Stereocomplex-Induced Gelation Properties of Polylactide/Poly(ethylene glycol) Diblock and Triblock Copolymers

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ABSTRACT: The ring-opening polymerization of L- or D-lactide was realized in the presence of dihydroxyl or monomethoxy poly(ethylene glycol) (PEG) with a number-average molecular weight of 2000. The resulting low-molar-mass poly(L-lactide) (PLLA)/PEG and poly(D-lactide) (PDLA)/PEG triblock and diblock copolymers were characterized with nuclear magnetic resonance (NMR), differential scanning calorimetry, size-exclusion chromatography, and X-ray diffractometric analysis. Bioresorbable hydrogels were successfully prepared from aqueous solutions containing both copolymers because of interactions and stereocomplexation between the PLLA and PDLA blocks. Gelation was evaluated with the tube inverting method and rheological measurements. A phase diagram was realized with gel–sol transitions as a function of concentration. The rheological properties of the hydrogels were investigated under various conditions through changes in the copolymer concentration, temperature, time, and frequency. It was concluded that the hydrogels constituted a dynamic and evolutive system because of the continuous formation/destruction of crosslinks and degradation. Further studies are underway to elucidate the degradation behavior and the potential of these substances as drug carriers or cell culture scaffolds. © 2011 Wiley Periodicals, Inc. J Appl Polym Sci 122: 1599–1606, 2011

Key words: biodegradable; block copolymers; hydrogels

INTRODUCTION

Hydrogels present growing interest for applications as controlled drug-delivery carriers and tissue engineering scaffolds because of their excellent biocompatibility due to the presence of large amounts of water.[1–7] Bioactive molecules can be physically entrapped in a hydrogel or chemically attached to the polymeric network. In the case of tissue engineering, cells can be temporarily entrapped inside a hydrogel for cell culturing. Hydrogels are usually formed by a hydrophilic polymer matrix crosslinked chemically through covalent bonds or physically through hydrogen bonds, crystallized domains, or hydrophobic interactions. They are particularly interesting for the release of poorly soluble drugs, proteins, genes, or nucleic acids, as the drugs can be protected from hostile environments, for example, the presence of enzymes, cells, or low pH values in the stomach.[4,5]

Among the various hydrogel systems, injectable and bioresorbable hydrogels appear to be the most promising. Kim and coworkers[8–10] reported hydrogels prepared from triblock copolymers containing both poly(ethylene glycol) (PEG) and poly(lactide-*co*-glycolide) blocks. A sol–gel transition was observed; its appearance depended on the concentration and composition of the copolymers. Hennink and coworkers[11–13] prepared a self-assembled hydrogel from dextran grafted with enantiomeric polylactide (PLA) oligomers. The hydrogel was formed by the stereocomplexation of poly(L-lactide) (PLLA) and poly(D-lactide) (PDLA) blocks. The authors affirmed that a degree of polymerization (DP) of 11 was the minimal value required to obtain dextran/PLA hydrogels.[11] Later on, Grijpma, Feijen, and coworkers[14,15] reported the formation of a hydrogel by stereocomplexation of water-soluble PLLA/PEG and PDLA/PEG star-shaped copolymers. Fujiwara et al.[16] obtained similar hydrogels. However, tetrahydrofuran was used to dissolve the copolymers.

In a series of articles,[17–19] we reported the synthesis, characterization, and stereocomplex-induced gelation of PLLA/PEG and PDLA/PEG copolymers. The copolymers were synthesized by the ring-opening polymerization of L- or D-lactide in the presence of monohydroxyl or dihydroxyl PEG with number-average molecular weights (M_n's) between 4600 and 20,000, with zinc lactate as the catalyst. Hydrogels were obtained from aqueous solutions containing both PLLA/PEG and PDLA/PEG block copolymers by stereocomplexation occurring between the PLLA and PDLA blocks. The rheological properties and

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drug-release behaviors of the hydrogels were also reported.

In the case of PLA/PEG hydrogels formed by PLLA/PDLA stereocomplexation, both the molar mass of PEG and the block length of PLA play a key role in the gelation process. PEGs with molar masses from 4600 to 20,000 have been used in the literature.[14–19] Nevertheless, hydrogels derived from low-molar-mass copolymers should be preferable for clinical applications insofar as the injectability is concerned. In this work, we synthesized a series of copolymers by the ring-opening polymerization of L- or D-lactide in the presence of dihydroxyl or monomethoxy poly(ethylene glycol) (mPEG) with M_n = 2000. The gelation behaviors of the copolymers were examined with the tube inverting method and rheological measurements. The results are reported herein in comparison with literature data.

