



Design and Preparation of AMPS-Based Hydrogels for Biomedical Use as Wound Dressings

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Received: 27 October 2006

Accepted: 19 February 2007.

ABSTRACT

Hydrogels from either 2-acrylamido-2-methylpropane sulfonic acid (AMPS-H⁺) or its sodium salt (AMPS-Na⁺) crosslinked with *N,N*'-methylene-bis-acrylamide (MBA) or ethylene glycol dimethacrylate (EGDM) have been prepared by redox-initiated free radical polymerisation to complete conversion. Different percentages of crosslinker and various concentrations of AMPS-H⁺ and AMPS-Na⁺ between 40-60% w/v were employed to obtain crosslinked hydrogels with different polymer contents and crosslink densities. The crosslinked polymers were swollen in water and the increasing water uptake followed as a function of time up to the equilibrium water content (EWC). It was found that the hydrogel sheets prepared from the highest monomer concentration (60% w/v) reached equilibrium at a slightly higher rate. In addition, the MBA crosslinker (≥ 1.0 mol %) had a significant effect on the water absorption profile and was found to be a more effective crosslinker than EGDM in terms of property modification. These results indicate that both type and concentration of monomer and crosslinker are highly influential on the degree of crosslinking which, in turn, affects the rate and capacity for water absorption of the resultant hydrogels. Thus, the balance between crosslink density and water absorption is of critical importance to their potential application as wound dressing materials.

Keywords: synthetic hydrogels, poly(2-acrylamido-2-methylpropane sulfonic acid), poly(2-acrylamido-2-methylpropane sulfonic acid) sodium salt, biomedical polymers, wound dressings.

1. INTRODUCTION

The development of synthetic hydrogels can be traced back to the studies of Wichterle and Lim [1] who employed 2-hydroxyethyl methacrylate (HEMA) as a hydrophilic monomer. The lightly crosslinked polymer of this material was used as a soft contact lens and, to a more limited extent, as a general biomedical polymer. Since then, much attention has been concentrated on synthetic hydrogels for their applications as biomaterials,

especially for wound dressings where the hydrogel assumes the skin's vital roles of protecting the inner tissues, retaining body fluids, maintaining the water balance, and regulating body heat [2-5]. The Biomedical Polymers Technology Unit at Chiang Mai University has previously studied synthetic hydrogels based on HEMA [6,7] and also chitosan for use as wound dressings. However, these materials still have some weak

points associated with their unsatisfactory skin adhesion and water absorption properties. Therefore, attention has recently turned to 2-acrylamido-2-methylpropane sulfonic acid (AMPS-H⁺) which is a strongly acidic ionic monomer and is easily dissolved in water. The polymer properties enhanced by AMPS-H⁺ are its hydrophilicity, thermal stability, stability over a broad pH range, resistance to hydrolysis and ionic character. The advantages of this synthetic hydrogel are that it is soft and flexible and, importantly (compared to HEMA), any residual unreacted monomer can be more easily removed by water due to the polymerisation being performed in an aqueous system. The result is that an already hydrated hydrogel is obtained because water is retained within a 3-dimensional crosslinked structure. This synthetic hydrogel has already attracted interest as a wound dressing [8-11] since it adheres to healthy skin but not to the wound surface, is easily removable/replaceable without any damage to the healing wound, while its gel transparency allows visual monitoring of the healing process.

The aim of this present work is to study the relationship between the crosslink density, as dependent upon the type and percentage of crosslinker and the monomer concentration, and the equilibrium water content. The monomers compared were AMPS-H⁺ and its sodium salt AMPS-Na⁺, while the two crosslinkers used were *N,N'*-methylene-bis-acrylamide and ethylene glycol dimethacrylate.

