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Synthesis and characterization of methoxy poly(ethylene glycol)-*b*-poly(*DL*-lactide-*co*-glycolide-*co*-ε-caprolactone) di block copolymers: Effects of block lengths and compositions

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Abstract: Methoxy poly(ethylene glycol)-*b*-poly(D,L-lactide-*co*-glycolide-*co*-ε-caprolactone) diblock copolymers, designated as MPEG-*b*-PDLLGCL, with different MPEG block lengths and DLL:G:CL ratios were synthesized via ring-opening polymerization in bulk using MPEG and stannous octoate as the initiating system. The diblock copolymers were characterized using a combination of FT-IR, ^{1}H-NMR, GPC and DSC. The percentage yields of the diblock copolymers were in excess of 90%. ^{1}H-NMR analysis confirmed that the PDLLGCL blocks contained at least some random character. From their DSC curves, the diblock copolymers were amorphous in morphology. Their glass transition temperatures decreased as the MPEG block length increased and as G and CL units were incorporated.

Introduction

Homo-, co- and terpolymers of D,L-lactide (DLL), glycolide (G) and ε-caprolactone (CL) have received much attention in the search for biodegradable polymers for potential use in biomedical [1] and packaging [2] applications. Each of the three homopolymers: poly(DL-lactide), polyglycolide and poly(ε-caprolactone) is biodegradable via a simple, non-enzymatic hydrolysis mechanism. The hydrolysis products are non-toxic. However, the properties of these homopolymers invariably only partially match the property requirements of the application such as biodegradation rate and mechanical properties. Co- and terpolymers of DLL, G and CL have all been reported either as random or block co- and terpolymers [3-8]. Random copolymers with different compositions and types of monomer units give a range of materials with different mechanical and biodegradable properties [9].

In packaging applications, these polyesters are difficult to apply to the film extrusion process due to the inherent brittleness of the polymer [10]. Recently, plasticizers such as poly(ethylene glycol) (PEG), methoxy poly(ethylene glycol) (MPEG), partial fatty acid esters, tributyl citrate, adipates and branched polylactides [11-17] have been used to improve the flexibility of polylactide by blending. However, partial migration of the plasticizer was observed [16]. Consequently, plasticizer molecules which are chemically bonded to polyester chains with different copolyester compositions are the focus of attention in this present paper.

MPEG has good hydrophilicity and biocompatibility and its use in the human body has been authorized by the USA Food and Drug Administration (FDA). MPEG has been used to prepare diblock copolymers to improve the hydrophilicity and biocompatibility of aliphatic polyesters [18]. The attachment of PDLL [19-21], PG [22], PCL [23-25] and their copolymers [26, 27] onto the ends of MPEG chains via ring-opening polymerization of their monomers initiated by the hydroxyl groups of MPEG has been reported.

Most of this previous work had concentrated on diblock copolymers consisting of MPEG and homo-/copolyester blocks. However, diblock copolymers comprising MPEG and PDLLGCL terpolymer blocks have not been reported. In this work, MPEG-*b*-PDLLGCL diblock copolymers have been prepared and characterized using stannous octoate (initiator) and MPEG (co-initiator) as the initiating system. The structures and thermal properties of diblock copolymers with varying MPEG block lengths and DLL:G:CL compositions have been investigated and their structure-property relationships are discussed.

Results and discussion

Characterization of diblock copolymers

All purified diblock copolymers had percentage yields higher than 90%. The structures of the diblock copolymers were characterized by FT-IR spectroscopy. Typical FT-IR spectra of MPEG5000 and the diblock copolymers MPEG5000-PDLL, MPEG5000-PDLLG and MPEG5000-PDLLGCL are shown in Figure 1.