EXPERIMENTAL

Materials

L-Lactide and D-lactide were obtained from Purac (Gorinchem, The Netherlands) and were recrystallized from ethyl acetate. Dihydroxyl PEG and mPEG with molar masses of 2000 g/mol were supplied by Fluka. Zinc lactate was purchased from Sigma.

Polymerization

Typically, predetermined amounts of L- or D-lactide and PEG2000 or mPEG2000 were introduced into a flask, with the initial molar ratios of ethylene oxide (EO) to lactyl (LA) repeat units being 1 : 1, 1.5 : 1, and 2 : 1. Zinc lactate was then added. After degassing, the flask was sealed *in vacuo*, and the polymerization was allowed to proceed at 140°C. After 7 days, the product was recovered by dissolution in CH_2Cl_2 and precipitation in ether. Finally, the product was dried under reduced pressure to a constant weight.

Preparation of hydrogels

Predetermined amounts of copolymer were dissolved in distilled water. The aqueous solutions were centrifuged to yield a homogeneous fluid. Gelation was then allowed to proceed at predetermined temperatures for various periods of time.

Measurements

Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded at room temperature with a Bruker spectrometer operating at 300 MHz with hexadeuterated dimethyl sulfoxide as the solvent. The chemical shifts (δ's) are given in parts per million with tetramethylsilane as an internal reference.

Differential scanning calorimetry (DSC) thermograms were registered with a PerkinElmer DSC 6 instrument, with the heating rate being 10°C/min. An amount of 10 mg of product was used for each analysis.

Size-exclusion chromatography (SEC) measurements were performed on a Waters apparatus equipped with a refractive index detector. Tetrahydrofuran was used as the mobile phase at a flow rate of 10 mL/min. A 1.0% (w/v) solution (20 μL) was injected for each analysis. Calibration was accomplished with polystyrene standards (Polysciences, Warrington, PA).

X-ray diffractometric analysis were carried out with an XPert diffractometer equipped with a Cu Kα (λ = 0.154 nm) source, an Inel monochromator, and a goniometric plate. The rheological properties were determined on a Carri-Med CSL2 rheometer of TA Instruments. For all the experiments, a cone-plate measuring geometry was used (steel, 4-cm diameter with an angle of 2° and a gap of 56 μm). A solvent trap was used to prevent water evaporation. Measurements were realized in the linear viscoelastic range.

Phase diagram

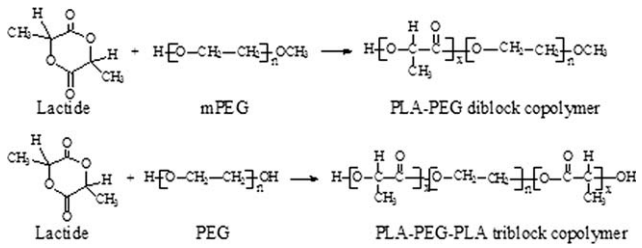
Aqueous solutions of $L_{13}EO_{45}L_{13}$ and $D_{12}EO_{45}D_{12}$ (2 mL; see the Results and Discussion section for explanation of these abbreviations) at different concentrations were mixed in 10-mL vials with inner diameters of 20 mm and magnetically stirred for 1 h at 25°C; the mixtures were allowed to stay for 24 h at 25°C for equilibrium. The vial was then slowly heated in a water bath within the range 5–80°C. The heating step was 5°C, and for each step, the vial was held for 10 min to reach equilibrium. The tube inverting method was then applied to evaluate the gel state.

RESULTS AND DISCUSSION

Synthesis and characterization

Diblock and triblock copolymers consisting of PEG and PLLA or PDLA blocks were synthesized by the ring-opening polymerization of L- or D-lactide in the presence of mPEG or PEG, respectively, with zinc lactate as the catalyst and as shown in Scheme 1. Zinc lactate was used as a catalyst instead of commonly used stannous octoate, which is slightly cytotoxic.[20]

Triblock copolymers were named with the abbreviation $L_xEO_yL_x$ or $D_xEO_yD_x$, and diblock copolymers were named L_xEO_y or D_xEO_y. In these abbreviations,



Scheme 1 Ring-opening polymerization of L- or D-lactide in the presence of mPEG or PEG with zinc lactate as a catalyst.

L, D and EO represent the PLLA, PDLA, and PEG blocks, respectively, and x and y represent the number-average DPs of the PLA and PEG blocks.

