APPENDICES

32nd Congress on Science and Technology of Thailand (STT.32)

"Science and Technology for Sufficiency Economy"

"Design and Preparation of Synthetic Hydrogels Based on 2-Acrylamido-2-Methylpropane Sulfonic Acid (AMPS) and its Sodium Salt (Na-AMPS) for Biomedical Use as Wound Dressings"

10-12 October 2006

at

Queen Sirikit National Convention Center
Bangkok
Thailand

Poster Presentation

Organized by

The Science Society of Thailand under the Patronage of His Majesty the King

In Conjunction

Chulalongkorn University

การออกแบบและการเตรียมไฮโดรเจลสังเคราะห์จาก 2-acrylamido-2-methylpropanesulfonic acid (AMPS) และเกลือ (Na-AMPS) สำหรับการประยุกต์ใช้งานทางด้านการแพทย์เพื่อใช้เป็นวัสดุปิดแผล

DESIGN AND PREPARATION OF SYNTHETIC HYDROGELS BASED ON 2-ACRYLAMIDO-2-METHYLPROPANESULFONIC ACID (AMPS) AND ITS SODIUM SALT (Na-AMPS) FOR BIOMEDICAL USE AS WOUND DRESSINGS

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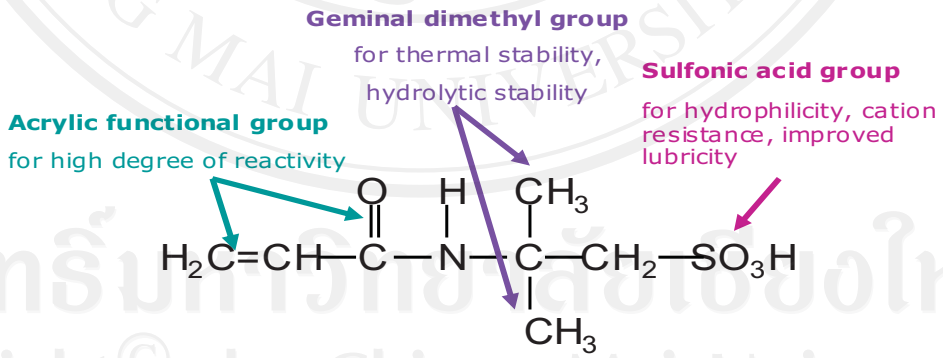
บทคัดย่อ: งานวิจัยนี้เป็นการออกแบบและการเตรียมไฮโดรเจลสังเคราะห์สำหรับการประยุกต์ใช้ด้านงานทางชีวการแพทย์เพื่อใช้เป็นวัสดุปิดแผล ซึ่งได้ทำการสังเคราะห์โพลิเมอร์แบบร่างแหจาก 2-acrylamido-2-methylpropanesulfonic acid (AMPS) และเกลือโซเดียม (Na-AMPS) โดยอาศัยขบวนการโพลิเมอร์ไรเซชั่นแบบฟรีแรดิคอลในน้ำซึ่งมีตัวริเริ่มแบบรีดอกซ์ ใช้เอทิลีนไกลคอลไดมีทาไคเลต(EGDM) เป็นสารเชื่อมไขว้ ในการทดลองได้ทำการศึกษาที่ความเข้มข้นของสารละลายมอนอเมอร์ AMPS และ Na-AMPS 30-50% โดยน้ำหนัก และที่ % EGDM ต่างๆ จากผลศึกษาพบว่าที่ความเข้มข้นของ AMPS และ Na-AMPS สูง จะได้แผ่นไฮโดรเจลที่มีรูปทรงที่ดี ในขณะที่ 30% จะได้แผ่นไฮโดรเจลที่มีความเหนียวและไม่คงรูป จากนั้นทำการศึกษาความสามารถในการดูดซับน้ำที่อุณหภูมิห้อง พบว่าในช่วงแรกแผ่นไฮโดรเจลจะสามารถดูดซับน้ำได้อย่างรวดเร็วและถึงสมดุลภายในเวลาเพียง 10 นาที ความเข้มข้นของ EGDM ไม่มีผลต่อความสามารถในการดูดซับน้ำอย่างมีนัยสำคัญ แต่มีผลต่อสมบัติเชิงกลของแผ่นไฮโดรเจลคือเมื่อเพิ่มปริมาณ EGDM จะทำให้แผ่นไฮโดรเจลที่ได้ฉีกขาดง่ายขึ้นและยืดหยุ่นได้น้อยลง

Abstract: This research is concerned with the design and preparation of synthetic hydrogels for biomedical use as wound dressings. Crosslinked polymers of 2-acrylamido-2-methylpropanesulfonic acid (AMPS) and its sodium salt (Na-AMPS) were prepared via free radical polymerization in aqueous solution using redox initiation. Ethylene glycol dimethacrylate (EGDM) was used as the crosslinker. Different crosslinker percentages of 1-3% mol/mol monomer and various AMPS and Na-AMPS monomer concentrations of between 30-50% w/v were employed to prepare crosslinked hydrogels with different crosslink densities. The results showed that the hydrogel sheets formed from the higher AMPS and Na-AMPS concentrations of 40 and 50% w/v were uniform and coherent whereas those from the 30% w/v concentration were weak and sticky. The water absorption properties of the hydrogel sheets were studied at room temperature. It was found that their initial rates of water absorption were very fast and reached their equilibrium water content (EWC) within 10 mins. The % crosslinker had little effect on the EWC of the hydrogel sheets at the same monomer content, for both AMPS and Na-AMPS, but did have a significant effect on the mechanical properties. The hydrated hydrogel sheets became weaker (i.e., lower tear strength) as the % crosslinker was increased.

Introduction: The development of synthetic wound dressings used for the treatment of burns is currently a subject of great commercial interest. Although work on synthetic wound dressings has been in progress now for many years, the last two decades especially have seen significant movements in the field. Before examining the range of hydrogels in this area, it is appropriate to note the properties that a successful wound dressing material should possess. Stated simply, the material should be flexible, strong, non-antigenic and permeable to water vapour and metabolites, whilst securely covering the wound to prevent bacterial infection. Hydrogels possess many of these properties and because of this they have been used extensively as wound dressing materials, sometimes alone but frequently in the form of composites principally to enhance their mechanical strength [1]. The use of 2-acrylamido-2-methylpropanesulfonic acid, AMPS, or its sodium salt, Na-AMPS, as a principal component of hydrogels for medical use is now well established. Their hydrogels are typically stable, 3-dimensional crosslinked polymer networks formed by free radical polymerisation in solution in water. They can be crosslinked by means of ultraviolet irradiation, thermal or redox initiation with a multifunctional crosslinking agent.

