

Esterification on Solid Support by Surface-Initiated Ring-Opening Polymerization of ϵ -Caprolactone from Benzylic Hydroxyl-Functionalized Wang Resin Bead

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ABSTRACT: Biodegradable poly(ϵ -caprolactone) (PCL) was formed on benzylic hydroxyl-functionalized Wang resin surface by surface-initiated ring-opening polymerization (SI-ROP). The SI-ROP of ϵ -caprolactone was achieved first by treating Wang resin with Tin(II) 2-ethylhexanoate [Sn(Oct)₂] to form Tin(II) complex, and then followed by polymerization of ϵ -caprolactone in anhydrous toluene at 60°C. Thus, the polymer-grafted Wang resin was characterized by Fourier transform infrared (FTIR) spectroscopy, differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), optical microscopy (OM), and field-emission scanning electron microscopy (FE-SEM). The FTIR spectroscopic analysis of polymer-grafted Wang resin (Wang-g-PCL) reveals the

formation of ester linkage between PCL and hydroxyl-terminated Wang resin. The DSC thermogram shows melting peak corresponding to PCL polymer on Wang resin surface. Thermogravimetric investigation shows increase in PCL content on the Wang resin surface in terms of percentage of weight loss with increase in reaction time. The formation of polymeric layers on the Wang resin surface can be directly visualized from OM and SEM images. © 2008 Wiley Periodicals, Inc. *J Appl Polym Sci* 111: 839–844, 2009

Key words: biodegradable; infrared spectroscopy; poly(ϵ -caprolactone); ring-opening polymerization; Wang resin; scanning electron microscopy

INTRODUCTION

The coating of solid substrates with biocompatible and/or biodegradable polymers has drawn a great deal of attention because of its potential applicability to biomedical areas such as passivation of prosthetic devices and implants, coating for drug-delivery devices, and scaffolds for tissue engineering.^{1–4} For polymeric coating of substrates, the “grafting-from” approach, based on surface-initiated polymerization (SIP), has intensively been studied because of its inherent superiority to over the other conventional techniques such as spin-casting and “grafting-onto” approach, in the aspects of robustness and controllability of density and thickness.^{5–7} In the process of SIP, polymer brushes are grown from initiators bound to surfaces by reacting with monomers in solution. Among various types of polymers, polymeric

films of biocompatible and biodegradable aliphatic polyesters, such as poly(lactic acid) (PLA), poly(ϵ -caprolactone) (PCL), and poly(*p*-dioxanone) (PPDX), were produced by surface-initiated ring-opening polymerization (SI-ROP).^{8–14}

There have been many efforts for polymeric coating of aliphatic polyesters on a variety of solid substrates via SI-ROP.^{8–14} Similar to synthesis in solution or bulk, organometallic catalysts, such as Sn(Oct)₂ and AlEt₃, have generally been employed for SI-ROP of biodegradable aliphatic polyesters from surfaces presenting hydroxyl or amino groups. For example, Yoon et al.⁸ reported the use of Sn(Oct)₂ to produce poly(*p*-dioxanone) (PPDO) brushes on gold and silicon oxide surfaces by ROP of *p*-dioxanone, and Husemann et al.⁹ used diethylaluminum alkoxides prepared from AlEt₃ as a catalyst to grow PCL brushes from gold surfaces presenting hydroxyl groups. Similar reaction conditions have widely been applied to SI-ROP for coating of various aliphatic polyesters, such as PLA,^{8,10} PCL,^{10,11} and PPDX^{11–13} on various types of substrates, such as gold,^{8–11} silicon oxide,^{8,11,12} and nanotubes.¹³

One of the obstacles to the generation of a highly uniform film of aliphatic polyesters via SI-ROP is the high crystallinity of most aliphatic polyesters.^{8,11}

