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Polymer 46 (2005) 3789–3794
polymer
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Poly(L-lactic acid) short fibers prepared by solvent evaporation using sodium tripolyphosphate

Yoichiro Mizutani[a,b,*], Masateru Hattori[a], Masahiko Okuyama[a], Toshihiro Kasuga[b], Masayuki Nogami[b]

[a]*R&D Center, NGK Spark Plug Co. Ltd, 2808 Iwasaki, Komaki, Aichi 485-8510, Japan*
[b]*Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466-8555, Japan*

Received 13 December 2004; received in revised form 21 February 2005; accepted 2 March 2005
Available online 7 April 2005

Abstract

A porous material consisting of biodegradable polymer fibers may be one of the best candidates for implants used in the regeneration of damaged tissue, because it has a continuous pore structure that would allow ingrowth of nutriments, tissues, blood vessels or cells. In the present work, short fibers of biodegradable poly(L-lactic acid) (PLLA) were successfully prepared by the dropwise addition of PLLA dissolved in methylene chloride to a poly(vinyl alcohol) (PVA) solution containing sodium tripolyphosphate with stirring. It was suggested that droplets of the PLLA solution form spheres coated with PVA, which are then deformed into fibrous shapes due to stirring. The length of fibers was 200–800 μm and was controlled by the stirring rate, the PLLA concentration of the droplets and the PVA concentration. A PLLA porous block could be easily prepared by sintering the PLLA fibers at 173 °C for 10 min. The material had a continuous pore structure with the average pore size of approximately 40 μm and porosity of about 80%.

Keywords: Poly(L-lactic acid); Short fiber; Porous material

1. Introduction

Recently, much attention has been paid to biodegradable porous polymers in medical applications for the regeneration of lost or damaged tissue in a living body [1–6]. Biodegradable porous polymers with a continuous pore structure have a great advantage in that they allow easy ingrowth of nutriments, tissues, blood vessels or cells, and new tissues may form in them when they are implanted in a damaged living tissue [7].

Non-woven fiber meshes consisting of a biodegradable polymer can be used as biomaterials because they have high porosity and a continuous pore structure [8,9]. Generally, the fibers are prepared by spinning techniques, such as melt spinning, dry spinning and wet spinning [10,11]. Since they are continuous fibers that are suitable for the fabrication of sheets or membranes, it may be difficult to shape them into a desirable block and to use them to prepare new composites. In the case of materials for bone regeneration, their biocompatibility can be improved by the addition of hydroxyapatite (HAp), because HAp is an inorganic component of hard tissue that exhibits high biocompatibility with bone cells. The length of fibers suitable for shaping or for homogeneously mixing HAp is believed to be less than 1 mm.

Our objectives in the present work are to prepare short poly(L-lactic acid) (PLLA) fibers utilizing a solvent evaporation technique and to prepare macroporous materials utilizing the fibers. The solvent evaporation technique has been reported to be an easy method of preparing polymer particles [12].

PLLA dissolved in methylene chloride is dispersed in a solution consisting of poly(vinyl alcohol) (PVA) as a surfactant. After evaporation of the methylene chloride, PLLA particles of several tens–hundreds μm in diameter are prepared as precipitate in the PVA solution. The shape of the resulting polymer is influenced by that of the polymer

* Corresponding author. Address: R&D Center, NGK Spark Plug Co. Ltd, 2808 Iwasaki, Komaki, Aichi 485-8510, Japan. Tel.: +81 568 76 1543; fax: +81 568 76 1295.
E-mail address: yo-mizutani@mg.ngkntk.co.jp (Y. Mizutani).

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doi:10.1016/j.polymer.2005.03.037

droplet in PVA solution; if the PLLA droplets can be dispersed as short fibers, PLLA short fibers are expected to be prepared.

Generally, PVA precipitates in the PVA solution after the addition of a salt consisting of sulfuric ion, phosphate ion, carbonate ion, sodium ion and/or potassium ion, as a coagulation agent [13]. When the PLLA droplets exist in the PVA solution with a coagulation agent, a PVA membrane is formed on the droplets. Concentrations of PVA and the agent are high around the interface between the PVA solution and the PLLA droplets, because the solvent in the PLLA droplets is slightly dissolved in the PVA solution. When the droplets of the PLLA solution are put into a PVA solution, they can be deformed into fibrous shapes by stirring. We anticipated the formation of the PLLA fibers via the above-described process.

