Biomaterials 33 (2012) 4309–4318

Contents lists available at SciVerse ScienceDirect

Biomaterials

journal homepage: www.elsevier.com/locate/biomaterials

In vivo biocompatibility and biodegradation of 3D-printed porous scaffolds based on a hydroxyl-functionalized poly(ε-caprolactone)

Hajar Seyednejad [a], Debby Gawlitta [b], Raoul V. Kuiper [c], Alain de Bruin [c], Cornelus F. van Nostrum [a], Tina Vermonden [a], Wouter J.A. Dhert [b], Wim E. Hennink [a,*]

[a] Department of Pharmaceutics, Utrecht Institute for Pharmaceutical Sciences (UIPS), Faculty of Science, Utrecht University, P. O. Box 80082, 3508 TB Utrecht, The Netherlands
[b] Department of Orthopaedics, University Medical Center Utrecht, P.O. Box 85500, 3508 GA Utrecht, The Netherlands
[c] Dutch Molecular Pathology Center, Department of Pathobiology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands

ARTICLE INFO

Article history:
Received 31 December 2011
Accepted 3 March 2012
Available online 20 March 2012

Keywords:
Functionalized polyester
Polycaprolactone
Biocompatibility
Biodegradation

ABSTRACT

The aim of this study was to evaluate the *in vivo* biodegradation and biocompatibility of three-dimensional (3D) scaffolds based on a hydroxyl-functionalized polyester (poly(hydroxymethylglycolide-co-ε-caprolactone), PHMGCL), which has enhanced hydrophilicity, increased degradation rate, and improved cell–material interactions as compared to its counterpart poly(ε-caprolactone), PCL. In this study, 3D scaffolds based on this polymer (PHMGCL, HMG:CL 8:92) were prepared by means of fiber deposition (melt-plotting). The biodegradation and tissue biocompatibility of PHMGCL and PCL scaffolds after subcutaneous implantation in Balb/c mice were investigated. At 4 and 12 weeks post implantation, the scaffolds were retrieved and evaluated for extent of degradation by measuring the residual weight of the scaffolds, thermal properties (DSC), and morphology (SEM) whereas the polymer was analyzed for both its composition (^{1}H NMR) and molecular weight (GPC). The scaffolds with infiltrated tissues were harvested, fixed, stained and histologically analyzed. The *in vitro* enzymatic degradation of these scaffolds was also investigated in lipase solutions. It was shown that PHMGCL 3D-scaffolds lost more than 60% of their weight within 3 months of implantation while PCL scaffolds showed no weight loss in this time frame. The molecular weight (M_w) of PHMGCL decreased from 46.9 kDa before implantation to 23.2 kDa after 3 months of implantation, while the molecular weight of PCL was unchanged in this period. ^{1}H NMR analysis showed that the degradation of PHMGCL was characterized by a loss of HMG units. *In vitro* enzymatic degradation showed that PHMGCL scaffolds were degraded within 50 h, while the degradation time for PCL scaffolds of similar structure was 72 h. A normal foreign body response to both scaffold types characterized by the presence of macrophages, lymphocytes, and fibrosis was observed with a more rapid onset in PHMGCL scaffolds. The extent of tissue–scaffold interactions as well as vascularization was shown to be higher for PHMGCL scaffolds compared to PCL ones. Therefore, the fast degradable PHMGCL which showed good biocompatibility is a promising biomaterial for tissue engineering applications.

1. Introduction

One of the main challenges in tissue engineering is designing suitable scaffolds that meet the crucial requirements for application in regenerative medicine. Both natural and synthetic polymers have been used for this purpose, however, the ability to adjust material properties and tailor their performance in terms of tissue response and biodegradation time makes synthetic polymers more attractive than natural polymers. The proper choice of polymer needs thoughtful considerations about the polymer's physical and chemical properties, degradation rate, and the ability to promote specific events at the cellular and tissue level [1]. Moreover, the polymeric scaffold should have good biocompatibility, which, as defined by Williams [2], means that it should be able to "perform as a substrate that will support the appropriate cellular activity, including the facilitation of molecular and mechanical signaling systems, in order to optimize tissue regeneration, without eliciting any undesirable local or systemic response in the eventual host". Besides biocompatibility, the physical architecture of the scaffold is also of great importance. Designing a three-dimensional structure comprising open-cells and interconnected pores [3] that allow facile communication between the biological cells dispersed within

* Corresponding author. Tel.: +31 30 253 6964; fax: +31 30 251 7839.
E-mail address: W.E.Hennink@uu.nl (W.E. Hennink).

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doi:10.1016/j.biomaterials.2012.03.002