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Biomaterials 21 (2000) 1181–1188

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**Biomaterials**

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# Photopolymers in orthopedics: characterization of novel crosslinked polyanhydrides

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Received 22 March 1999; accepted 5 January 2000

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## Abstract

Novel, high modulus, degradable polymers were prepared from methacrylated anhydride monomers of tricarballic acid (MTCA) and pyromellitylimidoalanine (MPMA-ala). Kinetic studies indicate that the time scale of photopolymerization of MTCA (< 30 s) is suitable for in vivo applications. Additionally, the tensile modulus of copolymers of these novel monomers with methacrylic anhydride (MA) ranged from 0.8 to 2.1 GPa, which lies between the modulus of trabecular and cortical bone. Degradation studies indicate that the copolymers of MTCA and MPMA-ala with MA are initially surface degrading, which is important to maintaining polymer strength through the degradation process. Monomers such as these that can be rapidly polymerized using ultraviolet or blue light into high modulus degradable materials have great potential in orthopedics. © 2000 Elsevier Science Ltd. All rights reserved.

*Keywords:* Crosslinked; Photopolymerizations; Degradable; Polyanhydrides

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## 1. Introduction

Traditional orthopedic fracture fixation technologies encompass autografts, allografts, and the use of permanent synthetic materials, such as metals and non-degradable plastics. Significant problems are associated with each of these techniques. For example, autografts cannot be used when large amounts of bone are required. Additionally, the site from which bone tissue is harvested may not recover to its preoperative state [1–3]. Allografts, on the other hand, overcome the bone supply problem, but they introduce foreign tissue that is accompanied by the risk of rejection [1–3]. Alternatively, permanent synthetic materials may be used, but they often become loose and irritating, requiring replacement or removal [1,2,4,5]. In the past 20 years, biodegradable rods and screws based primarily on poly(glycolic acid) (PGA) and poly(lactic acid) (PLA) have been successfully used in clinical settings but have been limited to low-load bearing applications due to insufficient strength [6]. Conse-

quently, a major area of research in biodegradable polymers for orthopedic applications is the development of higher strength materials [5,7–9].

This contribution reports on the development of novel photopolymerizable, biocompatible, degradable, crosslinking monomers based on methacrylated anhydrides. Photopolymerizable monomers have many advantages including easy processing into complex shapes by spatially controlling the incidence of light. Linear polyanhydrides have demonstrated biocompatibility through their successful use in drug delivery systems [10,11]; however, they do not have the required mechanical properties for many orthopedic applications. By crosslinking these polyanhydrides, a stronger network results. A photopolymerizable, crosslinking anhydride monomer that has been extensively studied in our lab is methacrylated sebacic acid (MSA) [12]. The tensile storage modulus of MSA lies between that of trabecular and cortical bone. Materials with increased modulus would expand the number of applications for which these novel materials are suitable.

Two avenues for increasing the modulus further are explored in this work. The first avenue is to increase the functionality of the crosslinking monomer. Increased monomer functionality has been shown to increase the crosslinking efficiency resulting in higher crosslink density [13] with a concomitant increase in modulus. MSA

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is a dimethacrylate; thus, a logical next step is to characterize the polymer developed from a trimethacrylate. The trimethacrylate monomer characterized in this study was methacrylated tricarballic acid (MTCA).

A second avenue for improving the efficiency of the crosslinking reaction is to use a stiffer monomer, which will be more likely to form effective crosslinks rather than primary cycles as compared to a more flexible crosslinking monomer [14–16]. Therefore, methacrylated pyromellitylimidoalanine (MPMA-ala) was studied because it incorporates a biocompatible aromatic imide [17] in the backbone of the polymer. Imides increase the rigidity of the backbone, which in and of itself leads to greater strength. Imides were initially incorporated into linear polyanhydrides by Staubli [18] in the form of trimellitic acid derivatives. Uhrich et al. [19] continued this work and developed imides based on pyromellitic anhydride and alanine. One potential drawback of the imide linkage may be brittle failure of the material; however, by copolymerizing monomers of varying composition this effect can be mitigated. Furthermore, a potential additional benefit of these imides is that they contain amino acids. This chemistry may be beneficial in future studies regarding biocompatibility. Biocompatibility of the linear polymer that incorporates PMA-ala has already been demonstrated [20].

## 2. Experimental section

### 2.1. Materials

Crosslinking methacrylated anhydride monomers were synthesized from multifunctional acids by reacting the acid with excess methacrylic anhydride at 80°C until the solid acid was consumed. A byproduct of the reaction is methacrylic acid. The general synthesis scheme for methacrylation of multifunctional acids is shown in Fig. 1.

