BIOCOMPATIBLE POLYMER BLENDS DERIVED FROM THE PHOTOPOLYMERIZATION OF POLYETHYLENE GLYCOL DIMETHACRYLATE-POLYLACTIDE MIXTURES*

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Introduction

Polyethylene glycol dimethacrylates (PEGDMAs) have been used as a resin component in dental applications and have been polymerized to form hydrogel with potential for soft tissue engineering.[1,2] PEGDMAs with high ethylene oxide (-CH_2CH_2O-) content are hydrophilic but relatively non-biodegradable. Previous research has also demonstrated that PEGDMAs are biocompatible *in vitro* with cells.[2]

Polylactide (PLA), an α-polyester that is biodegradable and biocompatible, has found use in a number of clinical applications.[3] PLA and its copolymers, e.g., poly (D,L-lactic-*co*-glycolic acid), and ABA type block copolymers of PLA and polyethylene glycol (PEG), have also been extensively studied as biomaterials for drug delivery and tissue engineering.[4]

Blending polymers is a low cost method to engineer materials with unique properties that cannot be achieved by the individual component.[5] For example, compared to the PLA or PEG components, blends of PLA and PEG were found to have different mechanical, thermal and degradation properties.[6] On the other hand, photopolymerization of monomer mixtures is widely used in dentistry to control the properties of polymeric matrices. A typical monomer system is composed of 2,2-bis[p-(2'-hydroxy-3'-methacryloxypropoxy)phenyl] (Bis-GMA) and triethylene glycoldimethacrylate (TEGDMA).[1]

In this study, blends of an activated PEGDMA monomer and a PLA polymer were prepared and subsequently photopolymerized to yield blends of poly(PEGDMA) with PLA. The effects of PLA content on miscibility, degree of vinyl conversion of the PEGDMA, the rheological and mechanical properties, and *in vitro* swelling behavior in a phosphate buffered saline (PBS) solution of the polymeric blends were studied. PEGDMA-PLA blends have potential application in the tissue engineering field and as novel tissue sealants due to their unique adhesion properties that will be addressed in a separate study.

Experimental

Materials. The PEGDMA monomer (number average molecular mass: 875 g/mol), camphorquinone (CQ) and ethyl 4-N,N-dimethylaminobenzoate (4-E) were purchased from Aldrich Corp. Phosphate buffered saline (PBS) was purchased from Sigma-Aldrich Corp. PLA (Resomer104, number average molecular mass: 2096 g/mol) was purchased from Boehringer Ingelheim Inc. The PLA particles were ground using a pestle and then sieved to achieve a particle size of less than 74 μm.

Preparation of poly(PEGDMA)-PLA Blends. The PEGDMA monomer was activated for blue light photopolymerization with 0.2 % CQ and 0.8 % 4-E (by mass fraction). PLA particulate powder was then mixed with the activated PEGDMA monomer at 10 %, 30 %, 50 % and 70 % (by mass fraction). These mixtures were stirred and then heated at 60 °C in an oven overnight to yield homogeneous liquids of increasing viscosities. These homogeneous liquids, composed of activated PEGDMA and PLA, were then poured into a mold sandwiched between mylar films and glass slides. Polymeric disks (approximate thickness of 1 mm and diameter of 10 mm) of poly(PEGDMA) and poly(PEGDMA)-PLA blends were prepared by visible light (wavelength = 470 nm) photo-polymerization of homogeneous mixtures for 120 s in a dental curing unit (Triad 2000 from Dentsply International Inc., with an approximate light intensity of 35 mW cm^{-2}, as measured by a radiometer at the specimen position) for further characterization.

Rheological Testing. Rheological properties of the PEGDMA monomer and the PEGDMA/PLA mixtures were studied by a Rhometrics ARES rheometer. Dynamic frequency sweeps and steady shear rate viscosities were measured using a cone-and-plate geometry (25 mm diameter, 0.1 rad).

Thermal Analysis. Thermal properties such as glass transition temperatures (Tg) of photopolymerized PEGDMA and PEGDMA/PLA blends were characterized by differential scanning calorimetry (DSC) (TA instruments Inc., Model: Q1000). All samples were subjected to two heating-cooling cycles at a ramp rate of 5 °C/min: First they were heated up to 100 °C, then held for 5 min, and then cooled to –80 °C.

Degree of Conversion (DC). The DC of PEGDMA/PLA blends and PEGDMA (control) after photopolymerization was determined using Fourier transform infrared spectrometry (FT-IR) (Magna 550, Nicolet Inc.). Uncured samples were first put between two KBr pellets that had been fixed on standard IR cards. IR spectra of samples before and after curing (120 s) were then collected. The DC was calculated using the area under a C=C absorption peak at 1637 cm^{-1}, utilizing the methacrylate carbonyl as an internal standard.