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In the previous studies, SI-ROP of PLLA, a crystalline polymer, and PPDO, a semicrystalline polymer, did not provide smooth polymeric films.^{8,11} Because crystallinity of polymers must be considered in SI-ROP for uniform coating, we focused on amorphous poly(1,5-dioxepan-2-one) (PDXO).¹⁵ PDXO has been known as a highly viscous and amorphous polymer with a glass transition temperature (T_g) of -39°C .¹⁶ PDXO also shows characteristic behaviors such as hydrolytic degradation and bioadsorption, and its main chain is composed of alternating ethylene glycol and β -hydroxypropionic acid.¹⁷

In this study, we formed a polymeric sphere of PCL on a Wang-resin surface by SI-ROP of ϵ -caprolactone with Tin(II) 2-ethylhexanoate as a catalyst and investigated the quality of the sphere, in particular, in the aspect of uniformity. Tin(II) 2-ethylhexanoate is one of the most widely used compounds for initiating the ring-opening polymerization of various lactones and lactides. Tin(II) 2-ethylhexanoate has been approved for surgical and pharmacological applications by the U.S. Food and Drug Administration.

The use of insoluble supports to mediate organic transformations has been developed extensively over the years. The solid phase chemistry is now considered almost routine for the synthesis of certain biological polymers or synthetic polymers with biological activity. Indeed, this is the basis for automated peptide synthesis that is routinely carried out by solid phase synthetic methods based on sequential addition of amino acids to an insoluble crosslinked polymeric support. The use of polymeric solid support (resin beads) for organic synthesis relies on interconnected requirements, preferably, as follows: (i) a crosslinked insoluble but solvent-swallowable polymeric material that is inert to the conditions of synthesis, and (ii) a successful synthetic procedure compatible with the linker and the solid phase. One of the most commonly available resins used is Wang resin, which is based on crosslinked polystyrene onto which 4-hydroxybenzyl alcohol moiety has been attached. One of the common transformations in solid-phase organic synthesis involves the construction of an ester linkage between a solid support and the other monomer. The ester linkage may be achieved, which has good stability to a variety of reaction conditions. Although different strategies generate such an ester linkage on solid support is available, here we report one of the convenient and straightforward method involving ring-opening polymerization of ϵ -caprolactone on hydroxyl-bound Wang resin.

EXPERIMENTAL

Materials

Toluene (from Aldrich) was purified by distillation over sodium. All other solvents and reagents were of analytical grade and used as received. ϵ -Caprolac-

tone was kindly provided by Samyang Company, Korea. Wang resin was supplied by Zeneca in a range of different load (1 to 4 mmol/g of OH functions, range of size 150–300 μm).

Surface-initiated ring-opening polymerization of ϵ -caprolactone

The Wang resin (1 g) was treated with $\text{Sn}(\text{Oct})_2$ (10 μmol) in 20 mL of dried toluene at 60°C for 1 h. The monomer, ϵ -caprolactone (10 mmol), was then added by syringe and the mixture was heated at 60°C . After the polymerization, the heterogeneous reaction mixture was intensively washed with chloroform, ethanol, THF, and water, and then sonicated in chloroform for 30 min, filtered (whatman 1) to remove any physisorbed homopolymer. Washing was done until no polymer was found in the filtrate. Finally, the Wang-g-PCL resin was dried under reduced pressure at room temperature for 24 h under flow of nitrogen.

Instrumentation

IR spectra were recorded using FTIR spectrophotometer (Bruker, EQUINOX 55) at a resolution of 4 cm^{-1} with a maximum of 100 scans at a wave numbers ranging from 500 to 4000 cm^{-1} . The thermal parameters of the Wang-g-PCL resin microparticles were measured under nitrogen flow (80 mL/min) by differential scanning calorimetry (DSC) at a heating rate $10^\circ\text{C}/\text{min}$ from 0 to 200°C and thermogravimetric analysis under nitrogen flow (80 mL/min) at a heating rate of $20^\circ\text{C}/\text{min}$ from ambient to 800°C using M/s TA Instruments. The surface morphology of the Wang-g-PCL resin microparticles was studied using optical microscopy (OM BX51 TF) and field-emission scanning electron microscope (FE-SEM) (SEM, Hitachi S-2250N, Japan).

