Characterization of Surgical Adhesives from UV-Polymerized Poly(PEG dimethacrylate-*co*-2-hydroxyethyl methacrylate) Copolymers

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SYNOPSIS

Polymer samples that could be used as wound adhesives were prepared from poly(ethylene glycol)dimethacrylate (PEGDMA) and 2-hydroxyethyl methacrylate (HEMA) copolymers in concentrations from 0 to 50 mol %. The UV copolymerization was initiated by 2,2-dimethoxy-2-phenylacetophenone (DMPA) and ultraviolet light intensities ranged from 0.1 to 0.5 mW/cm^2. The volume shrinkage during photopolymerization was observed using a dilatometric technique. The overall volume shrinkage was affected by the comonomer ratio and the nature of the PEGDMA comonomer. The rate of volume shrinkage was higher at higher ultraviolet light intensities. PEG(400)DMA-based copolymers exhibited lower glass transition temperatures than those of PEG(200)-based copolymers. The introduction of HEMA to the copolymers reduced both their glass transition and degradation temperatures. The equilibrium water-swelling ratio increased with increasing PEGDMA molecular weight and HEMA content. © 1995 John Wiley & Sons, Inc.

INTRODUCTION

Surgical dressings are biomaterials used for protecting wounds from infection or sutures from damage. The ideal surgical dressing for wounds must be capable of (i) protecting the area from mechanical damage; (ii) inhibiting the penetration of bacteria; (iii) preventing the rapid loss of fluids; (iv) withstanding the production of excess fluids; and (v) not harming the tissue when removed. Ideal surgical dressings are uncommon because some of the above requirements are contradictory. For example, a dressing should be impermeable for protection against bacteria, yet it must allow oxygen and moisture to diffuse so that the wound may heal.[1] Furthermore, after the dressing is removed, the healed tissue is often scarred. Scarring results because the skin and underlying tissue heal at unequal rates.

A promising alternative to the conventional surgical dressing is *a bioadhesive polymer* produced by an *in situ* reaction on a tissue. Bioadhesives may be polymeric materials that can interact with and be retained on biological tissue. Typically, a good bioadhesive has a high density of carboxylic residues and is a hydrophilic polymer. Important factors that result in a good bioadhesive include the extent of hydration and both the number and nature of hydrophilic sites on the polymer.[2] A wound bioadhesive could also be used as a controlled-release system. For example, a growth factor could be added to the wound adhesive in order to accelerate the healing and reduce the amount of scar formation, or an antibiotic may be added to prevent infection.[3]

A copolymer with both hydrophobic and hydrophilic moieities could serve as a good bioadhesive since the hydrophobic species would maintain the structural integrity of the system by resisting degradation from moisture, whereas the hydrophilic species would allow larger molecules like proteins to dissolve in the polymer. This work examines the feasibility of using various copolymers of poly(ethylene glycol)dimethacrylate (PEGDMA) and 2-hydroxyethyl methacrylate (HEMA) as wound adhesives. P(PEGDMA-*co*-HEMA) copoly-

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mers have already been identified by our group as ideal controlled-release systems because of their inertness and biocompatibility.[4]

In situ polymerizations offer two distinct conceptual advantages over preformed objects.[5,6] A conformal coating may be applied to an irregularly shaped area of tissue, and a large amount of the monomer mixture may be delivered through a small portal and assembled *in situ*.

An *in situ* photopolymerization on living tissue must meet[5] several requirements: (i) There must be minimal volume shrinkage of the material—otherwise, the desired surface contact will not be maintained; (ii) the heat of reaction must be low in order to avoid tissue damage; (iii) the intensity of the light source for the photopolymerization must not harm the tissue; (iv) the rate of reaction must be rapid enough that the patient does not become uncomfortable; and (v) the monomer mixture and the bioadhesive formed should not cause any inflammatory reaction with the body.

EXPERIMENTAL

Polymer Preparation

Comonomers used in the photopolymerizations were poly(ethylene glycol) 200 dimethacrylate [PEG-(200)DMA, Polysciences, Inc., Warrington, PA], poly(ethylene glycol) 400 dimethacrylate [PEG-(400)DMA, Polysciences, Inc., Warrington, PA], and 2-hydroxyethyl methacrylate (HEMA, Aldrich Chemical Co., Milwaukee, WI). The photoinitiator selected was 2,2-dimethoxy-2-phenylacetophenone (DMPA, Aldrich Chemical Co., Milwaukee, WI).

