

# The Role of 2-Acrylamido-2-methylpropanesulfonic Acid in Conductive Medical Hydrogel Electrodes

*Hyungsoo Kim<sup>1</sup>, Geoffrey P. Marks<sup>2</sup>, and Carlos Piedrahita<sup>1</sup>*

*(1) The Lubrizol Corporation, 29400 Lakeland Blvd, Wickliffe, OH 44092, USA (2) Lubrizol Limited, Derby, DE56 4AN, United Kingdom*

## Abstract

Hydrogel, a lightly cross-linked polymer network, can swell substantially in water taking on hydrophilic and conductive character with potential for biomedical applications. This paper will explore the use of 2-acrylamido-2-methylpropanesulfonic acid in conductive medical hydrogels prepared via UV polymerization to make an electrocardiogram electrode. Different hydrogel formulation strategies, where parameters studied include crosslinker concentration, pH, water content, humectant, polymer composition and neutralizing salt, were systematically investigated to improve properties including gel uniformity, moisture retention, conductivity, and skin adhesion.

## Introduction

A polymer hydrogel is a lightly cross-linked and highly hydrated polymer network with hydrophilic and conductive characteristics.<sup>1</sup> The properties of the hydrogel are affected by various factors: the hydrophilicity and/or ionic character of polymer chains, the components in the swelling medium, pH, and temperature.<sup>2-5</sup> The polymer hydrogel usually consists of hydrogen-bonded structures that can adhere to human tissue and be used for biomedical applications: drug delivery<sup>6,7</sup>, wound dressing<sup>8</sup>, biomedical adhesive<sup>9</sup>, medical electrodes, etc. Examples where hydrogels are used as medical electrodes are electrocardiograph electrodes, defibrillation electrodes, transcutaneous nerve stimulation electrodes, electrosurgical grounding pads, and iontophoretic drug delivery electrodes. The properties required for an effective hydrogel electrode are uniform electrical conductivity, hydrolytic stability, creep resistance, adhesion to skin, skin moisture resistance, and biocompatibility.<sup>10-14</sup> In addition, the hydrogel electrode should have some cohesive strength and lubricity to provide clean, residue free removal from the skin after application.<sup>15</sup>

UV polymerization is the preferred method for hydrogel electrode preparation where low viscosity monomer solutions need to flow into the complex shape and configuration of the medical electrode mold before curing. An example of a hydrogel-based electrode is shown in Figure 1. The electrode is a rectangular laminate of a backing or support material and the conductive hydrogel substrate. An electrical lead is inserted between the laminated layers, and the current is distributed by means of a metal foil or mesh as an extension to the electrical lead. The electric field causes the migration of counter-ions in the hydrogel toward the cathode and the ionized groups in hydrogel can be partially shielded.<sup>16</sup> As a result, the hydration extent of the hydrogel can be reduced locally in the cathode, and

this is also a function of the degree of ionization of polymer chains. Hydrogels made from polyacrylic acid are weak polyelectrolytes, and their ionic properties vary with the pH of the swelling medium. In contrast, hydrogels made from 2-acrylamido-2-methylpropanesulfonic acid are anionic over a wide pH range because the 2-acrylamido-2-methylpropanesulfonic acid monomer is a very strong sulfonic acid and is much less sensitive to local variations in swelling medium pH. The extent of hydration is therefore very uniform throughout the hydrogel under an electrical field or in the presence of metal cations.<sup>17-19</sup> For this reason, the use of 2-acrylamido-2-methylpropanesulfonic acid and its salts as a principal component of hydrogels for medical use is well known.<sup>20,21</sup> This paper will explore conductive medical hydrogel electrodes prepared via UV polymerization.



