FABRICATION AND CHARACTERIZATION OF CELLULOSE DERIVATIVES-BASED HYDROGEL

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ABSTRACT

Hydrogel materials have been extensively studied by many research groups owing to their wide application. The green approach in hydrogel fabrication might include polymers from natural sources. Cellulose derivative is a potential candidate because of its biocompatibility and readily availability. In this study, hydroxypropyl methyl cellulose (HPMC), hydroxypropyl cellulose (HPC), hydroxyethyl cellulose (HEC) and sodium carboxymethyl cellulose (CMC or NaCMC) shall be crosslinked with glutaraldehyde to confirm the ability to fabricate the cellulose-based hydrogel. The investigation showed that HPMC was not suitable for hydrogel fabrication due to low gel-time signal and small gel fraction (~10%). The gel time signal could be detected with only CMC solution. Accordingly, the CMC sample had the highest gel fraction (89%). CMC and HEC were comparable in water uptake (80 to 120%). HPC solution could be gelled at a higher concentration of glutaraldehyde and a completely gelled state of 100% gel fraction could be achieved. However, significantly large water uptake (up to 2000%) was detected with HPC - based samples.

Keywords: Celluloses, hydrogel, polymer, gel time, gel fraction, water uptake.

1. INTRODUCTION

Hydrogel is a polymeric network that has capability to absorb a large amount of water without being dissolved [1]. Hydrogel materials have been researched targets owing to their wide range of applications from robotic and tissue engineering [2] to agriculture [3]. In addition to good water absorption, the hydrogel should have a high gel fraction (about 85-95%) [4]. Therefore, the crosslinking density must be high enough. On the other hand, the dense structure might reduce water absorption. The ability to have a good interaction with water molecules of the hydrogel relates to hydrophilic groups in the original polymer chains such as hydroxyl, carboxyl, or amine. As a consequence, the hydrogel material is usually fabricated from highly hydrophilic polymers such as polyacrylic acid [5], polyacrylamide [6], and polyvinyl alcohol [7]. The polymeric network could be formed via physical or chemical bonding [8, 9]. The common crosslinker of glutaraldehyde could be added to form the covalent bonds for the network [10]. For the medical field, the biocompatibility and safety of the original polymer are the main concern and the polymer from natural sources might be a green approach. Therefore, cellulose with its environmentally friendly, biodegradable, and readily available characteristic is a potential starting material as the main matrix for the hydrogel [11].

Cellulose molecule contains many -OH groups which cause the hydrophilic property of the material. However, due to the hydrogen bonding, cellulose has a high ratio of crystallinity. The crystal force increases the intermolecular interaction and restrains the material to be dissolved in water. The modification of -OH groups cellulose molecules reduced the crystallinity and many dissolvable derivatives could be synthesized such as hydroxypropyl methyl cellulose (HPMC), hydroxypropyl cellulose (HPC), hydroxyethyl cellulose (HEC), and sodium carboxymethyl cellulose (CMC or NaCMC). HEC and CMC had been applied in the hydrogel fabrication and reported in several reports [12, 13] which indicated the potential of the research direction. However, to the best of our knowledge, there is no research that reports the direct comparison of these cellulose derivatives in hydrogel preparation and characterization.

In this study, the ability to crosslink the water-dissolved cellulose derivatives with glutaraldehyde shall be confirmed and compared. With the chemical crosslinking, the time required for the solution to transform into a gel state plays an important role in sample preparation. It could also be used as a preliminary result to predict the final hydrogel product [14]. Therefore, the gel time of the cellulose solution by adding glutaraldehyde shall also be conducted and compared to the PVA solution. The amount of formed gel in the same conditions as well as the ability of water absorbed by the sample shall be discussed.