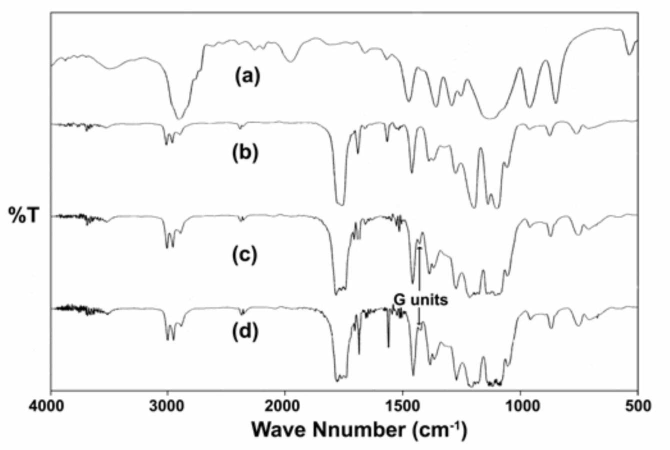


Fig. 1. FT-IR spectra of (a) MPEG5000, (b) MPEG5000-PDLL, (c) MPEG5000-PDLLG and (d) MPEG5000-PDLLGCL.

The major peaks are those appearing at 2900-3000 cm^{-1} (C-H stretching), 1760 cm^{-1} (C=O stretching), and 1100 cm^{-1} (O-CH$_2$ stretching). Comparison of the FT-IR spectrum of MPEG with those of the diblock copolymers confirms that the polymerization reaction between MPEG and the respective monomers occurred. This is indicated by the fact that the broad absorption band at 3500 cm^{-1} (O-H stretching) in the spectrum of MPEG5000 in Figure 1(a) is greatly diminished in the spectra of the diblock copolymers, Figures 1(b)-1(d), indicating that the free hydroxyl groups of MPEG had been consumed in the ring-opening polymerization of the lactide/glycolide/ε-caprolactone monomers. In addition, the CH_2 stretching bands of the G units at 1421 cm^{-1} can be observed from the FT-IR spectra of MPEG5000-PDLLG and MPEG5000-PDLLGCL. The corresponding spectra of MPEG2000 and its diblock copolymers showed similar results.

Chemical compositions of diblock copolymers

The compositions of the diblock copolymers were determined from their ^{1}H-NMR spectra by ratioing the peak areas corresponding to the ethylene oxide (EO) methylene protons at δ = 3.4-3.6 ppm, the DLL methine protons at δ = 5.0-5.3 ppm, the G methylene protons at δ = 4.5-4.9 ppm and the CL ε-methylene protons at δ = 3.9-4.2 ppm.

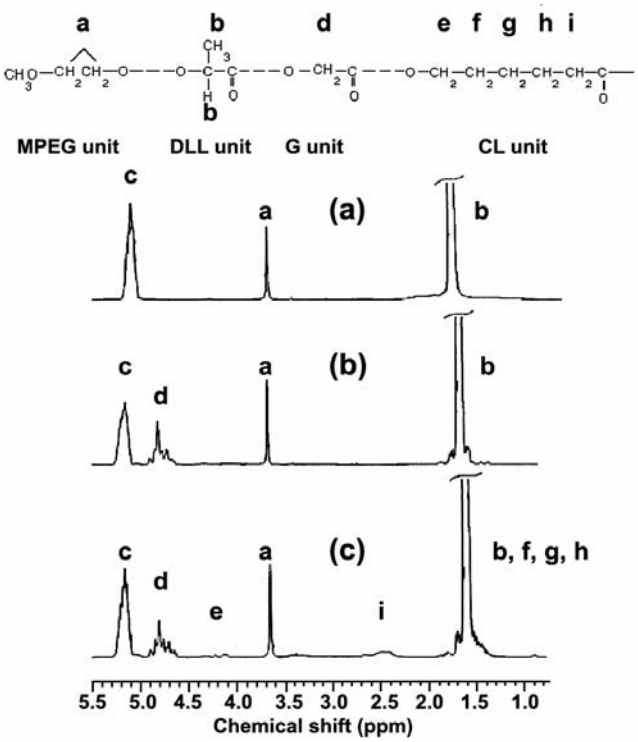


Fig. 2. ^{1}H-NMR spectra of (a) MPEG5000-PDLL, (b) MPEG5000-PDLLG and (c) MPEG5000-PDLLGCL (peak assignments as shown).

