# Enhanced Swelling Rate of Poly(ethylene glycol)-Grafted Superporous Hydrogels

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**ABSTRACT:** Hydrophilic poly(ethylene glycol) (PEG) grafts were introduced into superporous hydrogels (SPHs) to enhance the water absorption rate and swelling kinetics. PEG-grafted SPHs were prepared by copolymerization of acrylic acid and acrylamide monomers in the presence of PEG acrylate accompanied by a gas blowing foaming process to create superporous structures. PEG-grafted SPHs swelled 3 ~ 6 times faster than the control SPHs. The equilibrium swelling time was significantly reduced by introduction of hydrophilic PEG grafts and was further shortened by moisture. PEG-grafted SPHs containing 28 wt% of moisture reached their equilibrium swelling within 20 s. These PEG-grafted SPHs with fast swelling and superabsorbent properties may be useful for bioapplications where fast swelling kinetics is critical.

**KEY WORDS:** hydrogels, superporous hydrogels, swelling kinetics, superporous structure, poly(ethylene glycol).

## INTRODUCTION

**Over the past** decades, hydrogels have been extensively investigated for a broad range of pharmaceutical and biomedical applications, especially for developing controlled release drug delivery systems [1]. Hydrogels are three dimensional hydrophilic polymer networks formed by chemical and/or physical cross-linking [2]. They can absorb a significant amount of water but retain their three dimensional structure in the swollen state. Since the first report on the biomedical use of

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poly(2-hydroxyethyl methacrylate) hydrogel in 1960 [3], considerable progress has been made in the synthesis and applications of hydrogels.

One of the challenges in the application of hydrogels has been preparing hydrogels with fast responses in terms of swelling/deswelling, phase transition, and other physical changes. Most dried hydrogels swell very slowly, and their swelling to the equilibrium state takes a long time ranging from several hours to days due to the slow absorption of water into glassy hydrogels by diffusion. Even though slow swelling properties have been useful for controlled drug delivery, fast swelling hydrogels are critical for many other applications. Since the swelling of dried hydrogels is limited by slow diffusion of water, the most commonly used method for achieving fast swelling has been to make microparticles that have extremely short diffusion path length. The small size of microparticles, however, poses limitations for many applications.

Over the years, we have developed hydrogels that have both fast and superabsorbent properties. Hydrogels with superporous structures were prepared by using a gas blowing technique based on acid and sodium bicarbonate [4–6]. While microporous and macroporous hydrogels have pore sizes from 10~100 nm and 100 nm~10 μm, respectively, superporous hydrogels (SPHs) have pore sizes in the range of hundreds of micrometers. In superporous structures, the pores are interconnected to each other to generate open channels, allowing fast water absorption by capillary force. Due to their superporous structures, the swelling ratio usually is more than 100 and reaches its equilibrium within minutes. Based on these fast swelling and superabsorbent properties, SPHs have potential for various pharmaceutical and biomedical applications. For example, SPH composites have been developed as gastric retention devices [7,8]. The mechanical strength of SPHs was substantially increased by using a composite material, such as, Ac-Di-So®, a cross-linked carboxymethylcellulose which is commonly used as a disintegrant in pharmaceutical tablets. SPHs with interpenetrating polymer network structures were also developed to improve mechanical properties [9]. SPHs were investigated as novel peroral peptide drug delivery systems for drug targeting in the intestine [10–12].

In this study, to maximize the swelling rate of the SPHs, hydrophilic poly(ethylene glycol) (PEG) chains were introduced as grafted chains to the SPH network structure. The effects of the PEG grafting on the swelling properties of SPHs were investigated.

## EXPERIMENTAL PART

### Materials

Acrylic acid (AA, 99%), poly(ethylene glycol) acrylate (Mn = 375 g/mol), ammonium persulfate (APS, 99.9%), *N*,*N*′-methylenebisacrylamide (BIS, 99%), *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMED, 99.5%), and sodium bicarbonate (99.7%) were purchased from Aldrich (Milwaukee, WI). Acryl amide (AAm, 99%) and Pluronic® F127 were obtained from Fluka (Buchs, Switzerland) and BASF (Parsippany, NJ), respectively. The reagents were used without further purification. All solvents used in the study were reagent grade.

