Preparation of Porous Poly(L-lactic acid) Composite Containing Hydroxyapatite Whiskers

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A new type of porous biomaterial for bone repair was successfully prepared using poly(L-lactic acid) short fibers of ≈700 μm and hydroxyapatite whiskers (W-HAs) of 60 μm (in average length). When W-HAs of ≤70 wt % were introduced, the composites could have about 80% porosity including numerous, interconnecting pores of >10 μm in diameter. W-HAs play an important role in formation of the pores, which allow penetration of nutriments and ingrowth of bone cells.

A porous material with continuous pore structure is expected to be useful for implants used in the regeneration of damaged tissue, because the continuous pore would allow penetration of nutriments or ingrowth of tissues, blood vessels, or cells.[1–4] In the case of porous materials for bone regeneration, it is important that the pore size is enough to allow ingrowth of them, and the size is reported to be more than 10 μm.[5] A nonwoven fiber mesh consisting of a biodegradable polymer, such as poly(L-lactic acid) (PLLA), may be one of the best candidates for the biomaterials, because the connective large pores are easily formed by interlocking the fibers.[6–9] On the other hand, the biocompatibility for hard tissue can be improved by addition of hydroxyapatite (HA), because HA is the inorganic component of hard tissue in the living body and exhibits high biocompatibility with bone cells.[10,11] Some researchers have prepared dense composites of PLLA and HA.[12,13] However, almost HA particles, which show the excellent biocompatibility, are covered with PLLA. In the case of preparation of composites with sufficiently exposed HA, a biomimetic coating is one of the useful methods.[14,15] In the method, bone-like HA can be coated on the skeletal surface of porous polymer by soaking in simulated body fluid (SBF). However, the HA is difficult to be precipitated directly on the PLLA surface without an accelerator of HA nucleation.[16]

In the present work our objective is to prepare a PLLA/HA composite with both of interconnected pore structure and high biocompatibility. Our approach is to utilize HA whiskers as a part of frameworks in the PLLA short fiber mesh. We prepared two kinds of PLLA/HA porous composites containing HA whiskers (W-HAs) and HA fine particles (P-HAs) for discussion of the potential morphologies of HA in terms of the pore structures.

The PLLA short fibers were obtained by a solvent evaporation technique;[17] ten grams of PLLA solution (methylene chloride) was dropwise added to 500 mL of PVA solution including 0.01 wt % of poly(vinyl alcohol) and 0.1 mol/L of a coagulation agent, sodium tripolyphosphate with stirring for 20 h to complete evaporation of the solvent. The products were isolated by vacuum filtration, washed and dried. The products were identified as PLLA by X-ray diffractometry (XRD) (RU-200, Rigaku, Japan) and gel permeation chromatography (GPC) (HLC-8120GPC, Tosoh, Japan). Figure 1a shows the scanning electron microscopic (SEM) (S-2500, Hitachi, Japan) image of the PLLA short fibers. The average length and the average aspect ratio of the fibers were estimated from the SEM image to be ≈700 μm and ≈30, respectively. P-HAs were prepared by ball-milling a mixture of dicalcium phosphate dehydrate and calcium carbonate with Ca/P of 1.67 in water and, subsequently, drying at 120 °C for 24 h. The products were identified as HA by XRD. The average particle size of the agglomerates was determined to be 8 μm with a laser-scattering-type particle size distribution analyzer. W-HAs were prepared by hydrothermal treatment of calcium tripolyphosphate gel with 50 mmol/L of a nitric acid to adjust the pH value of 2.5 before the reaction at 140 °C for 24 h.[18,19] The products were identified as HA with a trace amount of anhydrous dicalcium phosphate by XRD. Figure 1b shows the SEM image of W-HA. The average length and the average aspect ratio were about 60 μm and 12, respectively. A porous material was prepared by mixing the PLLA short fibers and 50 wt % HA powders (W-HA or P-HA) in ethanol, filling them to a mold and sintering them at 170–180 °C. The pore diameter distribution was determined with a micrometrics mercury intru-

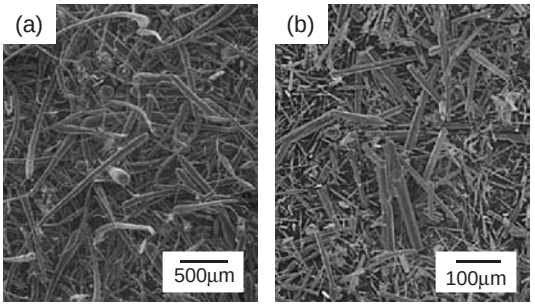

Figure 1. SEM images of (a) PLLA short fibers and (b) HA whiskers.

