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Synthesis of biodegradable poly(propylene fumarate) networks with poly(propylene fumarate)–diacrylate macromers as crosslinking agents and characterization of their degradation products

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Abstract

New biodegradable poly(propylene fumarate)-based polymer networks have been prepared by radical polymerization using poly(propylene fumarate) (PPF) and poly(propylene fumarate)–diacrylate (PPF–DA) macromers. Two PPF–DAs were synthesized incorporating one ($m = 1$) and two ($m = 2$) fumarate units, and were employed in the synthesis of the polymer networks. The PPF/PPF–DA double bond ratio and the molecular weight of PPF–DA were varied to assess their effects on the mechanical properties of the resulting polymer networks as well as on their equilibrium water content. The compressive strength at fracture of PPF/PPF–DA ($m = 1$) polymer networks increased from 11.2 ± 1.8 to 66.2 ± 5.5 MPa as the double bond ratio of PPF/PPF–DA ($m = 1$) decreased from 4 to 0.5. An increase in compressive modulus was also observed from 19.4 ± 1.8 to 340.2 ± 30.7 MPa for the same range of the double bond ratio of PPF/PPF–DA. Increasing the molecular weight of PPF–DA ($m = 2$) caused both the compressive strength at fracture and modulus of the corresponding polymer networks to increase to the ranges of 14.4 ± 4.2 to 88.2 ± 6.1 MPa and 28.0 ± 2.4 to 480.4 ± 35.9 MPa, respectively. Similarly, both were increased as the PPF/PPF–DA ($m = 2$) double bond ratio decreased from 4 to 0.5. The PPF/PPF–DA crosslinked polymer networks showed negligible equilibrium water content for all 10 formulations tested in this study. The degradation reaction of the PPF/PPF–DA polymer networks under basic conditions was investigated. The degradation products were isolated and characterized by NMR and GC/MS as fumaric acid, propylene glycol, and poly(acrylic acid-*co*-fumaric acid) of weight average molecular weight of 5080. These data demonstrate that biodegradable PPF/PPF–DA polymer networks should have great potential as polymer scaffolds for orthopedic applications in tissue engineering. © 2000 Published by Elsevier Science Ltd.

Keywords: Poly(propylene fumarate); Poly(ethylene glycol); In situ polymerization

1. Introduction

Biodegradable polymers have been explored recently because they show promise for temporary surgical and pharmacological applications. Aliphatic polyesters and anhydrides are the polymer families that have been recognized as the most attractive and promising. Several reviews highlight the recent developments in this area (for reviews, see Refs. [1–3]). In the field of tissue engineering, degradable biomaterials usually serve as a scaffold to provide mechanical support and a matrix for ingrowth of new tissue [4]. As new tissues form, the polymer degrades until it is entirely dissolved. The degradation products are eliminated through natural pathways such as metabolic processes.

Poly(propylene fumarate) (PPF) is one of these attractive polymers, which has been under investigation as a biodegradable and crosslinkable polymer composite for use in orthopedic applications for many years [5–8]. The fumarate double bond in PPF can be crosslinked with various reagents to form polymer networks. The crosslinking reaction can be carried out at a defect site using benzoyl peroxide initiator, which is particularly interesting for orthopaedic applications in filling irregularly shaped defects with minimal surgical intervention. The development of biodegradable polymer composites based on PPF for orthopaedic applications has been a subject of investigation in our laboratory [9–12]. Several PPF-based formulation methods have been

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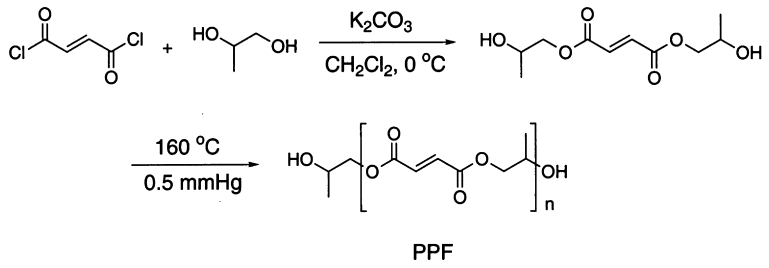

Fig. 1. Synthesis of poly(propylene fumarate).

evaluated by varying such parameters as the molecular weight of PPF and the choice of crosslinking reagents.

N-Vinyl pyrrolidone [11] (NVP) was usually used as a crosslinking reagent in PPF-based formulations, but any unreacted NVP [13] after in situ polymerization is of concern on account of its toxicity. Also, the poly(vinyl pyrrolidone) (PVP) crosslinks in the crosslinked PPF networks are non-degradable. Recently, we [14] have reported using poly(ethylene glycol)–dimethacrylate (PEG–DMA) as a crosslinking reagent to form PPF polymer networks. These PPF/PEG–DMA composites possessed ideal initial mechanical properties which, however, decreased in the wet state due to the hydrophilicity of PEG. In order to retain the favorable mechanical properties, high water absorption should be avoided.

Another important factor in the success of biomaterials development is the properties of the degradation products. Degradation of PPF-based polymer composites has been studied [7,9,15,16] to assess the mass loss and the change of mechanical properties, but characterization of the degradation products was not reported.

In this study, we attempt to develop biodegradable PPF-based polymer networks using PPF–diacrylate (PPF–DA) as a crosslinking reagent. We investigated the effects of double bond ratio of PPF/PPF–DA and molecular weight of PPF–DA on the mechanical properties of the crosslinked polymer networks as well as on their equilibrium water content. Finally, the degradation reaction of the PPF/PPF–DA polymer networks was studied and the degradation products were isolated and characterized by instrumental analysis.