### Preparation of AA/AAm SPHs

SPHs were produced by polymerization of monomers, AA and AAm, in the presence of BIS as a cross-linking agent. AAm (15% w/v) and AA (10% w/v) were dissolved in distilled water. BIS (0.25% w/v) and Pluronic® F127 (0.5% w/v) were added to the monomer solution. The pH of the solution was adjusted to 5.0∼5.1 by adding 8 M NaOH solution. A predetermined amount of the monomer solutions were poured into 50 mL polypropylene conical tubes (30 × 115 mm). After APS (0.6% w/v) and TEMED (0.4% w/v) were added, the solutions were shaken manually and kept at room temperature for 3.5 min. Sodium bicarbonate power (5% w/v) was added to the solution and immediately stirred with a spatula for several seconds so that gas bubbles could be generated and distributed evenly throughout the reaction solution. The solution was allowed to stand for more than 30 min to ensure complete polymerization. The resultant superporous hydrogel was dehydrated in ethyl alcohol and dried in an oven at 60°C for 12 h.

### Preparation of PEG-grafted AA/AAm SPHs

The procedure for PEG-grafted SPHs was basically the same as above, except for the addition of PEG acrylate to the monomer solution. A predetermined amount of PEG acrylate (5 or 10% w/v) was added to the monomer solution before initiating the polymerization. The other processes were carried out as described for making AA/AAm SPHs. The synthesized PEG-grafted AA/AAm SPHs were soaked in 80% ethyl alcohol for 1 h to remove residual unreacted monomers and impurities from the hydrogels, followed by dehydration in ethyl alcohol for 2 h. After removal of excessive ethyl alcohol on the surface by

gentle blotting, the SPHs were dried in a drying oven kept at 60°C for 12 h.

## The Swelling Ratio Measurements

To measure the weight to swelling ratio, hydrogels were cut into disks (12 mm in diameter and 2 mm in thickness) and then dried under vacuum for 24 h. The samples were immersed in an excessive amount of distilled water at room temperature and weighed at predetermined time intervals after removal of excessive surface water by lightly touching the samples with filter paper. The weight swelling ratios (S) of the SPHs were calculated from the following equation:

$$S = (W_s - W_d)/W_d$$

where $W_s$ and $W_d$ are the weights of swollen and dried hydrogels, respectively. The percentage swelling of hydrogels was defined as:

$$\text{Percentage swelling} = (S_t/S_{eq}) \times 100$$

where $S_t$ and $S_{eq}$ are the swelling ratio measured at a certain time (t) and the equilibrium swelling ratio, respectively.

For the swelling test with moist SPHs, the SPHs were moisturized in a water chamber at 37°C and taken out when their moisture content reached 28 wt%. PEG-grafted SPHs were hygroscopic, and thus they were moisturized at ambient conditions to have the same moisture content.

## Contact Angle Measurement

AA/AAm and PEG-grafted AA/AAm PEG hydrogels with the same chemical compositions were synthesized without the bubbling process and used for contact angle measurements, because the SPHs were not able to be measured due to their tendency to absorb water instantaneously through pores. Monomer solutions were polymerized in a glass mold of about 2 cm × 2 cm (0.4 mm in thickness) and then dried at room temperature for 24 h and in vacuo for another 24 h. Advancing contact angles of water droplets were measured using a goniometer (Rame-Hart, Inc., Mountain Lakes, NJ, USA).

### Scanning Electron Microscopy (SEM)

SEM was used to examine the morphology of the porous structure of hydrogels. A JEOL JSM-840 scanning electron microscope (Jeol USA, Inc., Peabody, MA) was used after coating the samples with gold using a Hummer Sputter Coater (Technics, Ltd). Images were captured using a digital capture card and Digital Scan Generator 1 (Jeol). Dried superporous hydrogels were cut to expose their inner structure. The pore size was determined from the SEM pictures.

## RESULTS AND DISCUSSION

### Preparation of PEG-grafted AA/AAm SPHs

Superporous hydrogels based on AA and AAm were synthesized in the absence and the presence of PEG acrylate using the gas blowing technique. Listed in Table 1 are the chemical compositions of the monomer solutions to prepare SPH samples. The process for making a superporous hydrogel is shown in Figure 1. To make homogeneous SPHs, the kinetics of foaming and polymerization processes is important. Therefore, the timing for this addition of the foaming agent and the onset of gelling had to be carefully controlled to produce homogeneous pore structures in hydrogels. It was observed for AA/AAm SPHs that 3.5 min after adding initiators was the optimum timing for the foaming process.

