



Original article

Optical monitoring the degradation of PLGA inverse opal film

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ABSTRACT

Implantable materials have broad applications in tissue engineering and *in vivo* sensors. It is essential to know the detailed information of the implantable materials during their degradation. In this paper, we developed a method to monitor the degradation process of a well-used biomaterial, poly(lactide-co-glycolide) (PLGA) by taking advantage of inverse opal structure. We found that mass loss, molecular weight and glass transition temperature of PLGA during the degradation process in Hank's artificial body fluid can be *in situ* monitored by measuring the optical properties of PLGA inverse opal.

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1. Introduction

Poly(lactide-co-glycolide) (PLGA), a biodegradable aliphatic polyester, has received vast interests for its excellent biodegradability, biocompatibility, nontoxicity and mechanical strength [1,2]. These properties of PLGA result in their extensive use in biomedicine and pharmacy, such as drug carriers for controlled-drug delivery and release, as well as scaffolds in tissue engineering [3,4]. One of the most important advantages of the PLGA is that the degradation time of which can be tuned by changing the monomers proportion of lactide (LA) and glycolide (GA). For the applications of the PLGA, it is necessary to monitor the degradation process of PLGA. Therefore methods have been developed to monitor the state of the material degradation, including surface plasma resonance (SPR) [5], fluorescence resonance [6], magnetic resonance [7] and so on [8,9]. However, these methods are either experiment-intensive or bio-incompatible for the *in situ* monitoring. Inverse opal which is composed of well-arranged uniform holes has been widely studied. It is generally fabricated by the replication of an opal template composed of ordered monodisperse spheres. The interaction of the light with the ordered structure results in an optical stop band, which can be measured as a reflection peak in reflection spectrum. Variations in the effective refractive index and lattice spacing of the inverse opal films can vary the light transportation and thus change the reflection spectrum. The properties have been used for the construction of sensors for monitoring chemical or biological reaction [10–16].

In this paper, we proposed to form a PLGA inverse opal on the PLGA film for *in situ* monitoring the decomposing process of bulk materials. When the inverse opal on the PLGA film was decomposed, it led a change in both microstructure and effective refractive index, and thus changed the optical properties. These changes can be even observed by naked eyes.

2. Experimental

The amorphous copolymer of lactide and glycolide (PLGA, L/G = 80/20 in molar ratio, viscosity average molecular weight $M_v = 300,000$) was purchased from Jinan Daigang (China) Co., Ltd. Monodisperse SiO₂ spheres were prepared by modified Stöber method [17]. Hank's artificial body liquid was prepared as reported [18].

Firstly, high quality SiO₂ opal templates were fabricated by vertical deposition method [19]. Secondly, the SiO₂ opal template was infiltrated by 10 wt% PLGA trichloromethane solution and dried under room temperature for 3 days, vacuum at 55 °C for 12 h and vacuum at 80 °C for 2 h. Thirdly, the SiO₂ opal/PLGA composite film was immersed in 2 wt% aqueous solution of hydrofluoric acid (HF). When the composite film floated from the substrate, SiO₂ particles were completely removed by successively etched with 1 wt% HF for 12 h at 4 °C. Finally, the PLGA inverse opal film was rinsed with deionized water for at least three times and dried by nitrogen flow. Before the PLGA films were used for degradation experiment, they were kept in evacuated desiccators at room temperature.

The PLGA inverse opal films were cut into 1 cm × 1 cm slices and rinsed with Hank's artificial body liquid solution for three times before using. Prior to the hydrolytic degradation, the initial mass (m_0), glass transition temperature (T_{g0}) and molecule weight

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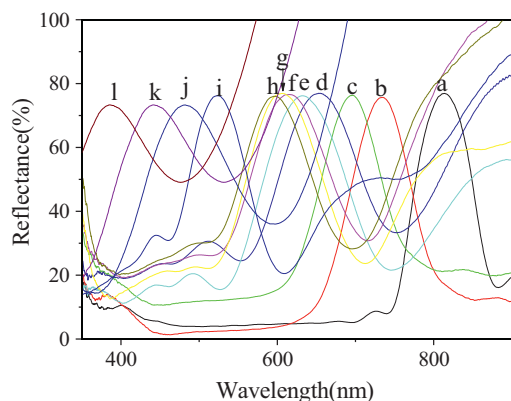


Fig. 1. The reflection spectra of dried PLGA inverse opals at different degradation stage ((a) 0 day, (b) 1 day, (c) 2 days, (d) 3 days, (e) 4 days, (f) 5 days, (g) 6 days, (h) 1 week, (i) 2 weeks, (j) 3 weeks, (k) 4 weeks, (l) 5 weeks).

