Synthesis and Characterization of Biodegradable Network Poly(ethylene glycol) Films with Elastic Properties

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ABSTRACT: Novel biodegradable network films with elastic properties were prepared from trimesic acid (Y) and poly(ethylene glycol)s (PEGs) with different molecular weights (MW) and/or 4,7,10-trioxa-1,13-tridecanediamine (I). Prepolymers prepared by a melt polycondensation were cast from *N*,*N*′-dimethylformamide solution and postpolymerized at 290°C for various times to form a network. The resultant films were transparent, flexible, and insoluble in organic solvents. The X-ray diffraction scattering pattern showed that all network films are amorphous. The densities of the network films decreased, whereas their water uptake increased with increasing MWs of PEG. The thermal and tensile properties were measured in dry and wet conditions and were affected remarkably not only by MWs of PEG, but also by the water uptake of the films. The glass transition temperatures (T_g) decreased with increasing MWs of PEG. $YPEG_{200}$ and $YPEG_{1000}$ films showed good elastomeric properties with an ultimate elongation of 225 and 277%, respectively, in dry condition. The tensile strength of 13 MPa and Young's modulus of 214 MPa were the highest for $YPEG_{200}$ among the network elastic films studied. All sample films in wet condition had lower T_g's and tensile properties. The hydrolytic degradation was measured by the weight loss of network films in a buffer solution with or without *Rhizopus delemar* lipase at 37°C. The degree and the rate of the degradation increased with increasing MWs of PEG, which is compatible with the increase in water uptake of the films. Incorporation of large amount of I moiety into $YPEG_{1000}$ film increased the glass transition temperatures, tensile strength and Young's modulus, but depressed elastic nature of the films. © 2007 Wiley Periodicals, Inc. J Appl Polym Sci 106: 2885–2891, 2007

Key words: poly(ethylene glycol); trimesic acid; 4,7,10-trioxa-1,13-tridecanediamine; networks; elastic properties; enzymatic degradation

INTRODUCTION

Biodegradable elastomers have significant potential for both biomedical applications such as artificial skin, drug delivery devices, and scaffolds for tissue engineering. There have been two general classes of biodegradable elastomers: thermoplastics and thermosets. While thermoplastics are prepared easily by melt or solvent processing, they degrade heterogeneously due to the mixture of crystalline and amorphous regions. This can lead to a rapid loss of mechanical properties as well as large deformation as the material degrades. On the contrary, thermosets offer more homogenous degradation which leads to linear loss of mass and mechanical properties as well as minimal deformation as the materials degrades.

Biodegradable network poly(ester–urethane) elastomers have been prepared from ethyl-2,6-diisocyanatohexanoate and a series of polyester triols[1] or a few hexahydroxy-terminated star-shaped prepolymers.[2] Recently, thermoset biodegradable elastomers have been synthesized by crosslinking vinyl-end group functionalized star-shaped poly(ε-caprolactone)-*co*-DL-lactide) prepolymers.[3–5] We have prepared several biodegradable network elastomers from multifunctional aliphatic and aromatic carboxylic acids and poly(ε-caprolactone) diols with a regular network structure, showing a wide range of thermal, mechanical, and degradation properties.[6,7]

Continuing our interests on the biodegradable regular network elastomers, we have synthesized the novel network poly(ethylene glycol) (PEG) films with elastic properties from trimesic acid and PEGs. The effects of molecular weights (MWs) of PEG on the thermal and mechanical properties as well as hydrolytic degradation were investigated. In addition, 4,7,10-trioxa-1,13-tridecanediamine (I) was copolymerized into the network PEG backbone to improve the mechanical properties of the films. The polyamides containing I moiety have been reported as biodegradable materials.[8,9]

PEG is known to be a nontoxic water soluble polymer and suitable for biomedical applications such as controlled drug release and tissue engineering.[10] The

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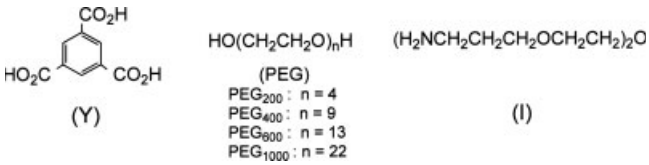

Figure 1 Chemical structures and codes of starting materials.

crosslinking of PEGs have been widely performed by ultraviolet irradiation[11] or end-functionalization with methacrylate and acrylate[12,13] mainly for preparation of hydrogels. But less attention has been paid to the regular network PEG films with elastic properties.