Methacrylated sebacic acid (MSA) was synthesized from sebacic acid (SA; Aldrich, Milwaukee, WI) and methacrylic anhydride (MA; Aldrich, Milwaukee, WI). Both reagents were used as received. This synthesis has been described elsewhere [21]. Briefly, SA and MA were reacted to produce the methacrylated monomer. A rotary evaporator (Yamato Scientific America Inc., Orangeburg, NY) attached to a vacuum pump (BOC Edwards, Wilmington, MA) was used to remove the excess methacrylic anhydride and the methacrylic acid produced during the reaction. The methacrylated monomer was precipitated in petroleum ether (Fisher Scientific, Fair Lawn, NJ) and isolated by filtration. The MSA was dried in a vacuum dessicator and stored at 4°C. Proton nuclear magnetic resonance (NMR) spectroscopy (300 MHz Varian VXR-300S; Palo Alto, CA) was used to verify the structure of MSA and to determine the molecular weight.

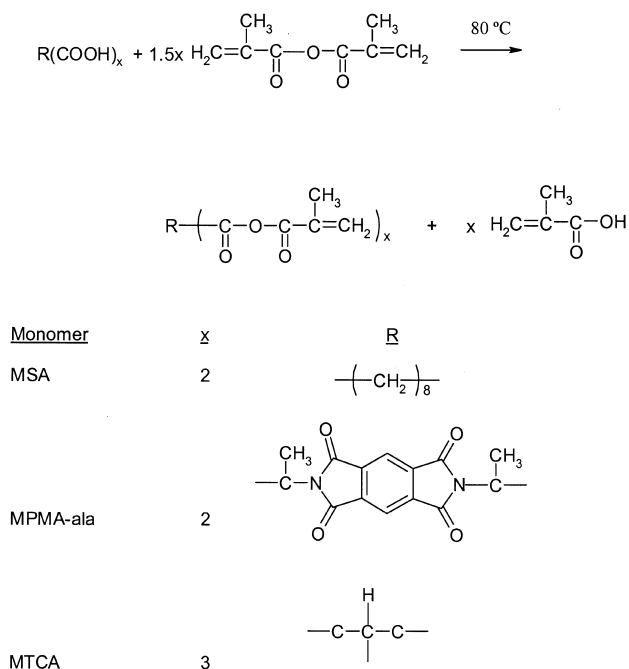


Fig. 1. Scheme for methacrylation of acid groups.

The ratio of the area of the methylene hydrogens ( $\delta 1.3$ ) to the area of the vinyl hydrogens ( $\delta 5.8$  and  $\delta 6.2$ ) indicated that, under our reaction conditions, MSA is an oligomer of 4.5 monomers, and thus has a molecular weight of 982 g/mol. The Fourier transform infrared spectroscopy (FTIR) spectrum (Nicolet Magna-IR 750; Madison, WI) of MSA showed the appearance of a carbon-carbon double bond peak at  $1640\text{ cm}^{-1}$  and the classic anhydride double peak at  $1810$  and  $1740\text{ cm}^{-1}$ .

Methacrylated tricarballic acid (MTCA) was synthesized similarly. Tricarballic acid (TCA; Aldrich, Milwaukee, WI) was used as received. MTCA was purified by washing in excess hexane (Fisher Scientific, Fair Lawn, NJ). This highly reactive solution was typically diluted with 20 wt% methacrylic anhydride and stored at 4°C. It is possible for both linear and ring containing oligomers to form during the reaction which presents difficulties during the interpretation of the NMR spectra. Thus, the molecular weight of the resulting trimethacrylate monomer was estimated by monitoring the polymerization reaction using both FTIR and differential scanning calorimetry (DSC). FTIR unequivocally determines the conversion of double bonds. Given the conversion of double bonds and knowing the theoretical heat evolved per double bond, heat release data from the DSC can be fit by adjusting the assumed functionality and molecular weight of the monomer. The functionality and molecular weight chosen corresponds to possible oligomers of the MTCA. Using this method, the best fit of the DSC data was obtained by assuming MTCA is

a trimethacrylate with a molecular weight of 911 g/mol. The FTIR spectrum of MTCA clearly shows the double peak of an anhydride linkage at 1790 and 1750  $\text{cm}^{-1}$  along with the carbon–carbon double bond peak at 1640  $\text{cm}^{-1}$ .

