Poly(ethylene glycol) Star Polymer Hydrogels

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ABSTRACT: Poly(ethylene glycol) (PEG) star polymer hydrogels were prepared by γ-irradiation of aqueous solutions of star PEG polymers. The swelling behavior of these gels in deionized water at 37 °C indicated that the gels prepared from PEG star polymers with a small number of long arms swelled to a greater extent than those prepared from PEG star polymers with a large number of short arms. PEG star polymers and branched PEG polymers were modified to incorporate acrylate groups on the ends of the polymer arms. These acrylated star or branched polymers were copolymerized with poly(ethylene glycol) diacrylate in the presence of UV light. The ensuing materials swelled to a greater extent than hydrogels prepared without acrylated star or branched PEG polymers. Number-average molecular weights were calculated using several rubber elasticity-based theories.

Introduction

Star polymers are three-dimensional hyperbranched structures in which linear arms of the same or different molecular weights emanate from a central core. The existence of numerous functional groups in a small volume makes these polymers important for use in biological and pharmaceutical applications. Biologically active molecules can be immobilized on the surface of the polymer gel or incorporated into the network.[1]

Hydrogels are useful in biomedical and pharmaceutical applications because of their biocompatibility, high water content, and rubbery state. In addition to being used as carriers of bioactive agents, they can also provide protection for these proteins or drugs.[2] Hydrogels may also be used in molecular imprinting applications. Molecular imprinting replicates the structure of a biological molecule on the surface or inside a network to create a material that "remembers" the original molecule. Molecularly imprinted polymers can be used as tailor-made separation materials, antibody- and receptor site-mimicking systems, enzyme-mimicking catalytic systems, or adsorbent-specific polymers.[3] Molecularly imprinted star hydrogels would have the additional advantage of possessing a large number of functional groups. These functional groups could be modified to give the polymer gel specific properties.[4−8]

Because poly(ethylene glycol) (PEG) is a nontoxic, water-soluble polymer that resists recognition by the immune system, hydrogels prepared from PEG star polymers are excellent candidates as biomaterials.[4] The focus of this research was to synthesize PEG star polymer hydrogels that could be used for new applications such as specific drug delivery or possibly targeting. These gels could be characterized using swelling techniques and investigated for use in biomedical and molecular imprinting applications.

Poly(ethylene glycol) Star Polymers. PEG has many properties that make it an excellent candidate as a biomaterial. PEG is soluble in water and many organic solvents including toluene, methylene chloride, ethanol, and acetone. PEG is nontoxic, has a rapid clearance from the body, and has been approved for several medical applications. One of the most important properties is that PEG resists recognition from the immune system. It also resists protein and cell adsorption.[4]

Covalent bonding of PEG to other molecules may enhance the properties of other molecules rendering them nonimmunogenic, water soluble, and protein rejecting. These molecules not only exhibit many of the properties of PEG, but they retain their biological activity. Because of the high mobility of PEG, molecules that are tethered to it exhibit activity similar to that of a freely soluble molecule. The proteins that are tethered to PEG are not denatured, and because their size is increased, their rate of clearance through the body is often increased.[9−11] PEG star polymers that terminate with a hydroxyl group must be prepared by the core-first anionic polymerization method. This method was prepared by Rempp and colleagues.[12,13] The "living" core is produced through anionic polymerization of divinylbenzene in tetrahydrofuran at −40 °C using potassium naphthalene as the initiator. More recently, a method was developed by Yen and Merrill[14] to create PEG star molecules from polyamidoamine (PAMAM) dendrimer cores.

PEG/PEO Hydrogels. As indicated in an excellent review by Graham,[15] hydrogels of PEG or the equivalent high molecular weight poly(ethylene oxide) (PEO) can be prepared by: (i) free radical or radiation cross-linking of high molecular weight PEO; (ii) cross-linking of high molecular weight PEO because of entanglements; (iii) end-linking by reaction of the hydroxyl groups on the ends of PEG; (iv) copolymerization of PEG with other polymers; and (v) molecular complexation by hydrogen bonding between high molecular weight PEG and other polymers.

Aqueous solutions of PEG become cross-linked under γ-radiation or electron beam radiation to form a hydrogel. Initiation occurs from the hydrolysis of water to produce a hydroxyl radical. The hydroxyl radicals react with the PEG chains to produce chain scission and chain branching. Ultimately, termination occurs when two

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main-chain carbon radicals combine to create a tetrafunctional cross-link junction. This results in the formation of a cross-linked polymer network.[16,17]

