

Spontaneous Transesterification Reactions Between Poly(lactide-*co*-glycolide) and Poly(trimethylene carbonate) at the Interface

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ABSTRACT: Poly(lactide) (PLA) and its copolymers can be made from naturally occurring materials. They are ideal candidates as sustainable materials to replace the petroleum based polymers. However, these polymers often are brittle so toughening is needed. One of the most effective toughening methods is to reactive blend brittle polymers with materials having very different rigidity. This approach requires that the two materials chemically bond with each other at the interface to compatibilize the blends. Thus, to design and make reactive systems is a key to the success of reactive blending. In this article, we studied toughening poly(lactide-*co*-glycolide) (PLGA) with a rubbery material poly(trimethylene carbonate) (PTMC). We observed that PTMC spontaneously reacted with PLGA during melt blending. The reaction produced

PLGA-*co*-PTMC copolymers that stayed at the PLGA/PTMC interface. Those copolymers not only helped to create a stable blend microstructure at a length scale of 100 nm but also promoted the bonding between the PLGA and PTMC domains. It is interesting that the reaction did not need a catalyst or initiator. We speculated that this reaction between PLGA and PTMC was a transesterification reaction. This reaction is easy to achieve and is expected to broaden the property range of the PLGA and other degradable polyesters, enabling them to replace certain types of petroleum based polymers. © 2010 Wiley Periodicals, Inc. *J Appl Polym Sci* 117: 2153–2158, 2010

Key words: sustainable polymers; toughening; degradable polymers; reactive blending; transesterification

INTRODUCTION

Poly(lactide) (PLA) is considered to be ideal renewable material to replace petroleum based polymers such as polypropylene and polystyrene.^{1,2} PLA and its copolymers have also been extensively studied for biomedical applications, such as controlled drug delivery, engineered tissue replacements, and other implantable medical devices.^{3–7}

PLA and its copolymers are strong and rigid, but brittle. Toughening PLA has been an important research topic.⁸ Various polymers such as polycaprolactone (PCL) and polyethylene have been studied to toughen PLA and proved being effective. However, these polymer are not compatible with PLA; copolymers such as poly(caprolactone-*co*-lactide) and poly(ethylene-*co*-lactide) have been added to the blends for good compatibilities.⁸

poly(trimethylene carbonate) (PTMC) has also been used to toughen PLA.⁹ It is a rubbery material at room temperature and can degrade through en-

zymatic degradation. The toughened materials can degrade completely, which is attractive for medical applications. To achieve good interfacial bonding for toughening, PTMC-*co*-PLA copolymers were premade and added into the blends for compatibilization.⁹ However, copolymers generally are difficult to make. Dispersing premade copolymers in blends is not efficient. Thus, addition of premade copolymers has not been used broadly.¹⁰ A more effective approach for compatibilization is reactive blending, a strategy to make copolymers *in situ* during melt blending. This reactive blending has been demonstrated to be more effective.¹¹ However, reactive blending systems usually need specially designed polymers or additives. In this article, we studied the reactions between PTMC and poly(lactide-*co*-glycolide) (PLGA) during blending. We observed that the reaction between these two polymers spontaneously occurred at melt blending temperature (~ 200°C). There is no need to use specially designed materials. The copolymers resulted from the reaction compatibilized the blends. We studied this reaction with thermal analysis, electron microscopy, and molecular weight measurements. This observed reaction is expected

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TABLE I
Characteristics of Polymers Used in this Work

Polymer	Supplier	M_n (kg/mol)	M_w/M_n
PLGA	Boehringer Ingelheim	440	1.4
PTMC	Synthesized in house	220	1.4
PLLA	Toyota motor	56	1.3
PCL	Aldrich	80	1.2
PTMC-anth	Synthesized in house	20	1.3
PLA-co-PTMC	Boehringer ingelheim	NA	NA

to provide a more effective and easier option for PLA toughening.

EXPERIMENTAL

Materials

Characteristics of the polymers used in this study are listed in Table I. Random copolymers PLGA (L/G = 85/15 wt) and poly(L-lactide-co-trimethylene carbonate) (L/TMC = 70/30 wt) PLA-co-PTMC were bought from Boehringer Ingelheim (Germany). PCL was bought from Aldrich. All these polymers were used as received.