Pyromellitylimidoalanine (PMA-ala) was synthesized from 1,3,4,5-benzene tetracarboxylic acid dianhydride (PMA; Aldrich, Milwaukee, WI), and D,L-alanine (Aldrich, Milwaukee, WI) as described previously [19]. Briefly, PMA and alanine (used as received) were reacted together in DMF at reflux (153°C) for 18–24 h. A precipitate forms as the DMF is removed under vacuum. The precipitate is isolated by filtration, washed with deionized water and ethyl ether, and dried in a vacuum desiccator.

Methacrylated PMA-ala is synthesized as described above. The NMR spectrum of MPMA-ala indicated that MPMA-ala is primarily doubly methacrylated with no oligomerization (ratio of vinyl hydrogens  $\delta 6.2$  and  $\delta 5.8$  to the aromatic hydrogens  $\delta 8.3$ ). The FTIR spectrum shows the characteristic anhydride linkage with the dual carbon–oxygen double bond peaks at 1820 and 1750  $\text{cm}^{-1}$ . Additionally, the carbon–carbon double bond was present at 1640  $\text{cm}^{-1}$ .

### 3. Characterization methods

#### 3.1. Dynamic mechanical analysis

The tensile storage modulus of the crosslinked polymer networks at 37°C was determined using dynamic mechanical analysis (DMA7e; Perkin-Elmer, Norwalk, CT). Cuboid samples approximately 4 mm  $\times$  10 mm  $\times$  1 mm were prepared using 0.5 wt% 2,2-dimethoxy-2-phenylacetophenone (DMPA; Ciba-Geigy, Hawthorne, NY). This concentration of initiator allows 75% of the incident light to pass through the entire sample. The samples were polymerized for 10–30 min on each side using longwave UV light (Blak-Ray; UVP, Model B 100 AP, Upland, CA) with a light intensity of approximately 8 mW/cm<sup>2</sup>. These polymerization conditions were chosen to ensure that maximum conversion was consistently obtained for each monomer composition. The temperature scan experiments were performed in extension mode at 1 Hz, static control was 110% tension, and dynamic control was amplitude control (5–15  $\mu\text{m}$ ). Similar conditions have been used by others [12,13] for high modulus materials.

#### 3.2. Degradation study methods

Degradation studies were performed on disks that were 15 mm in diameter and 1.5 mm thick. The disks were degraded in 200 ml of phosphate buffered saline (PBS; LabChem Inc., Pittsburgh, PA) which has an initial

pH of 7.4. The buffer volume was chosen to ensure that degradation is not inhibited by saturation of the solution. The pH of the system was monitored and the buffer was changed when the pH dropped to 6.8 or less. The degradation temperature was 37°C. The temperature and pH targets were chosen to simulate physiological conditions. Studies were performed in a still water bath (Precision Scientific Inc., Chicago, IL) and weight and dimensional changes were measured periodically.

#### 3.3. Differential scanning calorimetry

Differential scanning calorimetry (DSC; Perkin-Elmer, Norwalk, CT) with a monochromatic photoaccessory was used to obtain rates of polymerization for the novel monomers and comonomer systems. Rates of polymerization are determined from heat release curves using a theoretical enthalpy of converting a double bond to a single bond of 13.1 kcal/mol for methacrylates [22]. The polymerizations were initiated with 1 wt% of DMPA.

#### 3.4. Fourier transform infrared spectroscopy

FTIR was also used to determine the conversion of the DMA samples. Conversion was estimated from the ratio of the area of the carbon–carbon double bond peak to the area of the anhydride peak. The anhydride peak does change shape as polymerization proceeds, so this method is only approximate.

## 4. Results and discussion

The suitability of a photopolymer for an orthopedic application is governed by the particular characteristics of the polymer. In this work, we focused on two critical questions for the newly synthesized photocrosslinkable monomers: (1) how do these monomers react; and (2) what are the properties of the polymer product once formed (mechanical and degradation).