PEG is a highly hydrophilic polymer which is freely soluble in water. In this study, PEG was introduced as grafted chains in hydrogel structures to enhance the swelling kinetics. As shown in Figure 2, the polymerization of AA and AAm in the presence of PEG acrylate can lead to SPHs with hydrophilic PEG grafts. The density of the PEG grafts in hydrogels is expected to be a function of the PEG content in aqueous

*Table 1. Monomer composition for the preparation of superporous hydrogels.*

| Sample | Acrylic acid (% w/v) | Acrylamide (% w/v) | PEG acrylate (% w/v) | Contact angle (°C) | $S_{eq}$[b] |
|---|---|---|---|---|---|
| AA/Aam[a] | 10 | 15 | – | 71 | 400 |
| AA/AAm-PEG05 | 10 | 15 | 5 | 62 | 178 |
| AA/AAm-PEG10 | 10 | 15 | 10 | 60 | 131 |

[a]The other chemicals were fixed as the following: BIS = 0.25% w/v, Pluronic® F127 = 0.5% w/v, APS = 0.6% w/v, TEMED = 0.4% w/v, sodium bicarbonate = 5% w/v.
[b]Equilibrium swelling ratio.

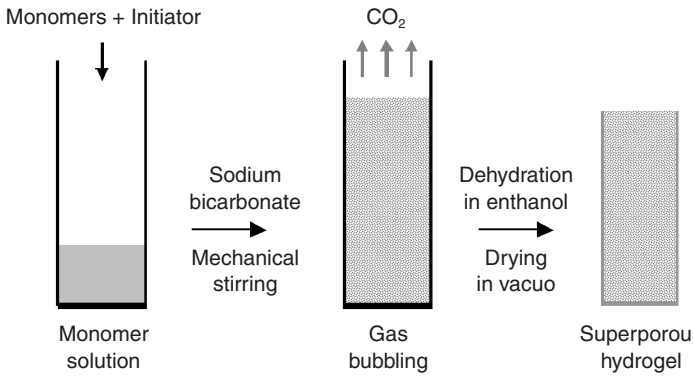


**Figure 1.** General procedure for making superporous hydrogels.

monomer solution. The introduction of grafted chains may increase the chain entanglement that can decrease the swelling rate and ratio. To minimize chain entanglement of the PEG grafts a low molecular weight PEG (Mw– 375 g/mol) was used to make the SPHs with grafted structure.

Pictures of AA/AAm-PEG05 SPH in the dried and hydrated states are shown in Figure 3. The superporous hydrogel instantly responded and swelled up on addition of water until it reached an equilibrium swelling point. The swelling ratios of hydrogels were more than 100 fold by weight. The volume of the hydrogel significantly increased after swelling while the original shape was maintained. Also, the hydrated hydrogel could be converted to the dried hydrogel with retention of the original size and shape. While AA/AAm SPHs showed the equilibrium swelling ratio of about 400 fold, the swelling ratios of PEG-grafted SPHs ranged from 130 to 180. The decrease in swelling ratio may be ascribed to enhanced chain entanglement by the introduction of the grafted chains. An increase in the PEG content from 5% to 10% (w/v) led to a slight decrease in the swelling ratio of the SPHs. Although the swelling capacity was reduced by the grafted structures, PEG-grafted SPHs still maintained superabsorbent properties with equilibrium swelling ratios exceeding 100 fold.

## Morphological Study

The morphology of superporous structures was examined with a scanning electron microscope (SEM). Dried superporous hydrogels