Mechanical Testing. Tensile tests of poly(PEGDMA) and poly(PEGDMA)-PLA blends (50 % PLA by mass fraction) were performed with a universal testing machine (Instron, model: 5500R) with a load cell of 100 N and a cross-head speed of 1 mm/min. Dog-bone shape specimens (length = 60 mm and width = 10 mm) were prepared in a mold by photopolymerization of the activated PEDGMA and PEGDMA-PLA blends.

***In Vitro* Soaking In Phosphate Buffered Saline (PBS).** Photopolymerized PEGDMA and PEGDMA-PLA blend (50 % PLA by mass fraction) disks (diameter = 10 mm and thickness = 1 mm) were soaked in a 0.01 mol/L phosphate buffered saline (PBS) solution, 25 mg sample/mL PBS. After soaking samples for 2 weeks, mass and dimensional changes were determined by differential weighing and differential size measurements using a caliper, respectively.

Statistical Analysis. Statistical analyses (n = 5) of the data of 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

Before photopolymerization, homogeneous mixtures of the PEGDMA and PLA were characterized as Newtonian fluids as determined by the steady shear viscosity measured as a function of shear rate (data not shown). Figure 1 shows the dynamic frequency sweep for PEGDMA and PEGDMA-PLA blends. In the frequency range studied, all samples showed a terminal relaxation behavior with G' (storage shear modulus) $\propto \omega^2$ (frequency) and G" (loss shear modulus) $\propto \omega$. Viscosity of the mixtures increases with increased PLA content and ranged from 0.1 (PEGDMA alone) to 10 $Pa{\cdot}s^{-1}$ (50 % PLA-PEGDMA blend).

After photopolymerization, the as-prepared poly(PEGDMA) and the poly(PEGDMA)-PLA blend specimens are transparent. DSC results confirm the good miscibility in the blends: a single glass transition was observed for all the blends. Furthermore, T_g of the blends is compositionally dependent and increases with the addition of PLA in the blends. The Fox equation is often applied to describe the compositional dependence of polymer blends:[7,8]

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

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. Figure 2 shows the calculated T_g of the blends from the Fox equation and the experimental T_g of the blends from DSC data. The experimental data are in good agreement with the values calculated by the Fox equation.

Figure 3 shows the DC of PEGDMA and its PLA blends after photo-polymerization. The average DC of the PEGDMA and the blends (10 % and 50 % PLA by mass fraction) are 83 %, 81 %, and 84 %, respectively. However, no statistical difference in DC was found between PEGDMA and the blends. Previous studies show that the addition of inorganic fillers or other additives can influence the DC of matrix dental resin monomers.[1,9] Adding low molecular mass PLA to the matrix-forming PEGDMA, however, does not change the DC of PEGDMA. It appears that the addition of the low molecular mass PLA (despite the increasing viscosity) does not interfere with the vinyl conversion of PEGDMA during photo-polymerization. However, FT-IR analyses of blends composed of the same photoactivated PEGDMA but with a high molecular mass PLA (molecular mass = 100,000) showed that the addition of the high molecular mass PLA significantly decreased the DC of PEGDMA (data not shown).

The poly(PEGDMA) and a poly(PEGDMA)-PLA blend (50 % PLA) have different tensile mechanical properties. Table 1 shows the tensile break strength, elastic modulus and break strain of poly(PEGDMA) and the blend. Poly(PEGDMA) has a statistically significant higher strength and modulus but a lower strain than those of its 50 % blends with PLA. The slight differences

Table 1. Tensile Mechanical Properties of poly (PEGDMA) and poly(PEGDMA) Blends with 50% PLA (By Mass Fraction)

Specimens	Break Strength [MPa]	s.d	Elastic Modulus [MPa]	s.d.	Break Strain [%]	s.d.
PEGDMA	1.33	0.06	15.9	1.7	9.0	1.2
PEGDMA-PLA	1.00	0.02	5.1	0.3	24.4	0.8

Standard deviations (s.d.) represent a measure of the standard uncertainty of these measurements.

