Gamma Radiation Synthesis and Swelling Properties of Hydrogels Based on Poly(ethylene glycol)/Methacrylic Acid (MAc) Mixtures

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ABSTRACT: In this work, gamma radiation was used to prepare hydrophilic hydrogels based on different mass ratios of poly(ethylene glycol) (PEG) and methacrylic acid (MAc) monomer. The thermal stability of hydrogels was characterized thermogravimetric analysis (TGA). The effect of temperature and pH, as external environments, on the equilibrium swelling of PEG/MAc hydrogels was also studied. The results showed that the gel fraction of PEG/MAc hydrogels is lower than that of PMAc hydrogel, in which the gel fraction of PMAc hydrogel was decreased greatly with increasing the mass ratio of PEG polymer in the initial solutions. The results showed that PEG/MAc hydrogels reached the equilibrium swelling state in water after 6 hours. It was found that the equilibrium swelling of PEG/MAc hydrogels displayed a transition change within the temperature range 30–40°C. This change in equilibrium swelling was illustrated by differential scanning calorimetry (DSC). However, it was observed that the equilibrium swelling of PEG/MAc hydrogels increases progressively with increasing the pH value from 4 up to 8. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 117: 1137–1143, 2010

Key words: gamma radiation; hydrogels; poly(ethylene glycol); methacrylic acid; swelling character; temperature and pH dependency studies

INTRODUCTION

Hydrogels are hydrophilic polymer networks that can absorb large amounts of water but remain insoluble because of the presence of crosslinks and entanglements.[1,2] However, there is a significant increasing attention for the responsive hydrogels, both for their intrinsic scientific interest and for their potential clinical applications. Hydrogels can be sensitive to the conditions of the external environment, in which the swelling behavior may be dependent on pH, temperature and ionic strength. Responsive hydrogels have been receiving increasing attention for their applications as drug delivery systems because of the advances in biotechnology and biochemistry have led to the discovery of a large number of therapeutic drugs.[3]

Poly(ethylene glycol) (PEG) is a biocompatible polymer with excellent biocompatibility and no-toxicity; it is often blended or compounded with other polymers to be used in the field of drug-controlled release systems.[4,5] In this regard, films of chitosan/PEG blend with ciprofloxacin hydrochloride as model drug incorporated at different ratios were obtained by a casting/solution evaporation method.[6] The results of controlled release tests showed that the amount of ciprofloxacin hydrochloride released increased with an increase in the ratio of PEG and decreased as the amount of drug loaded in the film increased. Also, thermoreversible gelation of block and star copolymers of PEG and poly(*N*-isopropylacrylamide) of varying architectures was prepared to study the structures and properties relationship.[7]

The preparation and characterization of poly(methacrylic acid)/PEG systems for drug delivery have been extensively investigated by Peppas research groups during the recent years. They were being interested to prepare novel complexation hydrogels of poly(methacrylic acid)-grafted-poly(ethylene glycol) [P (MAc-*g*-EG)] nanospheres.[8–16] In this respect, they have developed the production of [P (MAc-*g*-EG)] micro, nano and film hydrogels for oral delivery of proteins and glucose by methods without using large amounts of organic solvents or usage of stabilizers that could result in toxic side effects. In these research works, free radical bulk polymerization, a suspension polymerization technique and UV initiated free radical precipitation polymerization methods were used.

Apparently, the preparation of most responsive hydrogels was based on chemical initiation methods;

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few publications were based on ionizing radiation. In this regard, the physical properties of PEG/methacrylate-*co*-acrylic acid hydrogels, prepared by gamma radiation, were studied in terms of pH responsive as drug delivery material.[17] The application of radiation synthesized PEG/acrylic acid hydrogel as a colon-specific drug carrier, in which the release of Ketoprofen drug was studied as a function of pH.[18] Gamma radiation synthesis, characterization and adsorption of uranyl ions by hydrogels based on PEG/methacrylate copolymers, in the presence of triethyleneglycol dimethacrylate as crosslinking agent, was also studied.[19] We also are interested in the preparation of hydrogels by gamma or electron beam irradiation because radiation synthesis of hydrogels has special technical advantages; it allows the fabrication of noncontaminated products.[20–24] In this work, mixtures of different weight fractions of PEG and methacrylic acid monomer in aqueous solutions are exposed to gamma irradiation to obtain crosslinked network structure. The structure-property relationship of the formed hydrogels was investigated by FTIR spectroscopy and thermogravimetric analysis. The effect of pH and temperature on the swelling was also studied due to the potential applications in the biomedical and pharmaceutical fields. The compositions of PEG/MAc used in this work are different from the other compositions used in previous publications and without the use of crosslinking agent. Potentially, PEG/MAc systems will be recommended as carriers for colon drugs.