(M_{v0}) of each PLGA inverse opal slices were recorded. After that, they were sealed into bottles containing 25 mL Hank's artificial body liquid solution. The samples were incubated at 37.0 °C for different time length (up to 50 days). The pH of the solution was kept at 7.4 during the whole process. After decomposition, the films were removed from the Hank's artificial body liquid solution in turn, rinsed with deionized water and dried the surface by nitrogen flow. The samples were then dried in an oven at 37.0 °C for 5 days, after which the surface morphology, reflection spectra, mass (m_d), glass transition temperature (T_{gd}) and molecule weight (M_{vd}) were recorded.

3. Results and discussion

It is known that the reflection peak of inverse opal photonic crystal originated from the diffraction of light in the periodic structure. The normal reflection position of PLGA inverse opal films can be predicted by Bragg law: [19]

$$\lambda = 2d(f_{\text{PLGA}}n_{\text{PLGA}}^2 + f_{\text{air}}n_{\text{air}}^2)^{1/2} \quad (1)$$

where λ is the maximum reflection wavelength, d is the distance between crystalline planes in the (1 1 1) direction, n_{PLGA} and n_{air} are the refractive indices of the polymer and air, f_{PLGA} and f_{air} are their volume fractions ($f_{\text{PLGA}} + f_{\text{air}} = 1$). Fig. 1 gave the reflection spectra during the degradation process. Before degradation, the reflection peak of the PLGA inverse opal replicated from 410 nm SiO₂ sphere template was at 814 nm. This reflection peak shifted to short wavelength during degradation process. The position of the peak shifted fast in the first two days and then slowed down in the following days.

The morphology of the PLGA inverse opal film just replicated from the opal template composed of SiO₂ sphere with a diameter of 410 nm is shown in Fig. 2A. Hexagonally packed uniform voids can be clearly observed, indicating the formation of close-packed structure. Such ordered structure can be gradually decomposed. Fig. 2B shows the SEM image of the material soaked in Hank's artificial body liquid solution after 1 week. Although small breakages appeared from place to place, most of the place kept the ordered structure. At this stage these small breakages affected little on the optical properties. Two weeks later, the destruction spread over the film (Fig. 2C). However, the regularity of holes was still observed. Four weeks later, the order structure could only be observed in small area (Fig. 2D). This status kept for 6 weeks when the order structure disappeared thoroughly.

Curve a in Fig. 3A plotted the change of mass loss as a function of degradation time, which exhibits a linear relationship. The mass loss of the PLGA inverse opal was not significant, which was only 2.4% even after 5 weeks of degradation. This implied that no or little soluble products and oligomers were formed. The result corresponded to the first stage of PLGA biodegradation, which involved random chain scission. At the time, the molecular weight of PLGA decreased significantly, but no appreciable weight loss or soluble monomer products were formed [4]. Curve b in Fig. 3A showed the relationship between the average molecular weight and degradation time. The natural logarithmic of the number-average molecular weight ($\ln(M_v)$) of PLGA was plotted against degradation time, which showed that $\ln(M_v)$ of PLGA decreased linearly with the degradation time. After 7 weeks, the average molecular weight declined from 300,000 to ca. 120,000. Fig. 3B