2. EXPERIMENTAL SECTION

2.1. Materials

R = H or CH$_2$CH(OH)CH$_3$
Hydroxypropyl Cellulose
(HPC)

R = H or CH$_2$CH$_2$OH
Hydroxyethyl Cellulose
(HEC)

R = H or CH$_3$ or
CH$_2$CH(OH)CH$_3$
(Hydroxypropyl)methyl Cellulose
(HPMC)

R = H or CH$_2$COONa
Carboxymethyl Cellulose Sodium Salt
(CMC)
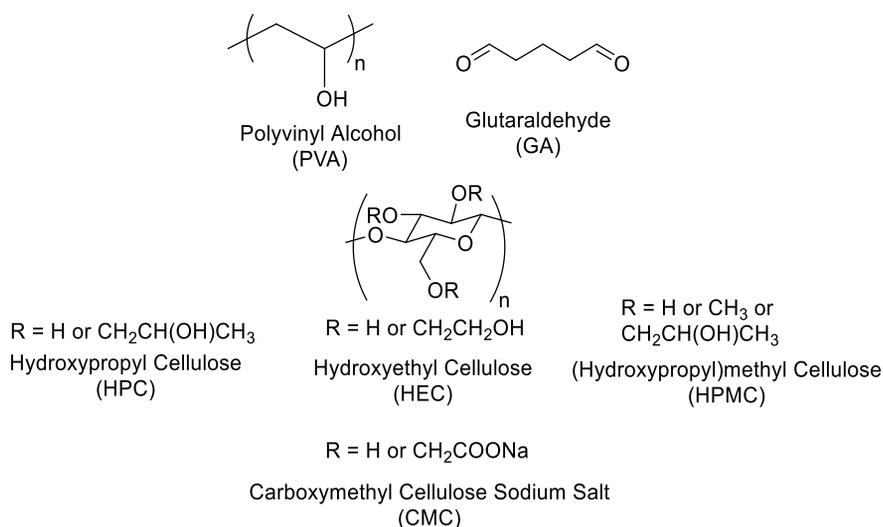
Figure 1. Chemical structures for GA, PVA, HPC, HPMC, and CMC.

The chemical structures for the materials in the research were presented in Figure 1. Polyvinyl alcohol (PVA) (hydrolysis degree: 85-90%) and glutaraldehyde (GA) (50% in water) were purchased from Shanghai Aladdin Bio-Chem Technology Co. LTD (China). HPC (viscosity (2 wt%, 20 ℃): 1000-5000 mPa.s) and HPMC (E15) were received from FUJIFILM Wako Pure Chemical Corporation (Japan) and Shandong Head (China), respectively. Sodium carboxymethyl cellulose (CMC) and hydroxyethyl cellulose (HEC) were products of Xilong Company (China). Hydrochloric acid (HCl) from Duc Giang Chemicals (Viet Nam) was used as a catalyst for the gelation process.

2.2. Method

Gel time measurement

The gel time measurement was conducted using the technique reported in our previous article [14]. The cellulose derivatives were weighed (2 wt% or 1.5 wt%) and dissolved in double distilled water. The mixture was constantly stirred at room temperature for few hours until a clear solution was formed. The polymeric solution was continued to be stirred for another one hour and kept overnight before conducting the next experiment. 50 mL polymeric solution was added to a 50 mL beaker using a measuring cylinder. GA (2 µL) was added to the solution by a micropipette and the mixture was stirred for 5 min. Then, HCl (0.2 mL) was added and mixed in 1 min before measuring with Brookfield viscometer (DV2T) and the gel timer GT-2000. The spindle in the glass rod form was dipped into the prepared solution. The level of the rod in the solution was maintained at the same position in all of the measurements with a safety lock. The spindle was set with a rotation speed of 1 rpm. The viscometer acquired data method was multipoint, i.e. the data were collected continuously. The data time interval was 5 s until the measurement finished. The device was set to be automatically stopped when the torque value is larger than 90%.