Methodology: AMPS was dissolved in water in various concentrations ranging from 30-50% w/v. In the case of Na-AMPS, an AMPS solution was cooled in an ice-bath and neutralized with sodium hydroxide solution [2]. Before polymerization, 1-3 % mol of EGDM per mol of monomer was added and the mixture stirred to give a homogeneous solution. Then 0.5% w/v of each of potassium persulfate as initiator, potassium metabisulfate as co-initiator and ferrous sulfate as redox catalyst were added. The solution was then quickly poured into a vertical glass mould with Teflon release liners. The polymerization reaction was allowed to proceed at room temperature for 24 hrs before post-curing at 60°C for 4 hrs. Finally, the hydrated hydrogel sheet, of approximately 1 mm thickness, was removed from the mould and its water absorption properties studied at room temperature [3-5].



2-acrylamido-2-methylpropanesulfonic acid (AMPS)

Results, Discussion, and Conclusions: The hydrogel sheets from the 40% and 50% w/v of AMPS and Na-AMPS contents gave good coherent thin sheets. In contrast, the hydrogel sheets from the 30% w/v concentration were weak and sticky. The water absorption of the hydrogel sheets were studied in deionized water at room temperature. It was found that the initial rates of water absorption were very fast and reached the equilibrium water content (EWC) within 10 mins. The % crosslinker had little effect on the EWC of the hydrogel at the same monomer content but did have a significant effect on the mechanical properties. As the % crosslinker increased, the tear strength of the hydrogel decreased.

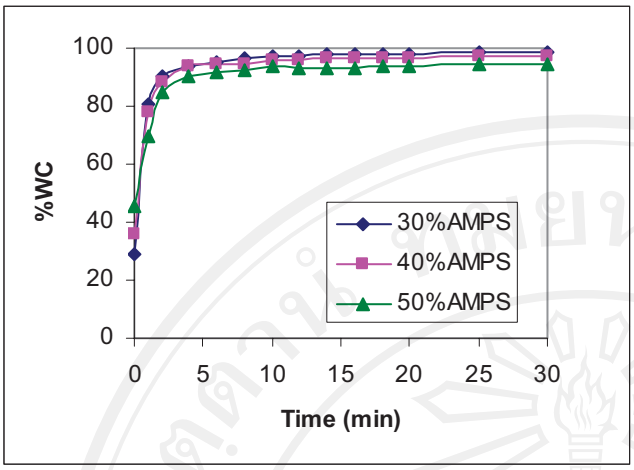


Fig. 1 : Increase in water content (WC) with time for hydrogel sheets prepared from 30-50% w/v AMPS with 1% mol of EGDM crosslinker.

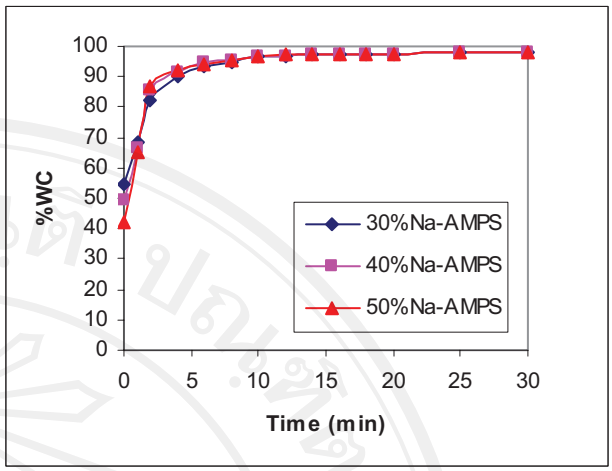


Fig. 2 : Increase in water content (WC) with time for hydrogel sheets prepared from 30-50% w/v Na-AMPS with 1% mol of EGDM crosslinker.

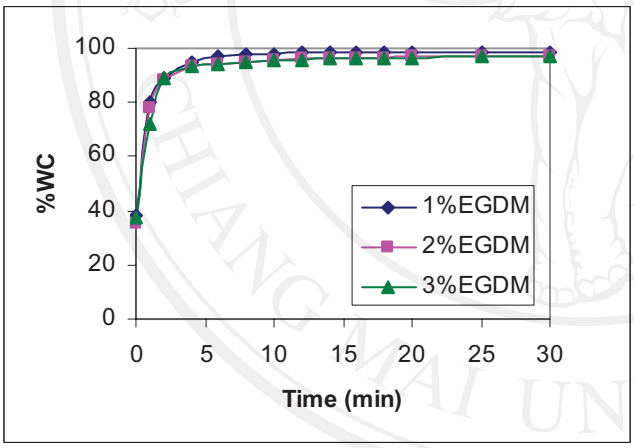


Fig. 3 : Increase in water content (WC) with time for hydrogel sheets prepared from 40% w/v AMPS with 1-3% mol of EGDM crosslinker.

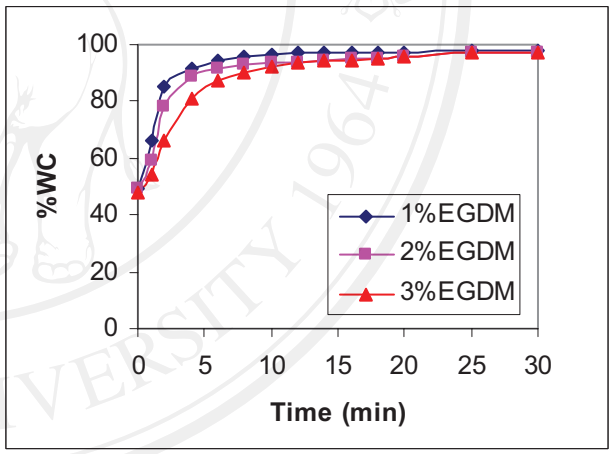


Fig. 4 : Increase in water content (WC) with time for hydrogel sheets prepared from 40% w/v Na-AMPS with 1-3% mol of EGDM crosslinker.

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Keywords: 2-acrylamido-2-methylpropanesulfonic acid (AMPS), sodium 2-acrylamido-2-methylpropanesulfonate (Na-AMPS), hydrogels, wound dressings

Chiang Mai University
Annual Research Conference

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This research is concerned with the design and preparation of synthetic hydrogels for biomedical use as wound dressings. Crosslinked polymers of 2-acrylamido-2-methylpropane sulfonic acid (AMPS) and its sodium salt (Na-AMPS) were prepared via free radical polymerization in aqueous solution using redox initiation. Ethylene glycol dimethacrylate (EGDM) was used as the crosslinker. Different crosslinker percentages of 1-3% mol/mol monomer and various AMPS and Na-AMPS monomer concentrations of between 30-50% w/v were employed to prepare crosslinked hydrogels with different crosslink densities. The results showed that the hydrogel sheets formed from the higher AMPS and Na-AMPS concentrations of 40 and 50% w/v were uniform and coherent whereas those from the 30% w/v concentration were weak and sticky. The water absorption properties of the hydrogel sheets were studied at room temperature. It was found that their initial rates of water absorption were very fast and reached their equilibrium water content (EWC) within 10 mins. The % crosslinker had little effect on the EWC of the hydrogel sheets at the same monomer content, for both AMPS and Na-AMPS, but did have a significant effect on the mechanical properties. The hydrated hydrogel sheets became weaker (i.e., lower tear strength) as the % crosslinker was increased.