EXPERIMENTAL

Materials

Figure 1 shows chemical structures and codes of the starting materials used in this study. Trimesic acid (Y) and 4,7,10-trioxa-1,13-tridecanediamine (I) were obtained from Tokyo Chemical Industry and used without further purification. Triethyl ester of trimesic acid (Y_E) was synthesized by refluxing Y and a large excess of ethanol in the presence of a small amount of concentrated sulfuric acid, and recrystallized from ethanol (mp.: 154°C). PEGs of the number average MWs of 200, 400, 600, and 1000 (g mol^{-1}) were kindly supplied by Sanyo-Chemical.

Preparation of prepolymers

Prepolymers from Y and PEGs and precopolymers Y, PEGs, and I were prepared by a melt polycondensation. In the case of copolymerization of I component, Y_E was chosen to keep mild reactivity. A typical example is as follows: A mixture of Y and PEG of various molecular weights (total amount of 4 g, molar ratio of PEG/Y = 3/2) were heated in a stream of nitrogen at 260°C for 10–150 min. As MWs of PEG increased, longer heating time was needed. However, the excess heating caused a gelation of the polymers. Then the heating was stopped just before the gelation occurred. The similar procedures of the polymerization described previously[14] were used. The precopolymers were prepared from Y_E, PEGs and I with total amount of 4 g, molar ratio of Y_E/a mixture of PEG and I = 2/3.

Film preparation and postpolymerization

The prepolymers and precopolymers obtained were cast on an aluminum plate from a 17 wt % dimethylformamide solution at 80°C. Then the cast film was heated at 290°C for various periods of time in a nitrogen atmosphere. After the postpolymerization, the film was peeled off from the plate and stored in a desiccators over silica gel. The network films obtained were transparent and insoluble in organic solvents such as dichloromethane and *N*,*N*-dimethylformamide. The polymer and copolymer films prepared were denoted by the monomer codes. The polymer from trimesic acid (Y) and PEG is called as $YPEG_n$, where subscript n is the molecular weight of PEG. The copolymer of PEG and I with Y is denoted as YIPEG(a/b), where a/b is a molar ratio of I and PEG.

Characterization

Fourier transform infrared (FTIR) spectra were recorded on a Perkin–Elmer model GX-2000 FTIR spectrophotometer using thin films. Wide angle X-ray scattering (WAXS) was performed with a Toshiba model ADG-301 X-ray diffractometer with nickel-filtered CuKα radiation. Differential scanning calorimetry (DSC) was made on a TA Instruments DSC 2920 differential scanning calorimeter with a heating rate of 10°C/min in a nitrogen atmosphere. To provide the same thermal history, each sample was preheated from room temperature to 100°C and rapidly cooled down to −100°C. Then the DSC scan was recorded by heating from −100 to 100°C. Thermomechanical analysis (TMA) was performed in a penetration mode under a pressure of 10 kg/cm^2 and a heating rate of 20°C/min in a nitrogen atmosphere, using a Seiko model TMA-100 thermomechanical analyzer controlled by a SSC-5200 disk station. The density of the film was measured using a sink and float method in potassium iodide aqueous solution at 37°C. Tensile properties were tested with a Shimadzu AG-1 autograph at a strain of 100% min^{-1} to measure tensile strength, elongation, and Young's modulus in dry condition (10% relative humidity) and wet condition (90% relative humidity) and the averaged value for 5–10 specimens was used.

