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Poly(ester urethane)-crosslinked carboxymethylchitosan as a highly water swollen hydrogel

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Abstract

This work focused on the synthesis and characterization of carboxymethylchitosan (CMC)-based hydrogels modified with polyester-containing polyurethane (PU). The polyester was first synthesized from the condensation between 1,6-hexane diol and malonic acid, then reacted with an excess of 1,6-hexamethylene diisocyanate (HDI), and followed by the reaction with ethylene glycol as a chain extender to gain PU. CMC was chemically crosslinked with a water soluble crosslinker in the presence of 1-60 wt% of PU to obtain highly water swollen CMC hydrogels. Upon addition of PU, the CMC hydrogel showed excellent water swellability (up to 400 times of the dried weight), and it seemed to decrease as decreasing PU percentage but still higher than those of unmodified CMC hydrogel (95 times of the dried weight). The drop of the water swellability was attributed to hydrophobic PU presenting in hydrophilic CMC, evidenced by the formation of PU microphase both in the bulk and surface of the hydrogel with average size ranging between 32 μm and 49 μm in diameter. Addition of PU was generally enhanced tensile strength properties of the hydrogel, while an opposite trend was observed for the elongation properties.

1. Introduction

Chitosan is a linear positively charged polysaccharide composing of β-(1,4)-2-amino-2-deoxy-D-glucopyranose units and is typically synthesized by alkaline deacetylation of chitin [1]. It shows a significant advantage over cellulose and starch due to its presence of amino groups in the structure, allowing for further chemical modifications and essentially extending its broad range for various applications [2]. However, its solubility solely in aqueous acidic solution limited its potential applications [3,4]. Incorporation of hydrophilic functional groups such as carboxymethyl groups led to the formation of water soluble derivatives [5]. Carboxymethylchitosan (CMC), an anionic derivative of chitosan, is typically synthesized through a carboxymethylation reaction of chitosan with monochloroacetic acid in basic solution [6]. This water soluble CMC exhibited various potential uses in biomedical applications [7], e.g. scaffold [8], drug delivery [9], healing [10] and tissue engineering [11] etc. Owing to its good water solubility, formation of CMC network is a promising approach in enhancing its capability to retain large amount of water without dissolved portion [12]. A number of researches have explored various approaches with the aim at formation of CMC hydrogel [13-15]. However, the mechanical properties of CMC hydrogel without addition of other functional polymers seemed to be deteriorated due to the formation of network structure. Hence, incorporation of CMC hydrogels with other polymers can overcome this drawback and broaden its use in a wider application [12,16-18]. Polyurethane (PU), a kind of polymer that consists of carbamate units (–NH-CO-) in the structure, is typically prepared from the reaction between polyol (hydroxyl-terminated prepolymer) and polyisocyanate [19]. Various kinds of polyol are employed in PU synthesis such as polycarbonate, polyether and polyester. It has been widely used in a number of applications, e.g. textile fibers [20, 21], elastomer [22], automative parts [23], medical parts [24-26], and foams [27-29]. Researches involving the interpenetration of PU into CMC network are rather limited. Precedent has been reported that incorporation of polyester-based PU into CMC hydrogel can improve its tensile strength [30].

In this work, synthesis of CMC hydrogel modified with polyester-based PU was presented (Figure 1). Polyester was first synthesized by the reaction between malonic acid and 1,6-hexanediol to obtain low molecular weight polyester (PHM) as a polyol precursor. PU was then prepared from the reaction of PHM polyol with hexamethylenediisocyanate (HDI) and an ethylene glycol chain extender. CMC hydrogel was then prepared via the crosslinking reaction in the presence of PHM-based PU with the use of hexamethylene-1,6-di-(aminocarboxysulfonate) (HAD) as a water soluble crosslinker. Percent crosslinking and water swelling properties of CMC hydrogel were also studied. Effect of PU concentrations on water swelling behavior, toughness properties and water contact angle of CMC hydrogel was investigated. Also, microphase separation of CMC hydrogel as a function of PU percentage was also determined.