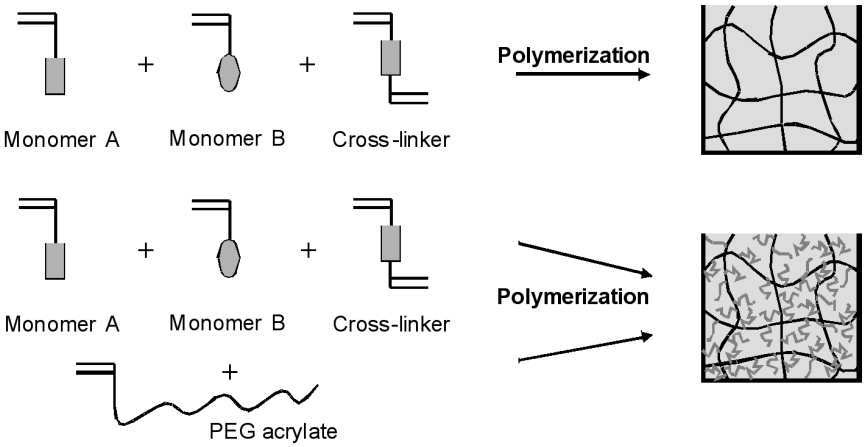


**Figure 2.** Hydrogel structures of AA/AAm SPH (top) and PEG-grafted AA/AAm SPH (bottom).

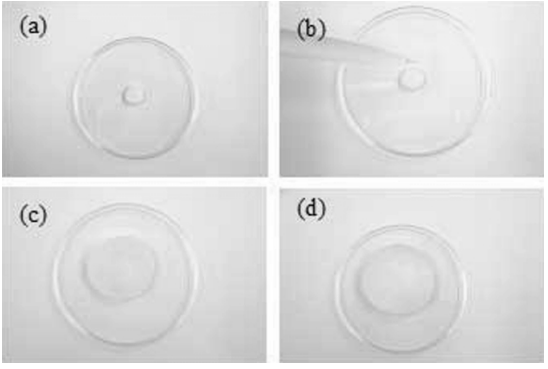


**Figure 3.** Fast swelling behavior of a dried hydrogel upon addition of water. (a) Dried hydrogel; (b) addition of distilled water to hydrogel; (c) 10 s after addition of 10 mL of distilled water; and (d) 10 s after addition of 15 mL of distilled water.

were cut to expose their inner structure as shown in Figure 4(a) the surface (top) and Figure 4(b) the inside (bottom) of a superporous hydrogel based on AA and AAm. As seen in this figure, the pores were spherical in shape with circular interconnections. The average diameter of the pores was approximately 100–250 μm, and some pores were as large as over 300 μm. All pores were connected to each other to form extensive capillary channels, and this is critical for fast swelling

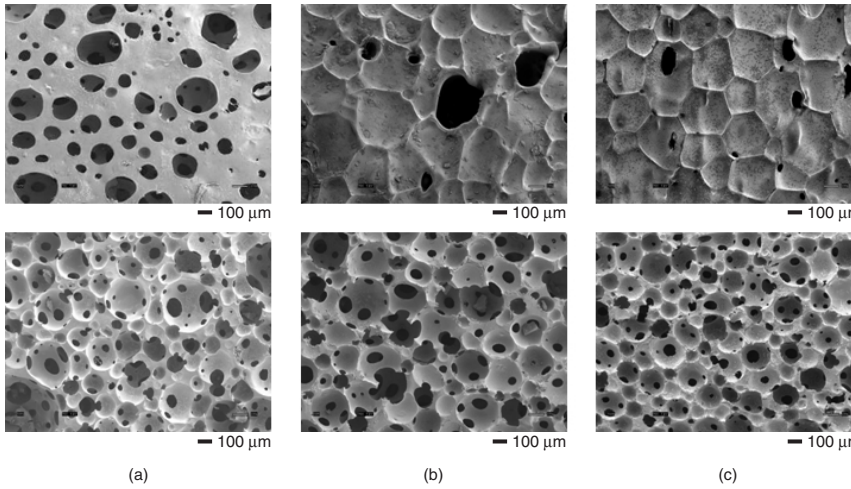


**Figure 4.** Scanning electron micrographs of the surface (top) and the inside (bottom) of superporous hydrogels: (a) AA/AAm SPH; (b) AA/AAm-PEG05 SPH; and (c) AA/AAm-PEG10 SPH.

of dried gels to the equilibrium state in a matter of minutes. Shown in Figures 4(b) and 4(c) are the surface and the inside of PEG-grafted superporous hydrogels. PEG-grafted SPHs had different surfaces than AA/AAm SPH. For both PEG-grafted hydrogels relatively non-porous surfaces were observed. Nevertheless the inside of the hydrogels was similar in porous structures to AA/AAm SPH. The pores were interconnected to each other to form the open channel system. The average diameters of the pores in Figure 4(b) and 4(c) were approximately 170 μm and 140 μm, respectively, and their size ranged from 100 μm to 250 μm.

