Characterization and Potential Application of Electro-Active Acrylamido-2-methyl Propane Sulfonic Acid/Acrylic Acid Copolymer Prepared by Ionizing Radiation

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A new electro active polymeric material was synthesized by gamma radiation induced copolymerization of 2-acrylamido-2-methyl propane sulfonic acid (AMPS) and acrylic acid (AAc). The prepared copolymer hydrogels were characterized by studying their swelling behavior in response to the environmental conditions such as pH and ionic strength. The electro active characteristics of AMPS/AAc hydrogels were evaluated by investigating their swelling rate, deswelling behavior, and bending behavior under the influence of the applied electric field. The effects of copolymer composition, applied voltage and ionic strength on the electro active characteristics of the prepared AMPS/AAc were also studied. The results show that the electro active characteristics increased by increasing AMPS content in the copolymer, ionic strength as well as applied voltage. Meanwhile, electro active property decreases by the increase of AAc content, as well as crosslinking density. The possibility of using the prepared hydrogel as a carrier for electric controlled drug delivery systems was examined by measuring the release of theophylline in response to the application of the electric field. The release of drugs showed complete dependence on the application of the electric field.

Keywords: Electro-active copolymer; swelling/deswelling; bending behavior; electric controlled drug delivery

1 Introduction

Hydrogels are hydrophilic polymer networks that have a capability to adsorb large amount of water. They are characterized by the presence of crosslinks, crystalline and amorphous regions, entanglements and rearrangement of the hydrophobic and hydrophilic domains (1). Studies of hydrogels are interesting in engineering, pharmaceuticals, food processing, biochemistry biotechnology and medicine. One of the most interesting properties of the hydrogel is their capability for reversible volume or shape change under the influence of external <u>stimulus</u> such as temperature, pH, ionic strength and electric field (2–5).

Recently, much interest focused on electro-active hydrogels which undergo deformation in response to a direct current (DC) electric field due to their potential scientific and technological importance. Different aspects of practical applications of electro-responsive hydrogels in robotics, sensors, artificial muscles system and other biomedical devices such as drug delivery systems were explored (6–11).

Even though the mechanism of electro-driven chemo mechanical motion of the electro active polymers under the influence of electric field has been discussed frequently, it is still controversial. This perceived controversy refers to the different theories used by the interested researchers to explain their observations. Osada et al. reported about a polymer gel with electrically driven mobility, and they interpreted the basic principle of electric field induced bending of hydrogel (12). Tanaka et al. reported about a hydrolyzed acrylamide collapsed in an acetone/water binary mixture upon the application of an electric field and they interpreted this phenomenon with the Flory-Huggins theory (13). On the other hand, Gong et al. reported on the electrokinetic modeling of the contractile phenomenon of the polyelectrolyte hydrogel and they interpreted the mechanism of the electric induced bending and contraction (14). Yuk and Lee demonstrated the reversible bending of the crosslinked acrylamide gel induced by an electric field in aqueous NaCl solution and they proposed a mechanism for that phenomenon (15). De Rossi et al. explained the anisotropic deswelling of polyvinyl alcohol/acrylic acid membranes at the anode by a local pH decrease associated with water electrolysis (16).

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Kwon et al. adopted a theory involving depletion polarization to explain gel bending in response to the electric field application (17).

Poly acrylic (AAc) acid is a week polyelectrolyte that possesses a pH and electric sensitive properties due to the charge density on the carboxylic groups whereas, 2-acrylamido-2-methyl propane sulfonic acid (AMPS) is a strong polyelectrolyte dissociated completely at wide pH range. It has been reported that the linear polymer containing sulfonated groups driven from AMPS exhibits an extensive coil type expansion in aqueous solution which may assist its response to the electric field stimulus (18). Materials of such properties, in addition to the facility of using gamma irradiation as a clean source of initiation and crosslinking which can simultaneously produce sterilized polymeric biomaterials free of initiators and, crosslinkers would encourage the synthesis and further characterization of new electroactive polymeric materials.

In this paper, electro-active copolymers, composed of AAc and AMPS at different compositions, were prepared by means of gamma irradiation as a source for initiation and crosslinking processes. Swelling characteristics and electro active behavior were characterized. The electro-active property of the copolymers was investigated. Practical applications such as deformable robots, based on bending behavior of the hydrogel, electrically active drug release, and on swelling deswelling behavior, were estimated.