The comonomer compositions were 25 or 50 mol % HEMA, the remaining being either PEG-(200)DMA or PEG(400)DMA. To each of these samples, 2.1 mol % of DMPA was added as a photoinitiator. Films were made by placing 4 mL of the sample into a 70 mm aluminum dish. The samples were then irradiated at 0.5 mW/cm^2 for 30 min under a nitrogen atmosphere using an ultraviolet light source (Ultracure, 100, Engineered Fiber Optic Systems, Buffalo, NY) which was set to deliver light in 90 s intervals. Similarly, the two homopolymers of PEG(200)DMAA and PEG(400)DMA were produced. All reactions were carried out at room temperature. After the photopolymerization was completed, the films were cured in a vacuum oven at 90 $\pm$ 4°C for about 16 h and stored in a dessicator until needed.

Volume Shrinkage Experiments

The change in volume during copolymerization was monitored. In a typical experiment, approximately 1 mL of the reacting sample was placed in an NMR tube, nitrogen was purged through, and the monomers were reacted under an ultraviolet light source (Ultracure, 100). Samples were exposed to light intensities ranging from 0.1 to 0.5 mW/cm^2 at 27–30°C. The change of height of the sample in the NMR tube was recorded with a cathetometer.

Thermal Analysis

The glass transition temperature, T_g, of each copolymer film was determined using a thermomechanical analyzer (TMA, Model 2940, TA Instruments, Inc., New Castle, DE). Approximately 5 $\times$ 5 $\times$ 1.5 mm^3 specimens of each film were placed under a 6.07 mm-diameter probe, which was set for a 0.02 N force. Each sample was first heated under nitrogen to 90°C at a rate of 20°C/min and was held at isothermal conditions for 10 min. The sample was then heated to 200°C at a rate of 5°C/min. A plot of the sample strain as a function of temperature was generated and analyzed to determine the glass transition temperature of each film.

A thermogravimetric analyzer (Hi-Res TGA, Model 2950, TA Instruments) was used to determine the temperature at which each copolymer degraded: T_d. A sample of 10–50 mg was cut from each copolymer film and heated from 30 to 300°C at a rate of 5°C/min, and its weight change was recorded. The degradation temperature of the copolymer was considered to be the temperature at which the percent weight decrease exceeded 1%.

Swelling Studies

Rectangular samples of 0.1–0.5 g were cut from each copolymer and placed in glass jars containing deionized water at a pH of about 5. The jars were kept in a water bath at a temperature of 30 $\pm$ 1°C. The weights of the samples were monitored on a regular basis. The samples were swelled until an equilibrium weight was obtained. After equilibrium swelling, the samples were allowed to dry at ambient conditions until a final dry weight was reached.

RESULTS AND DISCUSSION

Sample Preparation

The six copolymer films prepared varied in their hardness. The flexibility of the copolymer films was

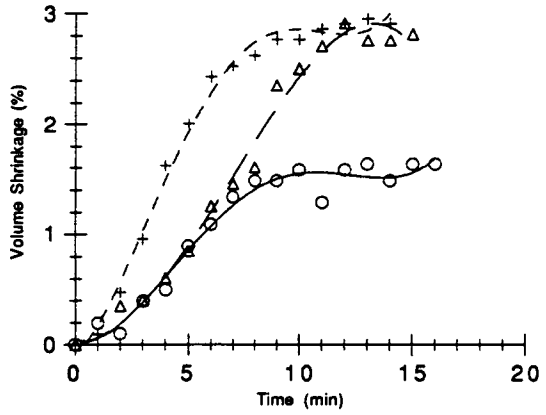

Figure 1 Volume change of PEG(400)DMA upon photopolymerization at various ultraviolet light intensities: (○) 0.1 mW/cm^2; (△) 0.3 mW/cm^2, (+) 0.5 mW/cm^2.

strongly influenced by both the molecular weight of the PEGDMA and the content of HEMA in the copolymer. Copolymers prepared with PEG(400)DMA were much more flexible than were those prepared from PEG(200)DMA. Copolymers containing PEG(400)DMA were cut with a scalpel, whereas films containing PEG(200)DMA could crack. The higher flexibility in the PEG(400)DMA copolymers was due to the larger number of ethylene glycol groups between crosslinks. In addition, as the molar composition of HEMA in a film increased, the flexibility of the film also increased. This is because HEMA reduced the number of crosslinks formed, thus redistributing the stress on the existing crosslinks.