RESULTS AND DISCUSSION

PCL was grafted on to the Wang resin surface, first by treating the Wang resin with Tin(II) 2-ethylhexanoate in toluene at 60°C and then the ϵ -caprolactone was polymerized on to Wang resin in the presence of Wang-Sn(Oct) complex by co-ordination insertion mechanism as shown in Figure 1. In the co-ordination-insertion mechanism, the initiating species is a tin alkoxide formed before the polymerization. Therefore, the initiator can be attached to the surface that presents a hydroxyl group by the Oct-OR exchange reaction and be transferred to the propagating polymer chain. To remove the physically adsorbed polymers, the resulting mixture was intensively washed with chloroform, ethanol, THF, and water, sonicated in chloroform for 30 min, and then

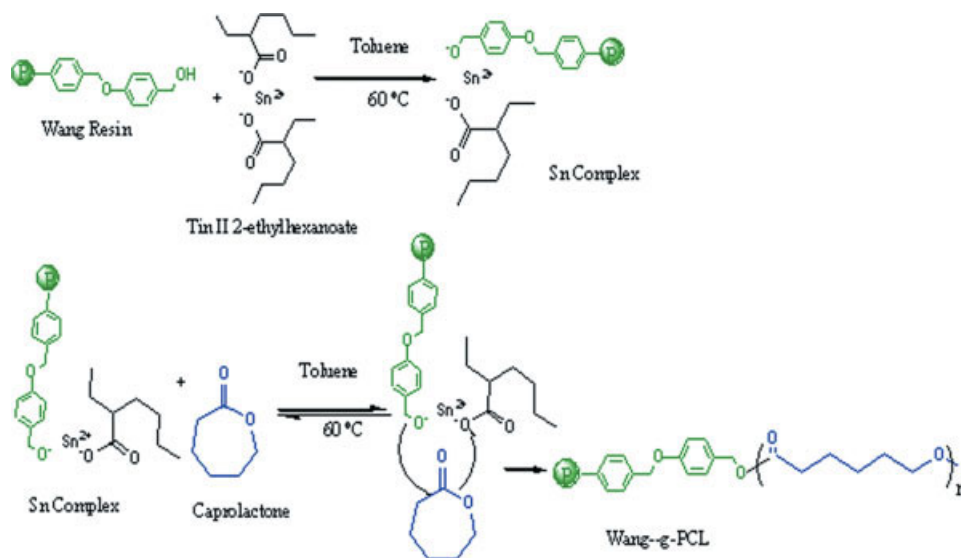


Figure 1 Schematic representation for surface-initiated ring-opening polymerization of ϵ -caprolactone on Wang resin surface. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

dried under a flow of nitrogen. The Wang resin-grafted-PCL thus formed was characterized by FTIR, DSC, TGA, OM, and SEM.

The attachment of PCL on the Wang resin surface is observed by the reduction in intensity of broad hydroxyl stretch at 3426 cm^{-1} (Fig. 2) accompanied by the appearance of an intense signal at 1726 cm^{-1} for the ester link between Wang resin and PCL. The FTIR (Fig. 2) spectrum of the Wang resin showed characteristic bands at 3426 cm^{-1} [Fig. 2(a)], which attributed to the primary O—H stretching of hydroxyl functional group. Figure 2(b) shows the IR spectrum of the Wang-g-PCL resin. The characteristic bands at 2916 cm^{-1} due to the C—H stretching, at 1726 cm^{-1} due to the C=O stretching of ester, at 1162 cm^{-1} due to the C—O—C stretching of ether indicated the presence of PCL layer on the Wang

resin surface. Specially, the appearance of C=O ester stretching band at 1726 cm^{-1} demonstrates the formation of PCL grafting on the Wang bead surface. Since, after the polymerization, the Wang resin beads were thoroughly washed until no polymer was found in the filtrate, it would be reasonable to conclude that the polymer layer observed on Wang resin surface is corresponding to the PCL covalently attached to the Wang resin.

