compressive modulus of dry scaffolds and 5 days degraded.

Conclusion: A novel hybrid PLGA scaffold using a hydrogel particle as a porogen at various weight percentages offers the necessary mechanical support for a wide variety of tissue engineering implants. Furthermore, the scaffold has the potential to be a multidrug delivery system. The addition of the porogen affected the scaffolds initially, up to 5 days, after which the PLGA matrix of the scaffolds behaved similarly.

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