JOURNAL OF MATERIALS SCIENCE: MATERIALS IN MEDICINE 13 (2002) 773–781

Thermal and mechanical properties of biodegradable hydrophilic-hydrophobic hydrogels based on dextran and poly (lactic acid)

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The thermal and mechanical properties of a new family of biodegradable hydrogels made of photocrosslinked dextran derivative of allyl isocyanate (dex-AI) and poly (D,L) lactide diacrylate macromer (PDLLAM) were studied. The changes of thermal and mechanical properties of the dex-AI/PDLLAM hydrogels as functions of dex-AI to PDLLAM composition ratio and immersion time in phosphate buffer solution at 37 °C were also investigated. Thermal property data showed that the chemical modification, crosslinking, swelling and hydrolytic degradation affected the glass transition and melting temperatures. Based on thermal data, no phase separation was observed in the bicomponent dex-AI/PDLLAM hydrogels. Mechanical property data showed that, by changing the composition ratio, dex-AI/PDLLAM hydrogels having a wide range of dry and swollen compression moduli could be obtained. The moduli of the dex-AI/DPLLAM hydrogels in dry state decreased with an increase in the PDLLAM composition due to the reduction in glass transition temperature of the hydrogels. The loss of mechanical strength in buffer solutions was attributed to the swelling-induced formation of 3D porous network structure in the early stage of immersion and the hydrolytic degradation of the PDLLAM in the late stage via the chain scission of ester linkages located in the PDLLAM backbone. Because swelling and degradation were composition dependent, the magnitude of the loss of mechanical strength was also composition-dependent.

Introduction

Biodegradable drug carriers represent an attractive means for drug administration because of the consistent slow drug release that minimizes drug toxicity. More specifically, there has been considerable interest in studying the unique properties of biodegradable hydrogels – water-swollen network polymers – as drug carriers [1]. The combination of high water content without premature structure dissolution makes hydrogel materials well suited to be drug carriers. The use of biodegradable hydrogels as drug carriers has become promising because the recent advancement in biotechnology has led to a great variety of pharmacologically active peptides and proteins that may be difficult to release adequately from existing non-biodegradable biomaterials. In addition, due to their good tissue biocompatibility and the possibilities of tailoring the permeability of the hydrogels for specific drugs, biodegradable hydrogels appear to be a viable alternative to existing drug carriers [2–5]. In the swollen state, the properties of hydrogels are strongly influenced by their water content. Many important properties of hydrogel-based drug carriers, such as permeability to hydrophilic or hydrophobic drugs, biocompatibility, rates of enzymatic or hydrolytic degradation and mechanical properties of hydrogels in the swollen state, can be directly related to their water content [6–8]. Thus, the swelling property of hydrogels is a critical factor for regulating all other important properties of hydrogels.

In our previous studies, we described the synthesis of a series of biodegradable hydrogels made from hydrophilic dextran derivative of either allyl isocyanate (dex-AI) or acryloyl chloride (dex-AC) and relatively hydrophobic poly (D,L) lactide diacrylate macromer (PDLLAM) [9, 10]. By adjusting the composition ratio of dextran derivatives to PDLLAM, hydrogel networks having a wide range of hydrophilicity to hydrophobicity, swelling and biodegradability could be obtained. The release kinetics of some model drugs (Indomethacin, albumin, insulin) and the biodegradation properties of this new class of biodegradable hydrogels have also been reported and confirmed that a wide range of release kinetics of

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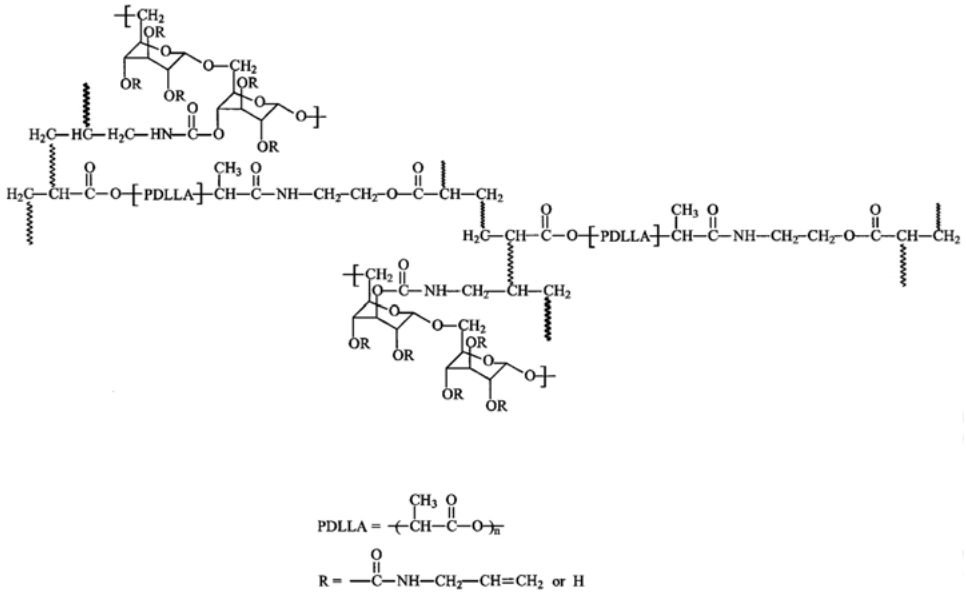

Figure 1 Schematic drawing of dex-AI/PDLLAM hydrogel network structure.

drugs could be obtained, depending on the composition ratio of dextran derivative to poly (D,L) lactide diacrylate macromer (PDLLAM) [11, 12, 13].