2 Experimental

2.1 Materials

Acrylic acid, of purity 99.9% and 2-Acrylamido-2-methyl propane sulfonic acid of purity 99.9% were purchased from Aldrich, Germany. All chemicals used were reagent grade (El Nasr) and were used as purchased without further purification.

2.2 Preparation of AMPS/AAc Copolymer Hydrogel

AMPS/AAc hydrogels of different copolymer compositions were prepared from their 40 wt% aqueous solutions using γ-irradiation at different irradiation doses which ranged from 20 to 50 kGy at a dose rate 4.8 kGy/h. The prepared gels were washed extensively in distilled water for 2 days to remove the unreacted monomers. AMPS/AAc potassium salt hydrogel was prepared by soaking the prepared hydrogels at 0.5 M solution of KCl (5).

2.3 Swelling Experiments

AMPS/AAc copolymers of different composition were allowed to swell in distilled water, buffer solutions, and electrolyte solutions of different ionic strengths in the absence and presence of an electric field. The degree of swelling at 5 min time intervals, and at equilibrium swelling, was calculated as follows:

$$\text{Swelling degree}(\%) = \frac{(W_s - W_o)}{W_o} \times 100$$

Where W_s and W_o are the weights of the swollen and the dry hydrogel, respectively.

3 Deswelling Measurements Under the Influence of an Electric Field

The equilibrated swelled AMPS/AAc hydrogels were cut into rectangular shaped plates and weighed. Two platinum electrodes were inserted into the hydrogels. When an electric field was used, water was released from the hydrogel at the anode side. The seeped water was removed by filter paper and the deswelled hydrogels were weighed at 5 min time intervals of. The deswelling degree was calculated as follows:

$$\text{Deswelling degree}(\%) = \frac{W_{after}}{W_{before}} \times 100$$

Where W_{after} and W_{before} are the weights of the swollen gel after and before the application of the electric field.

3.1 Bending Angle of the AMPS/AAc Hydrogel Under the Influence of Electric Field

Fully swollen AMPS/AAc hydrogels were held between t two carbon electrodes in the box of dimension $(20 \times 5 \times 2 \text{ mm})$ connected to the DC source. The distance between the two-carbon electrodes is 30 mm. The time needed for maximum displacement was considered as response time.

### 3.2 Preparation of Buffer Solutions of Different pH's

(Citric acid/trisodium citrate) and (sodium dihydrogen phosphate/ disodium hydrogen phosphate) were used to prepare buffer solutions ranged from 3−5 and 6−7, respectively (19). HCl was used to prepare solutions of pH values which ranged from 1−3.

3.3 Preparation of Theophylline-Loaded Gel

AMPS/AAc dry gels were immersed in a saturated aqueous solution of theophylline at room temperature 25°C until equilibrium, washed with distilled water, removed from the solution and kept in sealed polyethylene bag in refrigerator.

3.4 Electroresponsive Drug Release

AMPS/AAc gels loaded with theophylline were sandwiched between two carbon electrodes (Figure 1). The electric field
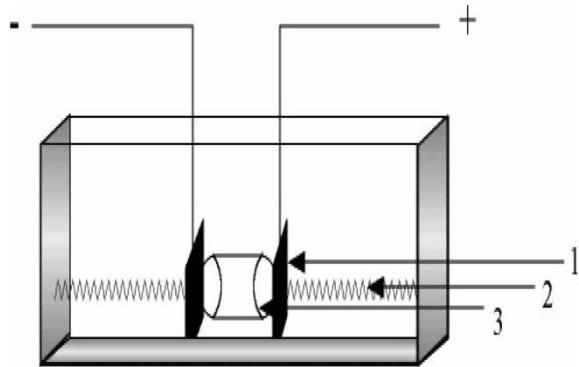
Fig. 1. Schematic diagram of the apparatus used to examine the electric field controlled drug delivery of AMPS/AAc hydrogel. (1) Two carbon electrodes, (2) spring wire and (3) drug loaded swollen AMPS/AAc hydrogel.

was applied to the hydrogel with on-off switching. The amount of drug released in response to the application of electric field (1 V) was measured spectrometrically by measuring the absorption at 270 nm using Milton Roy Spetronic 1201 spectrophotometer in the range from 190−900 nm.