2. Materials and methods

2.1. Preparation of poly(L-lactic acid) fibers

PLLA (M_w = 180,000–220,000) (Shimadzu Co., Japan) was dissolved in methylene chloride to give a 0.02–0.10 weight/volume (w/v) ratio. Ten gram of the PLLA solution was added dropwise to 500 mL of PVA solution containing 0–0.03 wt% of PVA (M_w = 22,000) (MP Biomedicals Inc., USA) and 0–0.15 mol/L of a coagulation agent with stirring (300–700 rpm) for 20 h to complete evaporation of the solvent. Na_2SO_4, K_2HPO_4, or $Na_5P_3O_{10}$ (sodium tripolyphosphate; STP) was used as the coagulation agent. Products precipitated in the PVA solution were isolated by vacuum filtration and washed several times with deionized water. The products were dried at room temperature for 1 day under a reduced pressure, using a vacuum pump. The morphology of the products was observed with a scanning electron microscope (SEM) (S-2500, Hitachi, Japan). The average length of the products was determined by randomly measuring 20–30 fibers in the SEM image of the products. The lengths of winding fibers were determined by estimating the stretched lengths of the fibers. Changes in molecular weight between the as-received PLLA and the resulting products were confirmed by gel permeation chromatography (GPC) (HLC-8120GPC, Tosoh, Japan). Their crystalline phases were identified by X-ray diffractometry (XRD) (RU-200, Rigaku, Japan). Their enthalpies of fusion (ΔH_f) were measured by differential scanning calorimetry (DSC) (DSC22, Seiko Instruments, Japan) at a heating rate of 5 °C/min.

2.2. Preparation of PLLA porous block

A stainless-steel mold of 7 mm inner diameter and 4 or 10 mm height was filled with PLLA fibers. After heating at 173 °C for 10 min to connect the PLLA fibers, the mold was cooled to room temperature and the sample was removed. The porosity of the sample was estimated by measuring its volume and weight. The pore structure of the sample was observed with an SEM. The pore diameter distribution of the sample was determined with a micrometrics mercury intrusion porosimeter (Poresizer 9320, Shimadzu, Japan).

3. Results and discussion

3.1. Preparation of poly(L-lactic acid) fibers

Fig. 1 shows SEM images of products prepared using a PVA solution with 0.1 mol/L of Na_2SO_4, K_2HPO_4, or STP. In the case of Na_2SO_4, the products are spherical (Fig. 1(a)). When the PVA solution includes K_2HPO_4, elliptical and spherical products are obtained (Fig. 1(b)). On the other hand, almost linear fibrous products can be prepared by using a PVA solution with STP (Fig. 1(c)).

Fig. 2 shows the XRD pattern of the products prepared using PVA solution with STP. The pattern exhibits significant peaks at 2θ = 14.9, 16.8, 19.1 and 22.3°, in agreement with the peaks at 15, 16, 18.5 and 22.5° for a homopolymer of PLA reported by Ikada et al. [14]. Fig. 3 shows GPC profiles of the as-received PLLA and the products. The profiles have a main PLLA peak at around 10 min and two small peaks of mobile phases in the range of 13–18 min. There are no significant changes in the molecular weight.

Fig. 4 shows DSC curves of the as-received PLLA, the spherical products prepared using PVA solution with Na_2SO_4 and the fibrous products prepared using PVA solution with STP. The as-received PLLA exhibits two endothermic peaks at the glass transition temperature (T_g) and the melting temperature (T_m) (Fig. 4(a)), whereas the others have a peak only at T_m (Fig. 4(b) and (c)). The enthalpies of fusion (ΔH_f), as determined from the area of the melting peak, for the as-received PLLA, the spherical product and the fibrous product are found to be 32, 34 and 42 J/g, respectively. The temperature of crystallization (T_c) is not observed in any profile. The degree of crystallinity can be estimated using