The compositions of the diblock and triblock copolymers were determined from ^{1}H-NMR, as reported in the literature.[17–19] The EO/LA ratio of the copolymers was determined from the integrations of NMR resonances belonging to the PEG blocks at 3.6 ppm and to the PLA blocks at 5.2 ppm.

Table I presents the structure, EO/LA ratio, DP, and M_n data of the various copolymers obtained from ^{1}H-NMR, according to the following equations:

$$\mathrm{DP_{PEG}} = M_{n\mathrm{PEG}}/44 \quad (1)$$

$$\mathrm{DP_{PLA}} = \mathrm{DP_{PEG}}/(\mathrm{EO/LA}) \quad (2)$$

$$M_n = 72 \times \mathrm{DP_{PLA}} + 44 \times \mathrm{DP_{PEG}} \quad (3)$$

$\mathrm{DP_{PEG}}$ was equal to 45, as derived from the M_n value of 2000, and $\mathrm{DP_{PLA}}$ ranged from 18 to 26 for the triblocks and from 18 to 75 for the diblocks. The EO/LA ratios of the copolymers were higher than in the feeds, according to Table I. This finding could be assigned to the fact that the conversion of lactide was not complete, and unreacted lactide was eliminated during the purification procedure, as previously reported.[17]

The M_n and M_n distribution of the copolymers were also determined by SEC. Figure 1(A) shows the SEC curves of the mPEG2000 and mPEG2000-initiated diblock copolymers. The peak of the copolymers appeared at elution times shorter than that of mPEG2000, which was in agreement with the attachment of PLA blocks. M_n ranged from 3300 to 7400. The molar mass distribution of the diblock copolymers was very narrow, with polydispersity indices [weight-average molecular weight (M_w)/M_n] in the 1.2–1.3 range. Figure 1(B) shows the SEC curves of PEG2000 and PEG2000-initiated triblock copolymers. Similar features were observed as in the case of the diblocks. M_n values determined by SEC appeared higher than those determined by ^{1}H-NMR. The difference was assigned to the fact that M_n values derived from SEC are based on the hydrodynamic volumes, in contrast to the absolute M_n values obtained by ^{1}H-NMR.[17]

The crystalline structure of the copolymers was examined with X-ray diffraction. Figure 2 shows the spectra of the PLLA–PEG copolymers. $L_{18}EO_{45}$ exhibited two main diffraction peaks at $2\theta = 18$ and 23.5°, characteristic of the PEG crystalline phase; this indicated that PEG blocks were able to crystallize in the copolymer. No diffraction peak characteristic of the PLA crystalline phase was visible because of the short PLA block length, although PLLA homopolymers are able to crystallize with $\mathrm{DP_{PLA}}$'s above 11.[21] The intensity of these two peaks was dramatically diminished on the spectra of $L_{26}EO_{45}$, $L_{56}EO_{45}$, and $D_{75}EO_{45}$, which presented a third peak at $2\theta = 17°$, characteristic of the PLA crystalline phase. These findings indicate that the crystallinity of PEG blocks was strongly influenced by the PLA blocks and vice versa.

It was also of interest to compare the spectra of the diblock $L_{18}EO_{45}$ and the triblock $L_9EO_{45}L_9$, which possessed the same total $\mathrm{DP_{PLA}}$ and EO/LA ratio. Both exhibited the two main diffraction peaks of PEG (Fig. 2). However, the peak intensity was much higher for $L_{18}EO_{45}$ than for $L_9EO_{45}L_9$; this indicated that the triblock structure disfavored crystallization of PEG much more than the diblock structure.

The thermal properties of the copolymers were determined by DSC (Table II). PEG2000 and mPEG2000 exhibited melting temperatures (T_m's) of

TABLE I
PLA–PEG Triblock and Diblock Copolymers Obtained by the Ring-Opening Polymerization of L- or D-Lactide in the Presence of PEG2000 and mPEG2000

Acronym	EO/LA[a]	Lactide conversion (%)[b]	$\mathrm{DP_{PLA}}$[c]	M_n[d]	M_w/M_n[e]
$L_9EO_{45}L_9$	2.6 (2.0[f])	77	18	4000 (3300[e])	1.2
$D_9EO_{45}D_9$	2.6 (2.0)	77	18	4200 (3300)	1.2
$L_{13}EO_{45}L_{13}$	1.7 (1.5)	88	26	5000 (3900)	1.2
$D_{12}EO_{45}D_{12}$	1.9 (1.5)	79	24	5000 (3700)	1.2
$L_{18}EO_{45}$	2.5 (2.0)	80	18	4100 (3300)	1.2
$D_{18}EO_{45}$	2.5 (2.0)	80	18	4100 (3300)	1.2
$D_{26}EO_{45}$	1.7 (1.5)	88	26	5100 (3900)	1.2
$L_{28}EO_{45}$	1.6 (1.5)	94	28	4900 (4000)	1.2
$L_{56}EO_{45}$	0.8 (1.0)	—	56	6800 (6000)	1.3
$D_{75}EO_{45}$	0.6 (1.0)	—	75	8300 (8300)	1.3