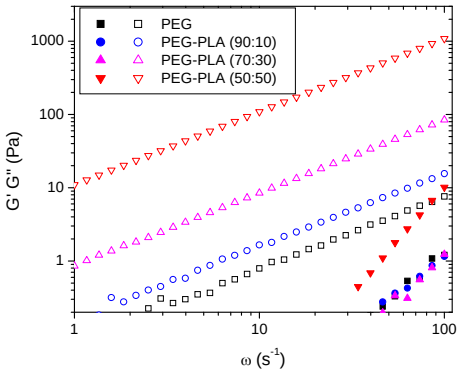

Figure 1. Dynamic frequency sweep of PEGDMA (designated here as PEG) and mixtures composed of the PEGDMA monomer and PLA.

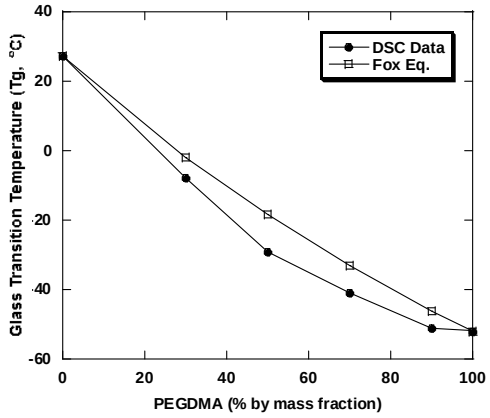

Figure 2. Variation of the calculated and experimental glass transition temperatures (T_g) with the composition of PEGDMA-PLA blends.

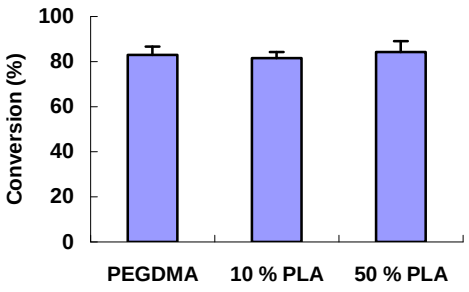

Figure 3. DC of PEGDMA and blends after photopolymerization. Error bars denote are standard deviation, and represent a measure of the standard uncertainty.

in strength (1.33 MPa ± 0.06 MPa of poly(PEGDAM) vs. 1.00 MPa ± 0.02 MPa of the blend) may be due to the introduction of defects during the preparation of the
blend. The decease in elastic modulus of the blend is due to the addition of low molecular mass PLA, which is less stiff than the crosslinked PEGDMA matrix. The addition of the relatively tough PLA into the relatively brittle poly(PEGDMA) matrix greatly improves the break strain of the blend. It was also noticed that the work of fracture (the area under the tensile stress-strain curve) is about twice as high for the blend than for the poly(PEGDMA) alone. Although the current tensile tests showed interesting mechanical properties of the polymeric blend, the low break tensile strength and elastic modulus may present challenges to their potential biomaterials applications. Blends composed of high molecular mass PLA hold promise due to the better PLA mechanical properties. Therefore, a new set of blends consisting of Poly(PEGDMA) with high molecular mass PLAs is under development and will be reported in the near future.

After soaking in PBS for 2 weeks, both poly(PEGDMA) and poly(PEGDMA) blends with 50 % PLA exhibited marked swelling. The mass increases are 59.9 % ± 1.5 % and 57.4 % ± 6.2 % for poly(PEGDMA) and the polymeric blend, respectively (no statistical difference). Because the poly(PEGDMA) specimens were broken into pieces during soaking, only the dimensional changes of the polymeric tougher blend were measured. The mean diameter increase of the polymeric blend disks is 19.0 % ± 0.3 % after soaking. The mass and dimensional increases of the polymeric blend may be due to the hydrophilic nature of poly(PEGDMA) and the low molecular mass of the PLA.

Future studies will assess the *in vitro* cellular biocompatibility of various poly(PEGDMA)-PLA blends compared to poly(PEGDMA).

Summary

Miscible liquid blends of photoactivated PEGDMA and low molecular mass PLA were prepared by simple heating. Subsequent photo-polymerization of the activated PEGDMA and PLA yielded clear polymeric blends. The addition of low molecular mass PLA did not change the DC but enhanced the toughness of poly(PEGDMA). This increase in the toughness of poly(PEGDMA) represented a significant improvement in mechanical behavior. Photopolymerizable PEGDMA-PLA blends offer a unique approach to a new class of biomaterials derived from the blending of biocompatible polymers with polymerizable, biocompatible monomers. This novel processing method provides a strategy for preparing polymer blends with a wide spectrum of properties from miscible polymers and photo-polymerizable monomers or oligomers.

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Disclaimer

Certain commercial materials and equipment are identified in this work for adequate definition of the experimental procedures. In no instance does such identification imply recommendation or endorsement by the National Institute of Standards and Technology that the material and the equipment identified is necessarily the best available for the purpose.

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