$$\text{Crystallinity (\%)} = \frac{(\Delta H_f - \Delta H_c)}{\Delta H_f^0} \quad (1)$$

in which $\Delta H_f - \Delta H_c$ is the difference between the enthalpies of melting and crystallization and ΔH_f^0 denotes the enthalpy of melting of a 100% crystalline PLLA sample. In the present work, the ΔH_f^0, value of 100 J/g reported by Nijenhuis et al. is used [15]. The crystallinities of the as-received PLLA and the spherical and fibrous products are estimated to be 32, 34 and 42%, respectively. The value of T_m for the as-received PLLA, the spherical product and the fibrous product are 176.8, 174.8 and 173.3 °C, respectively. In general, T_m increases with increasing crystallinity. However, in the case of the present samples, T_m decreases

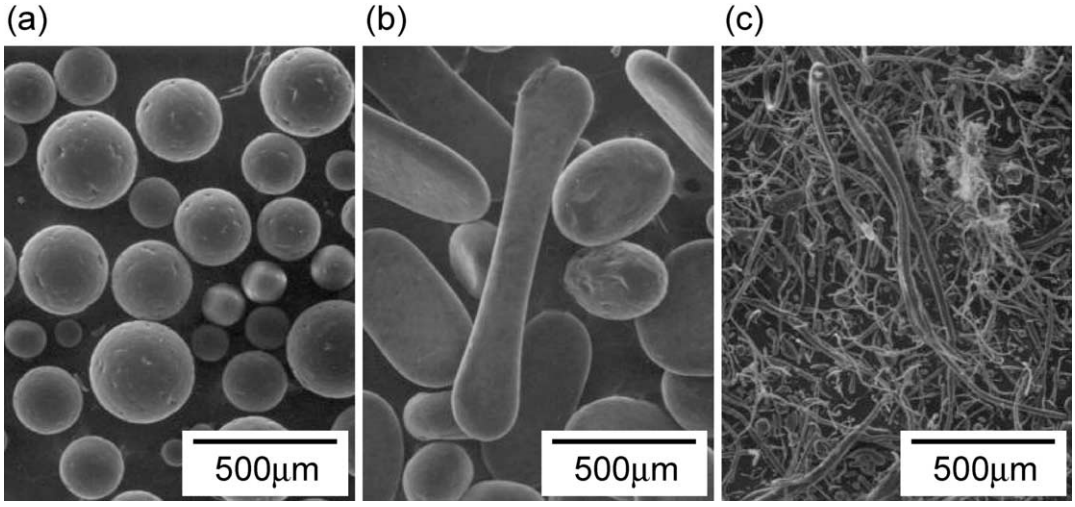

Fig. 1. SEM images of products prepared by addition of PLLA solution (0.07 w/v) into PVA solution consisting of 0.01 wt% PVA and 0.1 mol/L (a) Na_2SO_4, (b) K_2HPO_4, or (c) STP at stirring rate of 450 rpm.

negligibly with increasing crystallinity. Since the particle size is different among samples, the heat transmission rate of each sample is also assumed to be different; the smallest products, the PLLA fibers, are believed to have the fastest heat transmission rate among them.

The formation mechanism for the PLLA short fibers is explained as follows. When the PLLA solution is added dropwise to PVA solution with STP as a coagulation agent, a PVA membrane is formed on the dispersed droplets of PLLA solution. Due to the formation of the PVA membrane on the droplets, apparent viscosity of the droplets increases. When an external force is applied to the droplets upon stirring the solution, the spherical droplets are deformed to fibrous shapes. Crystallization of the PLLA fibers is considered to be enhanced by the deformation of the droplets due to the rearrangement of the PLLA molecules. After methylene chloride is completely evaporated, the PLLA fibers are left in the PVA solution. The PVA membrane on the PLLA fibers is removed by several washings with deionized water prior to drying.