In order to better understand some fundamental properties of this family of hydrogels and the effect of composition ratio on structure–property relationship, the thermal and mechanical properties of this new class of biodegradable hydrogels should be examined. The present work reports the thermal and mechanical properties of the dextran derivative of allyl isocyanate (dex-AI)/PDLLAM hydrogels as a function of composition ratio of dex-AI to PDLLAM.

Differential scanning calorimetry (DSC) was employed by others to study drug-hydrogel thermodynamic interaction, amounts of freezing water in hydrogels, thermal treatment of hydrogels [14–18]. In our work, DSC was used to examine the dependence of the thermal properties, such as glass transition temperature (T_g) and melting temperature (T_m), on the dex-AI to PDLLAM composition ratio and the duration of *in vitro* hydrolytic degradation.

Another very important property of biodegradable hydrogels that determines their potential for clinical use is their mechanical property and its change with the duration of biodegradation [14–22]. Our previous study has shown that the incorporation of the hydrophobic PDLLAM component into the dex-AI hydrogel resulted in hydrogel networks to exhibit improved structure integrity upon swelling [9, 10, 12]. However, because of the relatively fast hydrolytic degradation rate of the PDLLAM, the structure integrity of the dex-AI/PDLLAM hydrogels also depended on the incubation time as well as the composition ratio. Since hydrogel's structural integrity is directly related to its mechanical property, our second objective of this study was to examine the effects of composition ratio and *in vitro* hydrolytic degradation time on the mechanical property change of the dex-AI/PDLLAM hydrogels. We used compression testing method, a common method for mechanical property analysis [23, 24], to obtain mechanical properties of both dry and swollen dex-AI/PDLLAM hydrogels.

Materials and Methods

Poly (D,L) lactic acid (PDLLA) of molecular weight (MW) 740 was supplied by Boehringer Ingelheim Company. Dextran of MW 43 000 was purchased from Sigma Chemical Company. Dimethyl formamide (DMF), allyl isocyanate (AI), and 2,2-dimethoxy 2-phenyl acetophenone were obtained from Aldrich Chemical Company. Phosphate buffer solution (PBS) of pH 7.4 (0.1 M) was used.

Synthesis of dex-AI/PDLLAM hydrogels

The synthesis of hydrogel precursors, dex-AI and PDLLAM, was carried out according to our previously published methods [9, 10]. In brief, dextran reacted with AI in the presence of dibutyltin dilaurate catalyst to form a series of dex-AI of different degrees of substitution (DS) by AI (the number of AI groups per 100 anhydroglucose units). Specifically, the dex-AI used in this study had a DS 6. The synthesis of PDLLAM involved two steps: the conversion of –COOH end groups of PDLLA to –OH end groups and the subsequent incorporation of crosslinkable unsaturated units at the –OH chain ends of PDLLA. In this study, acrylates were used as the crosslinkable unsaturated units.

The photocrosslinking of the hydrogel precursors, dex-AI and PDLLAM, was performed in DMF at a concentration of 50% (w/v), in the presence of 2.5% (w/v) 2,2-dimethoxy 2-phenyl acetophenone. The solution was transferred onto a Teflon plate and converted to hydrogel form by exposure to a long wavelength ultraviolet light (365 nm, 8 W) for 3 h. The hydrogel formed had a diameter of 8 mm and thickness of 0.8 mm. Fig. 1 shows schematically one of the possible structures of the dex-AI/PDLLAM hydrogel. In the present study, the

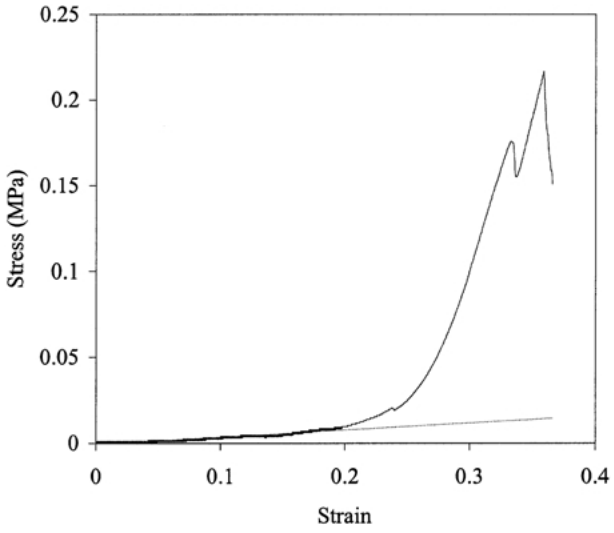

Figure 2 The compression stress-strain curve of the 100/0 dex-AI/PDLLAM hydrogel after two-day incubation in pH 7.4 phosphate buffer solution at 37 °C.

composition ratio of the dex-AI/PDLLAM hydrogels ranged from 100/0, 80/20, 50/50, 20/80 to 0/100.

Thermal analysis

The thermal properties of the hydrogels and their constituents were measured by DSC (TA model 2920). Ten mg of a sample was placed into an aluminum pan and sealed. The sample was cooled to − 50 °C and remained at this temperature for 2 min before heating to 250 °C at a rate of 20 °C/min under nitrogen environment. TA universal analysis software was used for the data analysis. Glass transition temperature (T_g) was determined at the inflexion point and melting temperature (T_m) was determined at the maximum peak from the DSC curve. The effects of chemical modification (synthesis of hydrogel precursors) and crosslinking (fabrication of hydrogel) on the change of the thermal property were studied. The effect of *in vitro* hydrolytic degradation on thermal property of the dex-AI/PDLLAM hydrogels was also investigated by incubating the hydrogels in pH 7.4 PBS at 37 °C for predetermined periods (up to 60 days), the hydrolyzed samples were then dried under vacuum for 48 h before DSC test.