#### 4.1. Characterization of reaction behavior

##### 4.1.1. Bulk polymerization rate

Characterization of the reaction behavior has several parts, one of which is determining the time it takes to polymerize these monomers to maximum conversion. Bulk polymerization time of the monomers impacts the ability to use these monomers in vivo (for example: filling a small bone defect in the operating room in a procedure similar to a dental restoration). Fig. 2 shows the rates of copolymerization of these monomers with MA compared to the homopolymerization of MA. Copolymerizations

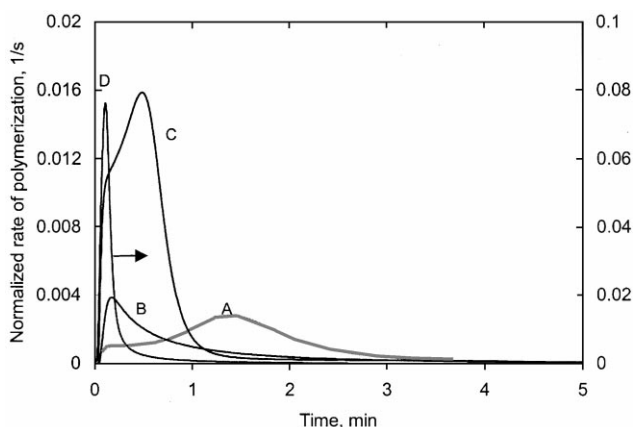


Fig. 2. Rates of polymerization for MA (A), 30/70 MA/MPMA-ala (B), 20/80 MA/MSA(C), and bulk MTCA(D). Polymerization temperature was 40°C using 1 wt% DMPA and a UV light intensity of 3 mW/cm<sup>2</sup>.

with MA are required to facilitate handling since MPMA-ala and MSA are solids at room temperature and MTCA is highly reactive. These curves illustrate the anomalous behavior that is characteristic of crosslinking behavior during the polymerization of multifunctional monomers including autoacceleration and autodeceleration. Compared to the homopolymerization of MA, the 30/70 wt% MA/MPMA-ala system reaches a slightly higher maximum rate, and the reaction is complete in a shorter time. Polymerization of a 20/80 wt% MA/MSA system results in a four-fold increase in the maximum rate and a decrease in the reaction time compared to the 30/70 wt% MA/MPMA-ala system. Bulk MTCA polymerizes 5-fold faster than the MA/MSA system. Studies performed on non-degradable monomers showed that trimethacrylates have higher rates of polymerization than comparable dimethacrylates [13], thus it is not surprising that the MTCA system has the highest rate of polymerization. Since MSA and MPMA-ala are both dimethacrylates, but are quite different chemically, the relative rates of polymerization depend on the reactivity of the methacrylate functionality in each environment. The MPMA-ala monomer is much more rigid, which limits the mobility of monomer, thus reducing the rate of polymerization and the final conversion of monomer to polymer.

Since maximizing the polymerization rate is an objective for a system used in vivo, the effect of comonomer concentration on the rate of polymerization was investigated. Fig. 3 illustrates the results for MTCA copolymerized with MA. Interestingly, the maximum rate of the homopolymerization of MTCA monomer is significantly faster than the maximum for the 30/70 wt% MA/MTCA system despite the slight differences in polymerization conditions. The extremely rapid rate of polymerization of bulk MTCA has tremendous advantages in

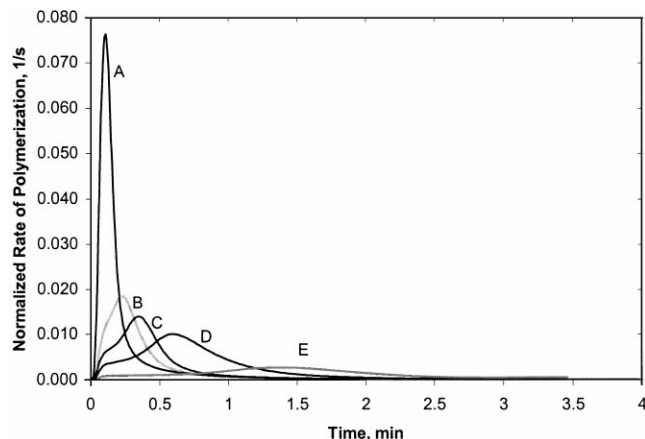


Fig. 3. Rates of polymerization for bulk MTCA (A), 30/70 MA/MTCA (B), 50/50 MA/MTCA (C), 70/30 MA/MTCA (D) and bulk MA (E). Polymerization temperature was 40°C using 0.5 wt% DMPA and a UV light intensity of 4 mW/cm<sup>2</sup> except for bulk MTCA which used 1 wt% DMPA and a UV light intensity of 3 mW/cm<sup>2</sup>.

terms of in vivo applications and manufacturing times of degradable implants. Since photopolymerizations are limited to optically thin layers (a few mm) a difference between 20 s and 1 min becomes quite significant if multiple layers are required to build a complex three-dimensional implant. In terms of fabrication, the number of layers could be on the order of 100, which translates into an hour less time required if the polymerization time for each layer is reduced from 1 min to 20 s.

