Hydroxyapatite/Poly(L-Lactide) Co-Electrospun Scaffold with Dual-Scale Alignments for Bone Regeneration

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Statement of Purpose: Human bone is a composite of hydroxyapatite (HA) and collagen nanofibers.[1] Structurally, lamellae of HA nanocrystals are aligned along the long axis of collagen fiber and contribute to strong mechanical properties of bone. Much attention has been directed at preparing bone regeneration scaffold using electrospinning, which is a versatile technique for fabricating submicron fibers from various materials with random or aligned fibrous assemblies.[2] In this study, HA/Poly(L-lactide) (PLLA) scaffold with dual-scale alignments, including a nano-scale HA alignment within fiber matrix and a micro-scale fiber alignment was co-electrospun from an HA/PLLA suspension. Both of the two alignments were found to enhance significantly the mechanical strength of the composite scaffold.

Methods: HA particles were synthesized using a metathesis method by gradually mixing $Ca(NO_3)_2 \cdot 4H_2O$ and $(NH_4)_2HPO_4$ solutions at a stoichiometric ratio. After heating and aging processes, HA particles were separated and suspended into N, N-dimethylformamide, which was then mixed with PLLA/dichloromethane solution and formed into spinning dope. Co-electrospun nanofibers were collected on a rotating drum and formed into a scaffold. The composition and morphology of HA/PLLA scaffold were characterized using XRD, FESEM, and TEM, respectively. The mechanical behavior of the scaffold was evaluated using tensile tests. In the case of the aligned scaffolds, the tensile stress was aligned along the fiber direction.

Results: Highly crystallized HA particles with rod-shape and a high aspect ratio (up to 50) were attained using the metathesis method (Figure 1). The HA particles were co-electrospun with PLLA (20/80, w/w), yielding fibers with an average diameter of 350 and a standard deviation of 50 nm. The HA particles were well aligned along the fiber long axis (Figure 2). Comparing XRD patterns of HA particles and that of HA/PLLA scaffold, it was found that the (002) peak (perpendicular to the particle z-axis) almost disappeared in the HA/PLLA scaffold, while the (300) peak (parallel to z-axis) substantially increased and

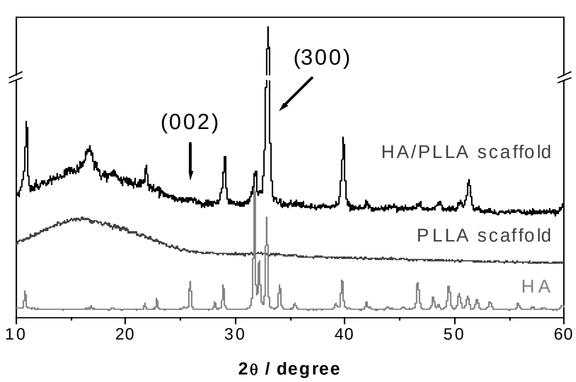

Figure 1. XRD patterns of HA particles, PLLA and HA/PLLA scaffolds

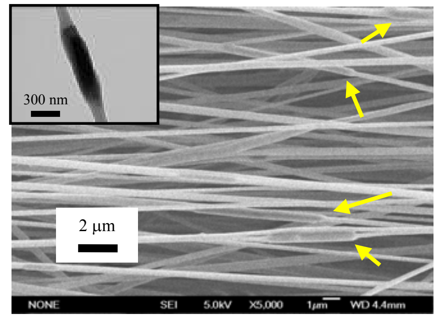

Figure 2. FESEM and TEM (inserted) images of HA/PLLA electrospun scaffold showing its morphology. Arrows indicate locations where aligned HA particles are visible.

became the most prominent peak (Figure 1). Because the scaffold specimen for XRD was so mounted that the long axis of composite fibers was kept perpendicular to the incident X-ray, it was proved that most of the incorporated HA particles are well aligned along the fiber direction. It was also found that such nano-scale HA alignment had significantly increased the modulus (E) of the composite scaffold compared to the PLLA one (p= 0.001) (Table 1). Moreover, HA alignment also promoted the tensile stress (σ) of random scaffolds (p< 0.001), which effect was less significant on that of aligned scaffold (p= 0.145). The micro-scale fiber alignment also improved the mechanical strength of the aligned composite scaffold compared with that of the random one (E, p= 0.001; σ, p< 0.001). The tensile strain (ε) of the aligned HA/PLLA scaffold was also lower than that of the random one (p<0.001). These results could indicate that PLLA chains in aligned fibers may be better oriented along fiber direction and undergo less cold-drawing under tensile stress.

Table 1. Tensile tests results of electrospun scaffolds. Values presented are mean± standard deviation of samples.

HA, wt%	Fibrous assembly	E, MPa	σ, MPa	ε, %
0	Random	75±13	2.7±0.3	34.9±4.9
20	Random	195±46	6.0±1.3	30.5±5.0
0	Aligned	375±157	16.5±3.1	20.1±6.0
20	Aligned	1498±315	19.4±3.3	3.5±1.1

Conclusions: Pure HA particles with high aspect ratio and crystallinity were co-electrospun with PLLA. The HA particles had high aspect ratio and were well aligned along the long axis of nanofibers. The spun composite fibers in the scaffold also aligned with each other in a micro-scale. The dual-scale alignments significantly contributed to the enhanced mechanical strength of the nanofibrous scaffold, which also mimicked bone in inorganic/organic composition and structure.

References:

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2. Li, D; Xia, YN. Adv Mater. 2004;16:1151-1170.