[a] Determined from the integration of ^{1}H-NMR bands belonging to PEG blocks at 3.6 ppm and to PLA blocks at 5.2 ppm.
[b] Lactide conversion (%) = $(\mathrm{EO/LA})_{\mathrm{theoretical}}/(\mathrm{EO/LA})_{\mathrm{experimental}}$.
[c] $\mathrm{DP_{PLA}} = \mathrm{DP_{PEG}}/(\mathrm{EO/LA})$.
[d] $M_n = M_{n\mathrm{PEG}} + \mathrm{DP_{PLA}} \times 72$.
[e] Measured by SEC with polystyrene standards.
[f] Theoretical values.

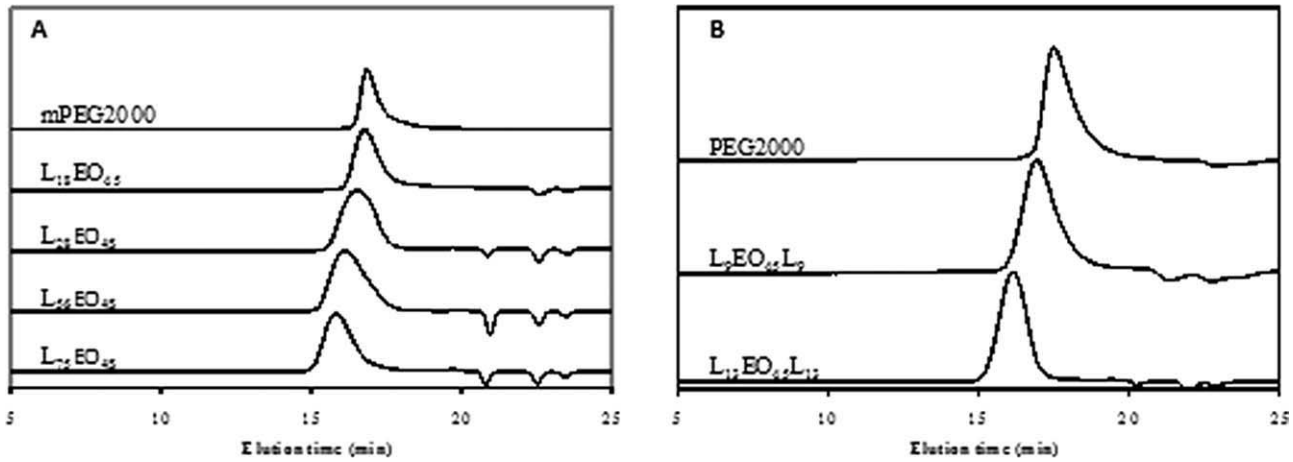


Figure 1 SEC curves of (A) mPEG2000 and mPEG2000-initiated diblock copolymers and (B) PEG2000 and PEG2000-initiated triblock copolymers.

57 and 58°C with a melting enthalpy (ΔH_m) of 150 J/g. In contrast, the T_m and ΔH_m values corresponding to the PEG block decreased strongly in the copolymers; this confirmed that the presence of PLA blocks disfavored the crystallization of PEG. The longer the PLA block length was, the lower the degree of crystallinity of PEG was, as reflected by the ΔH_m values. No melting peak assignable to the PLA blocks was observed for the triblock copolymers or for the $L_{18}EO_{45}$ and $D_{18}EO_{45}$ diblock copolymers because they were too short to crystallize. Melting was observed for longer PLA blocks ($D_{26}EO_{45}$, $L_{28}EO_{45}$, $L_{56}EO_{45}$, and $D_{75}EO_{45}$), and the corresponding T_m and ΔH_m values increased with PLA block length.

