In Situ Formation of Blends by Photopolymerization of Poly(ethylene glycol) Dimethacrylate and Polylactide

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Blends of cross-linked poly(ethylene glycol) dimethacrylate (PEGDMA) and poly(D,L-lactide) (PLA) were prepared by mixing photoactive PEGDMA (molecular mass: 875 g/mol) and PLA, and subsequently photopolymerizing the mixture with visible light. The effects of PLA molecular mass and mass fraction on the rheological properties of the PEGDMA/PLA mixtures, and on the degree of methacrylate vinyl conversion (DC), as well as blend miscibility, microstructure, mechanical properties, in vitro swelling behavior, and cell responses were studied. PLA-2K (molecular mass: 2096 g/mol) and PLA-63K (molecular mass: 63 000 g/mol) formed miscible and partially miscible blends with cross-linked PEGDMA, respectively. The addition of the PLA-2K did not affect the immediate or post-cure (>24 h) DC of the PEGDMA upon photopolymerization. However, the addition of PLA-63K decreased the immediate DC of the PEGDMA, which can be increased through extending the curing time or post-curing period. Compared to the cross-linked neat PEGDMA and PLA-2K/PEGDMA blends, PLA-63K/PEGDMA blends were significantly stronger, stiffer, and tougher. Both types of blends and the cross-linked PEGDMA swelled when soaked in a phosphate buffered saline (PBS) solution. The attachment and spreading of MCT3-E1 cells increased with increasing PLA-63K content in the blends. The facile and rapid formation of PEGDMA/PLA blends by photopolymerization represents a simple and efficient approach to a class of biomaterials with a broad spectrum of properties.

Introduction

Poly(ethylene glycol) dimethacrylates (PEGDMA) represent a class of cross-linkable oligomers and macromers with unique properties. The cross-linking reaction can be achieved by thermal polymerization or by photopolymerization, with the later process widely used in areas such as industrial coatings, adhesive materials, dental materials, and other biomaterials because of efficient, in situ, "on command" polymerization.[1−5] PEGDMAs are hydrophilic due to their ethylene oxide backbone and can be modified to be either bio-inert or biocompatible. PEGDMAs of 2000 g/mol or a higher molecular mass have been photopolymerized in aqueous solutions to form biocompatible hydrogels with potential applications in soft tissue engineering such as cartilage regeneration.[1,2] Lower molecular mass PEGDMAs have been copolymerized with poly(propylene fumarate) for use as injectable and cross-linkable composites[3] and have been incorporated as diluents in photopolymerizable resins designed for dental applications.[5]

Although PEGDMAs possess numerous attractive properties as biomaterials, some undesirable characteristics for use in tissue regeneration include weak mechanical properties and low biodegradability due to the hydrolytic stability at the ether linkages. One approach toward improving the mechanical properties and imparting biodegradability into PEGDMA networks is by copolymerizing PEG with a degradable polymer such as polylactide (PLA), a α-polyester that is widely used in industrial and clinical applications.[6,7] For example, acrylated PEGs have been co-photopolymerized with acrylated lactic acid oligomers to form networks for use as tissue engineering scaffolds.[8,9] The network's degradation and mechanical properties, as well as the cell adhesion to the scaffolds, can be modified by changing the molecular mass and mass fraction of acrylated PEG macromers. Block copolymers of PEG and PLA have been used to form degradable hydrogels,[10] nanospheres for drug or gene delivery,[11,12] and biomimetic surfaces.[13]

In addition to the copolymerization approach, blending of polymers has been extensively investigated for modifying material properties. Blending is a cost-effective method to tune the material properties of polymers and to impart desirable characteristics that are not found in either individual component alone.[14,15] The blend properties, such as mechanical properties, can be tailored by controlling the blend composition and morphology. Previous work has found that compared to the pure PLA or pure PEG, blends of PLA and PEG exhibit improved or better controllable mechanical, thermal, and degradative properties.[16,17] Although blending the cross-linked PEGDMA and PLA does not lead to complete polymer degradation, it does offer a way to create

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the porosity needed in tissue engineering applications. A similar approach consisting of blending immiscible polymers followed by leaching of one component has been used to prepare porous scaffolds.[14]

The goal of the current study is to investigate the feasibility of in situ fabrication of blends from photopolymerizable oligomers and biocompatible thermoplastic polymers. Specifically, this study is designed to investigate the structure−property relationships of PEGDMA/PLA blends prepared by a photopolymerization process as a prototype model system for preparing a series of biomaterials with easily adjustable properties. The PEGDMA/PLA system is chosen because both components are well characterized, widely used, and exhibit desirable properties for use as biomaterials.[1−7] Although PEGDMA is not readily biodegradable, blends composed of all biodegradable components (e.g., incorporating biodegradable linkages that would not radically change the gel properties) can also be prepared using the same approach.

In the current study, a photoactivated PEGDMA oligomer and two PLAs of different molecular masses were mixed and subsequently photopolymerized to yield blends of cross-linked PEGDMA with PLA. The effects of PLA content and molecular mass on the PEGDMA's degree of vinyl conversion, as well as on the blends' miscibility, mechanical properties, swelling behavior, and in vitro cellular responses were examined.

Materials and Methods

Certain commercial materials and equipment are identified in this paper in order to specify adequately the experimental procedure. In no case does such identification imply recommendation by the National Institute of Standards and Technology nor does it imply that the material or equipment identified is necessarily the best available for this purpose.