Water uptake

The equilibrium water contents were measured as follows: The resulting network films (20 mm × 20 mm, ~ 200 μm) were carefully dried and weighed, then soaked in about 20 mL of distilled water for 24 h at 37°C. The swollen film was removed from solution, and surplus water was wiped away with a tissue, and weighed. The water uptake of the network films was determined as follows:

$$DS = (W_{wet} - W_{dry})/W_{dry}$$

where W_{wet} is the weight of the swollen film and W_{dry} is the weight of the dry film. Each experiment was performed in duplicate and averaged.

Hydrolytic degradation

The enzyme used in this study is a lipase from *Rhizopus delemar* (specific activity of 669 unit mg^{-1} from Seikagaku Kogyo). The film specimens (20 mm × 20 mm, ~ 200 μm thickness) were placed in a small bottle containing 10 mL of 1/15 mol phosphate buffer solution (pH 7.2) with and without 600–900 unit mL^{-1} of the above-mentioned lipase. The vial was incubated at 37°C for various periods of time. After incubation the film was washed with water thoroughly, and dried at 40°C *in vacuo* to constant weight. The degree of degradation was calculated as the differences between the dry weight after degradation and the initial weight. The weight loss averaged for two specimens was employed. The variability was within ±3.2% for the weight loss of the films.

RESULTS AND DISCUSSION

Synthesis of network polymer films

Various network PEG films were prepared from trimesic acid, PEG, and/or I by the procedures described in the Experimental section. The chemical structure of network films from trimesic acid and PEG is shown in Figure 2. Figure 3 shows the IR spectra of $YPEG_{400}$ film postpolymerized at 290°C for various periods of time. The absorbance at 3460 cm^{-1} due to hydroxyl group decreased with increasing postpolymerization time, while the absorbance at 2920 cm^{-1} due to methylene groups remained unchanged. Since the postpolymerization proceeds through the reactions between the carboxyl group of multifunctional aromatic carboxylic acid and hydroxyl group of PEG, the change of absorption intensity ratio between —OH and ⟩CH_2, A_{OH}/A_{CH_2}, is a measure of the degree of reaction. For $YPEG_{400}$, for example, at the beginning of reaction, the ratio of hydroxyl and methylene groups in PEG_{400}, [OH]/[CH_2], is 2/18. The structure of PEG_{400} is given in Figure 1. The average repeating unit n of PEG_{400} is 9. Thus the number of methylene groups is estimated as 18. The ratio of [OH]/[CH_2] varied with the progress of reaction to become (2 − 2)/18 when

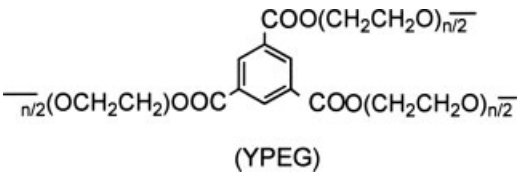

Figure 2 Chemical structures of polymers prepared from trimesic acid and PEGs of various molecular weights. The number of n is shown in Figure 1.

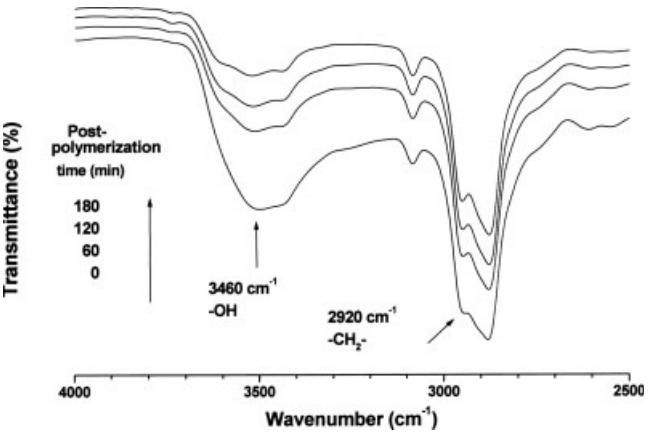

Figure 3 Infrared absorbance change of films at 290°C for various postpolymerization times.