Tab. 1. Chemical compositions of the diblock copolymers.

Diblock copolymer	$\overline{M}_n$ of MPEG (g/mol)	EO:DLL:G:CL (mol %)		DLL:G:CL (mol %)	
		Feed ratio[a]	^{1}H NMR[b]	Feed ratio[a]	^{1}H NMR[b]
MPEG2000-PDLL	2,000	10:90:0:0	8:92:0:0	100:0:0	100:0:0
MPEG2000-PDLLG	2,000	10:72:18:0	10:71:19:0	80:20:0	79:21:0
MPEG2000-PDLLGCL	2,000	9:72:14:5	10:71:14:5	80:15:5	78:16:6
MPEG5000-PDLL	5,000	22:78:0:0	21:79:0:0	100:0:0	100:0:0
MPEG5000-PDLLG	5,000	21:63:16:0	21:67:12:0	80:20:0	85:15:0
MPEG5000-PDLLGCL	5,000	21:63:12:4	20:66:10:4	80:15:5	83:12:5

[a] Calculated from comonomer feed ratios

[b] Calculated from ^{1}H-NMR spectra

The ^{1}H-NMR spectra of the diblock copolymers of MPEG5000 are shown in Figure 2 and the calculated compositions of EO:DLL:G:CL and DLL:G:CL mol % are given in Table 1. As would be expected, the copolymer compositions are similar to the comonomer feed ratios, indicating that the synthesis reactions proceeded to near-quantitative conversion.

Molecular weights of diblock copolymers

Molecular weight characterization was carried out by means of a combination of GPC and ^{1}H-NMR. The molecular weight characteristics are reported in Table 2. It was found that the $\overline{M}_n$ of all of the diblock copolymers from GPC and ^{1}H-NMR are slightly lower than the calculated $\overline{M}_n$ values from the feed ratios.

Tab. 2. Molecular weight characteristics and glass transition temperatures (T_g) of the diblock copolymers.

Diblock copolymer	$\overline{M}_n$ (g/mol)			MWD[b]	T_g (^{o}C)	
	Feed ratio[a]	GPC[b]	^{1}H-NMR[c]		Calculated T_g[d]	Observed T_g[e]
MPEG2000-PDLL	62,000	58,200	59,300	1.86	65	48
MPEG2000-PDLLG	62,000	54,400	58,100	1.78	59	37
MPEG2000-PDLLGCL	62,000	56,900	58,400	1.85	53	30
MPEG5000-PDLL	65,000	73,600	67,700	1.88	65	37
MPEG5000-PDLLG	65,000	68,800	65,000	1.83	61	28
MPEG5000-PDLLGCL	65,000	74,500	67,300	1.84	54	22

[a] Calculated from the comonomer feed ratios
[b] Obtained from GPC curves
[c] Calculated from ^{1}H-NMR spectra
[d] Calculated from equation (1)
[e] Mid-point of DSC glass transition

This may be interpreted in terms of degradation side reactions such as the transesterification taking place. All diblock copolymers gave similar unimodal GPC molecular weight distributions, an example of which is shown in Figure 3 in the MPEG5000-PDLLGCL.

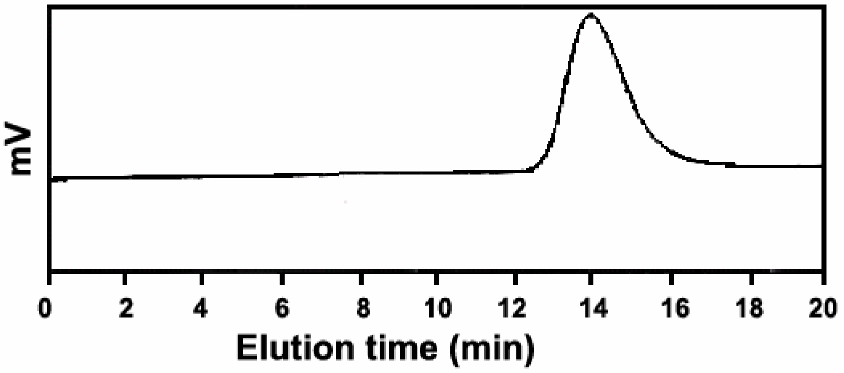


Fig. 3. GPC curve of the MPEG5000-PDLLGCL product.

