Poly(lactic acid) Inverse Opal as Implantable Photonic Bandgap Materials

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Macroporous poly(lactic acid) with inverse opal structure (IoPLA) was fabricated by colloidal crystal templating. IoPLA shows an intense near-infrared (NIR) reflection, which comes from the optical diffraction upon the periodic macroporous structure composed of uniformly sized pores. It is demonstrated that in vivo implantation of IoPLA leads to destruction of the inverse opal structure, causing a notable decrease in the intensity of the NIR reflection peak. IoPLA with this degradation-dependent optical property might become an implantable photonic bandgap material that can report the state of degradation and co-occurring events in a nondestructive, real-time manner.

Recent developments in micromolding techniques have enabled fabrication of a wide variety of microstructures.[1,2] One of the techniques, colloidal crystal templating facilitates fabrication of a regular macroporous structure with three-dimensional periodicity, the so-called inverse opal structure, of various kinds of organic and inorganic materials.[3,4] The fabricated macroporous materials are classified into photonic bandgap materials characterized by the optical reflection property in the visible and near-infrared (NIR) regions.[5] Based on this property, many kinds of polymeric macroporous materials have been fabricated for applications such as in situ monitoring of pH,[6] temperature,[7] biochemical reactions,[8] etc. However, there are few reports of fabrication of macroporous biodegradable polymers by colloidal crystal templating.

In this study, we have focused on poly(lactic acid) (PLA) as a component material of the macroporous structure. PLA is the most promising biodegradable polymer because of its excellent biodegradability, biocompatibility, processability, and harmlessness of the degraded products.[9,10] For these features, PLA has the potential for use as medical sutures, bone screws, temporary wound dressings, scaffolds for tissue engineering, and microchip devices for drug delivery systems (DDS).[11]

In all of these applications, monitoring of any degradation of PLA is an important subject for understanding the mechanism of in vivo degradation, release profile of loaded drugs, and cell behavior under tissue formation. In previous studies, several techniques such as magnetic resonance imaging (MRI),[12,13] X-ray computed tomography (CT),[14] radiolabeling, and fluorescent imaging[15] have been adopted for monitoring. On the other hand, the utilization of the optical reflection of a macroporous material for monitoring has not been reported.

The purpose of this study is to present macroporous PLA with inverse opal structure (IoPLA), which might enable in situ monitoring of degradation and co-occurring events such as drug release in a nondestructive, real-time manner. The IoPLA was prepared with poly(*dl*-lactic acid) (average molecular weight 30,000, Taki Chemical Co., Ltd.) according to the conventional fabrication procedure, which is mentioned below. Colloidal crystal templates (CC) were fabricated on a clean glass substrate by a modified gravity sedimentation method using 10 wt % colloidal dispersion of silica microspheres (mean diameter 400 nm, Polysciences, Inc.).[16]

Several drops of 30 wt % acetone solution of the polymer were carefully dropped on CC. The obtained composite film was then stored in a freezer for one day in order to complete the infiltration of the solution into the inter-particle voids of the templates. After completion of the infiltration, the composite film was immersed in a 2.3 wt % aqueous solution of hydrofluoric acid for two days at ca. 4 °C. The obtained IoPLA was rinsed with ion-exchanged water several times and then dried in an evacuated desiccator at room temperature.

In order to check removal of the etchant and the template from IoPLA, the composition of the fabricated IoPLA was investigated by energy dispersive X-ray spectroscopy (EDS) using an energy dispersive X-ray analyzer (HORIBA, EMAX ENERGY EX-250). The EDS spectrum of IoPLA showed intense signals from C (70.64%) and O (29.33%) and no signals from Si and F. Therefore, it can be said that the etchant and the template were completely removed from the IoPLA. The Fourier transformed infrared (FT-IR) spectrum of the IoPLA measured with a FT-IR spectrometer (JASCO, FT/IR-470) showed almost the same absorption profile as did a spectrum of neat PLA. This result indicates that the IoPLA has enough durability against the etchant.

Figure 1a is a SEM image of CC observed from normal to the sample surface using a field emission scanning electron microscope (FE-SEM, Hitachi High-Technologies, S-4800). A hexagonally close-packed layer, which is composed of uniform silica microspheres (mean diameter 400 nm), can be seen. The direction vertical to this layer corresponds to the (111) direction