The radiation dose needed to cross-link PEG chains depends not only on the molecular weight, but also on the concentration of PEG in the solution.[15] Stringer and Peppas[18] prepared hydrogels from aqueous solutions of PEO using γ-irradiation. The number-average molecular weight between cross-links varied from 3,500 to 32,000. This molecular weight between cross-links, $\bar{M}_c$, decreased with increasing radiation dosage, polymer molecular weight, and solution concentration. Kofinas et al.[19] also studied PEO gels prepared by irradiation. Polymer hydrogels were prepared using electron beam irradiation of aqueous solutions of PEO with molecular weights equal to 600 000, 1 000 000, or 5 000 000. These solutions with concentrations of 2, 4, and 6 wt/vol % were exposed to 4 Mrad of radiation. These gels also exhibited a decrease in the number-average molecular weight between cross-links with increasing molecular weight, but $\bar{M}_c$ increased with increasing concentration. Merrill and colleagues[20,21] prepared PEG star polymer hydrogels using electron beam irradiation. These hydrogels have a larger number of free hydroxyl ends than hydrogels prepared from linear PEG chains. Because the cross-linking occurs randomly between PEG chains, the hydroxyl groups remain available for activation. To obtain the same concentration of hydroxyl groups to star PEGs, linear chains with a molecular weight of 5,000 would have to be cross-linked. The cross-linking of such short chains is very difficult if not impossible; and if gels were to be formed from these chains they would have very low strength. These gels were prepared from 10 wt/vol % aqueous solutions of star polymers. Two different star polymers were used: those with a molecular weight of 229 000 and 43 arms, and those with a molecular weight of 371 000 and 30 arms. The equilibrium volume swelling ratios in water at 25 °C were equal to 1.3 for the star polymer gels and 2.8 and 3.0 for hydrogels prepared from linear PEO chains with a molecular weight 100 000 and 300 000, respectively. These gels rejected platelet adsorption when test in an ex vivo shunt model with the divinylbenzene cores shielded by the PEG arms.

PEG hydrogels have been used in a variety of biomedical applications, especially drug delivery and wound healing. These hydrogels, often used in combination with other polymers, have formed a basis for some commercial products. Vigilon, which is formed by radiation cross-linking of high molecular weight PEO chains, is used as a sheet wound-covering material. Cross-linked PEO Hypol foam also has been used in commercial wound healing and drug delivery materials.[15]

PEG hydrogels have been investigated for use as controlled release systems. Belcheva et al.[22] have studied the drug release profiles for hydrogels synthesized by γ-irradiation of high molecular weight PEO. Various drugs were incorporated into the gels by soaking them in solutions containing the drug or by incorporating the drug in the polymer solution before irradiation. The drug release was not dependent on pH. By varying the molecular weight of the PEO chain, different swelling properties and release profiles were obtained.

Several other researchers have investigated the drug release of PEG gels prepared by various methods.[23−26] The rate of drug release was found to depend not only on the method of preparation, but also on the cross-linking density, molecular weight of the PEO chains, and drug type used. These PEO gels can be synthesized for various applications including tailor-made drug delivery devices.[27]

The main goal of this research was to investigate the use of PEG star polymer hydrogels for use in biomedical or molecular imprinting applications. PEG star polymer hydrogels were prepared using irradiation techniques to investigate the effects of the number of star arms, length of star arm, and radiation dose on the network structure. PEG hydrogels containing acrylate groups were synthesized to examine the effect of incorporating acrylates into the gels. Equilibrium swelling studies were conducted on these gels to examine the network structure under various preparation conditions.

Experimental Section

Preparation of PEG Star Polymer Gels Prepared by Irradiation. Samples of PEG star polymers (Shearwater Polymers, Huntsville, AL) were dissolved in deionized water at concentrations of 10 wt % or 20 wt %. Three grades of star polymers were used: star-PEG 429 ($\bar{M}_n$ = 250 000; f = 13), star-PEG 423 ($\bar{M}_n$ = 450 000; f = 75), and star-PEG 432 ($\bar{M}_n$ = 624 000; f = 31), where f is the functionality or the number of arms, and $\bar{M}_n$ is the number-average molecular weight of the sample. According to the supplier, these star polymers were prepared by the core-first method (anionic polymerization) and had low polydispersity. Aqueous solutions of the star polymers were placed in a glovebox and bubbled with nitrogen for approximately 40 min. The solutions were poured into Petri dishes, covered with Saran Wrap®, and covered with the tops of the Petri dishes. All cross-linking reactions had to be conducted in nitrogen because PEG star polymers are known to degrade in atmospheric conditions and also because peroxide bond formation, which will change the reaction, had to be avoided. The samples were irradiated with γ-irradiation using a Co^{60} chamber (Purdue University, Pharmacy Department) at a dose rate of either 660 rad/min or 3330 rad/min for a total dose of 1 to 10 Mrad.

Characterization of PEG Star Polymer Gels Prepared by Irradiation. After irradiation, the gels were cut into disks of approximately 15 mm in diameter. The disks were weighed and then placed in deionized water at 37 °C. Periodically, the gels were taken out of the water and weighed in air and in heptane. After the gels reached an equilibrium weight, they were removed from the water and allowed to dry at room temperature. The weight swelling ratio of the gels was calculated as:

$$q = \frac{W_s}{W_d} \tag{1}$$

where W_s is the weight of the swollen sample and W_d is the weight of the dry sample.

Preparation of Acrylated Star PEG and Branched PEG Polymers. The acrylation procedure was carried out on samples of star PEG and branched PEG polymers. The star polymers used were star-PEG 432 (Shearwater Polymers, Huntsville, AL) having 31 arms with a number-average molecular weight of 624 000 g/mol. The branched PEG polymers (bPEGs) (Shearwater Polymers, Huntsville, AL) used had a number-average molecular weight of 10 000 g/mol with eight arms.