Materials. PEGDMA (M_n = 875 g/mol), dichloromethane, camphorquinone (CQ), and ethyl 4-*N*,*N*-dimethylaminobenzoate (4E) were purchased from Sigma-Aldrich Corp. and used as received. Dry phosphate buffered saline (PBS) powder (dissolved in 1 L deionized water at 25 °C to yield 0.01 mol/L PBS solution with 0.138 mol/L NaCl and 0.0027 mol/L KCl, pH = 7.4) was purchased from Sigma-Aldrich Corp. Poly(D,L-lactide) (PLA-2K, Resomer104, M_n = 2096 g/mol) was purchased from Boehringer Ingelheim Inc. The PLA particles were ground using a mortar and pestle and then sieved to achieve a particle size of less than 74 μm. PLA-63K (Medisorb, M_n = 63 000 g/mol) was purchased from Alkermes Inc. and used as received.

Preparation of Cross-Linked PEGDMA/PLA Blends. Blends were prepared using two different approaches depending on the PLA molecular mass. Blends of PEGDMA and PLA-2K were mixed directly (without solvent), followed by photopolymerization. Solvent mixing was used for the PEGDMA/PLA-63K blends. In both cases, PEGDMA was first activated for blue light photopolymerization with a redox initiator system consisting of 0.2% CQ (photooxidant) and 0.8% 4E (photoreducdant). PLA-2K was mixed with photoactivated PEGDMA at mass fractions of 0, 10, 30, 50, and 70% and stirred at 60 °C in the dark to yield homogeneous liquids. The mixtures were then poured into a circular mold sandwiched between two Mylar films and clamped between two glass slides. Disk specimens (≈ thickness of 1 mm and diameter of 10 mm) were cross-linked via visible light (λ = 470 nm) irradiation for 1 min per side in a dental curing unit (Triad 2000, Dentsply International Inc., intensity ≈ 35 mW cm^{-2}).

To prepare PEGDMA/PLA-63K blends (mass fraction = 10%, 30%, and 50%), photoactivated PEGDMA oligomer was vigorously mixed with PLA-63K dissolved in dichloromethane at 60 °C in the dark. The solvent was then removed under vacuum at 25 °C. Disks of PEGDMA/PLA-63K blends were prepared via photopolymerization in the same manner as used for the PLA-2K blends. Matrix assisted laser desorption ionization time-of-flight mass spectroscopy (MALDI-TOF MS) showed no evidence of PLA degradation during the blend processing at 60 °C.

Characterization of Cross-Linked PEGDMA/PLA Blends. *Rheology*. Rheological properties of nonactivated PEGDMA and PEGDMA/PLA mixtures were studied using a Rheometrics ARES rheometer. Dynamic modulus and steady shear rate viscosities were measured using a cone-and-plate geometry (25 mm diameter, 0.1 rad) at 25 °C.

Degree of Conversion. The degree of conversions (DC) for the cross-linked PEGDMA (control) and PEGDMA/PLA blends after photopolymerization were determined using transmission spectra obtained by Fourier transform infrared spectrometry (FT-IR) (Magna 550, Nicolet Inc.). Samples were sandwiched between two KBr pellets, placed on a fixed standard IR cards, and IR spectra of samples before and immediately after photopolymerization (1 min per side) were collected. The samples were sufficiently thin such that no saturation occurred. The DC was calculated using the area under the C=C absorption peak at 1637 cm^{-1}, and utilizing the methacrylate carbonyl as an internal standard. DC results are reported for data collected from at least 5 specimens for each sample.

Thermal Properties. Glass transition temperatures (T_g) of photopolymerized PEGDMA and PEGDMA/PLA blends, respectively, were characterized by differential scanning calorimetry (DSC) (TA instruments Inc., model Q1000). Samples were heated to 100 °C, held for 5 min, and then cooled to −80 °C under nitrogen. A ramp rate of 5 °C/min was used. Data reported are from the second heating−cooling cycle. The temperature at the midpoint of the corresponding heat-capacity jump in the second heating cycle was taken as T_g.

Microstructure. The microstructures were characterized using a Hitachi S-4700 field emission scanning electron microscope (FE-SEM). Specimens were fractured at room temperature and the exposed cross-sectional surfaces were imaged.

Mechanical Properties. Tensile tests were performed using a universal testing machine (Instron, model 5500R) with a 100 N load cell and a cross-head speed of 1 mm/min on dog-bone shape specimens (length = 60 mm, width = 10 mm, and thickness ≈ 2 mm). The elastic modulus was calculated from the elastic region of the stress−strain curve

(1% strain). Results are reported for data collected from at least 3 specimens for each material.

Soaking in PBS. In vitro soaking in PBS was performed as follows. Disk specimens (diameter ≈ 10 mm, thickness ≈ 1 mm) were soaked in a 0.01 mol/L PBS solution (pH = 7.4) with a soaking ratio of 1 g of specimen per 30 mL of PBS. After soaking the specimens for 2 weeks, the mass, diameter, and pH changes were determined by differential weighing, size, and pH measurements using a balance, caliper, and pH meter, respectively. Samples were measured in triplicates.

