Novel Biodegradable Amphiphilic Poly(ε-caprolactone)/ Poly(*N*-vinylpyrrolidone) Blends via Successive *In Situ* Polymerizations

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ABSTRACT: In this study, biodegradable blends of poly(ε-caprolactone) (PCL) and poly(*N*-vinylpyrrolidone) (PVP) were prepared by a new strategy in the following steps: (1) free radical polymerization of *N*-vinyl-2-pyrrolidone (NVP) in ε-caprolactone (CL); (2) ring-opening polymerization of ε-caprolactone in the presence of PVP to obtain the target blends. The structure of the blends was confirmed by FTIR and ^{1}H NMR, and the molecular weight of PCL and PVP were determined by GPC. SEM study revealed that this polymerization method could decrease the disperse phase size and improve the interphase when compared with solution-blending method. The phase inversion occurred when PVP content was 15–20 wt %. Subsequently, the PCL sphere dispersed in PVP matrix and its size decreased with the increase of PVP content. The contact angle results showed that PVP has a profound effect on hydrophilic properties of PCL/PVP blends. PCL/PVP blends are believed to be promising for drug delivery, cell therapy, and other biomedical applications. © 2008 Wiley Periodicals, Inc. J Appl Polym Sci 111: 1676–1683, 2009

Key words: amphiphilic; poly(ε-caprolactone); poly(*N*-vinylpyrrolidone); blends; ring-opening polymerization

INTRODUCTION

Biodegradable aliphatic polyesters have received great research interest for their environmental, medical, and pharmaceutical applications.[1–3] Being one of the famous inexpensive biodegradable aliphatic polyesters, polycaprolactone (PCL) is manufactured by ring-opening polymerization of ε-caprolactone (CL). PCL is very attractive not only as a substitute material for nondegradable polymers for commodity applications but also as a specific plastic in the medicine,[4–6] agricultural,[7] and tissue engineering field that includes tissue engineered skin,[8] drug delivery systems,[9,10] axonal regeneration,[11,12] and scaffolds for supporting fibroblasts or osteoblasts growth.[13,14] PCL chains may undergo enzymatic degradation through hydrolysis of its ester bonds by lipase, especially Pseudomonas lipase (PS),[15,16] cholesterol esterase,[17] and carboxyl esterase.[18] However, degradation kinetics of PCL is slow due to its hydrophobic and semicrystalline nature, which makes its resorption time longer than 2 years.[19] Furthermore, hydrophobic property of PCL can lead to complement activation and liver accumulation and lacking surface recognition functions for specific mucoadhesion or receptor recognition.[20–22] So, hydrophobic property brings difficulties for developing more advanced biomaterials from PCL.[23,24]

For improving its hydrophilic property, many researchers synthesized PCL copolymers or blends with ethylene oxide (EO)/poly(ethylene glycol) (PEG)[25] or polysaccharides (starch,[26] gellan, and dextrin[27,28]). PCL-based blends have also been produced by melt extrusion for biodegradable packaging applications.[29] Demirgöz et al.[30] developed a methodology for preparation of crosslinking commercial starch-based thermoplastic blends. Ciardelli et al.[31] found out that starch and gellan are two suitable materials for the production of PCL-based blends for selective laser sintered tissue engineering scaffolds. Müller[32] prepared poly(*p*-dopamine)-*b*-poly (ε-caprolactone) diblock copolymers (PPDX-*b*-PCL), with the aim to provide a way to tune the lifetime of the biomedical devices within the human body as PCL hydrolytic degradation is several orders of magnitude lower than that of PPDX. Incorporation of various functional groups into PCL has also been investigated.[33,34] While these investigations are

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informative, the preparation of functional polyesters usually involves tedious protection/deprotection chemistry and the use of organic solvents. As a result, such systems present significant challenges for industrialization.

Poly(*N*-vinyl-2-pyrrolidone) (PVP) has relatively fast hydrolytic degradation and can preserve platelet functions when the platelets contact the polymer surfaces as the chemical structures of water-soluble.[35] PVP can replace PEO as a food thickener, blood plasma substitute, binding agent for drug delivery, and so forth. As a result, PVP is considered a biocompatible and biodegradable material.[36] However, the study of PCL/PVP blends has been rarely performed, particularly in investigations on their wettability. In this article we reported on the preparation and the properties of PCL/PVP blends obtained by successive *in situ* polymerizations. The polymerization process was stable, facile, and avoided the use of organic solvent disposal. In comparison with the solution-blending, this method can improve the interphase and decrease size of disperse phase, moreover, the phase inversion occurred with the variation of PVP content, and correspondingly the hydrophilic properties of PCL/PVP blends were affected.