Since the PVA membrane can be precipitated only when the PVA solution contains STP, the PLLA short fibers can be prepared by the addition of STP to PVA solution. To clarify this, the following experiment was performed. To 20 mL of methylene chloride in a beaker, 25 mL of PVA solution containing the coagulation agent was added carefully to keep the two solvents separated. As a result, the PVA membrane was observed at the interface between the methylene chloride and the PVA solution containing STP. When the membrane was picked up using tweezers, it

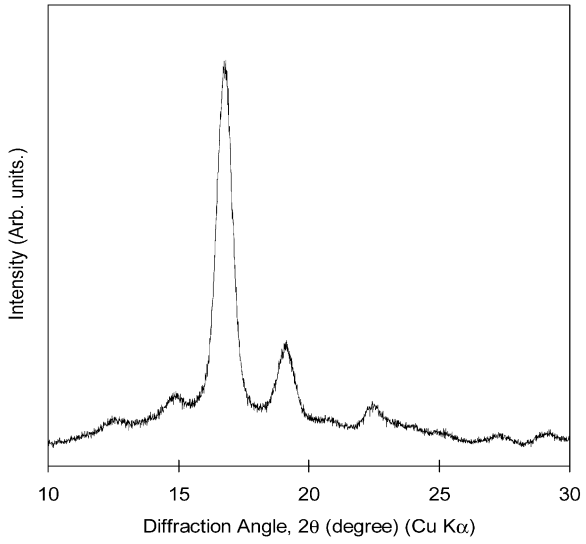

Fig. 2. XRD pattern of products prepared by addition of PLLA solution (0.07 w/v) into PVA solution consisting of 0.01 wt% PVA and 0.1 mol/L STP at stirring rate of 450 rpm.

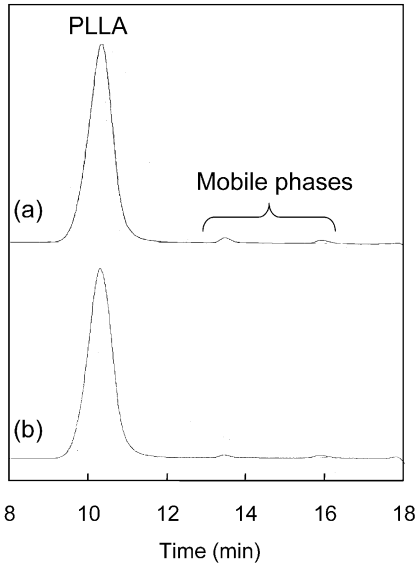

Fig. 3. GPC profiles of (a) as-received PLLA and (b) products prepared by addition of PLLA solution (0.07 w/v) into PVA solution consisting of 0.01 wt% PVA and 0.1 mol/L STP at stirring rate of 450 rpm.

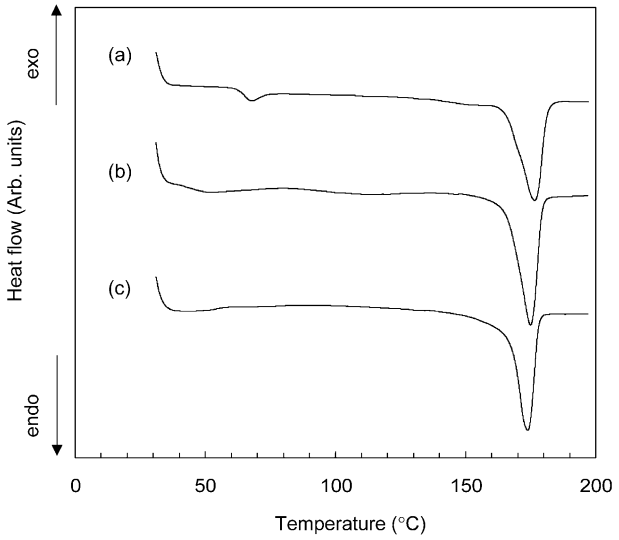

Fig. 4. DSC curves of (a) as-received PLLA and products prepared by addition of PLLA solution (0.07 w/v) into PVA solution consisting of 0.01 wt% PVA and (b) 0.1 mol/L Na_2SO_4 and (c) 0.1 mol/L STP at stirring rate of 450 rpm.

stretched like a thread; it was found to have high viscosity. On the other hand, the membrane was not formed when PVA solution containing Na_2SO_4 or K_2HPO_4 was used. STP would be an effective coagulation agent, because the number of oxygen atoms, which are related to hydrogen bond, in the tripolyphosphate ion is much larger than that of the others; the H_2O molecules hydrated with PVA molecules or PVA colloids dissolved in the solution were taken by the tripolyphosphate ions and PVA were easily precipitated under the presence of STP.