Mechanical properties

The mechanical properties of the dex-AI/PDLLAM hydrogels were measured by an Instron model 1122 (Instron Corporation) at 25 °C and 65% relative humidity. The hydrogel was placed onto the top plate of a compression load cell (2 kg full load capacity) and compressed between this plate and a parallel footer (diameter 6 mm) at a constant compression rate of 0.5 mm/sec until fragmentation of the hydrogel was produced. The thickness of the hydrogel was evaluated using a compressometer (Frazier Instruments, Hagerstown, MD). Initial compression modulus was used to represent the hydrogel strength. The strength of a hydrogel control was measured using a dry sample.

In order to examine the effect of swelling and degradation on the change of the hydrogel strength, the dex-AI/PDLLAM hydrogels were incubated in pH 7.4 PBS at 37 °C for predetermined periods (up to 60 days), the strength of the swollen samples were then measured the same way as the dry ones. For each type of hydrogels, five samples were used for the compression test. Mean value was calculated with a standard deviation.

A representative compression stress-strain curve is shown in Fig. 2. The initial compression modulus was calculated from this stress-strain curve.

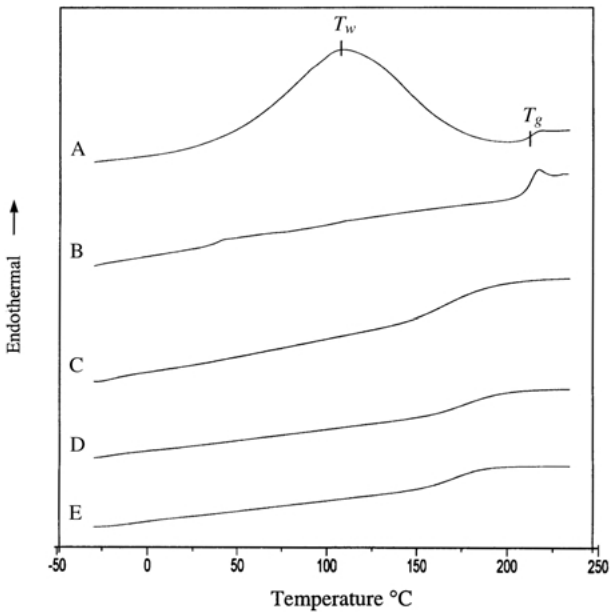

Figure 3 Differential scanning calorimetric curves of dextran, dextran derivative and dextran-based hydrogel. (A) undried dextran; (B) dried dextran; (C) dried dex-AI; (D) dried 0-day 100% dex-AI hydrogel; (E) dried 60-day 100% dex-AI hydrogel.

Results

Thermal properties

Thermal data of dextran, dex-AI, PDLLA, PDLLAM and their hydrogels are shown in Figs 3–5 and Table I.

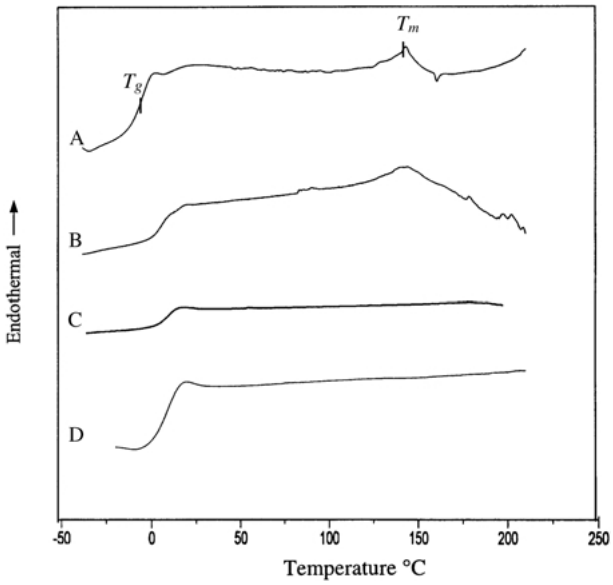

Figure 4 DSC curves of PDLLA, PDLLA derivative and PDLLA-based hydrogel. (A) PDLLA; (B) PDLLAM; (C) 0-day 100% PDLLAM hydrogel; (D) 20-day 100% PDLLAM hydrogel.

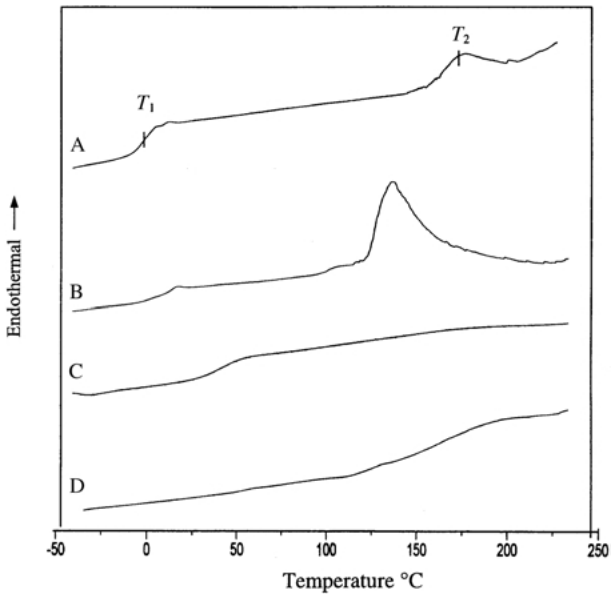

Figure 5 DSC curves of dextran and PDLLA bicomponent materials. (A) dried 50/50 dextran/PDLLA mixture; (B) dried 50/50 dex-AI/PDLLAM mixture; (C) dried 0-day 50/50 dex-AI/PDLLAM hydrogel; (D) dried 60-day 50/50 dex-AI/PDLLAM hydrogel.