#### 4.1.2. Network evolution versus crosslinker structure and functionality

As we try to tailor crosslinked polymer materials to specific applications, it is important to understand how the crosslinked network evolves. Previous studies [13–16] demonstrated that the monomer functionality and structure strongly affect the evolution of crosslinked networks. The distance and flexibility between functional groups affect the relative number of crosslinks, primary and secondary cycles formed during polymerization [14–16]. A primary cycle can occur during polymerization of multifunctional monomers when a growing polymer radical loops back on itself and polymerizes through a pendant double bond on the same chain. Secondary cycles develop when a polymer chain forms more than one crosslink with another polymer chain. The tendency to form primary and secondary cycles is a function of the monomer structure. Thus, by using a stiffer monomer, we hope to minimize the tendency to loop back on the growing chain and thereby increase the number of crosslinks relative to primary cycles.

Bulk polymerizations provide information about relevant rates of polymerization during the application of the material, but they do not provide insight into the

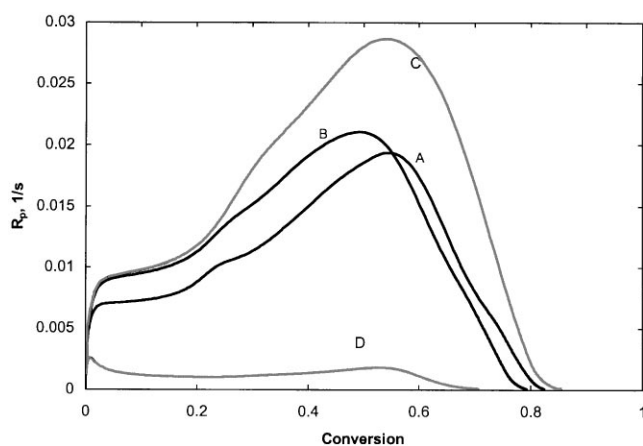


Fig. 4. Rates of polymerization versus conversion for pure HEMA (A), 2/98 mol% MSA/HEMA (B), 1/99 mol% MTCA/HEMA (C) and 5/95 mol% MPMA-ala/HEMA (D). Polymerizations were at 25°C using 1 wt% DMPA and 3 mW/cm<sup>2</sup> UV light intensity.

network evolution. The effect of monomer structure and functionality on the rates of polymerization is best evaluated by copolymerizing low concentrations of the crosslinking agents with a monovinyl monomer. Therefore, comonomer solutions of the novel monomers with 2-hydroxy ethyl methacrylate (HEMA) were prepared.

Fig. 4 shows the rates of polymerization versus conversion for solutions of the novel monomers in HEMA. Pure HEMA data is shown for reference. When a 2/98 mol% MSA/HEMA system is polymerized to form a relatively loosely crosslinked network, the initial rate increases compared to that of pure HEMA; the maximum rate is slightly higher and occurs at a lower conversion. The maximum conversion attained for HEMA crosslinked with MSA is slightly lower than that of pure HEMA. These observations indicate that MSA in HEMA forms a crosslinked polymer in which propagation becomes diffusion limited earlier than in pure HEMA. The addition of MSA to HEMA does not visibly affect the initial viscosity of the system; thus, the increased diffusional limitation to propagation is most likely due to the formation of crosslinks and secondary cycles.

A 1/99 mol% MTCA/HEMA system has the same number of double bonds available for crosslinking as the 2/98 mol% MSA/HEMA system. When a 1/99 mol% MTCA/HEMA system is polymerized, the initial rate increases compared to pure HEMA, and the slope of the autoacceleration portion of the curve is steeper. However, the final conversion remains essentially the same. Additionally, the maximum rate is significantly higher (30%) although it occurs at a similar conversion. Again, the initial viscosity is not significantly affected by the presence of the MTCA. Steeper acceleration of the polymerization rate is indicative of the formation of a greater

number of effective crosslinks. Propagation does become diffusion limited, but not early enough to reduce the final conversion significantly.

In contrast, the rate of polymerization of a 5/95 mol% MPMA-ala/HEMA mixture, which has 2.5 times the number of crosslinking double bonds as the previous systems, was very low and took 10 min to complete. The other three reactions were complete in 2 min. Interestingly, the addition of MPMA-ala visibly increased the initial viscosity, which typically improves the rate of polymerization to a point by reducing the rate of termination. However, the copolymerization of MPMA-ala and HEMA was slower than the homopolymerization of either one.