2. Experimental section

2.1. Materials

Propylene glycol, fumaryl chloride, benzoyl peroxide (BP), *N*,*N*-dimethyl-*p*-toluidine (DMT), and acryloyl chloride were purchased from Aldrich (Milwaukee, WI). Solvents such as methylene chloride, ethyl acetate and petroleum ether were purchased from Fisher (Pittsburgh, PA) and used as received. Fumaryl chloride was purified by distillation at 1 atm under nitrogen.

2.2. Synthesis of poly(propylene fumarate)

PPF was synthesized by a two-step reaction process described previously [12] (Fig. 1). Briefly, fumaryl chloride was added dropwise to a solution of propylene glycol in methylene chloride at 0°C under nitrogen in the presence of K_2CO_3. After addition of fumaryl chloride, the reaction mixture was stirred for an additional 2 h at 0°C and then water was added to dissolve the inorganic salt. The organic layer was separated and dried with Na_2SO_4. After filtration and evaporation of the solvent, the formed di-(2-hydroxypropyl) fumarate underwent transesterification reaction to produce PPF at a temperature of 160°C and a pressure of 0.5 mmHg. PPF was purified through solution precipitation in chloroform and petroleum ether. ^{1}H-NMR (250 MHz, $CDCl_3$): δ 1.28 (m, 3H, CH_3), 4.26 (m, 2H, CH_2), 5.27 (m, 1H, CH), 6.84 (bs, 2H, –CH=CH–).

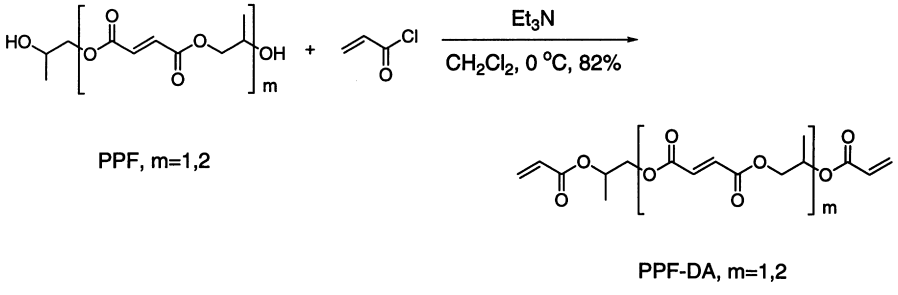

Fig. 2. Synthesis of PPF–DA ($m = 1, 2$).

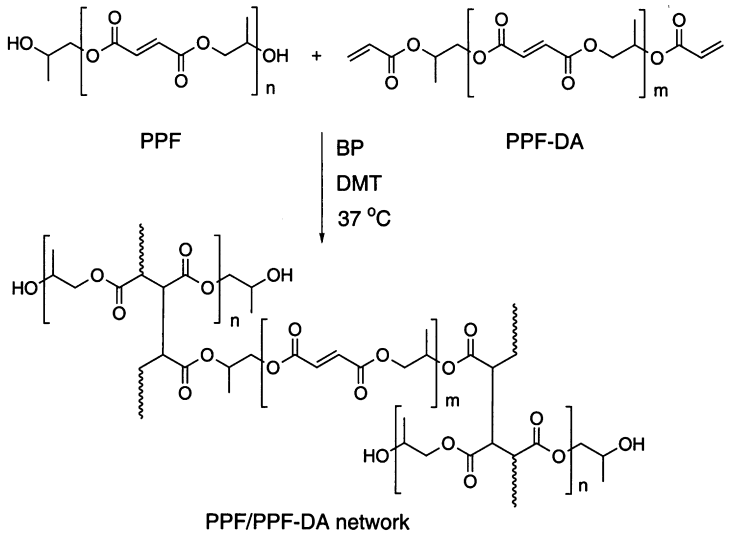

Fig. 3. Synthesis of PPF/PPF–DA polymer networks.

2.3. Synthesis of PPF–DA

Fig. 2 shows the synthetic reactions of PPF–diacrylate. A typical procedure for synthesis of PPF–DA ($m = 1$) is given here. Di-(2-hydroxypropyl) fumarate was obtained from the reaction of fumaryl chloride with propylene glycol as described above. To a solution of di-(2-hydroxypropyl) fumarate (23.2 g, 0.1 mol) in dry CH_2Cl_2 (200 ml) at 0°C was added triethylamine (30.3 g, 0.3 mol). After stirring for 10 min, acryloyl chloride (26 g, 0.3 mol) was added dropwise during approximately 2 h, causing formation of a white precipitate. The reaction mixture was stirred overnight at room temperature. The white precipitate was filtered off and the CH_2Cl_2 solvent was rotary evaporated. Ethyl acetate (250 ml) was added to the residue and the ethyl acetate solution was washed with aq. NaOH (5%), water and brine. After drying over Na_2SO_4, filtration of the mixture and solvent evaporation, PPF–DA was obtained (28.5 g, 83%). ^{1}H-NMR (250 MHz, $CDCl_3$): δ 1.32 (m, 3H, CH_3), 4.26 (m, 2H, CH_2), 5.24 (m, 1H, CH), 5.85 (m, 1H, –CH=CH_2), 6.05 (m, 1H, –CH=CH_2), 6.37 (dd, 1H, –CH=CH_2), 6.84 (bs, –CH=CH–). For synthesis of PPF–DA ($m = 2$), PPF ($m = 2$) obtained by the transesterification reaction was used instead of di-(2-hydroxypropyl) fumarate.