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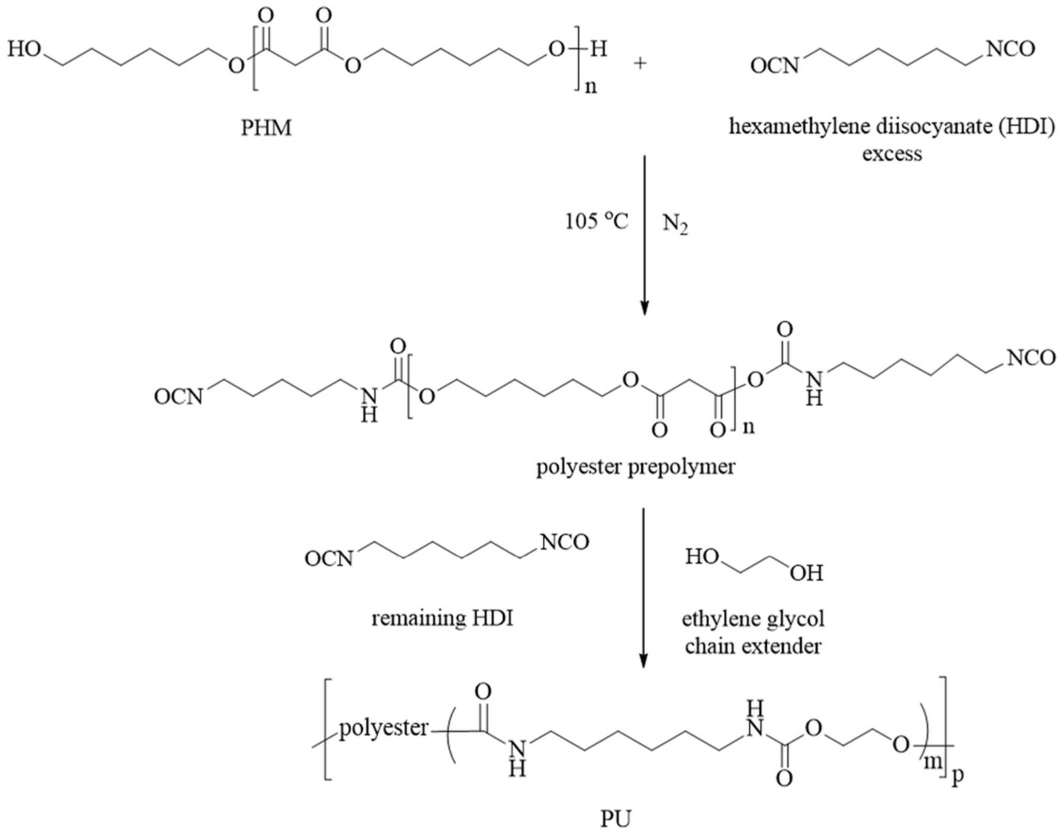

Figure 1. Synthetic scheme for the preparation of PHM-based PU.

2. Material and methods

2.1 Materials

Chitosan from shrimp (85% degree of deacetylation) (Taming Enterprise, Thailand), malonic acid, 99% (Acros), 1,6-hexanediol, 99% (Acros), dibutyltin oxide, 98% (Acros), sodium metabisulphite, $Na_2S_2O_5$ (Carlo Erba reagent) and 1,6-hexamethylene diisocyanate (HDI), 99% (Acros) were used as received. Ethylene glycol (Mallinckrodt) were fractionally distilled and stored under N_2 until used.

2.2 Syntheses

2.2.1 Preparation of CMC from chitosan

Chitosan was swollen in isopropanol for 12 h before the reaction with NaOH for 75 min, and it was then reacted with monochloroacetic acid at 60°C for 5 h. After adjusting pH of the solution with HCl solution until neutral, it was then precipitated in MeOH, and washed with a MeOH:H_2O mixture (70:30 v/v) to get rid of salts. It was filtered and then dried at 40°C under reduced pressure until dryness.

2.2.2 Preparation of polyester polyol from malonic acid and 1,6-haxanediol (PHM)

Malonic acid (2.91 g, 0.028 mol) and 1,6-hexanediol (3.42 g, 0.029 mol) were charged into a reaction flask in the presence of dibutyltin oxide catalyst (the molar ratio of malonic acid to 1,6-hexanediol was 1:1.04 in order to control the molecular weight of PHM). The mixture was stirred at 180°C for 24 h under reduced pressure. The mixture was cool down to room temperature under N_2 purging.