EXPERIMENTAL

Materials

Methacrylic acid monomer used in this study was a laboratory grade chemicals purchased from Merck Chemical Co. (Germany), and used as received. PEG, laboratory grade, of average molecular weight of 8000 was purchased from Milwaukee, WI.

Preparation of PEG/MAc hydrogels

The hydrogels were prepared by dissolving separately (0.955 g or 0.421 g) of PEG and (0.120 g or 0.266 g) of MAc in 5 mL of distilled water. The PEG and MAc solutions were then mixed with continuous stirring until complete miscibility was achieved. The hydrogels were prepared such that the weight fractions of PEG and MAc in the mixtures are 0.9/0.1 and 0.6/0.4 wt fractions. The mixtures were then poured into test tubes and de-oxygenated by purging nitrogen gas for 5 minutes at least and sealed. The tubes were then subjected to gamma irradiation. Irradiation to the required doses was carried out at a dose rate of 8.86 kGy/h. in the ^{60}Co gamma cell made in Russia. The contents were removed from the tubes, washed with hot water to get rid of unreacted materials.

Determination of gel fraction (%)

Samples of prepared hydrogels were accurately weighed (W_o) and then extracted with water using Soxhlet system, and then dried in vacuum oven at 80°C to a constant weight (W_1). The gel fraction (%) was calculated according to the following equation:

$$\text{Gel fraction } (\%) = (W_1/W_o) \times 100$$

Determination of MAc conversion (%)

Samples of the prepared hydrogels after removing from gamma source were dried and accurately weighed (W_f). The conversion (%) of MAc monomer was determined gravimetrically by a method based on back titration against NaOH. The conversion (%) was calculated according to the following equation (taking in consideration the initial weight (W_i) of MAc monomer in the feed solutions):

$$\text{Conversion } (\%) = [(W_i - W_f/W_i)] \times 100$$

Differential scanning calorimeter (DSC)

The differential scanning calorimetry (DSC) was carried out on Shimadzu DSC-50 calorimetry at a heating rate of 10°C/min under a flowing nitrogen gas at a rate of 20 mL/min.

IR spectroscopic analysis

The infrared spectra were performed using a FTIR spectrometer (model Mattson 5000) made by Unicam over the range 500–4000 cm^{-1}. A dry constant weight from each hydrogel was ground with 3 mg of KBr and pressed to form transparent discs. The samples for IR analysis were first dried in vacuum oven at 80°C for 24 hrs.

Thermogravimetric analysis (TGA)

The TGA thermograms were performed on a Shimadzu–50 instrument (Kyoto, Japan) at a heating rate of 10°C/min under flowing nitrogen (20 mL/min) from room temperature to 500°C. The primary TGA thermograms were used to determine the rate of thermal decomposition reaction.

Equilibrium swelling study of PEG/MAc hydrogels

Swelling studies were conducted on PEG/MAc hydrogels as a function of time (0–24 hrs). A known

dry weight of insoluble hydrogel (W_d) was immersed in water at 25°C and pH of 7. The samples were then removed and blotted on filter paper to remove excess water and weighed (w_s), in which the percentage swelling was calculated according to the following equation:

$$\text{Degree of swelling } (\%) = [(W_s - W_d)/W_d] \times 100$$

Swelling characters of PEG/MAc hydrogels in external conditions

Dry weight (W_d) of PMAc and PEG/MAc hydrogels were first immersed in water to the equilibrium state and then immersed in different temperatures (10–45°C) and different pH values (1–8) to the equilibrium state (24 hours). The samples were removed at each interval of time and weighed W_c and W_{pH}, respectively. The swelling in each case is calculated as follows:

$$\text{Swelling } (\%) \text{ at different temperatures} = [(W_c - W_d)/W_d]$$

$$\text{Swelling } (\%) \text{ at different pH values} = [(W_{pH} - W_d)/W_d]$$

RESULTS AND DISCUSSION

Formation of PEG/MAc networks by gamma radiation

The gel formation of acrylic monomers in solution by gamma radiation is well-known, in which the mechanism of crosslinking of polymers and polymerization of monomers in solution by ionizing radiation was early studied by Chapiro[25] and others.[26] The mechanism of crosslinking of the polymers of MAc monomers in aqueous solution by gamma radiation can be briefly outlined as follows:

1. The monomer (M—H) and the solvent (HO—H) absorb the gamma radiation and go to the transient activated states MH* and HOH*, which dissociate causing the formation of the radicals $M^{\bullet}$, $HO^{\bullet}$, and $H^{\bullet}$.
2. The transfer of radical from water to polymer increases the concentration of M radicals and increases the rate of crosslinking and gelation:

$$M - H + (H^{\bullet} \text{ or } HO^{\bullet}) \rightarrow PM^{\bullet} + HOH \text{ and}$$

3. Two polymer radicals $PM^{\bullet}$ with m and n repeat units combine to form a crosslinked point:

$$PM^{\bullet}{}_m + PM^{\bullet}{}_n \rightarrow M_m - M_n \text{ (crosslinked network)}$$

4. The interaction of the OH radicals with PEG is quite possible and will result to —O—$CH^{\bullet}$—CH_2— radical. These radicals may take place in both crosslinkng and interaction with monomer.

Effect of PEG/MAc ratio on gel fraction

PEG and methacrylic acid; both are soluble in water and have hydrophilic groups to form miscible solutions. Preliminary experiments were carried out to obtain homogenous hydrogels by studying irradiation dose and solvent volume. It was found that the appropriate irradiation dose to form homogenous hydrogels is 30 kGy of gamma radiation.

Figure 1 shows the effect of initial composition of PEG/MAc on the gel fraction (%) and conversion (%) of MAc. It should be noted that all the hydrogels were prepared at a constant dose of 30 kGy of gamma radiation. It can be seen that the gel fraction of PEG/MAc hydrogels decreases abruptly with increasing the ratio of PEG in the initial solutions. The gel fraction of PMAc was decreased from $\sim$ 100% to $\sim$ 66% by using 80% of PEG. The decrease observed in the gel fraction of PEG/MAc hydrogels caused by increasing the ratio of PEG is due to the lower sensitivity of PEG towards gamma irradiation compared to MAc monomer. Meanwhile, the conversion of MAc (%) was found to decrease with increasing the PEG ratio in the initial solution.

IR spectroscopic analysis

IR spectroscopic analysis was used to illustrate the structure and nature of bonding of PEG/MAc hydrogels. Figure 2 shows the IR spectra of the hydrogels based on PMAc, PEG, and PEG/MAc of different ratios prepared at a constant dose of 30 kGy of gamma irradiation. The IR spectrum of PMAc hydrogel showed an absorption peak around 2950 cm^{-1} arising from C—H stretching. The characteristic absorption peaks due to the C=O stretching of the carboxylic groups can be seen at 1730 cm^{-1}. The IR spectrum of PEG, beside the absorption bands at 2950 cm^{-1} due to C—H stretching, it showed characteristic bands at 1100 and 1340 cm^{-1} due to the bending vibration of C—O and C—H, respectively.[6] The IR spectra of the hydrogels based on PEG/MAc showed different features from those of PMAc and PEG, which indicates the existence of PEG in the free form inside and outside the networks of PMAc. Also, the intensity and broadness of

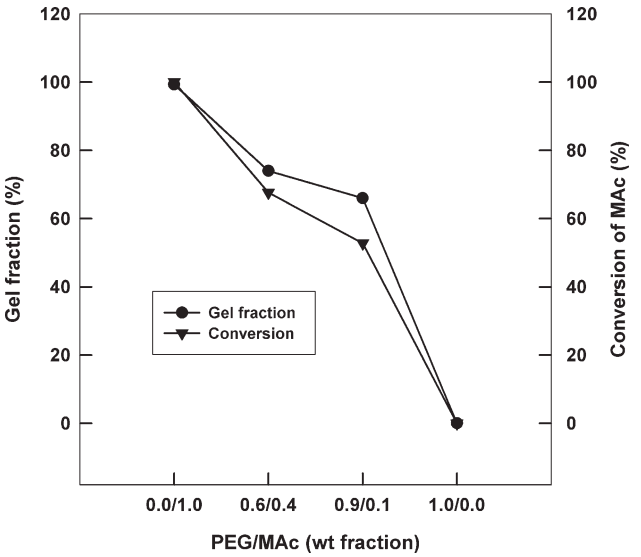

Figure 1 Effect of PEG/MAc composition in the initial solution on the gel fraction and MAc monomer conversion of the produced hydrogels prepared by gamma irradiation at a dose of 30 kGy.

the absorption bands increases with increasing the ratio of PEG polymer.