Keywords: 2-acrylamido-2-methylpropanesulfonic acid (AMPS), sodium 2-acrylamido-2-methylpropanesulfonate (Na-AMPS), hydrogels, wound dressings

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2nd International Conference on Smart/Intelligent Materials (SmartMat'-08)

Design and Preparation of a Bioresponsive Hydrogel for Biomedical Application as a Wound Dressing

22-25 April 2008

at
Imperial Mae Ping Hotel

Chiang Mai

Thailand

Oral Presentation (International)

Organized by

Design and Preparation of a Bioresponsive Hydrogel for Biomedical Application as a Wound Dressing

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Keywords: photopolymerisation, hydrogel wound dressing, sodium AMPS

Abstract. In this work, the sodium salt of 2-acrylamido-2-methylpropanesulfonic acid (Na-AMPS) was photopolymerised in aqueous solution with ethylene glycol dimethacrylate (EGDM) added as a crosslinking agent and 4,4'-azo-bis(4-cyanopentanoic acid) as the water-soluble photoinitiator. The aqueous solution was poured into a vertical sheet-forming mould consisting of two parallel plates covered with Teflon® sheets as release liners. Spacers were used to control the sheet thickness with a polymer mesh inserted in the middle to strengthen the hydrogel. The hydrogel sheets obtained were of 1.2 ± 0.2 mm thickness and showed good transparency, flexibility and skin adhesion. On immersion in distilled water at 37°C, it was found that the equilibrium water content (EWC) reached 98 ± 1% within 20 mins following which the equilibrium water retention (EWR) in ambient air was 21 ± 1% over a period of about 4 hrs. The water vapour transmission rate (WVTR) was measured at 37 ºC and was found to be 82 ± 2 g m^{-2} hr^{-1}. It is concluded that this Na-AMPS hydrogel sheet has properties which show potential for biomedical use as a wound dressing.

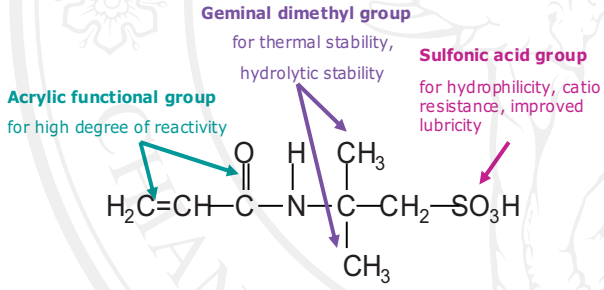
Introduction

In recent years, polymers have found increasing use in the field of wound healing. Hydrogels have attracted much research interest because of their unique properties which can meet the essential requirements of an ideal wound dressing including: immediate pain control, easy replacement, transparency to allow healing follow up, absorption and control loss of body fluids, barrier against bacteria, oxygen permeability, good handling, control of drug dosage, and promotion of cell proliferation [1,2]. Prior to the 1960s, wound dressings were considered to be only passive products that had a minimal role in the healing process. The landmark study by Winter [3] in 1962 initiated the concept of an optimal environment for wound repair and the active involvement of a wound dressing in establishing and maintaining such an environment. This awareness revolutionized the approach to wound care and paved the way for the development of wound dressings from being passive materials to more functionally active ones [4].In the case of synthetic hydrogels, photoinitiation by UV light is recognized as a very useful synthetic tool. Photoinitiation has various advantages over thermal or redox initiation such as being easier to control, more easily convertible into a continuous process, and offering the possibility of combining both polymerisation and sterilization into one technological step [5]. Wound dressings manufactured by the simultaneous radiation-induced crosslinking and sterilization of hydrophilic polymers were invented by Rosiak et al [6]. This

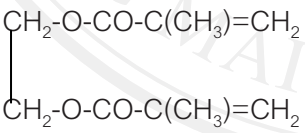
manufacturing process technology has been successfully and widely used in Europe, America and many countries but is still not practised in Thailand which continues to import biomedical hydrogel products at great expense. This present research work is therefore aimed at developing a capability to manufacture these products in Thailand with the initial emphasis on wound dressings.

Experimental: Hydrogel Synthesis

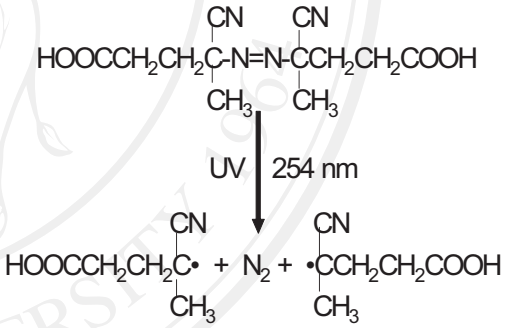
The water-soluble monomer used in this work was the sodium salt (Na-AMPS) of 2-acrylamido-2-methylpropanesulfonic acid (AMPS) [7]. An aqueous solution of Na-AMPS was prepared by dissolving AMPS acid (see structure below) in distilled water (40% w/v), cooling in an ice-bath, and then neutralizing to pH 7 with sodium hydroxide solution with stirring. 1.0 mol % of ethylene glycol dimethacrylate (EGDM) per mol of Na-AMPS was added as a crosslinking agent together with 0.1% w/v of 4,4'-azo-bis(4-cyanopentanoic acid) as photoinitiator [8]. The aqueous solution was poured into a vertical sheet-forming mould consisting of two parallel plates covered with Teflon® sheets as release liners. Spacers were used to control the sheet thickness with a polymer mesh inserted in the middle to strengthen the hydrated hydrogel. Photopolymerisation was carried out at room temperature using a commercially available UV lamp (254 nm).



2-acrylamido-2-methylpropanesulfonic acid (AMPS)



ethylene glycol dimethacrylate (EGDM)



4,4-azo-bis(4-cyanopentanoic acid)

After removal from the mould, one side of the hydrogel sheet was covered with a polyurethane film as a backing sheet and the other side covered with a polyethylene film as a release liner, as shown in Fig. 1 below.