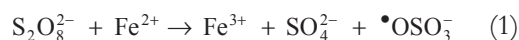
2. MATERIALS AND METHODS

The AMPS-H⁺ monomer was a commercial product (Aldrich, assay 99%) and was used without further purification. The AMPS-Na⁺ monomer was prepared from AMPS-H⁺ by neutralization in aqueous solution with sodium hydroxide (NaOH), as described in detail below. Potassium persulphate (K₂S₂O₈), ferrous sulphate (Fe(SO₄)₂) and potassium metabisulphite (K₂S₂O₅), which were employed as the initiator, co-initiator and

redox catalyst respectively, were also commercial products (Aldrich). The *N,N'*-methylene-bis-acrylamide (MBA) and ethylene glycol dimethacrylate (EGDM) crosslinkers were purchased from Fluka. Deionized water was used for measuring the water absorption properties of the hydrogel sheets.

AMPS-H⁺ and AMPS-Na⁺ solution polymerisations were carried out in distilled water as the solvent at room temperature using various monomer concentrations ranging from 40-60% w/v. In the case of AMPS-Na⁺ at a concentration of 40% w/v, the monomer solution was prepared by first dissolving 40 g of AMPS-H⁺ in about 30 ml of deionized water and adding to this solution 25 ml of a 30% w/v NaOH solution with cooling. The solution was then neutralised by titration with 1M NaOH to pH 7.00. Finally, the volume of the solution was adjusted to 100 ml with distilled water. The 50% w/v and 60% w/v AMPS-Na⁺ solutions were prepared using the same procedure using 50 g and 60 g AMPS-H⁺ respectively.

For polymerisation, 0.15% w/v of potassium persulphate (K₂S₂O₈), 0.08% w/v of ferrous sulphate (Fe(SO₄)₂) and 0.15% w/v of potassium metabisulphite (K₂S₂O₅) were added to the monomer solution as the initiator, co-initiator and redox catalyst respectively. This redox initiating system generated free radicals as shown in equation (1) below.



In addition, MBA and EGDM were employed as crosslinkers in concentrations ranging from 0.5 to 1.5% mol/mol monomer. The crosslinking reaction was performed in a beaker with gentle stirring before quickly pouring the solution into a 15 x 15 cm glass vertical mould with a spacer of thickness 0.8 mm. Gentle stirring was necessary in order to avoid the formation of air bubbles in the product. Adhesion of the hydrogel to the glass mould was prevented by using Teflon

sheets over the surface area of contact. The polymerisation reaction was allowed to proceed towards completion at room

temperature (25-28°C) and under 55-60% relative humidity for 24 hrs before removing the hydrogel sheet.

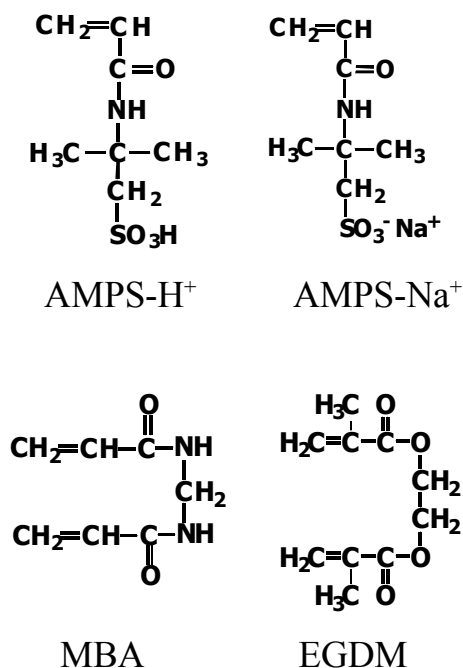


Figure 1. Chemical structures of the AMPS-H⁺ and AMPS-Na⁺ monomers and the MBA and EGDM crosslinkers.

The water absorption-time profile and equilibrium water content (EWC) were determined for each of the hydrogels in deionized water at room temperature. Before each determination, the hydrogel sheet was conditioned by allowing it to equilibrate in air at room temperature for at least 24 hours. Thus, the initial water content at time $t=0$ prior to immersion in the deionized water was, in essence, the EWC in air. The reasoning behind this was so that each sample moved from the same equilibrium state in air to the same equilibrium state in water. This ensured that the differences in osmotic driving force for water absorption between the samples could be related to their differences in composition and microstructure for the same osmotic shift

in equilibrium. The dimensions of the synthesized hydrogel sheets after equilibration in air and before immersion in water were 2 x 2 x 0.08 cm.