Volume Shrinkage Experiments

The copolymerizations studied resulted in a decrease in overall volume of the copolymer produced. This

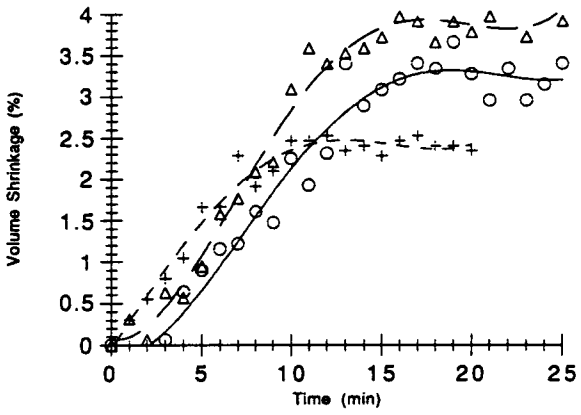

Figure 2 Volume change of a 75% PEG(400)DMA and 25% HEMA comonomer mixture upon photopolymerization at various ultraviolet light intensities: (○) 0.1 mW/cm^2; (△) 0.3 mW/cm^2; (+) 0.5 mW/cm^2.

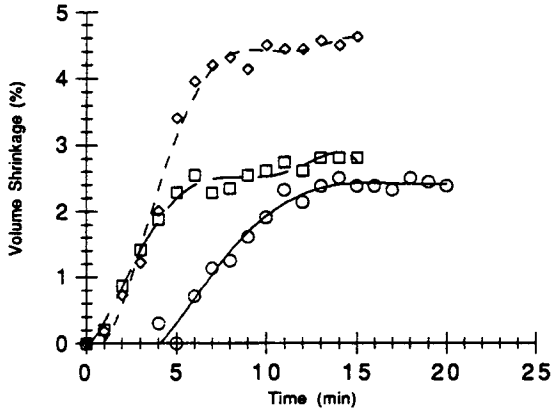

Figure 3 Volume change of a 50% PEG(400)DMA and 50% HEMA comonomer mixture upon photopolymerization at various ultraviolet light intensities: (○) 0.1 mW/cm^2; (△) 0.3 mW/cm^2; (+) 0.5 mW/cm^2.

volume shrinkage was typically below 4%. The ultimate volume shrinkage determined provided insights into the conversion achieved in the UV copolymerization reaction.

Figures 1–6 show the time dependence of volume shrinkage at various light intensities for each of the copolymers formed. For all six comonomer mixtures, the rate of volume shrinkage was larger at higher light intensities. This confirmed that the rate of polymerization was a function of the incident light intensity.

In general, the PEG(200)DMA-containing copolymers resulted in a larger volume decrease than did the PEG(400)DMA-containing copolymers. Figure 7 shows that addition of HEMA to the comonomer mixture resulted in a smaller volume shrinkage. An exception to this trend was seen for the 50 : 50 P(PEG(400)DMA-*co*-HEMA) copolymer.

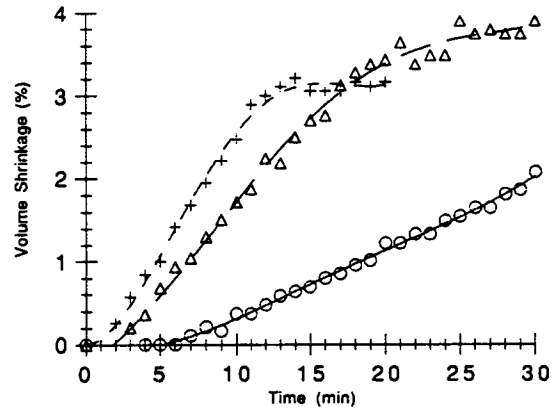

Figure 4 Volume change of PEG(200)DMA upon photopolymerization at various ultraviolet light intensities: (○) 0.1 mW/cm^2; (△) 0.3 mW/cm^2; (+) 0.5 mW/cm^2.

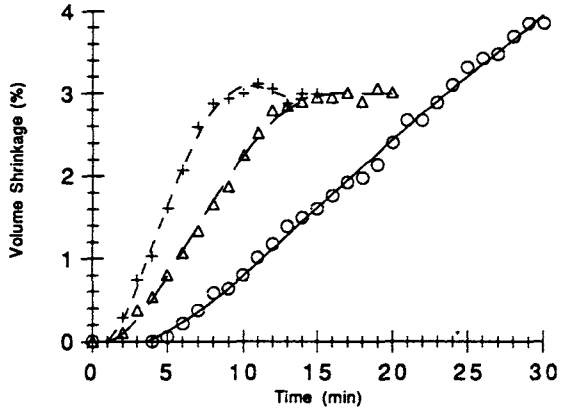

Figure 5 Volume change of a 75% PEG(200)DMA and 25% HEMA comonomer mixture upon photopolymerization at various ultraviolet light intensities: (○) 0.1 mW/cm^2; (△) 0.3 mW/cm^2; (+) 0.5 mW/cm^2.