2.4. Preparation of PPF/PPF–DA networks

Fig. 3 shows the synthesis of PPF/PPF–DA polymer networks and a typical procedure for their preparation is given here. PPF (1 g) was mixed with 1.04 g PPF–DA

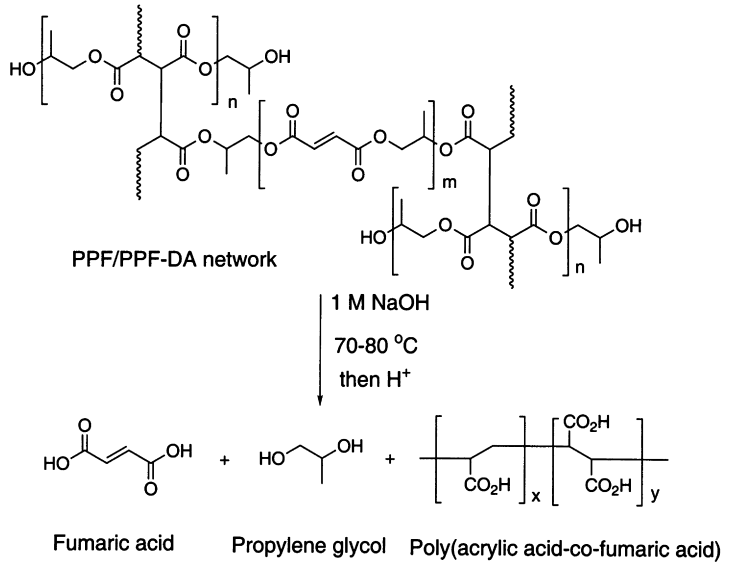

Fig. 4. Degradation reaction of PPF/PPF–DA polymer networks.

Table 1
Formulation of 10 PPF/PPF–DA ($m = 1, 2$) networks. The BP and DMT contents were 0.7 and 0.25 wt%, respectively, for all formulations. (The percentages of BP and DMT were based on the total amount of PPF and PPF–DA)

No.	*m*	Weight ratio of PPF/PPF–DA	Double bond ratio of PPF/PPF–DA
1	1	0	0
2	1	0.48	0.5
3	1	0.96	1
4	1	1.92	2
5	1	3.84	4
6	2	0	0
7	2	0.33	0.5
8	2	0.66	1
9	2	1.32	2
10	2	2.63	4

(the double bond ratio of PPF/PPF–DA is 1) at room temperature. Initiator solution (0.14 ml) (0.1 g BP per 1 ml CH_2Cl_2) was then added to the PPF/PPF–DA mixture. After thorough mixing on Vortexer, 5 μl DMT were added with rapid stirring, then, the mixture was molded as a cylinder or a film. For mechanical testing, the mixture was placed into cylindrical vials of 6 mm diameter. The vials were centrifuged at 2000 rpm for 5 min to remove any air bubbles and defects. The molds were then placed in a 37°C water bath. After 2 h, the cylinders were removed from the vials and cut into 12 mm long segments using a Diamond Saw (SBT Inc. San Clemente, CA). For degradation studies, PPF/PPF–DA network films were obtained by polymerization of the PPF/PPF–DA mixture in a Teflon mold with 1 mm depth.

2.5. Degradation reaction of PPF/PPF–DA networks

The degradation reaction of PPF/PPF–DA networks was carried out under strongly basic conditions (Fig. 4). PPF/PPF–DA (1.7 g) networks were placed into 100 ml 1 M NaOH solution and the reaction mixture was stirred at 70–80°C under a nitrogen atmosphere until the polymer networks completely dissolved (approximately 4 days). The solution pH was adjusted to 1 by addition of 5% aq. HCl. The acidic solution was rotary evaporated to give a slushy residue. For NMR studies, the residue was extracted with acetone-d_6 (10 ml) for 20 min at room temperature. For GC and GC/MS, acetone was used to extract the degradation products. The undissolved residue was washed with acetone and dried under vacuum. To the slightly orange solid was added freshly prepared diazomethane in ether [17] at room temperature until the yellow color of diazomethane persisted, suggesting completion of the reaction. As expected, gas evolution (N_2) was observed during this reaction. The ether was rotary evaporated and the product was extracted into $CHCl_3$ for GPC measurement.

2.6. Characterization

The molecular weights of PPF and degradation copolymer were determined relative to polystyrene standards in chloroform by gel permeation chromatography with a differential refractometer detector (Waters 410, Milford, MA). A Styragel HR2 column (300×7.8 mm^2, 5 nm, mixed bed, Waters, Milford, MA) and a Phenogel guard column (50×7.8 mm^2, 5 nm, mixed bed, Phenomenex) were employed with a chloroform eluent flow rate of 1 ml/min.