Thermal decomposition behavior of PEG/MAc hydrogels

The dissociation energies of the covalent bonds C—H, C—C, C=O, C—O, and O—H were reported to be 414, 347, 741, 351, and 464 kJ/mol, respectively.[27] According to these values, the average complete dissociation energy (ACDE) for PMAc and PEG can be calculated as follows:

$$\begin{aligned}\mathrm{ACDE(PMAc)} &= \mathrm{C{-}H}(5\times 414) + \mathrm{C{-}C}(3\times 347) \\ &\quad + \mathrm{C{-}O}(1\times 351) + \mathrm{C{=}O}(1\times 741) \\ &\quad + \mathrm{O{-}H}(1\times 464) = 4667/11 = 424.3\,\mathrm{kJ/mol} \\ \mathrm{ACDE(PEG)} &= \mathrm{C{-}H}(4\times 414) + \mathrm{C{-}C}(1\times 347) \\ &\quad + \mathrm{C{-}O}(2\times 351) + \mathrm{O{-}H}(2\times 464) \\ &= 3633/9 = 403.7\,\mathrm{kJ/mol}\end{aligned}$$

Thus, it may be expected that the formation of hydrogels based on different ratios of PEG and MAc will eventually results in materials with higher thermal stability than pure PEG. Thermogravimetric analysis (TGA) was used to investigate experimentally the thermal stability of the hydrogel based on 100% MAc and PEG/MAc of different ratios. Figure 3 and Table I shows the initial TGA thermograms and the percentage weight loss percentage at different decompositions temperatures taken from the

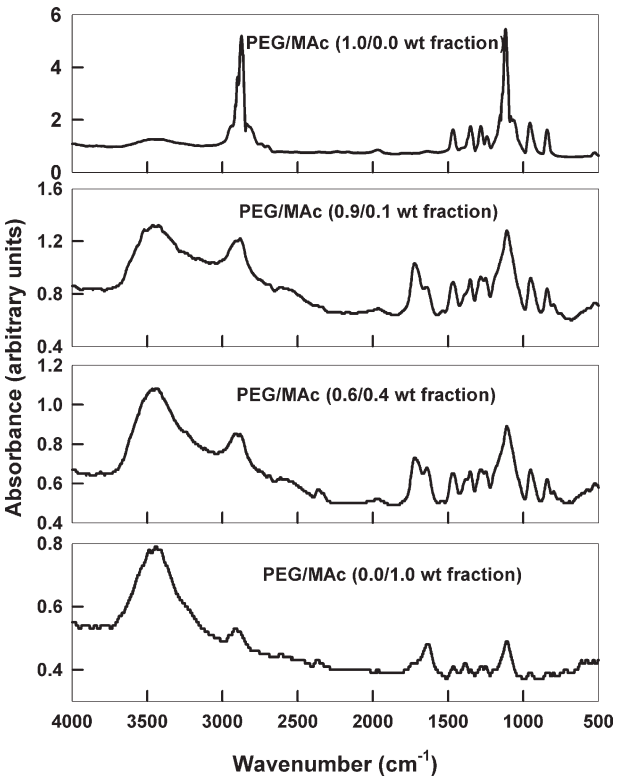

Figure 2 IR spectra of hydrogels based on PMAc, PEG and PEG/MAc hydrogels of different compositions prepared by gamma irradiation at a dose of 30 kGy.