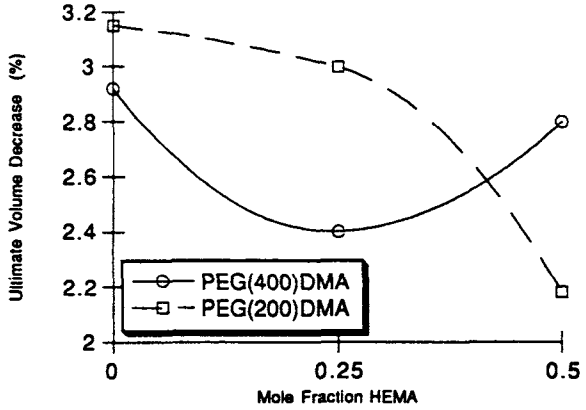

Figure 7 Ultimate volume decrease of the copolymers studied as a function of the amount of HEMA in the copolymers.

In this case, a larger volume shrinkage was seen with the addition of HEMA.

Thermal Characteristics

TMA studies are a simple technique for determining dimensional changes of a polymer sample. The results of the TMA experiments are listed in Table I. The glass transition temperatures of the PEG(400)DMA-containing copolymers were lower than those of the PEG(200)DMA-containing copolymers. The increased flexibility in the PEG(400)DMA-containing copolymers from the larger number of ethylene glycol groups between crosslinks allowed more flexibility and lower glass transition temperatures.

In general, the glass transition temperature of the copolymers decreased as their HEMA content increased due to the steric hindrance during polymerization. An exception to this trend was for the 50:50 P(PEG(200)DMA-*co*-HEMA) copolymer. The amount of crosslinking in this copolymer was probably lower. However, the increased HEMA content might allow for additional hydrogen bonding between the hydroxy groups. As a result, "physical crosslinks" might be forming and enhancing the strength of the copolymer.

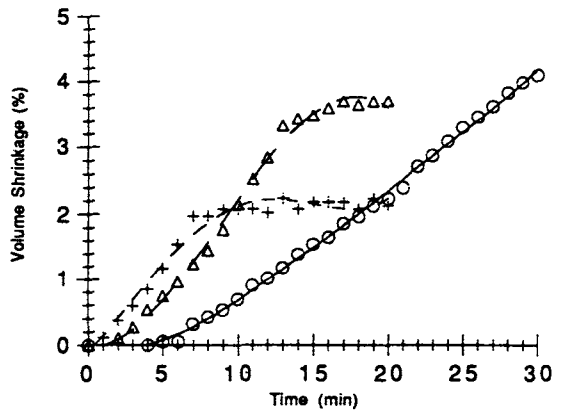

Figure 6 Volume change of a 50% PEG(400)DMA and 50% HEMA upon photopolymerization at various ultraviolet light intensities: (○) 0.1 mW/cm^2; (△) 0.3 mW/cm^2; (+) 0.5 mW/cm^2.

The TGA experiments were used to determine the degradation temperature of each copolymer. The weight of each copolymer sample was recorded as it was heated. The degradation temperature of the copolymer was assumed to occur at the point at which the sample had a 1% decrease in weight. The results of the TGA experiments are also listed in Table I. The PEG(400)DMA-containing copolymers degraded at higher temperatures than did the PEG(200)DMA-containing copolymers. The additional ethylene glycol groups between crosslinks in the PEG(400)DMA copolymers resulted in the higher degradation temperatures because they were

Table I Glass Transition and Degradation Temperatures of Copolymers

Copolymer Composition	T_g (°C)	T_d (°C)
100% PEG(400)DMA	−7.2	248
75% PEG(400)DMA + 25% HEMA	−16.5	236
50% PEG(400)DMA + 50% HEMA	−22.7	233
100% PEG(200)DMA	61.5	209
75% PEG(200)DMA + 25% HEMA	58.0	209
50% PEG(200)DMA + 50% HEMA	73.8	208

better able to dissipate the added energy. The PEG(200)DMA-containing copolymers were more densely crosslinked and more sterically hindered. Therefore, they would degrade at lower temperatures.