In practice, when a sample of a hydrogel is immersed in water, there will be an osmotic driving force encouraging the water to enter the free volume within the hydrogel, as shown in Figure 2 [12]. When this osmotic driving force becomes balanced by the opposing force exerted by the polymer chains in resisting further expansion (a resistance which increases with crosslinking), an equilibrium will be reached. The water content (WC) at this point is termed the 'equilibrium water content', EWC.

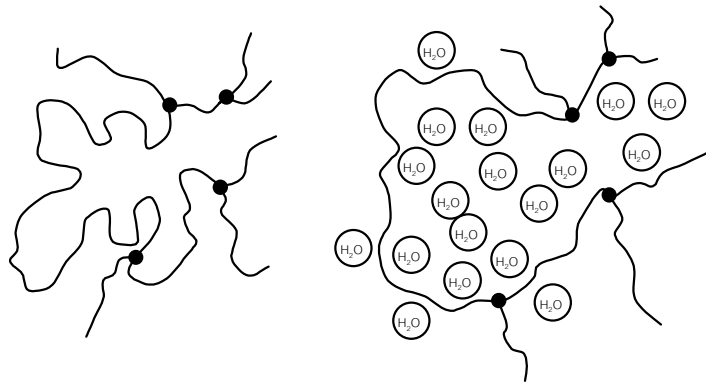


Figure 2. Absorption of water into a crosslinked hydrogel chain segment [12]. (● crosslinking units)

The water content (WC) of a hydrogel, expressed as a weight percentage (% w/w), is given by equation (2).

$$WC = \frac{\text{wt. of swollen} - \text{wt. of dry polymer}}{\text{wt. of swollen polymer}} \times 100\% \quad (2)$$

3. RESULTS AND DISCUSSION

The water absorption versus time (WC-time) profiles for the hydrogel sheets (thickness 0.8 mm) prepared from the two AMPS-H⁺ and AMPS-Na⁺ monomers at various monomer concentrations are shown in Figures 3 and 4. The effects of the type and concentration of crosslinker used are shown in Figures 5-7.

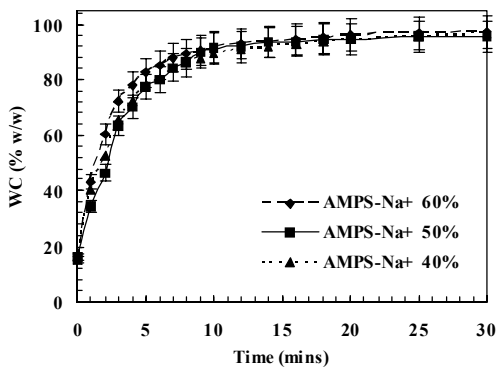


Figure 3. WC-time profiles of the AMPS-H⁺ hydrogels prepared from different monomer concentrations (40-60% w/v).

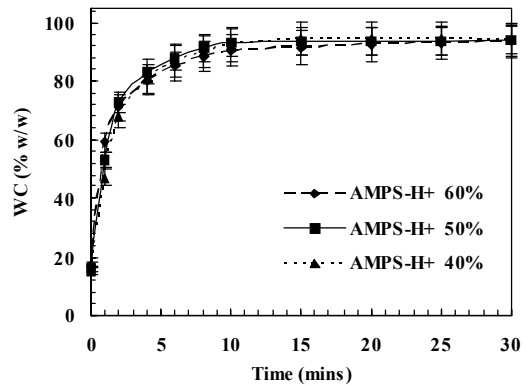


Figure 4. WC-time profiles of the AMPS-Na⁺ hydrogels prepared from different monomer concentrations (40-60% w/v).