Generally, either the incorporation of AI onto dextran backbone (dex-AI synthesis) or the hydrolytic degradation of all hydrogels reduced their corresponding T_g values. However, the incorporation of acrylate units onto the two chain ends of PDLLA (PDLLAM synthesis) and the photocrosslinking of the individual hydrogel precursors to form hydrogels (i.e. 100% dex-AI or 100% PDLLAM hydrogel) increased T_g.

Fig. 3 shows DSC data of five dextran samples: undried dextran and dried dextran, dex-AI, 0-day 100% dex-AI hydrogel and 60-day incubated 100% dex-AI hydrogel. The large endotherm peak around 116.6 °C in Curve A was due to the evaporation of water entrapped inside dextran and was further confirmed by its absence in the corresponding dried sample shown in Curve B. This dried dextran had a T_g at 222.7 °C. This T_g was shifted to a lower temperature (172.5 °C) after the incorporation of AI onto dextran backbone (Curve C). Upon photocrosslinking of dex-AI into hydrogel, the T_g of the 100% dex-AI hydrogel (179.0 °C in Curve D) was higher than that of the dex-AI precursor. After hydrolytic degradation of the 100% dex-AI hydrogel in PBS at 37 °C for two months, its T_g was shifted to a lower value (173.3 °C in Curve E) than that of the initial 0-day 100% dex-AI hydrogel.

The DSC profiles of dried PDLLA, PDLLAM, 0-day 100% PDLLAM hydrogel and 20-day hydrolyzed 100% PDLLAM hydrogel are shown in Fig. 4. The appearance of a small melting endotherm in the PDLLA (152.1 °C in Curve A) and PDLLAM samples (159.3 °C in Curve B), prior to crosslinking, indicates both polymers have very low degree of crystallinity. After crosslinking, the melting endotherm peak disappeared (Curve C), indicating no crystallinity in the 100% PDLLAM hydrogel. The T_g of the PDLLA and PDLLAM were 9.6 °C (Curve A) and 12.4 °C (Curve B), respectively. Photocrosslinking of PDLLAM into hydrogel form increased its T_g to 16.2 °C (Curve C), while the 20-day degradation of the 100% PDLLAM hydrogel lowered its T_g to 7.3 °C (Curve D).

Fig. 5 displays the DSC data of dried 50/50 dextran/PDLLA mixture (a physical mixture of dextran and PDLLA with a composition ratio 50 to 50), 50/50 dex-AI/PDLLAM mixture, 0-day 50/50 dex-AI/PDLLAM hydrogel and 60-day hydrolyzed 50/50 dex-AI/PDLLAM hydrogel. The crosslinking of dex-AI with PDLLAM at a composition ratio of 50/50 resulted in only one T_g (38.1 °C in Curve C), indicating that no phase separation occurred in the 50/50 dex-AI/PDLLAM hydrogel. After the hydrolytic degradation of this hydrogel in PBS for two months, its T_g appeared around 170.5 °C (Curve D). A comparison of the thermal data of the 0-day 50/50 dex-AI/PDLLAM hydrogel (Curve C) with 0-day uncrosslinked 50/50 mixture of dex-AI and PDLLAM (Curve B) indicate that the uncrosslinked mixture had a melting peak at 138.4 °C, while the corresponding hydrogel did not. The T_g observed in this uncrosslinked 50/50 dex-AI/PDLLAM mixture (21.3 °C) was lower than the crosslinked 50/50 dex-AI/PDLLAM hydrogel and was suspected from the contribution of the PDLLAM component. This was further confirmed by comparing the DSC curves of this uncrosslinked mixture of hydrogel precursors with the uncrosslinked mixture of dextran and PDLLA (Curve A).

Mechanical properties

The initial moduli of the dex-AI/PDLLAM hydrogels as a function of their composition ratio and *in vitro* degradation time are summarized in Table II. Among all hydrogels tested, the 100% 0-day dex-AI hydrogel had the highest modulus (7.82 MPa). In this 0-day group, the modulus of the dex-AI/PDLLAM hydrogel decreased gradually as the PDLLAM composition in the hydrogel increased, and the 100% PDLLAM hydrogel had the lowest modulus (1.17 MPa).

Generally, there was a large reduction in the modulus of the swollen hydrogel (2-day immersion) comparing to

TABLE I Thermal properties of the dex-AI/PDLLAM hydrogels and their components

Samples	100/0		50/50		0/100	
	T_g	T_w	T_1	T_2	T_g	T_m
Undried dextran	222.9	116.6	—	—	—	—
Dried dextran, PDLLA or dextran/PDLLA mixture	222.7	—	15.9	197.2	9.6	152.1
Dried dex-AI, PDLLAM or dex-AI/PDLLAM mixture	172.5	—	21.3	138.4	12.4	159.3
Dried 0-day dex-AI/PDLLAM hydrogels	179.0	—	38.1	—	16.2	—
Dried and hydrolyzed dex-AI/PDLLAM hydrogels	173.3[a]	—	—	170.5[a]	7.3[b]	—

[a]60-day incubation, [b]20-day incubation.

TABLE II Initial compression modulus (MPa) of dex-AI/PDLLAM hydrogels as a function of degradation time and composition ratio

Time (days)	100/0	80/20	50/50	20/80	0/100
0	7.82 ± 0.71	6.01 ± 0.36	2.56 ± 0.26	1.39 ± 0.19	1.17 ± 0.05
2	0.19 ± 0.02	0.45 ± 0.05	0.51 ± 0.07	0.77 ± 0.12	0.91 ± 0.08
30	0.10 ± 0.06	0.31 ± 0.08	0.27 ± 0.02	0.12 ± 0.02	0.05 ± 0.01
60	0.09 ± 0.02	0.07 ± 0.01	0.04 ± 0.02	—*	—*

*Completely degraded.

its dried unswollen sample, and the higher the dex-AI (hydrophilic component) composition was, the larger the reduction in modulus became. For example, the 100% dex-AI hydrogel had the lowest two-day swollen modulus (0.19 MPa) among all the hydrogels. As the PDLLAM composition increased, the two-day swollen moduli increased from 0.19 MPa for 100/0, 0.45 MPa for 80/20, 0.51 MPa for 50/50, 0.77 MPa for 20/80 to 0.91 MPa for 0/100 dex-AI/PDLLAM hydrogels.

