

# Hollow Porous Poly(lactic acid) Microspheres

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**ABSTRACT:** On the basis of the water solubility of poly(*N*-vinyl-2-pyrrolidinone), hollow porous poly(lactic acid) microspheres (HPPLAs) were prepared by a water-in-oil-in-water multiple-emulsion solvent evaporation method. The influence of the concentration of the stabilizer Span80 in the oil phase on the morphology was investigated. It was found that when the content of Span80 solutions was 3.5 wt %, most HPPLAs were about 2  $\mu\text{m}$  in diameter. Field scanning electron microscopy results show that the HPPLAs were porous and hollow. The structure and crystal form of the HPPLAs were characterized by Fourier transform infrared spectroscopy and X-ray

diffraction analysis. Using these HPPLAs as degradable templates, we successfully synthesized Litchi-like polystyrene (PS) microspheres about 2  $\mu\text{m}$  in diameter by the emulsion method. When used as drug carriers, these HPPLAs would be convenient in which to embed drugs, whereas the Litchi-like PS microspheres may have potential as new materials for polymer modification. © 2007 Wiley Periodicals, Inc. *J Appl Polym Sci* 107: 1189–1193, 2008

**Key words:** composites; emulsion polymerization; synthesis; degradation

## INTRODUCTION

Poly(lactic acid) (PLA) and its copolymers are among the most commonly used biodegradable polymers in the development and manufacture of biodegradable sustained release systems such as implants and microspheres.<sup>1</sup> Moreover, the advantages of PLA include availability from renewable resources and a reduction in carbon dioxide emissions generated during manufacturing compared to conventional commodity plastics.<sup>2</sup> In recent years, microspheres of biodegradable polymers such as poly(DL-lactic acid) and poly(DL-lactic-co-glycolic acid) have attracted much interest due to their good biodegradability.<sup>3,4</sup>

Multiple emulsions are complex systems, named *emulsions of emulsions*, in which the particles of the dispersed phase include smaller dispersed particles that belong to the continuous phase and have two interfaces. In multiple emulsions, each dispersed particle forms a vesicular structure with one or more aqueous compartments separated from the aqueous phase by a film of the oily phase.<sup>5–12</sup> Water-in-oil-in-water ( $W_{\text{in}}/O/W_{\text{out}}$ ) multiple emulsions are composed of aqueous microparticles contained in oily particles, which in turn, are dispersed in an aqueous phase.<sup>9–11,13,14</sup> Because of their structure, multiple emulsions may have numerous applications in the cosmetics, pharmaceutical, and food industry and in

different separation techniques.<sup>6,7,11,13</sup> In this study, we prepared hollow porous poly(lactic acid) microspheres (HPPLAs) by a  $W_{\text{in}}/O/W_{\text{out}}$  multiple-emulsion solvent evaporation method. Using these HPPLAs as a degradable template, we successfully synthesized Litchi-like polystyrene (PS) microspheres by the emulsion method.

## EXPERIMENTAL

### Material

We prepared PLA (viscosity average molecular weight ( $M_v$ ) =  $8.0 \times 10^4$ ).<sup>15</sup> Poly(*N*-vinyl-2-pyrrolidinone) (PVP) was purchased from Sinopharm Chemical Reagent Co., Ltd. (Liaoning, China) Poly(vinyl alcohol) (PVA;  $1750 \pm 50$ ), *n*-pentyl alcohol, and sodium dodecyl sulfate were obtained from Chemical Medical (Group) Shanghai Chemical Reagent Corp. (Shanghai, China) Polysorbate 80 (Tween 80) was purchased from Shantou Xilong Chemical Co., Ltd. (Guangdong province, China) Dichloromethane (DCM) was purchased from Tianjin Damao Chemical Factory. The lipophilic emulsifier sorbitan monooleate (Span 80) was obtained from Tianjin No. 3 Chemical Reagent Factory (Tianjin city, China). Styrene and potassium persulfate were obtained from Sinopharm Chemical Reagent Co., Ltd. (Liaoning, China).