the network structure of film was completely developed. Thus, the following equation is defined:

$$[OH]/[CH_2] = (2 - y)/18$$

and

$$y = 2 - (18[OH]/[CH_2])$$

Here y is the number of reacted hydroxyl groups. The degree of reaction (D_R) is calculated as

$$D_R = (y/2) \times 100\ (\%)$$

To obtain the quantitative [OH]/[CH_2] ratio in network films, the calibration curve between A_{OH}/A_{CH_2} made by the known diols and alcohols was used.[15]

Figure 4 shows the dependence of D_R on the postpolymerization time at 290°C for the various periods of time for $YPEG_{400}$. D_R value increases at the initial stage of postpolymerization and approximately

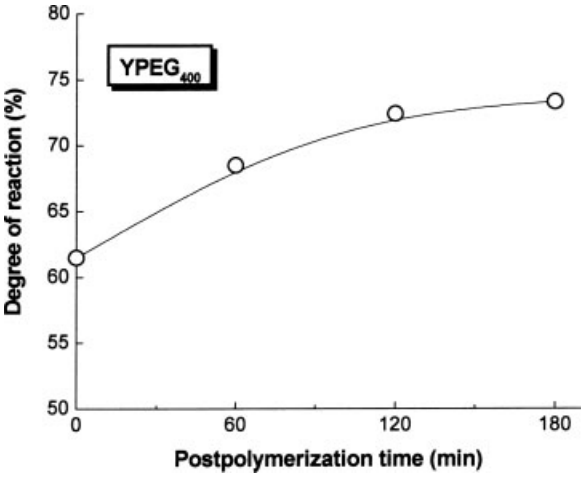

Figure 4 Degree of reaction of YPEG400 film versus postpolymerization time.

TABLE I
D_R Values of the Network Films Postpolymerized at 290°C

Polymer code	Postpolymerization time (min)	D_R (%)
$YPEG_{200}$	90	77
$YPEG_{400}$	180	73
$YPEG_{600}$	240	70
$YPEG_{1000}$	300	74
YI	60	72

leveled off after 180 min. Thus the postpolymerization was performed at 290°C for 180 min for $YPEG_{400}$. D_R values of $YPEG_n$ network films postpolymerized at 290°C for 90–300 min are summarized in Table I. With increasing MWs of PEG, it takes the longer reaction time for the YPEG films to attain equilibrium. All PEG films show D_R values higher than 70%, indicating that network structure was formed.

The D_R values of YI film is estimated by the similar procedure using the intensity ratio of carboxyl group at 1724 cm^{-1} (A_{COO}) and methylene group at 2960 cm^{-1} (A_{CH_2}). The intensity of A_{COO} decreases, while that of A_{CH_2} is unchanged with increasing postpolymerization time, since the absorption at 1724 cm^{-1} due to the ester group decreased with increasing postpolymerization time. To obtain the quantitative [COO]/[CH_2] ratio in network films, the calibration curve between A_{COO}/A_{CH_2} made by the known various esters was used (Fig. 5). D_R values increased with time and approximately leveled off after 60 min. D_R value of YI is shown in Table I.

The network copolymer films of Y, PEG_{1000} and I were postpolymerized at 290°C for 120–180 min. D_R values of them could not be estimated since the suitable absorption peak to determine D_R values did not appear in FTIR curve. But we confirmed the intensity ratio of carboxyl group at 1724 cm^{-1} (A_{COO}) and amide group at 1648 cm^{-1} (A_{NHCO}) leveled off after 120–180 min, depending on the copolymer compositions. D_R values of both pure network polymers ($YPEG_{1000}$ and YI) are 74 and 72%, respectively, suggesting strongly that those of these network copolymers from Y, PEG, and I are in the range of 74 and 72%.