#### 4.2. Characterization of the mechanical properties

One measure of the suitability of the newly developed novel materials is the tensile storage modulus at 37°C. The tensile storage modulus is a measure of the force required to produce a given percent elongation. Alternatively, tensile strength measures the force required to break the sample. For many orthopedic applications, the material moduli should lie between that of trabecular and cortical bone depending on the implant site. The tensile storage modulus of cortical bone ranges from 17–20 GPa, and for trabecular bone, the range is 50–100 MPa depending on its density [23]. The modulus is one measure of the material's suitability for either a load-bearing application, such as repair of a major defect in the femur, or a low-load bearing application such as reconstruction of a facial bone.

Mechanical property data can also indicate the relative degree of crosslinking of the polymer, and thus, is another tool to supplement the polymerization studies for examining crosslinking efficiencies. The theory of rubber elasticity states that the crosslinking density is proportional to the tensile storage modulus in the rubbery region divided by the temperature at which the modulus is determined [24]. By determining the relative degree of crosslinking in the polymers formed from these new monomers, further insight into the effect of monomer functionality and structure on network development is gained. This insight aids in optimizing and designing monomers to produce networks for specific applications.

A summary of the mechanical properties of the polymers of MA, and copolymers of MA and MSA, MTCA, and MPMA-ala is given in Table 1. The range of tensile storage moduli was 0.8–2.1 GPa, which lies within the desired range between the moduli of trabecular and cortical bone. Poly(MTCA) had the largest modulus. Poly(MTCA) may have an advantage over poly(MSA) and poly(MPMA-ala) in its ease of processing, which consistently leads to materials with a significantly higher modulus. MA also polymerizes to form a high modulus material; however, methacrylic anhydride monomer can

Table 1  
Summary of modulus data, relative crosslinking density, conversion and initial concentration of pendant double bonds for the crosslinked polyanhydride networks. Relative crosslinking density is the ratio of the tensile storage modulus to temperature (373 K) in the rubbery plateau. FTIR was used to determine the conversion. There was a small shoulder for the samples labeled (a) thus conversion was not 100% but was nearly so

| Network composition     | Tensile storage modulus at 37°C (GPa) | Relative crosslinking density (KPa/K) | Conversion (%) | Initial concentration of pendant double bonds (mol/l) |
|-------------------------|---------------------------------------|---------------------------------------|----------------|---|
| Poly(MA)                | 1.2                                   | 2200                                  | 42             | 6.5   |
| 20/80 Poly(MA/MSA)      | 1.2                                   | 7.5                                   | a              | 1.8   |
| 30/70 Poly(MA/MTCA)     | 1.9                                   | 960                                   | 80             | 3.5   |
| 50/50 Poly(MA/MTCA)     | 2.1                                   | 2790                                  | 71             | 4.3   |
| 70/30 Poly(MA/MTCA)     | 1.8                                   | 3210                                  | 60             | 5.2   |
| 30/70 Poly(MA/MPMA-ala) | 1.2                                   | 950                                   | 78             | 3.4   |
| 50/50 Poly(MA/MPMA-ala) | 1.0                                   | 1200                                  | 70             | 4.2   |
| 70/30 Poly(MA/MPMA-ala) | 0.8                                   | 890                                   | 61             | 5.1   |

be toxic at very low concentrations and the slow rate of polymerization and low conversion of MA may preclude its use as a scaffold material.

Copolymers of MA and MTCA have the highest crosslinking density. These results are consistent with the polymerization data shown in Fig. 4. Pure poly(MA) has the next highest crosslinking density. This result is interesting because MA is a small molecule, and thus, one would expect it to form primary cycles easily. However, because it is small, the initial concentration of pendant double bonds is a minimum of 30% higher than for the other monomer systems. This high initial concentration of pendant double bonds results in higher concentrations of crosslinks even at lower crosslinking efficiencies.

MA/MPMA-ala copolymers have higher crosslinking densities than the copolymer of MA and MSA. While the results for the MA/MSA copolymer seem unreasonably low, this value is based on repeated measurements of the crosslinking density. In addition, a higher crosslinking density using MPMA-ala over MSA is theorized since MPMA-ala has a stiffer pendant group, which should be less prone to cyclization. The length of the crosslinking monomer is also important. NMR data for MPMA-ala indicate that it is primarily monomeric, where MSA is oligomeric (4.5mer). As such, the size of MSA significantly increases the distance between crosslinks and reduces the crosslinking density. Thus, while the data indicate that the stiffer methacrylate (MPMA-ala) is forming a greater number of effective crosslinks than MSA, the molecular weight of the monomer is also a contributing factor.

