Poly(diol citrate) nanocomposites with enhanced mechanical properties for soft tissue engineering

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Statement of Purpose: Due to the stiffness and lack of elasticity of commonly used polymers in tissue engineering, our laboratory has developed a novel family of biodegradable elastomeric polyesters referred to as poly(diol citrates) [1]. However, the mechanical properties that can be obtained may not meet the demanding requirements of musculoskeletal tissues. In this study we describe the fabrication and mechanical characterization of a novel elastomeric nanocomposite material in which the macrophase consists of a poly(diol citrate) elastomer and the nanophase consists of a poly(L-lactic acid) (PLLA) nanofibrous network.

Methods: Poly(diol citrate) prepolymers were created as described elsewhere [1]. The PLLA nanofibrous nanocomposite was fabricated via thermally induced gelation followed by coating with poly(diol citrate) pre-polymer and polymerization [2]. Porous nanofibrous nanocomposite scaffolds were prepared through the addition of salt particles during the gelation step.

Non-porous samples were tested for ultimate tensile strength, Young's modulus, and strain at break using ASTM D412a. The compressive modulus of porous scaffolds was evaluated in unconfined compression using a stepwise stress/relaxation test [3]. Data are expressed as means ± standard deviation with statistical significance calculated using two-tail *t*-test or analysis of variance.

Results/Discussion: Nanofibrous networks were created with PLLA concentrations of 5% or 10%. The addition of a nonelastic nanoscale PLLA to elastomeric poly(diol citrates) significantly increased the mechanical properties while maintaining elasticity (**Table 1)**. For the tensile strength, modulus, and elongation, a statistically significant difference was found when comparing the PDC control (no PLLA) and the PLLA-PDC nanocomposites, confirming that the mechanical properties could be significantly increased using nanofibrous composite elastomers. Comparing between composites reinforced with different amounts of PLLA, there is an increase in the mechanical properties with increasing PLLA concentration from 5% to 10%. The increase in mechanical properties with the addition of PLLA nanofibrous networks may be due to mechanical interlocking and/or interactions between the nanofibers and the elastomer chains.

Table (1) - Mechanical properties of PDC nanocomposites

Sample	TS (MPa)	YM (MPa)	Elong (%)
5% PLLA-PDC 80-3	2.2 ± 0.2	7.5 ± 1.4	211 ± 52
10% PLLA-PDC 80-3	3.4 ± 0.9	13.1 ± 2.9	302 ± 38
10% PLLA-PDC 120-2	13.0 ± 3.2	85.1 ± 5.5	71 ± 28
PDC 80-3	1.4 ± 0.05	1.2 ± 0.1	207 ± 24
PDC 120-2	1.9 ± 0.3	1.9 ± 0.3	163 ± 29
5% PLLA	0.2 ± 0.05	10.1 ± 1.1	2.65 ± 0.69
10% PLLA	0.7 ± 0.08	29.2 ± 8.3	4.28 ± 0.98

(PDC = poly(1,10-decanediol-co-citrate), TS = tensile strength, YM = Young's modulus, Elong = elongation at break, 80-3 = polymerized at 80°C for 3 days without vacuum, 120-2 = polymerized at 120°C without vacuum for 1 day followed by 1 day with vacuum)

The effect of post-polymerization conditions on the nanocomposite's mechanical properties was also assessed. Increasing the post-polymerization temperature increased the tensile strength and modulus of the nanocomposite (**Table 1**). This suggests that it is possible to tailor the mechanical properties of the nanocomposite to specific soft tissue engineering applications. When compared to native tissue, the tensile mechanical properties of the highly polymerized 10% PLLA-PDC compare favorably to that of human cartilage (TS = 3.7-10.5 MPa), ligament (YM = 65-541 MPa), and coronary arteries (TS = 1.4-11.14 MPa)

Since poly(diol citrate) composites are targeted for tissue engineering, porous nanocomposites scaffolds were created. The addition of PLLA nanofiber meshes to PDC significantly increased the mechanical properties (**Figure 2**). In addition, for a 10% PLLA-PDC porous nanocomposite, the compressive modulus was 439 ± 106 kPa, similar to that of human (581 ± 168 kPa) and bovine (310 ± 180 kPa) articular cartilage. This is important as a tissue engineering scaffold should have mechanical properties that match that of the host tissue at the site of implantation.

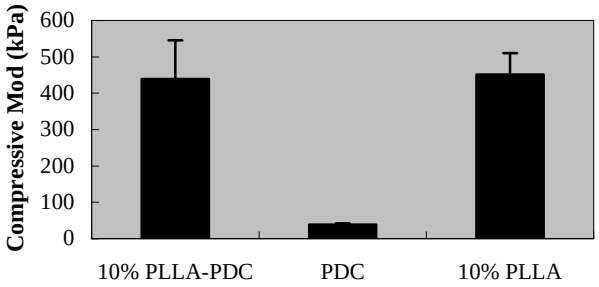

Figure 2 – Compressive modulus of porous nanocomposites

Conclusions: The incorporation of nanophase PLLA into a PDC elastomer increased the mechanical properties while still maintaining elasticity. In addition, it was demonstrated that the mechanical properties could be adjusted by varying the concentration of the nanophase or polymerization conditions. The range of mechanical properties that can be obtained was similar to many soft tissues. These results warrant further study of poly(diol citrate nanocomposites for soft tissue engineering.

References:

1. Yang J. Adv Mater. 2004;16: 511-516.
2. Ma P. J Biomed Mater Res. 1999;46:60-72.
3. Korhonen RK. J Biomech. 2002;35:903-909.