4 Results and Discussion

Copolymer hydrogels composed of AAc and AMPS of different compositions were prepared using gamma radiation induced crosslinking copolymerization. The effect of comonomer compositions on the conversion and gel content of the copolymers was studied and shown in Table 1. The data shows that both conversion and gel content decrease as a function of increasing AMPS content in the comonomer feed solution. This may be due to the low tendency of AMPS to form crosslinking network structure compared with that of AAc.

4.1 Swelling Behavior of AMPS/AAc Hydrogels

Swelling behavior is an important consideration in the application of dynamic hydrogel to control of solute transportation,

Table 1. Effect of copolymer composition on conversion and gelation degrees and equilibrium swelling of AMPS/AAc hydrogel

AMPS content in the comonomer feed solution (wt%)	Conversion (%)	Gelation (%)	Equilibrium Swelling (%)
0	95.75	92.12	1036
25	95.11	88.44	8093
50	90.86	81.69	19258
75	96.78	69.72	24835
100	94.20	60.98	30253

"e.g. control drug delivery". Swelling and deswelling of polyelectrolyte hydrogels can be induced by augmenting electrostatic swelling forces associated with the ionizable charge groups content in the polymeric matrix which are affected by environmental conditions.

Table 1 shows the effect of comonomer composition on the swelling behavior of the prepared hydrogels in distilled water. It is clear that equilibrium swelling increases by increasing the AMPS content in the copolymer. This can attributed not only to the presence of a high amount of strong hydrophilic (SO_3H) groups, but also to the copolymer gel content which decreases by increasing the AMPS content in the copolymer.

The AMPS/AAc hydrogels of different copolymer compositions were also allowed to swell in buffer solutions of pH values ranging from 1 to 8, and the results are shown in Figure 2. For all copolymer compositions, swelling equilibrium increases as the pH value increases and reaches its maximum at pH 3. Thereafter, as the pH values increase higher than pH 3, a dramatic decrease in the swelling equilibrium was observed and was then followed by a slight increase in the equilibrium swelling up to pH 6. As pH values exceed pH 6, a further reduction in the equilibrium swelling occurred.

The above mentioned data can be explained as follows, at pH 1, all the copolymers are in a relatively collapsed state and possessed the lowest swelling degrees. The swelling of the copolymers at pH 1 are directly related to the AMPS content in the copolymer i.e., the swelling degree increases by an increasing AMPS content. The sharp increment in the equilibrium swelling above pH 2 could be attributed to the complete ionization of the strong acidic SO_3H groups depending on its pKa value at value near pH 2 (20). The drastic decrease in the swelling at pH values higher than pH 3 may be due to the change in the ionic strength accompanied by changing the medium from an aqueous HCl solution to 0.2 M citrate buffer solutions. The slight increment in the swelling degree at pH values above pH 4 up to pH 6 is
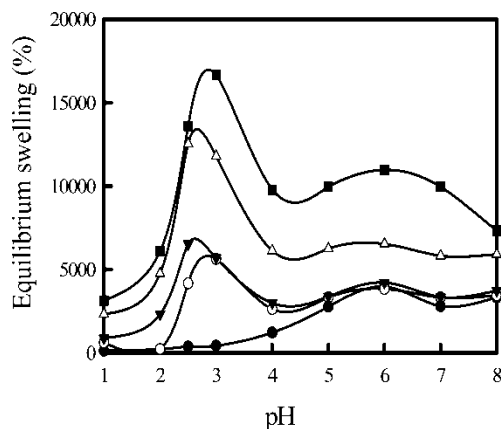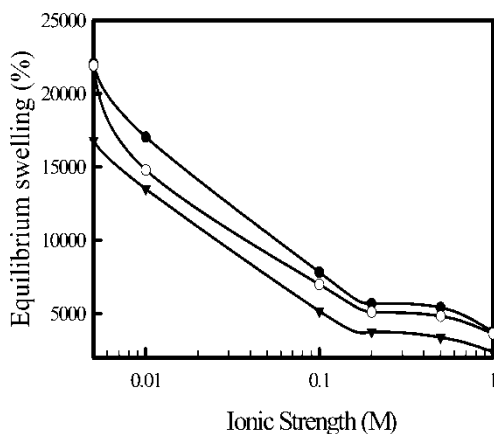

Fig. 2. pH dependent swelling of AMPS/AAc hydrogels of different AMPS content (wt%); (●) 0, (○) 25, (▼) 50, (▽) 75 and (■) 100.