After the first heating, the molten samples were quenched in liquid nitrogen, and a second heating was performed to determine the glass-transition temperature (T_g) and cold crystallization temperature (T_c). T_g was not detected for the PEG homopolymers because they crystallized extremely fast. In contrast, T_g and T_c appeared in the DSC curves of the copolymers. T_g ranged from −43 to 6°C an T_c ranged from −18 to 37°C for the diblocks, and T_g ranged from −40°C to −33°C and T_c ranged from −6 to 17°C for the triblocks.

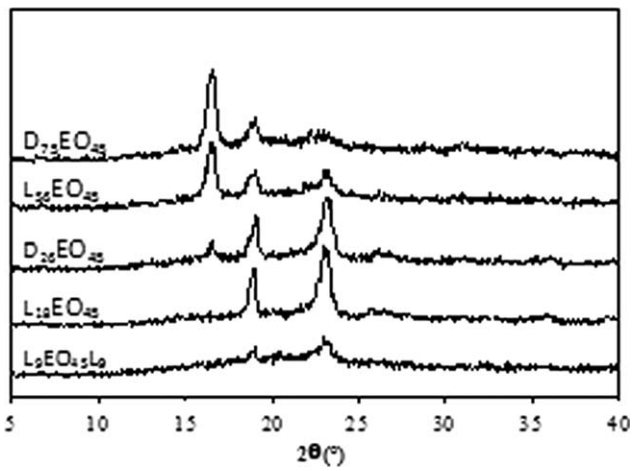


Figure 2 X-ray diffraction spectra of the PLA/PEG diblock and triblock copolymers.

Hydrogel formation

Aqueous solutions of the PLLA/PEG and PDLA/PEG copolymers were mixed under magnetic agitation. A hydrogel could be formed because of specific interactions between the L and D blocks, which led to stereocomplexation. Hydrogel formation was detected by the vial inverting method and confirmed by rheological measurement.

TABLE II
Thermal Properties of PLA/PEG Block Copolymers Obtained by Ring Opening Polymerization of L- or D-Lactide in the Presence of PEG or Mpeg

Acronym	T_m (°C)[a]	ΔH_m (J/g)[a]	T_g (°C)[b]	T_c (°C)[b]
PEG2000	57	150	—	—
$L_9EO_{45}L_9$	39	88	−40	−6
$D_9EO_{45}D_9$	38	96	−40	−10
$L_{13}EO_{45}L_{13}$	37	80	−33	17
$D_{12}EO_{45}D_{12}$	37	83	−33	17
mPEG2000	58	150	—	—
$L_{18}EO_{45}$	—[c]	—	—	—
$D_{18}EO_{45}$	52	141	−43	−18
$D_{26}EO_{45}$	51	113	−40	−3
$L_{28}EO_{45}$	51	113	−40	1
$L_{56}EO_{45}$	50	66	−21	24
$D_{75}EO_{45}$	48	28	6	37

[a] Obtained from the first heating.
[b] Obtained from the second heating.
[c] Not determined.

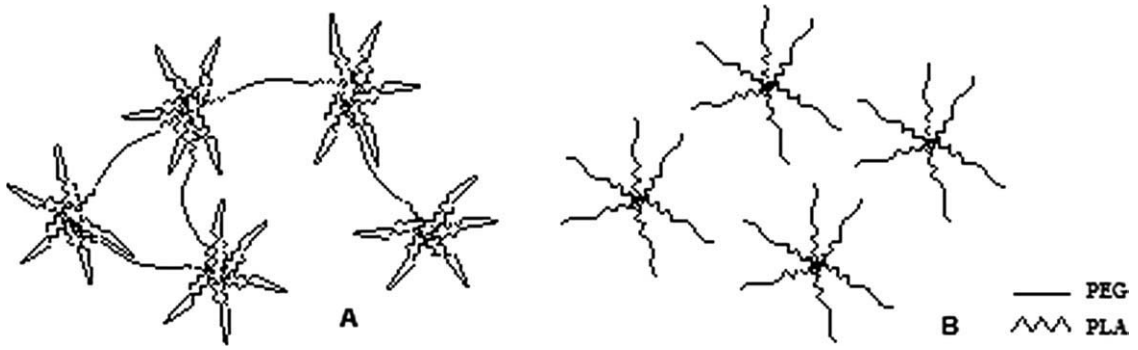


Figure 3 Schematic presentation of (A) PLA/PEG triblock copolymers and (B) diblock copolymers in aqueous solution at concentrations above the critical micellar concentration.