Cell Culture. Culture of osteoblast-like cells (MC3T3-E1) was performed following a previously reported procedure.[18] Briefly, MC3T3-E1 cells (Riken Cell Bank, Hirosaka, Japan) were maintained in α-modification of Eagle's minimum essential medium (Biowhittaker, Walkersville, MD) with a volume fraction of 10% fetal bovine serum (Gibco-BRL-Life Technologies, Rockville, MD) and 60 mg/L kanamycin sulfate (Sigma, St. Louis, MO) in a fully humidified atmosphere with a volume fraction of 5% CO_2 at 37 °C. The medium was changed twice a week. Cultures were passaged with EDTA-containing (1 mmol/L) trypsin solution (mass fraction of 0.25%; Gibco, Rockville, MD) once a week. Passage #3 cells were used in this study. All disk specimens (diameter ≈ 10 mm and thickness ≈ 1 mm) were cleaned 3 times using 70% ethanol (disinfectant) for 1 min at a soaking ratio of 2 mL/specimen, dried, and then placed in 12-well plates with one disk per well. Each disk was washed with 2 mL of media, and then fresh media was placed on each disk for an overnight extraction in the cell incubator. For phase contrast microscopy, disk specimens were cultured with cells in a 12-well plate (50 000 cells per well) for 1 d and imaged using an inverted phase contrast microscope (Nikon TE300, Melville, NY). Cells on tissue culture polystyrene (TCPS) (control) were also prepared and observed. For the fluorescence microscopy studies, cells after 1 d culture on disk specimens were stained with calcein-AM (live cells, green) and ethidium homodimer-1 (dead cells, red).

Statistical analyses of the data for DC, mechanical tests, and PBS soaking were performed using a Student's *t* test with a level of significance of $p < 0.05$.

Results and Discussion

Rheological Properties of Mixtures. Before photopolymerization, mixtures of PEGDMA and PLA-2K were homogeneous and behaved as Newtonian fluids, as the steady shear viscosity remained constant over a wide range of shear rates (data not shown). This is expected since both components are of relatively low molecular mass and are miscible. The viscosity of the mixtures increased with increased PLA content and ranged from 0.1 Pa·s for the pure PEGDMA to 10 Pa·s for the 50% PLA-2K mixture. Figure 1A shows the dynamic frequency sweep for the PEGDMA/PLA-2K mixtures at various PLA compositions. In the frequency (ω) range studied, all samples shows terminal relaxation behavior with G'' storage shear modulus) > G' (loss shear modulus), $G' \propto \omega^2$ (frequency), and $G'' \propto \omega$. The observed terminal relaxation behavior is consistent with the samples' viscoelastic behavior and also suggests that the mixtures are single-phase.[19]

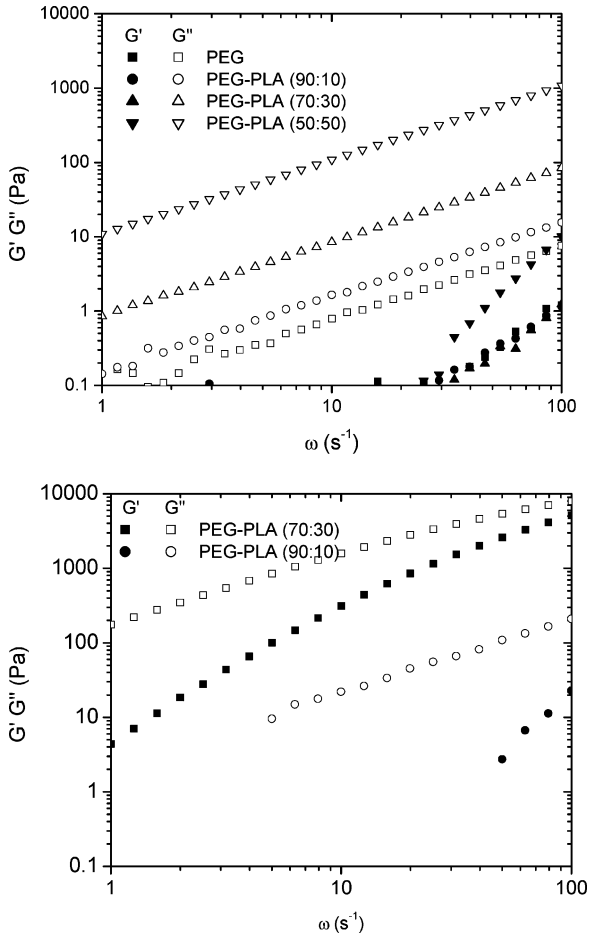

Figure 1. Dynamic frequency sweep for PEGDMA/PLA-2K mixtures (top) and PEGDMA/PLA-63K mixtures (bottom).

Homogeneous PEGDMA/PLA-63K mixtures became non-Newtonian at high shear rates due to high molecular mass of this PLA. The dynamic frequency sweep for PEGDMA/PLA-63K mixtures (Figure 1B) shows significantly higher loss and storage moduli than those of the mixtures with PLA-2K at the same composition. The viscosity for 10% and 30% PLA-63K blends are 2.2 Pa·s and 176 Pa·s, respectively. The viscosity is an important material parameter since it can affect the reaction kinetics and degree of conversion for the PEGDMA.[20]

Degree of Vinyl Conversion (DC). FTIR was used to determine the degree of conversion for the PEGDMA and its blends. As shown in Figure 2A, no statistical differences in DC are found between the pure cross-linked PEGDMA and PEGDMA/PLA-2K blends immediately after photopolymerization. Although previous studies have shown that the addition of inorganic fillers can influence the DC of methacrylate dental monomers during photopolymerization,[21] the addition of up to 50% low molecular mass PLA-2K does not interfere with the reaction kinetics and vinyl conversion of PEGDMA, despite an increase in the viscosity.