attributed to the dissociation of the carboxylic groups of poly acrylic acid within the hydrogel network. The last reduction in the equilibrium swelling is accompanied by changing the buffer solution type from 0.2 M citrate to 0.2 M phosphate. Such a reduction in swelling might also be attributed to the change in ionic strength resulting from the difference in the ionization degree between citrate and phosphate salts (21).
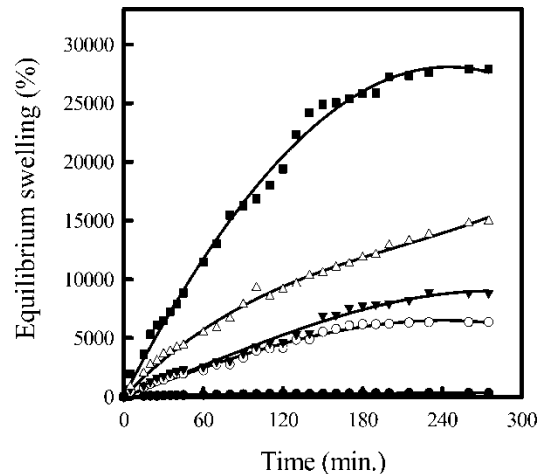
To study the effect of ionic strength on the equilibrium swelling of AMPS/AAc hydrogel, the hydrogel was allowed to swell in different aqueous electrolyte solutions of pH 4 and of various electrolyte concentrations i.e., ionic strength. Figure 3 showed the relation between the ionic strength of the solution and the equilibrium swelling of the prepared copolymer in a semi-log plot. It is obvious that the equilibrium is highly dependent on the ionic strength of the medium. Also, the type of the electrolyte affects the copolymer-swelling ratio. The increase in the ionic strength leads to a decrease in the swelling degree of the hydrogel. The reduction in swelling degree increased in the order:

Sodium chloride > Sodium phosphate > Sodium citrate.

The aforementioned results can be referred to the association state of COOH and SO_3H groups; and their hydration affinity in such solutions. The dissociation degree of citrate and phosphate salts is not the same and therefore, their ionic strength is different. On the other hand, according to Donnan osmotic pressure equilibrium, the increase in the movable counter ions concentration in the solution leads to the decrease in the osmotic pressure within the hydrogels, and affects their swelling ability (22). The mobility of counter ion depends on the degree of ionization of the electrolytes. The higher the ionizing degree of solute, the higher the immovable counter ion. The solutes used here ranged from weakly ionized (sodium citrate) to the fully ionized salt (sodium chloride). This may cause the variation in the reduction of the copolymer swelling degree.

Fig. 4. Time dependent swelling of AMPS/AAc hydrogel of different AMPS content; (●) 0, (○) 25, (▼) 50, (△) 75 and (■) 100 wt%.

Figures 4 and 5 show the time dependent swelling behavior of AMPS/AAc hydrogels in absence and under the influence of electric field, respectively. Under both conditions, the data show that the swelling degree and swelling rate increase by increasing the AMPS content in the copolymer to reach a maximum for a pure AMPS hydrogel. Also, it is clear that the application of the electric field increases the swelling degree and fastens the swelling rate of the hydrogel. The increase in the swelling degree and rate under the influence of the electric field can be explained as follows; the application of the electric field increases the ionization rate of both SO_3H and COOH groups owing to the migration of H^+ to the cathode. This allows the ionized acidic groups to combine with a large number of water molecules in a short time.
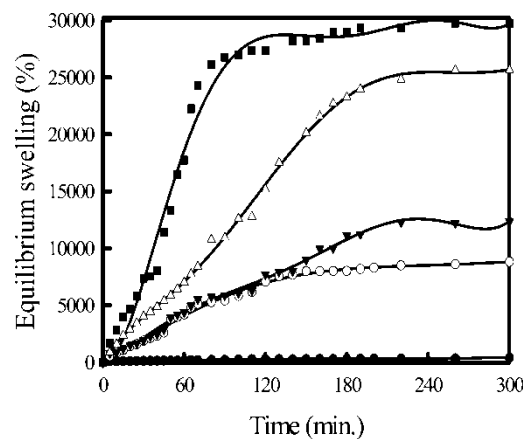