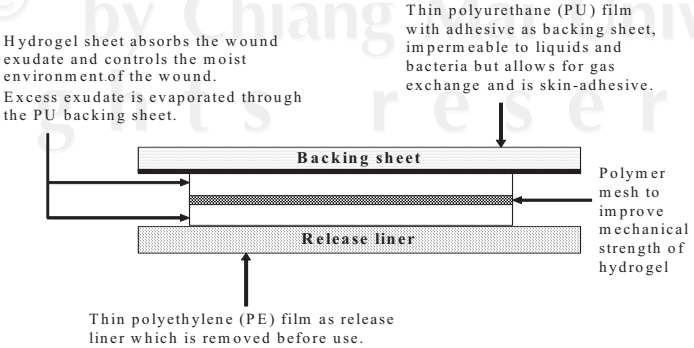
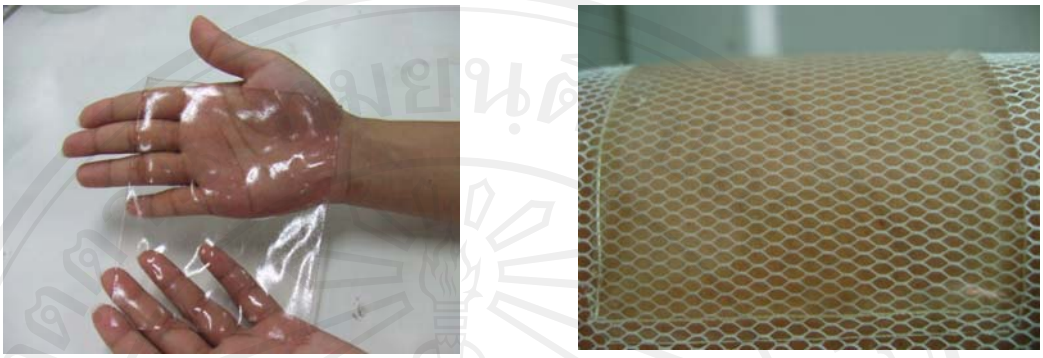


Figure 1. Prototype hydrogel wound dressing showing its multilayer construction.

Results and Discussion: Physical properties

The Na-AMPS hydrogel sheets as obtained from synthesis were 1.2 ± 0.2 mm in thickness and showed good transparency, elasticity, tear strength and skin adhesion. Photographs of the sheet both with and without the reinforcing polymer mesh are shown in Fig. 2 below.



(a) without the reinforcing polymer mesh (b) with the reinforcing polymer mesh

Figure 2. Photographs showing the Na-AMPS hydrogel sheet

Water absorption and retention: After equilibration in air, the unreinforced hydrogel sheet, still partially hydrated, was immersed in distilled water at 37 ºC and its increase in weight with time followed to constant weight at equilibrium. The water content (WC) was calculated using the following expression:

$$WC\ (wt\ \%) = [(W_w - W_d)/W_w] \times 100 \qquad (1)$$

where W_d and W_w are the dry and wet weights of the hydrogel respectively. The WC-time profile is shown in Fig. 3. When the equilibrium water content (EWC) had been reached, the hydrogel was removed from the water and re-equilibrated in air at room temperature, again to constant weight. The water retention (WR) of the hydrogel was plotted as a function of time, as shown in Fig. 4.

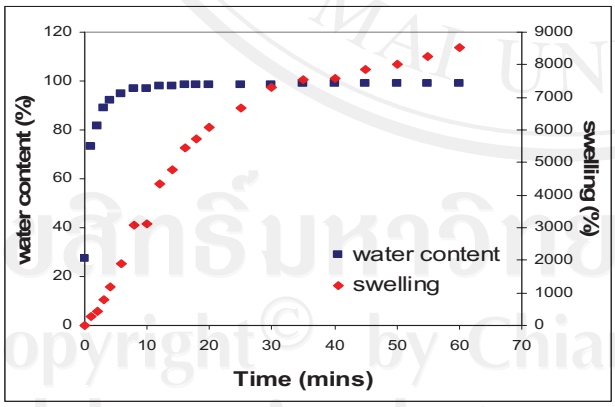


Figure 3. Water absorption - time profile for the hydrogel sheet when immersed in distilled water at 37°C.

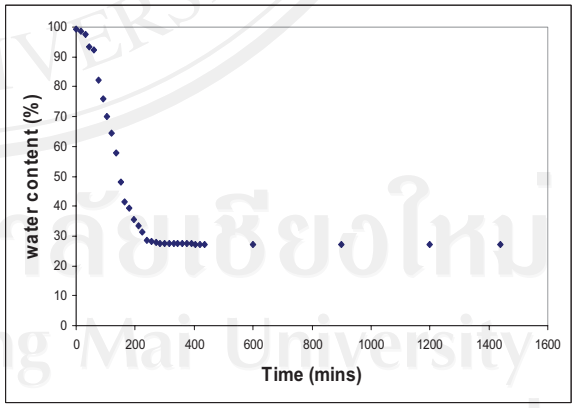


Figure 4. Water retention - time profile for the hydrogel sheet when left in air at room temperature (continuous from Fig. 3)

As the WC-time profile in Fig. 3 shows, an equilibrium water content (EWC) of 98 ± 1% was obtained within 30 mins. Following on from this, when this same sample was removed from the water and left in air to re-equilibrate, as shown in the WR-time plot in Fig. 4, an equilibrium water retention (EWR) of 21 ± 1% was obtained over a period of about 4 hrs.

Water vapour transmission: The water vapour transmission rate (WVTR) of the hydrated sheet (after equilibration in air) was measured using the ASTM E96-90 (1990) Water Cup Method [9]. The WVT-time profile is shown in Fig. 5. From the linear plot, a WVTR value of 82±2 g m^{-2} hr^{-1} was obtained which, for medical purposes, is deemed to be a suitable rate for the controlled evaporative water loss from a second-degree burn.

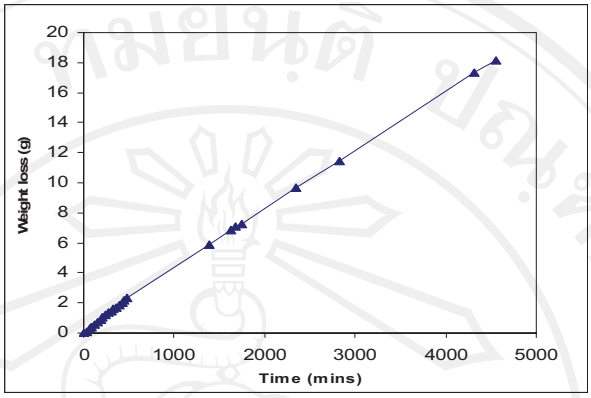


Figure 5. Water vapour transmission - time profile for the Na-AMPS hydrogel sheet at 37°C and 55-60% relative humidity.