## Swelling Kinetics of Superporous Hydrogels

Generally, conventional hydrogels take several hours to days to swell to their equilibrium states depending on their dimensions. As seen in Figure 4, superporous hydrogels have a lot of open channels that allow water absorption by capillary force, thus they can swell in a short time length. The swelling kinetics of AA/AAm SPH and PEG-grafted SPHs in distilled water are shown in Figure 5. All SPH samples were completely dried in a vacuum oven at 60°C for more than 24 h before measuring their swelling ratios. The AA/AAm SPHs swelled to equilibrium sizes in less than 10 min. The swelling of dried AA/AAm SPH samples took about 10–20 min to reach their equilibrium

points; this is similar to the results obtained in the previous studies [6,9]. Generally, the SPHs based on AA and AAm were observed to reach their equilibrium swelling ratios in 5–30 min depending on the preparation conditions such as drying conditions, the chemical composition and the amount of foaming agent ($NaHCO_3$) used. Compared with several hours to days necessary for conventional hydrogels, the swelling rate of SPHs is extremely fast. This fast swelling property results from the existence of homogeneous open channels throughout the hydrogels that make water intrusion easy. On the other hand, there was a dramatic difference in the equilibrium swelling time between AA/AAm SPHs and PEG-grafted SPHs (AA/AAm-PEG05 and AA/AAm-PEG10). The PEG-grafted SPHs showed much faster swelling and swelled to their equilibrium within 2–3 min. The swelling of the hydrogels containing a higher content of PEG grafts occurred even more quickly.

It was reported that superporous hydrogels demonstrated a remarkably faster swelling in "moisturized" state than in dry state [6]. As shown in Figure 6, moisturizing significantly affected the swelling kinetics. For both AA/AAm and AA/AAm-PEG SPHs, the swelling

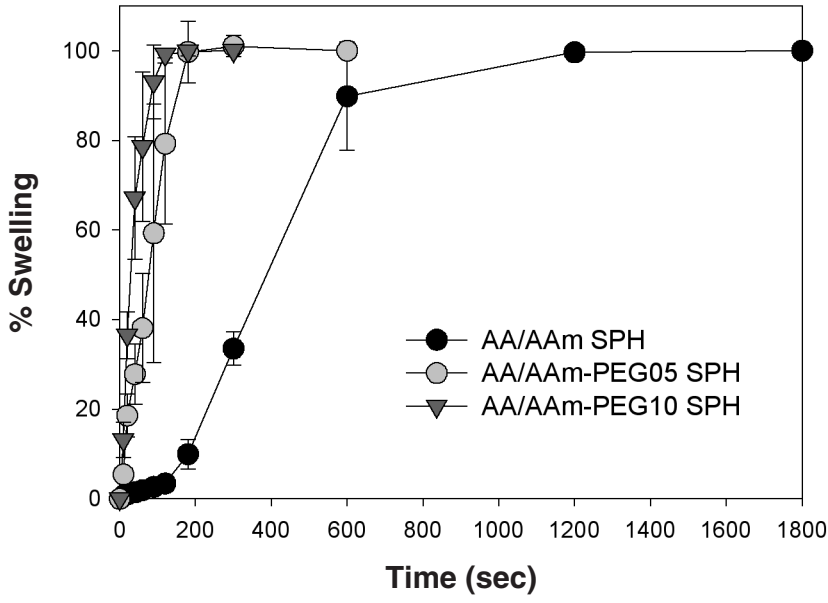


**Figure 5.** Swelling kinetics of superporous hydrogels: (a) AA/AAm SPH; (b) AA/AAm-PEG05 SPH; and (c) AA/AAm-PEG10 SPH.