Fig. 3. Effect of ionic strength of different electrolyte solutions on the equilibrium swelling of AMPS/AAc hydrogel in aqueous HCl solution (pH 4); (●) sodium citrate, (○) Sodium phosphate and (▼) sodium chloride.
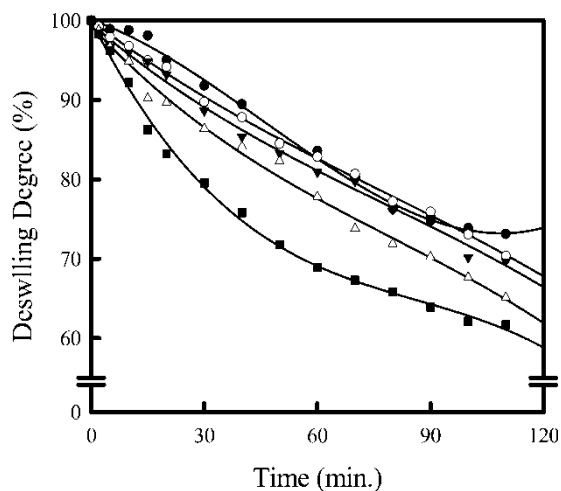

Fig. 5. Time dependent swelling of AMPS/AAc hydrogel of different AMPS content under the influence DC electric field of 12 V. AMPS content in the copolymer (wt%); (●) 0, (○) 25, (▼) 50, (△) 75 and (■) 100 wt%.

4.2 Electro-driven Chemo-mechanical Interactions within Electro-responsive Hydrogels
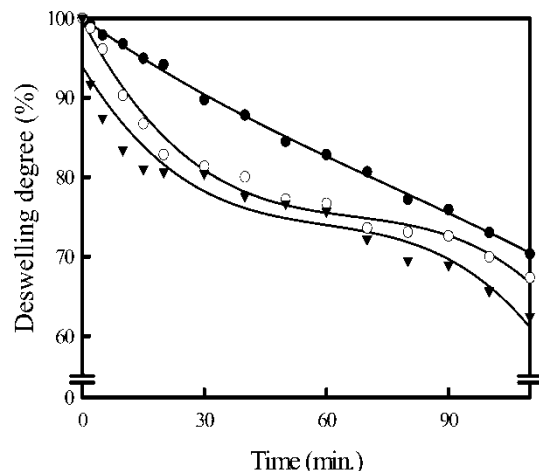
There are two major classes of chemo mechanical interactions within the electro active hydrogel in response to the application of the electric field (23). The first is the equilibrium swelling and swelling behavior generated by the electrostatic repulsive forces between the fixed charged groups in the hydrogel causing electric sensitive swelling/deswelling character (24). The second is the non-equilibrium electro-kinetics transduction associated with the relative flow of the electrolyte solution through the matrix containing ionized groups causing bending behavior of the hydrogel under the electric stimuli. The above mentioned interactions would depend on the magnitude and distribution of the fixed charge groups within the hydrogel and their response to the environmental conditions such as pH, ionic strength and applied electric fields (25).

Water deswelling behavior of AMPS/AAc hydrogel of different comonomer compositions under the influence of electric field was studied. Figure 6 shows the water deswelling rate of AMPS/AAc hydrogel of different comonomer compositions under the influence of a DC electric field of 5 V. As the AMPS content increases in the copolymer, its deswelling rate increases in response to the application of the electric field. Figure 7 shows the deswelling rate of AMPS/AAc copolymer as a function of the applied voltage. It obvious that, the increase in the applied voltage, leads to increase in the hydrogel de-swelling rate. The higher the potential applied, the higher the hydrogel sample response. On the other hand, Figure 8 shows the phenomenon of electric field induced deswelling is clearly shown by switching the electric field on and off.

Systems, which undergo shape change and produce contractile force in response to the environmental stimuli is called chemo-mechanical systems. Such systems can transform chemical energy directly into chemical work to give isothermal energy conversion. Electro-responsive chemo-mechanical behavior of AMPS/AAc hydrogel of different compositions as a function of the applied voltage was investigated.

The constant electric voltage across two parallel plate electrodes can cause AMPS/AAc hydrogel, held in an aqueous electrolyte solution such as KCl, to bend towards the cathode due to the voltage induced motion of ions. In other words, the electric field causes the migration of K^+ counter ions in the hydrogel toward the cathode, resulting in partial shielding of the ionized groups; SO_3^- and COO^- (5). This