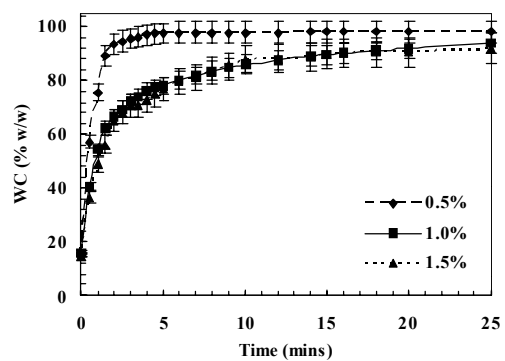


Figure 5. WC-time profiles of the AMPS-H⁺ 40% w/v hydrogels with varying concentrations (0.5-1.5 mol %) of MBA crosslinker.

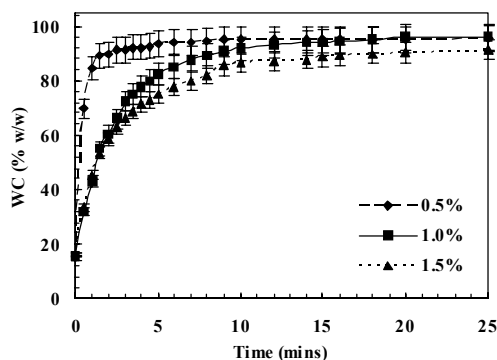


Figure 6. WC-time profiles of the AMPS-Na⁺ 40% w/v hydrogels with varying concentrations (0.5-1.5 mol %) of MBA crosslinker.

The WC-time profiles of the AMPS-H⁺ and AMPS-Na⁺ hydrogels in Figures 3 and 4 show only slight differences with concentration. These differences are not considered to be significant over the 40-60% w/v concentration range studied despite the varying polymer contents. Furthermore, a similar EWC level of 95-100% was attained in each case after approximately 20 mins. The most noticeable effect of increasing the monomer concentration seemed to be to increase the mechanical strength and coherency of the hydrogel sheet as prepared. Since the hydrogels could not be tested mechanically, their mechanical strength and coherency were judged manually by simply stretching and pressing the sheet. Sheets prepared from higher concentrations of monomer and crosslinker were noticeably stronger when pressed or stretched and showed greater dimensional stability (not too elastic).

In this study, the 40-60% w/v monomer concentration range was initially chosen because this range had been suggested by many previous workers [8-11]. AMPS-H⁺ and AMPS-Na⁺ hydrogels prepared within this concentration range are suitable for wound dressing applications since they can be cast into good quality sheets with appropriate levels of elasticity and water absorption. Monomer concentrations >60% cause problems due to

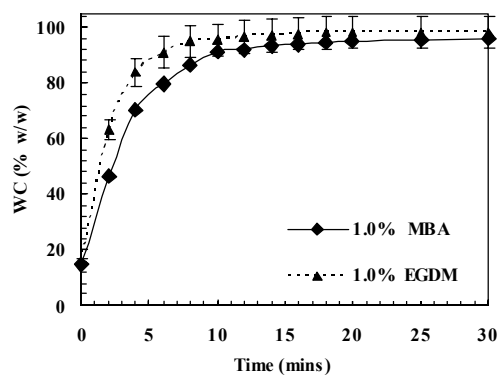


Figure 7. Comparison of the WC-time profiles of AMPS-Na⁺ 50% w/v hydrogels using 1.0 mol % (relative to monomer) EGDM and MBA crosslinkers.

high viscosity and rapid self-polymerisation. On the other hand, monomer concentrations <40% give rise to hydrogel sheets which are very soft, tacky, and therefore difficult to remove from the mould. Also, from an economic perspective, the cost of the monomer needs to be taken into account since a higher monomer concentration will increase the production cost of the hydrogel.