DSC thermograms of Wang-g-PCL (a) and Wang resins (b) are shown in Figure 3. The Wang resin, basically a benzylic hydroxyl-functionalized polystyrene crosslinked with divinyl benzene shows a thermal transition at 107.6°C , which corresponds to polystyrene glass transition, whereas the PCL-grafted-Wang resin has a transition at 45.9°C corresponding to the melting of PCL. Since the Wang

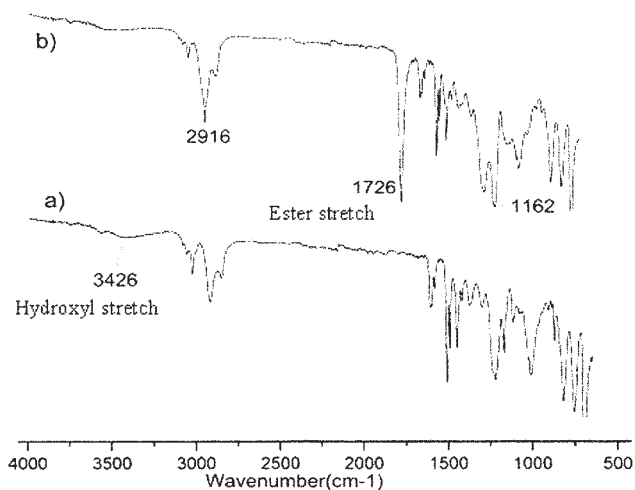


Figure 2 FTIR spectra of (a) Wang resin and (b) Wang-g-PCL resin.

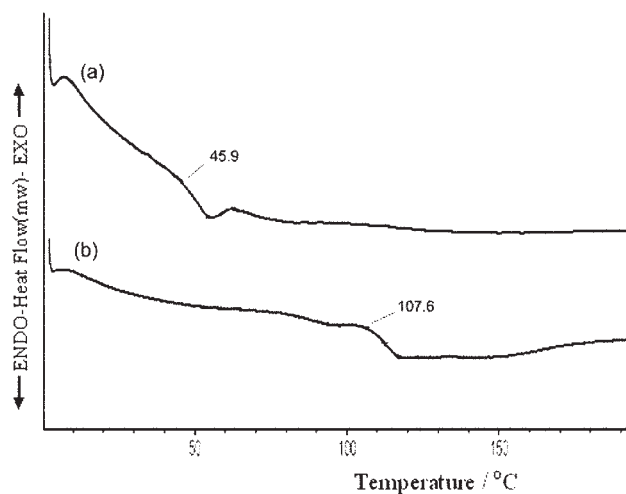


Figure 3 DSC thermograms of (a) Wang resin-g-PCL and (b) Wang resin.

resin beads are thoroughly washed to remove any physisorbed homopolymers, we can draw the conclusion that the melting transition observed at 45.9°C in the curve of Wang-g-PCL is corresponding to the melting of the PCL covalently attached to Wang resin surface.

The TGA thermograms of Wang resin and Wang resin grafted with PCL were obtained by heating the samples from ambient to 800°C at a heating rate of 20°C/min under nitrogen atmosphere and shown in Figure 4. From the Figure 4(b), it is clear that the Wang resin undergoes single-stage degradation between 330 and 480°C with weight loss of 92.75%, whereas the Wang-g-PCL [Fig. 4(a)] undergoes degradation in two stages: the first stage is from 250 to 330°C with weight loss of 19.60% and the second stage is from 330 to 480°C with weight loss of 69.49. The first (lower) temperature weight loss (19.60%) corresponds to PCL, whereas the second and higher temperature weight loss (69.49%) corresponds to Wang resin. This low-temperature weight loss of 19.60% between 250 and 330°C clearly indicates the grafting of PCL on to Wang resin. Further, the growth of the polymer around Wang resin beads was monitored by TGA at different stages of the polymerization and the TGA thermograms of Wang-g-PCL at different stages of polymerization; 9, 17, 24, 36 h, and Wang resin are shown in Figure 5. Figure 5 shows that all PCL-grafted samples undergo two-stage thermal degradation; however, the weight loss increases with increase in duration of grafting polymerization and the results are presented in Table I. Table I shows that the Wang resin polymer bead after 9-h grafting process shows 8.31% weight loss, with increase in grafting duration the percentage of