Fig. 7. Time dependent deswelling of AMPS/AAc hydrogel of comonomer composition AMPS/AAc (75/25 wt%) under the influence of DC electric field of (●) 5 V, (○)7 V and (▼) 10 V.
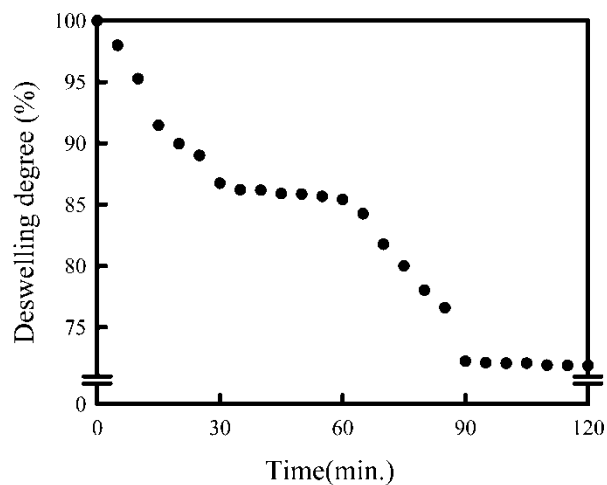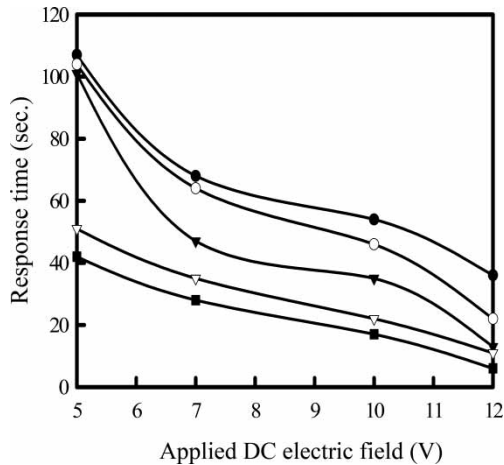
Fig. 6. Time dependent deswelling of AMPS/AAc hydrogels of different AMPS content under the influence of DC electric field of 5 V. AMPS content in the copolymer (wt %); (●) 0, (○) 25, (▼) 50, (△) 75 and (■) 100.
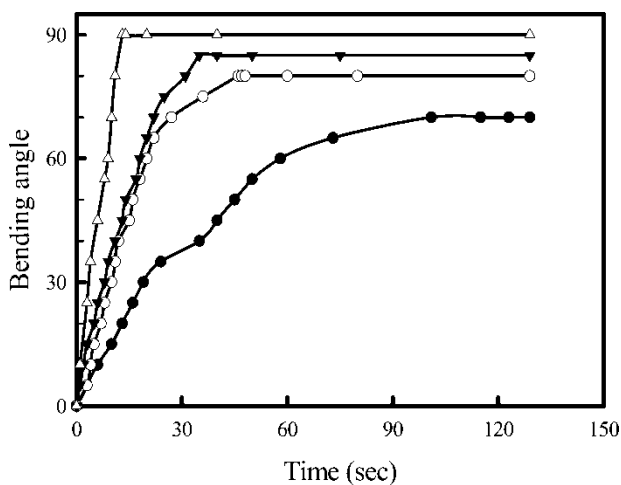
Fig. 8. Deswelling behavior of AMPS/AAc hydrogel due to on/off switching of electric field of 5 V.
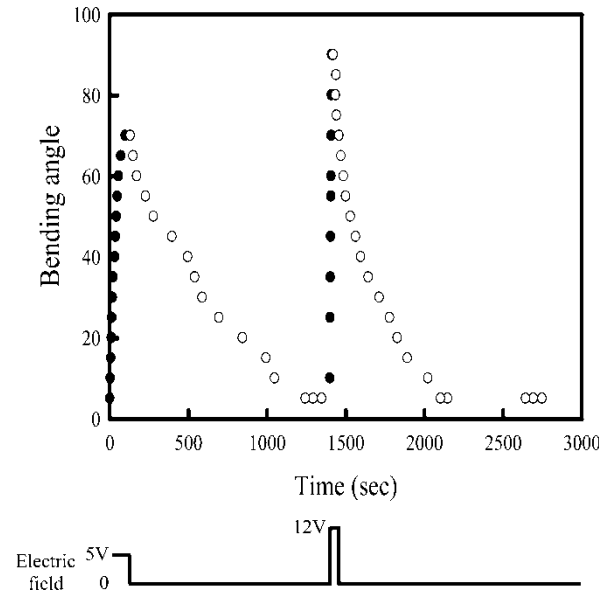
Fig. 9. Effect of the applied DC electric field on the response time of AMPS/AAc copolymer of different AMPS content (wt%); (●) 0, (○) 25, (▼) 50, (▽) 75 and (■) 100.

