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LETTER

Development of layered porous poly(L-lactide) for bone regeneration

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Biodegradable porous materials called scaffold have been used for cell culture in tissue engineering. Poly(L-lactide) (PLLA) and poly(ε-caprolactone) (PCL), typical biodegradable polymers, have been considered as the candidates for polymeric scaffolds [1–7]. These scaffolds should have proper mechanical properties comparative to target tissues to be regenerated. For example, scaffolds for bone tissue may need to have much higher mechanical properties than for softer tissues. However, such polymeric scaffolds have much lower mechanical properties than bone tissue, and may easily be collapsed when implanted into damaged part of bone tissue. In this study, therefore, layered structure was introduced to improve the mechanical properties of porous PLLA scaffold. In this newly developed structure, a porous core region is surrounded by a solid layer that works as load bearing structure. This kind of layered structure is very similar to the bone structure in which porous cancellous bone is surrounded by cortical bone.

Porous structure of PLLA was fabricated by the solid–liquid phase separation and freeze-drying methods [6, 8]. In the first process, PLLA pellets were dissolved in 1,4-dioxane to make 3 and 7 wt% solutions. These solutions were then filled into a test tube in which a PLLA film with a thickness of 250 μm was inserted. The PLLA dioxane solutions in test tubes were cooled from the bottom surfaces at a constant rate by using liquid nitrogen to induce solid–liquid phase separation. The phase-separated samples were then dried under vacuum at −5 °C for about 1 week to remove the solvent completely. Cylindrical samples were obtained and then trimmed to be a cylinder with 8.5 mm diameter and 11 mm length. For each of the samples, the diameter and length were measured at three different positions and averaged values were then used to estimate the volume of the cylinder. The density of the sample was evaluated from the volume and weight. Porosity (volume fraction of pores) of the scaffold was then estimated from the densities of PLLA solid and the scaffold. Compression tests of the scaffolds were performed using a conventional mechanical testing machine at a loading rate of 1 mm/min. Five specimens were tested for each of the samples. Elastic moduli were then estimated from the initial slope of the stress–strain curves. Compressive strength values were also evaluated at the critical points where the stress–strain curves reached the first inflection points that corresponded to the end of elastic deformation behavior. A field-emission scanning electron microscope (FE-SEM) was also used to observe the microstructures of the porous samples and the deformation behavior of the porous samples at the critical point.

FE-SEM microphotographs of the mono- and layered-structural scaffolds made from 3 wt% solution are shown in Fig. 1. The mono-structure shows homogeneous distribution of pores with larger holes that are produced by solvent exhaust. It is seen that the solid layer is firmly connected to the porous core region. For the 3 wt% scaffolds, the range of pore size is about 10–100 μm, and for the 7 wt%, the range is 10–55μm. The size of solvent exhaust hole is 90–120 μm. The porosity values of the scaffolds are shown in Fig. 2. The porosities tend to decrease with increase of PLLA concentration. The porosities of both mono-scaffolds are much higher than

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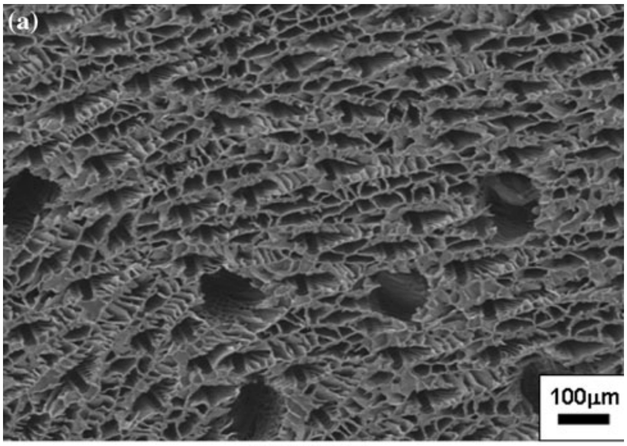
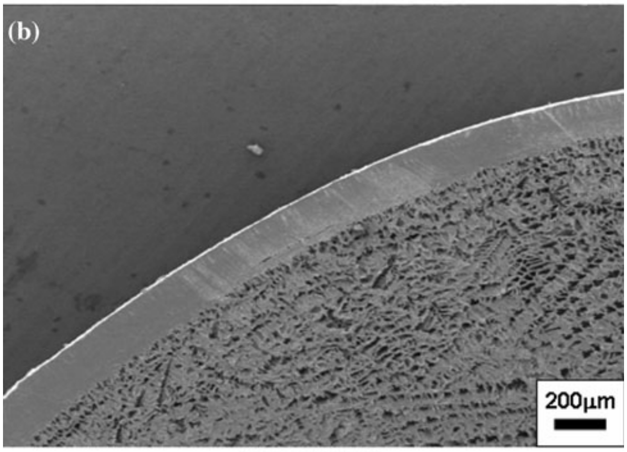


Mono-structure



Layered-structure

Fig. 1 Porous microstructures of PLLA scaffolds. **a** Mono-structure. **b** Layered-structure