FTIR analyses of blends composed of the same photoactivated PEGDMA and PLA-63K show that the addition of the high molecular mass PLA significantly decreases the

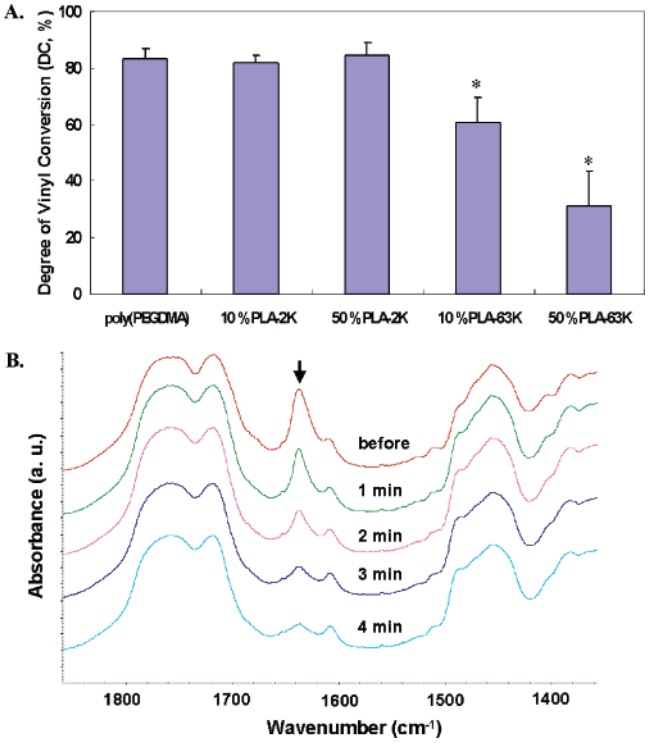

Figure 2. (A) Degree of vinyl conversion (DC) of pure cross-linked PEGDMA (poly(PEGDMA)) and its blends with PLA-2K and PLA-63K. Stars indicate that data are statistically different. (B) FTIR spectra of 50% PLA-63K blends before and after photopolymerization for 1, 2, 3, and 4 min/side. Arrow indicates the C═C absorption peak.

DC of PEGDMA for the same reaction time (Figure 2A). However, FTIR of post cured samples show significant increase in conversion indicating that the DC of PLA-63K blends could be greatly enhanced through longer curing times and/or post-curing periods. For example, after photopolymerization for 2, 3, and 4 min on each side of the sample, the DC of 50% PLA-63K blends increased from 31% (1 min per side) to 63%, 82%, and 89%, respectively (Figure 2B). In addition, 24 h after photopolymerization for the sample that was cured for 1 min per side, the DC increased from 31% to 83%. Similar post-curing behaviors have also been observed for the curing of dimethacrylate dental monomers.[21,22] Additional polymerization due to the extent of the post-cure period is presumably due to diffusion-controlled reactions of methacrylate groups with radical species remaining in the network.[22]

Previous studies on photopolymerization of dimethacrylate-based resins have shown that the cross-linking kinetics, and subsequently the DC, were strongly affected by the chemical structure and viscosity of the monomer mixtures.[23−26] Although PEGDMA/PLA-2K mixtures had increased viscosities relative to the pure PEGDMA, the reaction kinetics and DC was not strongly affected in this system. The effect of viscosity on the reaction kinetics was manifested in the PEGDMA/PLA-63K mixtures, although other factors, such as morphology, could also affect the reaction kinetics. It should be noted that the ultimate DC is not affected by the initial viscosity as the cross-linked PEGDMA, PEGDMA/PLA-2K blend, and PEGDMA/PLA-63k blend all had comparable final DC (≈ 83%) 24 h after photopolymerization.

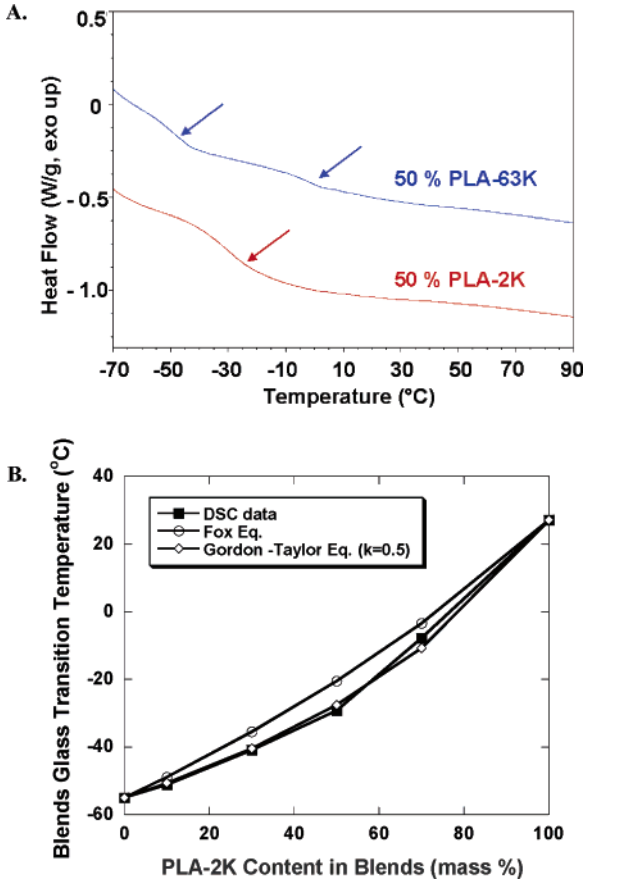

Figure 3. Glass transition temperatures of the blends. (A) Representative DSC data of 50% PLA-2K blends and 50% PLA-63K blends, and (B) glass transition temperatures of PLA-2K blends from DSC results and from calculations using the Fox and the Gordon-Taylor models.