Similar to the glass transition temperatures, the degradation temperatures of the copolymers studied decreased as their HEMA content increased. Again, the HEMA introduced an additional stress in the copolymer network which caused the copolymer to degrade at lower temperatures. An anomaly to this trend was also seen for the 50 : 50 P(PEG(200)DMA-*co*-HEMA) copolymer. Hydrogen bonding and "physical entanglements" may have strengthened this copolymer.

Swelling Studies

The swelling agent used for the swelling studies was deionized water. The pH of the water was constant at about 5, which is the pH of human skin. By studying the swelling of the copolymer films, comparisons of crosslinking among the copolymers could be made.

Within the first 30 h, all copolymer samples reached their equilibrium swelling. As expected, the PEG(400)DMA-containing copolymers swelled much more than did the PEG(200)DMA-containing copolymers. Furthermore, as the molar percent of HEMA in each copolymer was increased, the swelling ratio also increased. Both of these facts verify that the crosslinking density decreased as the molecular weight of the PEGDMA increased and as the amount of HEMA added increased. Figures 8 and 9 show the swelling data for PEG(400)DMA copolymers and PEG(200)DMA copolymers, respectively.

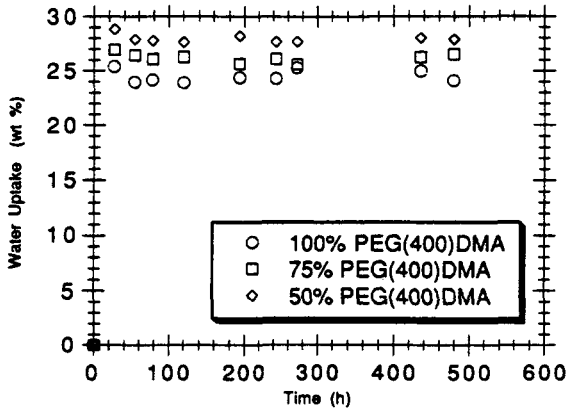

Figure 8 Water-swelling data for each of the three PEG(400)DMA copolymers tested.

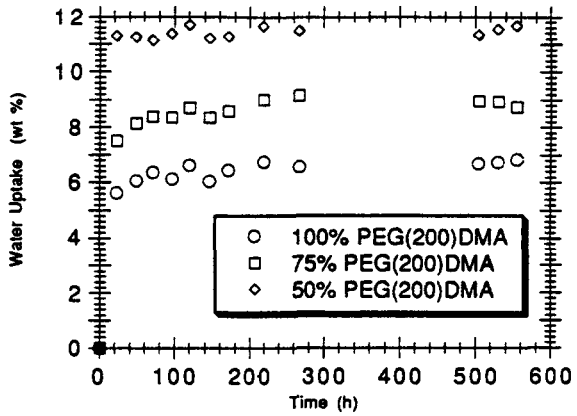

Figure 9 Water-swelling data for each of the three PEG(200)DMA copolymers tested.

Desirable Properties of Wound Dressing Materials

These results of the characterization analysis of the copolymers are indicative of the excellent properties of low shrinkage during UV polymerization, thermal stability, and swelling in water, which would contribute to the development of good *in situ* surgical adhesives. Based on the previous studies, it must be concluded that PEG(400)DMA and its copolymers with HEMA would be more desirable networks for wound dressings because they are rubbery at room temperature and because they can lead to a minimal unreacted residual monomer after polymerization, as the reaction can lead to almost 100% conversion without vitrification.

CONCLUSIONS

The research reported here provided insight into the behavior of various P(PEGDMA-*co*-HEMA) copolymers which can be used as wound adhesives. The rate of volume shrinkage and, consequently, the rate of polymerization increased as the ultraviolet light intensity used to promote the reaction increased. The ultimate volume shrinkage of PEG(400)DMA-containing copolymers increased with higher light intensities, but the ultimate volume shrinkage of PEG(200)DMA-containing copolymers decreased with higher light intensities.

The addition of HEMA to the copolymer tended to reduce the ultimate volume decrease of the polymerizing mixture. PEG(200)DMA-based copolymers had higher glass transition temperatures than those of PEG(400)DM-based copolymers.

The swelling of PEG(400)DMA-containing copolymers in water was over twice that of PEG(200)DMA-

containing copolymers. The introduction of HEMA moieties to the copolymers prepared resulted in a noticeable increase in swelling. Finally, the crosslinking density of the copolymers studied was reduced as the molecular weight of the PEGDMA and mole fraction of HEMA were increased.

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