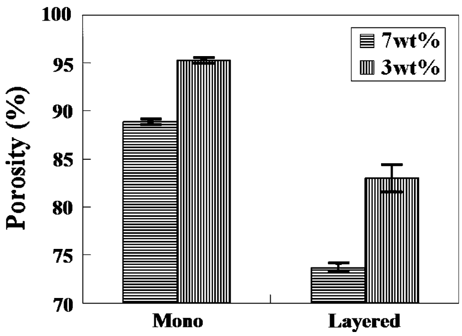


Fig. 2 Porosity values of PLLA scaffolds

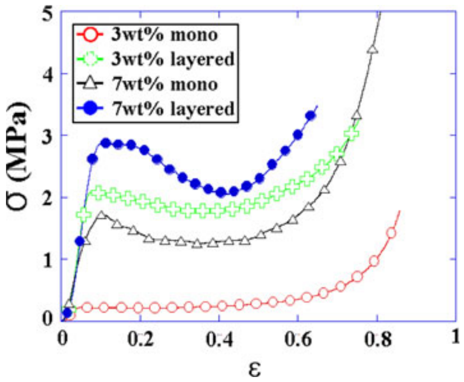
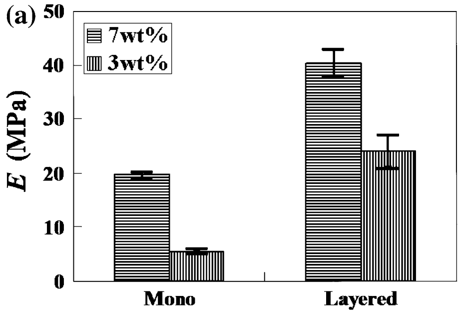
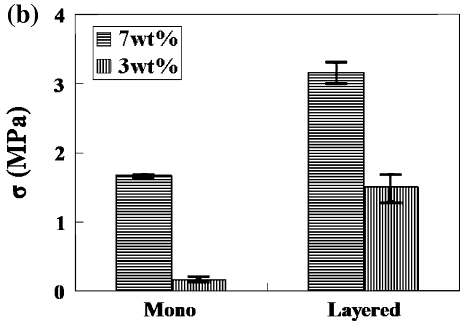


Fig. 3 Typical stress–strain curves of PLLA scaffolds under compression



Elastic modulus

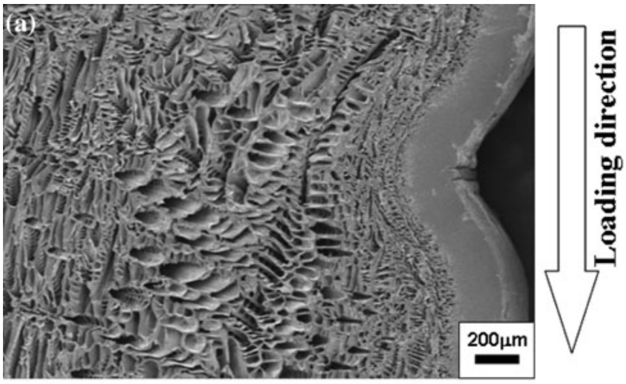


Compressive strength

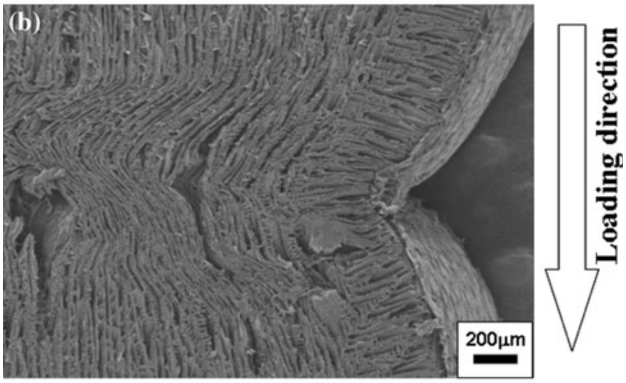
Fig. 4 Compressive mechanical properties. **a** Elastic modulus. **b** Compressive strength

those of the layered scaffolds as a result of the higher density of the solid layer.

Typical stress–strain curves of the PLLA scaffolds under compression are shown in Fig. 3. All of the stress–strain relations exhibited initial linear parts recognized as elastic deformation region. The critical point can be understood as the end of the linear elastic deformation region and also the onset of irreversible nonlinear deformation mode such as buckling as shown in Fig. 5. After the linear elastic deformation, the stress–strain curves showed constant or decreasing stress corresponding to the onset and growth of the buckling deformations. The compressive mechanical properties are shown in Fig. 4. The elastic moduli of the 3 and 7 wt% layered scaffolds are two and three times larger than those of the mono-scaffolds, respectively. On the other hand, the compressive strength values of the 3 and 7 wt% layered scaffolds are two and nine times larger than those of the mono-scaffolds, respectively. It is thus clearly seen that both the elastic modulus and strength are effectively improved by the



Mono-structure



Layered-structure

Fig. 5 Deformation behaviors of 7 wt% PLLA scaffolds at critical points. **a** Mono-structure. **b** Layered-structure

layered structure. The one-way ANOVA test was conducted as a statistic analysis and the significance level, P, were calculated. For the mean modulus and strength, the P values were $P < 0.0004$ and $P < 0.0002$, respectively. It is therefore concluded that the experimental data are valid to discuss the effect of layered structure on these mechanical properties. FE-SEM micrographs of deformed 7 wt% scaffolds at the critical points are shown in Fig. 5. These micrographs show longitudinal cross-sectional views of the specimens. The deformation of the mono-scaffold is characterized by localized buckling of the walls of cell structures. The deformation mechanism of the layered structure is buckling of the solid outer layer, resulting in the much higher compressive strength than the mono-scaffolds as shown in Fig. 4b.

In summary, layered structure was successfully introduced to improve the compressive mechanical properties of biodegradable PLLA scaffolds. The layered scaffold consists of a porous core region and a solid outer layer. The porosity of scaffold tends to decrease by the layered structure, while the compressive modulus and strength are greatly improved due to the load bearing function of the solid outer layer. At the critical point of compressive deformation process, the deformation of the layered scaffold is characterized by buckling of the solid outer layer, while the mono-scaffold exhibits localized buckling deformation of the cell walls. It is thus concluded that the mechanical properties of PLLA scaffolds can be controlled by changing the thickness of the solid outer layer in order to satisfy the desired properties that may be compatible to the target tissues to be regenerated.

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