In vitro and in vivo degradation behavior of elastic PLCL scaffolds for vascular tissue engineering

Kim, YH[1], Lee, J[1], Jung, H[1], Kim, S-H[2], Kim, SH[2]
[1]Dept. of Materials Science & Engineering, Gwangju Institute of Science and Technology, Gwangju 500-712, Korea
[2]Biomaterials Research Center, Korea Institute of Science and Technology P.O. Box 131,Cheongryang, Seoul 130-650,Korea

Introduction

Many recent studies have reported that mechanical stimuli enhanced the development and function of engineered vessel tissues. For such stimuli-enhanced (mechano-active) tissue engineering, it is necessary to develop very elastic scaffolds that can withstand cyclic mechanical strain without cracking or significant permanent deformation. We prepared very elastic poly(lactide-co-caprolactone) (PLCL) scaffolds for vascular tissue engineering[1-3] and examined the cytocompatibility and degradation behavior.

Materials and Methods

PLCL (50:50, Mn~280,000) was polymerized at 150 ℃ for 24 hr in a glass ampoule containing 1,6-hexanediol and stannous octoate. PLCL was processed into cylindrical scaffolds (ID 4mm, pore size 150±50 ㎛, porosity 90 %) by extrusion/particulate leaching technique. In vitro biodegradation test; The tubular scaffolds were cut into pieces (length 5 cm) and placed in closed bottles containing PBS on a shaker table at 37 □ for up to 1 year. The specimens were weighed and analyzed by GPC and NMR. In vivo implantation test (Fig. 1); The cylindrical scaffolds (length 1 cm) were seeded with smooth muscle cells (SMCs) and implanted into the subcutaneous dorsum of 5 week-old male athymic mice. Implants were harvested to measure the dried weight, and the polymeric scaffolds were extracted by chloroform for 5 h and analyzed by GPC and NMR.

Results and Discussion

The PLCL copolymers were basically random and amorphous. However, two Tg were observed in DMA and also in DSC thermograms. Furthermore, microdomains (about 17 nm size) were indicated on SAXS profile and finally confirmed by TEM. Therefore, the PLCL copolymer was probably composed of a soft matrix of mainly ε-caprolactone moieties and hard domains containing more L-lactide units, to exhibit a rubber-like elasticity in a virtue of a physically crosslinked structure.

The SMCs-seeded scaffolds were implanted into nude mice subcutaneously for up to 15 weeks to monitor the in vivo degradation. In addition, they were degraded in vitro for up to 1 year to compare the results each other. All the scaffolds degraded slowly in vivo and in vitro even in the form of highly porous thin membrane. However, the degradation rate was somewhat faster for in vivo than for in vitro (Fig. 2). This should be explained by that enzymes might have played a certain role in the degradation in the body. In addition, the ε-caprolactone moieties degraded faster than L-lactide units did in these PLCL scaffolds, although their hydrophilicities were in the opposite order (Fig. 3). This behavior appeared more prominently in the in vivo case. This should be resulted from that the amorphous regions composed of mainly ε-caprolactone units might have been firstly attacked by water as water can penetrate into the amorphous regions easier than the hard domains containing more L-lactide.

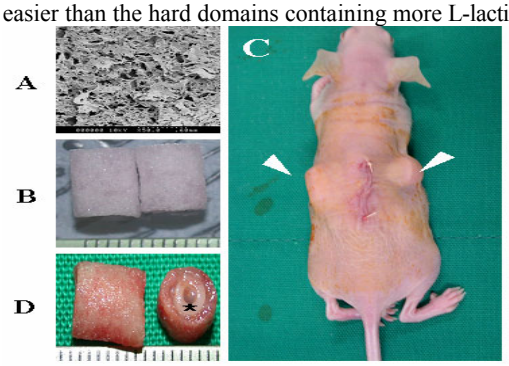

Fig. 1. Implantation of PLCL scaffolds seeded with SMCs; (A) Surface of SMCs-seeded scaffolds, (B) scaffolds (C) scaffolds implanted subdermally, (D) explanted scaffolds

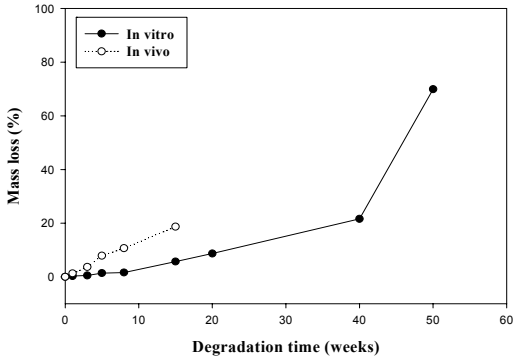

Fig. 2. Mass loss (wt %) of PLCL scaffolds on degradation time in vitro (filled circles) and in vivo (open circles).

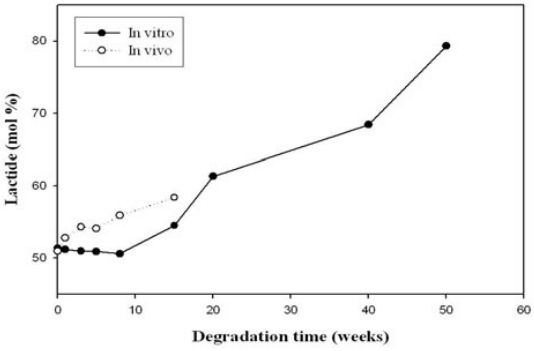

Fig. 3 Change of L-lactide contents in PLCL scaffolds on time in vitro (filled circles) and in vivo (open circles).

References

1. S.I.Jeong, S.H.Kim, Y.H.Kim, et al, J. Biomat. Sci., Polymer Ed., 15, 645-60 (2004).
2. S.I.Jeong, B.-S.Kim, S.W.Kang, J.H.Kwon, Y.M.Lee, S.H.Kim, Y.H.Kim, Biomaterials, 25, 5939-46 (2004)
3. S.I.Jeong, J.H.Kwon, J.I.Lim, S.H.Kim, Y.H.Kim, et al., Biomaterials, 26, 1405-11 (2005)