$L_{56}EO_{45}$ and $D_{75}EO_{45}$ were not be tested for hydrogel formation by stereocomplexation because they were not soluble in water. The $L_9EO_{45}L_9$/$D_9EO_{45}D_9$ copolymers did not form hydrogels for concentrations in the copolymers of up to 60%. In contrast, aqueous solutions of $L_{12}EO_{45}L_{12}$/$D_{13}EO_{45}D_{13}$ formed hydrogels at a concentration of 30%. In blends of L- and D-lactic acid oligomers, a minimum DP of 7 is required for stereocomplexation.[21] When L- and D-lactic acid oligomers are coupled to dextran, yielding Dex-(L)lactate and Dex-(D)lactate, respectively, the minimum DP of the lactic acid oligomers is 11 for stereocomplexation. Obviously, longer lactic acid chains are required to obtain the stereocomplexes because of steric hindrance due to dextran.[11] We deduced from these observations that the minimum DP of lactic acid oligomers in the case of the PLA–PEG–PLA triblock copolymers based on PEG2000 was between 9 and 12.

In contrast, no hydrogel was obtained from the mixing of aqueous solutions of the L/D diblock copolymers $L_{18}EO_{45}/D_{18}EO_{45}$ and $L_{28}EO_{45}/D_{26}EO_{45}$, although the DPs of the lactic acid oligomers blocks were longer than those of the triblock copolymers. PLA/PEG diblock and triblock copolymers formed flower micelles for concentration in copolymers above the critical micellar concentration. When the micelle concentrations increased, hydrogels could be formed by the formation of hydrophobic microdomains. In the case of the PLA–PEG–PLA triblock copolymers, two micelles could be linked by the same PLA–PEG–PLA chain, as shown in Figure 3(A). The tridimensional network leading to hydrogel formation was then more easily formed than in the case of the diblock copolymers [Fig. 3(B)].

Stereocomplexation is a specific interaction between PLA chains of opposite chirality and enhanced hydrophobic interactions between PLA chains. Hydrogels formed by stereocomplexation (when L/D PLA–PEG copolymers aqueous solutions are mixed) are thus obtained at concentrations below the concentrations allowing hydrogel formation by only hydrophobic interactions.

Detection of stereocomplexes

Stereocomplexes have been detected by X-ray diffraction analysis in films obtained by solvent evaporation by the mixture of organic solutions of PLA/PEG triblock copolymers.[22–24] They have also been detected by RX diffraction analysis in aqueous mixed dispersions of PEG–PLLA–PEG and PEG–PDLA–PEG copolymers. In this case, stereocomplexes were not observed at 25 and 37°C but only after heating for 1 h at 75°C.[25]

In contrast, well-defined stereocomplex peaks were detected at 25° by X-ray diffraction in lyophilized samples and gels resulting from the mixing of $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ (Fig. 4). The $D_{12}EO_{45}D_{12}$ spectra showed three weak peaks corresponding to

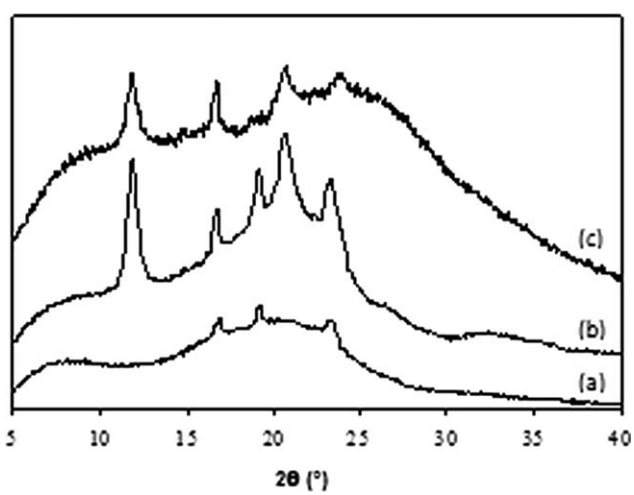


Figure 4 X-ray diffraction spectra of (a) $D_{12}EO_{45}D_{12}$, (b) 40% lyophilized sample of $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$, and (c) 40% hydrogel of $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$.