PTMC was synthesized through ring opening polymerization. Trimethylene carbonate (500 g, from Boehringer Ingelheim and used as received) and tin 2-ethylhexanoate (7.5 mL, 9% in toluene, Aldrich) were added into a 1 L round bottom flask in a dry box. The flask was vacuum/purged with nitrogen for three cycles then heated slowly under nitrogen to 140°C in an oil bath. The reaction mixture was further heated under nitrogen at 160°C overnight (*ca.* 16 h). After reaction, the mixture was dissolved in THF followed by precipitating in methanol. Purification was repeated three times by dissolving in THF and precipitating in methanol to remove residual monomer and low molecular weight oligomers. The polymers were dried in a vacuum oven until no weight change can be observed. Typically, yield was above 85%. Anthracene-labeled PTMC (PTMC-anth) was made by polymerizing TMC with 9-anthracenemethanol (Aldrich) as the initiator and tin 2-ethylhexanoate as the catalyst.

The molecular weights of these polymers were measured by size exclusion chromatography (SEC, Agilent 1100 unit equipped with Phenogel 5 micron columns), using tetrahydrofuran (THF) as the mobile phase with a flow rate of 1 mL/min. The molecular weight was obtained for all the samples based on the coupled light scattering (measured at 18 angles with Dawn EOS, Wyatt) and RI detection (Optilab DSP, Wyatt). A fluorescence detector (G1321A, Agilent) was used to detect the PTMC-anth at the excitation wavelength of 358 nm and the emission wavelength of 402 nm.

Blend preparation

The composition of the blends studied in this work was summarized in Table II. Three blends were made through melt blending (LGT-*m*1, LGT-*m*2, and LGT-anth-*m*), where LG stands for PLGA, T for PTMC, T-anth for fluorescence-labeled PTMC, and *m* for melt blending). Two blends were made through solvent blending (LGT-*sol* and LGT-anth-*sol*, where *sol* stands for solvent blending). Before blending, all the polymers were dried with a desiccant dryer (Dri-Air hopper dryer) at 57°C for 12 h. Melt blending was done with a batch mixer (Haake, Germany) at 180–215°C and a blade rotation speed of 50–100 rpm. The blending time was 7 min for LGT-*m*1 and LGT-*m*2. A small piece of blend was sampled at 1, 3, 7, and 12 min for LGT-anth-*m*. After blending finished, the samples were pressed immediately with a hot press at 225°C for 4 min followed by quenching to room temperature within 1 min. The intermediate samples of LGT-anth-*m* were quenched in liquid nitrogen.

For solvent blending, PLGA and PTMC were dissolved in chloroform separately at a concentration of about 2 wt %. The two solutions were then mixed at a PLGA/PTMC ratio of 80/20 (wt) by stirring at room temperature for 12 h. After that, the solvent was evaporated by continuously purging the flask with dry nitrogen. Then the blends were further dried in a vacuum oven at 40°C for 2 weeks.

Thermal analysis

Differential scanning calorimetry (DSC) was performed on a PerkinElmer Pyris unit with about 10 mg of polymer samples. To remove thermal history of the samples, the samples were first annealed at 150°C for 2 min and then cooled to -40°C at 20°C/min and held for 2 min. The samples were then heated at a rate of 20°C/min from -40 to 150°C. The glass transition temperatures (T_g) of the polymers and the blends were determined as the onset temperature of the transitions.

TABLE II
PLGA/PTMC Blends and the Blending Methods.
The Weight Ratios of PLGA to PTMC for All the
Blends are 80/20

Blend	Added copolymer (wt)	Blending methods
LGT- <i>m</i> 1	0	Melt blending
LGT- <i>m</i> 2	2%	Melt blending
LGT- <i>sol</i>	0	Solvent blending
LGT-anth- <i>m</i>	0	Melt blending
LGT-anth- <i>sol</i>	0	Solvent blending

Morphology characterization

The morphology of the blends was characterized using transmission electron microscope (TEM, Jeol 1210). To increase contrast between PLGA/PTMC, the blend was stained with RuO_4 .¹² The stained blends were then microtomed into 70 nm thick slices at room temperature using a diamond knife. Scanning electron microscope (SEM, Jeol JSM-5900LV) was also used to determine the morphology of some blends. The fractured surface of the blends was prepared by fracturing a piece of sample in liquid nitrogen. The surface was coated with a 5-nm thick Pt layer to prevent static accumulation.