EXPERIMENTAL

Materials

ε-Caprolactone, CL (Aldrich, Shanghai, China) was dried over CaH_2 for 7 days and distilled at reduced pressure prior to use. *N*-vinyl-2-pyrrolidone, NVP (Shanghai povidone trade Company, Shanghai, China) was dried under reduced pressure for several hours to remove traces of water before use. Azodiisobutyronitrile (AIBN), ethyleneglycol, and Tin(II) octanoate ($Sn(Oct)_2$) used in this study were all purchased from Shanghai Chemical Reagents Company (Shanghai, China) and used without further treatment.

Polymerization of NVP in ε-caprolactone

Freshly distilled NVP was dispersed in ε-caprolactone monomer at 80°C with the assigned weight ratio, and a homogeneous transparent mixture was observed. Then 0.2 wt % AIBN was added and kept stirring for 24 h at 80°C for the polymerization of NVP. Later, a clear and viscous mixture was obtained.

Preparation of PCL/PVP blends

Certain amount of the obtained PVP/CL mixture was kept under vacuum at 100°C for 20 min to remove residual NVP monomer and residual traces of the water. After this, 0.02 wt % ethylene glycol was added and stirring for 30 min. Stirring was performed then 0.2 wt % $Sn(Oct)_2$ was added, the mixture was kept stirred for 24 h at 180°C for the polymerization of ε-caprolactone. The blends obtained were denoted as V5 (PVP 5 wt %), V10 (PVP 10 wt %), V15 (PVP 15 wt %), V20 (PVP 20 wt %), V25 (PVP 25 wt %), V35 (PVP 35 wt %), V45 (PVP 45 wt %).

Measurements

FTIR spectroscopy was carried out with a Nicolet AVATAR 360FTIR spectrometer in the range of 4000 to 500 cm^{-1}, with a resolution of 2 cm^{-1}. The Waters-991 model GPC was used to evaluate the weight average molecular weight (M_w) and the polydispersity (M_w/M_n), and the molecular weights were calibrated with polystyrene standards. The M_w of the PCL in the PCL/PVP blends was over 6.0×10^4 g mol^{-1}, and the polydispersity (M_w/M_n) of it was just 1.38–1.5. The M_w of the PVP was 1.2×10^4 g mol^{-1}, and the polydispersity was 1.4–1.6. Nuclear magnetic resonance (NMR) was recorded on a Bruker Avance DMX500 spectrometer in $CDCl_3$ with tetramethylsilane as internal standard. The characteristic signals around 4 ppm due to the proton of the last —CH_2— group next to —COO— group in PCL segment and 3.2 ppm of —CH— group in main chain of PVP in ^{1}H NMR spectrum were clearly observed. The ratio of PVP and PCL in blends was confirmed via comparing the square of above protons. The results were shown in brackets next to corresponding blends as follows: V5(95 : 4.87), V10(90 : 9.84), V15(85 : 13.77), V20(80 : 17.03), V25(75 : 23.81), V30(70 : 27.25), V35(65 : 32.93), V40(60 : 36.75).

SEM (JEOL JSM 5600 LV) analysis of fractured sections of blends was performed to gain insight into the morphology. DSC measurements were carried out on an NETZSCH DSC 200 PC calibrated by In standards. All the samples were firstly heated to the maximum annealing temperature, $T_{max} = 200$°C, for 3 min to eliminate the PCL crystalline residues formed during the preparation procedure. For nonisothermal crystallization experiments, the series of samples after eliminating heat history were cooled to −50°C at 10°C min^{-1} and then heated to 200°C by a scan rate of 10°C min^{-1}.

The contact angles (Dataphysics OCA40) of the upper surface of 20×20 mm^2 samples were measured at room temperature by the sessile drop method, using a 5 μL water droplet in a telescopic goniometer. The telescope had a magnification power of 7× and was equipped with a protractor of 0.3° graduation.

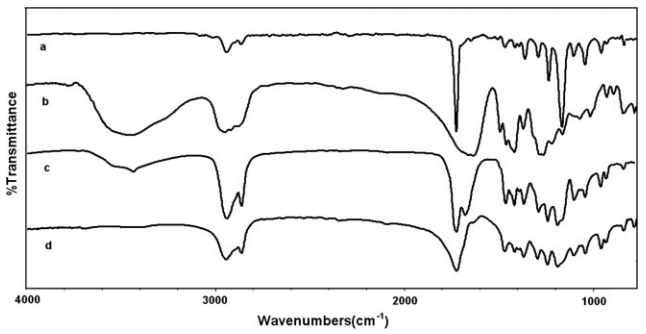

Figure 1 The FTIR spectra of (a) PCL, (b) PVP, (c) V20, and (d) the vacuum dried V20 after dissolved in water.