Summary

On the basis of these experimental results, it is considered that this photopolymerised Na-AMPS-based hydrogel shows considerable potential for biomedical use as wound dressing. The hydrogel sheet exhibits fast water absorption to a high equilibrium water content with an appropriate balance of water vapour transmission. The mechanical properties can be improved by using a polymer mesh as a reinforcing framework. The multilayer construction shown previously in Fig. 1 provides the basis for a prototype wound dressing for possible commercialization provided that the hydrogel is shown to be non-toxic to cells. This biological evaluation is part of the further work which is currently in progress.

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42nd World Polymer Congress
(Macro 2008)

"Synthetic Hydrogels Prepared via Photopolymerisation for Biomedical Use as Wound Dressings"

29 June – 4 July 2008

at
Taipei International Convention Center

Taipei

Taiwan

Oral Presentation (International)

Synthetic Hydrogels Prepared via Photopolymerisation for Biomedical Use as Wound Dressings

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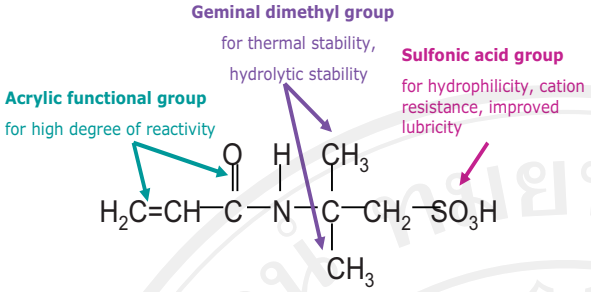
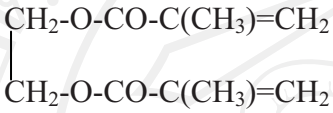
Introduction. In recent years, hydrogels have attracted much research interest as biomaterials in applications such as contact lenses and wound dressings. Because of their unique properties, hydrogels meet the essential requirements of ideal wound dressings including: immediate pain control, easy replacement, transparency to allow healing follow up, absorb and prevent loss of body fluids, barrier against bacteria, oxygen permeability, good handling, control of drug dosages and so on [1]. In the case of synthetic hydrogels, photoinitiation by UV light is recognized as a very useful synthetic tool. Photoinitiation has various advantages over thermal or redox initiation such as being easier to control, more easily convertible into a continuous process, and offering the possibility of combining both polymerisation and sterilization into one technological step [2-7].

Wound dressings manufactured by simultaneous radiation-induced crosslinking and sterilization of hydrophilic polymers were invented by Rosiak et al [2]. The wound dressing manufacturing process technology was successfully and widely used in Europe, America and many other countries. This type of process technology is still not practised in Thailand which continues to import biomedical hydrogel products at great expense. This present research work is therefore aimed at developing a capability to manufacture these products in Thailand with the initial emphasis on wound dressings. While the good biocompatibility and water transport properties of hydrogel sheets are essential to the application, it is also important to understand how the chemical structure of the hydrogel can improve the handling ability and general mechanical properties. Ideally, a wound dressing should be able to (a) create and maintain a moist environment, (b) protect the wound from secondary infection (c) absorb wound fluids and exudates, (d) reduce wound surface necrosis, (e) prevent wound desiccation, (f) stimulate growth factors, and also be (g) elastic, (h) non-antigenic and (i) biocompatible [8].

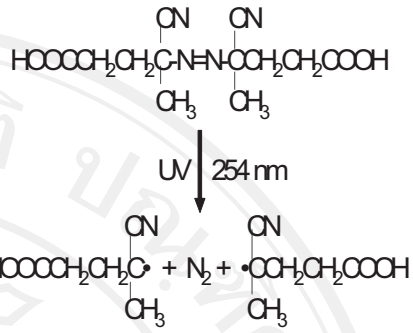
The use of 2-acrylamido-2-methylpropane sulfonic acid(AMPS) and its salts as principal monomers for hydrogels in medical use is now well established [9]. The acrylic unit in the AMPS monomer minimizes chain transfer reactions and permits high molecular weight generation compared with other sulphonic acid monomers. The AMPS monomer is known for its hydrolytic stability and a high tolerance towards divalent cations, thereby maintaining its capacity for propagation. Especially, it is a water soluble monomer and easy to convert to its sodium salt in aqueous solution [10-13].



2-acrylamido-2-methylpropanesulfonic acid (AMPS)



ethylene glycol dimethacrylate (EGDM)



4,4-azo-bis(4-cyanopentanoic acid) [14]

Methods: Hydrogel Synthesis

The water-soluble monomer used in this work was the sodium salt (Na-AMPS) of 2-acrylamido-2-methylpropanesulfonic acid (AMPS). An aqueous solution of Na-AMPS was prepared by dissolving AMPS in distilled water (40% w/v), cooling in an ice-bath, and then neutralizing to pH 7 with sodium hydroxide solution with stirring. Various concentrations of 0.1, 0.5 and 1.0 mol % of ethylene glycol dimethacrylate (EGDM) per mol of Na-AMPS were added as a crosslinking agent and the mixtures stirred to give homogeneous solutions. 0.1% w/v of 4,4'-azo-bis(4-cyanopentanoic acid) was then added as photoinitiator and each solution poured into a vertical glass mould with Teflon release liners. Photopolymerization was carried out at room temperature for 10 mins using a commercially available UV lamp. Finally, the hydrated hydrogel sheet was removed from the mould and its water transport properties studied.

Analysis of Hydrogel Properties

Water Transport Properties

After equilibration in air, the hydrogel was immersed in distilled water at room temperature (37 ºC). and its increase in weight with time was followed. The water content (WC) can be calculated using the following expression:

$$WC\ (wt\ \%) = [(W_w - W_d)/W_w] \times 100$$

where W_d and W_w are the dry and wet weights of the hydrogel respectively.

When the equilibrium water content (EWC) had been reached, the hydrogel was removed from the distilled water and re-equilibrated in air at room temperature to constant weight. The water retention (WR) of the hydrogel was plotted as a function of time.

The water vapour transmission rate (WVTR) was measured using the ASTM E96-93 (1990) Water Cup Method.