The structures of PPF and PPF–DA were analyzed by

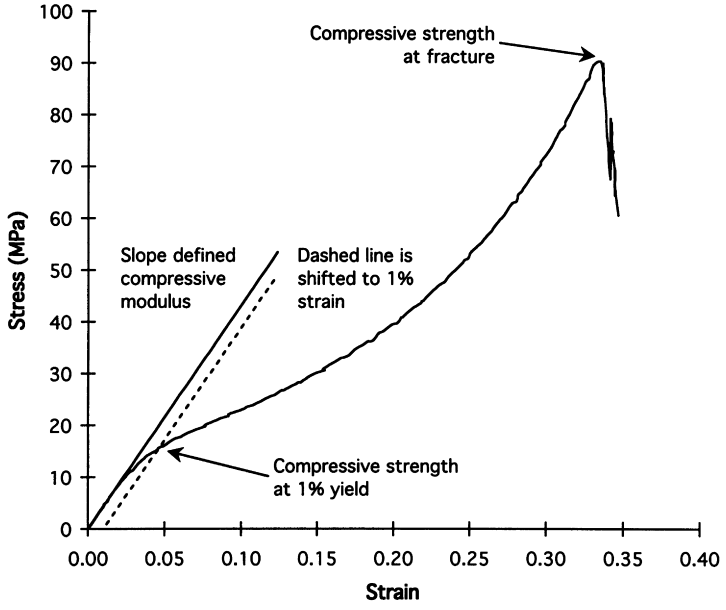

Fig. 5. Typical stress–strain curve of the compression test performed on the crosslinked PPF/PPF–DA polymer networks defining compressive strength at yield, compressive strength at fracture, and compressive modulus.

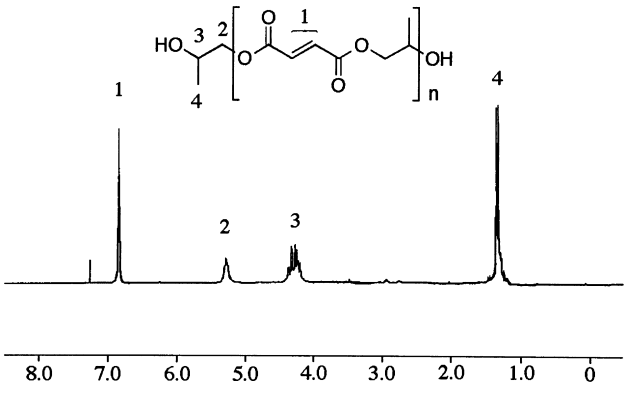

Fig. 6. ^{1}H NMR spectrum of PPF.

NMR and FTIR. NMR spectra were acquired in $CDCl_3$ on a Bruker AC-250 spectrometer. FTIR spectra were obtained on a Nicolet 550 spectrometer (Madison, WI) using neat samples. For the analysis of the degradation products, analytical gas chromatography (GC) was carried out on a HP 5890A instrument equipped with a AT1701 capillary column (0.25 mm × 30 m) and FID detectors. Analytical GC conditions were 80°C for 5 min, ramp at 10°C/min to 250°C, hold 10 min. GC/MS spectra were obtained on a Finnigan MAT 95 equipped with a DB-5 capillary column (0.25 mm × 30 m).

The mechanical properties of the PPF/PPF–DA networks under compression were determined according to the method reported before [11]. Ten formulations were designed to assess the effects of molecular weight of PPF–DA and double bond ratio of PPF/PPF–DA on the compressive strength at yield, compressive strength at fracture, and compressive modulus. The different formulations are presented in Table 1. Compressive testing for strength and modulus was conducted on an 858 Material Testing System mechanical testing machine (MTS System Corp., Eden Prairie, MN) following the guidelines set in ASTM F451-95. Cylindrical samples 12 mm high and 6 mm in diameter were compressed in a dry state at a cross-head speed of 1 mm/min until failure, with the stress versus strain curve recorded throughout. The compressive strength at fracture was defined as the maximum stress carried by the specimen during the test (the peak of the stress–strain curve). The compressive modulus was calculated as the slope of the initial linear portion of the stress–strain curve. The compressive strength at the yield was determined by drawing a line parallel to the slope defining the modulus, beginning at 1.0% strain. The intersection of this line with the stress–strain curve was recorded as the compressive strength at yield. A typical stress–strain curve of this compression test and the mechanical property definitions are presented in Fig. 5.

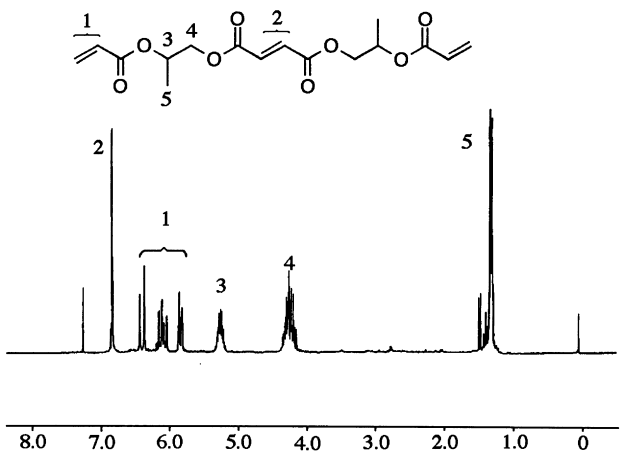

Fig. 7. ^{1}H NMR spectrum of PPF–DA ($m = 1$).

The equilibrium water content of PPF/PPF–DA polymer networks was determined by gravimetry measurements [14] with cylindrical specimens of 6 mm diameter and 12 mm height prepared as outlined for the mechanical testing. The fabricated PPF/PPF–DA networks were rinsed with methylene chloride (10 ml), air-dried for one day, and vacuum-dried for 6 h. The weight of the dried specimens was then recorded (W_1). Subsequently, the specimens were immersed in phosphate buffered saline (PBS, pH 7.4) at room temperature. The weight of the specimens was monitored periodically and recorded when it reached an equilibrium value (W_2) (approximately after 24 h). The equilibrium water content was calculated as $[(W_2 - W_1)/W_2] \times 100\%$.