RESULTS AND DISCUSSION

The PCL/PVP blends were prepared via successive *in situ* polymerization of the *N*-vinyl-2-pyrrolidone (free radical polymerization) and ε-caprolactone monomers (ring-opening polymerization) in one reactor. During the *in situ* compounding process, the free radical polymerization of *N*-vinyl-2-pyrrolidone was firstly performed using ε-caprolactone as solvent, and subsequently, the ring-opening of ε-caprolactone was initiated in the presence of *in situ* prepared PVP component. The structures of blends were investigated by FTIR, ^{1}H NMR, GPC, SEM, and CA measurements.

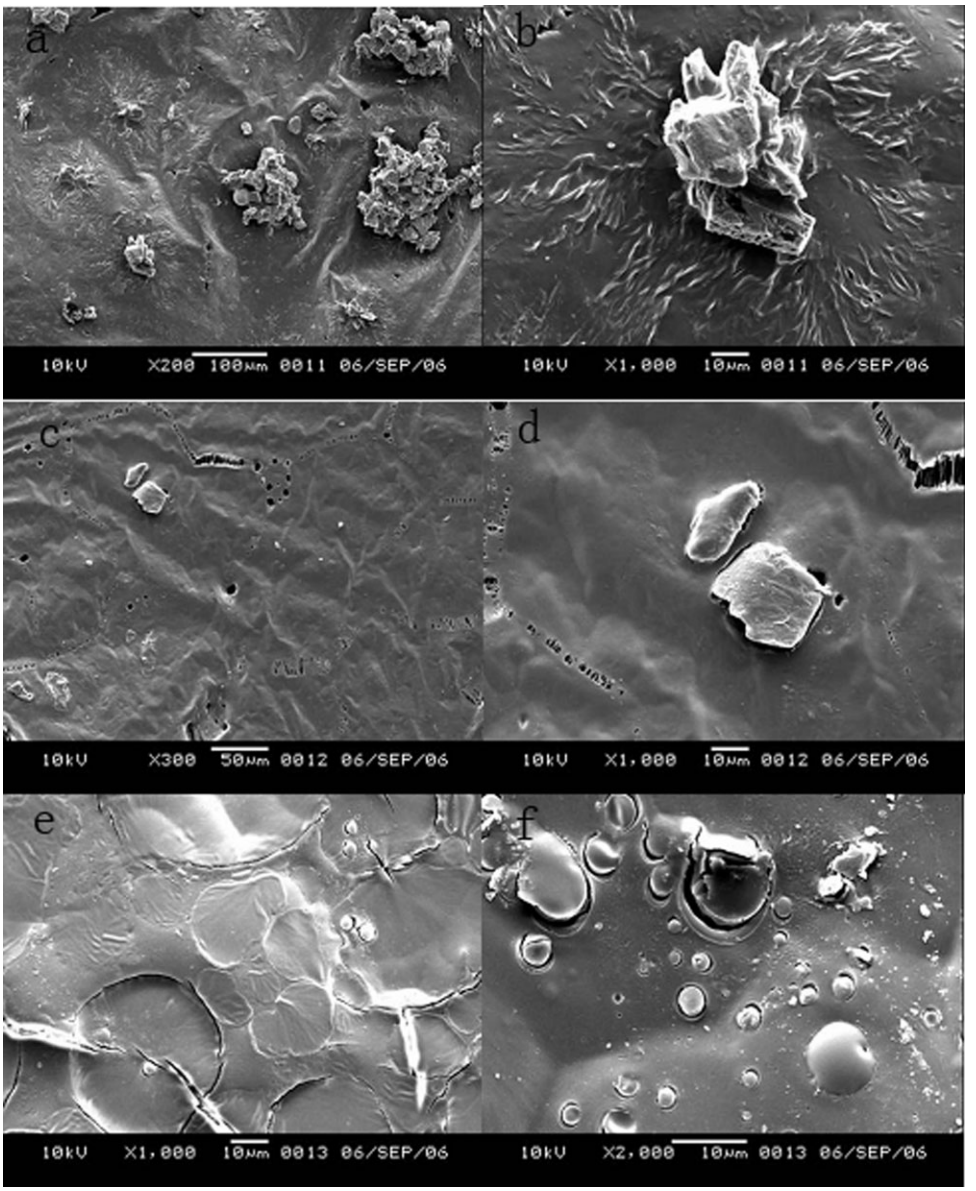

Figure 2 SEM of PCL/PVP prepared by solution-blending: (a, b) V5, (c, d) V10, (e, f) V15.