Thermal Properties. After photopolymerization, the PEGDMA/PLA-2K blends were miscible as confirmed by the DSC results. A single glass transition temperature (T_g) was observed for all blend compositions (Figure 3A). In addition, the T_g was compositionally dependent and increased with increased PLA content (Table 1). The Fox and Gordon-Taylor equations[27−29] are often applied to describe the compositional dependence of T_g of miscible blends. The Fox equation is[30]

$$\frac{1}{T_g} = \frac{W_1}{T_{g1}} + \frac{W_2}{T_{g2}} \quad (1)$$

The Gordon-Taylor equation is[31]

$$T_g = T_{g1} + kW_2 \frac{T_{g2} - T_{g1}}{W_1 + kW_2} \quad (2)$$

where W_1 and W_2 are the mass fractions of component 1 and 2 in the blend and T_{g1}, T_{g2}, and T_g are the glass transition temperatures of component 1, 2, and the blend, respectively. The fitting parameter k is related to the interaction between the components in the blend. Figure 3B shows the theoretical blends T_g calculated from both the Fox and Gordon-Taylor equations ($k = 0.5$) and the T_g determined from the DSC data. The experimental results are in good agreement with the values calculated by the Fox and Gordon-Taylor equa-

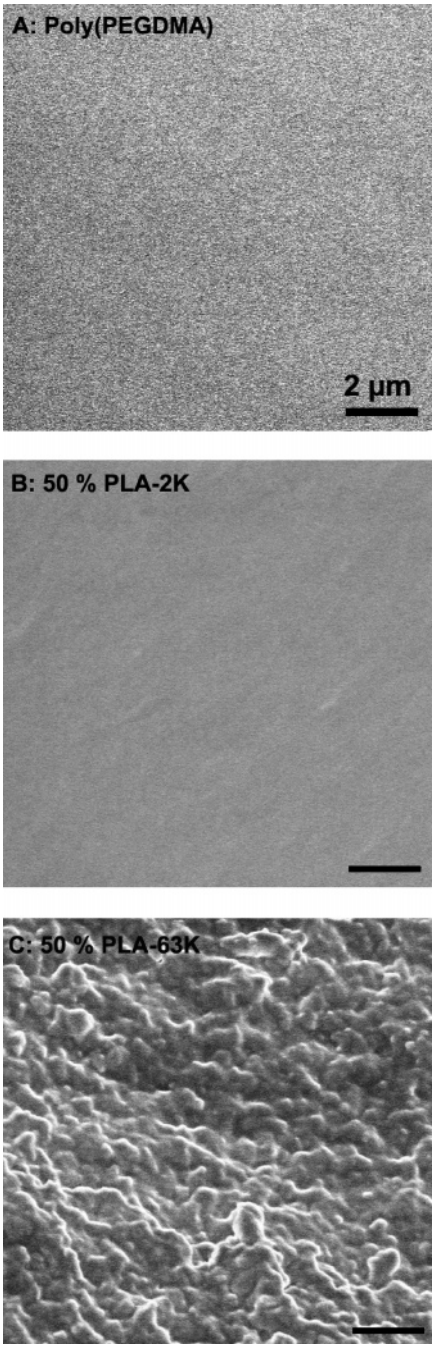

Figure 4. Scanning electron microscopy images of the fractured surfaces of (A) poly(PEGDMA), (B) 50% PLA-2K blends, and (C) 50% PLA-63K blends. Scale bar: 2 μm.

Table 1. Glass Transition Temperatures of Crosslinked PEGDMA and PEGDMA/PLA Blends

PLA content (mass %)	0%	10%	30%	50%	70%	100%
T_g of PLA-2K blends (°C)	−55.0	−51.2	−40.9	−29.2	−7.8	27.1
T_{g1} of PLA-63K blends (°C)	−55.0	N/A	−55.0	−46.4	−46.0	N/A
T_{g2} of PLA-63K blends (°C)	N/A	N/A	−9.2	−1.5	22.4	40.9

tions, thus demonstrating that the PEGDMA/PLA-2K blends are miscible. In addition, the low value of k (<1) suggests

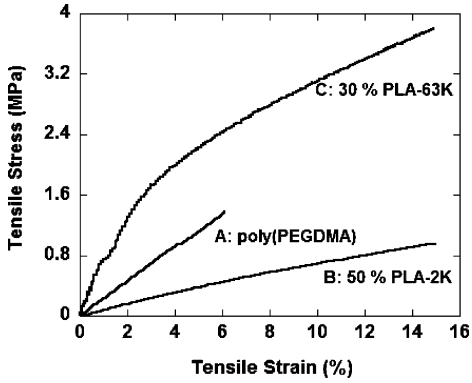

Figure 5. Representative tensile stress−strain curves of (A) poly(PEGDMA), (B) 50% PLA-2K blends, and (C) 30% PLA-63K blends.