Fig. 5 shows the relationship between the average length of PLLA short fibers and the PLLA concentration of droplets. The length increases with increase of PLLA concentration. In the case of high concentration of PLLA droplets, the droplets can be elongated by the shear stress of stirring because of their high viscosity. On the other hand, in the case of low concentration, the elongated droplets are broken by the shear stress.

Fig. 6 shows the relationship between the average length of PLLA short fibers and the stirring rate. At the stirring rate of $\geq$300 rpm the PLLA solution could be dispersed as droplets in the PVA solution, whereas the stirring rate of $<$ 300 rpm was too slow for the PLLA droplets to be obtained in the PVA solution. Fig. 6 indicates that the length of the PLLA droplets is influenced by the stirring rate; the length decreases with increasing the stirring rate. The droplets are elongated by the reasonable shear stress, and the elongated droplets are broken by the high shear stress when they are stirred at the fast rate.

Figs. 7 and 8 show the relationship between the average length of the PLLA fibers and the concentrations of STP and PVA, respectively. The average length is estimated to be about 700 μm and it is independent of the STP concentration. When the PVA solution includes 0.15 mol/L of STP, PVA precipitates before the addition of the PLA solution and PLA fibrous products cannot be prepared. On the other hand, the average length decreases with increasing PVA concentration. The PLLA fibers of 200–800 μm length can be prepared by controlling the PVA concentration. Since PVA also acts as a surfactant, the surface tension of the dispersed PLLA droplets decreases with increasing PVA concentration. Droplets with a small volume can be stably dispersed in the PVA solution with a high PVA concentration. As a result, the length of stretched droplets was reduced. The short PLLA fibers form at a high concentration of PVA. Since the present fibers have no uniformity in diameter, that is, they have some narrow parts; it is difficult to determine their exact aspect ratios. In the present work, the average ratios were estimated to be ~30. The ratios were independent of STP and PVA concentrations.

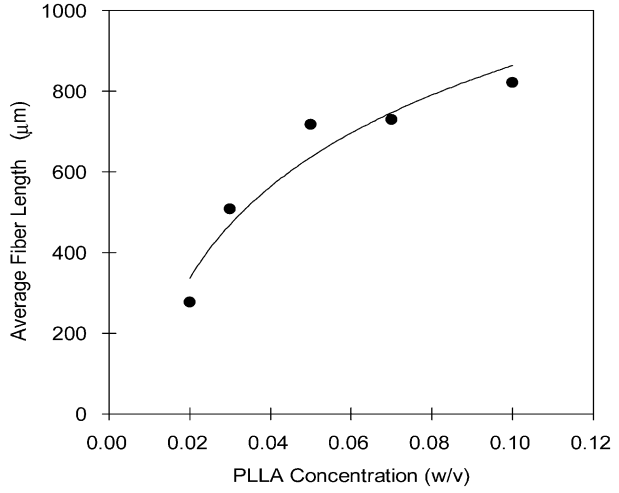

Fig. 5. Average fiber lengths of products derived from addition of PLLA solution into PVA solution consisting of 0.01 wt% PVA and 0.1 mol/L STP at stirring rate of 450 rpm as a function of PLLA concentration of droplets.