**Figure 1.** Example of a conductive medical hydrogel

## Experimental

### Materials

AMPS<sup>®</sup>2404 (2-acrylamido-2-methylpropanesulfonic acid), AMPS<sup>®</sup>2405 (2-acrylamido-2-methylpropanesulfonic acid, sodium salt), and AMPS<sup>®</sup>2411 (2-acrylamido-2-methylpropanesulfonic acid, ammonium salt), were used as supplied by the The Lubrizol Corporation. The lithium and potassium salts of the AMPS<sup>®</sup> 2404 were prepared in water (50%wt) by reaction with LiOH and KOH, respectively. Acrylic acid used as a comonomer, N,N'-methylene-bis-acrylamide (MBAM) as the crosslinker, and glycerol as the humectant were used as received from EMD Chemicals. 2-Hydroxy-2-methyl-1-phenyl-propane-1-one, Darocur<sup>®</sup>1173, from Ciba Specialty Chemicals was used as the photoinitiator.

### Hydrogel Preparation and Characterization

An example of a conductive medical hydrogel formulation is given in Table 1. To produce the hydrogel, 20 parts of glycerol were added to 60 to 80 parts of AMPS<sup>®</sup>2405 (50 wt% in water) and 0.08 parts of the MBAM crosslinker. Acrylic acid may be added as a comonomer, so the total monomer content is approximately 30 to 40%wt. Water may be added to adjust the total monomer content. Sodium hydroxide (50%wt in water) can be used to adjust the pH of the formulation (typically between 4.5 to 6) if needed. The monomer solution was purged with N<sub>2</sub>, at 2 SCFH, for three minutes to remove dissolved oxygen and then 0.05 part of the Darocur<sup>®</sup>1173 photoinitiator was added and mixed. The resulting

solution was poured into a Petri dish, and polymerized using a Fusion UV 300S instrument by passing the Petri dish through the instrument twice using a belt speed of 20 ft/min. The thickness of the resulting hydrogel was 50 mil. The total UVA and UVB energy densities used in curing the hydrogel were  $\sim 1.0 \text{ J/cm}^2$ . The electrical resistance or resistivity of the hydrogel was measured by using a concentric ring probe (ASTM D257-99). The work of adhesion of the hydrogel on stainless steel was measured with a Texture Analyzer TA-XTRi using a 7 mm stainless probe with 5g load and probe speed at 1 mm/sec.

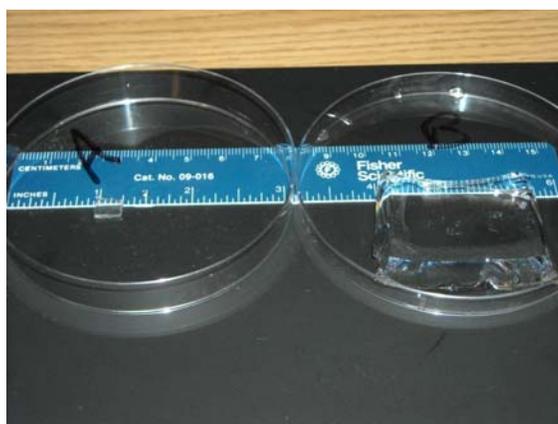
**Table 1.** The formulation of conductive medical hydrogel

Ingredient	Parts by weight
AMPS monomer, sodium salt (50 wt% in water)	60 to 80
Acrylic acid	0 to 30
Sodium Hydroxide (50 wt% in water)	variable to adjust pH around 4.5 to 6
Water	0 to 20
Glycerol	20
Crosslinker	0.08 (0.2 PHM, part per hundred monomer)
Photoinitiator	0.05 (0.125 PHM)