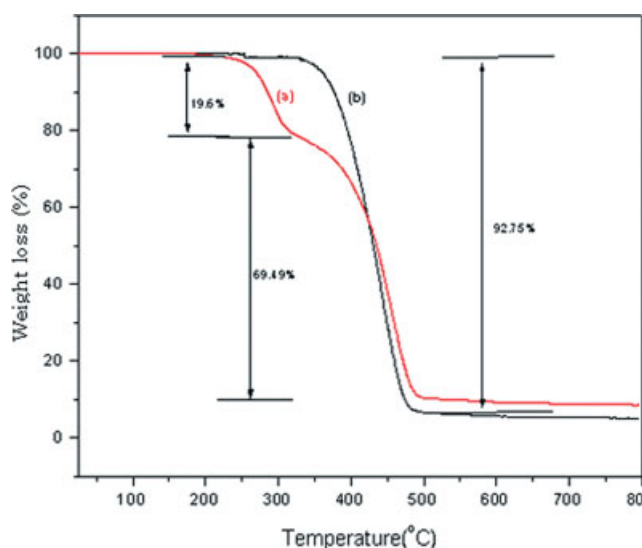


Figure 4 TGA thermograms of (a) Wang resin-g-PCL and (b) Wang resin. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

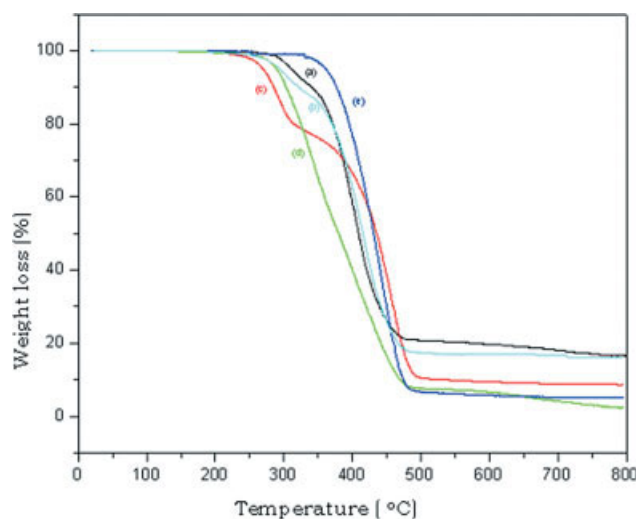


Figure 5 TGA thermograms of Wang resin-g-PCL at different reaction time (a) 9 h, (b) 17 h, (c) 24 h, (d) 36 h, and (e) Wang resin. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

weight loss increased from 8.31 to 21.89% in the temperature range of 250–330°C. Based on the first stage (250–330°C) weight loss, it is reasonable to conclude that the percentage of PCL grafting on the Wang resin surface increased from 8.31 to 21.89%. It is interesting to note that the Wang resin act as the center of the core around which polymer layers are built by grafting process, which means that Wang resin bead behave as a reactor of polymerization.

The surface topography of the PCL-grafted-Wang resin was examined by OM. Figure 6 presents the OM images of the surface topology of the PCL-grafted-Wang resin [Fig. 6(a,b)] and Wang resin bead [Fig. 6(c,d)] at different magnifications. PCL-grafted-Wang resin bead surface [Fig. 6(a,b)] shows a relatively rough surface when compared with Wang resin bead surface [Fig. 6(c,d)]. Wang-g-PCL surface was found to be unevenly covered by the polymer as seen from the OM images. Since, after the polymerization, the Wang resin beads were thoroughly washed until no polymer was found in the filtrate, it would be reasonable to conclude that the polymer layer observed on Wang resin surface is corresponding to the PCL covalently attached to the Wang resin.