Gel fraction

After adding GA and HCl to the polymer solution using the above procedure, the mixture was poured into a petri dish and the water was gradually evaporated in ambient conditions to form the hydrogel film. The remained water in the hydrogel materials was further removed in an oven at 60 ℃ for 8 h. The dried materials were weighed to obtain values of W_{total}. Then, the material was dipped into a large amount of water for at least 48 h. The samples were filtered and dried to obtain W_{gel}. Gel fraction was calculated using the following equation:

$$GF\% = 100 \ x \ W_{gel}/W_{total}$$

Water uptake

The formed hydrogel was washed with double distilled water and put into an oven (60 ℃, 8h) to obtain a dried gel with a mass of W_d. The materials were dipped into water at room temperature and weighed again to get the mass values of wet gel (W_w). The water uptake (WU) was calculated using the equation:

$$WU\% = 100 \ x \ (W_w - W_d)/W_d$$

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectroscopy was performed with FTIR Shimadzu 8400s (Japan). The materials with and without crosslinking were compared using transmission mode with thin film samples. The experiment was conducted in the range of 4000 to 400 cm^{-1} and the final spectrum was an average result of 40 scans.

3. RESULTS AND DISCUSSION

The gel time results of the cellulose derivatives solution were shown in Figure 2a and b. For comparison, a similar experiment was conducted with PVA solution (3 wt%) (Figure 2c). The sample with PVA showed a typical curve for gel time measurement. The torque value was undetectable and remained unchanged during the initial time. When the crosslinking reaction was activated, the viscosity of the solution was drastically increased and torque could reach the maximum value. However, the result for the cellulose derivatives was different in comparison to the PVA solution.
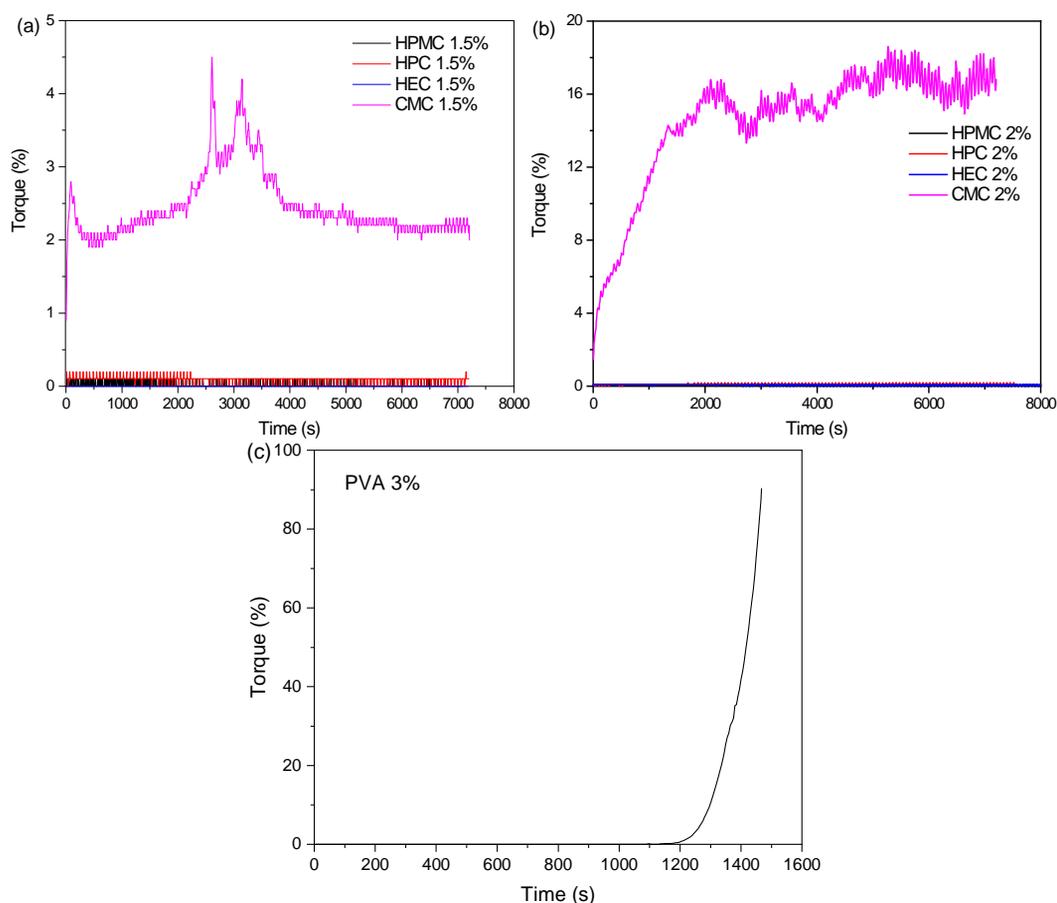
Figure 2. Torque as a function of time of cellulose derivatives solution – (a) 1.5 wt%, (b) 2 wt% and (c) PVA (3 wt%) (2 μL GA and 0.2 mL HCl).