Acrylate pendant groups were added to the ends of the arms of star PEG polymers and bPEGs using an esterification reaction between PEG and acryloyl chloride. In a 250-mL three-neck reactor, 1.0 g of the star PEG polymers or bPEGs was dissolved in a solution containing 100 mL of tetrahydrofuran (99+%, Aldrich Chemical Co., Milwaukee, WI) and 30 mL of toluene (anhydrous, 99+%, Aldrich Chemical Co.,

Milwaukee, WI). The mixture was stirred at room temperature until the star PEG polymers or bPEGs were dissolved. Subsequently, 0.6 mL of triethylamine was added to the solution, and the solution was purged with nitrogen for approximately 10 min. To the degassed solution, 3 mL of acryloyl chloride (99% purity, Aldrich Chemical Co., Milwaukee, WI) was added through the septum during a period of 30 min. The temperature was raised to 40 °C, and the mixture was stirred for 16 h at 40−45 °C.

Upon completion of the reaction, the triethylamine hydrochloride salt was removed from the solution by vacuum filtration. The solvent containing tetrahydrofuran, toluene, and the excess of acryloyl chloride was removed by vacuum evaporation at 30−40 °C. The product was washed and precipitated in ether and acetone several times. The acrylated PEG was dried under vacuum at 30 °C for a day and stored under nitrogen.

The degree of modification was determined by ^{1}H NMR spectroscopy by integrating the areas under the proton peaks of the PEG molecule with respect to the proton peaks of the acryloyl moiety.

Preparation of Acrylated PEG Star Polymer/PEGDA Gels. Hydrogels of acrylated PEG star polymers copolymerized with poly(ethylene glycol) diacrylate (PEGDA) were prepared using two different samples of PEGDA. These samples were designated as PEGDA (x = 400) and PEGDA (x = 4000), where x represents the average molecular weight of the PEG segment. Because PEGDA (x = 400) is a liquid, and PEGDA (x = 4000) is a solid, two different methods of preparation were used to prepare the acrylated star polymer gels containing these materials.

Acrylated PEG star gels containing PEGDA (x = 4000) (Polysciences, Inc., Warrington, PA) were prepared from aqueous solutions of PEGDA (x = 4000). In a typical experiment, 0.1 g of PEGDA (x = 4000) was dissolved in 2.0 mL of deionized water. To this solution, 0.02 g of acrylated star PEGs or bPEGs and 0.01 g of the water-soluble initiator, Irgacure 2959 (2-hydroxy-1-[4-(hydroxyethoxy)phenyl]-2-methyl-1-propanone) (Ciba Specialty Chemicals, Tarrytown, NY), were added to the solution. The solution was placed in a glovebox that was purged with nitrogen. The solution was stirred and bubbled with nitrogen for 40 min to remove oxygen which acts as a free radical scavenger. The solution was then pipetted between two microscope slides with 0.7-mm Teflon spacers between them and was exposed to UV light for 20−30 min.

Acrylated PEG star gels containing PEGDA (x = 400) (Polysciences, Inc., Warrington, PA) were prepared in a similar manner. Irgacure 2959, the water-soluble initiator, was not used because these gels were prepared using a lower water content than the gels prepared with PEGDA (x = 4000). The initiator, 2,2-dimethoxy-2-phenyl-acetophenone (DMPA) (Aldrich Chemical Co., Milwaukee, WI) was dissolved in the PEGDA (x = 400). Typically, 0.015 g of DMPA was dissolved in 1.5 g of PEGDA (x = 400). Subsequently, 0.1 g of acrylated star PEGs or bPEGs and 1.0 mL of deionized water were added to the DMPA/PEGDA solution. The solution was placed in the glovebox that was purged with nitrogen, and the solution was stirred and bubbled with nitrogen. The solution was pipetted between two microscope slides with 0.7-mm Teflon spacers between them and was exposed to UV light for 20 min.

Immediately after polymerization, the gels were cut into disks of approximately 15 mm in diameter, and the disks were weighed. The disks were either dried at room temperature or placed in deionized water at 37 °C. The gels placed in deionized water were weighed periodically until reaching an equilibrium weight. The weight swelling ratio was calculated using eq 1. All swelling studies were conducted in triplicate.

Results and Discussion

Preparation of PEG Star Polymer Gels Prepared by Irradiation. PEG star polymer gels were synthesized satisfactorily by γ-irradiation techniques as described in the previous section. In general, PEG hydrogels that were irradiated with less than 10 Mrad were too soft to work with, and swelling studies could not be conducted with these samples. Samples were prepared with 10 wt % and 20 wt % star polymers. The samples prepared with 10 wt % star polymers were very soft and fragile, and broke apart during swelling within the first 2 h. The samples containing 20 wt % star-PEG 429 were also very soft, and when swelling studies were performed, they broke apart within the first 4 h.

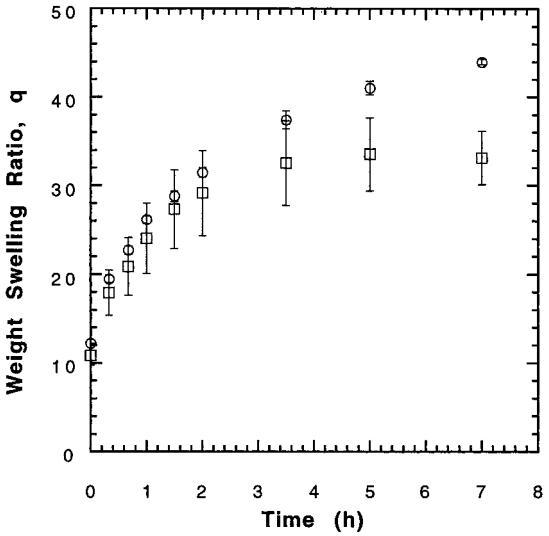

Figure 1. Weight swelling ratio in water at 37 °C versus time for PEG star hydrogels prepared from star-PEG 432 (○) and from star-PEG 423 (□). All data are in triplicate, and error bars indicate one standard deviation.