While these polymers do not have the high modulus required for load bearing cortical bone replacement, they are still good candidates for low load and structural applications. Furthermore, these novel monomers could become candidates for cortical bone replacement with the successful addition of fillers or reinforcing fibers

[12,25]. The monomer based on MTCA is particularly promising because it has the higher initial modulus; it is easily handled versus the solid monomers of MSA and MPMA-ala; and it reacts on a clinically acceptable time-scale (<2 min).

#### 4.3. Characterization of the degradation properties

In addition to having adequate initial moduli, materials must have mass degradation rates that are suitable for the application, and they must maintain their strength as they degrade. If a material degrades too slowly, then new tissue may not develop properly. The scaffold may impede physical expansion of the new tissue or somehow interfere with signaling between cells that might be necessary for maturation of the tissue. On the other hand, if a material degrades too quickly, then the growing tissue may not have adequate mechanical properties to support the load imposed on the area.

Modes of degradation include bulk and surface degradation. Bulk degrading materials lose strength rapidly without significant mass loss. Thus, a bulk degradation mechanism is often undesirable because the defect area becomes significantly weaker while providing insufficient space for new tissue to grow. Bulk degradation occurs in the polyesters PLA and PGA because water can penetrate the polymer matrix before significant hydrolysis of the ester bonds occurs.

Alternatively, surface degrading polymers degrade like a bar of soap. Consequently, the mass loss of a surface degrading polymer is proportional to the surface area. Additionally, surface degrading polymers have been shown to maintain their strength as they degrade [12]. Surface degradation occurs when the polymer is resistant to solvent penetration but at the same time has linkages that are highly susceptible to solvent attack. Thus, when anhydride linkages, which are highly susceptible to

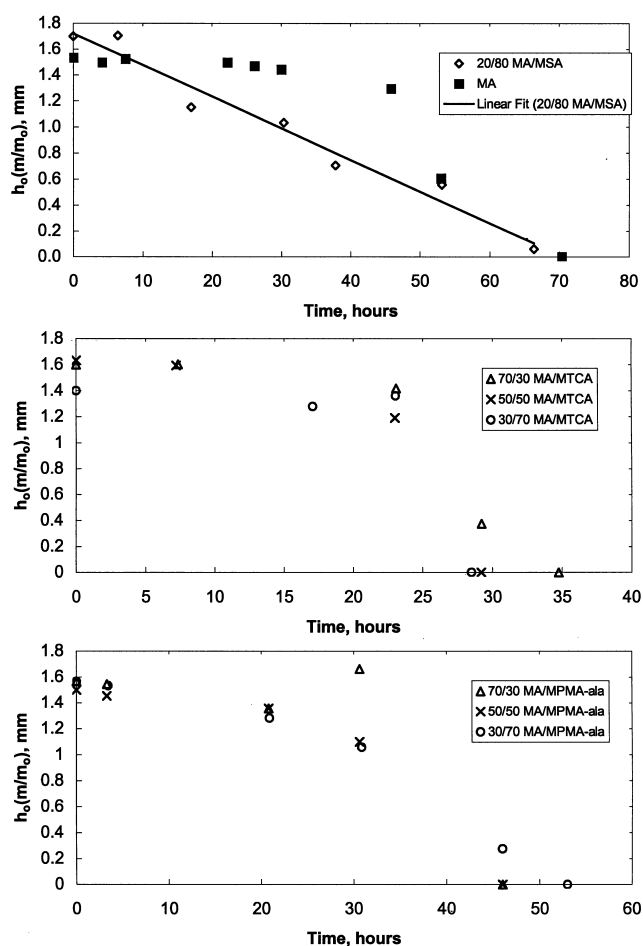


Fig. 5. Degradation rates for MA, MSA and copolymers of MA and the novel monomers MTCA and MPMA-ala. These studies were performed in PBS at 37°C. Disks had dimensions 15 mm × 1.5 mm initially.

hydrolysis, are combined with a hydrophobic backbone, such as SA, the polymer undergoes surface degradation. If the polymer is also crosslinked, further resistance to solvent penetration is imparted.