2.2.3 Preparation of PHM-based PU

PHM polyol prepared in the previous step was used as a polyester soft segment to prepared PU. It was prepared *via* a reaction between PHM polyol and an excess of HDI to obtain polyester with isocyanate groups at both ends, and followed by the reaction between the isocyanate-terminated PHM and ethylene glycol chain extender (Figure 1). PHM and HDI (1:2.5 molar ratio) were charged into a round-bottom flask filled with N_2. The temperature was adjusted to 105°C for 2 h to obtain PHM prepolymer. Ethylene glycol chain extender (0.5 molar equivalent of PHM and

HDI) was then added into the prepolymer to commence the chain extending reaction for 2 h. The molecular weight of the polymer was determined using GPC technique.

2.2.4 Preparation of hexamethylene-1,6-di-(aminocarboxysulfonate) (HDA) as a crosslinker

The mixture of HDI (5 g, 0.03 mol) and $Na_2S_2O_5$ solution (6 g, 0.03 mol in 12 ml H_2O) was stirred overnight at room temperature under N_2 atmosphere. It was then poured in acetone to precipitate the product and it was then filtered and dried under reduced pressure. After dissolving in water, the product was repetitively precipitated in acetone and dried to gain white powder of HDA.

2.2.5 Preparation of poly(ester urethane)-modified carboxymethylchitosan (CMC-PU)

A CMC mixture (2.5 g in 50 mL water) was mixed with PU solution (50 mL of THF) and HDA solution (0.25 g HDA in 10 mL water). After 2 h of stirring, it was cast into a glass mold to obtain a 10×10 cm^2 sample film, which was stored at 60°C for 24 h.

2.3 Characterization

2.3.1 Characterization

Proton nuclear magnetic resonance spectroscopy (^1H NMR) was conducted on a 400 MHz Bruker NMR spectrometer with $CDCl_3$ solvent. Fourier-transform infrared spectroscopy (FTIR) was carried out on a Perkin-Elmer Model 1600 Series FTIR Spectrophotometer. Gel permeation chromatography (GPC) was performed on PLgel 10 μm mixed B2 column (1 $mL\cdot min^{-1}$ at 30°C) with an RI detector using tetrahydrofuran (THF) as a solvent. Morphology of the films was conducted on LEO 1455 VP scanning electron microscopy (SEM) with an accelerating voltage of 20 kV. Contact angle measurement was performed on a Krüss DSA 10 Contact Angle Meter at room temperature and the results were reported from with the average of five different measurements. Tensile strength and elongation of the films were measured on a Universal Testing Machine (Instron Model 55R4502), following an ASTM D882 standard method.

2.3.2 Measurement of percent crosslinking

The 2×2 cm^2 sample films were immersed into water for 48 h to dissolve uncrosslinked PU, CMC and HDA. The chemically crosslinked CMC hydrogel was filtered and washed with water and acetone to remove uncrosslinked portions, and then dried at 60°C under reduced pressure for 24 h. Percent crossilinking was estimated from the following equation;

$$\text{Percent crosslinking (\%)} = (W_2 / W_1) \times 100$$

where W_1 and W_2 are dried weights of the films before and after the dissolution, respectively. The reported values are the average of five different measurements.

2.3.3 Measurement of water swelling properties

Water swelling properties of CMC hydrogel was investigated from the measurement of equilibrium water content (EWC) values. After crosslinking, the 2×2 cm^2 sample films were immersed into containers having an excess of water in order to obtain fully swellen films. After 24 h, the swollen films were removed from the containers, dried off an excess of water on the film surface and then weighed (Wsw1). The films were dried for another 48 h at 50°C under reduced pressure and then they were again weighed (Wd). EWC1 values were estimated from this equation;

$$\text{EWC1 (\%)} = (W_{sw1} - W_d) \times 100 / W_d$$

To investigate water swellability of the pre-dried films, the same films used to investigate EWC1 were immersed into water for another 48 h. The swollen films were removed from the container, removed water on the film surface and then weighed (W_{sw2}). The calculation of EWC2 values was following;

$$\text{EWC2 (\%)} = (W_{sw2} - W_d) \times 100 / W_d$$

The reported values are the average of five different measurements.