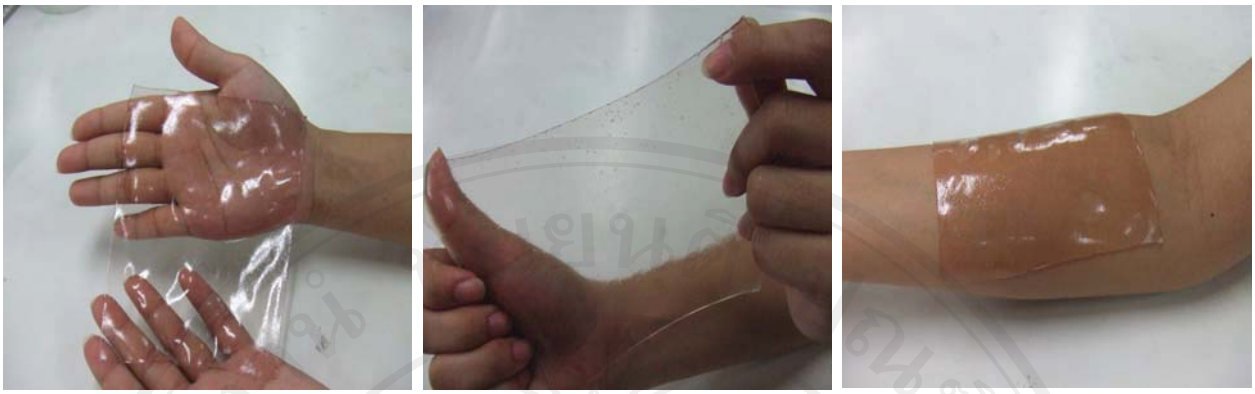


Figure 1 : Hydrogel sheets from 40% w/v Na-AMPS with 1% mol EGDM

The hydrated hydrogel sheets obtained direct from synthesis were of 1.20 ± 0.20 mm thickness. It was found that the hydrogel obtained using 1.0% mol of EGDM (Figure 1) showed slightly better coherency, transparency, flexibility and skin adhesion compared with 0.1 and 0.5% mol EGDM.

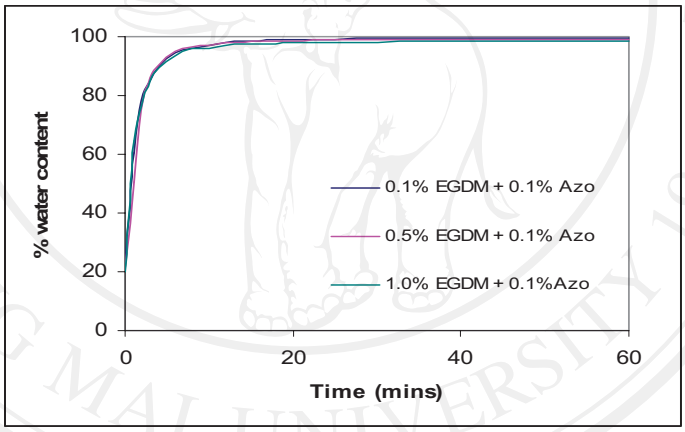


Figure 2: Water content - time profiles in water for hydrogel sheets prepared from 40% w/v Na-AMPS with various % mol of EGDM crosslinker.

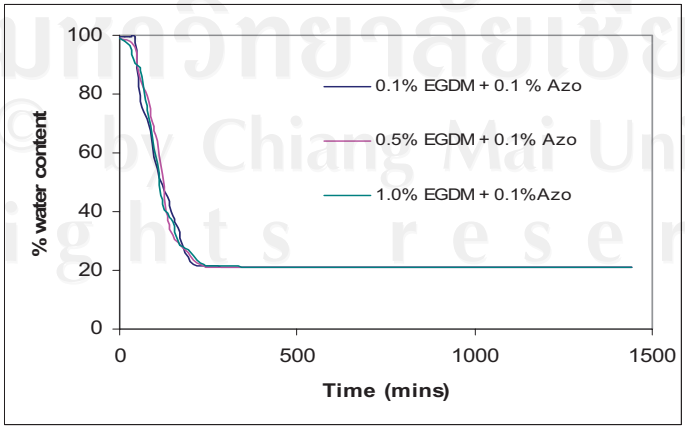


Figure 3 : Water content - time profiles in air (after EWC in water) for hydrogel sheets prepared from 40% w/v Na-AMPS with various % mol of EGDM crosslinker.

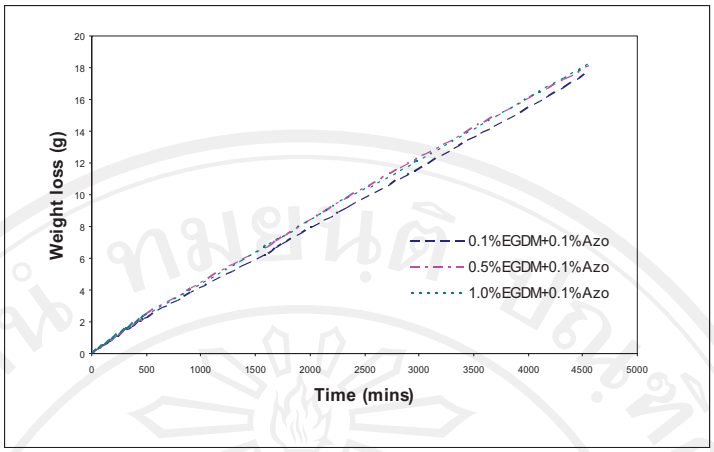


Figure 4 : Water vapour transmission - time profiles for hydrogel sheets prepared from 40% w/v Na-AMPS with various % mol of EGDM crosslinker.

After initial equilibration in air, the still partially hydrated sheets absorbed water very quickly when immersed in distilled water, reaching an EWC of 98 ± 1% within 20 mins (Figure 2). This is a reflection of the strong osmotic effect of the sodium sulfonate ($Na^+SO_3^-$) groups in the polymer structure. The effect of the EGDM crosslinker concentration is relatively small over the 0.1-1.0 mol % range studied. When removed from the water and exposed to air at room temperature, the sheets partially dehydrated to an equilibrium water retention (EWR) of 21 ± 1% over a period of about 4 hrs (Figure 3). Finally, Figure 4 shows linear water vapour transmission rate (WVTR) plots with time which further defines the hydrogels water transport capability. Their WVTR were measured at 37 ºC and were found to be in the range of 82 ± 2 g m^{-2} hr^{-1}.

Oxygen Permeability

The oxygen permeability (Dk) was obtained using a 210T Permiometer and the equation

$$Dk = L(i - i_0)\ V / n\ F\ A\ Ps$$

where

L = thickness (mm)
i_0 = current obtained for N_2-zero in all cases
i = current obtained for O_2-passing through the hydrogel
F = Faraday constant = 96490 x 10^6 µA.s.mol^{-1}
A = area of gold electrode = 0.1278 cm^2
Ps = oxygen tension = 760 mmHg S.T.P.
N = number of electron involved = 4
V = standard gas molar volume = 22.4x10^3 ml

If the constant terms are combined, the equation becomes

$$Dk = i\ (\mu A) \times L\ (mm) \times (6 \times 10^{-11})$$

It was found that the Dk of the Na-AMPS hydrogel sheets were about 300 x 10^{-11} cc.mm./cm^2.s.mmHg, significantly higher than other hydrogel polymers such as polyHEMA for which the Dk is 145 x 10^{-11} cc.mm./cm^2.s.mmHg [15].