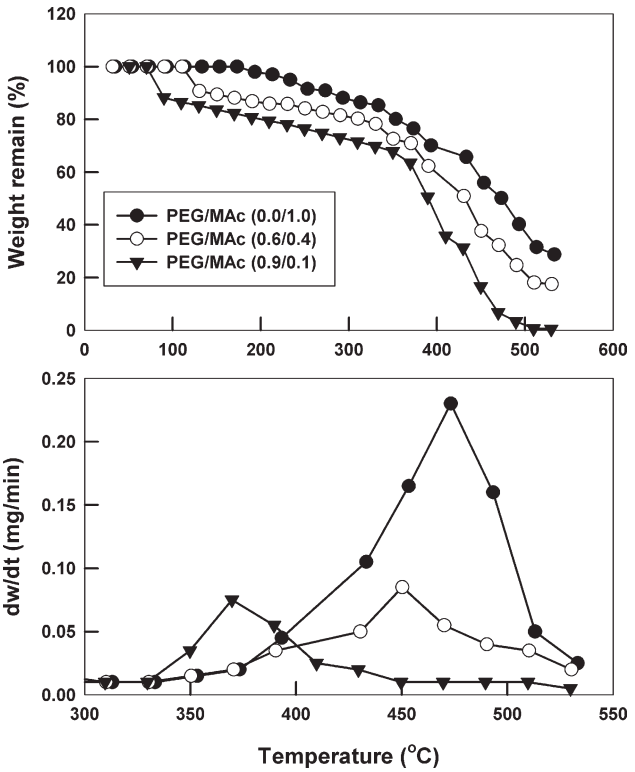

Figure 3 TGA thermograms and rate of reaction curves for PMAc and PEG/MAc hydrogels of different compositions prepared by gamma irradiation at a dose of 30 kGy.

TABLE I
Weight Loss (%) and Temperatures of the Maximum Rate of Reaction for PEG/MAc Hydrogels Prepared by Gamma Radiation at a Dose of 30 kGy

PEG/MAc (Weight Fraction)	Weight Loss (%)						T_{max} (°C)
	200°C	250°C	300°C	350°C	400°C	500°C	
PEG/MAc (0.0/1.0)	2.0	8.0	9.1	14.7	23.9	23.9	473.2
PEG/MAc (0.6/0.4)	10.2	12.9	15.5	24.5	34.7	72.3	450.3
PEG/MAc (0.8/0.1)	11.6	16.2	19.5	27.5	39.3	78.5	369.7

corresponding TGA thermograms. It should be noted that all the gels were prepared at a constant dose of 30 kGy of gamma radiation. It can be seen that all the hydrogels undergo similar thermal decomposition behavior indicating the compatibility between crosslinked PMAc and PEG polymer. However, the major thermal decomposition occurs within the temperature range 300–500°C, in which the hydrogel based on 100% MAc monomer displayed the highest thermal stability at the different heating temperatures. Also, the thermal stability, in terms of weight loss %, was found to decrease with increasing the ratio of PEG polymer in the feeding solutions.

The derivative of the TGA thermograms (DTGA) curves for the gels based on 100% MAc and PEG/MAc mixtures hydrogels is shown in Figure 3. The temperatures at which the maximum values of the rate of reaction (T_{max}) occur are shown in Table I. The T_{max} is in accordance with the results of the percentage weight loss at different heating temperatures and the theoretical calculations based on the average complete dissociation energies.

Swelling behavior of PEG/MAc based hydrogels

Figure 4 shows the swelling kinetics in water at 25°C for PMAc and PEG/MAc hydrogels of different compositions formed at a constant dose of 30 kGy of gamma irradiation. It can be seen that the degree of swelling for all the hydrogels increases progressively within the initial time of swelling up to 6 hours and after that the equilibrium state is reached. The degree of swelling of PEG/MAc hydrogels displayed a systematic trend in accordance with composition. However, the degree of swelling was decreased greatly with increasing the ratio of PEG polymer in the initial solutions. This is due to the higher hydrophilic character of PMAc and also arises from "the formation of H-bonds between acid group of MAc and —OH group of PEG chains."

Effect of temperature on the equilibrium swelling of PEG/MAc hydrogels

Figure 5 shows the effect of temperature on the equilibrium swelling of PMAc and PEG/MAc

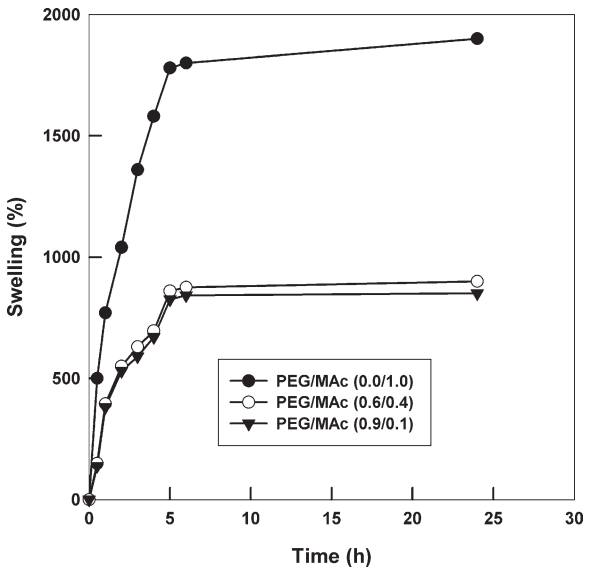

Figure 4 Swelling kinetics in water at 25°C and pH = 7 for PMAc and PEG/MAc hydrogels of different compositions prepared by gamma irradiation at a dose of 30 kGy.