The moduli of the swollen hydrogels decreased further as incubation time increased beyond two days, and the rate of loss of this swollen modulus increased with an increase in the PDLLAM (hydrolytic degradable component) composition in the hydrogels. For example, during a 2–60 day immersion period, the percentages of reduction in the swollen moduli of the 100/0, 50/50 and 0/100 dex-AI/PDLLAM hydrogels were 53%, 92% and 100%, respectively. In fact, the 100% PDLLAM hydrogel disappeared in PBS about the 50-day immersion period.

Discussion

Thermal properties

Dextran-based materials

A comparison of the DSC traces between dextran and dried dextran (Fig. 3) indicated the presence of loosely bound water in the undried dextran due to the large amounts of hydroxyl groups on the dextran backbone, i.e. the endothermal peak at 116.6 °C (Curve A in Fig. 3) disappeared in the totally dried dextran (Curve B in Fig. 3). Similar behavior was also observed by Ravichandran *et al*. [25] when they studied the DSC of hydrophilic poly (NVP-AA)-PEG polymer. They attributed the endothermic transition at 125 °C to the loss of loose and bound water.

The T_g of dextran observed in our study was high (222.7 °C) and no crystallinity was observed. Our thermal data appeared to confirm Kakizaki *et al*.'s [26] findings that dextran is an amorphous biopolymer and its T_g is higher than 150 °C. The strong hydrogen bonding among the dextran macromolecules is believed to be the cause of its high T_g.

The T_g of dex-AI was lower than that of dextran. This could be attributed to the replacement of –OH group with AI group that would reduce the number of hydroxyl groups available for hydrogen bonding and increase the distance between the macromolecules due to the bulky AI group. As a result, a smaller degree of intermolecular hydrogen bonding would be formed, i.e. lower T_g.

The 100% dex-AI hydrogel had a relatively higher T_g (179.0 °C) than the dex-AI polymer (172.5 °C). This is because crosslinking reduced the segmental movement of dex-AI and increased its T_g. Since the dextran polymer backbone is not hydrolytically degradable and the urethane linkage in the crosslinker is relatively stable in PBS, the 100% dex-AI hydrogel was structurally stable in PBS, and its T_g did not decrease significantly with the duration of immersion (3% reduction over 60 days). The slight reduction in T_g after a two-month incubation might come from the decrease in crosslinking density of the hydrogel by the osmotic force due to the high water content in the hydrogel, which was found to be 67% at 69-day incubation according to our previous degradation study [27].

PDLLA based materials

Due to the addition of acrylate derivative end groups into PDLLA chain ends, the synthesis of PDLLAM (MW 1,096) increased the MW of PDLLA (MW 740) and thus increased its T_g slightly. Similar to the T_g data of the 100% dex-AI hydrogel, the 100% PDLLAM hydrogel had a higher T_g (16.2 °C) than the PDLLAM precursor (12.4 °C) due to the reduction in free volume from crosslinking. The disappearance of the crystalline nature of the PDLLAM upon crosslinking shows that crosslinking reaction would prohibit crystallization. Because network structure increases the constraints of segmental mobility imposed by crosslinked PDLLAM, a phenomenon that renders the system with no freedom for spatial rearrangement, i.e. no crystallinity and T_m were observed in the 100% PDLLAM hydrogel.

It is apparent from the results in Fig. 4 that the T_g of the 100% PDLLAM hydrogel decreased as incubation time progressed. This behavior might be attributed mainly to the random chain scission of the ester linkages in the PDLLAM backbone as well as the reduction in the crosslinking density of the network structure. For example, due to hydrolytic degradation, 38% of the original weight of the 100% PDLLAM hydrogel was lost during 20-day incubation period [23, 27]. The reduction in MW of polymer and crosslinking density would result in a lower T_g. The decrease in T_g as a result of hydrolytic degradation of poly-L-lactic acid (PLLA) was also reported by Migliaresi *et al*. [14]. They found that the T_g of high MW PLLA decreased gradually from 70.6 °C to 46.7 °C over a period of 779 days incubation in Ringer solution at 37 °C. During this incubation period, the MW of the PLLA decreased from 103,000 to less than 4,900.

Dextran-PDLLA based materials

As shown in Curves A and B in Fig. 5, the 50/50 mixture of dextran/PDLLA and dex-AI/PDLLAM have two temperatures corresponding to their constituent polymers forming their own domains. A comparison between these DSC curves of the two mixtures with the ones before