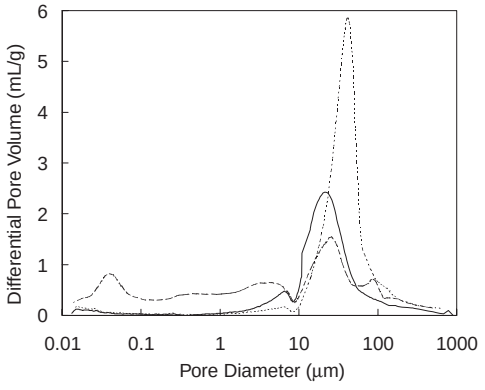

Figure 2. Pore diameter distributions of PLLA-N (dotted line ·····), PLLA-W (solid line —), and PLLA-P (broken line - - -).

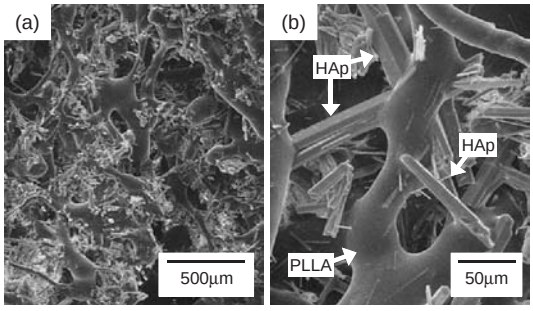

Figure 3. SEM image of PLLA-W. (b) is highly magnified image.

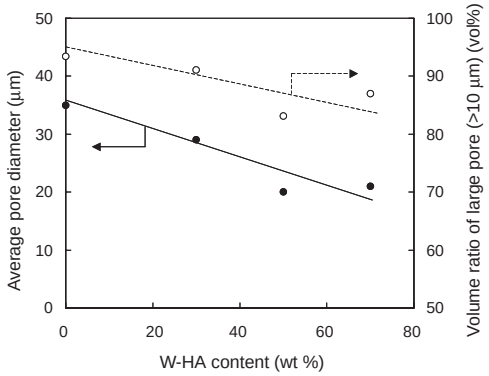

Figure 4. Average pore size and volume ratio of large pore (>10 μm) of PLLA-W prepared by sintering PLLA short fibers and W-HAs as a function of W-HA content.

sion porosimeter (Poresizer 9320, Shimadzu, Japan). The pore structure was observed with an SEM. The compressive strengths of the composites were measured by bone strength tester (TK-252C, Muromachi Kikai, Japan).

Figure 2 shows the pore diameter distributions of the PLLA porous block without HA (PLLA-N) and those with W-HA (PLLA-W) and P-HA (PLLA-P). The average pore diameters are 35, 20, and 5 μm, respectively. The distribution curves show that PLLA-N and PLLA-W have a peak of large-sized pore diameter of >10 μm; the pores are enough to allow penetration of nutriments or ingrowth of bone cells. The volume ratios of the large-sized pores (>10 μm) for PLLA-N, PLLA-W, and PLLA-P are 93, 83, and 46%, respectively. The porosities of the PLLA-N, PLLA-W, and PLLA-P are 79, 78, and 84%, respectively. Although their porosities are almost close, the volume ratios of large-sized pores for the PLLA-N and PLLA-W are much larger than that for PLLA-P. Figure 3 shows the SEM image of PLLA-W. This indicates that PLLA short fibers bonded the adjacent PLLA short fibers and W-HAs by softening of the PLLA during heat treatment. The bonding of them forms the continuous large-sized pores. Almost surface of HAs is exposed, because W-HA exists as a part of framework in the material or on the surface of PLLA. W-HA would be useful as a biocompatible additive for the present porous material using the nonwoven fiber mesh. On the other hand, few continuous large-sized pores are formed in the PLLA-P, because most of P-HAs are agglomerated on the surface of PLLA and in the space between the PLLA short fibers.

Figure 4 is the relationship between average pore size and porosity and W-HA content. The average pore size is found to decrease from 40 to 20 μm with increasing W-HA content, since the length of PLLA fibers is larger than that of W-HA. According to SEM observation, the agglomeration of W-HAs, which formed the small-sized pores, increases with increase of W-HA content. The volume ratios of large pore (>10 μm) also decrease with the increase in W-HA content, but they are in the high values of about 80 vol %.

The compressive strengths of the PLLA-W with 0, 30, 50, and 70 wt % W-HA are estimated to be 300 to 400 kPa.

In summary, we could prepare the PLLA/HA porous composite, where the numerous connective large-sized pores were formed by utilizing HA whiskers. The average pore diameter could be controlled by introducing HA whiskers. The high volume ratios of large pore (>10 μm) and porosity is expected to be applied to a biomaterial for bone regeneration.

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