Experiments for the equilibrium water content measurement were conducted in triplicate while those for the mechanical testing were repeated five times. The data are expressed as mean ± standard deviation. Single factor analysis of variance (ANOVA) was used to assess the statistical significance of the results. Scheffe's method was employed for multiple comparison tests at a significance level of 95% ($p < 0.05$).

3. Results and discussion

3.1. Synthesis of PPF and PPF–DA

PPF was synthesized by a two-step sequence discovered in our laboratory. Di-(2-hydroxypropyl) fumarate was obtained by the reaction of fumaryl chloride with propylene glycol. Transesterification of di-(2-hydroxypropyl) fumarate without any added catalyst produced PPF. The molecular weight of PPF could be controlled by varying the transesterification time. In this study, the PPF having a number average molecular weight of 1700 Da ($n = 11$) and polydispersity index of 1.98 was obtained after 15 h transesterification. In its ^{1}H NMR spectrum (Fig. 6), four multiplets were observed. The signal at 6.84 ppm was assigned to the olefinic protons while the 1.27-ppm peak was attributed to the methyl protons. The other two signals at 5.28 and 4.28 ppm belonged, respectively, to the methine and methylene protons of the propyl diol. The integration ratio of the vinyl protons to the methyl protons was 2/3.6,

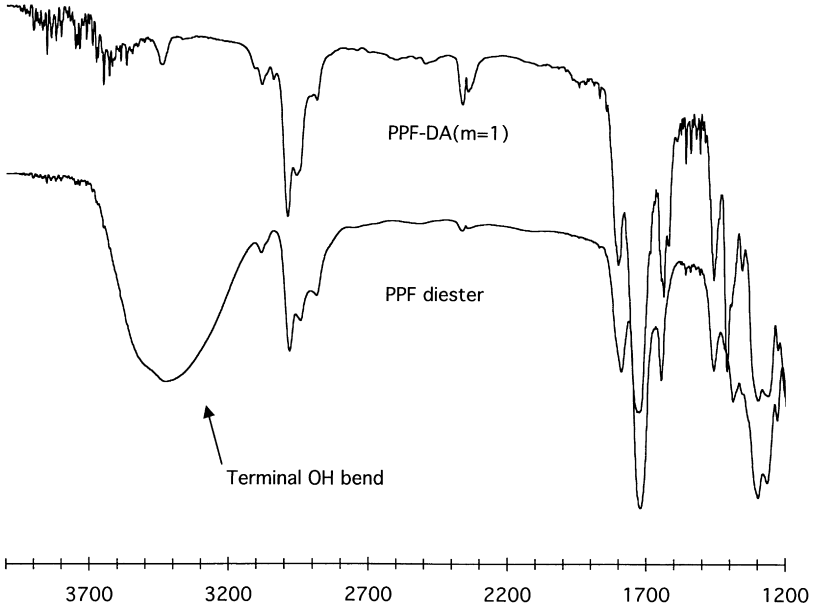

Fig. 8. FTIR spectra of (a) PPF oligomer and (b) PPF–DA ($m = 1$).

which is close to the 2/3.4 calculated based on the number average molecular weight of PPF. This agreement indicated no loss of polymer unsaturation during the two-step synthesis.

Two PPF–DAs with $m = 1$ and 2 were synthesized by reaction of the appropriate PPF with acryloyl chloride. It was found from the ^{1}H NMR spectrum (Fig. 7) of PPF–DA ($m = 1$) that integration ratio of acryl protons to fumarate protons was 3 to 1. This ratio suggested that both terminal hydroxyl groups in di-(2-hydroxypropyl) fumarate were derivatized with an acrylate group. Further evidence for reaction at both ends came from the FTIR spectrum (Fig. 8) of PPF–DA, which showed no OH stretching band in the region of 3500–3100 cm^{-1}. The PPF with $m = 2$ was produced in the same way using PPF with $m = 2$ obtained after 4 h transesterification. The integration ratio of acrylate to fumarate vinyl protons allows determination of the molecular weight of PPF–DA. The ^{1}H NMR spectrum gave the ratio of 3:2, which implies presence of an average number of two fumarate units in this PPF–DA.

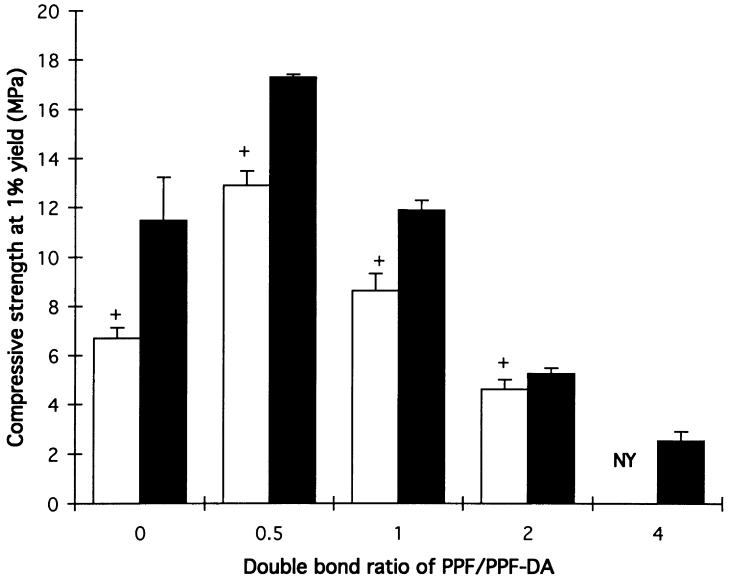

Fig. 9. Dependence of compressive strength at yield of crosslinked PPF/PPF–DA polymer networks on both the double bond ratio of PPF/PPF–DA and the molecular weight of PPF–DA ($m = 1$, white bar; $m = 2$, black bar). Error bars stand for means ± standard deviation for $n = 5$. A symbol " + " represents the statistically significant difference of pairwise comparison for crosslinked PPF/PPF–DA networks with different molecular weights of PPF–DA ($p < 0.05$). The symbol "NY" indicates that the polymer network did not exhibit a linearly elastic yield point and thus a compressive strength at yield could not be obtained.