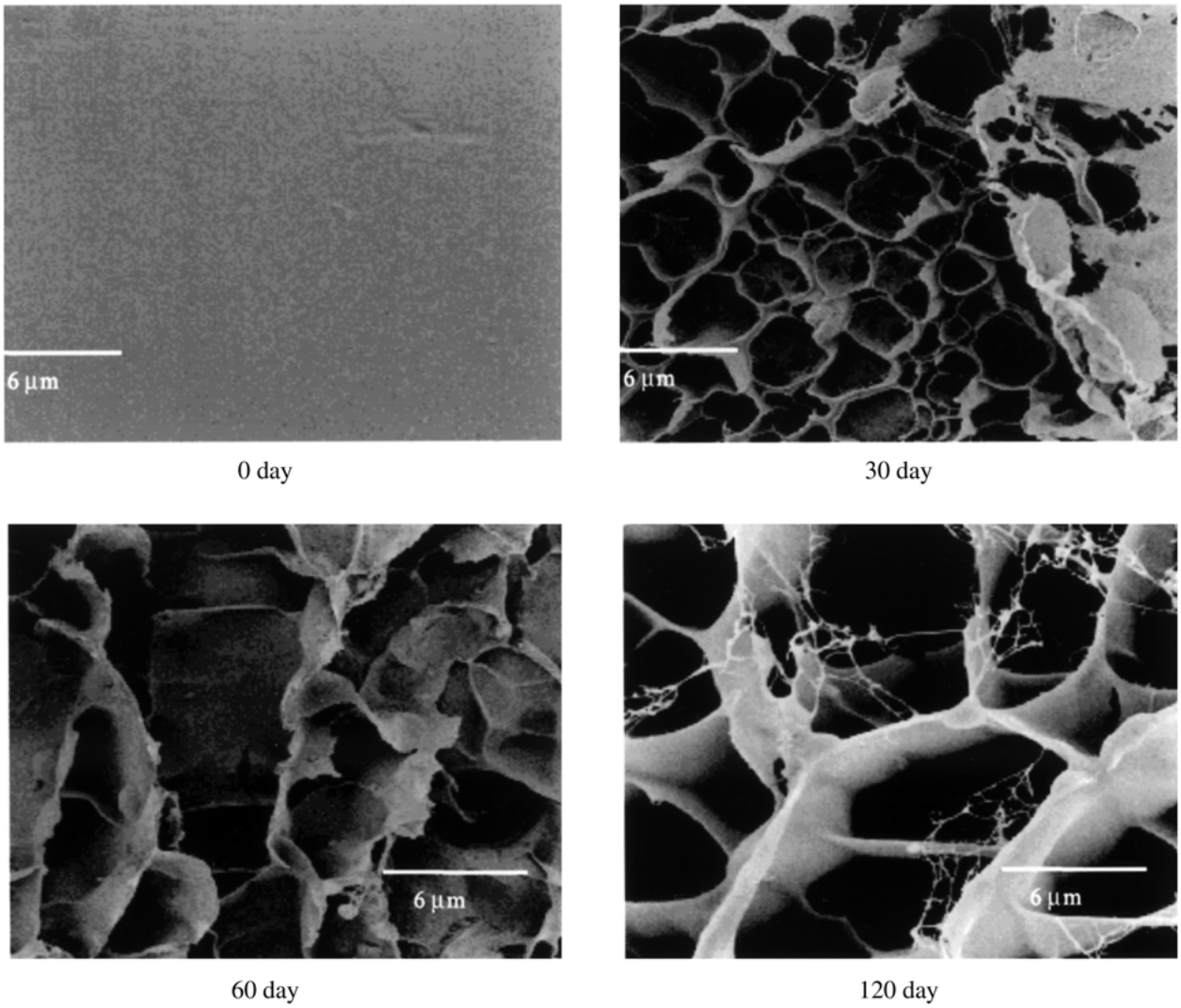

Figure 6 Scanning electron images of 50/50 dex-AI/PDLLAM hydrogels after immersion in pH 7.4 phosphate buffer solution. (A) 0 day; (B) 30 days; (C) 60 days; (D) 120 days.

mixing (Figs 3 and 4) indicated that there might exist some kind of weak interaction in the mixture. For example, the T_1 and T_2 in the 50/50 dextran/PDLLA mixture (Curve A in Fig. 5) were higher than the T_g and T_m of PDLLA (Curve A in Fig. 4), respectively. The intermolecular hydrogen bonding between dextran and PDLLA in the 50/50 mixture might be the cause for the increase in T_1 and T_2 from T_g and T_m of PDLLA. This kind of interaction in mixtures was also reported by others [16, 28]. Carelli *et al*. [16] found that when a model drug, progesterone (PGT), was entrapped in a crosslinked poly (ethylene oxides) (cr-PEO) matrix, the peak for the fusion of PGT in the matrix was considerably broader than a free PGT. They suggested that the existence of interaction between PGT and the amorphous polymer chain of cr-PEO was the cause for this change. Pitarresi *et al*. [28] studied the interaction between the α, β-poly (N-hydroxyethyl)-DL-aspartamide (PHEA) hydrogel and dimyristoilphos-phatidylcholine (DMPC) lipsome. There is no change of T_m and ΔH according to the calorimetric scans, thus PHEA hydrogel did not interact with DMPC. On the other hand, it showed that the entrapped drug, 4-biphenylacetic acid (BPAA), interacted with DMPC lipsome, causing a decrease of the T_m value of DMPC lipsome.

In the 50/50 dex-AI/PDLLAM bicomponent hydrogel, there was only one T_g (38.1 °C) observed (Curve C in Fig. 5). This clearly demonstrated that no phase separation occurred in this hydrogel. The calculated T_g of a totally miscible 50/50 dex-AI/PDLLAM blend using the following empirical equation is 29.7 °C [29].

$$1/T_g = w_1/T_{g1} + w_2/T_{g2}$$

where $w_1 = w_2 = 0.5$ for 50/50 dex-AI/PDLLAM hydrogel, $T_{g1} = 179.0$, $T_{g2} = 16.2$. The experimentally observed T_g of 50/50 hydrogel was 22% higher than the calculated 50/50 blend. This difference between experimental and calculated T_g must be attributed to the crosslinking nature in the 50/50 hydrogel that the 50/50 blend did not have, i.e., a crosslinked network structure would increase T_g of the miscible blends. For example, Eschbach and Huang [30] synthesized a hydrophilic-hydrophobic binary system of poly (2-hydroxyethyl methacrylate)(PHEMA) and polycaprolactone (PCL). A crosslinked interpenetrating polymer network of PHEMA/PCL (90/10 w/w) had its T_g 95 °C that was 16 °C higher than the T_g of the PHEMA/PCL (90/10 w/w) copolymer.