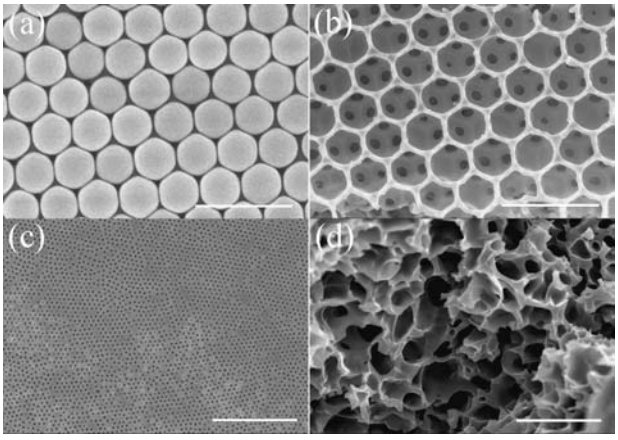

Figure 1. SEM images of (a) colloidal crystal template, (b), (c) IoPLA with different magnification, (d) implanted IoPLA in subcutaneous tissue (scale bars in (a) and (b): 1 μm, (c) and (d): 10 μm).

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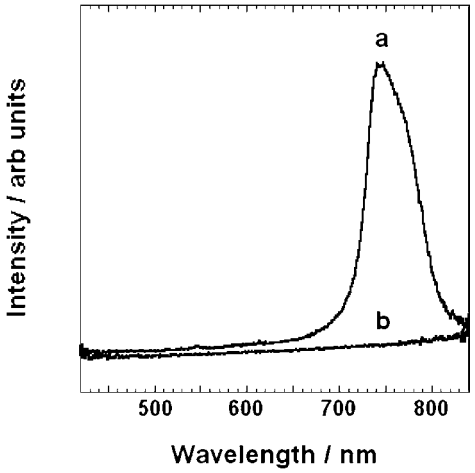

Figure 2. Optical reflection spectra of (a) IoPLA and (b) implanted IoPLA in subcutaneous tissue.

of the face-centered cubic (fcc) lattice. The SEM image of the IoPLA (Figure 1b) shows the inverted structure against the structure of CC. That is, the periodic structure composed of the silica spheres and interparticle voids were inverted into the structure of air spheres (ca. 400 nm) and polymer frameworks, respectively. The black spots in Figure 1b correspond to inter-pore channels between the upper and lower layers. According to Figure 1c, the periodicity of the pore arrangement is maintained on a scale over several tens of micrometers.

Figure 2a shows the optical reflection spectrum of IoPLA measured with a fiber optic spectrometer (Ocean Optics, HR4000-CG). IoPLA showed intense reflection centered at 744 nm with an incidence of white light normal to the sample surface. According to the modified version of the Bragg equation,[17] the pore diameter was estimated to be 402 nm, which is in reasonable agreement with the SEM image (Figure 1b). This indicates that the observed reflection is derived from the optical diffraction upon the periodic macroporous structure composed of uniformly sized pores.

Since the optical reflection of IoPLA is derived from the structural regularity with respect to porosity, pore sizes, and pore arrangement, it is expected to change simultaneously with deterioration of the regularity through biodegradation by in vivo implantation. Figure 1d shows a SEM image of implanted IoPLA in the subcutaneous tissue of the lower backs of mice for a month. The irregular porous structure, which consists of large, distorted pores, can be seen in contrast to the images of non-implanted IoPLA with a regular porous structure (Figure 1c). The observed irregular structure is considered to be formed through the fusion of the original uniform pores as a result of heterogeneous erosion of the polymer frameworks in the in vivo environment.

Figure 2b shows the reflection spectrum of the implanted IoPLA. As anticipated from the SEM observation, the implanted IoPLA did not give a distinct optical reflection peak. The absence of the reflection peak means that the IoPLA suffers from excess structural modulation through biodegradation that is insufficient to diffract incident NIR light. The spectral change should be caused by variations in either volume fractions for the pores and polymer frameworks, in the refractive index of the polymer framework, in the distance between lattice planes, or in a combination of these.

Although the process of degradation cannot be read from the present two spectra (Figures 2a and 2b), measurement of the reflection spectra over time might disclose the mode of degradation through spectral change with respect to peak intensity, peak width, and maximum reflection wavelength. From the recent in vitro degradation experiments, it was revealed that the optical reflection of IoPLA varied gradually from an intense, sharp peak to a feeble, broad one with a simultaneous variation in the reflection wavelength. Such the behaviour may be related to the degradation mechanism characteristic of IoPLA. Further investigation on this topic is now in progress.

In summary, macroporous PLA with inverse opal structure was successfully fabricated by colloidal crystal templating. It shows NIR reflection caused by the Bragg diffraction of incident light upon the periodic macroporous structure. In addition, it was revealed that in vivo implantation extinguished the three-dimensional structural periodicity and the reflection peak in the NIR region. The results of this study should contribute to fabrication of an implantable photonic bandgap material that enables in situ monitoring of biodegradation and co-occurring events in a nondestructive, real-time manner.

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