

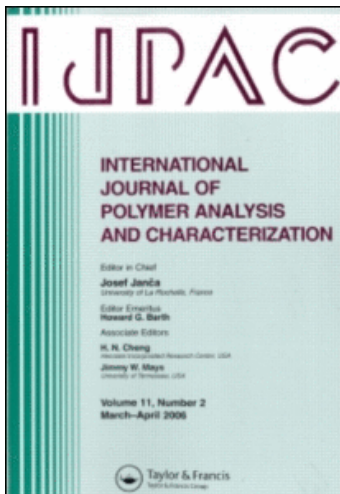
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Preparation and Morphology Study of Biodegradable Chitosan/Methoxy Poly(ethylene glycol)-*b*-Poly(ϵ -caprolactone) Nanocomposite Films

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Abstract: Nanocomposite chitosan-based films containing nanoparticles of methoxy poly(ethylene glycol)-*b*-poly(ϵ -caprolactone) (MPEG-*b*-PCL) diblock copolymer were prepared by forming nanoparticles in chitosan solution before suspension-solution casting. Films with chitosan/MPEG-*b*-PCL composite ratios of 90/10, 80/20, and 70/30 (w/w) were prepared and investigated. From FT-IR analysis, it was found that intermolecular bonds exist between chitosan and MPEG-*b*-PCL. The film surface and cross section of the nanocomposite films was studied by scanning electron microscopy (SEM). The surfaces of the nanocomposite films were found to be rougher than those observed for the chitosan film. Nanoparticles of approximately 200 nm in size with spherical shape were dispersed in the nanocomposite films. In addition, the nanopores were found at the film and cross section surface. The thermal properties of the nanocomposite films were determined by differential scanning calorimetry

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and found to be strongly dependent upon the composite ratios. Film transparency of the nanocomposite films was lower than that obtained for the chitosan film. It was found that the film transparency decreased as the MPEG-*b*-PCL ratios increased.

Keywords: Chitosan films; Diblock copolymer; Methoxy poly(ethylene glycol); Nanocomposite films; Nanoparticles; Poly(ϵ -caprolactone)

INTRODUCTION

Chitosan is a biopolymer that has received great deal of attention in a variety of applications because of its biodegradability and biocompatibility.^[1,2] Because of its excellent film-forming property, chitosan can be used effectively as a film-forming material to carry active ingredients such as minerals or vitamins for food packaging applications^[3,4] and hydrophilic or hydrophobic drugs for drug delivery applications.^[5,6] However, chitosan film does not promote prolonged drug release due to its fast dissolution rate in aqueous media. Hydrophobic drug-loaded poly(lactide-*co*-glycolide) microparticles have been incorporated into chitosan films to improve drug release profiles.^[7] Incorporation of microparticles of biodegradable aliphatic polyesters microphases such as poly(ϵ -caprolactone) and polylactide into chitosan films has been also studied to improve their moisture sensitivity.^[8,9] Methoxy poly(ethylene glycol)-*b*-poly(ϵ -caprolactone) (MPEG-*b*-PCL) diblock copolymer is a biodegradable polymer that has been widely investigated in drug delivery applications.^[10–13] MPEG is hydrophilic block that can improve biocompatibility of PCL hydrophobic block.^[11]

The modified spontaneous emulsification-solvent diffusion method (modified-SESD method) for nanoparticle preparation was proposed first by Murakami et al.^[14] Poly(D,L-lactide-*co*-glycolide) was dissolved in volatile water-miscible organic solvents, acetone, and ethanol instead of acetone and dichloromethane, which were used in the original SESD method.^[15] Higher energy apparatus, such as a homogenizer or a sonicator (usually applied in larger scale preparation of polymer nanoparticles), was not used for this technique.

In this article, nanocomposite MPEG-*b*-PCL nanoparticles dispersed in chitosan film were prepared and characterized. The MPEG-*b*-PCL nanoparticles were prepared in chitosan solution by using a modified SESD method before film casting. The nanocomposite films were analyzed by FT-IR, SEM DSC, and UV-vis spectroscopic methods to determine the morphology, thermal properties, and film transparency, respectively.