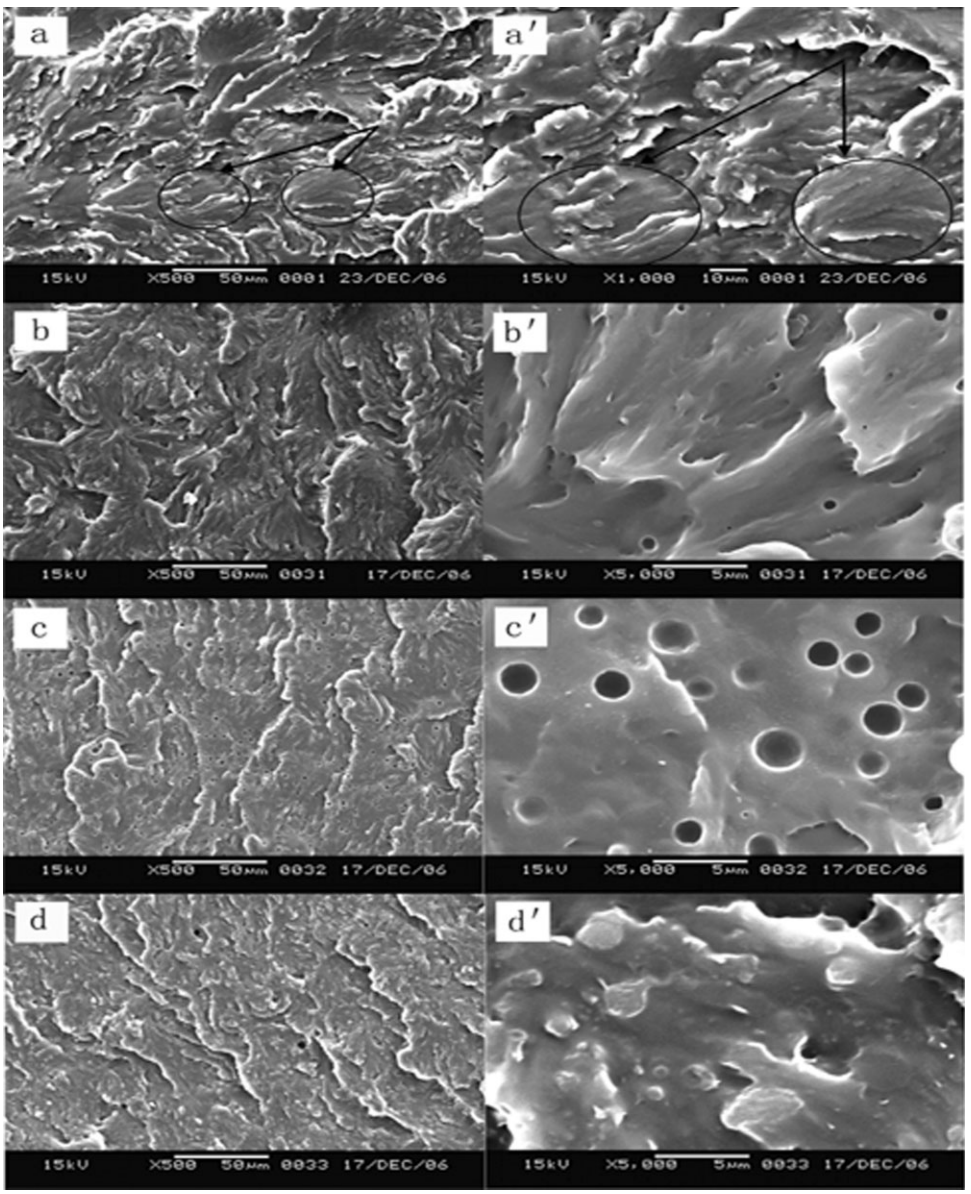

Figure 3 SEM of PCL and etched surface of PCL/PVP blends by water: (a, a′) PCL, (b, b′) V5, (c, c′) V10, (d, d′) V15.

