



Biodegradable elastomer for soft tissue engineering

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ABSTRACT

In this work we present the synthesis of a biodegradable, elastomeric material with a wide range of mechanical properties. The synthesis of the material was done by condensation polymerization of malic acid and 1,12-dodecandiol. The synthesized materials have low Young's modulus ranging from about 1 to 4 MPa and a high elongation at break of 25–737% depending on the crosslinking density of the system. The cell growth observed under microscope showed good proliferation at 3 days of culture indicating good biocompatibility and support of L929 cells growth. The fabrication of 3D scaffold from these materials using the super critical CO₂ foaming method was also attempted. This method of scaffold fabrication is appropriate for materials that are easily hydrolysable and it also has the advantage of being a solvent free process. These materials are generally soft, biocompatible and biodegradable making them suitable for tissue engineering of soft tissues that are elastic in nature like muscles and blood vessels.

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1. Introduction

Design of new materials has been one of the many challenges in the field of biomedical engineering. Most of the common biodegradable synthetic biopolymers are linear thermoplastics that are relatively stiff in nature which results in a very poor mechanical compliance with the soft and elastic native tissues [1–3]. Therefore biodegradable elastomers development has been receiving much attention lately.

There have been a number of developments in biodegradable elastomers in the recent years. There are two main classes of synthetic biodegradable elastomers; thermoplastic [4–7] and thermoset [8–13]. While thermoplastic elastomer materials offer synthetic control and ease of processing, the majority of these materials contain crystalline domains and the elasticity is not as superior as the thermosetting elastomers. Thermoset elastomers are rubbery at 37 °C giving them a highly elastic property. However, many of these elastomers require challenging and costly synthesis methods and some also require use

of initiators and catalysts which may be detrimental for cells survival [14–17]. Some elastomers may be less synthetically challenging to prepare but the mechanical properties are still quite high relative to some soft tissues and hence may be more suitable for the stiffer soft tissues like cartilage and tendon [18].

In this work, we report the synthesis, characterization and scaffold fabrication method for an elastomeric biodegradable polymer that has a wide range of mechanical properties. The tensile strength can range from 0.21 to 4.16 MPa and Young's modulus from 0.98 to 4.04 depending on the curing conditions which can be easily modified.

2. Materials and methods

2.1. Synthesis of poly (diol malates)

Malic acid and 1,12 dodecandiol used in this study were purchased from Sigma–Aldrich, USA at 99% purity for both materials. Different curing conditions and molar ratios of acid to diol have been attempted in this study as summarized in Table 1. It is to be noted that crosslinking could take place due to the fact that the diacid contains a secondary alcohol.

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Table 1

Different curing conditions and molar ratios of acid to diol attempted in this study.

Polymer	Molar ratio of acid to diol	Equivalent ratio of COOH to OH functional group	No. of post curing days	
			140 °C	160 °C
A	1:1	2:3	21	0
B	1:1	2:3	36	0
C	1:1	2:3	5	16
D	1:1	2:3	12	17
E	1:2	2:5	36	0
F	1:2	2:5	16	13
G	1:2	2:5	22	31

The required amount of malic acid and diol were mixed in a three neck flask and purged with high purity nitrogen gas. The set up was heated to 140 °C by silicon oil bath under constant stirring. The solution at this stage is denoted as the pre-polymer. Once the chemicals were homogeneously mixed, the material was then poured into a mold and sent for post curing. After post curing, the materials were rinsed in water to remove residue monomers and are then ready for characterization.

2.2. Material characterization

Indication of crosslinking was monitored by following the changes in the functional groups using Attenuated Total Reflectance (ATR); Fourier Transform InfraRed (FTIR) Perkin Elmer GX2000. Before the runs, the FTIR system was purged with nitrogen overnight to remove any moisture inside the system. The background spectrum was taken in air at 4 cm⁻¹ resolution for 16 times accumulations.

Mechanical properties of the elastomers were tested using Instron Microtester 5848. Samples were cut into rectangular shape of 6 × 0.5 × 18 mm (W × T × L). The crosshead speed was set at 5 mm/min. The Young's modulus that was obtained was used to calculate the crosslinking density based on the theory of rubber elasticity using the following equation below.

$$N = E/3RT \quad (1)$$

where n is the crosslinking density (mol/m³), E is the Young's modulus (Pa); R is the universal gas constant (8.3144 J/mol K); T is the absolute temperature (K), which is 298 K in this case.

The degradation studies were obtained by monitoring the weight loss over immersion time. Each sample was immersed in 15 mL PBS solution and incubated at 37 °C. The PBS solution would be changed frequently to maintain the pH at around 7.4. Weight loss was obtained by comparing the initial weight (W_0) and the weight measured at fixed intervals (W_t).

$$\text{Weight loss (\%)} = [(W_0 - W_t)/W_0] \times 100 \quad (2)$$

2.3. Cell attachment and proliferation

After sterilization of the materials, they were cut into circular shapes and placed in the 24-well plate together

with the control. A cell solution with cell density 5×10^5 /ml of L929 mouse fibroblast is prepared for cell seeding. 100 µl of cell solution is added onto each well plate and are incubated at 37 °C and 5% CO₂ for 1 h before adding 500 µl of complete medium to each scaffold. The cells were observed under the Nikon eCLiRse TS 100 Optical Microscope at the 3rd day of culture.

2.4. Scaffold fabrication using supercritical CO₂ (SCCO₂)

For scaffold fabrication, a partially cured polymer was placed inside the supercritical CO₂ chamber and then heated up to the saturation temperature ($T_{\text{saturation}}$) at 120 °C. The pressure in the chamber was increased to saturation pressure ($P_{\text{saturation}}$) of 3500 psi once the desired saturation temperature is achieved. The whole process of scaffold fabrication is as shown in the steps below:

3500 psi(2 h) → 500 psi(10 min) → 3500 psi(1 h)
 → 100 psi post cure in SCCO₂
 Machine (overnight).

3. Results

3.1. Polymer characterization

Fig. 1a and b show the FTIR analysis of the elastomers and pre-polymer. The elastomers showed very similar prominent peaks at 1690–1750 cm⁻¹ which could be assigned to carbonyl (C=O) groups. The peaks at about 2931 cm⁻¹ is assigned to methylene groups which were found in all the spectra of the elastomers. The broad peaks centered at 3475 cm⁻¹ are assigned to the hydrogen bonded hydroxyl group stretching vibration. It is very obvious that this peak showed up much more strongly in the pre-polymers compared to the elastomers. For example, in Fig. 1a, the ratio of the OH peak relative to the methylene peak is about 0.68 and 0.063 for the pre-polymer and elastomer D, respectively. In Fig. 1b, the ratio was 0.90–0.11 for the pre-polymer and elastomer G, respectively. This reflected the uncured –OH groups from the diol in the pre-polymer.

The crosslinking density of the elastomers presented in Fig. 2 showed an increase of crosslinking density with the first step (140 °C) curing time as expected. However, the second step curing (at 160 °C) seems to be more effective in increasing the crosslinking density. The crosslinking density for the first group of elastomers (A to D) seemed to have reached saturation at curing condition of C.

3.2. Mechanical properties

Typical stress strain curves of the elastomers are shown in Fig. 3; exhibiting elastomeric characteristics. After sample failure, no permanent deformation was found in all the samples which also indicates elastomeric behavior of the materials. The tensile strength and Young's modulus ranged from 0.21 ± 0.04 to 4.16 ± 0.90 MPa and 0.98 ± 0.17 to 4.04 ± 0.78 MPa, respectively, depending on the crosslinking density and acid to diol molarity. As seen in Table 2,

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