## Results and Discussions

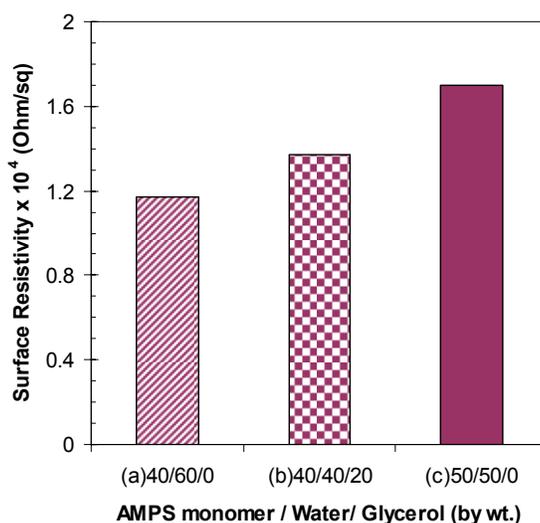
### Water and Humectant Effect

Water not only plasticizes the hydrogel, lowers its  $T_g$  and improves the adhesive properties, but water also provides electrical conductivity due to its high dielectric constant. When the water is uniformly distributed throughout a hydrogel, the adhesive and conductive properties of the hydrogel are maintained during the applications under the electrical field and/or in the presence of additives. A higher water content in a hydrogel is beneficial if the hydrogel can maintain its creep resistance and its adhesive properties at high water content. Water-swelling of hydrogel with AMPS monomer is demonstrated in Figure 2.



**Figure 2.** Water-swelling of hydrogel with AMPS monomer sodium salt: Water: Glycerol = 40: 40: 20 by wt. (a) Left: before water-swelling ( $\frac{1}{4} \times \frac{1}{4} \text{ in}^2$ ), and (b) Right: a swollen hydrogel after immersed in de-ionized water for 24 hrs ( $1\frac{3}{4} \times 1\frac{3}{4} \text{ in}^2$ )

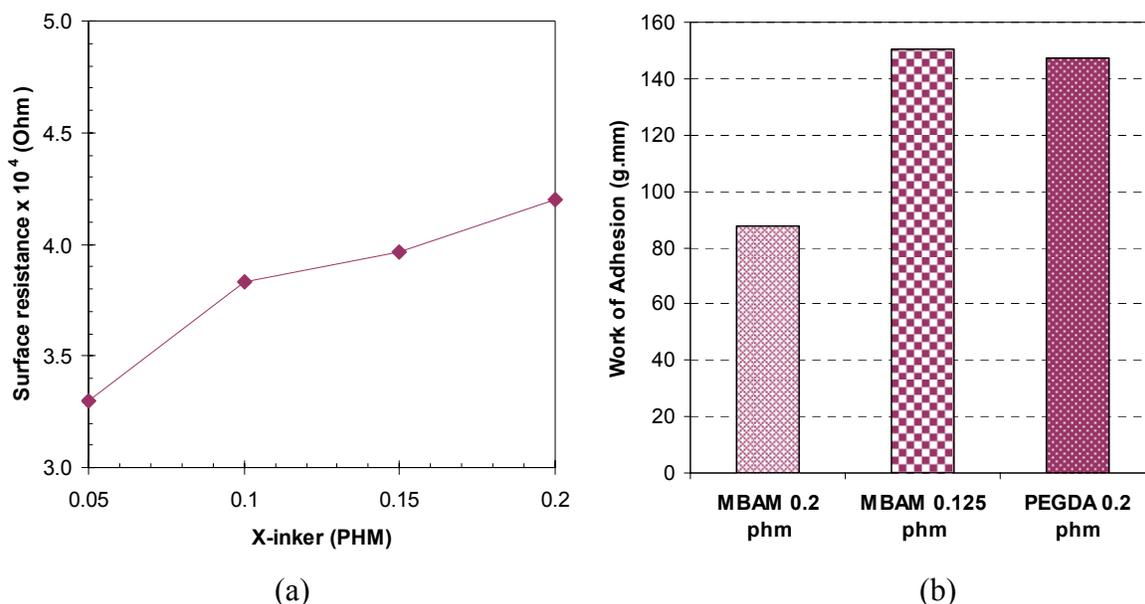
A polymer electrode needs to maintain its shape and adhesive/electrical properties during use. An increase in the applied voltage or its application time can lead to hydrogel de-swelling followed by a change in  $T_g$ . Too much water in the formulation can cause the hydrogel to be too soft, leading to creep in use, causing the gel to flatten-out, requiring rheology modifier or more crosslinker in the polymer hydrogel. Water miscible and polar humectants such as glycerol, propylene glycol, and poly(ethylene)glycol are used to keep water in the hydrogel. It should be noted that the use of humectant can help the hydrogel adhesion by lowering  $T_g$ , but can affect the hydrogel electrical properties due to its relatively low dielectric constant compared to water. Figure 3 shows that the hydrogel resistivity increases when water content decreases, by being replaced by either glycerol or monomer. The concentration ratio of monomer, water, and glycerol should be optimized to meet both the desired electrical and adhesive properties.