EXPERIMENTAL SECTION

Materials

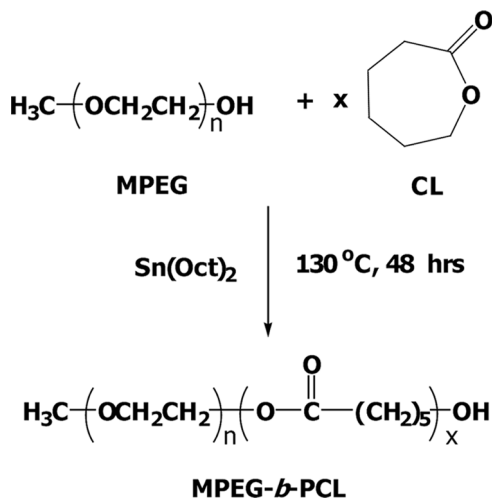
Chitosan (90% deacetylation and molecular weight of 80 KDa) was purchased from Seafresh Chitosan Lab Co., Ltd. (Thailand) and used without further purification. Methoxy poly(ethylene glycol) (MPEG) with a molecular weight of 5,000 g/mol (Fluka, Germany) was dried at 120°C under vacuum for 4 h before use. The ϵ -caprolactone (CL) monomer (99%, Acro, USA) was purified by drying with CaH₂ followed by distillation under reduced pressure before storage over molecular sieves in a refrigerator. Stannous octoate (Sn(Oct)₂, 95%, Sigma, USA), acetic acid (99.7%, Merck, Germany), and Tween-80 (Labchem, Australia) were used as received.

Synthesis of MPEG-*b*-PCL

MPEG-*b*-PCL was synthesized by ring-opening polymerization of CL monomer in bulk at 130°C for 48 h under nitrogen atmosphere. MPEG:CL feed mole ratio of 1:526 was used. Sn(Oct)₂ and MPEG were used as the initiating system. Sn(Oct)₂ concentration of 0.04 mol% was used. The polymerization reaction is illustrated in Scheme 1. The product MPEG-*b*-PCL was purified by dissolving it in chloroform before precipitation in cool *n*-hexane, and then drying it to constant weight under vacuum at room temperature. With to this procedure, purified MPEG-*b*-PCL was obtained with approximately 95% yield.

Characterization of MPEG-*b*-PCL

The structure of MPEG and the obtained MPEG-PCL were studied by Fourier transform-infrared (FT-IR) spectroscopy using a Perkin-Elmer Spectrum GX FTIR spectrophotometer with air as the reference. The resolution of 4 cm⁻¹ and 32 scans were used in this work. Chemical composition of the MPEG-*b*-PCL was determined by ¹H-nuclear magnetic resonance (NMR) spectrometry using a Bruker Advanced DPX 300 ¹H-NMR spectrometer. CDCl₃ was used as a solvent at room temperature, and tetramethylsilane was used as the internal standard. The number-average molecular weight (M_n) and molecular weight distribution (MWD) were determined by gel permeation chromatography (GPC) using a Waters 717 plus Autosampler GPC equipped with a Ultrastyrage[®] column operating at 30°C and employing a refractive index detector. Tetrahydrofuran was used as the solvent at a flow rate of 1 mL/min. The thermal properties of the polymers were characterized by non-isothermal differential scanning calorimetry (DSC) using a Perkin-Elmer Pyris Diamond DSC.



Scheme 1. Polymerization reaction of MPEG-*b*-PCL.

For DSC, approximately 10 mg of the sample were placed in a sealed aluminum pan and heated at the rate of 10°C/min under helium flow to measure the melting temperature (T_m) and the heat of melting (ΔH_m).

Preparation of Nanocomposite Films

MPEG-*b*-PCL nanoparticles were prepared by the modified SESD method in chitosan solution using Tween-80 as a surfactant. The chitosan solution was prepared using 1% (v/v) acetic acid aqueous solution as the solvent. The preparation of nanocomposite film was typically undertaken as follows. MPEG-*b*-PCL was dissolved in 2 mL acetone/ethanol (4/1

Table 1. Composition of nanocomposite films

Chitosan/diblock copolymer (w/w)	Chitosan ^a (mg)	Diblock copolymer ^b (mg)
100/0	200	–
90/10	180	20
80/20	160	40
70/30	140	60

^aamount of chitosan in 20 mL 1% (v/v) acetic acid solution.

^bamount of diblock copolymer in 2 mL acetone/ethanol (4/1 v/v) mixture solvents.

[v/v]). The MPEG-*b*-PCL solution was then added drop-wise into 20 mL chitosan solution containing 1% (w/v) Tween-80. This mixture was stirred at 600 rpm. The chitosan/MPEG-*b*-PCL composite was prepared, and its composite ratio is summarized in Table I. The organic solvent was removed in a fume hood over a 5 h period. The MPEG-*b*-PCL nanoparticles suspended in chitosan solution was obtained. Then, the film casting was done on a Petri dish and subsequently dried at 30°C for 72 h. The prepared film was kept under vacuum at room temperature for a week before characterization.