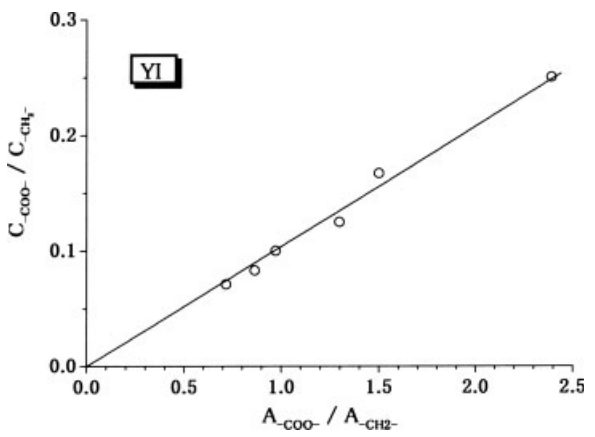

Figure 5 Calibration curve between A_{1724}/A_{2920} and [COO]/[CH_2] made by the known esters.

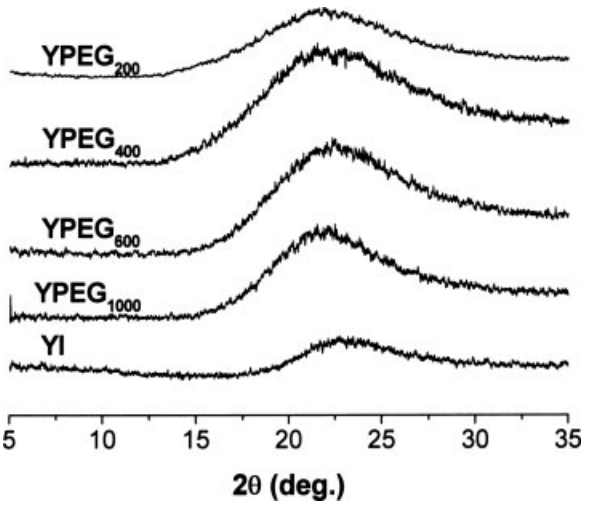

Figure 6 WAXS patterns of various network films.

Thermal properties of postpolymerized films

Figure 6 shows the typical WAXS intensity curves of the network $YPEG_n$ and YI films. All films give the amorphous patterns, showing that crystallization of PEG chain did not occur in these network films in ambient conditions. The copolymer network films also showed only amorphous halo in the WAXS patterns. However, DSC measurement, as shown in Figure 7, showed that $YPEG_{1000}$ gave cold crystallization at −33°C and melting endotherm at 19°C.

Figure 7 shows typical DSC scans for some network films. Endothermic changes due to glass transition (T_g) are observed for all films. T_g values of

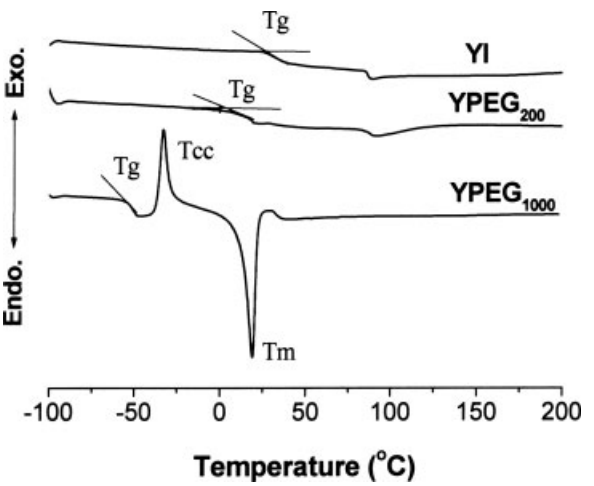

Figure 7 DSC curves of some network films.

TABLE II
Thermal Properties of the Network Films in the Dry and Wet Conditions

Polymer code	T_g (°C) dry/wet	T_{cc} (°C) dry/wet	T_m (°C) dry/wet
$YPEG_{200}$	6.6/−0.6		
$YPEG_{400}$	−34.7/−51.6		
$YPEG_{600}$	−37.8/−64.2		
$YPEG_{1000}$	−54.2/−67.6	−32.9/–[a]	19.0/–[a]
$YIPEG_{1000}$(50/50)	−50.3/−69.2	−13.1/–[a]	25.1/–[a]
$YIPEG_{1000}$(75/25)	−37.5/−64.7		
$YIPEG_{1000}$(80/20)	−31.4/–[b]		
$YIPEG_{1000}$(90/10)	−10.4/–[b]		
YI	26.4/−32.4		

[a] The peaks were not detectable.
[b] Not determined.