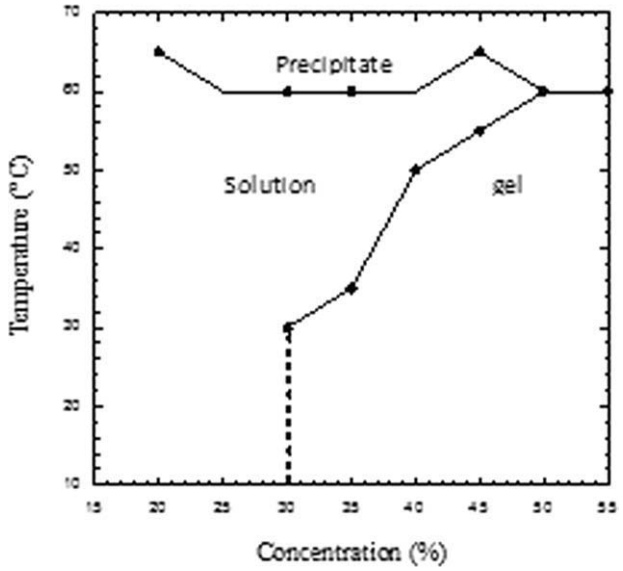


Figure 5 Phase diagram of $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ mixed aqueous solutions.

the PLA crystalline phase ($2\theta = 17°$) and PEG crystalline phase ($2\theta = 19$ and 23,5°). The peaks were not well defined because of the low crystallinity of PLA and PEG blocks in $D_{12}EO_{45}D_{12}$ and the waxy aspect of the copolymer. In contrast, two intense peaks at $2\theta = 12$ and 21° corresponding to stereocomplex were detected on the spectra of the lyophilized sample; this resulted from the mixing of $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ at 40%. The third peak characteristic of the stereocomplex at $2\theta = 24°$ overlapped with the peak of PEG at $2\theta = 23.5°$. The peaks corresponding to stereocomplex were also detected in a hydrogel sample of $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ at 40%. In this case, the peaks corresponding to the PEG crystalline phase disappeared because PEG is in an amorphous state in water.

Phase diagram

The phase diagram of the $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ aqueous solutions was realized by the tube inverting method, as shown in Figure 5. It was characterized by a critical gel concentration of 30%, which was quite high and in agreement with the short PEG and PLA blocks.

The mixing of aqueous solutions of the L/D copolymers showed a transition from gel to sol with increasing temperature. The gel–sol transition temperature increased with increasing concentration in the copolymers, which was in agreement with the higher stability of gels at high concentrations.

Precipitation of the copolymers was observed at temperatures of about 60–65°C. The precipitation temperature was not affected by the concentration of the copolymers within the investigated concentration range of 15–55 wt %, as already shown for PEO–PLA–PEO copolymers and Pluronics.[26] Precipitation of the copolymers was attributed to PEG chain dehydration at high temperature.

Rheological measurements

Figure 6 shows the variation of the storage modulus (G') and loss modulus (G'') of the 25% $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ aqueous solution as a function of deformation. The crossover point, $G' = G''$, has been proposed as an indicator of the sol–gel transition.[27] At low deformations, the samples were in a hydrogel state because G' was higher than G'' and turned to a viscous solution when the deformation increased. The limit deformation, below which the gel state was observed, was found to be 10%. This limit deformation depends on the concentration of the copolymers. It reached 30% for a concentration of 27%. Above the limit deformation, the network was too soft, and the number of nods, which increased with increasing concentration in the copolymers, was too low to support the imposed deformation and maintain the gel state. Temperature plays a main role in hydrogel formation. The kinetics of gelation were studied at 10, 25, and 35°C for samples of $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ at 30% (Fig. 7). Gelation time is a function of temperature at which the hydrogel is formed. Considering the gelation time at the crossover point $G' = G''$, the gelation time was 10 min at 35°C, 40 min at 25°C, and 210 min at 10°C. An increase in temperature enhanced the macromolecules' mobility and then supported the establishment of a link between the PLA blocks.

Physical hydrogels are dynamic systems where the nods of the network are formed and destroyed continually, in contrast to chemical hydrogels, in which links are established in a permanent way. Increasing the temperature from 10 to 35°C involves

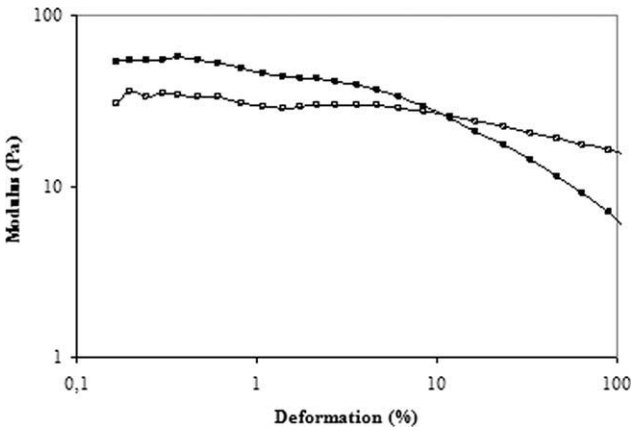


Figure 6 Variation of (■) G' and (□) G'' of the 25% $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ sample as a function of deformation (25°C, 1 Hz).