Fig. 11. Effect of applied voltage (on/off switching) on the bending time and bending angle.

reduces the hydration extent of the layers facing the cathode. Figure 9 shows the response of the copolymer under the effect of an electric field of different applied voltage. It is clear that the AMPS rich copolymers possess a faster response than those rich in AAc. Also, the increase in the applied voltage increases the responsiveness of the hydrogels by reducing the time needed for response.

Figure 10 shows time dependent bending angle under the influence of a DC electric field of different voltage. The Figure shows that the equilibrium bending angle, as well as the bending speed, is directly related to the applied voltage. As the applied voltage increases in the order of 5, 7, 10, and 12, the bending angle varied to be 71, 79, 84, and 90°, respectively. Similar to the bending angle, bending speeds are 1.27, 3.07, 3.73 and 7.98 degrees per

second as the applied voltage increases in the same order. In the same manner, Figure 11 shows the effect of the applied voltage on both the bending angle and bending response time by switching variable electric field (5 V and 12 V) on and off. It is obvious that the higher applied volt, 12 V, induced a faster response with a wider angle than those achieved under the influence of an electric field of 5 V.

Another important factor affecting the electro-driven chemo-mechanical behavior of the prepared hydrogel is the aqueous electrolyte solution concentration. Figure 12
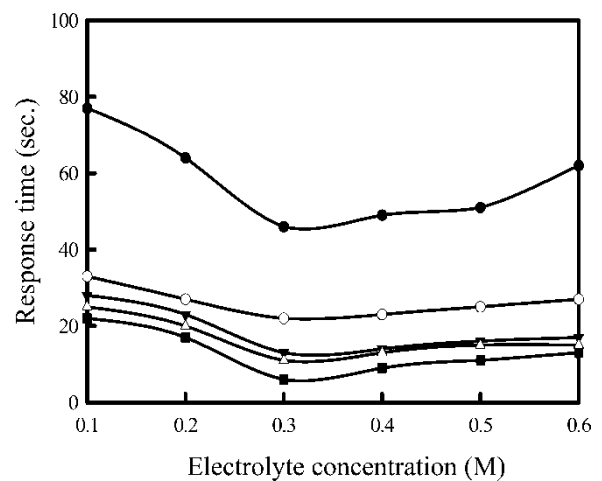

Fig. 10. Time dependent bending of AMPS/AAc copolymer under the influence of DC electric field of different voltage; (●) 5 V, (○) 7 V, (▼) 10 V and (△) 12 V.
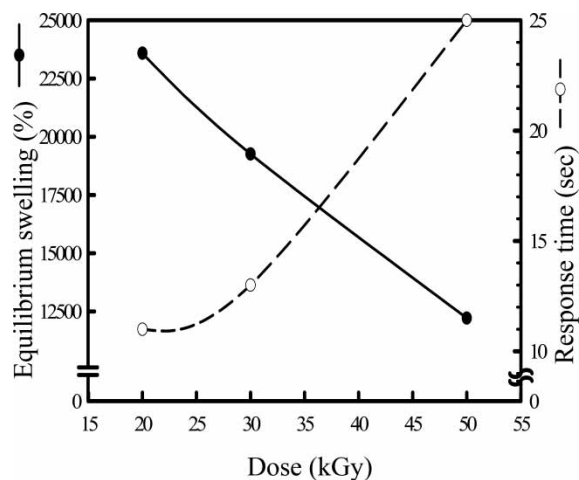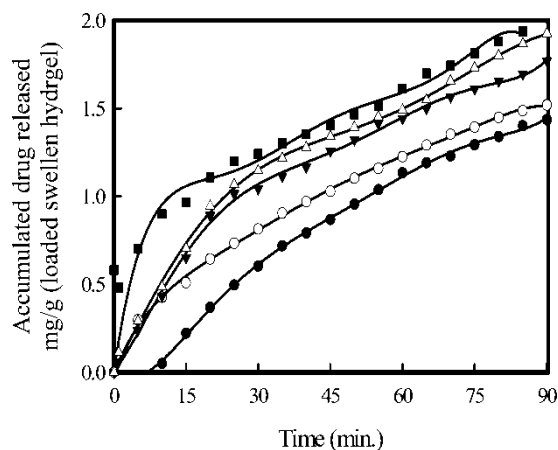