2.3.4 Measurement of tensile strength and percent elongation

The rectangular films with 1.0 cm width were tested using 30 mm gage length and the crosshead rate of 10 mm/min. Tensile strength and percent elongation at break were estimated using the following equation;

$$\text{Tensile strength } (N\cdot mm^{-2}) = \frac{\text{Breaking force (N)}}{\text{Cross-sectional area of the sample } (mm^2)}$$

$$\text{Percent elongation at break (\%)} = \frac{\text{The increase in length at breaking point (mm)} \times 100}{\text{Cross-sectional area of the sample } (mm^2)}$$

The reported values were the average of five different measurements.

3. Results and discussion

3.1 Synthesis and characterization of PHM

PHM was prepared *via* polycondensation between malonic acid and 1,6-hexanediol. A slight excess of 1,6-hexanediol was used to control its molecular weight and to obtain hydroxyl terminals (1:1.04 molar ratio of malonic acid:1,6-hexanediol, respectively). Nitrogen purging throughout the reaction in combination with high reaction temperature should continuously remove water and enhance the reaction equilibrium to the condensation product. According to ^{1}H NMR spectra (Figure 2a), the formation of ester linkage was confirmed by the appearance of signal *e* (3.3 ppm, $\text{-OC-C}\underline{\text{H}}_2\text{-CO-}$) and signal *f* (4.1 ppm, $\text{-OC-O-C}\underline{\text{H}}_2\text{-CH}_2\text{-}$) corresponding to the methylene protons adjacent to the ester linkage in PHM, in combination with the disappearance of signal *a* (3.5 ppm, $\text{HOOC-C}\underline{\text{H}}_2\text{-COOH}$) corresponding to the methylene proton of malonic acid. In good agreement with ^{1}H NMR, FTIR spectra showed the change from the broad signal (1702 cm^{-1}), which are characteristics of the carboxylic acid functional group, of malonic acid to the sharp peak (1720 cm^{-1}) of the ester linkage and the hydroxyl ends of PHM (Figure 2b).

The molecular weight of PHM, determined from the integration ratio of signal *f* in conjunction with the protons at the chain terminals (signal *b*), was approximately 900 g·mol^{-1} (Figure 2a), whereas the molecular weight determined from GPC technique was 1,500 g·mol^{-1} (polydispersity index, PDI = 1.42). The low molecular weight PHM obtained in this reaction was typical for polycondensation. It should be mentioned that the molecular weight of PHM prepared from sulfuric acid-catalyzed condensation was higher (3,400 g·mol^{-1}) but its distribution was slightly broader (1.57), comparing to that using dibutyltin oxide catalyst (PDI = 1.42). In this work, the low molecular weight of PHM was more desirable than the high molecular weight one to avoid feasible macroscopic phase separation of hydrophobic polyester in hydrophilic CMC in the film preparation step.

3.2 Synthesis of PHM-based PU

^{1}H NMR technique confirmed the formation of PHM-based PU by observing the appearance of signal *j* (3.13 ppm), corresponding to methylene protons adjacent to urethane functional groups (Figure 3a). The disappearance of signal *e* (3.50 ppm), corresponding to methylene protons at the chain terminal of PHM, indicated the complete reaction between PHM and HDI. However, the absence of signal *i* (3.20 ppm) indicated that there was no HDI remaining in PU structure although an excess of HDI was used. In good agreement with ^{1}H NMR results, FTIR exhibited the existence of C=O (1682 cm^{-1}) and N-H (3320 cm^{-1}) functional groups of the urethane linkage but there was no isocyanate group (2276 cm^{-1}) remaining after the reaction (Figure 3b). This was attributed to the formation of ester oligomers containing hydroxyl functional groups remaining from PHM preparation step, which can readily react with HDI and inhibited the chain extension reaction, resulting in the disappearance of HDI and essentially gaining the low molecular weight of PU. From GPC results, the molecular weight and PDI of PU were 4,100 g·mol^{-1} and 1.60, respectively, signifying the increase of these values as compared to those of PHM (1,500 g·mol^{-1}, MWD 1.41). The influence of the low molecular weight of PU on the properties of PU-modified CMC would be discussed in details in the next section.