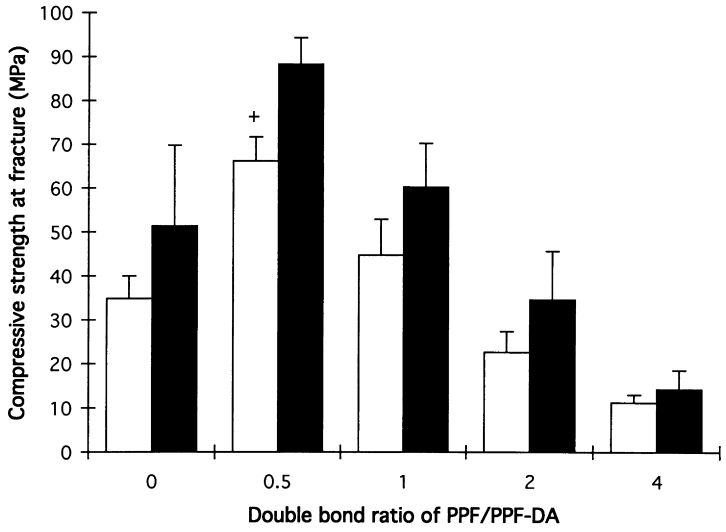

Fig. 10. Dependence of compressive strength at fracture of PPF/PPF–DA polymer networks on both the double bond ratio of PPF/PPF–DA and the molecular weight of PPF–DA ($m = 1$, white bar; $m = 2$,black bar). Error bars stand for means ± standard deviation for $n = 5$. A symbol " + " represents the statistically significant difference of pairwise comparison for crosslinked PPF/PPF–DA networks with different molecular weights of PPF–DA ($p < 0.05$).

3.2. Mechanical properties

The compressive strength at yield, compressive strength at fracture, and compressive modulus of 10 formulations tested are shown in Figs. 9–11. The compressive strength at fracture of PPF/PPF–DA ($m = 1$) ranged from 11.2 ± 1.8 to 66.2 ± 5.5 MPa and the modulus was in the range of 19.4 ± 1.8 to 340.2 ± 30.7 MPa. The compressive strength at yield varied from 4.6 ± 0.4 to 12.9 ± 0.6 MPa. All three mechanical properties increased as the double bond ratio of PPF/PPF–DA decreased ($p < 0.05$). The decrease of the PPF/PPF–DA double bond ratio increases the fraction of the more reactive acrylate group, which increased the efficiency of crosslinking, creating a more densely crosslinked polymeric network. When the double bond ratio of PPF/PPF–DA was zero (absence of PPF), the compressive strength at yield, strength at fracture, and modulus dropped to 6.7 ± 0.4, 34.8 ± 5.2, and 127.5 ± 17.2 MPa, respectively. Formation of polymer networks from PPF–DA alone indicated that the fumarate groups in PPF–DA might also be involved in the crosslinking reaction. The self-polymerization of PPF–DA rather than crosslinking

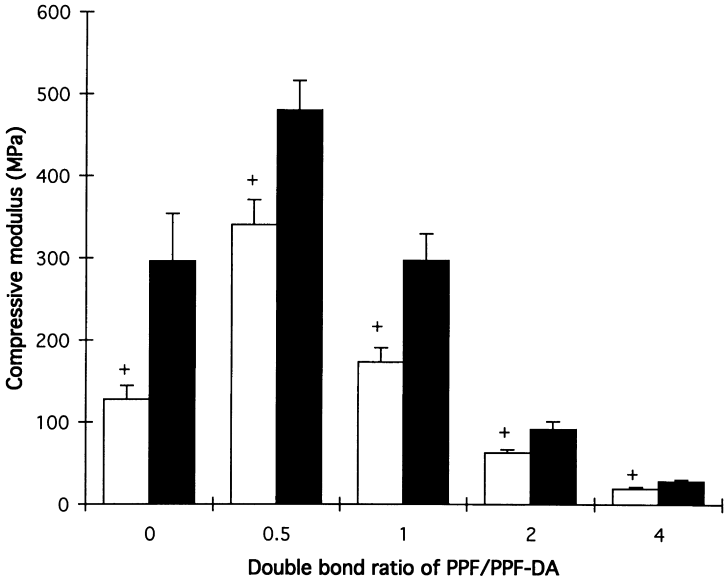

Fig. 11. Dependence of compressive modulus of crosslinked PPF/PPF–DA polymer networks on both the double bond ratio of PPF/PPF–DA and the molecular weight of PPF–DA ($m = 1$, white bar; $m = 2$, black bar). Error bars stand for means ± standard deviation for $n = 5$. A symbol " + " represents the statistically significant difference of pairwise comparison for crosslinked PPF/PPF–DA networks with different molecular weights of PPF–DA ($p < 0.05$).