Structure analysis

FTIR spectra of PCL/PVP blends are analyzed and compared with those of pure PCL and pure PVP. The absorption bands at 2950–2860 cm^{-1}, corresponding to the symmetrical and antisymmetrical CH_3 and CH_2 stretching, were present in both the PCL and PVP macromonomer spectra [Fig. 1(a,b)]. As shown in Figure 1(a–c), the broad band at about 3382 cm^{-1}, arising from the symmetric and antisymmetric O—H stretching mode, appeared except in the PCL macromonomer [Fig. 1(a)]. That attributed to lipophilic property of PCL and hydrophilic property of PVP. The intensities of the absorption bands will increase with the hydrophilic property of materials. FTIR spectrum of PCL/PVP blend with 20 wt % PVP [Fig. 1(c)] showed that the intensities of the absorption bands were lower than PVP. The band at 1681 cm^{-1} was assigned to carbonyl group of PVP, whereas the band located at 1727 cm^{-1} corresponded to the $\overset{O}{\overset{\|}{C}}$ stretching vibration of the carboxyl group in PCL chain. These bands were present in blend spectrum at Figure 1(c) which indicated. PVP component is expected to dissolve completely during the treatment of blends in water. Then the insoluble component was collected and vacuum dried at 80°C for 24 h, and analyzed again by FTIR [Fig. 1(d)]. The corresponding spectrum showed that the absorption bands in the 3600 to 3200 cm^{-1} vanished and the band at 1681 cm^{-1} was not detected any more, which confirmed PVP dissolution.

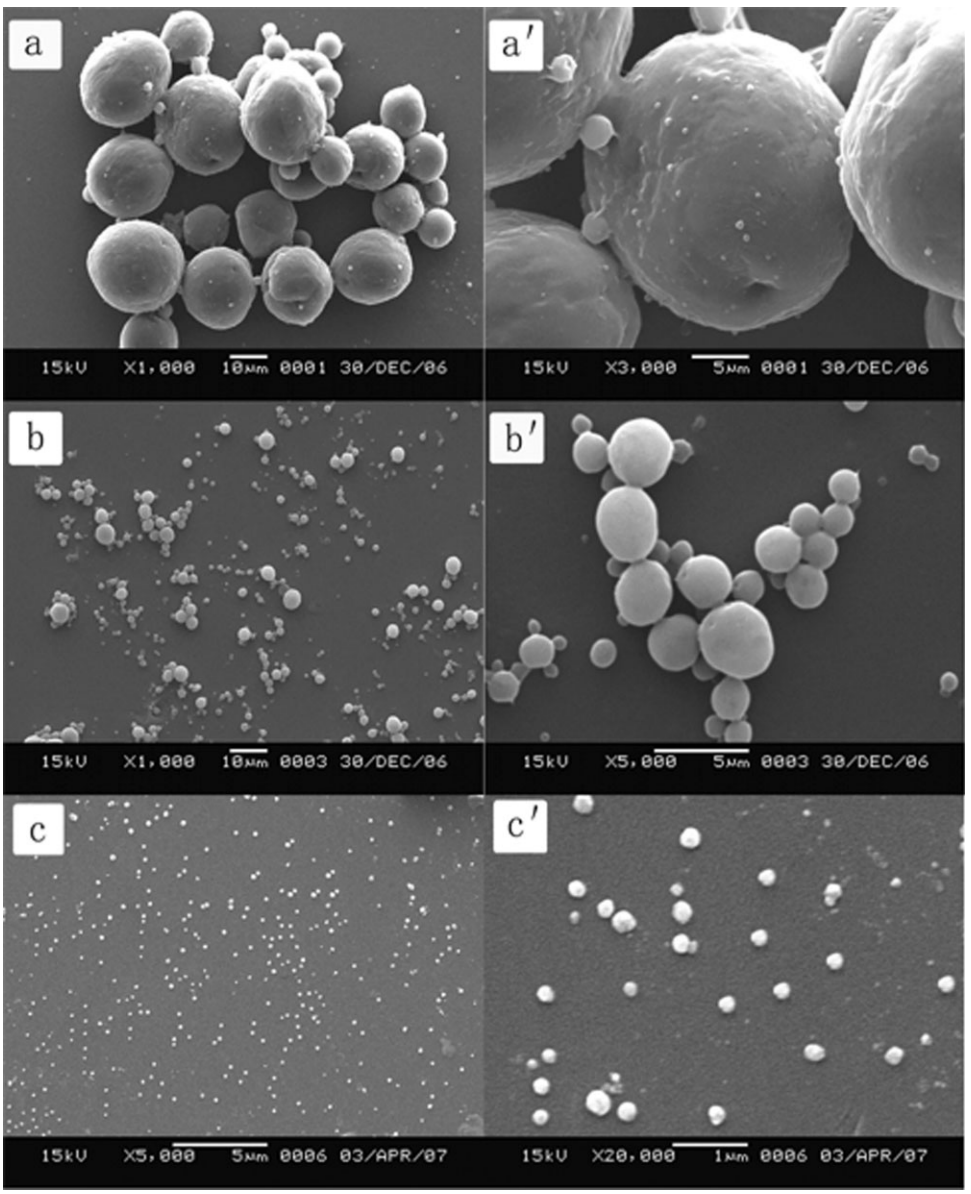

Figure 4 SEM images of the PCL microspheres prepared after the dissolution of the PVP phase from PCL/PVP blends: (a, a′) V25, (b, b′) V35, (c, c′) V45.