that the interactions between PLA-2K and PEGDMA are weak.[27,29]

In contrast, PLA-63K blends exhibit two T_gs for all blend compositions investigated (Figure 3A). The two T_gs are between the T_g of cross-linked PEGDMA and PLA-63K (Table 1), suggesting partial mixing of the two phases resulting in the formation of a cross-linked PEGDMA-rich and a PLA-rich phase. Using the Fox equation (eq 1), the mass fraction of PEGDMA in the cross-linked PEGDMA-rich phases are calculated to be 100, 88, and 87 for the 30%, 50%, and 70% PLA-63K blends, respectively. Similarly, the mass fraction of PLA-63K in the PLA-rich phase are calculated to be 56.8, 64.5, and 85.8 for the 30%, 50%, and 70% PLA-63K blends, respectively. Similar mixing behavior has been observed in other blend systems, such as partially miscible blends of poly(D,L)-lactide and poly(methyl methacrylate).[29]

SEM results also suggest partial miscibility of the PLA-63K blends (Figure 4). The fractured cross-sectional surfaces of both cross-linked PEGDMA and 50% PLA-2K blends are smooth and featureless. In contrast, the cross-sections of the fracture surfaces for the 50% PLA-63K blend are rough with particulate-like structures, suggesting that more energy is consumed during the fracture; and therefore, these blends should have improved mechanical properties.

Mechanical Properties. The mechanical properties were determined using tensile testing. Figure 5 shows the representative tensile stress−strain curves for cross-linked PEGDMA, 50% PLA-2K, and 30% PLA-63K blends. Table 2 lists the tensile break strength, tensile break strain, elastic modulus, and the work of fracture (the estimated area under stress−strain curves, a representation of toughness).

The 30% PLA-63K blend is the strongest, stiffest, and toughest among the three samples. The break strength and strain for the 30% PLA-63K blends are nearly tripled and the elastic modulus is doubled compared to those of cross-linked PEGDMA. The addition of the higher molecular mass more viscoelastic PLA-63K to the blends, and its partial miscibility with PEGDMA networks contributed to the improved mechanical properties.

Cross-linked PEGDMA has a higher strength but a lower strain than the 50% PLA-2K blends. The differences in strength may be due to the low molecular mass of the PLA-2K, which without molecular entanglement, may act to plasticize the network. The addition of the tougher PLA-2K

Table 2. Mechanical Properties of Pure Crosslinked PEGDMA (Poly(PEGDMA)) and Its Blends with PLA

	PEGDMA	50% PLA-2K	30% PLA-63K	PLA[32]
tensile break strength (MPa)	1.3 ± 0.1	1.0 ± 0.1	3.7 ± 0.5	34.0
tensile break strain (%)	5.4 ± 0.7	14.4 ± 0.5	17.3 ± 2.2	4.0
elastic modulus (MPa)	28.8 ± 3.2	9.4 ± 0.5	65.6 ± 13.9	2600.0
area under stress−strain curves (J/m)	3.6 ± 0.5	7.2 ± 0.2	32.1 ± 5.7	N/A

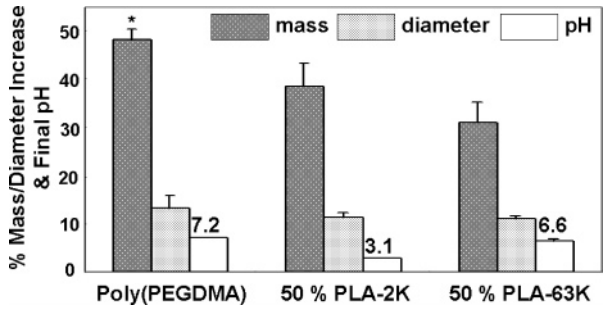

Figure 6. Final pH of the PBS solution and the percent of mass or diameter increase of poly(PEGDMA), 50% PLA-2K, and 50% PLA-63K blends, after soaking in 0.01 mol/L PBS solution for 14 d at a soaking ratio of 1 g of specimen per 30 mL of PBS solution. Star indicates statistical differences.

into the more brittle cross-linked PEGDMA matrix greatly improves the break strain of the blend and the work of fracture.

Compared to PEGDMA networks alone, PEGDMA/PLA blends show versatile mechanical properties depending on the PLA molecular mass and composition. Both PLA-63K and PLA-2K blends greatly improve the toughness of the pure PEGDMA network. PLA-63K blends are significantly stronger and stiffer than cross-linked PEGDMA; by contrast, PLA-2K blends are somewhat weaker and less stiff than cross-linked PEGDMA, illustrating the effect of molecular mass of PLA on the mechanical properties of these blends. The mechanical properties of blends are expected to increase with increased PLA content and molecular mass. This study demonstrates that facile and simple blending methods can be used to control the mechanical properties (e.g., modulus, strength, and toughness) of polymeric blends synthesized by the photoinitiated polymerization.