Although the hydrolytic degradation of polymers is generally believed to decrease their T_g, the T_g of the 60-day hydrolyzed 50/50 dex-AI/PDLLAM hydrogel was

found to be 348% higher than the unhydrolyzed 50/50 dex-AI/PDLLAM hydrogel. This phenomenon can be explained as below. Based on our previous studies of the degradation property of dex-AI/PDLLAM hydrogel [11, 31], the 100% PDLLAM hydrogel was found to totally disappear in PBS at about 50 days. Therefore, after two-months incubation in PBS in the present study, the PDLLAM component of the 50/50 dex-AI/PDLLAM bicomponent hydrogel would degrade completely and only the dex-AI component remained. Thus, the T_g of the 60-day hydrolyzed 50/50 dex-AI/PDLLAM hydrogel (170.5 °C) reflected the glass transition of the 60-day hydrolyzed dex-AI component, which had a T_g of 173.3 °C, a 1.6% difference that was well within the experimental error of DSC. The broadening of the T_g of the 60-days hydrolyzed 50/50 dex-AI/PDLLAM hydrogel (Fig. 5, Curve D) also indicated that the polydispersity of dex-AI increased, which might come from the chain cleavage of dex-AI. Our previous studies [11, 23] showed that, after two-months incubation, a loose 3D porous network structure formed in the hydrogel as the PDLLAM component degraded and diffused out of the hydrogel (Fig. 6). This process of swelling and hydrolytic degradation induced porous network structure formation would lead to a significant increase in osmotic pressure within the hydrogel due to the large amounts of water uptake, i.e. 28% increase in water content from 2 to 69 days incubation period. Such an increase in osmotic pressure might facilitate the fragmentation of the dex-AI backbone and an increase in its polydispersity.

Mechanical properties

Our mechanical property data (Table II) showed that the 0-day 100% dex-AI hydrogel had the highest modulus and it decreased with an increase in the PDLLAM composition in the hydrogel (0-day data). This relationship might be attributed to the relative magnitudes of the T_g of the hydrogel precursors to the temperature at which the mechanical property was tested. The modulus of the 100% dex-AI hydrogel tested in this study reflected its mechanical strength in a glassy state, i.e. the temperature of compression testing (25 °C) was far below the T_g of the 100% dex-AI hydrogel (179 °C). However, the T_g of the PDLLAM (12.4 °C) was below the compression testing temperature. Therefore, the incorporation of the PDLLAM component into the dex-AI hydrogel would reduce the T_g of the 100% dex-AI hydrogel and shift the T_g of the bicomponent hydrogels closer to our testing temperature for mechanical property, and hence reduce the moduli of the bicomponent hydrogels. The level of reduction in modulus depended on the composition ratio and became larger with an increase in the PDLLAM composition. Finally, the 100% PDLLAM hydrogel had the lowest modulus.

In the two-day swollen hydrogels, the swollen moduli of hydrogels showed composition-dependence that was opposite to the 0-day unswollen hydrogels and might be attributed to the composition-dependent swelling and the formation of various degree of 3D porous network structure. According to our previous study of the dex-AI/PDLLAM hydrogels [31], the swelling ratios dex-AI/PDLLAM hydrogels reduced from 349% for 100/0, 82% for 50/50 to 33% for 0/100 dex-AI to PDLLAM composition ratios during two-day immersion period. In the present study, the moduli of dex-AI/PDLLAM hydrogels increased from 0.19 MPa for 100/0, 0.51 MPa for 50/50 to 0.91 MPa for 0/100 dex-AI/PDLLAM hydrogels. Therefore, we suggest that, as the PDLLAM composition increased, the hydrophobicity of the hydrogel increased, swelling in the hydrogel decreased, thus the modulus increased accordingly. This composition-swelling relationship was also reflected in the surface morphology of these hydrogels. As shown in Fig. 7, at the end of 2-day immersion, the 100/0 dex-AI/