Characterization of PEG Star Polymer Gels Prepared by Irradiation. Swelling studies were conducted on hydrogels prepared from 20 wt % star-PEG 423 and 20 wt % star-PEG 429 aqueous solutions that had a total radiation exposure of 10 Mrad. Figure 1 shows the weight swelling ratio as a function of time for these gels during the first 8 h. All studies reported here were done in triplicate, and the error bars represent one standard deviation. Both star-PEG 423 and star-PEG 432 gels showed an increase in the weight swelling ratio as a function of time for the first 4 h. The uptake of water by these gels during the first 3 h was studied using the following equation proposed by Peppas[28]:

$$q = kt^n \tag{2}$$

This equation relates the uptake of water in a thin polymer film as a function of time where q is the weight swelling ratio at time t, and k is the kinetic constant that depends on the characteristics of the polymer and solvent. The diffusional exponent, n, can be used to relate the time dependence on the water uptake rate. Polymer relaxation does not affect transport in Fickian diffusion (n = 0.5), whereas relaxation processes become rate limiting with Case II transport (n = 1). Both diffusion and relaxation affect transport in the anomalous regime (0.5 < n < 1.0).

Equation 2 could not be used to model water diffusion into initially swollen gels. This model was modified to correct for the initial weight swelling ratio, q_o, of the gel:

$$q = q_o + kt^n \tag{3}$$

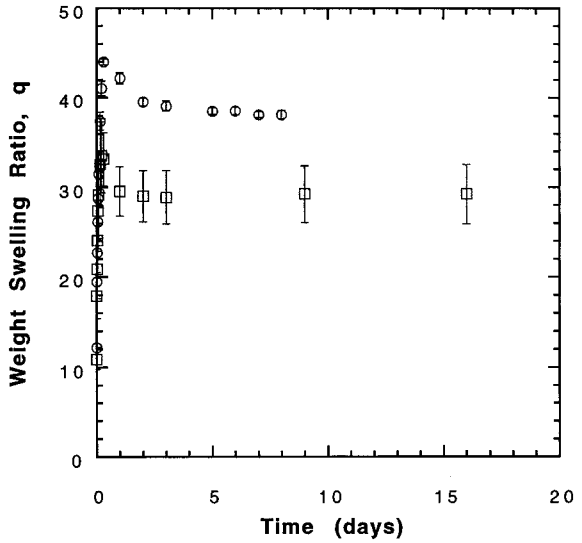

Figure 2. Long-term response of the weight swelling ratio in water at 37 °C versus time for PEG star hydrogels prepared from star-PEG 432 (○) and from star-PEG 423 (□). All data are in triplicate, and error bars indicate one standard deviation.

The swelling data were fit to this equation where $n = 0.51$ with a correlation coefficient, $r = 0.997$, for hydrogels prepared from star-PEG 432, and $n = 0.50$ with $r = 0.991$ for hydrogels prepared from star-PEG 423. Therefore, the diffusion of water into these gels during the first 3 h can be described as Fickian diffusion.

After 4 h, the weight swelling ratio of hydrogels prepared from star-PEG 423 began to level off, whereas the weight swelling ratio of hydrogels prepared from star-PEG 432 continued to increase slowly for up to 8 h (Figure 1). After the first 8 h, the weight swelling ratio began to drop to an equilibrium value for both of these gels as presented in Figure 2. During this time, the un-cross-linked PEG diffused out of the gel and the system came to the final equilibrium state.

This was determined by comparing the weights of samples that were dried immediately after cross-linking to the weights of samples that were dried after swelling. Samples that were dried after swelling weighed significantly less than those that were dried immediately after cross-linking: thus, it is assumed that un-cross-linked PEG diffused out of the gels before reaching the final equilibrium state.

Both hydrogels prepared from star-PEG 423 and star-PEG 432 exhibited an average overshoot of 15% defined by eq 4:

$$\text{overshoot} = \frac{q_m - q_e}{q_e} \tag{4}$$

In this equation, q_m is the maximum weight swelling ratio and q_e is the equilibrium weight swelling ratio.

Hydrogels prepared from star-PEG 432 had an equilibrium weight swelling ratio equal to 38, and hydrogels prepared from star-PEG 423 had an equilibrium weight swelling ratio equal to 29. Hydrogels prepared from star-PEG 423 produced a more highly cross-linked structure than hydrogels prepared from star-PEG 432 due to the smaller number-average molecular weight per arm and the larger number of arms. The extent of swelling was confirmed by calculating the number-average molecular weight between cross-links for these gels.