As can be seen in Figure 2, most of the samples showed no response within the investigated time. The CMC solution was the exception which showed an increase in the signal. Compare to the gel time curve of PVA solution, there was no stabilized period detected during the initial time in the CMC case. The signal quickly reached a high value when the data recording process was begun. However, the maximum torque value, in this case, could not be larger than 5%. This phenomenon is similar to the result with PVA 1.5 wt% solution reported in the previous article [14] and could be explained with the same mechanism. Similarly, when the polymer concentration was increased to 2 wt%, the experiment with CMC was the unique result which could give the change in the signal. The torque value was increased right after the measurement started which indicated that the crosslinking reaction had occurred. The highest torque of 18% was achieved and the value fluctuated in the vicinity of 16%. A higher concentration of polymer might yield a better torque. However, the larger viscosity of the original polymer solution might cause trouble in dispersing the GA crosslinker as well as the HCl catalyst and it might lead to the formation of defect in the final hydrogel structure. For other cellulose derivatives (HEC, HPC, and HPMC), there are two possible reasons for the low signal result. The first possibility was that the crosslinking reaction did not occur. Another explanation might include the slow reaction rate and the change of the signal was too small to be detected. Besides monitoring the viscosity, the ability of the material to be swelled and not dissolved in water is strong evidence for the formation of the three-dimensional network structure. In the next investigation, the gel fraction experiment was performed to confirm the existence of the crosslinking bonds in the samples.
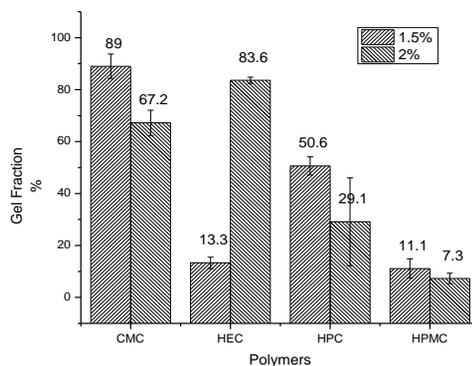
Figure 3. Gel fraction of hydrogel formed with cellulose derivatives solution.