Chain microstructure of diblock copolymers

The chain microstructures of polyester blocks are reflected in the fine structures of the ^{1}H-NMR spectra. The appearance of multiple resonances for the same proton can be attributed to the presence of different monomer sequences and therefore slightly different chemical environments in the copolymer chain. The α-CH_2 and ε-CH_2 protons in the CL units and the CH_2 protons in the G units are seen to be particularly sensitive to this. The bands at 2.4 and 4.1 ppm, corresponding to the α-CH_2 and ε-CH_2 protons in the CL units, respectively are split into two quite distinct triplets adjacent to one another suggesting randomization of the CL units in the copolyester chains [28, 29]. The band at 4.9 ppm corresponding to the CH_2 protons of the G units also show different resonance lines indicating various sequences of lactyl units (half-lactide units) and glycolyl units (half-glycolide units) [30]. This fine structure is a result of the different monomer sequences in the copolyester block.

Thermal properties of diblock copolymers

Thermal analysis of the diblock copolymers was carried out by means of differential scanning calorimetry (DSC). The DSC curves of the MPEG2000 and MPEG5000 show melting transition temperatures of 46 and 56 ^{o}C and heats of melting of 145.3 and 174.7 J/g, respectively (first heating scans), as shown in Figure 4.

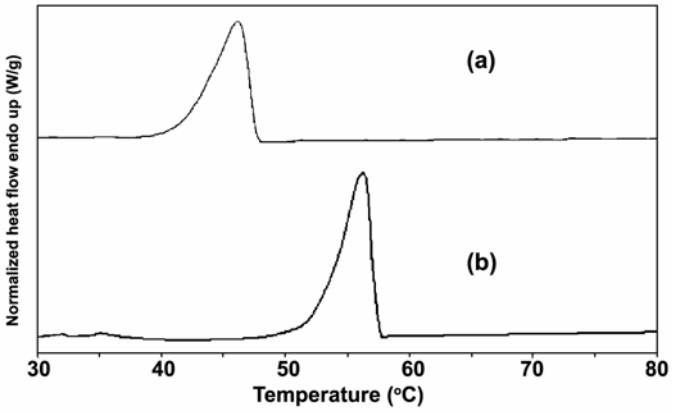


Fig. 4. DSC thermograms showing the melting endotherms of (a) MPEG2000 and (b) MPEG5000.

The DSC curves of the diblock copolymers each exhibited glass transitions over the range of 20-50 ^{o}C, as shown in Figure 5 and summarized in Table 2. It is significant to note that the crystallizability of the MPEG blocks in all of the diblock copolymers was suppressed when connected to the amorphous polyester blocks. The T_g of the diblock copolymers decreased with increasing the MPEG molecular weight and by incorporating glycolide and ε-caprolactone units into the polyester chain. Each experimentally observed T_g of the diblock copolymers can be compared with the weight-averaged value calculated from the Fox Equation (1) for a random copolymer

$$\frac{w_{DLL}}{T_{gDLL}}+\frac{w_{G}}{T_{gG}}+\frac{w_{CL}}{T_{gCL}}=\frac{1}{T_{gDLLGCL}} \qquad (1)$$

where w_{DLL}, w_G and w_{CL} are the respective weight fractions of the DLL, G and CL units, as calculated from the corresponding mole fractions from ^{1}H-NMR. T_{gDLL} (338 K), T_{gG} (308 K) and T_{gCL} (213 K) are the respective T_g (K) values of the PDLL, PG and PCL homopolymers, as obtained from the reference literature [31]. The calculated T_g values of the diblock copolymers from the Fox Equation are summarized in Table 2. It is found that the T_g value from the DSC curves are generally lower than the calculated T_g values from the Fox Equation. These results suggest that the MPEG blocks can act as an internal plasticizer to decrease the T_g of the diblock copolymers. This is most clearly observed in the T_gs of MPEG2000-PDLL and MPEG5000-PDLL which are considerably lower than the T_g of the PDLL homopolymer.