**Figure 3.** Effect of water / glycerol on the resistivity of the hydrogel with AMPS monomer sodium salt

### Cross-linker Effect

The complex configuration of the electrode requires monomer solutions with a low enough viscosity to flow into and completely fill the electrode-shaped mold. However, the cured polymer hydrogel needs to maintain its shape and adhesive/electrical properties in use under the electric field, at elevated temperatures and in the presence of water. To achieve the proper viscoelastic properties from a low viscosity monomer solution, chemical crosslinking and/or physical coiling/crosslinking is used. Chemical crosslinking is preferred in UV polymerization where low molecular weight polymers tend to be formed due to the quick viscosity increase followed by limited radical diffusion. Increasing crosslinking density can expel water from the hydrogel due to the dense network formed. High crosslink densities can also decrease ion mobility, increasing the hydrogel resistance (decreasing conductivity), as shown in Figure 4 (a). Highly crosslinked networks also have limited segmental molecular motion at the interface of the hydrogel and substrate. The longer the chain length in the crosslinked polymer gel, the lower  $T_g$  because of the easy segmental motion, resulting in improving the work of adhesion, as shown in Figure 4 (b). When the MBAM crosslinker was replaced by polyethyleneglycol diacrylate (PEGDA, MW=700) at equal weight basis, the adhesion improved because the net crosslinking density decreased due to the relatively high molecular weight of PEGDA (MW= 700) compared to MBAM (MW= 154.19).



**Figure 4.** (a) Effects of crosslinker on hydrogel resistance. The hydrogels were prepared from AMPS monomer sodium salt and water (50:50) and no glycerol was used. (b) Effect of crosslinker on adhesion. The hydrogel composition was AMPS monomer sodium salt/Water/glycerol = 40:40:20.

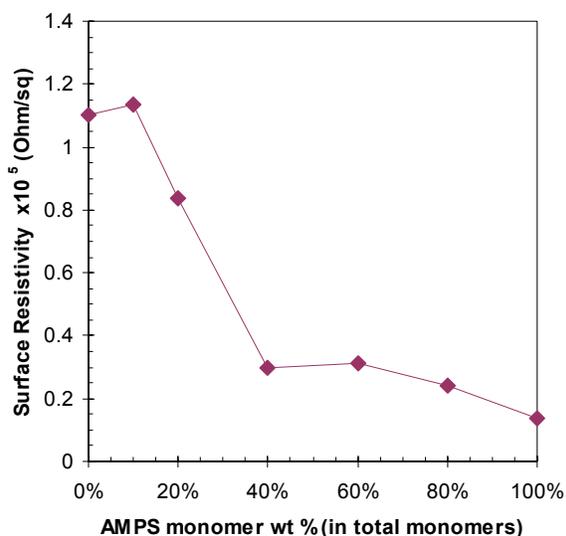
### Monomer Composition

The adhesive and electrical properties of the polymer hydrogel are not only affected by the identity of the swelling medium and crosslinker but they are also determined by the polymer composition, which controls the hydrophilicity at various conditions. The sulfonic acid in AMPS monomer is a very strong acid, and the resulting anionic charges repel each other. This charge repulsion affects the polymer's conformation providing more free volume where more liquid can be present. Because of this increased amount of liquid present within the polymer's conformation, the electrical current can flow more easily as the result of the diffusion of electrolytes soluble in liquid phase. Thus more AMPS monomer in the hydrogel leads to a lower resistivity (higher conductivity), as shown in Figure 5 (a). More free volume replaced by the liquid phase can also plasticize the hydrogel and lower  $T_g$  improving the hydrogel adhesive properties, thus more AMPS monomer in the hydrogel led to improved adhesion, as shown in Figure 5 (b). The complete dissociation of AMPS monomer in the hydrogel due to the strong acid nature of sulfonic acid led to greater water swelling as shown in Figure 5 (c), and this indicates that hydrogels containing AMPS monomer provides more flexibility in hydrogel formulation. The ionic character of AMPS monomer can maintain electrical properties of the hydrogel at a wide pH range. However, acrylic acid is protonated and non-ionic at low pH (< 3) so hydrogels consisting of only acrylic acid showed pH dependent electrical and adhesive properties, as shown in Figure 6.