Fig. 12. Effect of ionic strength on the response time of AMPS/AAc hydrogels of different compositions under the influence of DC electric field of 12 V. AMPS content in the copolymer (wt %): (●) 0, (○) 25, (▼) 50, (△) 75 and (■) 100.
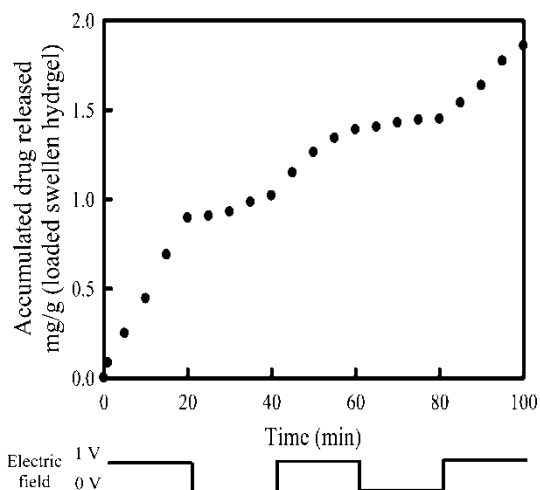
Fig. 13. Effect of irradiation dose on equilibrium swelling and response time of AMPS/AAc hydrogel.

Fig. 15. Electro-controlled release of theophylline from AMPS/AAc hydrogel by switching the applied electric field on and off.

shows that the response time of the AMPS/AAc hydrogel of different copolymer compositions becomes shorter as the electrolyte concentration increases reaching a minimum at 0.3 M (26). Thereafter, any further increase in the electrolyte solution does not possess any significant effect on the response time. This behavior can be explained by the Donnan osmotic pressure equilibrium. The increase in the movable counter ions concentration in the solution leads to the decrease in the osmotic pressure within the hydrogel which forced it to shrink, i.e., the higher the movable counter ions concentration, the faster shielding of the ionizable groups facing the cathode and consequently, the faster response to the applied electric field. The extra increase in the concentrations of the movable counter ions (>0.3 M) did not possess any decrease in the response

time due to the complete shielding of the ionizable groups of the matrix.

In addition to the applied voltage and electrolyte concentration, the degree of crosslinking may play a role in the response of the hydrogel to the electric field. Figure 13 shows the effect of irradiation dose on equilibrium swelling, as well as response time. As the irradiation dose (used for preparation of the hydrogel) increased, the equilibrium swelling also decreased, and a delay in the response time is observed. This behavior is attributed to the increase in crosslinking density of the hydrogel network, which reduces the free spaces available for swelling (27).

4.3 Electro-controlled Drug Release from AMPS/AAc Hydrogel

A release profile of theophylline as a model drug based on the electro responsiveness of the prepared AMPS/AAc hydrogel is shown in Figures 14 and 15. Figure 14 shows the effect of polymer composition on the theophyline release throughout the AMPS/AAc hydrogels. It is clear that the release of theophyline increases with time. Also, as the APMS content in the copolymer increases, the amount and the rate of released theophyline increases. The increase in AMPS content in the copolymer increases its ability to release the loaded drug under the influence of applied electric field. This is due to the high sensitivity of AMPS to the electric field.

The electro-controlled drug release of theophylline from AMPS/AAc hydrogel is shown in Figure 15. On the application of the DC electric field of 1 V, a rapid continuous release of theophylline is observed, while as soon as the electric field switched off, the release process is restricted. These results can be explained in the light of partition diffusion mechanism. The diffusion of the soluble loaded drug through out the matrix increases as network dehydration increases.

Fig. 14. Time dependent release of theophylline under the influence DC 1 volt from AMPS/AAc hydrogel of different AMPS content (wt %): (●) 0, (○) 25, (▲) 50, (▽) 75 and (■)100 in H_2O.

5 Conclusions

The AMPS/AAc copolymer hydrogels were synthesized by means of γ-radiation. The prepared hydrogel exhibited high sensitivity to the environmental stimuli such as pH, ionic strength and electric field. The electric responsive properties of the AMPS/AAc hydrogel were investigated in relation to the chemical composition, ionic strength and applied voltage. The magnitude and rate of the electric response was found to be dependent on the AMPS content, ionic strength and applied voltage. The release of theophylline, as a model drug, from AMPS/AAc hydrogel in response to the application of the electric field was investigated. The results obtained showed that the copolymer composition and electric field affected the release of drugs.

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