RESULTS AND DISCUSSIONS

PLGA and PTMC have strong interfacial bonding

The glass transition temperatures of PTMC and PLGA (DSC measurements) are -8 and 62°C , respectively. The blends of these two polymers (PTMC/PLGA weight ratios from 5/95 to 50/50) all have two glass transitions around the T_g s of the two component polymers. This indicates that PLGA and PTMC are thermodynamically immiscible with each other and they do not mix at a molecular level. As shown in Figure 1, PLGA (lighter domains) and PTMC (darker domains) were phase-separated, regardless of whether the blends were melt-mixed [Fig. 1(a,b)] or solvent-mixed [Fig. 1(c)]. Addition of PLA-co-PTMC copolymer did not cause any significant change in morphologies [Fig. 1(b)] compared to that without copolymer [Fig. 1(a)]. In all these cases, the size of the PTMC dispersed domains was about 100–500 nm.

The TEMs did not show significant difference between the morphologies of melt-mixed blends [Fig. 1(a,b)] and solvent-mixed blends [Fig. 1(c)]. However, in cryofractured surface, significant differences were observed between the solvent-mixed blends [low temperature, Fig. 2(a)] and melt-mixed blends [high temperature processing, Fig. 2(b,c)]. In the solvent-mixed blend (LGT-sol), small holes were seen on the fractured surface [Fig. 2(a), LGT-sol]. This indicates that the PTMC particles were pulled away during cryofracturing, which suggests the bonding between PLGA and PTMC in this blend was weak. In the melt-mixed blends LGT-m2 where PLA-co-PTMC was added [Fig. 2(b)], there was no obvious hole left on the fractured surface. This means that the bonding between PLGA and PTMC was strong and could survive the cryofracture processes. This strong interfacial bonding may be attributed to the copolymer added in the blend. However, it is interesting that there was no hole in the cryofractured surface in the PLGA/PTMC blend without

added PLA-co-PTMC copolymer [Fig. 2(c), LGT-m1]. The interfacial bonding in this blend must be strong. Therefore, although LGT-m1, m2, and LGT-sol had similar morphology, they had different interfacial

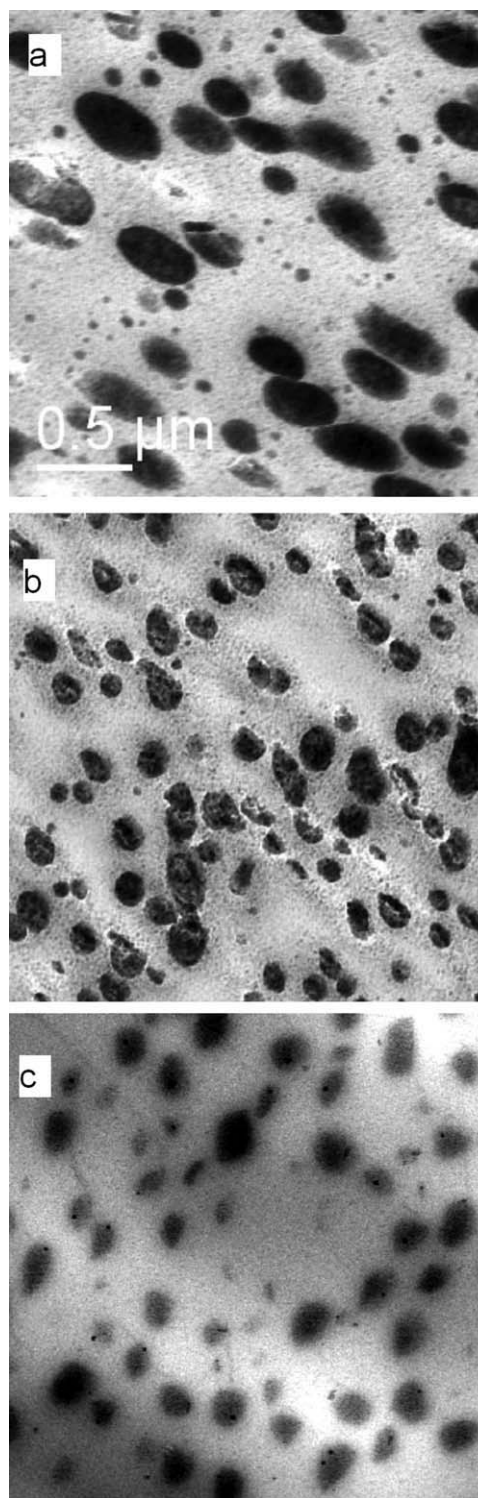


Figure 1 TEM morphology of the PLGA/PTMC blends. (a) melt blending without copolymer (LGT-m1), (b) melt blending with copolymer (2 wt %) (LGT-m2), and (c) solvent blending without copolymer (LGT-sol). The scale bars of all the three are the same.