Characterization of Chitosan and Nanocomposite Films

FT-IR spectroscopy was used to characterize the functional groups of both chitosan and MPEG-*b*-PCL in the nanocomposite films. The FT-IR spectra of the films were obtained with a resolution of 4 cm⁻¹ and 32 scans. The film surface and cross section were studied by scanning electron microscopy (SEM) using a JEOL JSM-6460LV SEM. The film cross section was obtained after cutting the film with paper scissors. Before SEM measurement, the films were sputter-coated with gold to enhance the surface conductivity. The thermal properties were measured by the DSC technique as described above. The film transparency was determined by UV-vis spectroscopy using a Perkin-Elmer Lambda 25 UV-visible spectrophotometer at 660 nm. This method was reported by Rhim et al.^[4]

RESULTS AND DISCUSSION

Characterization of MPEG-*b*-PCL

The chemical composition of MPEG-*b*-PCL was determined from the ¹H-NMR spectrum by calculating the ratio of the integral peak areas corresponding to the ethylene oxide (EO, repeating units of MPEG) methylene protons at $\delta = 3.6\text{--}3.7$ ppm and the CL ϵ -methylene protons at $\delta = 4.0\text{--}4.2$ ppm. The ¹H-NMR spectrum of MPEG-*b*-PCL is shown in Figure 1. From the peak area integrations of the peaks a and b in Figure 1, the copolymer composition can be determined as EO:CL = 18:82 (mol%) corresponding to the MPEG:CL mole ratio of 1:502. As could be expected, this copolymer composition is similar to the MPEG:CL feed mole ratio (1:526). Therefore, the synthesized reaction was taken to near-quantitative conversion.

The M_n and MWD of MPEG-*b*-PCL obtained from GPC were 62,300 g/mol and 1.8, respectively. The M_n obtained from GPC was very similar to that obtained from the feed ratio (65,000 g/mol).

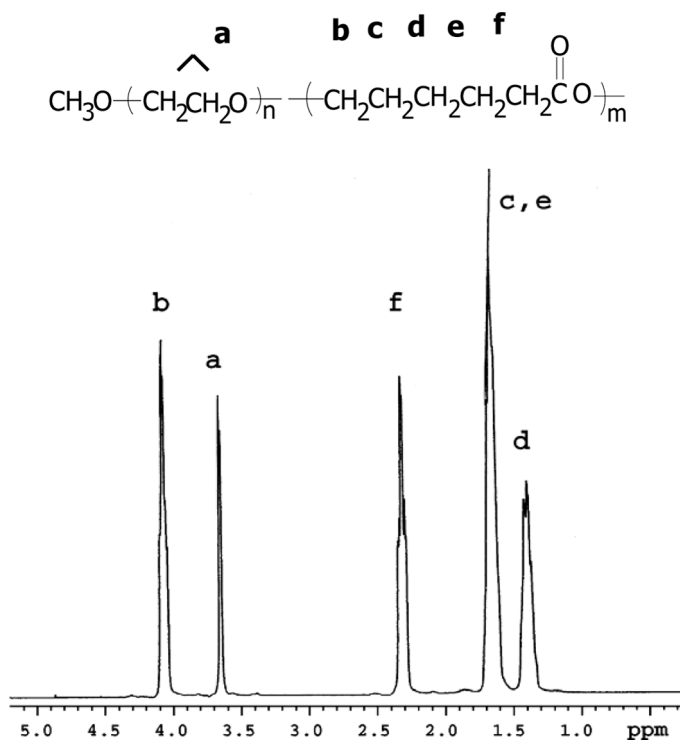


Figure 1. ¹H-NMR spectrum of MPEG-*b*-PCL.

FT-IR Analysis of Nanocomposite Films

The intermolecular bonds in chitosan and PEG or polylactide have been studied by FT-IR.^[16–17] The amine, residual amide, and hydroxyl groups of chitosan can form intermolecular hydrogen bonds with the ether and carbonyl groups in PEG and polylactide. The FT-IR spectrum of chitosan film is shown in Figure 2, spectrum (a). It shows the absorption bands at 1,654 and 1,587 cm⁻¹. These bands correspond to the amide carbonyl group (amide I) and the free amino groups, respectively. The FT-IR spectrum of MPEG-*b*-PCL is presented in Figure 2, spectrum (e). It shows the strong carbonyl band of PCL units at 1,724 cm⁻¹ and CH stretching vibration band of MPEG units at 2867 cm⁻¹. The FT-IR spectra of nanocomposite films are shown in Figure 2, spectra (b)–(d). These spectra demonstrate characteristic absorption bands of chitosan and MPEG-*b*-PCL. It was found that the intensity of carbonyl bands increased as the MPEG-*b*-PCL ratios increased. In addition, the free amino band of chitosan shifted to lower wave numbers in composites