The gel fraction result for different cellulose derivatives in the same conditions was shown in **Error! Reference source not found.**. The fixed GA amount and reduced solution concentration led to a higher ratio of GA/polymer. Therefore, lower polymer concentration yielded a higher gel fraction in most of the investigated samples as can be observed in **Error! Reference source not found.**. However, the sample of 1.5 wt% of HEC possessed a high gel fraction. This might be due to the primary alcohol structure of HEC had contributed to a better activation for the crosslinking reaction at a high polymer concentration. Further research must be conducted to confirm this assumption. The gel fraction of HPMC samples was the smallest (~ 11%) while the CMC solution could give the highest value (89%). This result is in agreement with the obtained gel time curves (Figure 2). In which, the torque value of the CMC sample was quickly increased while both of the HPCM solutions of 1.5 and 2 wt% could not show any change in the signal. Compare to other derivative chemical structures (Figure 1), HPMC has the smallest number of -OH groups. The crosslinking reaction rate depends strongly on the density of the -OH group in the polymer chain. This might be the main reason for the small gel fraction of the HPMC sample. With CMC, its chemical structure includes acrylate which could be hydrolyzed to the -COOH group under the acidic conditions of the hydrogel. These acid functional groups could form hydrogen bonding and it might strengthen the intermolecular interaction and form the physical linking in addition to the covalent bonding between polymer molecules. The acid group in CMC also could play a role as an additional catalyst for the GA crosslinking reaction.
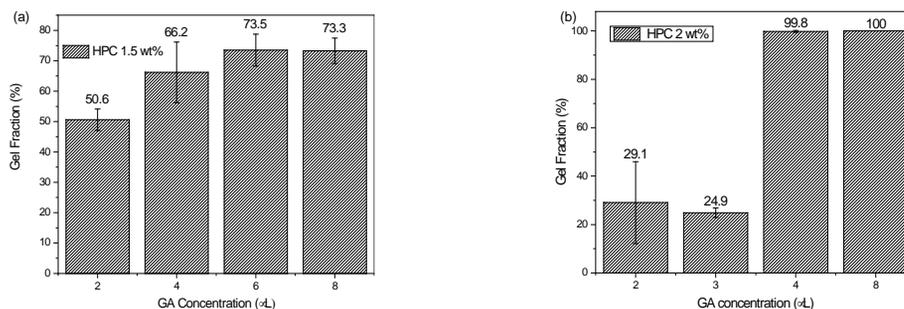
Figure 4. Gel fraction of samples fabricated from HPC solution with varied GA concentrations:
(a) 1.5 wt% HPC, (b) 2 wt% HPC

However, the above explanation could not be applied to the HPC case. The chemical structure of HPC also contained many -OH groups, but the gel fraction was small. Therefore, the next investigation was focused on the effort to improve the gel fraction of the HPC sample by increasing the amount of GA crosslinker. The gel fraction results of HPC with varied GA amounts were summarized in Figure 4. As can be seen, when the GA concentration was

increased, the gel fraction could be improved. The gel fraction of approximately 100% was obtained with 2 wt% of HPC and 4 or 8 μL GA. Although the gel fraction was higher when the concentration of the polymer was reduced, the maximum value was approximately 73% with 1.5 wt% solution.