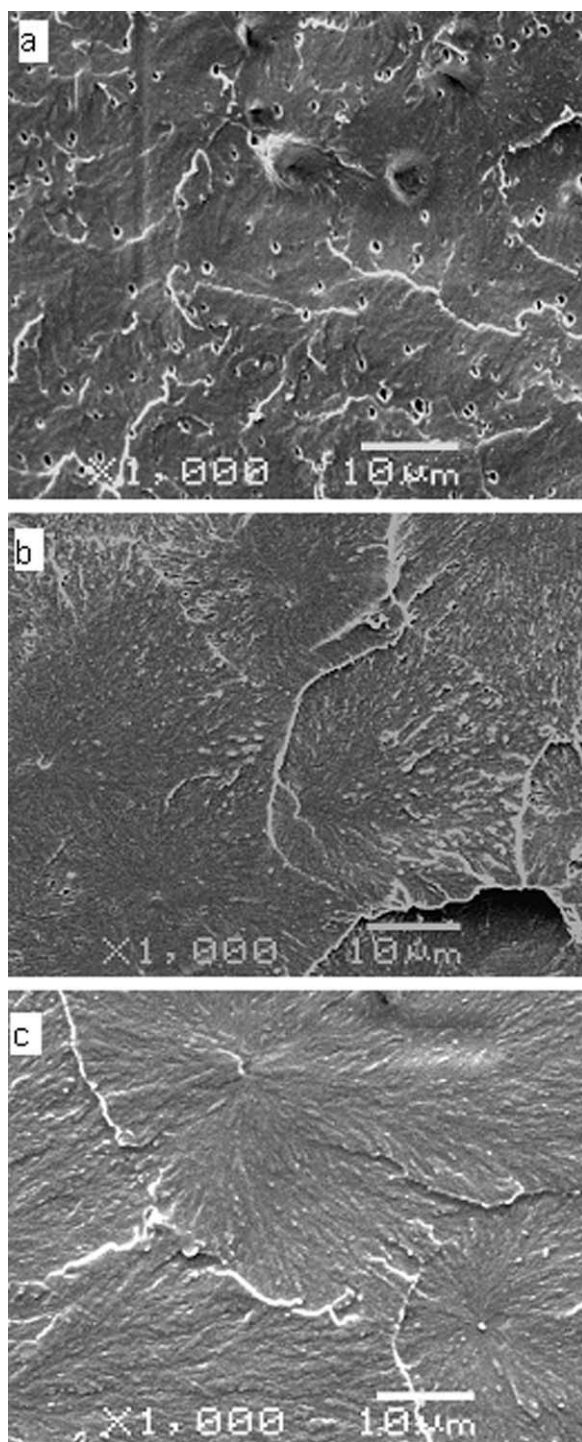


Figure 2 SEM images of cryofractured surfaces of (a) solvent-blended LGT-*sol* without copolymer, (b) melt-blended LGT-*m2* with 2 wt % copolymer, and (c) melt-blended LGT-*m1* without copolymer. There were holes in the solvent-blended sample because the dispersed domains fell off, indicating weak interfacial adhesion in this blend.

bonding. Overall, the melt-mixed blends had stronger PLGA/PTMC interfacial bonding than the solvent-mixed blend, regardless of whether the pre-made PLA-*co*-PTMC copolymer was added or not.

One speculated reason is the PLGA and PTMC must have reacted with each other during melt mixing and resulted in the formation of copolymers *in situ* at interface. These copolymers reinforced the PLGA/PTMC interfacial bonding. Such reaction did not occur in the solvent-mixed blend as the temperature was low compared to that for melt mixing. Therefore, the PLGA/PTMC interfacial bonding in solvent-mixed blends was weak. The reaction between PLGA and PTMC likely is a transesterification reaction that occurred at high temperatures during melt processing.