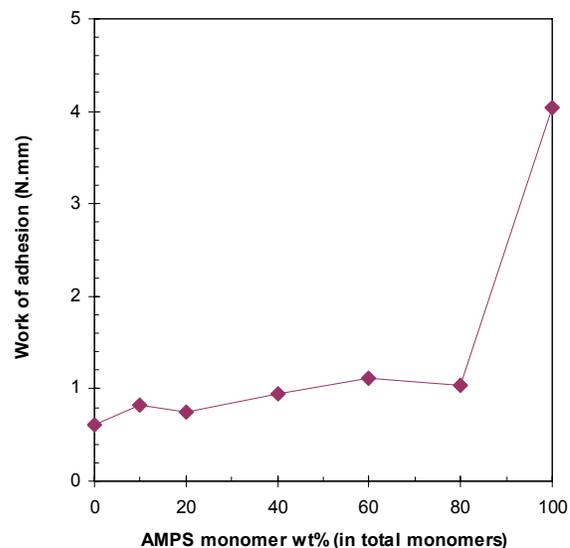
### Neutralizing Counter Ion

Metal ions like lithium are added to improve the electrical properties of polymeric electrolytes because the total flux of ions increases under the electrical field, but that is not always the case in hydrogel electrodes. Figure 7 shows the effect of the counter ions on the resistivity of hydrogel prepared with AMPS monomer. Except for the lithium ion, there was no significant variation of electrical property as

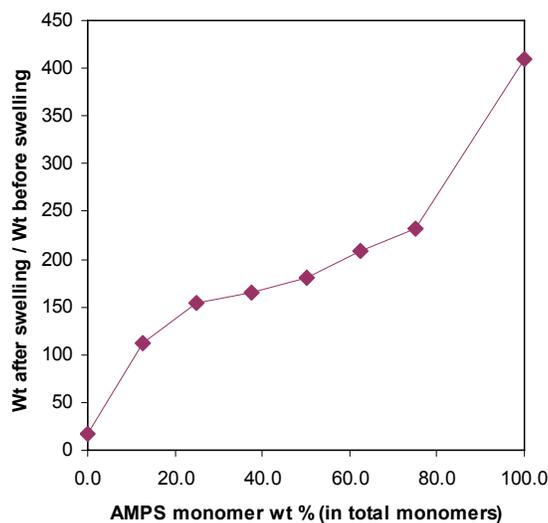
an effect of counter ion and the lithium salt of AMPS monomer showed the highest resistivity (lowest conductivity).



(a)