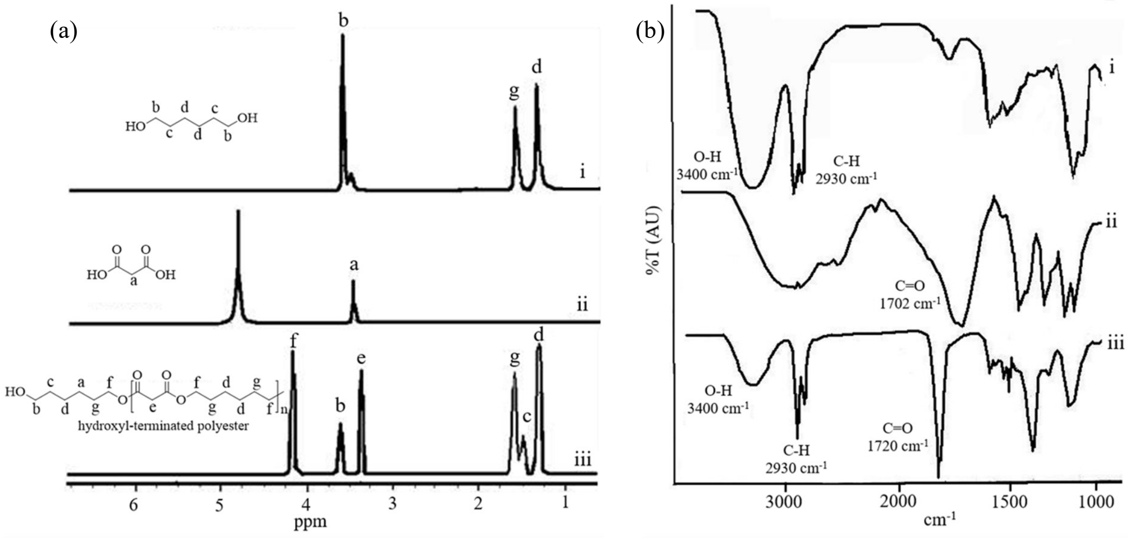

Figure 2. (a) ^{1}H NMR and (b) FTIR spectra of (i) 1,6-hexanediol, (ii) malonic acid and (iii) PHM.

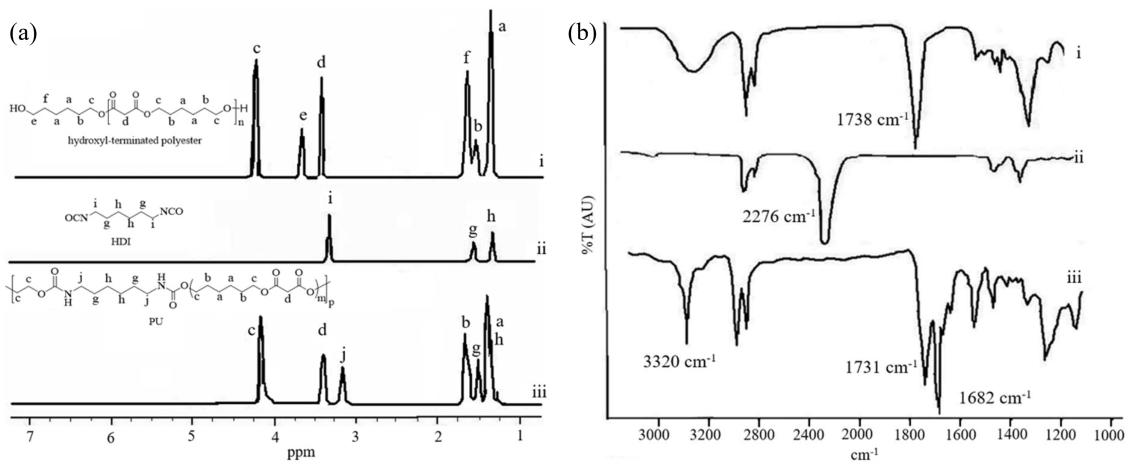

Figure 3. (a) ^{1}H NMR and (b) FTIR spectra of (i) PHM, (ii) HDI and (iii) PHM-based PU.