$YPEG_n$, YI and copolymer films are summarized in Table II. T_g of YI is much higher than those of $YPEG_n$ films due to the intermolecular hydrogen bonding of polyamide chains. T_g's decrease gradually with increasing MWs of PEG, suggesting that the longer PEG chains enhance the mobility of networks. As expected, incorporation of I moiety into $YPEG_{1000}$ increases T_g's.

T_g's were measured in wet condition for $YPEG_n$ films by DSC. The values are also listed in Table II. T_g's in wet condition are lower than those in dry condition, probably due to the plasticizing effect of the absorbed water into the films.

Density and water uptake of postpolymerized films

Densities and water uptakes of various network $YPEG_n$ films and copolymer films are summarized in Table III. Densities of $YPEG_n$ films decrease with increasing MWs of PEG, because the crosslinking density of the network films decrease with an increase of MWs of PEG. The copolymerization of I component to $YPEG_{1000}$ gradually reduces the densities of YPEG films due to the lower densities of YI. The water uptake of $YPEG_n$ films appreciably increases with increasing the MWs of PEG, which would be ascribed to the lower crosslinking density of polymers: The increase in MW of PEG makes the network size larger, thus larger network size makes easier penetration of water into inside of films. It is noteworthy that $YPEG_{1000}$ absorbs water as much as 221%. Water uptake of copolymer films decrease with increasing I content due to the lower water content of YI.

TABLE III
Density and Water Uptake of the Network Films

Polymer code	Density (g/cm^3)	Water uptake (%)
$YPEG_{200}$	1.301	6.5
$YPEG_{400}$	1.289	37
$YPEG_{600}$	1.280	93
$YPEG_{1000}$	1.258	221
$YIPEG_{1000}$(50/50)	1.250	231
$YIPEG_{1000}$(75/25)	1.246	110
$YIPEG_{1000}$(80/20)	1.240	84
$YIPEG_{1000}$(90/10)	1.235	52
YI	1.230	21

Tensile properties of postpolymerized films

Tensile properties of the postpolymerized films were measured for $YPEG_n$, YI and $YIPEG_{1000}$ copolymers in dry and wet conditions. Figure 8 shows the typical shapes of the stress–strain curves of films in dry condition. Table IV summarizes the tensile strength at break, ultimate elongation and Young's modulus of the postpolymerized films. In dry condition, $YPEG_{200}$ and $YPEG_{1000}$ show good elastic properties with a maximum strain of 225 and 277%, respectively. After the samples had deformed under the stress, they immediately recovered the original dimensions. The tensile strength at break and Young's modulus of $YPEG_{200}$ is higher than those of $YPEG_{1000}$, while the elongation of the former is lower than that of the latter, which would be ascribed to the differences of crosslinking density of both polymers. Tensile strength at break and Young's modulus, in dry condition, decreases in the order of $YPEG_{200} > YPEG_{1000} \gg YPEG_{400} \sim YPEG_{600}$ and elongation in the order of $YPEG_{200} \sim YPEG_{1000} \gg YPEG_{400} \sim YPEG_{600}$. It is noteworthy here that $YPEG_{200}$ film is the biodegradable elastomer with higher Young's modulus (214 MPa).

YI is a hard and tough film, which is responsible for the intermolecular hydrogen bonding of the polyamide chains. As expected, the tensile strength at break and Young's modulus of YI film are higher than those of YPEG films. YI exhibits a clear yield point and behaves as a thermoplastic. To improve

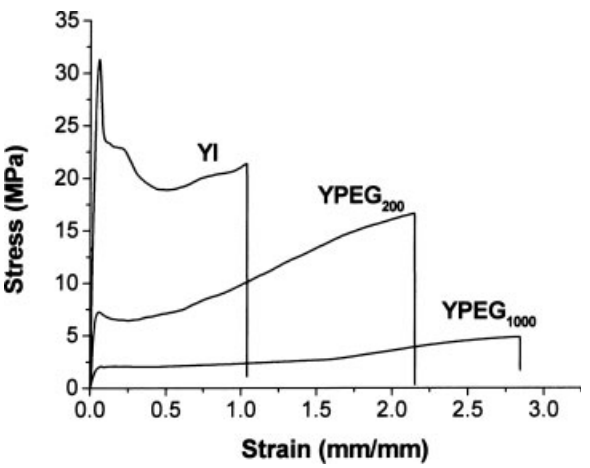

Figure 8 Typical stress–strain curves of some network films.