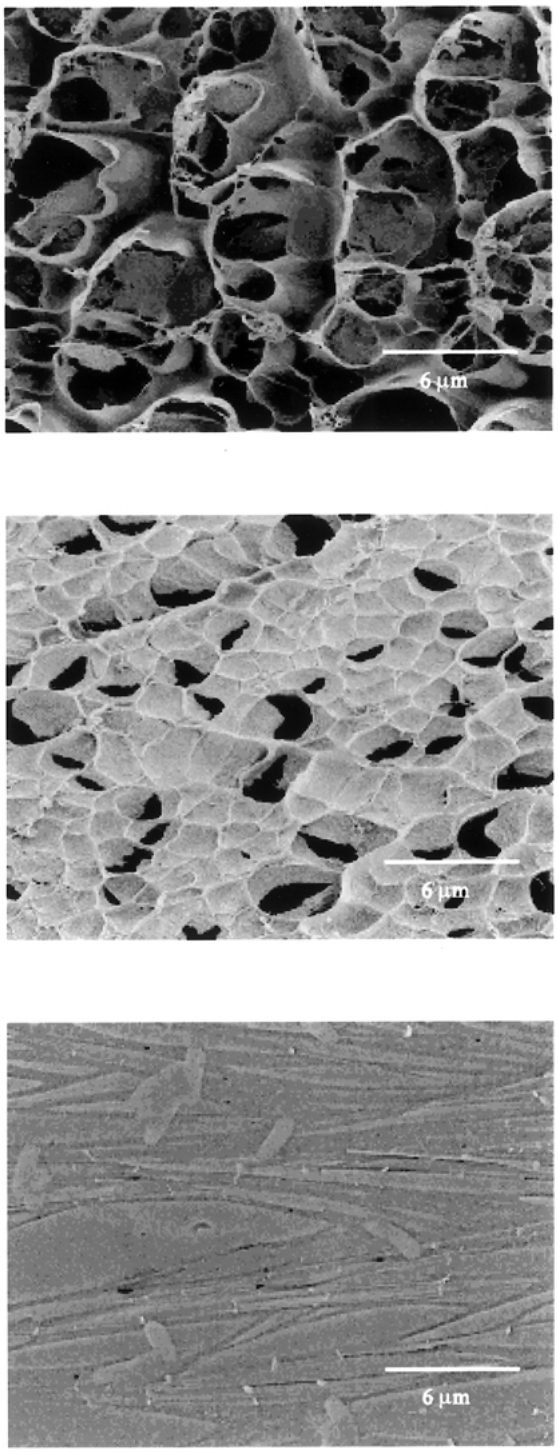

Figure 7 Scanning electron images of dex-AI/PDLLAM hydrogels after 2-day immersion in pH 7.4 PBS at 37 °C. (A) 100/0; (B) 50/50; (C) 0/100 dex-AI/PDLLAM.

PDLLAM hydrogel showed the most open 3D porous structure (Fig. 7A), followed by the 50/50 dex-AI/PDLLAM hydrogel (Fig. 7B), and the 0/100 dex-AI/PDLLAM hydrogel had the most compact and dense structure (Fig. 7C). Therefore, the number and size of swelling-induced pores were the highest in the 100/0 dex-AI/PDLLAM hydrogel and decreased as the PDLLAM composition increased. This composition-dependent morphological change at two-day immersion led to the largest modulus reduction in the 100/0 dex-AI/PDLLAM hydrogel (97%), followed by the 50/50 dex-AI/PDLLAM hydrogel (80%) and the 0/100 dex-AI/PDLLAM hydrogel had the smallest reduction (22%) from its 0-day modulus.

At a constant composition ratio, the moduli of the dex-AI-PDLLAM hydrogels decreased with incubation time. This loss in mechanical strength was attributed to either the swelling-induced formation of 3D porous network structure or/and the hydrolytic degradation of the PDLLAM via the chain scission of ester linkages located in the PDLLAM backbone [11, 31]. The magnitude of swelling-induced loss of modulus was composition ratio dependent and occurred in the early stage of immersion; the higher the swelling was, the larger the loss of modulus became. The loss of mechanical strength after the early stage of immersion was attributed to the hydrolytic degradation of the PDLLAM component in the dex-AI/PDLLAM hydrogels; the higher the PDLLAM composition was, the larger the loss of modulus became. This PDLLAM composition dependence of modulus loss after two days immersion was consistent with the weight loss data from our previous study [27]. We found that the weight losses of the 100/0, 50/50 and 0/100 dex-AI/PDLLAM hydrogels were 10%, 43% and 100% from 2 to 60 day incubation period, respectively. Their loss of modulus was 53%, 92% and 100%, respectively.

These swelling and degradation dependent mechanical properties of hydrogels were also consistent with other reported studies [20, 23, 30, 33]. For example, Miyachi *et al*. [20] found that the Young's modulus of the swollen copoly(N-hydroxypropyl-L-glutamine/L-leucine) hydrogel increased from 0.205 to 14.80 MPa when swelling ratio decreased from 10.4 to 1.8. According to Eschbach and Huang [30] the incorporation of 10% hydrophobic PCL in IPN structures decreased the equilibrium water content (at 20 °C for 72 h) of the modified PHEMA hydrogel by 17%. Due to this lower water content, the swollen tensile modulus of the IPN hydrogel increased by a factor of 3.1. Because of their very short study period, the hydrolytic degradation effect on the tensile modulus was not reported. Vervoort *et al*. found that a significant reduction in inulin hydrogel resistance to compression occurred after the hydrogel was incubated in Novozym 230 solutions for seven days [23]. As inulinase concentration increased in the Novozym 230 solution, the loss of hydrogel mechanical strength increased. Because enzymatic degradation of the hydrogels caused a loss of network integrity by hydrolysis of the hydrogel backbone. This resulted in a decreased resistance to compression.

Conclusion

The present study focused on the effects of composition ratio and *in vitro* hydrolytic degradation of dex-AI/PDLLAM hydrogels on their thermal and mechanical properties. The DSC data revealed that the 100% dex-AI hydrogel was relatively stable in PBS, with a small reduction in T_g. Due to the hydrolytic degradation of the PDLLAM in PBS, the T_g of the 100% PDLLAM hydrogel, however, decreased very rapidly after incubation. The presence of only one T_g in the 50/50 dex-AI/PDLLAM hydrogel indicated that there was no phase separation in the bicomponent hydrogel. Some noteworthy differences in the mechanical property of the dex-AI/PDLLAM hydrogels were observed. As the PDLLAM composition increased, the modulus of the 0-day unswollen hydrogel decreased gradually, because the increase in the PDLLAM composition converted the hydrogel from a glassy to rubbery state due to the very low T_g of the PDLLAM component. It has been shown that the formation of 3D porous network structure upon swelling was responsible for the large reduction in the compression modulus of the hydrogel at a very early immersion stage and such early stage modulus reduction became smaller in dex-AI/PDLLAM hydrogels having higher PDLLAM composition. In the late stage of immersion, due to the hydrolytic degradation the PDLLAM component and loss of structure integrity, the rate and extent of mechanical strength loss increased as the PDLLAM composition increased.

Acknowledgment

The authors would like to express their gratitude to the College of Human Ecology, Cornell University for their financial support to Yeli Zhang and the Boehringer Ingelheim company for their kind supply of low molecular PDLLA samples.

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Received 29 November 2000
and accepted 19 July 2001