In Vitro Soaking in PBS. All samples swell significantly after soaking in PBS for 2 weeks (Figure 6). The mass increase for the cross-linked PEGDMA is higher ($p < 0.05$) than that for the blends. However, the increase in specimen diameter is not statistically different among the three samples. As illustrated in Figure 6, the pH of PBS is relatively

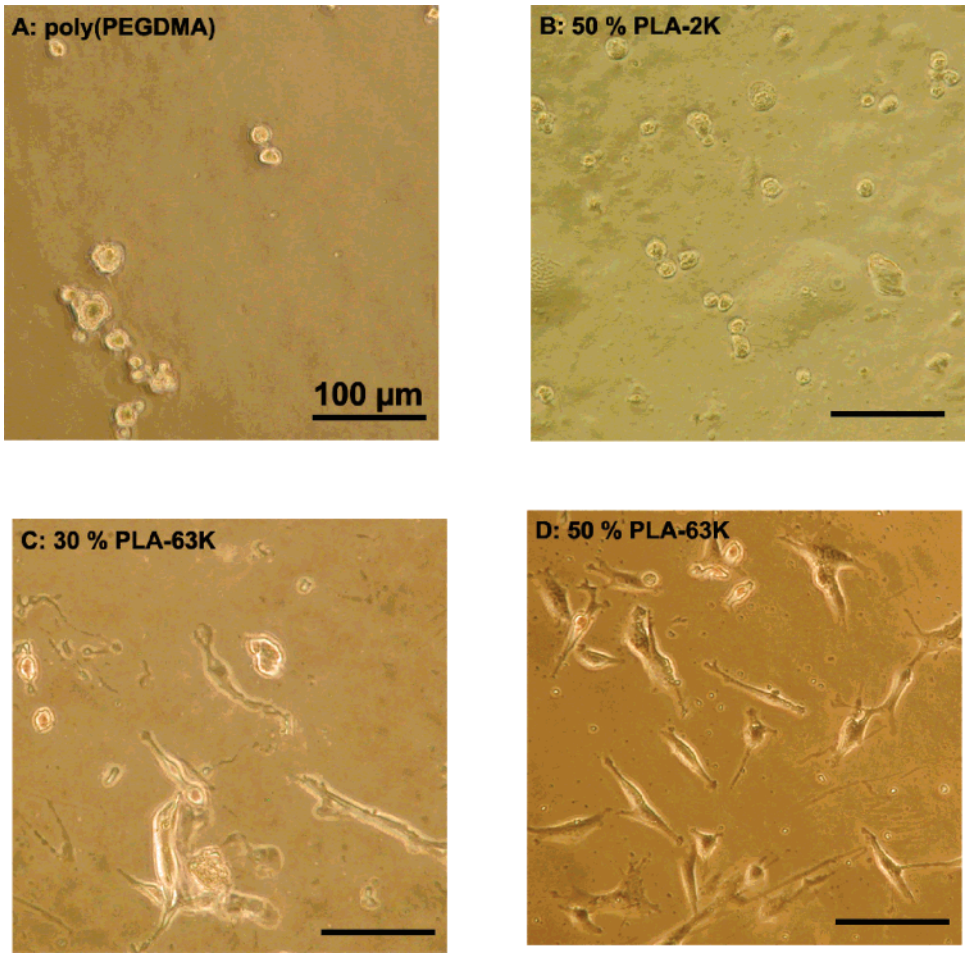

Figure 7. Phase contrast microscopy images of (A) poly(PEGDMA), (B) 50% PLA-2K, (C) 30% PLA-63K, and (D) 50% PLA-63K after cell culture for 1 d. Scale bar: 100 μm.

