9C-10 関節修復のための2層構造 scaffold の創製と評価

Development and Characterization of Dual-Layered Scaffold for Articular Regeneration.

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1. INTRODUCTION

Injured or diseased articular joint remains one of the major concerns in regenerative medicine[1]. Although recent years, tissue engineering is developing rapidly, various medical techniques for the repair of articular cartilage and bone have limited healing capacity [1-3]. Articular joints are composed of different kinds of tissues such as cartilage and bone and its features reflect the compositional functions of these tissues. These complex mechanical functions provide the essential mechanism for load-support and stress relaxation on the joints[3]. Therefore, it is very difficult to regenerate natural joint systems with such complex functions. Also, the current regenerative treatments of cartilage and bone have many problems such as meronecrosis, lack of thickness and complex damages. There are needs to improve the current treatment. Recent trends in tissue engineering have aimed to have the same functional scaffolds of articular joint.

In this study, bioabsorbable polymers such as poly(L-lactic acid) (PLLA) and poly(ϵ -caprolactone) (PCL) and a bioactive ceramics such as hydroxyapatite (HAp) were used to develop functional dual-layered scaffolds with porous structures, biocompatibility, biodegradability, interconnectivity and proper mechanical properties.

2. EXPERIMENTAL

The scaffolds composed of PLLA, PCL and PLLA/HAp were fabricated by the solid-liquid phase separation method and the freeze drying method. PLLA and PCL pellets were firstly dissolved in 1,4-dioxane with the solute concentrations of 3 and 7wt%. The solutions were filled into a polypropylene (PP) box and frozen at -30°C in a refrigerator to induce phase separation (see Fig.1). PLLA/HAp composite scaffold was also prepared by the solid-liquid phase separation and subsequent sublimation of solvent. Typically, a PLLA/HAp porous structure was prepared by the following step: PLLA/HAp (90:10) and dioxane solution was put into beaker (50 mL, warmed at 60°C). The solution was immediately put into the PP box and transferred into the refrigerator (-30°C). Frozen PLLA, PCL and PLLA/HAp scaffolds were orthogonally aligned and stacked on top of each other. A contact pressure of 0.6-1 kPa was applied on the top side by placing weights. The layered scaffolds were maintained at -30°C in the refrigerator for 24h and then placed in a freeze-drying vacuum vessel as shown in Fig.1.

Compression testing of these scaffolds was performed to estimate the compressive mechanical properties using a universal testing machine using a 1kN load cell. The compressive moduli were measured from the stress-strain relations obtained. Field emission scanning electron microscope (FE-SEM) was used to characterize the microstructures of the layered scaffolds.

3. RESULTS AND DISCUSSION

Typical stress-strain curves under compression are shown in Fig.2. The graphs show a typical deformation behavior characterized by two-step elastic deformation caused by two different elastic moduli of PCL and PLLA or PLLA/HAp.

The first and second-compressive moduli, E1 and E2, are shown in Fig.3. Fig.(a) shows the moduli of PLLA-PCL system and Fig.(b) shows the moduli of PLLA/HAp-PCL composite scaffold. E1 is thought to be mainly related to the elastic deformation of the softer layer, that is, PCL layer. On the contrary,

Fabrication -30°C

Fig.1 Fabrication process of layered scaffold.

Fig.2: Compressive stress-strain curves.

E2 is primarily related to the elastic deformation of the harder layer, that is, PLLA or PLLA/HAp layer. The moduli of the fabricated from 7wt% PLLA solution exhibited much higher moduli as a result of much denser porous structure. It is reasonably seen that E2 is larger than E1 since E2 is mainly related to the modulus of the harder layer.

FE-SEM microphotographs of PLLA-PCL and PLLA/HAp-PCL scaffolds are shown in Fig.4. It is clearly seen that the scaffolds fabricated from 7wt% PLLA solution have much denser porous structures than the 3wt% scaffolds. This structural difference is considered to be the primarily reason for the difference of elastic modulus shown in Fig.3. In each of these scaffolds, an interlayer exists between the two layers. In the PLLA-PCL scaffold, the interlayer is thought to be a polymer blend of PLLA and PCL. On the contrary, in the PLLA/HAp-PCL scaffolds, the interlayer is likely composed of PLLA, PCL and HAp. Actually, HAp particles are observed in the interlayers.

4. CONCLUSIONS

In this study, novel dual-layered scaffolds were successfully fabricated from bioabsorbable polymers and bioactive ceramics. These scaffolds are aimed at regeneration of articular tissues composed of cartilage and bone. Compressive testing results showed that these scaffolds have dual elastic modulus. The first modulus is related to the soft layer and the deformation of the hard layer affects the second modulus.

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(a) PLLA-PCL

(b) PLLA/HAp-PCL

Fig.3: Double compressive moduli.

(a) PLLA3-PCL3

(b) PLLA/HAp3-PCL3

(c) PLLA7-PCL7

(d) PLLA/HAp7-PCL7

Fig.4: FE-SEM micrographs of microstructures of dual-layered scaffolds.