The number-average molecular weight between cross-links, $\bar{M}_c$, was calculated using two methods: the Peppas−Merrill equation[29,30] and the Cima−Lopina equation.[31] The Peppas−Merrill equation applies to swollen networks of cross-linked polymers prepared under conditions such that the cross-links were introduced in solution:

$$\frac{1}{\bar{M}_c} = \frac{2}{\bar{M}_n} - \frac{\frac{\bar{v}}{V_1}[\ln(1 - v_{2,s}) + v_{2,s} + \chi v_{2,s}^2]}{v_{2,r}\left[\left(\frac{v_{2,s}}{v_{2,r}}\right)^{1/3} - \frac{2}{F}\left(\frac{v_{2,s}}{v_{2,r}}\right)\right]} \tag{5}$$

Here $\bar{M}_n$ is the number-average molecular weight of chains before cross-linking, $v_{2,r}$ is the polymer volume fraction of the gel after cross-linking but before swelling, $v_{2,s}$ is the polymer volume fraction of the swollen network, χ is the polymer/solvent thermodynamic interaction parameter, V_1 is the molar volume of the swelling agent, $\bar{v}$ is the specific volume of the polymer, and F is the junction functionality.

In the Peppas−Merrill equation, $\bar{M}_n$ was set equal to the molecular weight of the star arm. The polymer volume fractions, $v_{2,r}$ and $v_{2,s}$, were determined from the volume swelling ratio, Q:

$$v_2 = \frac{1}{Q} \tag{6}$$

The volume swelling ratio was calculated by:

$$Q = \frac{V_{g,s}}{V_p} \tag{7}$$

where $V_{g,s}$ is the volume of the swollen gel, and V_p is the volume of the dry polymer. The volume of the swollen gel was calculated using:

$$V_{g,s} = \frac{W_a'' - W_h''}{\rho_h} \tag{8}$$

where W_a'' is the weight of the swollen gel in air, W_h'' is the weight of the swollen gel in heptane, and ρ_h is the density of heptane. The volume of the dry gel was calculated in a similar manner:

$$V_p = \frac{W_a - W_h}{\rho_h} \tag{9}$$

W_a and W_h are the weights of the swollen gel in air and in heptane, respectively.

The specific volume of the polymer, $\bar{v}$, was calculated using

$$\bar{v} = \frac{1}{\rho} \tag{10}$$

where ρ_p is the density of the dry polymer. The density of the dry polymer was calculated using the volume of

Table 1. Number-Average Molecular Weight between Cross-links for PEG Star Polymer Gels Prepared by Irradiation

grade	$\bar{M}_n$ per arm	Cima−Lopina $\bar{M}_c$	Peppas−Merrill $\bar{M}_c$ ($F = f$)	Peppas−Merrill $\bar{M}_c$ ($F = 4$)
Star-PEG 423 ($f = 75$)	5970	4000	2500	2400
Star-PEG 432 ($f = 31$)	20000	9700	7100	6600

the dry polymer, V_p, as calculated in eq 9, and the weight of the dry polymer, W_d:

$$\rho_p = \frac{W_d}{V_p} \tag{11}$$

The Peppas−Merrill equation does not accurately describe radiation cross-linked star gels because it does not account for a bimodal distribution of cross-links. The Peppas−Merrill equation was modified by Cima and Lopina[31] to account for a bimodal distribution of functionalities, i.e., tetrafunctional radiation-induced cross-links and F-functional junctions at the star cores:

$$\frac{1}{M_c} = \frac{2}{M_a} - \frac{\frac{\bar{v}}{V_1}[\ln(1 - v_{2,s}) + v_{2,s} + \chi v_{2,s}^2]}{v_{2,r}\left[\left(\frac{v_{2,s}}{v_{2,r}}\right)^{1/3} - \left(\frac{2}{F_1} + \frac{1}{(M_a/M_c - 1)F_2}\right)\left(\frac{v_{2,s}}{v_{2,r}}\right)\right]} \tag{12}$$

In this equation, M_a is the molecular weight of the star arm, $v_{2,r}$ is the polymer volume fraction of the gel after cross-linking but before swelling, $v_{2,s}$ is the polymer volume fraction of the swollen network, χ is the polymer/solvent thermodynamic interaction parameter, V_1 is the molar volume of the swelling agent, $\bar{v}$ is the specific volume of the polymer, F_1 is the junction functionality ($F_1 = 4$ for tetrafunctional radiation-induced cross-links), and F_2 is the star functionality.

Table 1 compares the average $\bar{M}_c$ calculated using the Cima−Lopina equation, the Peppas−Merrill equation with $F = 4$ for tetrafunctional radiation-induced cross-links, and the Peppas−Merrill equation with $F =$ star functionality for 20 wt % star-PEG 423 and 20 wt % star-PEG 432 gels prepared by irradiation. Table 1 values were calculated using $\chi = 0.42$ as indicated by Good and Cantow.[32] These values show that hydrogels prepared from star-PEG 423 create a more tightly cross-linked network with an average $\bar{M}_c$ equal to 4000 than star-PEG 432 with an average $\bar{M}_c$ equal to 9,700 (based on the Cima−Lopina equation).

The $\bar{M}_c$ values are very sensitive to changes in χ, the polymer solvent thermodynamic interaction parameter. Thus, the calculation of $\bar{M}_c$ using the above equations requires a very accurate determination of the χ-factor.

Preparation of Acrylated Star PEG and Branched PEG Polymers. Star-PEG 432 ($\bar{M}_n$ =624 000; $f = 31$) was acrylated according to the procedure described in the previous section. The yield of the reaction was 85% with a degree of modification of approximately 45% (about 14 arms per star as determined by ^{1}H NMR). A very accurate determination of the degree of modification was difficult to obtain because of the large ratio of PEG protons to acryloyl chloride protons.