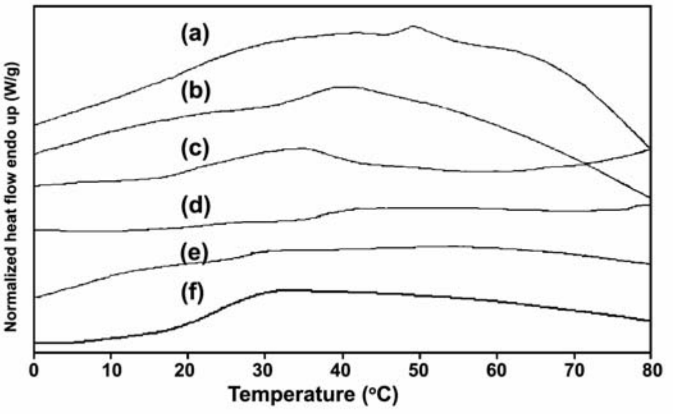


Fig. 5. DSC thermograms of (a) MPEG2000-PDLL, (b) MPEG2000-PDLLG, (c) MPEG2000-PDLLGCL, (d) MPEG5000-PDLL, (e) MPEG5000-PDLLG and (f) MPEG5000-PDLLGCL.

Conclusions

Diblock copolymers consisting of MPEG and PDLLGCL blocks with different MPEG block lengths and DLL:G:CL compositions have been successfully synthesized using MPEG and $Sn(Oct)_2$ as the initiating system. The random monomer sequencing in the polyester blocks can be observed from their ^{1}H-NMR spectra and is supported by decreased T_g values. In addition, the T_g values of the diblock copolymers also decreased with increasing MPEG block length.

These results suggest that amorphous MPEG-*b*-PDLLGCL diblock copolymers with different MPEG block lengths and copolyester compositions provide a range of materials that might be of interest for use as biodegradable colloids, films and foams in biomedical and packaging applications. The design of novel polymers with controlled microstructures is a way of tailoring polymer properties to meet the stringent demands of speciality applications.