Transesterification

To prove the transesterification hypothesis, the products of the reactions need to be identified. However, it is not convenient to complete this with traditional analytical tools such as FTIR or NMR. The reason is that only a few bonds in a large polymer chain ($\sim 10^3$ bonds per chain) may be involved in the reaction. These traditional tools do not have enough sensitivity to detect this low reaction fraction. In this article, we studied the reaction using fluorescence-labeled polymers. Fluorescence labeling combined with size exclusion chromatography (SEC) has been used in the literature to monitor the extent of chemical reactions between reactive polymers during melt blending.^{13–16} The rationale is that if a fluorescence-labeled polymer reacts with a nonlabeled polymer that has a much higher molecular weight compared to the labeled one, the resulting copolymers from the reactions should have fluorescence-labeled segments and their molecular weights should be higher than that of the initially labeled one. When the reaction system is analyzed with SEC, this copolymer should be detected with a fluorescent detector without interference from either the initial labeled polymer (due to difference in molecular weight) or the nonlabeled polymer (due to lack of fluorescent activity).

Anthracene-labeled PTMC (PTMC-anth) was used for this purpose. Its molecular weight (20 kg/mol) was made much lower than that of the PLGA (400 kg/mol) such that if it reacts with the PLGA the product should have a molecular weight significantly higher than its own and can be easily identified (the unreacted high M_w PLGA is not detectable with the fluorescence detector). The blends were prepared through both melt blending (LGT-anth-*m*) and solvent blending (LGT-anth-*sol*) with the same compositions and following the same procedures as those used for LGT-*m1* or LGT-*sol*. The blends were dissolved in THF and a fluorescence detector coupled with SEC was used to test the molecular weight changes. Only PTMC-anth and any possible

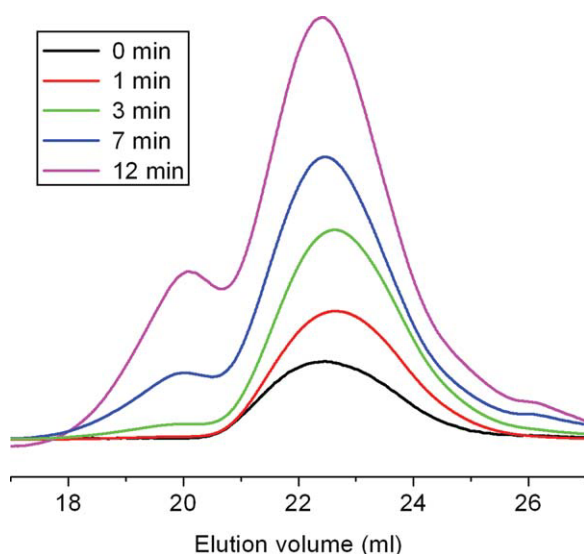


Figure 3 Molecular weight measurement (SEC) curves show the conversion of transesterification between PLGA/PTMC-anth as a function of reaction time. A high molecular weight copolymer (lower elution volume) was produced after melt blending. Because the PLGA was not detectable, only the PTMC-anth or PTMC-anth-co-PLGA was visible in the elution curves. Curves from the bottom to top represent the reactions of 0, 1, 3, 7, and 12 min.

product of PLGA-co-PTMC-anth copolymers are visible to the fluorescence detector.

Figure 3 shows the SEC curves from the fluorescence detector. The 0 min curve represents the starting PTMC-anth material. There was only one peak. This indicates that the initial material had one molecular weight component. After the PTMC-anth was melt-blended with the PLGA, a second peak at a lower elution volume (higher molecular weight) appeared. The peak height increased with increasing the melt blending reaction time. This indicates that a higher molecular weight polymer was produced with its production increasing with reaction time. The only possible explanation is that the PTMC-anth reacted with the PLGA and produced a higher molecular weight copolymer. However, in LGT-anth-sol, no extra peak was observed in the SEC curves, which suggested that no detectable reaction happened between these two polymers during solvent blending, a low temperature mixing process. Such results suggest the chemical reaction between the PLGA/PTMC occurred at high temperature during melt blending. The *in situ* formed PLGA-co-PTMC copolymers stayed at the PLGA/PTMC interfaces and reinforced the interfacial bonding.

Based on the earlier molecular weight results, it can be estimated that about 9.5% of the PTMC-anth reacted with the PLGA after 7 min. If we assume all the copolymers were at the interface, these copolymers could have an interfacial areal density of up to

0.014 chains/nm². This density is equivalent to a 10 nm distance between the copolymer molecules at the interface. The radius of gyration of the copolymer molecule is about 18 nm, estimated from the average molecular weight of PLGA and PTMC. Thus, these copolymer molecules touched each other at the interface. Because these copolymers are composed of PLGA and PTMC, they can effectively enhance the interfacial bonding between these two polymers.