TABLE IV
Tensile Properties of the Network Films in the Dry and Wet Conditions

Polymer code	Tensile strength at break (MPa)	Young's modulus (MPa)	Elongation at break (%)	Deformation
$YPEG_{200}$				
Dry	13.0 ± 1.5	214 ± 4.0	225 ± 10	Elastic
Wet	4.47 ± 0.43	13.1 ± 0.4	117 ± 12	Elastic
$YPEG_{400}$				
Dry	1.60 ± 0.17	6.02 ± 0.18	34.8 ± 5.3	Elastic
$YPEG_{600}$				
Dry	1.26 ± 0.19	2.18 ± 0.06	27.9 ± 6.7	Elastic
$YPEG_{1000}$				
Dry	4.54 ± 0.15	54.7 ± 1.3	277 ± 15	Elastic
Wet	0.4 ± 0.13	1.87 ± 0.13	19.5 ± 0.13	Elastic
$YIPEG_{1000}$(50//50)				
Dry	0.68 ± 0.04	1.85 ± 0.14	47.6 ± 7.7	Elastic
$YIPEG_{1000}$(80/20)				
Dry	3.99 ± 0.10	7.69 ± 2.64	116 ± 4	Elastic
$YIPEG_{1000}$(90/10)				
Dry	18.9 ± 2.0	260 ± 26	217 ± 26	Plastic
YI				
Dry	30.6 ± 0.8	888 ± 15	106 ± 1	Plastic
Wet	0.37 ± 0.05	5.78 ± 0.18	7.09 ± 1.0	Plastic

the mechanical properties of $YPEG_{1000}$, I component was introduced into $YPEG_{1000}$ as a comonomer unit. The resultant tensile properties of $YIPEG_{1000}$ copolymers are also summarized in Table IV. Larger amount of I component incorporation into $YPEG_{1000}$ enhances the tensile properties for $YIPEG_{1000}$ (90/10) with higher tensile strength of 18.9 MPa and higher Young' modulus of 260 MPa but plastic. Other copolymers of $YIPEG_{1000}$ (80/20) and (50/50) did not give the enhanced mechanical properties but did the elastic properties.

The hydrophilic $YPEG_n$ and YI films exhibit the quite different tensile behaviors in wet condition. All film exhibited no yield points. The tensile properties of the wet network films are given in the Table IV. The tensile properties such as strength, Young's modulus, and elongation of $YPEG_{200}$, $YPEG_{1000}$, and $YIPEG_{1000}$ films in wet condition are much lower than those in dry condition. However, these films are still elastic except for $YIPEG_{1000}$ (90/10). Much reduced tensile properties was caused by the plasticizing effect of absorbed water described above. The largest reduction of the tensile properties is appeared for $YPEG_{1000}$ film probably because it uptakes much larger amount of water (221%) among the network films prepared.

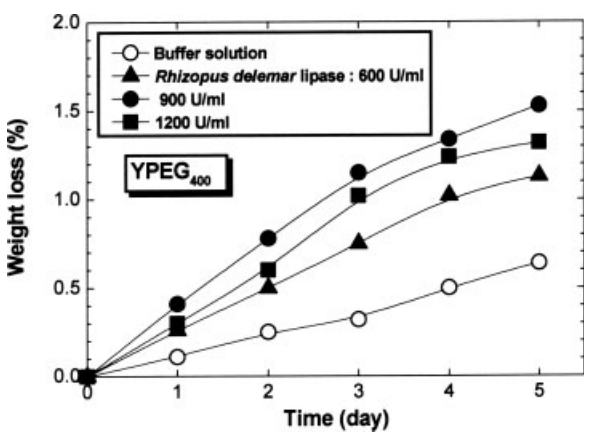

Figure 9 Weight loss of $YPEG_{400}$ film against time in a buffer solution with or without *Rh. delemar* lipase at 37°C.