Conclusions : From the analysis of the Na-AMPS hydrogels, it was found that the Na-AMPS hydrogel sheets have good properties for use as wound dressings such as high equilibrium water content and good oxygen permeability. On the basis of these experimental results, it was shown that UV irradiation is a powerful tool for producing hydrogels with potential for biomedical use as wound dressings. Further work is looking at how the mechanical properties can be improved by using a reinforcing polymer mesh inside the hydrogel. This would improve the tear strength which is a common weakness in hydrogel sheets.

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"Sodium AMPS Hydrogels for Use as Wound Dressings"

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Sodium AMPS Hydrogels for Use as Wound Dressings

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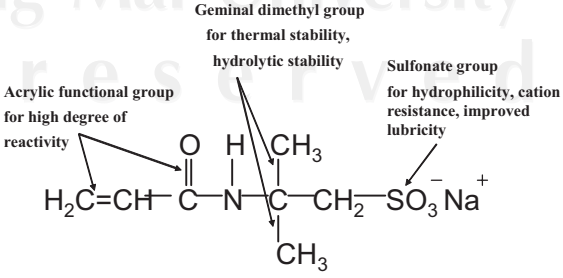
Abstract – The concept of using a synthetic hydrogel as a moist wound dressing for second degree burns has been studied in this work**.** The sodium salt of 2-acrylamido-2-methylpropanesulfonic acid (Na-AMPS) was photopolymerised in aqueous solution using an azo compound and Irgacure 184 as photoinitiators. Various properties of the hydrogels such as water absorption, water vapour transmission, residual monomer, oxygen permeability and peel strength were determined. It was found that Irgacure 184 gave less residual monomer. However, both the azo compound and Irgacure 184 gave hydrogel sheets with good water absorption, appropriate water vapour transmission, high oxygen permeability and good skin adhesion for use as a wound dressing.

Keywords : Sodium AMPS, photopolymerisation**,** hydrogel, wound dressing, biomedical applications

1. Introduction

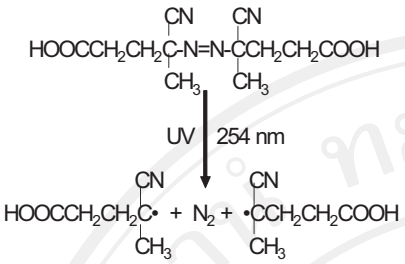
Since the pioneering work of Wichterle and Lim on crosslinked poly(2-hydroxyethyl methacrylate) (polyHEMA) hydrogels [1], and because of their hydrophilicity and biocompatibility, hydrogels have been of great interest to biomaterial scientists. For example, both natural and synthetic hydrogels have been of interest for use as wound dressings for second degree burns. During the past 20 years, the field of photopolymerisation has become of central importance in polymer science and technology. In the case of synthetic hydrogels, photoinitiation by UV light is recognized as a very useful synthetic tool. Photoinitiation has various advantages over thermal or redox initiation such as being easier to control, more easily convertible into a continuous process, and offering the possibility of combining both polymerisation and sterilization into one technological step [2]. Photoinitiators and crosslinkers are amongst the main factors to consider for producing hydrogels with good mechanical stability [3].

At present, Thailand continues to import biomedical hydrogel products at great expense. This present research work is therefore aimed at developing a capability to manufacture these products in Thailand with the initial emphasis on wound dressings.

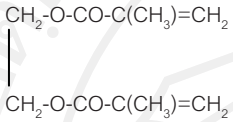


sodium 2-acrylamido-2-methylpropanesulfonate (Na-AMPS)

Photoinitiator-Crosslinker System I

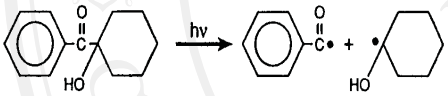


4,4-azo-bis(4-cyanopentanoic acid)

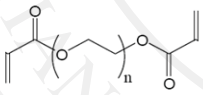


ethylene glycol dimethacrylate (EGDM)

Photoinitiator-Crosslinker System II



Irgacure 184



Ebecryl 11 = PEG400 DA

2. Experimental

2.1 Preparation of Na-AMPS Solution

The water-soluble monomer used in this work was the sodium salt (Na-AMPS) of 2-acrylamido-2-methylpropanesulfonic acid (AMPS). An aqueous solution of Na-AMPS was prepared by dissolving AMPS acid in distilled water (40% w/v), cooling in an ice-bath, and then neutralizing to pH 7 with sodium hydroxide solution.

2.2 Hydrogel Synthesis

In System I, 1.0 mol % of EGDM per mol of Na-AMPS was added into 40% w/v aqueous NaAMPS solution as crosslinker together with 0.1% w/v of 4,4'-azo-bis(4-cyanopentanoic acid) as photoinitiator.

In System II, Irgacure 184 as photoinitiator was first dissolved in Ebecryl 11 as crosslinker in a w/w ratio of 10:3 and 0.25% w/v of this solution added into the 40% w/v Na-AMPS solution.

The aqueous solutions were each poured into a vertical sheet-forming mould consisting of two parallel glass plates covered with Teflon® sheets as release liners. Spacers were used to control the sheet thickness with a polymer mesh inserted in the middle to strengthen the hydrated hydrogel. Photopolymerisation was carried out at room temperature using a commercially available UV lamp (254 nm), as shown in Fig. 1 below.

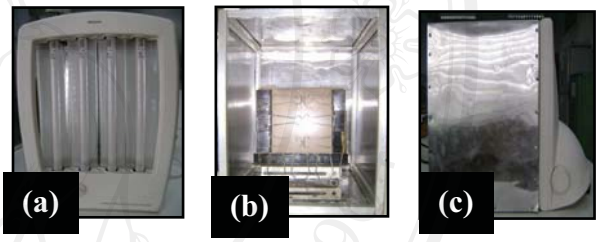


Figure 1. *UV polymerisation apparatus*

(a) UV lamp

(b) Mould inside an aluminium cabinet

(c) UV lamp in contact with the cabinet

2.3 Analysis of the Hydrogel Sheets

Water Transport Properties

After equilibration in air, each hydrogel sheet was immersed in distilled water at the physiological temperature (37ºC) and its increase in weight with time was followed. The water content (WC) was calculated using the following expression:

$$WC\ (wt\ \%) = [(W_w - W_d)/W_w] \times 100\ \%$$

where W_d and W_w are the dry and wet weights of the hydrogel respectively.

When the equilibrium water content (EWC) had been reached, the hydrogel was removed from the distilled water and re-equilibrated in air at room temperature to

constant weight. The water retention (WR) of the hydrogel was similarly plotted as a function of time.

The water vapour transmission rate (WVTR) was measured using the standard ASTM E96-93 (1990) Water Cup Method.