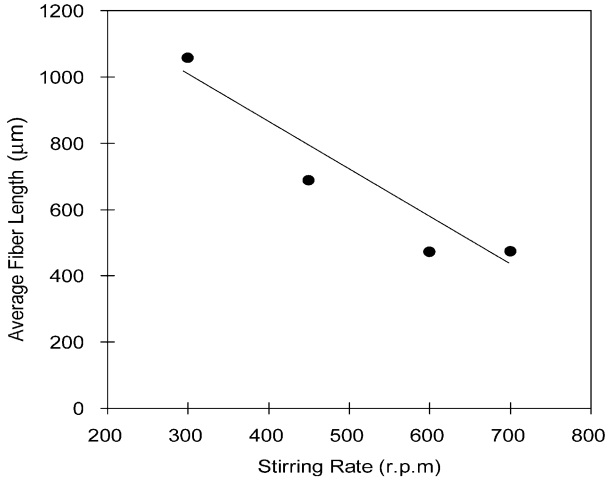

Fig. 6. Average fiber lengths of products derived from addition of PLLA solution (0.07 w/v) into PVA solution consisting of 0.01 wt% PVA and 0.1 mol/L STP as a function of stirring rate.

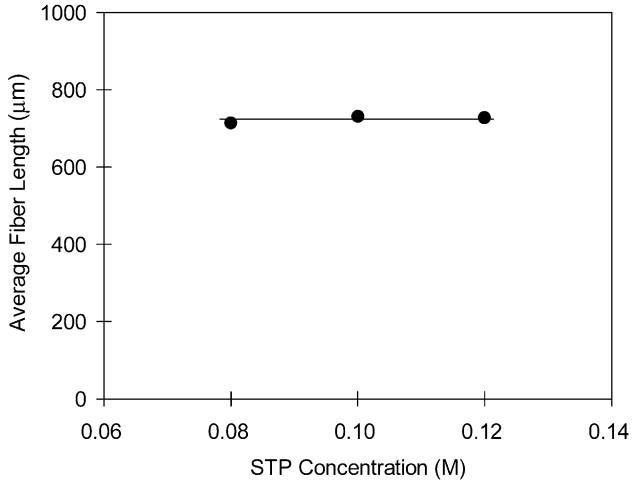

Fig. 7. Average fiber lengths of products derived from addition of PLLA solution into PVA solution (0.07 w/v) consisting of STP and 0.01 wt% PVA at stirring rate of 450 rpm as a function of STP concentration.

3.2. Fabrication of PLLA porous block

Fig. 9 shows PLLA porous blocks consisting of PLLA short fibers. The blocks are easily prepared by heating a mold filled with the fibers.

Fig. 10 shows SEM images of the PLLA blocks. The PLLA fibers are found to be bonded to one another and continuous pores are formed between the fibers. Fig. 11 shows the pore diameter distribution of the PLLA block. The average pore diameter is about 40 μm. Growth of cells or tissues into porous materials with average interconnecting pore diameters of 40 μm for a bone defect and ≥ 30 μm for a lesion of a knee meniscus has been reported so far [7, 16]. The pore sizes in the PLLA porous block are sufficient to allow the ingrowth of nutriments, tissues, blood vessels or cells into the material. The PLLA porous material fabricated in the present work is expected to be useful as a scaffold for tissue regeneration.

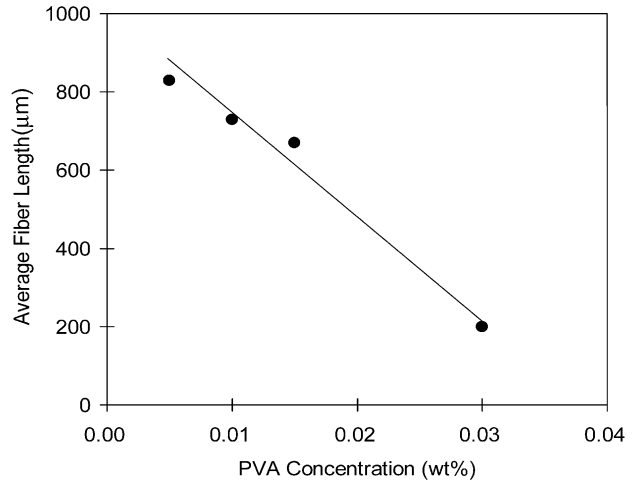

Fig. 8. Average fiber lengths of products derived from addition of PLLA solution (0.07 w/v) into PVA solution consisting of PVA and 0.1 mol/L STP at stirring rate of 450 rpm as a function of PVA concentration.