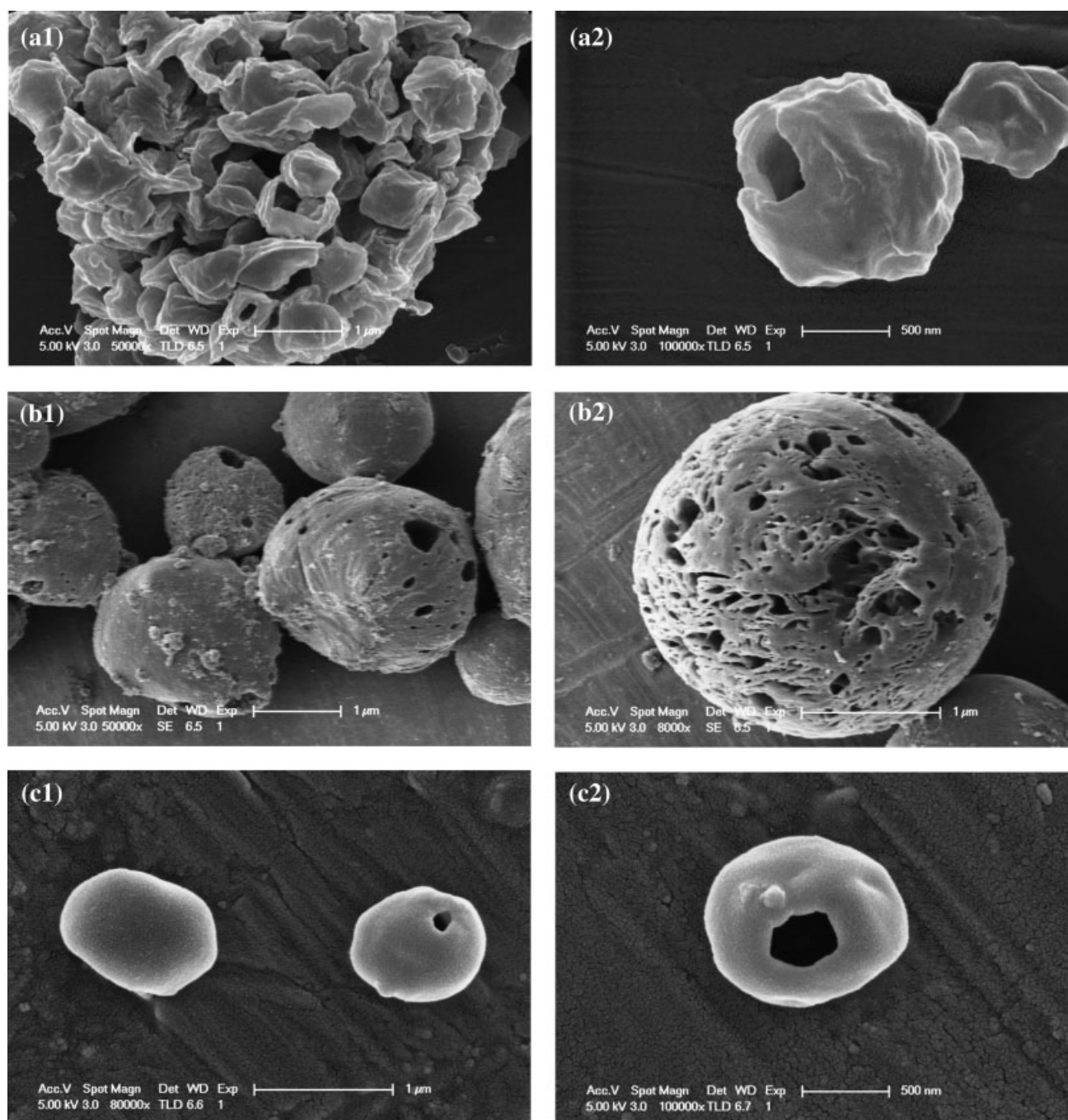
### Sample preparation

#### HPPLAs

A modified  $W_{\text{in}}/O/W_{\text{out}}$  double-emulsion solvent evaporation method was used to prepare the HPPLAs. To obtain the water-in-oil ( $W_{\text{in}}/O$ ) emul-