3.3 Preparation and properties of PU-modified CMC (CMC-PU)

Percent crosslinking and EWC studies

In this work, 10 wt% of water soluble HDA was used to chemically form CMC network. Percent crosslinking and EWC of CMC hydrogel without incorporation of PHM-based PU was first investigated as a control sample. According to the results in Figure 4a, percent crosslinking seemed to increase as increasing the percentage of HDA crosslinker (10-70 wt% of HDA added), and this was attributed to the formation of the dense network structure as higher amount of the crosslinker incorporated. This rationalization was in good agreement with EWC properties observed (Figure 4b). CMC hydrogel exhibited 9,500% EWC1 (95 times of the original dried weight) as only 10 wt% of HDA incorporated and continuously decreased to 1,100% EWC1 (11 times of the original dried weight) as 70 wt% of HDA was added. The same phenomena were also observed in case of EWC2. EWC values constantly decreased owing to the increase in the crosslinker concentration in CMC network and essentially forming dense network structure.

To study the effect of PHM-based PU on the crosslinking and EWC properties, 1-60 wt% of PU was added to CMC network to form CMC-PU hydrogel (10 wt% of HDA used as the crosslinker). Percent crosslinking of CMC-PU did not show any significant change as the concentration of PU in CMC increased (Figure 5A). It was hypothesized that PU was physically blended or interpenetrated in CMC due to the absence of isocyanate functional groups in PU chains, as evidenced by ^{1}H NMR and FTIR (Figure 3), to actively react with CMC. As a result, increasing PU concentration did not enhance percent crosslinking of the system.

EWC1 and EWC2 were determined to investigate swelling behavior of CMC-PU hydrogel (Figure 5B). Addition of 1 wt% PU into CMC hydrogel exhibited an excellent EWC1 up to 40000% (400 times of the original dried weight) and continuously decreased to 10000% EWC1 as increasing PU concentration to 60 wt%. The decrease in EWC of the hydrogel was attributed to the hydrophobicity of PHM soft segment in PU structures, which essentially influenced the water swellabillity of CMC-PU hydrogel. It is noteworthy to mention that EWC2 was drastically decreased as compared to EWC1 in all cases. Additional network formation when drying of CMC-PU hydrogel might take place, resulting in the lowering in its water swellability. EWC2 maintained at *ca.*35,000% when 30-60 wt% of PU was added. This signified that no or only slight further reaction occurring as more than 30 wt% PU was incorporated.

Morphological studies

SEM evidenced the existence of microphase separation of PU in the hydrogel as observed on surface (Figure 6b-6d) and also in the bulk (Figure 6b′-6d′) of the CMC containing 10-50 wt% of PU and this observation was compared with those of CMC-HDA (without PU), crosslinked with 10 wt% HDA (Figure 6a and 6a′). CMC-HDA samples (without PU) exhibited no microphase separation, while CMC-PU showed a number of spherical PU microphases dispersed in CMC matrix. The size of the PU microphase continuously increased from 32±9 μm (ranging 17-44 μm), 39±11 μm (ranging 27-50 μm) to 49±13 μm (ranging 33-72 μm) as increasing the PU percentage in CMC from 10 wt%, 30 wt% to 50 wt%, respectively. The formation of the PU microphase was probably due to the hydrophobic character of PU diffusing in hydrophilic CMC matrix. The increase in PU percentage (from 10 wt% to 50 wt%) thus enhanced this separation as indicated by the increase in size and size distribution of the microphase.

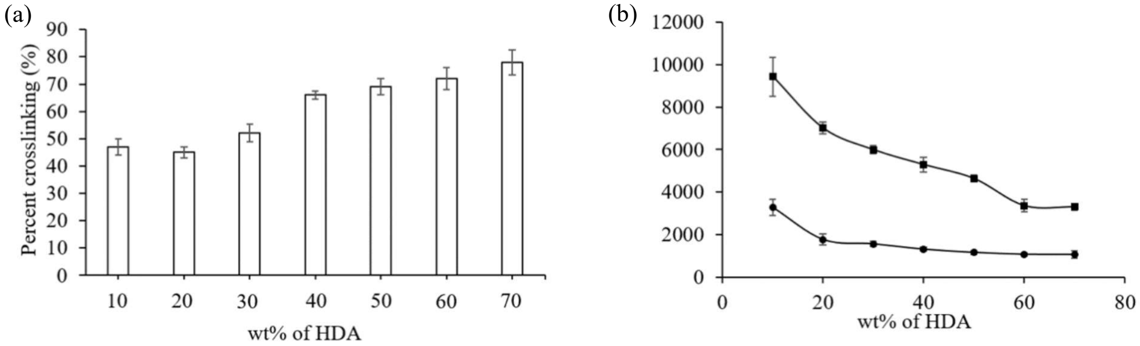

Figure 4. (a) Percent crosslinking and (b) EWC1 (■) and EWC2 (●) of CMC hydrogel (without PU) crosslinked with various amounts of HDA crosslinker.