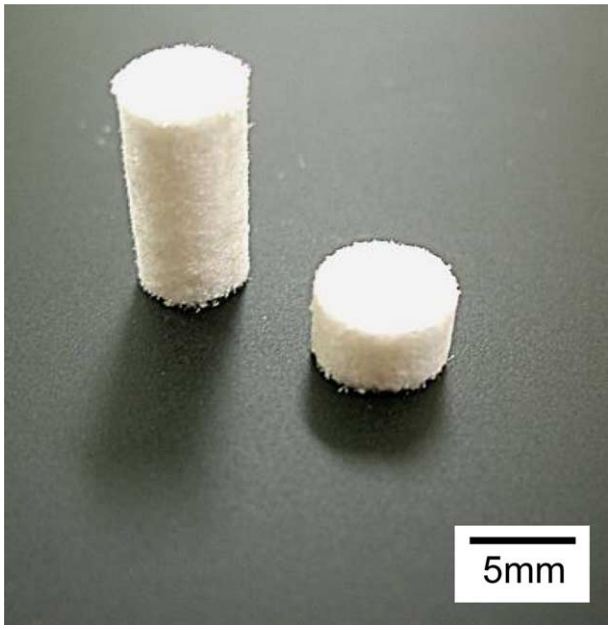

Fig. 9. PLLA porous blocks prepared by heating PLLA fibers at 173 °C for 10 min.

4. Conclusion

PLLA short fibers were successfully prepared by a solvent evaporation technique using a PLLA solution and PVA solution containing STP. STP plays an important role in the formation of a PVA membrane on the dispersed droplets of PLLA solution in PVA solution. The droplets were deformed in fibrous shapes by the external force by stirring. The length of fibers was 200–800 μm, which was controlled by the stirring rate, the PLLA concentration of the droplets and the PVA concentration. A PLLA porous block was easily prepared by interlocking PLLA fibers. It

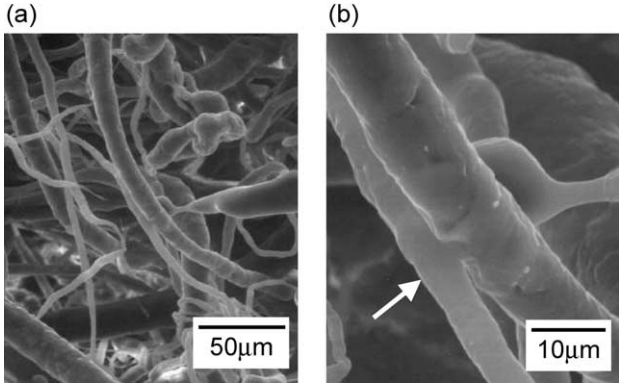

Fig. 10. SEM images of the PLLA porous block. White arrow in (b) marks a point where two fibers are bonded to each other.

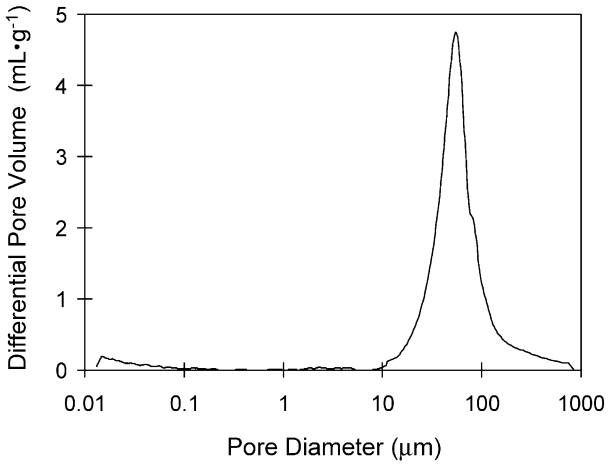

Fig. 11. Pore distribution of the PLLA porous block.

has a structure of interconnecting pores with diameters of 40 μm on average. The material is believed to be applicable as a biomaterial for tissue repair.

Acknowledgements

The present work was supported in part by a grant from the NITECH 21st Century COE Program 'World Ceramics Center for Environmental Harmony'. The authors are indebted to Atushi Suzuki (NGK Spark Plug Co., Ltd) for performing the GPC measurement and for helpful discussions.

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