A sample of the bPEG ($\bar{M}_n$ = 10 000; $f = 8$) was also acrylated according to the procedure above. The reaction between the bPEG polymers and acryloyl chloride produced a larger degree of modification than the star PEGs. The degree of modification was 71% (approximately 6 arms per bPEG) as determined by ^{1}H NMR.

Table 2. Composition of PEGDA ($x = 4000$) Hydrogels

	sample A	sample B	sample C	control
PEGDA ($x = 4000$) (wt %)	4.7	4.7	3.8	4.2
Water (wt %)	94.3	93.6	95.0	95.4
Y = acrylated star (wt %)	0.5	1.1		
Y = acrylated bPEG (wt %)			0.8	
ratio Y/PEGDA	0.11	0.23	0.21	

In comparison of the ^{1}H NMR spectra, the acrylation of the bPEGs produced a purer product than the acrylation of the star PEGs. The removal of water from the star PEG chain was difficult, and a large excess of acryloyl chloride was needed to modify the hydroxyl ends. Acryloyl chloride reacts with water to produce acrylic acid, which inhibits the acrylation of the star PEG arms, thus decreasing the degree of modification for the star PEGs.

Preparation of Acrylated PEG Star Polymer/PEGDA Gels. PEGDA ($x = 4000$) gels were prepared using various amounts of acrylated bPEGs or acrylated star PEGs as shown in Table 2. These gels were prepared containing approximately 95% water. This large amount of water was needed to dissolve the PEGDA ($x = 4000$). After polymerization, a layer of liquid covered the gel. Syneresis occurred in which water was "pushed" out of the network during cross-linking.

The PEGDA ($x = 4000$) gels prepared were transparent and almost colorless. These gels were soft, rubbery, and fragile. After drying, the gels were slightly brown in color. Gels were also prepared containing no acrylated star PEGs or bPEGs as a control sample with composition shown in Table 2.

Gels containing PEGDA ($x = 400$) were prepared according to the procedure described in the previous section. Various amounts of water and various amounts of acrylated star PEGs (Table 3) or acrylated bPEGs (Table 4) were used. These gels were rubbery and flexible yet highly cross-linked. These gels were not fragile like the gels prepared with PEGDA ($x = 4000$).

PEGDA ($x = 400$) gels containing acrylated star PEG polymers were opaque, whereas those containing acrylated bPEG polymers were translucent. The higher the concentration of acrylated star PEGs used, the more opaque the samples became. Samples were prepared containing no acrylated star PEGs or bPEGs to be used as a control groups with compositions shown in Table 3.

Characterization of Acrylated PEG Star Polymer/PEGDA Gels. Swelling studies were conducted on hydrogels containing acrylated star or bPEG polymers. PEGDA ($x = 4000$) gels with compositions shown in Table 2 were placed in deionized water at 37 °C, and the weight was monitored as a function of time. The weight swelling ratio was calculated using eq 1.

Figure 3 shows the dynamic swelling behavior of sample A containing 0.5% acrylated star polymers and 4.7% PEGDA ($x = 4000$) during the first 4 h. The weight swelling ratio increased from an initial value of approximately 20 to a value of approximately 25 after 4 h. These gels continued to swell over time as shown in Figure 4. The weight swelling ratio reached 29 after 3 days. The gels became more fragile with time, and

Table 3. Initial and Equilibrium Weight Swelling Ratios for PEGDA (x = 400) and Acrylated Star PEG Polymer Hydrogels

	sample D	sample E	sample F	control 1	control 2
PEGDA (x = 400) (wt %)	59.5	54.3	39.0	57.6	40.5
Water (wt %)	39.3	39.7	56.7	41.8	59.1
acrylated star (wt %)	0.6	5.4	3.9		
ratio star/PEGDA	0.01	0.10	0.10		
initial weight swelling ratio, q	1.51	1.57 ± 0.05	2.34 ± 0.07	1.71 ± 0.07	2.32 ± 0.08
equilibrium weight swelling ratio, q	2.08	1.94 ± 0.05	2.68 ± 0.07	1.78 ± 0.07	2.43 ± 0.08

Table 4. Initial and Equilibrium Weight Swelling Ratios for PEGDA (x = 400) and Acrylated Branched PEG Polymer Hydrogels

	sample G	sample H	sample I
PEGDA (x = 400) (wt %)	55.5	75.0	32.9
water (wt %)	38.3	23.4	63.3
acrylated bPEG (wt %)	5.6	0.8	3.4
ratio bPEG/PEGDA	0.10	0.01	0.10
initial weight swelling ratio, q	1.53	1.21	
equilibrium weight swelling ratio, q	1.84	1.61	2.97

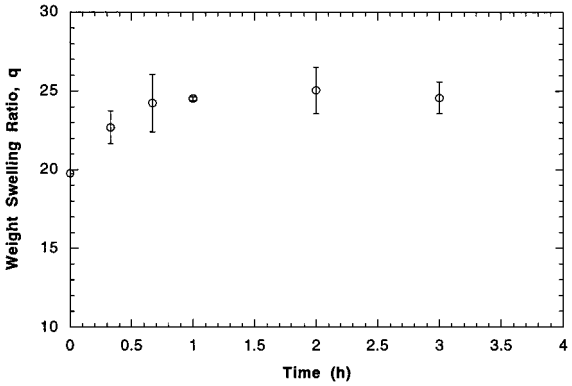

Figure 3. Weight swelling ratio in water at 37 °C as a function of time for swelling of PEG hydrogels prepared from an aqueous solution of 0.5 wt % acrylated star PEG 432 ($\bar{M}_n$ = 624 000; f=31) and 4.7 wt % PEGDA with PEG molecular weight of 4000. All data are in triplicate, and error bars indicate one standard deviation.