In contrast, it is clearly shown in Figures 5 and 6 that the crosslink density in the hydrogel structure does significantly influence the water content. The “crosslink density” is often defined as the mole fraction of monomer units which are crosslink points. Crosslinking provides anchoring points for the polymer chains and these anchoring points restrain excessive movement and maintain the position of the chain in the network. Thus, when a higher concentration of crosslinker is employed, the number of crosslink points in the polymer network increases, resulting in a denser and more compact hydrogel structure. Therefore, the rate of diffusion of water molecules into the hydrogel decreases. From the experimental results, it can be concluded that the hydrogel with higher crosslink density synthesized from a higher crosslinker concentration gives a lower EWC with a slower rate of water absorption. Also, the hydrogel takes a longer time to approach

equilibrium as the % crosslinker is increased to 1.0 and 1.5 mol %. This is because a hydrogel with a higher crosslink density shows more resistance to matrix expansion and therefore absorbs less water more slowly. Consequently, water diffuses less readily inside the loose hydrogel structure since the interactions between the water molecules and the sulfonic/sulfonate groups are more restricted. This is supported by the observation that the lower crosslink density gives softer and more elastic hydrogel sheets. Finally, Figure 7 shows that, at the same 1.0 mol % level of incorporation, EGDM has less effect as a crosslinker than MBA. This could be the result of incomplete reaction of the EGDM and/or less uniformity in its

crosslink distribution throughout the hydrogel matrix. Overall, it was observed that these synthetic hydrogels can absorb relatively large amounts of water quickly within 10 mins. On immersion in water, the hydrogels expanded dramatically from approximately 2 x 2 x 0.08 cm to 6 x 6 x 0.25 cm, as shown in Figure 8. Hydrogels such as these are often referred to in the literature as “high water-absorbing polymers” (HWAPs). Their hydrophilic, water-solubilizable substituents have a high affinity for water but their hydrophobic main chains and crosslinks prevent them from dissolving. Hence, they swell rather than dissolve when immersed in water.

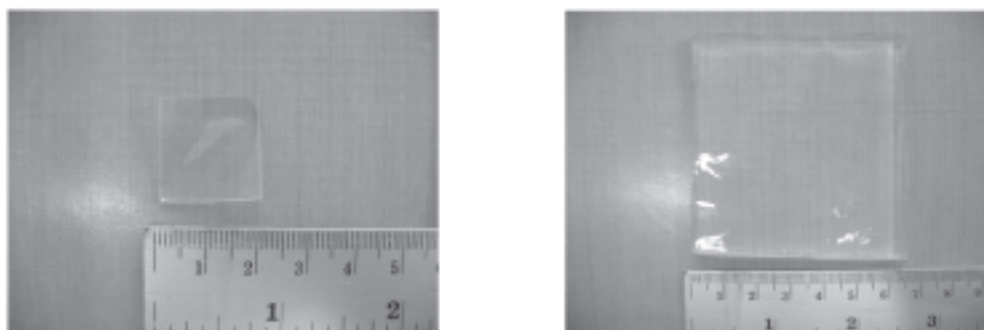


Figure 8. Hydrogel sheets synthesized from AMPS- Na^+ 60% w/v crosslinked with MBA 1.0 mol %; (a) hydrogel sheet after equilibration in air (2 x 2 x 0.08 cm) and (b) swollen hydrogel sheet after immersion in water to an equilibrium water content (6 x 6 x 0.25 cm).

4. CONCLUSIONS

The EWC of the hydrogel sheets could be controlled most effectively via the type and concentration of crosslinker employed. Monomer concentrations of between 40-60% w/v produced hydrogels with similar water absorption profiles over the same time intervals. However, the profiles changed significantly when higher percentages of crosslinker (0.5-1.5 mol %) were used. This was due to the fact that higher crosslink densities could be attained which produced more compact 3-dimensional hydrogel structures which, in turn, affected the free

volume for water uptake within the gel. Monomer type and concentration tended to have more effect on the mechanical strength and coherency of the hydrogel sheets. These findings illustrate the importance of finding the appropriate balance between monomer concentration and crosslink density in designing new hydrogels which can be employed as wound dressing materials. This balance is being extended to include other essential properties such as water vapour transmission and skin adhesion. The results of this ongoing work will be described in a future paper.

ACKNOWLEDGEMENTS

This work was supported by research grants from the Nano-science and Nano-Technology Research Centre, Chiang Mai University, and the National Metal and Materials Technology Center (MTEC). This support is gratefully acknowledged.

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