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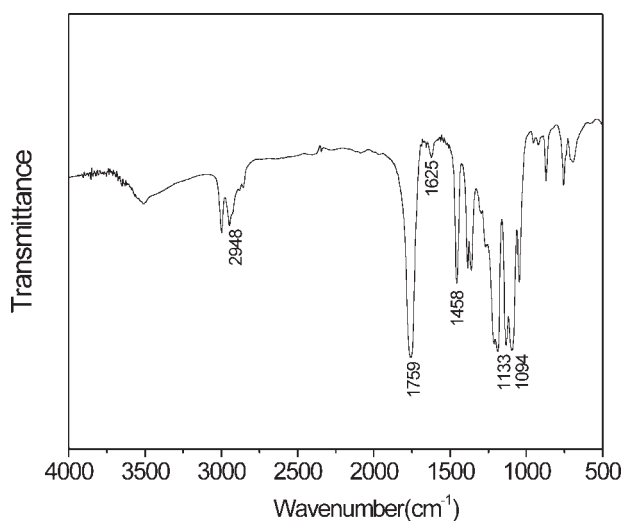
**Figure 1** SEM photographs of the HPPLAs. The concentrations of Span80 in the oil phase were (a1,a2) 1.5, (b1,b2) 3.5, and (c1,c2) 5.0 wt %.

sion, 3 mL of a 26.7 wt % PVP aqueous solution and 20.0 g of DCM containing 1.0 g of PLA, 1.0 g of PVP, and Span 80 were mixed and emulsified in a homogenizer with stirring at a speed of 900 rpm for 30 min. To prepare the  $W_{in}/O/W_{out}$  emulsion, the  $W_{in}/O$  emulsion was injected into 100 mL of a 1 wt % PVA aqueous solution ( $W_{out}$ ) with a glass syringe and emulsified with stirring at speed of 700 rpm for 30 min in a flask. Then, the temperature of this  $W_{in}/O/W_{out}$  emulsion was increased to 40°C, and the

emulsion was stirred at 700 rpm under atmosphere until the organic solvent DCM evaporated from the emulsion droplets completely, and then, by centrifugal separation, distilled water washing, and vacuum drying separately, the HPPLAs were obtained.

#### Litchi-like PS microspheres

For the water phase, 0.7 g of sodium dodecyl sulfate was dissolved in 50 mL of  $H_2O$ . Then, 0.1 g of *n*-



**Figure 2** FTIR spectra of the HPPLAs.

pentyl alcohol was added, and the solution was mixed evenly.

For the oil phase, 10 g of HPPLAs were dispersed in 15 g of styrene evenly by an ultrasonic dispersion technique.

To prepare the oil-in-water emulsion, the previous oil was dropped in the previous water solution with stirring at a speed of 200 rpm at 20°C for about 10 min in a flask. After 15 min, the temperature was increased to 60°C. Then, under the protection of inert N<sub>2</sub> gas, 5 mL of 3 wt % potassium persulfate was added drop by drop within 30 min. After 1 h, the temperature was raised and kept at 75°C for 8 h. Finally, by emulsion breaking, centrifugal separation, distilled water washing, and vacuum drying separately, the Litchi-like PS microspheres were obtained.

### Measurements

Field scanning electron microscopy photographs were taken on a JEOL JSM-6700F field scanning electron microscope (JEOL, Japan). Fourier transform infrared (FTIR) spectroscopy spectra were measured with a Nicolet Nexus-870 spectrometer (Madison, WI). Differential scanning calorimetry (DSC) was conducted with a Mettler Toledo DSC-821E instrument (Im langado, Switzerland) under a nitrogen atmosphere at a flow of 80 mL/min. X-ray diffraction (XRD) analysis was carried out to confirm the crystal form of PLA and the HPPLAs. A Japanese D/max-γB rotating diffractometer (Tokyo, Japan) was used with a Cu Kα line ( $\lambda = 0.15418$  nm), a tube voltage of 40 kV, and a tube current of 80 mA.