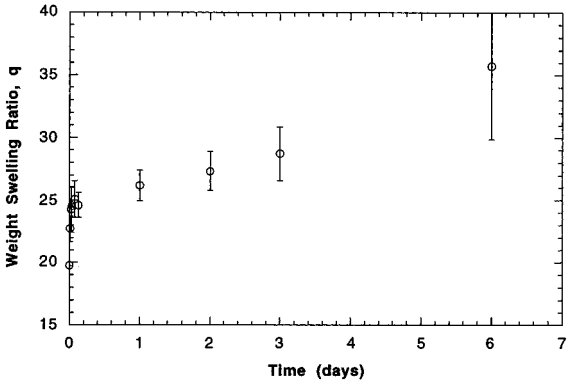

Figure 4. Long-term response of the weight swelling ratio in water at 37 °C as a function of time for swelling of PEG hydrogels prepared from an aqueous solution of 0.5 wt % acrylated star PEG 432 ($\bar{M}_n$ = 624 000; f = 31) and 4.7 wt % PEGDA with PEG molecular weight of 4000. All data are in triplicate, and error bars indicate one standard deviation.

after 6 days, the swelling studies were discontinued because the gels were difficult to work with. After approximately 50 days, these gels had completely dissolved in the water. The dry weights of the samples that approximated using a sample which was not swollen in water.

Dynamic swelling studies were conducted for 4 h with samples with a ratio of acrylated star PEG to PEGDA

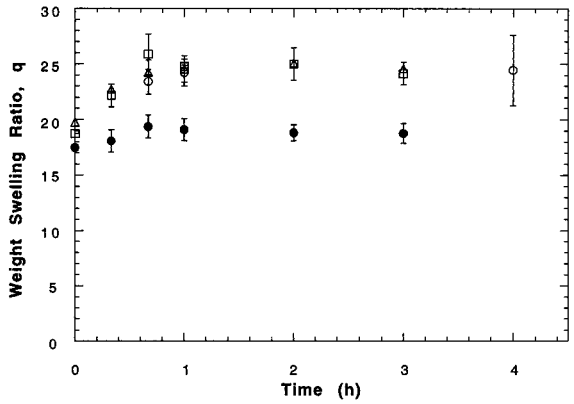

Figure 5. Weight swelling ratio in water at 37 °C as a function of time for swelling of PEG hydrogels containing PEGDA with PEG molecular weight of 4000 (●), PEGDA and acrylated branched PEG ($\bar{M}_n$ = 10 000; f = 8) with a ratio of bPEG/PEGDA = 0.21 (□), PEGDA and acrylated star PEG 432 ($\bar{M}_n$ = 624 000; f = 31) with a ratio of star PEG/PEGDA = 0.11 (△), and PEGDA and acrylated star PEG 432 ($\bar{M}_n$ = 624 000; f = 31) with a ratio of star PEG/PEGDA = 0.23 (○). All data are in triplicate, and error bars indicate one standard deviation.

(x = 4000) of 0.23, with samples with a ratio of acrylated bPEG to PEGDA (x = 4000) of 0.21, and with the control sample. The compositions are shown in Table 2. The swelling behavior of these gels along with a sample with a ratio of acrylated star PEG to PEGDA (x = 4000) of 0.11 is shown in Figure 5. The weight swelling ratios for the gels containing acrylated star PEGs or acrylated bPEGs increased during the first hour from approximately 19 to 24, and the weight swelling ratio of the control sample increased from approximately 18 to 19. After the first hour, the weight swelling ratios of all of the samples did not change significantly during the next 3 h. Thus, the PEGDA (x = 4000) gels containing acrylated star PEGs or acrylated bPEGs swelled more than the control sample.

PEGDA (x = 400) gels with compositions shown in Tables 3 and 4 were weighed and placed in deionized water at 37 °C immediately after cross-linking. The initial weight swelling ratio (immediately after cross-linking but before swelling) and the equilibrium weight swelling ratio were calculated using eq 1. These results for PEGDA (x = 400) and acrylated star PEG gels are shown in Table 3. Gels prepared with a high water content had a higher initial and equilibrium weight swelling ratio than the gels prepared with a low water content.