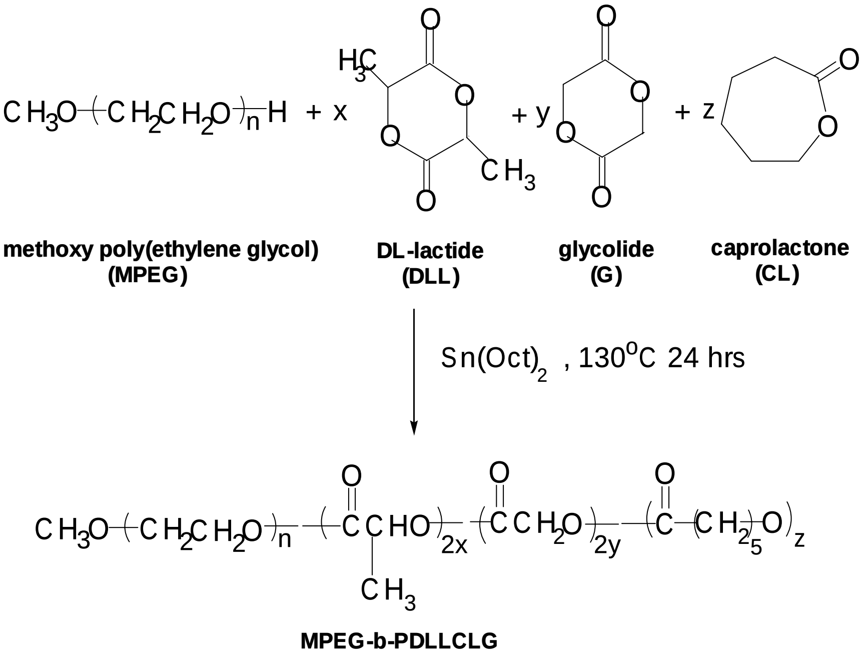
Experimental part

Materials

MPEG with molecular weights of $\overline{M}_n$ = 2000 and 5000 g/mol, previously referred to as MPEG2000 and MPEG5000 respectively, (Fluka, Germany), were dried in a vacuum oven at 120 °C for 4 hrs before use. DLL and G were synthesized by well established procedures from DL-lactic acid (90%, Fluka, Switzerland) and glycolic acid (99%, Acros, USA) respectively. Each was purified by repeated recrystallization from distilled ethyl acetate. CL (99%, Acros, USA) was purified by drying with CaH_2 followed by distillation under reduced pressure before being stored over molecular sieves in a refrigerator. Stannous octoate (95%, Sigma, USA), $Sn(Oct)_2$, was used without further purification.

Synthesis of diblock copolymers

The diblock copolymers with different DLL:G:CL monomer feed mole ratios (100:0:0, 80:20:0 and 80:15:5 mol%) and MPEG molecular weights (2000 and 5000 g/mol) were each synthesized in bulk at 130 ^{o}C for 24 hrs under a dry nitrogen atmosphere, as represented in Scheme 1. The molecular weights of the polyester blocks were approximately 60,000 g/mol. MPEG and $Sn(Oct)_2$ were used as the initiating system with the $Sn(Oct)_2$ concentration kept constant at 0.02 mol %. The as-polymerized diblock copolymers were purified by dissolving in chloroform before being precipitated in cool n-hexane. Finally, they were dried to constant weight in a vacuum oven at room temperature before characterization.



Scheme 1. Reaction scheme for the synthesis of MPEG-*b*-PDLLGCL.

Characterization of diblock copolymers

The chemical structures of the diblock copolymers were confirmed by Fourier-transform infrared (FT-IR) spectroscopy using a Perkin-Elmer Spectrum GX FT-IR Spectrometer with air as the reference. The FT-IR spectra were obtained using the KBr disk method with a resolution of 4 cm^{-1} and 32 scans. Diblock copolymer solutions in methylene chloride were dropped onto the KBr disks before being dried in a vacuum oven at room temperature for 1 week.

Copolymer compositions and microstructures of the polyester blocks were characterized by ^{1}H-NMR spectrometry using a Bruker Avance DPX 300 ^{1}H-NMR Spectrometer. Spectra were obtained from copolymer solutions in deuterated chloroform ($CDCl_3$) using tetramethysilane (TMS) as internal reference.

Number-average molecular weights, $\overline{M}_n$, and molecular weight distributions, MWD, were determined by gel permeation chromatography (GPC) using a Waters 717 plus Autosampler GPC equipped with an Ultrastyragel® column operating at 40 ^{o}C and employing universal calibration. THF was used as the solvent at a flow rate of 1 ml/min. The $\overline{M}_n$ values of the diblock copolymers were also determined from the ^{1}H-NMR spectra using the MPEG molecular weights as a reference.

Thermal analysis was carried out by means of differential scanning calorimetry (DSC) using a Perkin-Elmer DSC Pyris Diamond. For DSC analysis, copolymer samples of 5-10 mg in weight were heated at 10 ^{o}C/min under a helium atmosphere over a temperature range of 0-80 ^{o}C in order to observe their glass transition (T_g) and melting (T_m) temperatures from their second heating scans. For the second heating scans, the diblock copolymers were first heated to 200 ^{o}C before fast cooling (quenching) according to the DSC instrument's own default cooling mode before the second run.

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