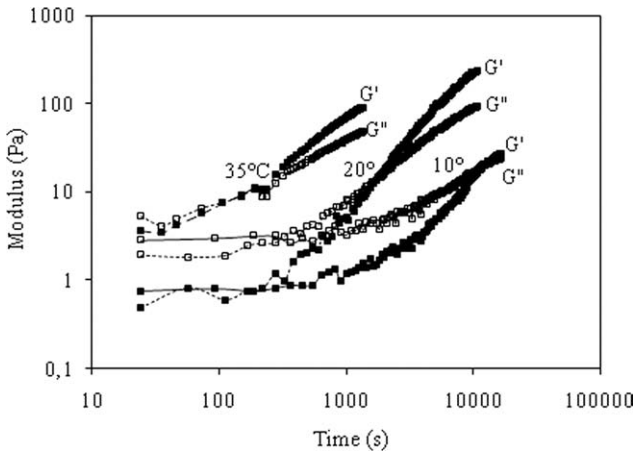


Figure 7 Variation of (■) G' and (□) G'' of the 30% $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ sample as a function of time at 10, 25, and 35°C (1 Hz, 1% deformation).

a reduction in the gelation time. In the meantime, an antagonist phenomenon appears. The degradation of PLA chains tends to reduce the number of nods in the network. The viscoelastic modulus was monitored for a 30% hydrogel of $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ at 25 and 37°C as a function of time over a period of 13 days (Fig. 8).

At 25°C, the modulus increased rapidly for the first 2 days. Then, G' still increased much more slowly, and G'' tended to remain at a constant value. After 13 days, the gel had a strong elastic component because G' was about 3400 Pa, and G'' was about 700 Pa. In the first hours, G' and G'' were higher for the hydrogel at 37°C than for the hydrogel at 25°C. However, after 30 h, both moduli began to decrease because of degradation, in particular, G'. At 25 and 37°C, network formation was prevalent over degradation in the first hours; this resulted in a strong increase of G' and G''. At 25°C, the degradation of PLA chains proceeded very slowly, and the moduli slowly increased over the whole period of time. In contrast, at 37°C, degradation was more pronounced; this resulted in decreases of G' and G''.

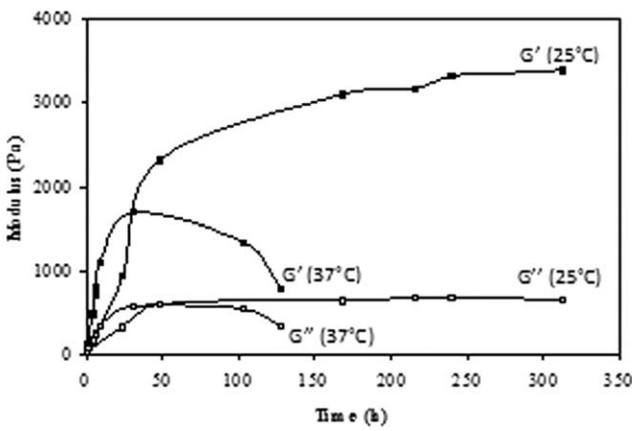


Figure 8 Variation of (■) G' and (□) G'' of the 30% $L_{13}EO_{45}L_{13}/D_{12}EO_{45}D_{12}$ sample as a function of time at 25 and 37°C (1 Hz, 1% deformation).

CONCLUSIONS

PLA/PEG block copolymers were prepared by the ring-opening polymerization of L(D)-lactide with low-toxic zinc lactate as a catalyst, in the presence of PEG or mPEG with $M_n = 2000$. The resulting triblock and diblock copolymers were semicrystalline materials. PEG blocks crystallized in all cases, whereas PLA ones crystallized when the DP of PLA was above 26. Hydrogels were obtained from water-soluble triblock copolymers because of stereocomplexation between the PLLA and PDLA blocks but not from diblock ones. Stereocomplex was detected in hydrogels in a dry or swollen state when the DP of PLA was above 12. The gel-to-sol transition was detected from the tube inverting method. The higher the concentration was, the higher the transition temperature was. Rheological measurements showed that the gelation time was shortened with increasing temperature. Degradation occurred during the gelation process, especially at 37°C. Further studies are underway to evaluate the potential of these degradable and injectable hydrogels as drug carriers or cell culture scaffolds.

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