Table 2
Equilibrium water content (wt%) of crosslinked PPF/PPF–DA polymer networks after equilibrium in PBS as a function of the double bond ratio of PPF/PPF–DA and the molecular weight of PPF–DA

Double bond ratio of PPF/PPF–DA	$m = 1$	$m = 2$
0	0.90 ± 0.03	0.55 ± 0.22
0.5	0.67 ± 0.04	0.65 ± 0.12
1	1.37 ± 0.13	0.87 ± 0.14
2	0.82 ± 0.11	0.96 ± 0.32
4	0.72 ± 0.08	0.79 ± 0.08

to PPF may dominate and generate long crosslinks, decreasing the mechanical properties, when the PPF/PPF–DA double bond ratio was decreased enough.

When the propylene fumarate chain linking two acrylate groups in PPF–DA was lengthened, this provided an additional crosslinkable fumarate double bond, leading to an increase of mechanical properties. The compressive strength at yield, strength at fracture, and modulus of the PPF/PPF–DA ($m = 2$) increased to the ranges of 2.5 ± 0.4 to 17.3 ± 7.5 MPa, 14.4 ± 4.3 to 88.2 ± 6.1 MPa, and 28.0 ± 2.4 to 480.4 ± 35.9 MPa, respectively, in the same range of PPF/PPF–DA ($m = 2$) double bond ratio. Again, it was observed that as the PPF/PPF–DA double bond ratio decreased, the mechanical properties increased ($p < 0.05$). These results demonstrate that the mechanical properties of PPF/PPF–DA polymeric networks can be tailored by varying not only the PPF/PPF–DA double bond ratio, but also the length of the PPF–DA. In comparison with other crosslinked PPF composites [5,11,14], the PPF/PPF–DA polymeric networks tested in this study showed improved mechanical properties. While they do not possess similar strengths as nondegradable PMMA bone cement [11], which has a compressive strength at yield and modulus of 46 and 1150 MPa, these networks do provide a wide range of mechanical properties upon varying the double bond ratio of PPF/PPF–DA or the length of PPF–DA suitable for orthopedic applications [7].

The equilibrium water content of PPF/PPF–DA polymer networks was measured and the results are given in Table 2. The water uptake was minimal, ranging from 0.55 ± 0.22 to 1.37 ± 0.13 wt% while there were no differences among the different polymer formulations. Unlike PPF/PEG–DMA networks [14], PPF/PPF–DA networks showed very low water absorption, probably due to the hydrophobic properties of both PPF and PPF–DA. The low water absorption capacity may protect the networks against diminution of their mechanical properties in the wet state.

3.3. Degradation products

Fig. 4 shows the degradation reaction of PPF/PPF–DA polymer networks. Strongly basic conditions were used to enhance the degradation rate. After hydrolysis of all ester linkages in the PPF/PPF–DA networks over the course of a few days, all degradation products were dissolved in basic water. In order to extract possible acidic products, the basic degradation solution was acidified by addition of 5% HCl.

Degradation products were first analyzed by gas chromatography (GC). Acetone was chosen as a solvent to extract the monomeric products, because the possible degradation products, fumaric acid and propylene glycol, have relatively high solubility in acetone while poly(acrylic acid-*co*-fumaric acid) is barely soluble in it. Two products with retention times of 4.7 and 15.7 min were detected. Based on GC/MS, both peaks have the same molecular weight of 116 and showed major fragments at $m/e = 59$ and 99, respectively. Analysis of the MS pattern (Fig. 12) suggested that the two products were fumaric acid and propylene glycol acetonide.

Support for these structural assignments resulted from NMR analysis of the degradation products extracted into deuterated acetone. Both ^{1}H NMR and ^{13}C NMR spectra of the product mixture in acetone-d_6 are shown in Fig. 13. In the ^{1}H NMR spectrum, four signals were found at 6.66, 3.82, 3.43, and 1.08 ppm. The large singlet peak at 6.66 ppm could belong to the two vinyl protons of fumaric acid, while the other three peaks arise from propylene glycol acetonide-d_6. The ^{13}C spectrum further confirmed these assignments. The carbonyl group was found at 167.6 ppm, while the

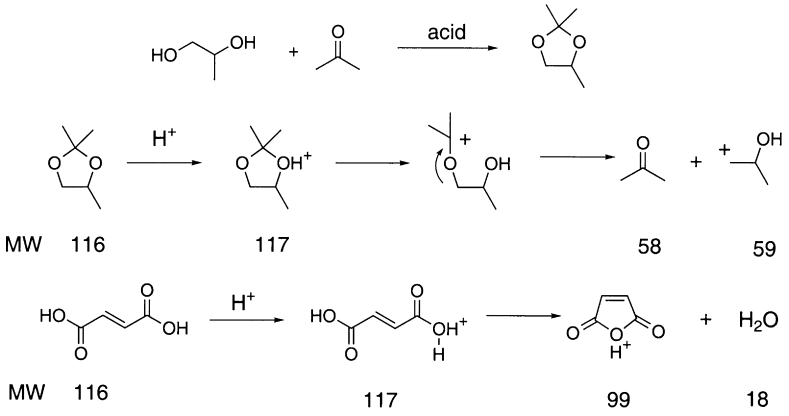

Fig. 12. MS/CI fragmentations of degradation products extracted by acetone.