TABLE I
TGA Data of Wang-g-PCL

	Percentage of weight loss at	
	250–330°C	330–480°C
Wang resin	No loss	92.39
9 h	8.31	70.73
17 h	10.10	70.73
24 h	19.60	59.76
36 h	21.89	68.88

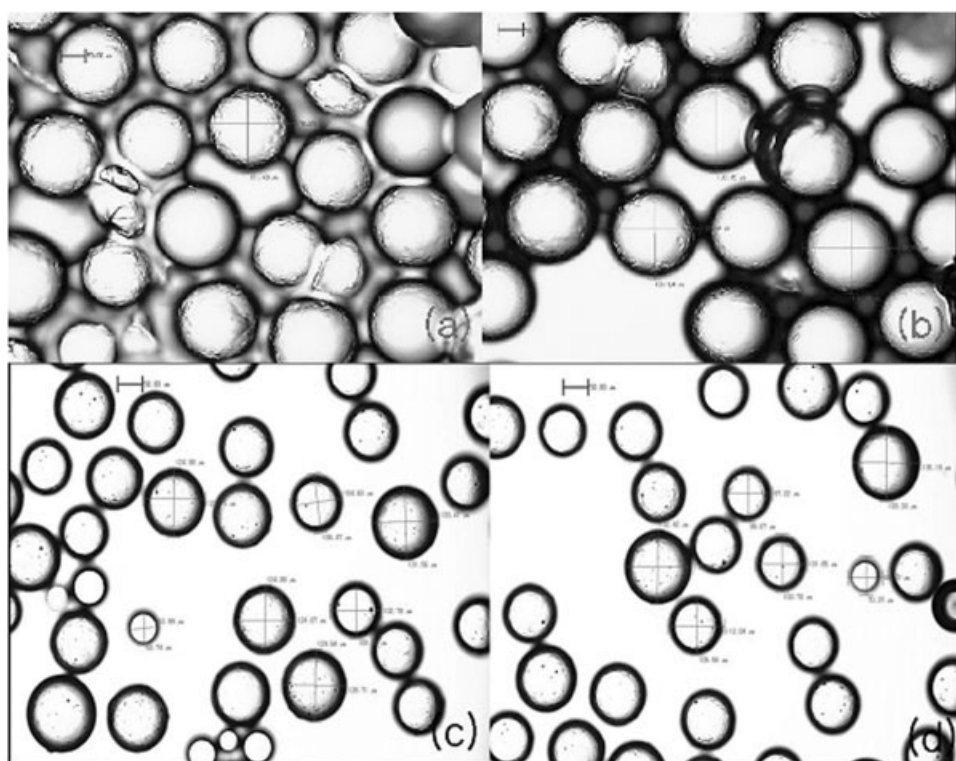


Figure 6 Optical micrographs of Wang-g-PCL (a, b) and Wang resin (c, d) at different magnifications.

Scanning electron microscopy (SEM) was used to directly observe the polymer layer wrapped around the Wang resin surface. SEM images show the spherical nature of the support was retained on

transformation. The SEM images of Wang resin at different magnifications are shown in Figure 7. Figure 7 shows a smooth and spherical surface, whereas the Wang-g-PCL resin bead (Fig. 8) shows