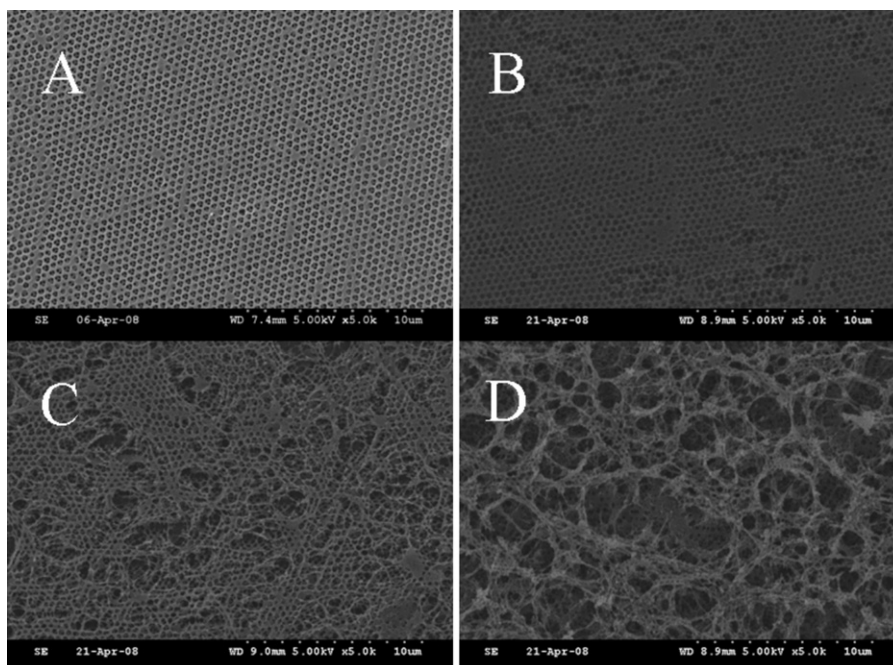


Fig. 2. SEM images of surfaces of PLGA inverse opal films at different degradation stage ((A) 0 week, (B) 1 week, (C) 2 weeks, (D) 4 weeks).

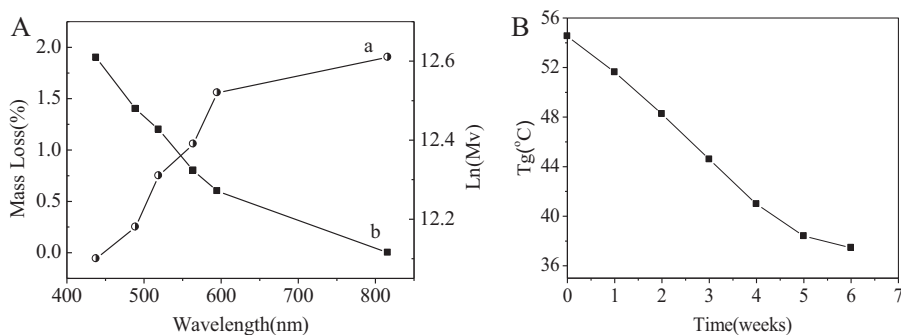


Fig. 3. The time-dependent changes of the mass (curve a in A), the average molecular weight (curve b in A) and the T_g (B) during the PLGA degradation process.

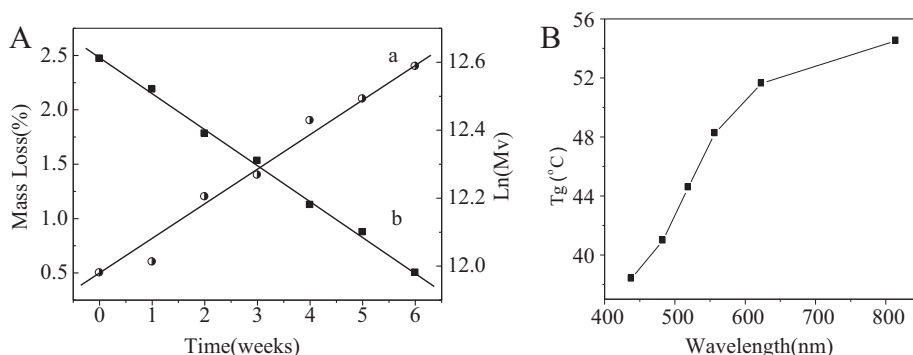


Fig. 4. The dependence of the mass (curve a in A), the average molecular weight (curve b in A) and the T_g (B) on the optical reflection peak center (in wavelength) during the PLGA degradation process.

plotted the T_g of the degraded PLGA films against degradation time. The decrease of T_g was caused by the increase in chain mobility and flexibility, which supported that the shorter amorphous chains attributed to continuous hydrolysis [4]. In the six weeks, the T_g decreased about 17 °C, which was somewhat different with the literatures [4].

In this work, the PLGA was amorphous and without thermal treatment, so the degree of crystallinity of PLGA film was very low. During degradation process, voids formation in the PLGA film was easier than that in the PLGA after thermal treatment. The relationships between reflection peak and mass loss, L_n and T_g were shown in Fig. 4A and B. These figures showed that the mass loss, molecule weight and T_g changed in monotone with the reflection peak position during the degradation process. Therefore, by using the reflection results we could predict some important parameters of the degradation state, which could be only detected *ex situ* in general. In practical applications, optical measurement would be useful for monitoring or trailing the degradation process of implantable material.

4. Conclusions

In conclusion, inverse opals were fabricated with PLGA, a type of material with degradation performance in Hank's artificial body liquid solution. The changes of PLGA degradation were monitored by a non-contact optical method. By measuring the reflection spectra of the PLGA inverse opal, we can monitor the change of mass loss, L_n , M_v and T_g of PLGA during degradation. The method showed here might provide a new *in situ* method for monitoring the change of bio-degradable materials.

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