Dynamic swelling studies were conducted on four of the PEGDA (x = 400) samples. Two of the samples contained acrylated star PEG with a ratio of acrylated star PEG to PEGDA (x = 400) equal to 0.10, whereas the other samples contained no acrylated star PEG polymers and were used as control samples. Sample F and Control 2 were prepared using twice as much water as Sample E and Control 1 (with compositions shown

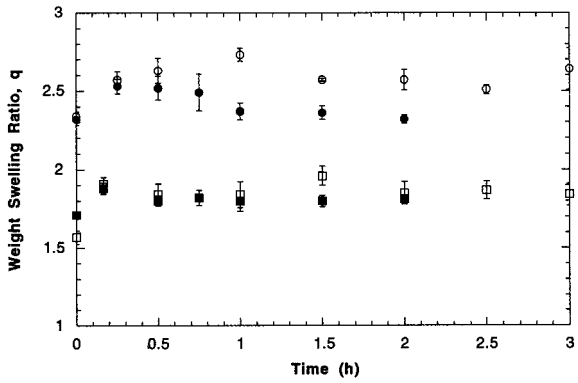

Figure 6. Weight swelling ratio in water at 37 °C as a function of time for swelling of hydrogels prepared containing PEGDA with PEG molecular weight of 400 and 39.7 wt % of water (■), PEGDA, acrylated star PEG 432 ($\bar{M}_n$ = 624 000; f = 31), and 41.8 wt % of water (□), PEGDA and 56.7 wt % of water (●) (corresponding to twice as much water as in the formulation designated by the symbol (■)), PEGDA, acrylated star PEG 432 ($\bar{M}_n$ = 624 000; f = 31), and 59.1 wt % of water (○) (corresponding to twice as much water as in the formulation designated by the symbol (□)). All data are in triplicate, and error bars indicate one standard deviation.

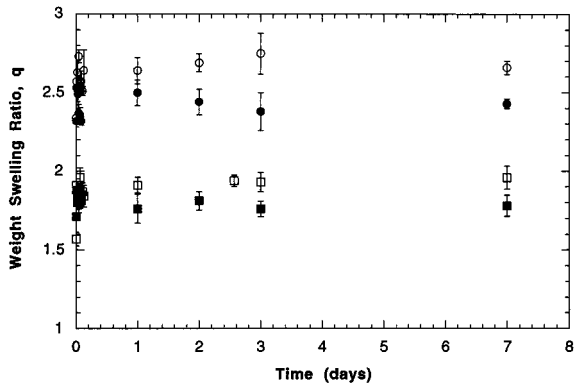

Figure 7. Long-term response of the weight swelling ratio in water at 37 °C as a function of time for swelling of hydrogels prepared containing PEGDA with PEG molecular weight of 400 and 39.7 wt % of water (■), PEGDA, acrylated star PEG 432 ($\bar{M}_n$ = 624 000; f = 31), and 41.8 wt % of water (□), PEGDA and 56.7 wt % of water (●) (corresponding to twice as much water as in the formulation designated by the symbol (■)), PEGDA, acrylated star PEG 432 ($\bar{M}_n$ = 624 000; f = 31), and 59.1 wt % of water (○) (corresponding to twice as much water as in the formulation designated by the symbol (□)). All data are in triplicate, and error bars indicate one standard deviation.

in Table 3). The weight swelling ratio as a function of time for these gels is shown in Figure 6. The weight swelling ratio for the gels containing the acrylated star PEGs and the control samples increased slightly during the first 3 h (Figure 6). At longer times, as shown in Figure 7, the weight swelling ratios of the samples containing acrylated star PEG polymers were higher than the corresponding control samples. The samples prepared with twice as much water had a higher weight swelling ratio than the samples prepared with the lower water content.

The initial and equilibrium weight swelling ratios for the PEGDA (x = 400) samples containing acrylated branched PEG polymers is shown in Table 4. Again, the samples prepared with the larger water content had a larger initial and equilibrium weight swelling ratio than the samples prepared with a low water content. The weight of the PEGDA (x = 400) gels remained stable for periods of approximately 2 months.

Conclusions

Satisfactory PEG star polymer hydrogels were prepared from 20 wt % aqueous solutions of PEG star polymers that were exposed to 10 Mrad γ-irradiation. Swelling studies were conducted in deionized water at 37 °C. Gels prepared from star-PEG 423 (number-average molecular weight = 450,000; 75 arms) swelled to approximately 29 times their dry weight whereas gels prepared from star-PEG 432 (number-average molecular weight = 624,000; 31 arms) swelled to approximately 38 times their dry weight. The number-average molecular weight between cross-links was calculated to be approximately 4000 for star-PEG 423 and approximately 9700 for star-PEG 432 using the Cima−Lopina equation.[31] Thus, hydrogels prepared from star PEG polymers containing a smaller number of short arms produced a more highly cross-linked structure than hydrogels prepared from star PEG polymers containing a large number of longer arms.

Poly(ethylene glycol) diacrylate hydrogels containing acrylated star polymers or acrylated branched polymers were prepared by UV polymerization. Gels were prepared with either PEGDA (x = 4000) or PEGDA (x = 400), where x represents the average molecular weight of the PEG segment. When placed in water at 37 °C, PEGDA (x = 4000) gels containing acrylated star PEG polymers or acrylated branched PEG polymers swelled to a greater extent than the control sample, which did not contain acrylated bPEGs or star PEGs. Samples containing acrylated star PEGs or acrylated bPEGs swelled from an initial weight of approximately 19 times their dry weight to approximately 24 times their dry weight, whereas the control sample swelled from approximately 18 times its dry weight to approximately 19 times its dry weight after 4 h.

PEGDA (x = 400) gels containing acrylated star PEG or acrylated bPEG polymers were prepared using various amounts of water. The larger the amount of water used to prepare the gels, the higher the initial and equilibrium weight swelling ratios were. Samples containing acrylated star PEG polymers or acrylated bPEG polymers swelled to a greater extent in deionized water at 37 °C than the control samples containing no acrylated star PEGs or bPEGs.

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