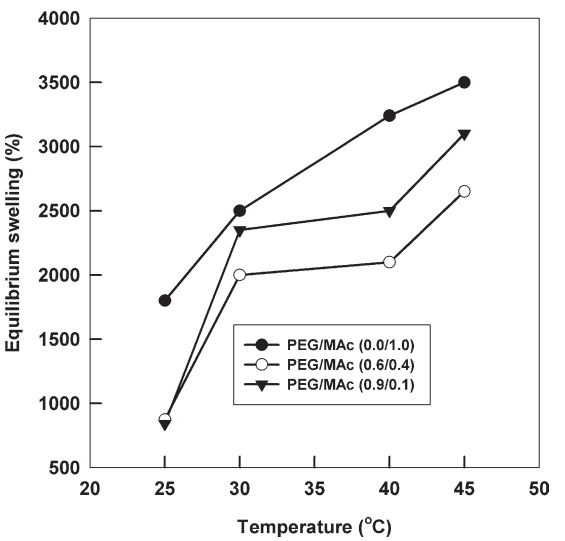

Figure 5 Effect of temperature on the equilibrium swelling (%) for PEG/MAc hydrogels of different compositions prepared by gamma irradiation at a dose of 30 kGy.

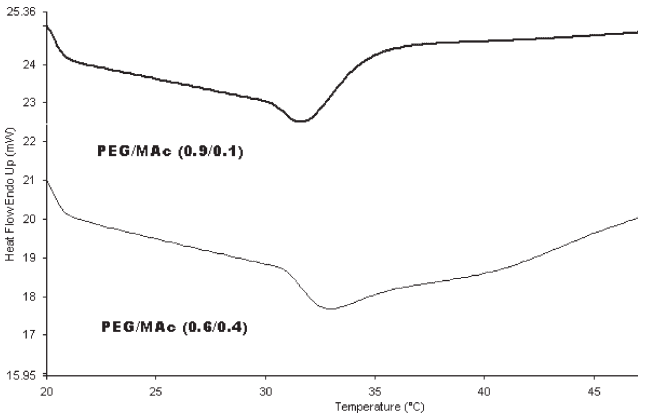

Figure 6 DSC scans of PEG/MAc hydrogels of different compositions prepared by gamma irradiation at a dose of 30 kGy.

hydrogels. It can be seen that there is a transition change in the equilibrium swelling of PEG/MAc hydrogels over the temperature range 30–40°C, while the equilibrium swelling of PMAc increases progressively by increasing temperature up to 45°C. PEG is a model of temperature unresponsive hydrophilic hydrogel segment, while PMAc is a typical pH sensitive polymer.[6] Therefore, the transition change is probably due to the formation of copolymer networks.

The transition change in equilibrium swelling within the temperature range 30–40°C is illustrated by differential scanning calorimetry (DSC) technique as shown in Figure 6. It is clear that all the PEG/MAc hydrogel compositions showed endothermic transitions upon heating. The transition temperatures, i.e. the temperature of the endothermic peaks

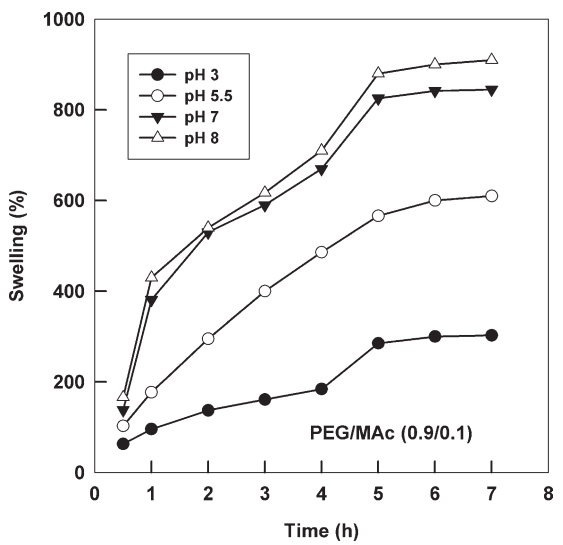

Figure 7 Effect of pH value on the equilibrium swelling (%) for the hydrogel composition PEG/MAc (0.9/0.1 wt fraction) as a function of swelling time.