After investigating gel time and gel fraction as the preliminary results, the formed hydrogel materials were washed with water to remove unreacted chemicals and dried to prepare for the next characterization. The water uptake results for CMC and HEC - based hydrogel, i.e. the amount of water absorbed by the samples, were shown in Figure 5. The water was quickly absorbed by the samples and the result was saturated after 20 min. The results for CMC or HEC samples were comparable. However, the HPC case showed a significantly different water uptake value as can be observed in Figure 6. Interestingly, the result of approximately 2000% could be obtained with the HPC case. The amount of water absorbed for HPC hydrogel was more than 10 times larger than that of other cellulose derivatives-based samples. Moreover, the water absorbed by the HPC hydrogel could not be saturated even after 120 min. A large amount of water uptake might be related to the HPC's chemical structure of propyl alcohol which caused less interaction between HPC molecules. As a result, the free volume in the HPC-based hydrogel was larger and the material was able to maintain more water inside the structure.
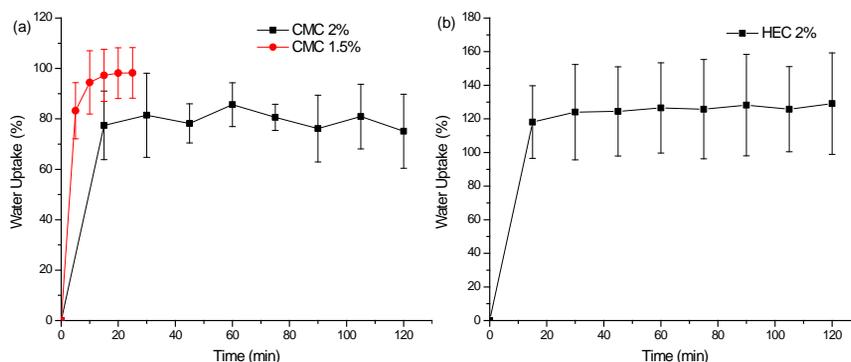
Figure 5. Water uptake of hydrogel samples based on: (a) CMC and (b) HEC.
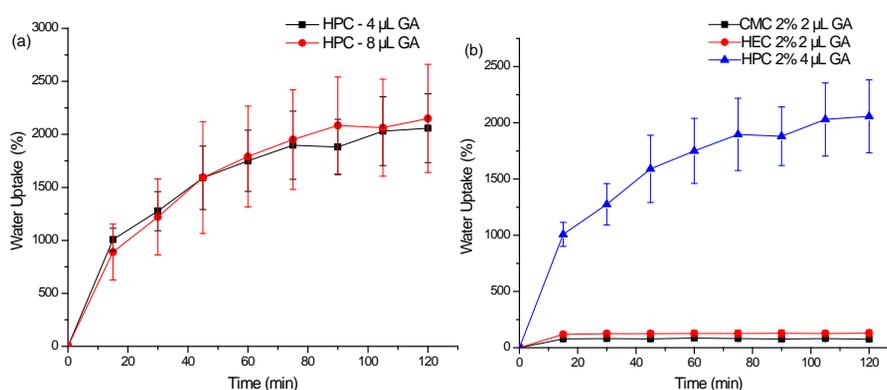
Figure 6. Water uptake of (a) HPC -based hydrogel with varied GA concentration and (b) HPC and cellulose derivatives-based hydrogel (2 wt% polymer solution).
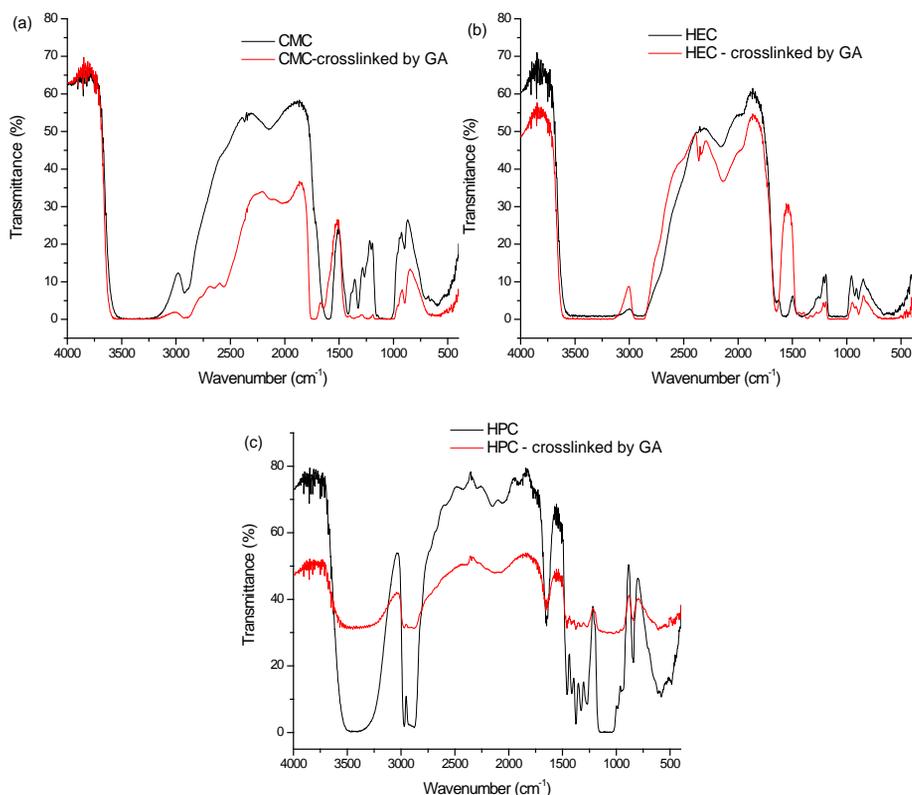
Figure 7. FTIR of cellulose derivatives with (red) and without (black) crosslinking by glutaraldehyde: (a) CMC, (b) HEC, (c) HPC