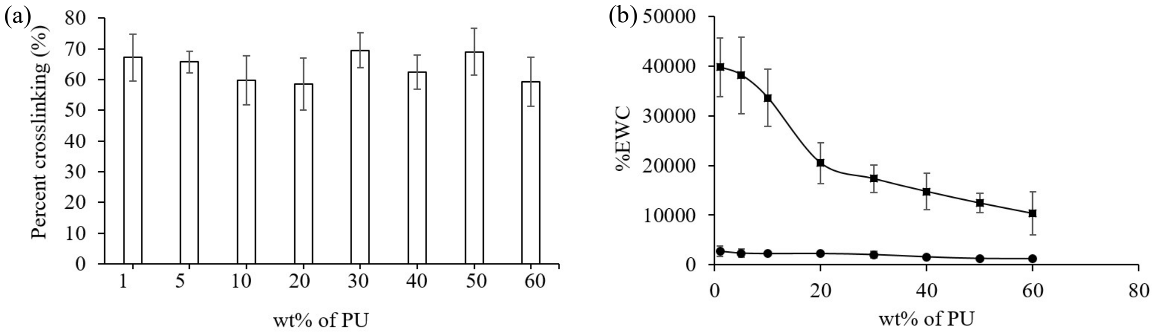

Figure 5. (a) Percent crosslinking and (b) EWC1 (■) and EWC2 (●) of CMC-PU hydrogel as a function of weight percentage of PU.

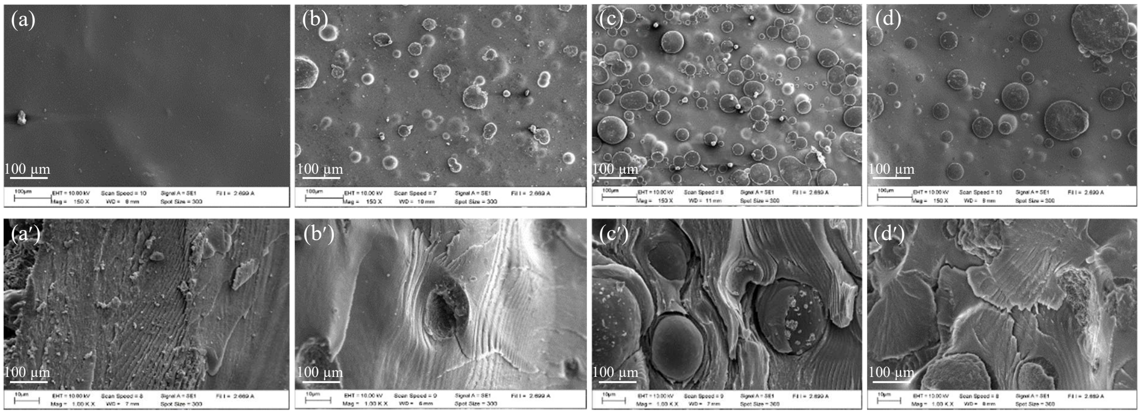

Figure 6. Surface (a-d) and cross-sectional (a′-d′) morphologies of (a-a′) CMC-HDA hydrogel (without PU), (b-b′) CMC-PU hydrogel with 10 wt% of PU, (c-c′) CMC-PU hydrogel with 30 wt% of PU and (d-d′) CMC-PU hydrogel with 50 wt% of PU.