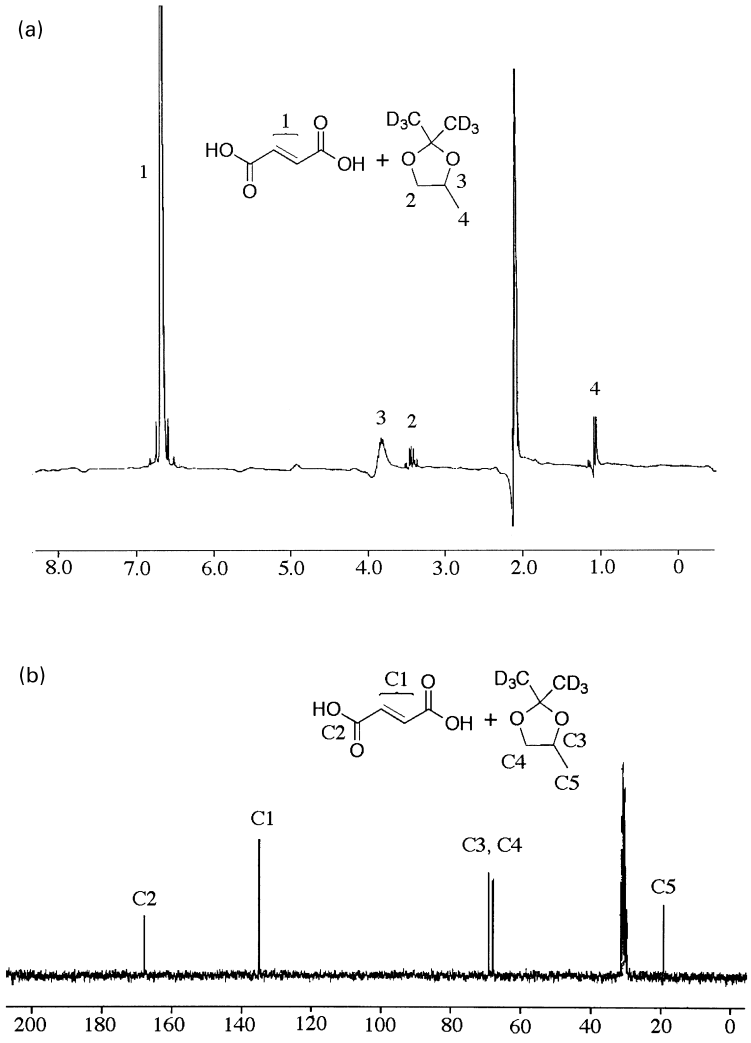

Fig. 13. ^{1}H NMR (a) and ^{13}C NMR (b) spectra of the degradation products extracted into acetone-d_6. Both the singlet signal at 2.09 in (a) and the multiplets at 31.75 ppm in (b) belong to acetone-d_6.

chemically equivalent vinyl carbons were at 134.7 ppm. The methyl carbon in propylene glycol acetonide was assigned to the peak at 19.0 ppm, while the other two carbons should be at the peaks at 67.5 and 68.9 ppm.

Propylene glycol acetonide came from the reaction of propylene glycol and acetone under acid catalysis. Formation of acetonides has been widely used in organic synthesis for protection of a diol group [18]. During the work-up of the degradation reaction, strong acid, HCl, was used to convert the degraded sodium salts to the corresponding acids in order to render them soluble in organic solvents. When acetone was used as the extracting solvent, the propylene glycol was converted completely to its acetonide under the acidic conditions.

Fumaric acid resulted from the uncrosslinked fumarate unit in both PPF and PPF–DA. This result indicated that only a fraction of the fumarate double bonds in PPF participated in the crosslinking reaction to form PPF polymer networks. Our failure to detect acrylic acid was not surprising because the double bond of an acrylate group in PPF–DA is much more reactive to radicals than that of a fumarate group because it is less sterically crowded. The absence of acrylic acid in the degradation product mixture indicated that all acrylate groups in PPF–DA were consumed in the crosslinking reaction, even though the double bond ratio of PPF/PPF–DA exceeded 1. This result implies that self-polymerization of PPF–DA was also involved in the crosslinking reaction.

The acetone-insoluble degradation product, poly(acrylic acid-*co*-fumaric acid), did not dissolve in other organic solvents including $CHCl_3$. In order to determine the molecular weight of this copolymer, it was converted to the corresponding methyl ester. Esterification of carboxylic acids by diazomethane is a convenient and efficient method [19]. After treatment with diazomethane, the esterified copolymer was soluble in $CHCl_3$ for GPC measurement. The GPC result showed that this material had a number average molecular weight of 2340 and a weight average

molecular weight of 5080. These molecular weights are well below the threshold value of 70 000 for hydrophilic polymers that are passively excreted by the kidneys [20].

4. Conclusions

New biodegradable poly(propylene fumarate)-based polymer networks were synthesized by radical reaction of PPF and newly synthesized PPF–DA. The PPF/PPF–DA polymer networks possessed strong mechanical properties. The compressive strengths and modulus of the PPF/PPF–DA polymer networks tested in this study spanned a wide range and were mainly affected by the PPF/PPF–DA double bond ratio and the molecular weight of PPF–DA. All cross-linked networks showed very low water absorption. These polymer networks degraded by hydrolysis of the ester linkage to water soluble products. The degradation products were identified as biocompatible propylene glycol, fumaric acid, and poly(acrylic acid-*co*-fumaric acid). The good mechanical properties and degradation to biocompatible products bode well for the potential applications of PPF/PPF–DA polymer networks as biomaterial scaffolds in orthopedic tissue engineering.

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