The FTIR spectra of CMC, HEC, and HPC before and after crosslinking were shown in Figure 7. Because the results were obtained by using transmission mode, part of the FTIR spectrum might not be observed when the film samples were not thin enough. Therefore, the comparison could only be conducted with the wavenumber of 2500 to 1500 cm^{-1}. With CMC, the original sample contained a peak at 1600 cm^{-1} which was typical for COO$^-$ groups. In the crosslinked CMC samples, there were two peaks in this area: 1641 and 1740 cm^{-1} which represented the vibration of C=O in COOH groups. This result indicated that the sodium salt of COONa in CMC had been transformed into COOH due to the acidic condition of the hydrogel fabrication process. This phenomenon could reconfirm the low water uptake result because of the hydrogen bonding caused by -COOH groups. The peak at 1641 cm^{-1} might be original from the hydrogen bonding between the adsorbed water and cellulose molecules [15, 16]. With HEC, in addition to the 1641 cm^{-1} peak, the pure HEC spectrum also contained another peak at 1587 cm^{-1}. However, this peak could not be detected in the crosslinked sample. It might be due to the increase of hydrogen bonding between ether groups in the HEC hydrogels and further investigation must be conducted to confirm this assumption. With HPC, there was no significant difference between the samples before and after experiencing crosslinking. This phenomenon might be related to the low density and large water absorption of HPC samples. The hydrogen bonding of water with the HPC polymer chain was dominant and other vibrations could not be observed.

4. CONCLUSIONS

The hydrogel materials based on cellulose derivatives of CMC, HEC, and HPC were fabricated successfully by crosslinking with GA. The investigation of gel time showed the only signal from the CMC solution. The result was in agreement with gel fraction

characterization when CMC samples had the largest amount of gel (89%) under the same conditions. HEC could have a high gel fraction with the solution at 1.5 wt%. However, HPMC samples without gel time signal and low gel fraction (~10%) were concluded to be not suitable as a based polymer for hydrogel material. Samples prepared from HPC could achieve a completely gelled state (~100% gel fraction) when the GA amount was larger than 4 μL per 50 mL of 1.5 or 2 wt% solutions. The water uptake of HEC and CMC -based hydrogel was from 80 to 120%. In another hand, a significantly large amount of water could be absorbed by the HPC-based hydrogel (up to 2000%). The investigation of FTIR showed that the functional groups of -COONa in CMC were transformed into -COOH and it might affect the ability to absorb water of the hydrogel.

REFERENCES

1. Mahinroosta M., Jomeh Farsangi Z., Allahverdi A., Shakoori Z. - Hydrogels as intelligent materials: A brief review of synthesis, properties and applications, Materials Today Chemistry **8** (2018) 42-55.

2. Taylor D.L., in het Panhuis M. - Self-Healing Hydrogels, Advanced Materials **28** (2016) 9060-9093.

3. Guilherme M.R., Aouada F.A., Fajardo A.R., Martins A.F., Paulino A.T., Davi M.F.T., Rubira A.F., Muniz E.C. - Superabsorbent hydrogels based on polysaccharides for application in agriculture as soil conditioner and nutrient carrier: A review, European Polymer Journal **72** (2015) 365-385.

4. Ahmed E.M. - Hydrogel: Preparation, characterization, and applications: A review, Journal of Advanced Research **6** (2015) 105-121.

5. Elliott J.E., Macdonald M., Nie J., Bowman C.N. - Structure and swelling of poly(acrylic acid) hydrogels: effect of pH, ionic strength, and dilution on the crosslinked polymer structure, Polymer **45** (2004) 1503-1510.

6. Elbarbary A.M., El-Rehim H.A.A., El-Sawy N.M., Hegazy E.-S.A., Soliman E.-S.A. - Radiation induced crosslinking of polyacrylamide incorporated low molecular weights natural polymers for possible use in the agricultural applications, Carbohydrate Polymers **176** (2017) 19-28.

7. Kumar A., Han S.S. - PVA-based hydrogels for tissue engineering: A review, International Journal of Polymeric Materials and Polymeric Biomaterials **66** (2017) 159-182.