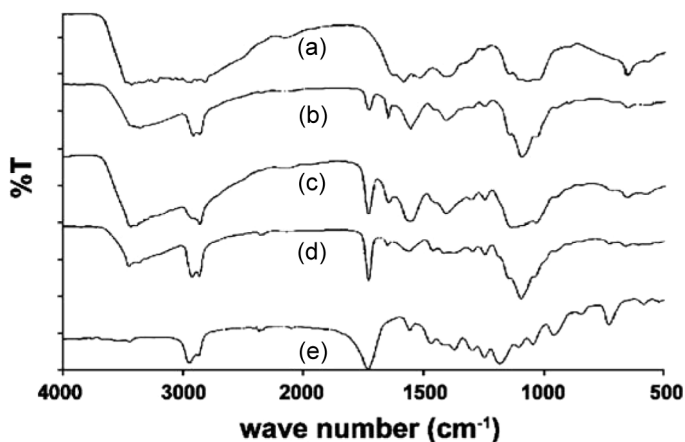


Figure 2. FT-IR spectra of (a) chitosan, (b) 90/10, (c) 80/20, (d) 70/30 (w/w) chitosan/MPEG-*b*-PCL nanocomposite films, and (e) MPEG-*b*-PCL.

with MPEG-*b*-PCL. The low wave number shift of the free amino band of chitosan can be attributed to its interaction with MPEG-*b*-PCL. This may be explained by the fact that hydrogen bonds between ether groups of MPEG and hydroxyl group of chitosan occurred. This result can be explained by the formation of the MPEG blocks in the shell of MPEG-*b*-PCL nanoparticles.^[18]

Structure of Nanocomposite Films

Thickness of the chitosan and nanocomposite film was determined by SEM analysis. It was found to be in the range of 15–25 μm . The SEM micrographs of the surface and cross section of nanocomposite films are shown in Figures 3 and 4, respectively, for 70/30 (w/w) chitosan/MPEG-*b*-PCL nanocomposite film. The surfaces of nanocomposite films were rougher than those of chitosan film. Increasing roughness of the film surfaces was observed as the MPEG-*b*-PCL ratios increased. In addition, the nanopores were observed on the film surface when the MPEG-*b*-PCL ratio was increased up to 20 (w/w). This might be due to the MPEG-*b*-PCL nanoparticles, which were self-condensed and phase separated from the chitosan matrix during the drying process.

The film cross sections were rougher than its surfaces and clearly exhibited the MPEG-*b*-PCL nanoparticles dispersed into chitosan film. The nanoparticle sizes were approximately 200 nm (or less) with spherical shape. In addition, the number of nanoparticles increased when the

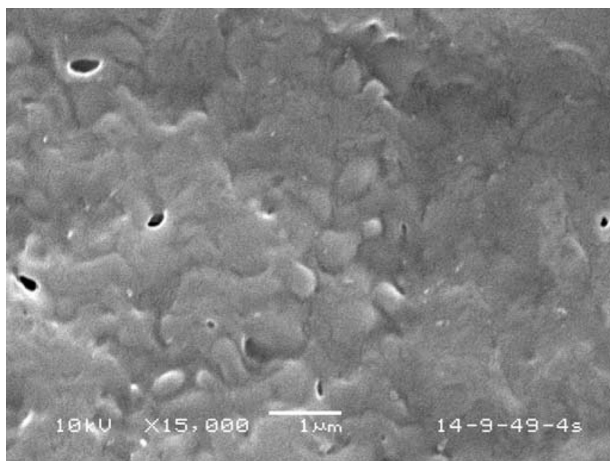


Figure 3. Surface of 70/30 (w/w) chitosan/MPEG-*b*-PCL nanocomposite film.

MPEG-*b*-PCL ratio increased. The size of the nanoparticles was independent of the MPEG-*b*-PCL ratios.

According to the results reported by Olabarrieta et al.^[8] and Suyatma et al.^[9] the sizes of the particles in their composite chitosan-based films were in the micrometer ranges. Thus, the very small particle size (nanometer range) reported by this work could have superior properties. That is, nanocomposite films could show much more consistent properties than microcomposite films.

