Novel Biointegrative Cross-linked Degradable Polyurethane Scaffold Matrix

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Introduction: Current synthetic resorbable scaffolds made from thermoplastic polyesters and polyurethanes using techniques such as such as particulate leaching, lyophilization, electrospinning, nonwoven technology, etc. are sub-optimal in forming high void content inter-connected open-cells with controlled pore architecture, resilience and controllable degradation rates. Biologic scaffolds such as collagen and HA suffer from a lack of 3-D structure, low permeability, inadequate compressive stiffness and resilience, fast degradation rates and risks host immune system rejection limiting their and the synthetic scaffold's potential utility for TE applications[1,2]. Biomerix has developed a family of patented, cross-linked, biointegrative, biostable elastomeric and resilient polycarbonate urethane-urea (PCPU-U) macroporous matrix scaffolds consisting of fully interconnected and accessible open-cells with high void content (>95%). The biocompatible composition, inter-connected porosity and cross-linked induced fast resilient recovery have been shown to be essential for effective and efficient cell culture and tissue-material interactions leading to superior performance over existing scaffolds with good host tissue interface, unfettered cellular infiltration and proliferation, and organized ECM synthesis in multiple animal models and approved implantable devices for neurovascular, soft tissue orthopedics, ventral hernia, etc. [3,4]

This purpose of this study was to develop a family of cross-linked degradable polyester urethane-urea scaffolds (PSPU-U) while expanding and maintaining the structural and biocompatible advantages of the PCPU-U scaffolds.

Methods: The segmented PSPU-U scaffold consists of a biocompatible biostable hard segment (HS) derived from diphenylmethane diisocyanate (MDI) and degradable soft segment (SS) derived from polyols of polycaprolactone (PCL) and its copolymers with other polyesters such as polylactic acid (PLLA), polyglycolic acid (PGA), etc. PSPU-U scaffolds were made by a process that includes a polymerization reaction between MDI and polyols in presence of cross-linkers and chain extenders, and a simultaneous blowing reaction between MDI and water that produces CO2 leading to an in situ cross-linked porous foam; it is followed by a controlled high temperature thermal combustion reticulation process that converts the porous foam to an open cell matrix by removing the cell windows formed during the foaming process. Scaffolds were characterized for morphology and in vitro (37C, pH-7.4 buffer) performance. They were seeded with articular chondrocytes at a concentration of $2x10^6$ cells/ml and cultured for 1, 2, and 4 weeks to test is utility in cartilage repair. The tissue constructs were then formalin fixed and evaluated by histology.

Results: The foaming and reticulation process produces tightly controlled pore distribution and mechanical performance, and are much less time consuming and less costly than biological and synthetic scaffolds.

Fig. 1 shows the SEM of the 3-D fully interconnected accessible open-cells (pore ~ 250 μ) with high void content (>95%) MDI-70PCL /30PLLA reticulated resilient matrix that has an *in vitro* degradation profile of about 24 months. Fig 2 shows that the moderately crosslinked MDI-85PCL / 15 PGA matrix has a slower in vitro degradation profile compared to the three MDI-70PCL /30PGA matrices owing to the standard degradation and universally followed control mechanism of incorporating larger proportion of slower degrading PCL in the SS copolymer. However, for the same 70 PCL/30PGA SS copolymer ratio and approximately same HS:SS ratio, a range of in vitro profiles from 4 months (low x-links) to 16 months (moderate x-links) were obtained for the MDI-70PCL/30PGA matrices. This unique degradation control mechanism of extending the degradation profile for same SS composition is attributed to the difference in the cross-linking, a novel feature that is not available or attainable in thermoplastic polyesters or polyester urethanes. The SS degradation products were the same as those obtained from resorbable aliphatic polyesters. Biostable HS (<1% by volume) has been shown to undergo total resorption[1]. MDI -PCL scaffolds seeded with articular chondrocytes cultured for 4 weeks, showed cartilage nodule formation throughout and de novo deposition of proteoglycan-rich cartilage matrix in both macroscopic and microscopic observations (Fig 3).

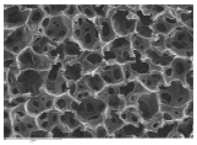

Fig.1

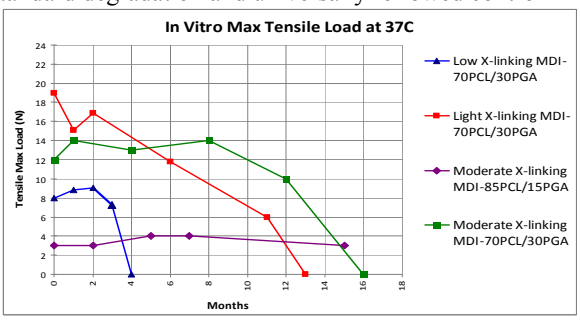

Fig. 2

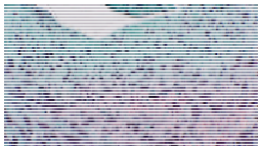

Fig. 3

Conclusions: PSPU-U scaffolds with novel ways to control its degradation profiles and with similarities in chemical composition (carbonate vs. polyester), morphology (>95% connected voids) and resilient properties to biostable PCPU-U have been successfully developed. They have been shown to be effective as biocompatible scaffolds for robust chondrocytes culture.

References:

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