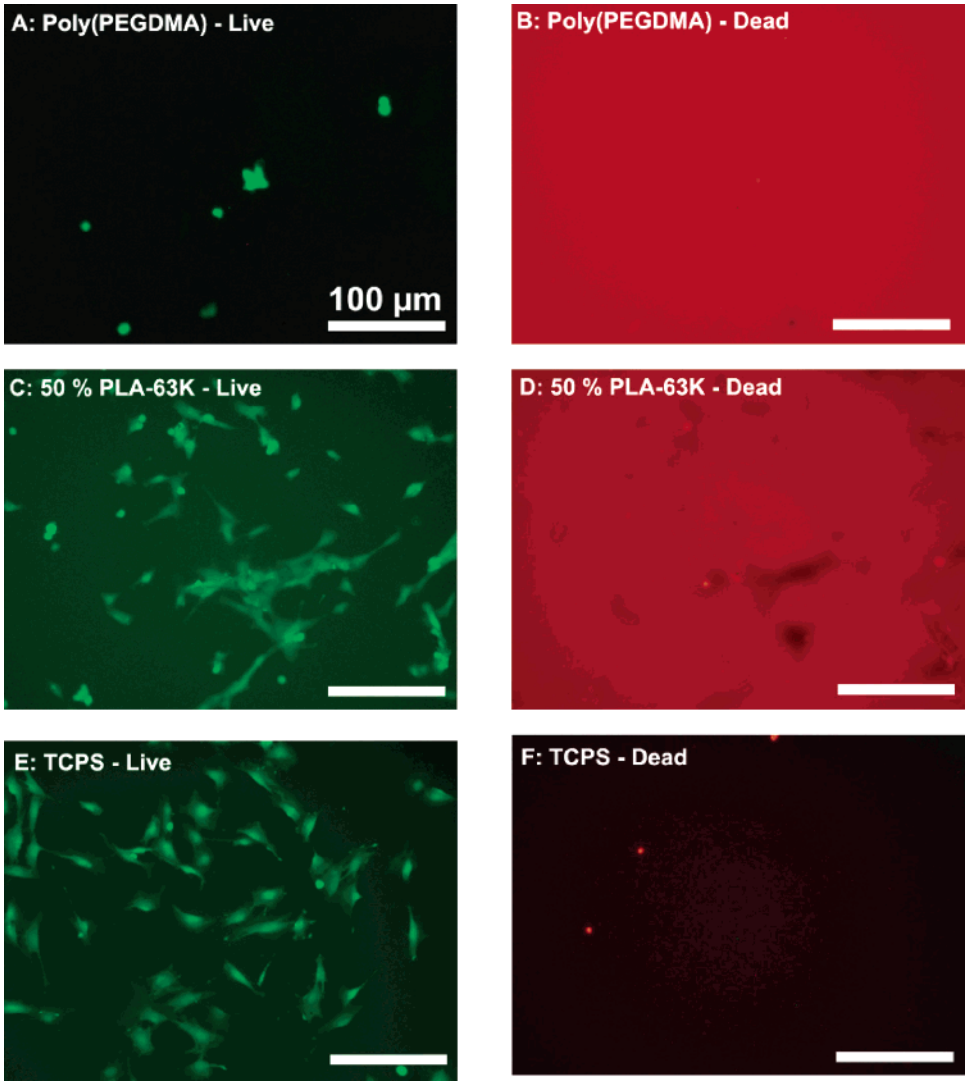

Figure 8. Fluorescence microscopy of cells cultured on poly(PEGDMA) and its blends with PLA for 1 d. (A, B) poly(PEGDMA). (C, D) 50% PLA-63K. (E, F) control: tissue culture polystyrene (TCPS). (A), (C), and (E) are live stained cells and (B), (D), and (F) are dead stained dead cells. Images on the left and right are the same field of view with different fluorescence filters (Left: green, live; Right: red, dead). Scale bar: 100 μm.

unchanged with cross-linked PEGDMA, moderately lowered with the 50% PLA-63K blend, but dramatically decreased with the 50% PLA-2K blend.

The mass and dimensional increases of the cross-linked PEGDMA are expected due to its hydrophilic nature. Water diffuses into the cross-linked PEGDMA moiety, thereby increases the mass and causes the specimens to swell. However, the mass and diameter changes of the PLA blends may be a combination of water absorption by the hydrophilic PEGDMA and mass loss of PLA (as indicated by the pH decrease in the medium). The mass loss of PLA could either be from the leaching or degradation of PLA, which is consistent with the decreased pH in PBS. Separate degradation studies will be investigated to determine the degradation behavior of these blends.

In Vitro Cell Culture. Phase contrast microscopy (Figure 7) and fluorescence microscopy (Figure 8) were used to characterize specimens after 1 d culture with MC3T3-E1 osteoblast-like cells. Cells remain viable on the cross-linked PEGDMA, as demonstrated by the live/dead staining (Figure 8A). It should be noted that, although cells adhered and spread on the TCPS around the sample (not shown), cells appeared to be rounded and clumped on cross-linked PEGDMA surfaces (Figures 7A and 8A), indicating that cells did not adhere well on the cross-linked PEGDMA. Similar nonadhering behavior, due to the protein resistant properties of PEG-based hydrophilic polymers, has been documented.[33]

Light microscopy results show that osteoblast-like cells did not exhibit their normal adherent morphology and appeared rounded on and around the 50% PLA-2K blends (Figure 7B). Moreover, live/dead staining shows that the cells are dead both on and around the specimens (i.e., TCPS). The in vitro soaking tests in PBS suggest that the medium containing the 50% PLA-2K blend became acidic. The pH of the culture medium after 1 d of cell culturing with 50% PLA-2K specimens indeed decreased significantly, as indicated by the change of medium color from red (i.e., neutral pH) to yellow (i.e., acidic pH). Even though the 50% PLA-2K specimens were pre-extracted before the cell experiments, low molecular mass lactic acid likely remains in the specimens during cell culture and cause a lowering of the pH and cell death.

Live/dead staining shows that cells on both 30% PLA-63K and 50% PLA-63K specimens were viable (Figure 8, parts C and D). In addition, the number of cells that adhered and spread on the specimens increased with the PLA-63K content in the blends (Figure 7, parts C and D). As observed under light microscopy, the degree of cell adhesion and spreading on 50% PLA-63K blends is comparable to that of the control (TCPS) after 1 day.

High molecular mass PLA is biocompatible and supports osteoblasts adhesion and spreading.[34] Previous studies have investigated the possibility of adjusting the cellular behavior of PEG-based polymers through their block copolymers.[4] In this study, blending with PLA-63K offers a simple method to control the cellular behavior (e.g., cell adhesion and spreading) of cross-linked PEGDMA.

Conclusions

Miscible or partially miscible blends of cross-linked PEGDMA and PLA were prepared using a combination of blending and photopolymerization processes. Through a careful selection of components (e.g., the molecular mass and mass fraction of PLA) and control of the processing conditions (e.g., photopolymerization period), the properties of blends such as DC, mechanical properties, swelling, and cell adhesion can be modified or enhanced compared to cross-linked PEGDMA alone. Photopolymerizable PEGDMA/PLA blends, as a prototype model system, represent a class of biomaterials derived from the blending of biocompatible polymers with polymerizable moieties. Compared to copolymerization approaches,[8−10] the processing method used in this study provides a strategy for preparing biocompatible blends with a broad spectrum of properties from a variety of polymers and photopolymerizable monomers, oligomers, or macromers. Likewise, blends using the method developed from this study may provide more material choices and superior properties for applications in tissue engineering, drug delivery, and tissue sealant.

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