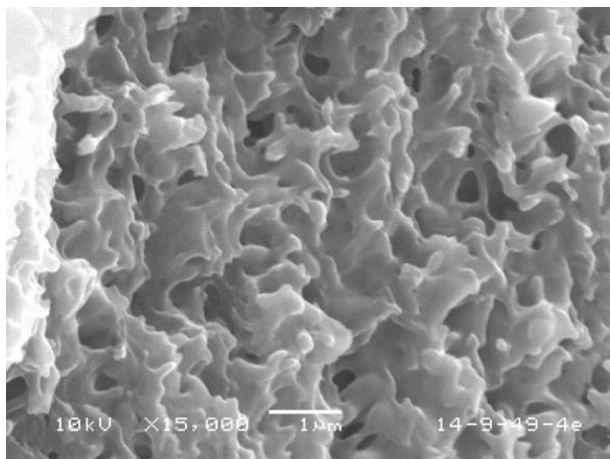


Figure 4. Cross section of 70/30 (w/w) chitosan/MPEG-*b*-PCL nanocomposite film.

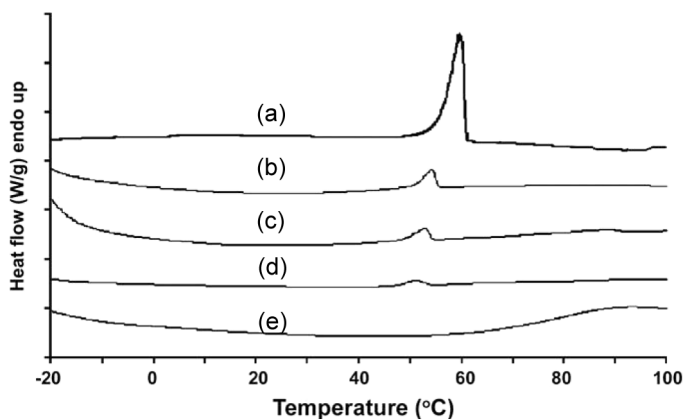


Figure 5. DSC thermograms of (a) MPEG-*b*-PCL, (b) 70/30, (c) 80/20, (d) 90/10 (w/w) chitosan/MPEG-*b*-PCL nanocomposite films, and (e) chitosan film.

However, it should be noted that the interfacial phases between the nanoparticle surface and the chitosan matrix seemed to be miscible. This may be due to the hydrophilic MPEG blocks, which formed as the outer shell of nanoparticles, being miscible with the hydrophilic chitosan matrix. This hypothesis can be confirmed by the FT-IR result, as described previously. In addition, the film cross section exhibits more nanoporous structure than that observed at its surface.

Thermal Properties of Nanocomposite Films

The DSC thermograms of chitosan film, nanocomposite films, and MPEG-*b*-PCL powder are shown in Figure 5 and the thermal properties are summarized in Table II. It was found that the T_m and ΔH_m of the nanocomposite film decreased as the chitosan ratios increased. This could be attributed to crystallization disturbance of chitosan in the composite state. The DSC results confirm that the chitosan and the MPEG-*b*-PCL have some interaction as indicated by FT-IR and SEM results.

Table 2. Thermal properties and transparency of films

Chitosan/diblock copolymer (w/w)	T_m (°C)	ΔH_m (J/g)	Transparency (% T_{660})
100/0	—	—	78.7
90/10	51	2.7	37.2
80/20	53	10.2	29.2
70/30	54	15.8	27.2

This also demonstrates that the crystallinity of MPEG-*b*-PCL in nanocomposite films is controlled by composite ratios.

Film Transparency of Nanocomposite Films

All films were transparent. The colors of chitosan and nanocomposite films had slight yellowish and whiteness tints, respectively. The percentage transmittance at λ_{\max} 660 nm (%T₆₆₀) was used for studying the film transparency. The results of %T₆₆₀ are shown in Table II. It was found that the film transparency decreased with increasing MPEG-*b*-PCL ratios.

CONCLUSIONS

The suspension of MPEG-*b*-PCL nanoparticles in chitosan solution was successfully prepared by using the modified SEDS method. Nanocomposite chitosan-based films with chitosan/MPEG-*b*-PCL composite ratios of 90/10, 80/20, and 70/30 (w/w) were obtained from the casting of nanoparticles suspended in chitosan solution. The intermolecular bonds between chitosan and MPEG-*b*-PCL were indicated by the low wave number shift of the free amino bands of the chitosan from FT-IR results and by thermal property change of MPEG-*b*-PCL from DSC results. The nanoparticles were observed from SEM micrographs of film cross sections, with approximate particle sizes of 200 nm and spherical shape. The film transparency of the nanocomposite films decreased when the MPEG-*b*-PCL ratios increased.

The nanocomposite chitosan-based films, containing nanoparticles, may have potential for use as food packaging and in drug delivery applications. Hydrophobic active compounds can be loaded in the nanoparticles.

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