## RESULTS AND DISCUSSION

### Morphology of the HPPLAs

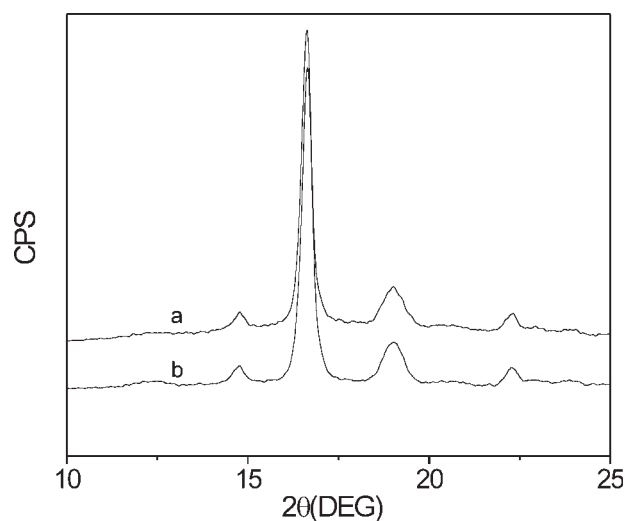
HPPLAs were successfully prepared by  $W_{in}/O/W_{out}$  multiple-emulsion solvent evaporation, as shown in

Figure 1 As clearly shown in Figure 1(b1,b2), the HPPLAs were hollow and porous; moreover, the obtained HPPLAs were about 2  $\mu\text{m}$  in diameter.

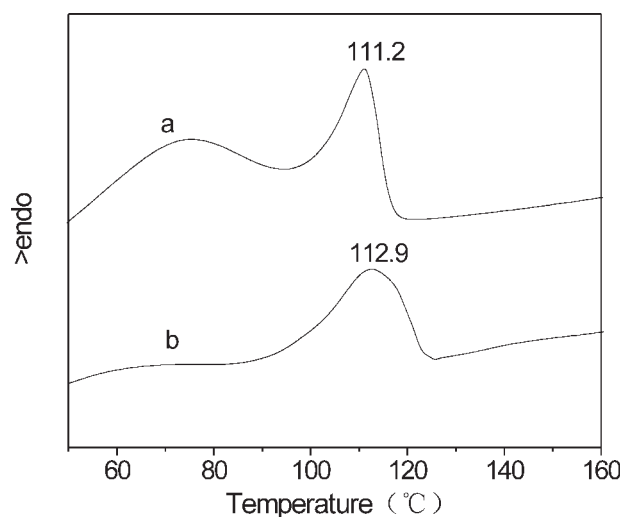
Span80 concentration in the oil phase is known to be a key factor that affects the morphology of microspheres. In this study, 1.5, 3.5, and 4.5 wt % Span80 solutions were used as oil phases to examine the effect of Span80 concentration on the morphology of the microspheres. Figure 1 illustrates the morphologies of the microspheres for the corresponding Span80 concentrations, respectively. When the concentration of Span80 was 1.5 wt %, the HPPLAs were not orbicular and without porous structure, even in the fragment shown as Figure 1(a1,a2). When the concentration of Span80 decreased to a certain degree, the emulsion was unstable; therefore, the HPPLAs were not orbicular and without porous structure, even when broken into fragments. When the concentration of Span80 was raised to 4.5 wt %, the HPPLAs were similar to orbicular and with hollow structure but not porous, as shown in Figure 1(c1,c2). A higher Span80 concentration increased the viscosity of the oil phase, which may have caused PVP to be dispersed unevenly and to agglomerate easily; moreover, the higher viscosity also inhibited DCM from diffusing from the  $W_{in}$  phase to the  $W_{out}$  phase. Therefore, when PVP dissolved, the remaining hollows were fewer and bigger. Consequently, the approximate concentration of Span80 to prepare the HPPLAs, as shown in Figure 1(b1,b2), was 3.5 wt %.

### Characterization of the HPPLAs

Figure 2 shows the FTIR spectra of the HPPLAs. In Figure 2, shown are the characteristic peaks for PLA:



**Figure 3** X-ray diffraction scans for the samples: (a) PLA and (b) HPPLAs.



**Figure 4** DSC curves of the samples: (a) PLA and (b) HPPLAs.

$\nu_{\text{C=O}}$  at  $1759\text{ cm}^{-1}$ ,  $\nu_{\text{C=O}}$  at  $1625\text{ cm}^{-1}$  (weak, intermolecular hydrogen bond),  $\nu_{\text{asC-O-C}}$  at  $1133\text{ cm}^{-1}$ ,  $\nu_{\text{sC-O-C}}$  at  $1094\text{ cm}^{-1}$ ,  $\nu(-\text{CH}_2)$  at  $2948\text{ cm}^{-1}$ , and  $\delta(-\text{CH}_3)$  at  $1458\text{ cm}^{-1}$ . Figure 3 illustrates the XRD patterns for PLA and the HPPLAs. Four main diffraction peaks, as shown in Figure 3, at about  $2\theta = 14.8, 16.6, 19.0,$  and  $22.3^\circ$  were observed, which corresponded with the  $\alpha$ -crystal PLA with helix conformation for  $2\theta = 15, 16, 18.5,$  and  $22.5^\circ$ , respectively.<sup>16</sup> No significant difference was found between the XRD patterns for PLA and the HPPLAs, which implied that when HPPLAs were prepared by the  $W_{\text{in}}/O/W_{\text{out}}$  multiple-emulsion solvent evaporation from PLA, the crystal form of PLA did not change. Figure 4 shows the DSC heating scan of PLA and the HPPLAs. The peak at about  $111.2^\circ\text{C}$  in

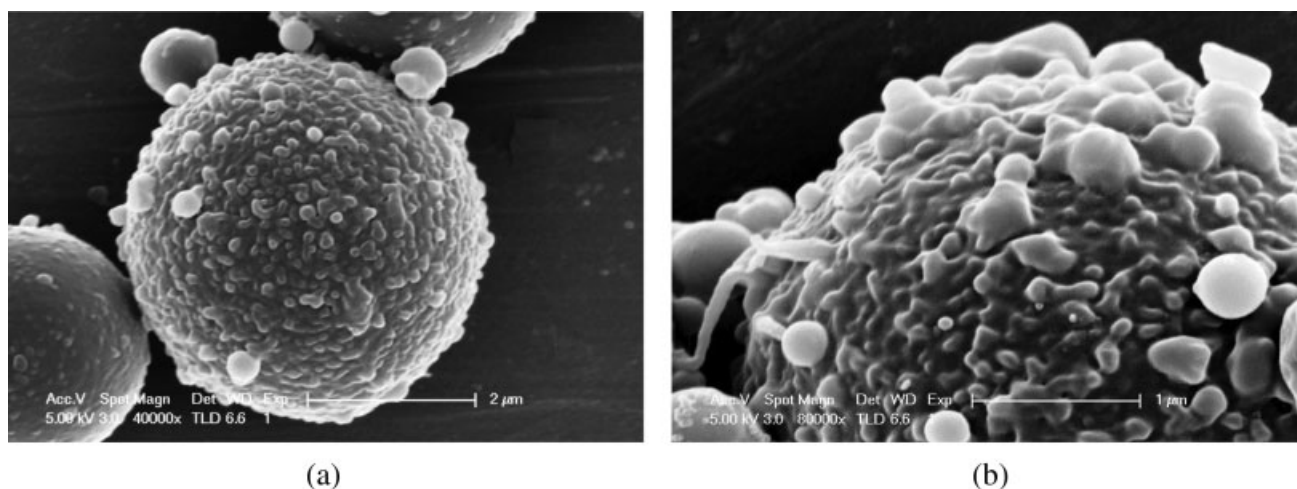
Figure 4(a) corresponds to the melting process of PLA. Another broad peak at about  $112.9^\circ\text{C}$  in Figure 4(b) corresponded to the melting process of the HPPLAs. This slight change may have been caused by a small amount of PVP entrapped in the HPPLAs (the melting point of the PVP used was  $125^\circ\text{C}$ ).

### Morphology of Litchi-like PS microspheres

With the HPPLAs as a degradable template, Litchi-like PS microspheres were successfully prepared by the emulsion method, as shown in Figure 5. As clearly shown in Figure 5(a,b), the PS microspheres are much like Litchi, a chief fruit in the region of Guangzhou, Guangdong Province, China. Moreover, the obtained PS microspheres were about  $2\text{ }\mu\text{m}$  in diameter. We deduced that styrene monomers were polymerized *in situ* in the center hollow site of each of the HPPLAs to form a PS microsphere at first; then, the PS microsphere grew there. When the PS microsphere grew bigger and reached the inner surface of the HPPLA shell, the PS grew out of the pores in shell of the HPPLA; during this period, HPPLAs were being degraded all the time. After the HPPLAs were degraded, the shell of the HPPLAs was broken into fragments, and Litchi-like PS microspheres appeared. This phenomenon was just like a hatching egg; when the shell of egg is broken into fragments, the chicken comes out.