Peel Strength

A peel strength test can be used to give an indication of the ease of removal of a hydrogel from a substrate. This gives important information about the strength of the adhesive bond between the hydrogel and the substrate which, in practice, would be the skin. The shear force required to remove a hydrogel from a substrate can be quantified provided that the test is carried out at a constant 90° angle. The instrument used in this work was a Hounsfield Tensile Tester with a withdrawal speed of 500 mm/min, hydrogel strip length of 25 mm and a 100 N load cell.

Residual Monomer

Ion chromatography (IC) was used for separating and quantifying anions (SO_3^-) present in an aqueous extract of the hydrated hydrogel. In a typical analysis, 5 mM of KOH solution was used as the eluent over an analysis time of 40 mins. The instrument used was a Dionex DX600 Ion Chromatograph supported by Chromeleon Client 6.50 software.

Oxygen Permeability

The oxygen permeability (Dk) was obtained using a 210T Permiometer and the equation

$$Dk = i\,(\mu A) \times L\,(mm) \times (6 \times 10^{-11})$$

where

L = hydrogel sample thickness (mm)

i = constant current obtained for O_2 passing through the hydrogel

3. Results and Discussion

The hydrated hydrogel sheets obtained direct from synthesis were of 1.20 ± 0.20 mm thickness and exhibited good coherency, transparency, flexibility and skin adhesion.

Water Transport Properties

As the WC-time profiles in Fig. 2 show, equilibrium water contents (EWC) of 98 ± 1% were obtained within 30 mins. Following on from this, when the samples were removed from the water and left in air to re-equilibrate, as shown in the WR-time plots in Fig. 3, equilibrium water retentions (EWR) of 25 ± 2% were obtained over a period of about 4 hrs.

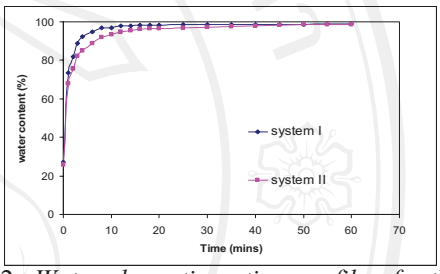


Figure 2. *Water absorption - time profiles for the hydrogel sheets when immersed in distilled water at 37°C.*

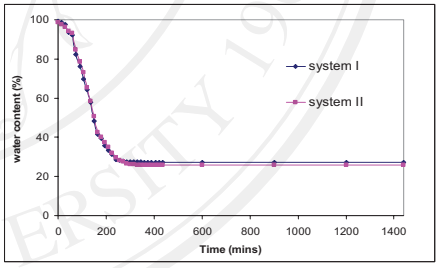


Figure 3. *Water retention - time profiles for the hydrogel sheets when left in air at room temperature (continuous from Fig. 2)*

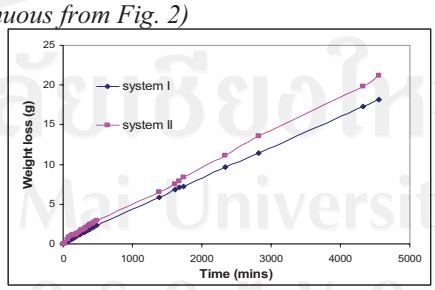


Figure 4. *Water vapour transmission - time profiles for the hydrogel sheets at 37°C and 55-60% relative humidity.*

The water vapour transmission (WVT)-time profiles are shown in Fig. 4 above. From the linear plots, WVT rates of 82±2 g m^{-2} hr^{-1} were obtained which, for medical purposes, is deemed to be a

suitable rate for the controlled evaporative water loss from a second-degree burn.

Peel Strength

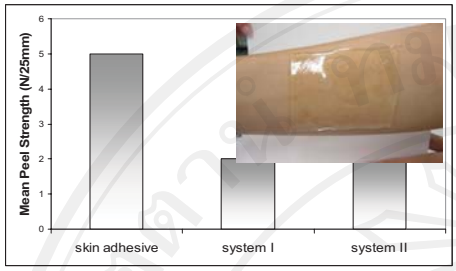


Figure 5. *Peel strengths of System I and System II hydrogels compared with a commercial skin adhesive material.*

Both hydrogel sheets from System I and System II showed good skin adhesion to healthy skin but not too high that it was painful to remove.

Oxygen Permeability

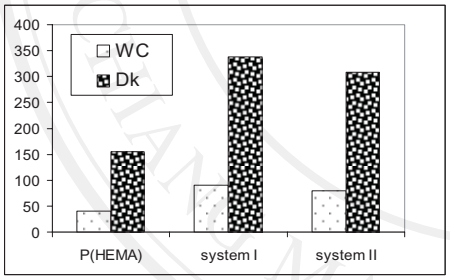


Figure *6. Oxygen permeabilities (Dk, cc.mm/cm2.s.cm Hg) and corresponding water contents (% WC) of the hydrogel sheets compared with poly(HEMA).*

It was found that the Dk values of the Na-AMPS hydrogel sheets were about 300 x 10^{-11} cc.mm./cm^2.s.mm Hg, significantly higher than other hydrogel polymers such as polyHEMA for which the Dk is about 145 x 10^{-11} cc.mm./cm^2.s.mm Hg [4].

Residual Monomer

From the ion chromatograms, the residual Na-AMPS monomer is calculated from the peak area compared with a standard calibration curve of % Na-AMPS versus peak area. The residual monomer concentrations from System I and System II were found to be less than 0.25% and 0.05% respectively.

4. Conclusions

The Na-AMPS synthetic hydrogels from this work showed a good balance of properties as would be required for a wound dressing such as good coherency, transparency and flexibility. High water absorption is essential for a hydrogel to be able to absorb wound exudate yet maintain a moist environment. At the same time, water absorption and water vapour transmission need to be balanced. The hydrogel sheets showed good skin adhesion to healthy skin while being easy to remove from a wound surface when hydrated. The hydrogel sheets from both System I and System II exhibited high oxygen permeability values (Dk) which are advantageous for their use as wound dressings from the point of view of allowing oxygen exchange to and from the wound surface. It was found that System I gave more residual monomer than System II by a factor of about 5 from which it can be concluded that the photoinitiator in System II gave a more complete polymerisation reaction than that in System I.

Acknowledgements

The presenting author (CW) wishes to thank the Department of Chemistry, Chiang Mai University, and the Biomaterials Research Unit, School of Chemical Engineering and Applied Chemistry, Aston University, Birmingham, UK, for providing the research facilities and the Rajamangala University of Technology I-SAN, Kalasin Campus, for financial support.

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JOURNAL PUBLICATION

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

Kanarat Nalampang, Nantarat Suebsanit, Chinanat Witthayaprapakorn and Robert Molloy

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