Degradation was characterized using disks with a large diameter compared to the height to mimic one-dimensional degradation. If degradation occurs just on the circular surfaces of the disks, then the relationship between mass and time is as follows:

$$h_0 \left( \frac{m}{m_0} \right) = h_0 - kt, \quad (1)$$

where  $h_0$  is the initial height of the sample,  $m$  is the sample mass,  $m_0$  is the initial mass,  $k$  is the kinetic constant for surface degradation, and  $t$  is the degradation time. Both the radius and sample density are constant in a purely one-dimensional surface degradation. Consequently, a plot of the product of normalized mass loss

and initial height versus time is linear for a surface-degrading polymer.

Fig. 5 shows the rate of mass loss versus time for a series of copolymers of MA and MTCA, copolymers of MA and MPMA-ala, 20/80 MA/MSA and MA. From the linear trend for 20/80 MA/MSA in Fig. 5, it is evident that this copolymer surface degrades. Pure MA and the copolymer 20/80 MA/MSA are completely degraded after 70 h. Disks of poly(MA) are initially hard and smooth on the surface and remain so for approximately the first 24 h. Then poly(MA) begins to swell just prior to the dramatic change in the slope of the degradation curve. The dramatic change in slope may indicate a change in the degradation mechanism.

Copolymers of MA and MTCA show little composition effect on the degradation rate. There is also an initial linear trend followed by a dramatic decline in mass. Again, there is evidence of swelling in these samples at the end of the degradation, indicating that they are not degrading entirely by a surface mechanism. The copolymers of MA and MPMA-ala also did not show significant differences in degradation rate with composition. However, the higher concentrations of MPMA-ala seem to impart a more surface degrading character to the polymer as evidenced by a more linear and extended degradation period.

There are several possible reasons for the faster degradation rates of MTCA and MPMA-ala polymer samples compared to polymers of MA and MSA. TCA is more hydrophilic than SA as indicated by the higher solubility of TCA in water. While poly(MTCA) is the most highly crosslinked, the presence of unreacted acid groups may enhance its hydrophilicity compared to the other polymers. In addition, MSA has eight carbon atoms between anhydride linkages, while MTCA has only 2–3. Thus, MTCA has a significantly higher density of anhydride linkages than MSA, which also increases MTCA's susceptibility to hydrolysis. Poly(MPMA-ala) may also be more hydrophilic than poly(MSA). Uhrich et al. [19] have shown that increasing the content of PMA-ala in a linear copolymer of PMA-ala and SA increases the hydrophilicity of the polymer. Thus, the increased hydrophilicity of the polymers containing MTCA and MPMA-ala may overshadow the benefits of increased crosslinking density resulting in higher degradation rates.

While these results indicate degradation rates that are too fast for many of the intended orthopedic applications, our laboratory has designed other more hydrophobic monomers that can be copolymerized with these monomers to reduce the degradation rates [26]. For example, the degradation rates of copolymers of MSA and methacrylated 1,6-bis(carboxyphenoxy) hexane (MCPH) have been shown to fall between the rate of poly(MSA), which degrades in a few days, and poly(MCPH), which takes several months to degrade completely [26]. An alternative strategy is the use of

semi-interpenetrating polymer networks (semi-IPNs) [26]. Linear hydrophobic polymers can be combined with MTCA or MPMA-ala monomers. The linear polymers are physically incorporated in the resulting crosslinked network during polymerization. The hydrophobic linear polymer hinders the penetration of water, thus increasing the degradation time [26]. Using these strategies, we can incorporate MTCA and MPMA-ala to improve the mechanics of the network, biocompatibility (with amino acid content) and polymerization rate, while MCPH can be used to control the degradation timescale.

## 5. Conclusions

Two novel multifunctional monomers were synthesized that are photopolymerizable and react to form highly crosslinked degradable networks. Advantages of photopolymerizable monomers are many including easy processing into complex shapes by spatially controlling the incidence of light. The rate of polymerization of MTCA is sufficiently rapid for use in a clinical application. The mechanical property data indicated that these novel monomers react to form polymer networks that have tensile storage moduli that lie between those of trabecular and cortical bone. Furthermore, this work indicates that an increase in modulus and crosslinking density can be achieved by using a trimethacrylate or a stiffer dimethacrylate. Degradation rates of these networks are also important in determining their usefulness for a specific application. The degradation rates of the novel polymers are relatively fast, but the rates could be tailored by copolymerizing with more hydrophobic monomers or developing semi-IPNs.

## Acknowledgements

The authors gratefully acknowledge funding from the National Science Foundation (BES-9734236) and a NIH Training grant (5T32GM08345-08 to JSY).

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