Water contact angle studies

Water contact angle of CMC-PU hydrogel (10-50 wt% of PU) was investigated in comparison with those of unmodified CMC and CMC-HDA hydrogels (without PU) crosslinked with 10 wt% HDA (Figure 7). It should be notified that a high degree of water contact angles signified low water wettability of the sample surface. Water contact angle of CMC-PU hydrogel increased from 67 to 82 degree when PU concentrations increased from 10 wt% to 50 wt%, while those of both unmodified CMC and CMC-HDA hydrogels were 64 degree. The high percentage of PU enhanced the formation of hydrophobic surface probably due to the migration of hydrophobic PU to the hydrogel surface. This result agreed well with the SEM observation of spherical PU microphase on the surface of CMC hydrogel with the larger size as increasing the PU percentage in the hydrogel (Figure 6b-6d).

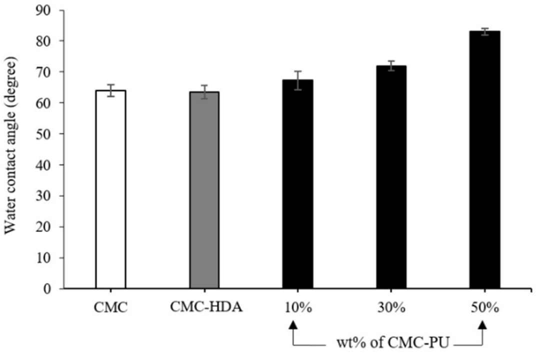

Figure 7 Water contact angle of unmodified CMC, CMC-HDA hydrogel (without PU) and CMC hydrogel containing 10-50 wt% of PU

Toughness property studies

Toughness properties of CMC-PU hydrogel having 10-50 wt% of PU were investigated in comparison with those of unmodified CMC and CMC-HDA hydrogels (without PU) crosslinked with 10 wt% of HDA (Figure 8). Incorporation of PU in CMC generally increased tensile strength of the hydrogel, while its percent elongation showed an opposite trend. The increase of PU in the hydrogel from 10 wt% to 50 wt% did not show any trend of tensile strength improvement. Conversely, the increase of PU in the hydrogel exhibited an enhancement in its toughness properties indicated by a significant increase in percent elongation from 28% to 67% as PU percentage increased from 10 wt% to 50 wt%.

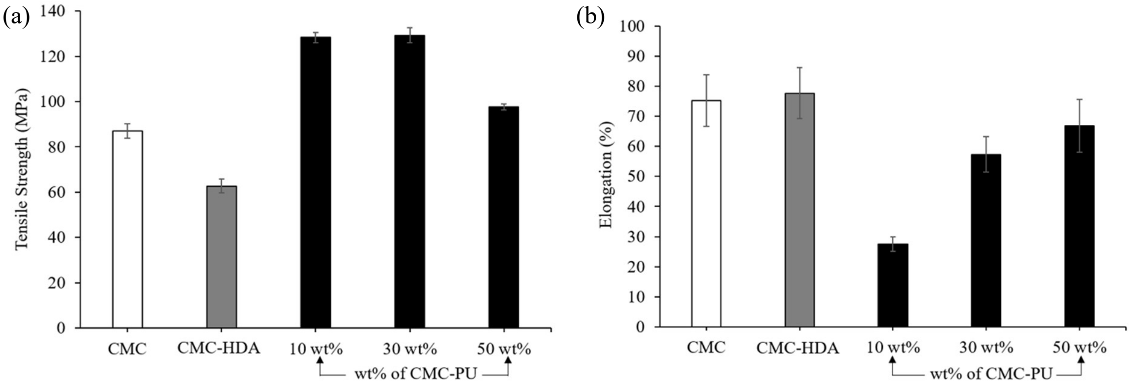

Figure 8 (a) Tensile strength and (b) percent elongation of unmodified CMC, CMC-HDA hydrogel (without PU) and CMC hydrogel containing 10-50 wt% of PU

4. Conclusions

CMC-based hydrogel modified with polyester (PHM)-containing PU was successfully prepared. It was chemically crosslinked with water soluble HDA to gain highly water swollen networks. The properties of the hydrogel were tuned by incorporating PU into CMC hydrogel. Increasing PU content in the hydrogel resulted in the decrease in its water swellability probably owing to the formation of interpenetrating PU in CMC hydrogel. The hydrogel surface was enriched with PU as observed by the presence of spherical PU microphase on its surface, as well as the enhancement in surface hydrophobicity when the PU content was increased. Introducing PU into CMC hydrogel generally enhanced its tensile strength, while an opposite trend was observed for the elongation properties.

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