Hydrolytic degradation of postpolymerized films

Figure 9 shows the weight loss of $YPEG_{400}$ film versus incubation time in a phosphate buffer solution

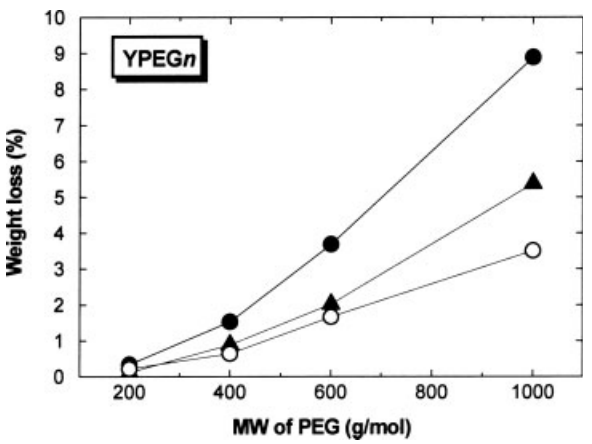

Figure 10 Effect of molecular weights of $YPEG_n$ on the weight loss of the films degraded in a buffer solution with or without *Rh. delemar* lipase at 37°C: (○) is weight loss in a buffer solution without *Rh. delemar* lipase; (●) is weight loss in a buffer solution containing *Rh. delemar* lipase ; (▲) is a net weight loss caused by *Rh. delemar* lipase.

with *Rh. delemar* lipase at 37°C. The weight loss profile in the absence of the lipase is also shown. The degradation was performed in three different enzymatic concentrations of 600, 900, and 1200 U mL^{-1}. The degradation rate is the highest in the concentration of 900 U mL^{-1}. The weight loss increases almost linearly with incubation time. Weight loss was hardly observed for YI film with and without the lipase, indicating that the amide linkage is reluctant to the hydrolysis. Figure 10 shows the weight loss of $YPEG_n$ films degraded in phosphate buffer solution with or without *Rh. delemar* lipase at 37°C for 5 days. Weight loss increases with increasing MWs of PEG, which is compatible with the water uptake of $YPEG_n$ films described above. The higher the water uptake, the greater is the weight loss. Moreover, the increase of network space with an increase of the chain length between crosslinked sites may assist the attack of lipase to the network leading to the faster enzymatic degradation.[6,7] It is important to identify which bond was cleaved during the degradation, i.e., the ester bond between the PEG and Y segments, or the ether bond of the PEG segments. The former was expected to be preferred as esters are more susceptible to hydrolysis than ethers. The scission of ester bond between poly(ethylene terephthalate) and PEG with some enzymes have been reported for polyethylene oxide/poly(ethylene terephthalate) copolymers.[16] The degradation products of the $YPEG_n$ films are presumably Y, PEG, and these oligomers.

CONCLUSIONS

Novel biodegradable network films were prepared from trimesic acid (Y) and PEGs with various molecular weights and/or 4,7,10-trioxa-1,13-tridecanediamine (I). Water uptake of network polymers increased linearly with increasing the MWs of PEG, whereas their densities decreased. The tensile properties of network films depended greatly on MWs of PEG. $YPEG_{200}$ and $YPEG_{1000}$ films showed good elastic properties with an ultimate elongation of 225 and 277%, respectively, in dry condition. Wet condition markedly decreased the glass transition temperature and the tensile properties of the network films. The degree and the rate of the degradation in a buffer solution with *Rh. delemar* lipase at 37°C increased with increasing the molecular weight of PEG, which is compatible with an increase in water uptake. $YPEG_{200}$ elastomer with the higher tensile strength and Young's modulus would be promising as a novel type of biodegradable thermoset elastomer for the environmental and biomedical applications.

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