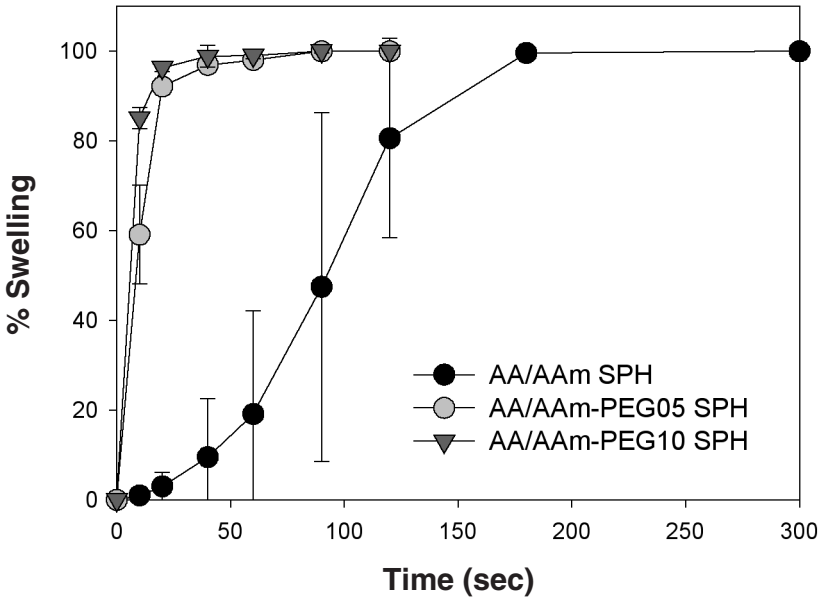


**Figure 6.** Swelling kinetics of moisturized superporous hydrogels (28 wt%): (a) AA/AAm SPH; (b) AA/AAm-PEG05 SPH; and (c) AA/AAm-PEG10 SPH.

rates were 3~6 times faster than for the corresponding dried hydrogels. The equilibrium swelling time of AA/AAm SPH samples was reduced to 2–3 min. The PEG-grafted SPHs showed almost instant swelling behaviors with the introduction of water and their measured swelling times were in the range of 20–30 s.

The differences in swelling kinetics between SPHs with or without PEG grafts were more significant at the initial stage of swelling (Figure 7). The PEG-grafted hydrogels showed much faster swelling than AA/AAm SPHs, not only in the dried state, but also in the moisturized state, and their swelling rates increased as the PEG content increased. For dried samples, the PEG-grafted hydrogels swelled to almost their equilibrium states (the swelling ratios of more than 130) in 2 min, while the AA/AAm SPHs swelling ratio was less than 10 for the same time period. The AA/AAm-PEG10 samples swelled to their equilibrium state within less than 2 min. On the other hand, PEG-grafted hydrogels containing 28% moisture instantly swelled in aqueous media and reached their equilibrium states within 20 s. Such a dramatic enhancement in swelling kinetics results from the introduction of hydrophilic PEG grafts into hydrogel structures. The contact

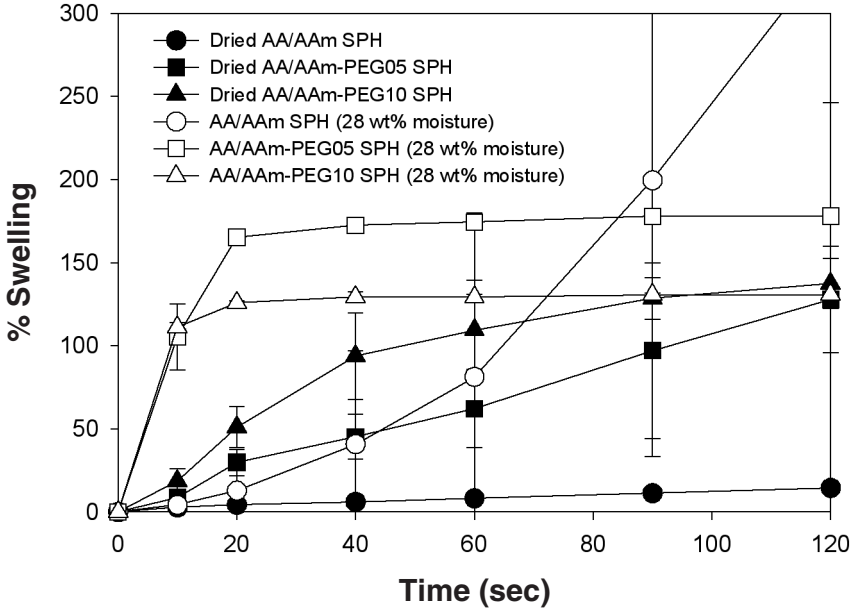


**Figure 7.** Comparison of initial swelling kinetics of dried (closed) and moisturized hydrogels (open).

angle measurement data (Table 1) showed that the surfaces of PEG-grafted hydrogels were more hydrophilic than the SPH without PEG grafts. Generally, good capillary action requires surfaces with good water wettability. PEG has been often used to reduce interfacial free energy and enhance wettability on hydrophobic polymer surfaces [13,14]. The introduction of hydrophilic PEG grafts make it possible for the SPHs to have enhanced wettability, leading to the accelerated water absorption rate.

## CONCLUSIONS

PEG-grafted SPHs were prepared to accelerate the swelling kinetics of the current SPHs. The PEG-grafted hydrogels demonstrated a much faster swelling behavior than the hydrogels without PEG grafts. These SPHs, with fast swelling and superabsorbent properties, are being evaluated for drug delivery and biomedical applications where fast swelling to large sizes is critical.

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