Biodegradable Microfibers Containing Hydroxyapatite Nanospheres for Bone Tissue Engineering

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Introduction

Various methods can be used to produce polymeric tissue engineering scaffolds (Atala A and Lanza RP, Eds., Methods of Tissue Engineering, 2002, Academic Press). Electrospinning has been found to be a simple, effective and versatile technique to fabricate nanofibrous structures for tissue engineering applications. Using nanofibrous structures is advantageous because it was found that cells attach and organize well around fibrous structures with fiber diameter smaller than the cells themselves (Elsdale TJ, Cell Biol. 1972;54:626-637). It has been shown that biodegradable polymers such as poly (hydroxybutyrate-co-hydroxyvalerate) (PHBV) can be electrospun into nano-fibers provided that the electrospinning parameters are optimized (Tong HW and Wang M, Key Engg Mater, 2006; Vol.334-335: in press). In bone tissue engineering, it is ideal that the scaffolds are osteoconductive. The incorporation of bioceramics such as hydroxyapatite (HA) into scaffolds can render these scaffolds osteoconductive (Wang M, Biomaterials, 2003; 24:2133-2151). Therefore, investigations were made into the electrospinning of PHBV microfibers containing HA nanoparticles.

Materials and Methods

The PHBV (M_w = 310,000) containing 2.9 mol% of hydroxyvalerate was commercially available and used as-received. To prepare a PHBV solution, 3 g of PHBV was dissolved in 20 ml of chloroform (analytical grade) to achieve a 15wt% polymer solution concentration. To prepare an HA/PHBV solution for fabricating composite fibers, depending on the composition of the fiber to be made, an amount of HA nanoparticles was added to the PHBV solution and the HA/PHBV solution was homogenized. In this investigation, PHBV solutions containing 0, 10 and 20% HA were used.

The HA nanoparticles used for making composite fibers were produced in-house through a nanoemulsion process (Zhou WY, et al., J Mater Sci-Mater M. 2006; in press). These particles were found to be carbonated HA (CHA) and were spherical, with diameters being 10-30 nm.

Membranes made of composite fibers were produced using an electrospinning apparatus (Tong HW and Wang M, Key Engg Mater, 2006; Vol.334-335: in press). Under the application of 25 kV by a high voltage power supply, the HA/PHBV solution was stretched by the electric force into ultra-fine fibers, and the fibers were collected as a non-woven fibrous mesh on a grounded plate. All electrospun membranes were then analyzed by using a scanning electron microscope (SEM) while the HA particles in and on the fibers could be detected by using energy dispersive X-ray spectroscopy (EDX).

Results and Discussion

The morphology of electrospun HA/PHBV composite fibers are shown in Fig.1, alongside with the CHA nanospheres (Fig.1d). For pure PHBV, the fiber surface was smooth while the average fiber diameter was about 1 μm (Fig.1a), which approaches the profile of the natural ECM. For 10% HA/PHBV, the fiber surface was still smooth but the CHA nanospheres could not be readily found on the fibers (Fig.1b). When the HA content was increased to 20%, some CHA nanospheres were seen to be on the fibers (Fig.1c). The fiber surface was very rough and the presence of HA was confirmed by the Ca and P peaks in the EDX spectra obtained (Fig.2). It appeared that at high HA content, HA nanospheres could be both incorporated in and attached to PHBV fibers.

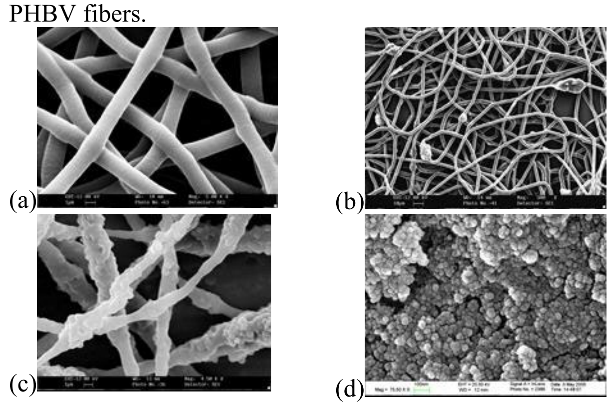

Figure 1. SEM micrographs of (a) PHBV fibers, (b) 10% HA/PHBV fibers, (c) 20% HA/PHBV fibers, (d) CHA

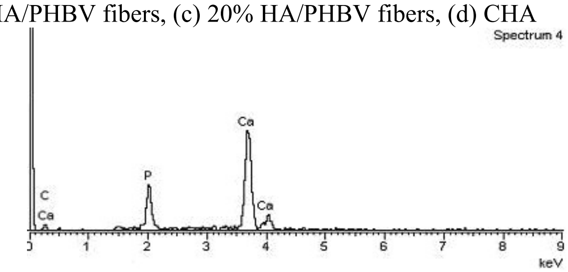

Figure 2. An EDX spectrum obtained from a 20% HA/PHBV composite fiber

Although some suppliers can provide HA nano-powders, the surface area of their HA nanoparticles is normally ~15 m^2/g. The surface area of CHA nanospheres synthesized in the current study reached 50 m^2/g, which is significantly higher. The high surface area of these nanospheres is expected to provide better osteoconductive properties. Furthermore, the CHA nanospheres resemble more chemically bone apatite and due to their higher resorption rate, are more suitable than pure HA nano-powders for bone tissue engineering.

Conclusions

CHA nanospheres of high surface area could be synthesized using a nanoemulsion process. It was possible to electrospin HA/PHBV composite fibers which may contain up to 20% of HA nanospheres. The incorporated and attached CHA nanospheres in composite fibers should render the fibrous membranes osteoconductive, making them suitable for bone tissue engineering.