Transesterification was reported occurring in bisphenol-A polycarbonate (PC)/poly(butylene terephthalate) (PBT) blends.¹⁷ The accepted reaction mechanism is that the carbonate groups and ester groups recombine or exchange, resulting in the formation of new carbonate and ester groups. At the molecular level, this reaction is a nucleophilic substitution reaction. We speculate that the reaction between PLGA and PTMC in the present system is also a transesterification reaction. It seems that the spontaneous transesterification reaction occurs only between polyesters and polycarbonates. To prove this, we repeated the same melt blending experiments with poly(L-lactide) (PLLA) and PCL blends. SEMs of cryofractured surface of the blends were shown in Figure 4; the PCL particles fell off from the PLLA matrix. This is similar to that of the solvent-mixed PLGA/PTMC blends (LGT-sol), except that the particles or holes were larger. This indicates that the interfacial bonding between PLLA and PCL was weak and no significant amounts of copolymers were produced. However, when a catalyst tin 2-ethylhexanoate was added to the system during melt

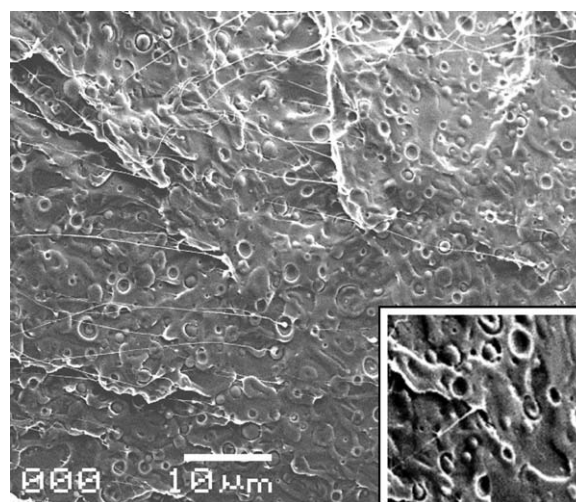


Figure 4 SEM of a cryofractured surface of the PLLA/PCL blend prepared through melt blending (the same way as the LGT-m1 was prepared. Figure 2(a). Inset was a higher magnification picture of the same fracture surface to demonstrate the dispersed PCL particles fell off from the PLLA matrix. This demonstrated that PLGA/PTMC had stronger interfacial adhesion than the present PLLA/PCL.



Figure 5 A piece of PLGA/PTMC (80/20 wt) film (about 1 mm thick) was placed over a word “Medtronic” (left). The word is legible. A piece of PLGA/PCL film with similar thickness was placed over a same word. The word is illegible (right). This indicates the PLGA/PTMC film is more transparent than the PLGA/PCL film. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

mixing, the blends became transparent. This change suggests that the dispersion domain sizes in the blends became smaller, indicating that some reaction between PLLA and PCL might occur after the catalyst was added. This observation was similar to what was reported by Harada.¹⁸ Comparing this with the PLGA/PTMC melt blend where transesterification occurred without a catalyst, one may speculate that polycarbonate (such as PTMC) is more susceptible to reactions with polyesters (such as PLLA or PCL).

The occurrence of transesterification between polycarbonates and polyesters can be spontaneous at high temperature; while that between polyesters needs added catalysts. Steric effects or electric characteristics of the carbonate groups may attribute to this high activity.^{19,20} For example, the carbon atom in the carbonate group of PTMC has a charge of 0.72 electrons, while the carbon atom of the ester group of PLGA has a charge of 0.56 electrons.²⁰ This higher charge in carbonate may make the groups more susceptible to nucleophilic attack compared to ester groups.

It is also important to notice that the present PLGA/PTMC blends are transparent even the system is immiscible. As shown in Figure 5, a piece of PLGA/PTMC blend film (about 1 mm thick) was placed over a word “Medtronic.” For comparison, a film of a PLGA/PCL blend (same matrix and thickness) was also placed over a same word. The word

underneath the PLGA/PTMC film is more legible than that underneath the PLGA/PCL blend. Transparency of a polymer is an important property for many applications. The good transparency of the PLGA/PTMC blends can be a big advantage for these materials to compete with others.

In summary, the PLGA/PTMC blends can be self compatibilized at melt processing temperatures. The blends have improved toughness and good transparency. It is expected that reactive blending with PTMC provides a convenient yet effective method to upgrade PLGA and other degradable polyesters.

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