Morphology analysis

The SEM analysis was performed to investigate the morphology of PCL/PVP blends with different weight ratios of PVP and blends with same ratios prepared by different methods. The SEM images are presented in Figures 2–4. Figure 2 showed the morphology of solution-blended PCL/PVP, and Figure 3 showed the morphology of successive *in situ* polymerization blends. In Figure 2, when the PVP content was 5% [Fig. 2(a,b)], PVP was the disperse phase acting like raised tuberous thing with pleating PCL around. When the content of PVP added to 10% in blends [Fig. 2(c,d)], tuberous and crevices were both shown in images. When the content of PVP added to 15% in blends [Fig. 2(e,f)], the disperse phase as like-spheres existed in PCL bulk with more and small sizes, however there were also clear cracks in the interphase. Two phase structure were also shown in Figure 3(b,b′,c,c′,d,d′), with comparatively uniform disperse phase size compared with blends as same ratio in Figure 2. In conclusion, based on the analysis of morphology in Figures 2 and 3, the images demonstrate that an obvious phase-separation happens in both preparation blends. Then compared with disperse degree of PVP in blends, we can confirm that the preparation method played a dominant role. The later preparation method was useful for PCL and PVP blends. So we focus on successive *in situ* polymerization PCL/PVP blends and detail studying on the morphology of blends with different ratio as following.

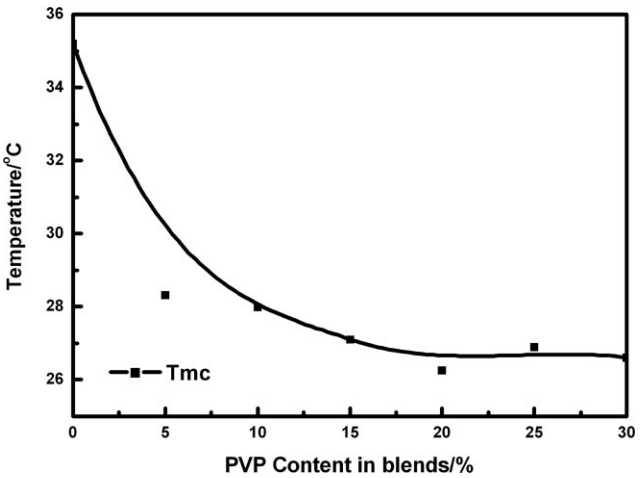

Figure 5 The relationship of Tmc and PVP content in blends.

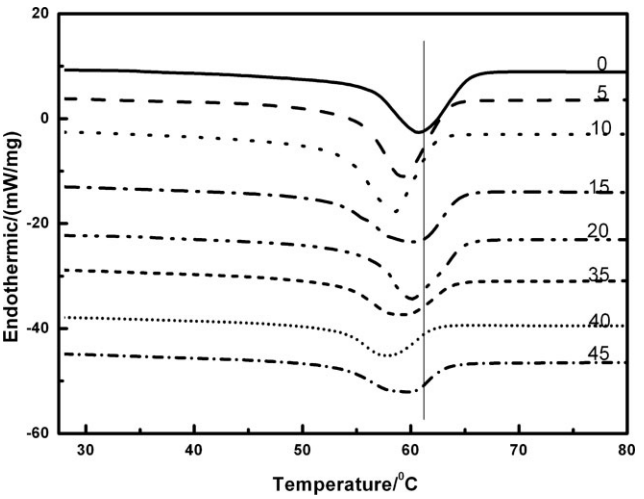

Figure 6 The curves of second heating scan in DSC, the numbers exhibit the PVP feeding ratio of samples.

Firstly, many whole spherulites were showed in morphology of pure PCL [arrow in Fig. 3(a,a′)], they were about 36 μm, corresponding to crystallization of PCL. But the spherulites were hardly observed in the following blends [Fig. 3(b–d′)]. The reason was that the PCL crystallization was restricted with the presence of PVP. It was confirmed clearly by DSC. Figure 5 showed that the Tmc of blends were decreased with the PVP content increase, especially from 0 to 10%. Figure 6 and Table I showed that the heat curves in second heating scan as well as the corresponding data of all samples. The values of ΔH_m can be compared with 139.5 J/g, corresponding to a 100% crystalline PCL.[37] Following this, the crystallinity of samples can be easily estimated. The results were also given in Table I.