8. Kamoun E.A., Kenawy E.-R.S. - Chen X., A review on polymeric hydrogel membranes for wound dressing applications: PVA-based hydrogel dressings, Journal of Advanced Research **8** (2017) 217-233.

9. Hennink W.E., van Nostrum C.F. - Novel crosslinking methods to design hydrogels, Advanced Drug Delivery Reviews **54** (2002) 13-36.

10. Mansur H.S., Sadahira C.M., Souza A.N., Mansur A.A.P. - FTIR spectroscopy characterization of poly (vinyl alcohol) hydrogel with different hydrolysis degree and chemically crosslinked with glutaraldehyde, Materials Science and Engineering: C **28** (2008) 539-548.

11. Chang C., Zhang L. - Cellulose-based hydrogels: Present status and application prospects, Carbohydrate Polymers **84** (2011) 40-53.

12. Capanema N.S.V., Mansur A.A.P., de Jesus A.C., Carvalho S.M., de Oliveira L.C., Mansur H.S. - Superabsorbent crosslinked carboxymethyl cellulose-PEG hydrogels for potential wound dressing applications, International Journal of Biological Macromolecules **106** (2018) 1218-1234.

13. Seki Y., Altinisik A., Demircioğlu B., Tetik C. - Carboxymethylcellulose (CMC)–hydroxyethylcellulose (HEC) based hydrogels: synthesis and characterization, Cellulose **21** (2014) 1689-1698.

14. Dung T.T.P., Khanh V.B., Phuc H.N.H., Thao P.N.T., Dung T.L., Hau T.V., Tien H. V., Lam T.H., Giang H.N. - Gelation time characterization method for polyvinyl alcohol-based hydrogel, Science and Technology Development Journal **24** (2021) 2049-2057.

15. Cichosz S., Masek A. - IR Study on Cellulose with the Varied Moisture Contents: Insight into the Supramolecular Structure, Materials **13** (2020) 4573.

16. Oh S.Y., Yoo D.I., Shin Y., Seo G. - FTIR analysis of cellulose treated with sodium hydroxide and carbon dioxide, Carbohydrate Research **340** (2005) 417-428.

TÓM TẮT

CHẾ TẠO VÀ PHÂN TÍCH HYDROGEL TRÊN NỀN DẪN XUẤT CỦA CELLULOSE

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Vật liệu hydrogel đã được nghiên cứu chuyên sâu bởi nhiều nhóm nghiên cứu nhờ vào tiềm năng ứng dụng rộng rãi của chúng. Phương pháp tiếp cận xanh trong quá trình chế tạo hydrogel là sử dụng các polymer có nguồn gốc tự nhiên. Dẫn xuất của cellulose là ứng cử viên tiềm năng bởi vì tính tương thích sinh học và dễ dàng tiếp cận. Trong nghiên cứu này, hydroxypropyl methyl cellulose (HPMC), hydroxypropyl cellulose (HPC), hydroxyethyl cellulose (HEC) và sodium carboxymethyl cellulose (CMC or NaCMC) sẽ được nối ngang bằng glutaraldehyde để xác nhận khả năng chế tạo hydrogel trên nền cellulose. Khảo sát cho thấy HPMC không thích hợp do tín hiệu đo đạc thời gian gel thấp và hàm lượng gel nhỏ (~10%). Dung dịch CMC là mẫu duy nhất cho tín hiệu thời gian gel và có hàm lượng gel cao nhất (89%). CMC và HEC có độ hấp thụ nước tương đồng nhau (80-120%). HPC chỉ có thể hình thành gel (khâu mạng) với hàm lượng glutaraldehyde cao hơn và trạng thái hoàn toàn gel (100% hàm lượng gel) có thể đạt được. Tuy nhiên, lượng lớn nước hấp thụ (lên đến 2000%) đã được xác nhận với các mẫu trên nền HPC.

Từ khóa: Cellulose, hydrogel, polymer, thời gian gel, hàm lượng gel fraction, độ hấp thụ nước.