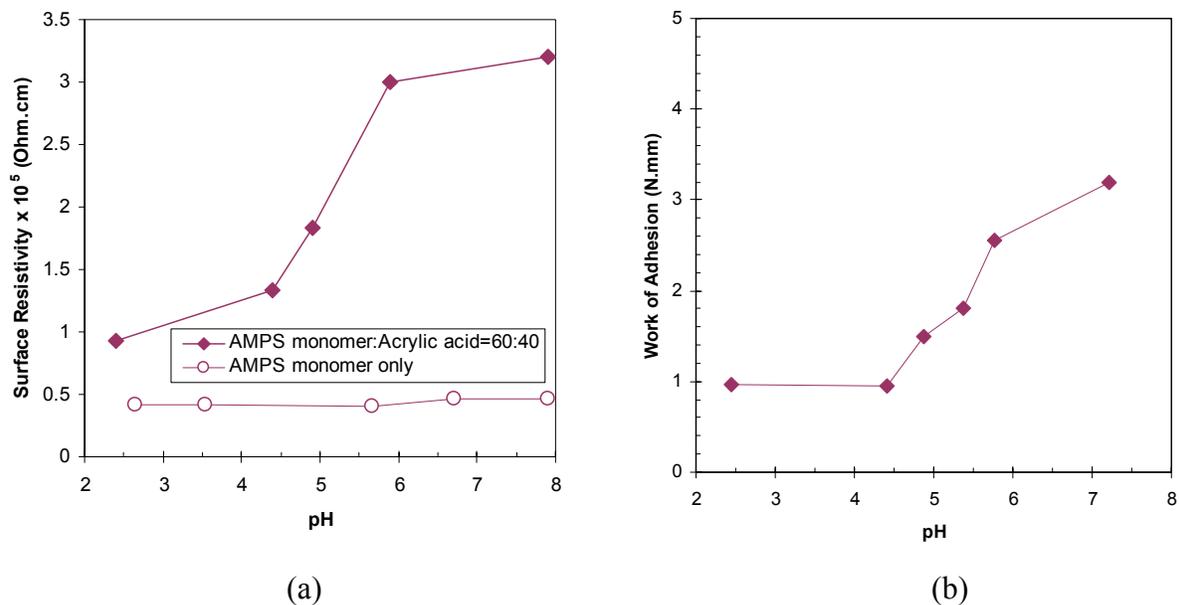


(b)

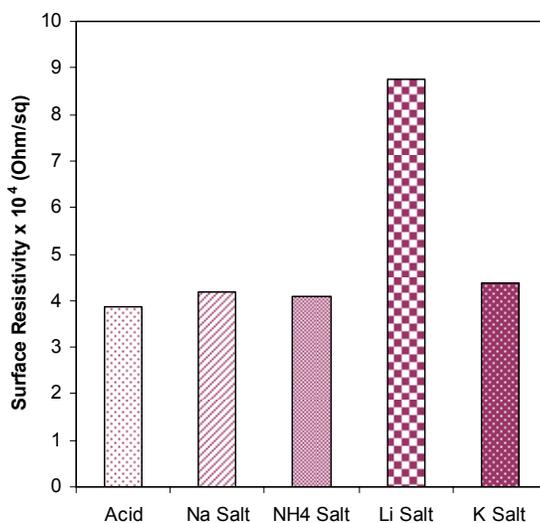


(C)

**Figure 5.** (a) Effect of AMPS monomer content on resistivity of hydrogels (b) Effect of AMPS monomer content on adhesion of hydrogels (c) Effect of AMPS monomer content on water swelling of hydrogels at pH = 4. The monomers used were AMPS monomer sodium salt and acrylic acid and the crosslinker (MBAM) amount was 0.3 mole % based on total monomers. The weight ratios of total monomers: water: glycerol were (a) 40: 40: 20, (b) 30: 30: 40, and (c) 40: 40: 20, respectively.



**Figure 6.** (a) Effect of pH content on resistivity (b) Effect of pH on work of adhesion. The crosslinker (MBAM) amount was 0.3 mole % based on total monomers in all cases. The weight ratio of total monomers: water: glycerol was 30: 30: 40.



**Figure 7.** Effect of counter ions on the resistivity of hydrogels with AMPS monomer and its salts. The weight ratio of AMPS monomers: water: glycerol was 40: 20: 20.

## CONCLUSIONS

Hydrogels made with AMPS monomers were prepared via UV polymerization and assessed for use in conductive medical electrode applications. It was shown that highly crosslinked hydrogel networks expelled the water from the hydrogel and decreased the electrical conductivity due to a loss of water within the conformational free volumes. Parameters that affect the  $T_g$  of the hydrogel such as water content and humectant content should be optimized to meet both the desired electrical conductivity and adhesive properties. The strong anionic charges of AMPS monomer, due to the sulfonic acid, led to a hydrogel with a soft and well-plasticized structure at a wide range of pH conditions. This is because the sulfonate anionic charges repel each other providing more free volume within the polymer's conformation where the liquids e.g., water and humectant can be present. As a result of the liquids in the free volume, the electrical conductivity and the adhesive properties of the hydrogel are improved by using AMPS monomers in medical hydrogel electrode applications.

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