Secondly, when the fracture surface of blends was etched with water, the PVP was removed and the two phases were observed, and the morphologies showed great differences with increase of PVP content. In Figure 3(b–d′), the black holes corresponded to the extracted PVP phase. The holes increased in number with increasing PVP content from 5 to 10 wt %. When PVP content was 15 wt %, the holes seemed to disappear, it was similar when PVP content was further increased to 20 wt %. The change in morphology was attributed to the phase inversion. With further increasing the PVP content, the etched surface of blends collapsed. The samples were prepared by following steps. The blends with high content of PVP were shattered and then immersed into ethanol for 2 h to allow the dissolving of the PVP. The PCL were separated by centrifugation. And the morphology of the PCL will be described in detail in the next paragraph.

When the content of PVP exceeded 20 wt %, SEM images of etched blend samples showed microspheres with a decreasing diameter with increasing PVP content [Fig 4]. As PVP content was 25 wt %, phase inversion completed, that is to say, the phase morphology of the blends changed from PVP dispersed/PCL matrix to PCL dispersed/PVP matrix system. The PCL phase was spherical, completely isolated by PVP matrix, and the PVP component existed mainly in the gap of PCL spheres as the continuous phase in the blends. By etching the PVP matrix with solvent, the PCL spheres were easily obtained. For V25 system, the diameter of PCL microsphere size was distributed in 2–26 μm and many little spheres adhered to the big PCL spheres. The size was really poorly. On the other hand, for V35 system, the PCL spheres became much smaller (2.7 μm in diameter) and more uniform. With a further increasing of PVP content to 45 wt %, the size of the PCL spheres decreased dramatically and the size was about 0.25 μm averagely. The above series

TABLE I
Parameters of Heating Scan for Various Samples

Samples	T_m (°C)	ΔH_m (J/g)	Crystallinity[a] (%)	Samples	T_m (°C)	ΔH_m (J/g)	Crystallinity[a] (%)
PCL	61.09	81.96	58.75	V20	60.16	52.50	47.04
V5	59.28	62.93	47.49	V35	59.78	39.89	43.99
V10	58.51	62.59	49.85	V40	58.28	31.08	37.13
V15	60.36	55.91	47.15	V45	59.54	29.03	37.84

[a] Using 139.5 J/g as the heat of fusion for a 100% crystalline material.

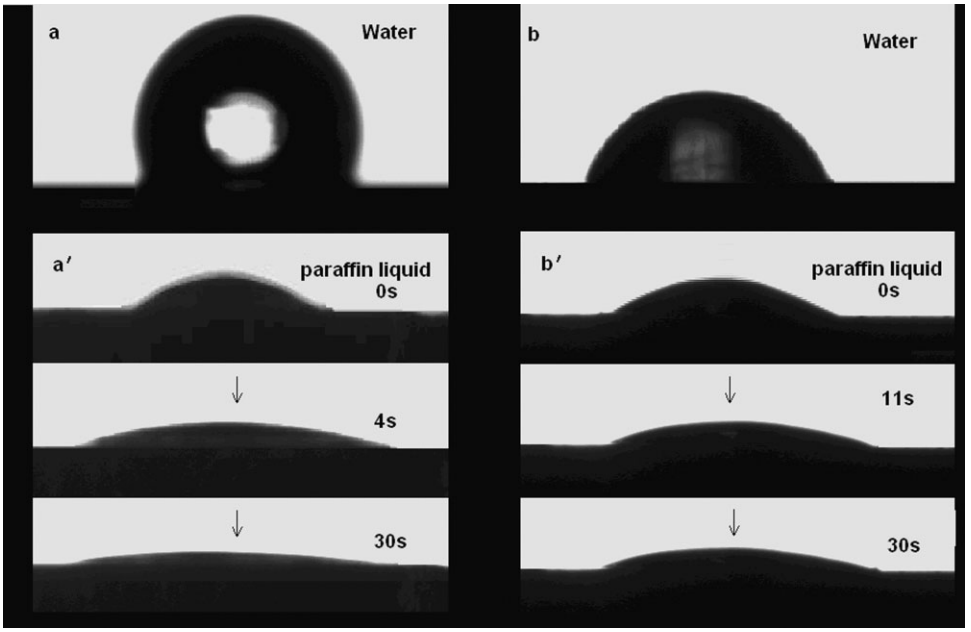

Figure 7 The shape of a water and oil droplet on the surface of (a, a′) PCL and (b, b′) V20 in different time.

of experiments demonstrated that PCL microspheres with controllable size could be conveniently prepared by varying the PVP content.