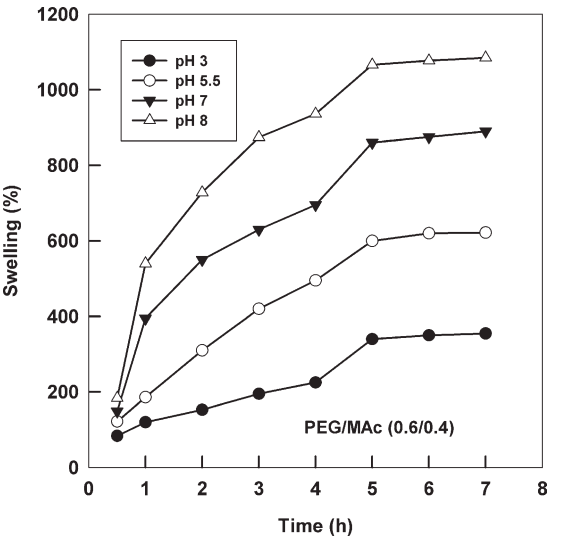

Figure 8 Effect of pH value on the equilibrium swelling (%) for the hydrogel composition PEG/MAc (0.6/0.4 wt fraction) as a function of swelling time.

of PEG/MAc hydrogels, were found to be in the range of 31.7–33.1°C.

Effect of pH on the equilibrium swelling of PEG/MAc hydrogels

The effect of pH values on the equilibrium swelling of PEG/MAc at different time intervals, prepared at a constant dose of 30 kGy of gamma irradiation is shown in Figures 7 and 8. It should be noted that the hydrogel samples in the dry state were immersed in different buffer solutions at 25°C. The effect of pH on the degree of swelling can be observed, in which it increases progressively by increasing the pH values from 3 to 8. Also, it can be seen that the pH-sensitivity increases with increasing the MAc ratio in the feeding solutions. At low pH values of 3 and 4, the PEG/MAc gels were in collapsed state due to the hydrogen bonding between the carboxylic acid groups of PMAc and the hydroxyl groups of PEG chains.[3] At high pH value of 8, the equilibrium swelling of the PEG/MAc (60/40% and 90/10%) feed ratios was approximately 3 times that of the equilibrium swelling of the same gels ratios at a pH of 3.

Swelling of hydrogels occurred due to electrostatic repulsion within the network caused by the ionization of the carboxylic acid groups. At high pH values, the carboxylic groups were ionized and the hydrogen bonds formed between PMAc and PEG at low pH values are broken. In a study on the preparation and characterization of pH-responsive PMAc-*g*-EG nanospheres, it was found that the equilibrium swelling volume at pH of 7.5 produced from MAc/EG molar feed ratios of 1 : 1, 2 : 1, and 4 : 1 is 100, 200, and 400 times that of the equilibrium swelling at pH 3.3, respectively.[13] The higher change in

equilibrium swelling from low to higher pH values for the prepared nanospheres was attributed to the rich ionizable carboxylic acid groups. However, the low change in the equilibrium swelling from low to higher pH values in this work is due to low contents of ionizable carboxylic acid groups and high contents of PEG in the feed ratios.

CONCLUSIONS

The synthesis of hydrogels by ionizing radiation offers technical advantages, in which the crosslinking occurs in the absence of initiators. In this work, gamma radiation was utilized successfully to form copolymer network hydrogels based on different ratios of PEG and methacrylic acid (MAc). It has been found that the swelling characters in water and thermal stability depend largely on the composition of the initial solutions of preparation. The results showed that the thermal stability of PEG/MAc hydrogels decreases with increasing the ratio of PEG. The use of MAc as a component in these hydrogels leads to increasing the time of equilibrium swelling, which may represent an advantage in some applications. Moreover, it was found that the swelling of PEG/MAc hydrogels was affected by the pH values near the pK_a of PMAc. For all the PEG/MAc hydrogels, it was observed that the equilibrium swelling in undergoes a transition change within the temperature range 30–40°C.

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