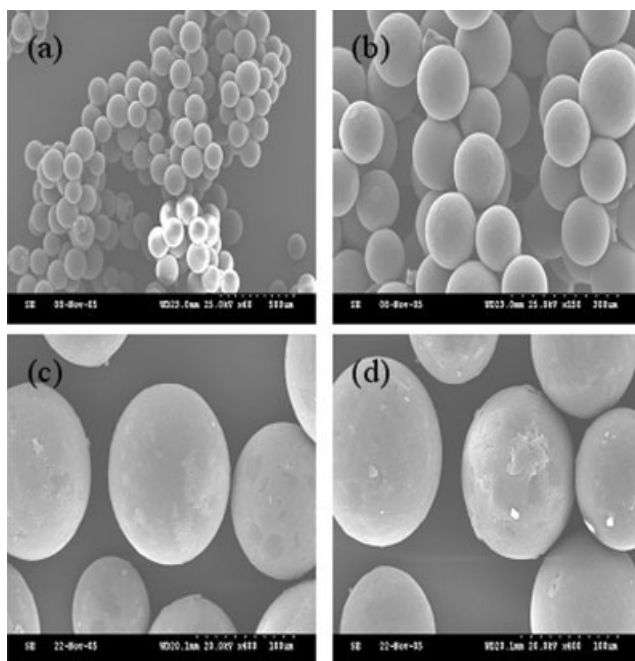


Figure 7 SEM images of Wang resin at different magnifications.

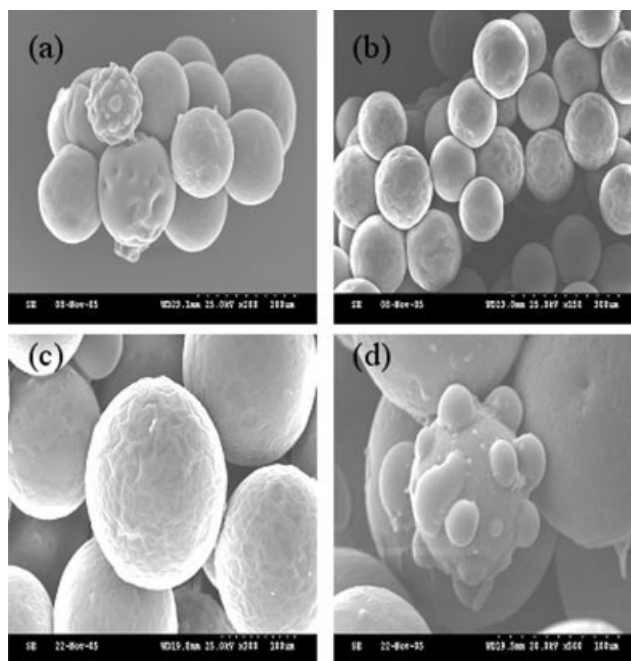


Figure 8 SEM images of Wang-g-PCL at different magnifications.

rough, but spherical surface. It is important to retain the overall morphology of the resin throughout the reactions, the shape of the resin support and particularly the growth of the polymer around beads as the conversion of PCL increases. Moreover the resin support keeps homogeneous in size and distribution all along the polymerization process, which indicates that the bead behave as a reactor to polymerization. This study also revealed that the polymer is covalently attached to the support and growth apart from the solid support.

CONCLUSIONS

We have successfully demonstrated the SI-ROP of ϵ -caprolactone on Wang resin solid substrates catalyzed by $\text{Sn}(\text{Oct})_2$. This surface-grafted Wang resin was characterized by FTIR, DSC, TGA, OM, and FE-SEM. The FTIR spectroscopic analysis reveals the formation of ester linkage between PCL and hydroxyl-terminated Wang resin. The DSC thermogram shows melting peak corresponding to PCL polymer on Wang resin surface. Thermogravimetric investigation shows increase in PCL content on the Wang resin surface with increase in reaction time. The OM and SEM photographs clearly demonstrate the formation of PCL polymer layer on the Wang resin surface without altering the spherical nature of Wang resin bead. It is a step toward development of a coating technique where biodegradable aliphatic polyester is used as a coating material. In addition to the coating, the fabrication of solid substrates with biodegradable polymer will be important in studying the cell bio-

logy on the surface, considering a growing interest in tissue engineering.

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