Contact angle measurement

Contact angle measurements are widely used as a simple, sensitive technique for quantifying the hydrophilic/hydrophobic property of a surface.[38] Therefore, aqueous static and dynamic contact angle measurements were carried out to investigate the change of contact angle in the presence of PVP. Figure 7 showed the shape of a water and paraffin liquid droplet on the surface of PCL and of V20 blend. When water was dripped on bare PCL, it was oncoming spheroid ($\theta = 107°$). However, When water was dripped on the surface of V20, it was just hemispheroidal ($\theta = 72.9°$). Then the shapes of oil (paraffin liquid) on the same samples were also observed. It was found that the oil droplet flatted rapidly in both samples. The detailed difference of samples can be revealed in the value of contact angle shown in Table II.

TABLE II
Contact Angle of Solvent on the Surface of PCL and V20

Solvent	Contact angle (°)			
	Time (s)	PCL	Time (s)	V20
Water	0	107	0	72.9
Paraffin liquid	0	25.1	0	34.8
Paraffin liquid	4	13.5	11	20.3
Paraffin liquid	30	8.6	30	17.3

For further investigating the hydrophilic property, Figure 8 showed the dynamic water contact angle of PCL and different blends. PCL was hydrophobic with a water contact angle of 112°–105°; error was lower than 1.3%. On the opposite, the PCL/PVP blends were hydrophilic, and the contact angles decreasing dramatically in the first several seconds and retaining at the lower angle for long time. Another characteristic of blends was confirmed that the ending water contact angle decreased with increase of PVP content.V5 system was ended at 67°, and V10 was at 63°, V15–V20 was at 57°–55°, then V25 system just at 40°. That were also corresponding to the foregoing SEM result. It was thus confirmed

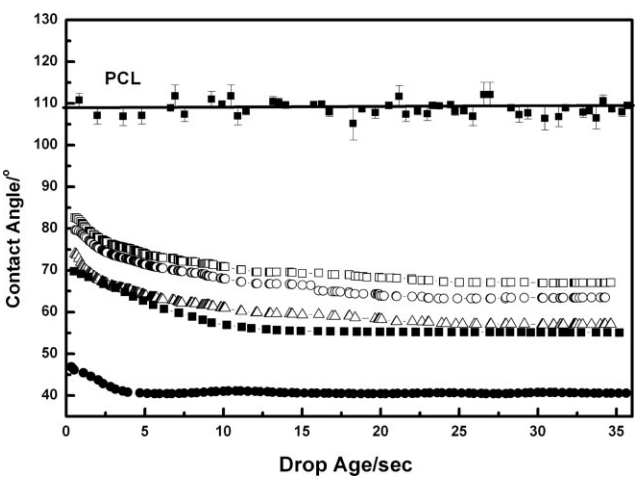

Figure 8 Relationship between the drop age and the water contact angles of PCL and V5 (□), V10 (○), V15 (△), V20 (■), V25 (●).

that PVP has a profound effect on hydrophilic properties of the blends. The surfaces with contact angles in the range of 54°–61° have been reported to be optimal for cell adhesion which is greatly favored by hydrophilic surfaces with intermediate wettability.[38] The results showed that PCL/PVP blends, especial V15–V20, can become new biodegradable material for biomedical applications.

CONCLUSIONS

In conclusion, we demonstrated a facile approach to prepare PCL/PVP blends by successive *in situ* polymerization of CL : NVP with different ratio. The process consisted of firstly radical polymerization of *N*-vinyl-2-pyrrolidone in CL and secondly *in situ* anionic ring opening polymerization of CL in the presence of *in situ* prepared PVP component. Compared with the solution-blending, this preparation method is useful to morphology development as more uniformity disperse phase and comparatively steady interphase. The GPC confirmed that the M_w of the PCL in this system exceeded 6.0×10^4 g mol^{-1} as well as low polydispersity (M_w/M_n), and the M_w of the PVP neared 1.2×10^4 g mol^{-1}. The morphology of the blends showed island phase morphology with the PVP dispersed/PCL matrix characteristics when the content of PVP was lower than 15 wt % (V15). Then the phase morphology showed PCL spheres dispersed/PVP matrix characteristics when the PVP content was 25 wt % (V25) or more. The phase inversion occurred between 15 and 20 wt % PVP. The contact angle associated with the surface property of blends, and it showed that PVP has a prominent effect on the hydrophilic properties of blends. The hydrophilic surface of V15–V20 blend could be optimal for cell adhesion, which was an evidence for that PCL/PVP blends were promising substitute material for drug delivery, cell therapy, and other biomedical applications.

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