### Characterization of the Litchi-like PS microspheres

Figure 6 shows the FTIR spectra of the Litchi-like PS microspheres. The presence of benzene identified for the following characteristic vibrations were present:  $\nu_{\text{C=C}}$  at  $1600, 1500,$  and  $1447\text{ cm}^{-1}$ . Compared with Figure 2, no obvious characteristic peaks for PLA



**Figure 5** SEM photographs of the Litchi-like PS microspheres: (a) Litchi-like PS microspheres and (b) surface of the Litchi-like PS microspheres.

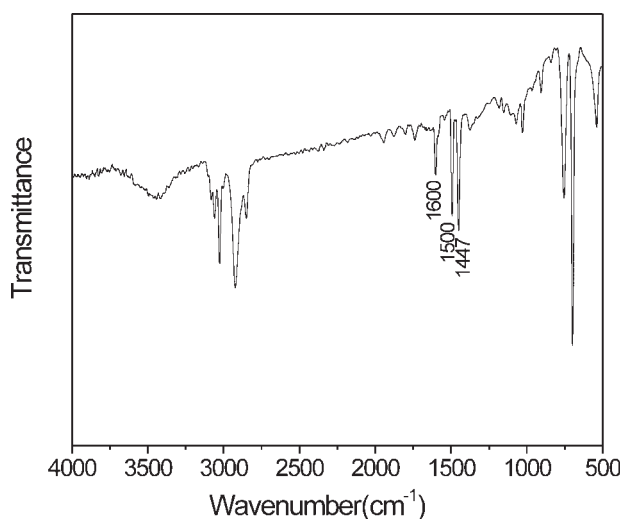


Figure 6 FTIR spectra of the Litchi-like PS microspheres.

were found:  $\nu_{C=O}$  at  $1759\text{ cm}^{-1}$ . Figure 7 shows the DSC heating scans of PS and the Litchi-like PS microspheres. The peaks corresponding to the melting process of PS and the Litchi-like PS micro-

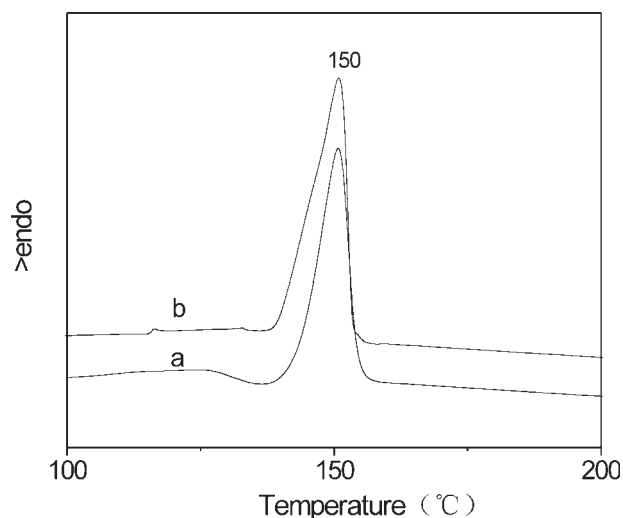


Figure 7 DSC curves of the samples: (a) PS and (b) Litchi-like PS microspheres.

spheres were both at about  $150^{\circ}\text{C}$ . These facts implied that before the Litchi-like PS microspheres appeared, the shell of the HPPLAs was degraded and dissolved.

## CONCLUSIONS

HPPLAs about  $2\text{ }\mu\text{m}$  in diameter were successfully prepared by a  $W_{\text{in}}/O/W_{\text{out}}$  multiple-emulsion solvent evaporation method. Span80 concentration in the oil phase was an important factor affecting the morphology of the HPPLAs, and the approximate concentration was 3.5 wt %. When prepared by this method, the crystal form of PLA did not change. Moreover, with HPPLAs as a degradable template, Litchi-like PS microspheres about  $2\text{ }\mu\text{m}$  were prepared by an emulsion method.

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