Carbohydrate Polymers 90 (2012) 1634–1641

Contents lists available at SciVerse ScienceDirect

Carbohydrate Polymers

journal homepage: www.elsevier.com/locate/carbpol

Preparation of pH- and ionic-strength responsive biodegradable fumaric acid crosslinked carboxymethyl cellulose

Emine Akar[a], Aylin Altınışık[b], Yoldaş Seki[b,*]

[a] Dokuz Eylül University, Graduate School of Natural and Applied Sciences, Department of Chemistry, 35160 Izmir, Turkey
[b] Dokuz Eylül University, Faculty of Science, Department of Chemistry, Kaynaklar Campus, 35160 Izmir, Turkey

ARTICLE INFO

Article history:
Received 30 March 2012
Received in revised form 10 July 2012
Accepted 16 July 2012
Available online 28 July 2012

Keywords:
Carboxymethylcellulose
pH-responsive
Biodegradability
Fumaric acid
Hydrogel

ABSTRACT

A novel biodegradable sodium carboxymethyl cellulose (NaCMC)-based hydrogel was synthesized by using fumaric acid (FA) as a crosslinking agent at various ratios. Hydrogels (CMCF) were characterized using Fourier transform infrared spectroscopy (FTIR), thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), X-ray diffraction analysis (XRD), scanning electron microscopy (SEM), and atomic force microscopy (AFM). Swelling behaviors of hydrogels were investigated in distilled water, various salt, and pH solutions. The FTIR results indicated the crosslinking between carboxyl groups of FA with hydroxyl group of NaCMC through ester formation. AFM analyses showed that roughness of hydrogel surface decreased with increasing crosslinker concentration. The swelling capacity decreased with an increase in charge of the metal cation ($Al^{3+} < Ca^{2+} < Na^{+}$). In order to investigate reversible pH sensitivity of CMCF hydrogels, pH-dependent swelling was studied at pH 2 and 10. Reversible pH-responsiveness of CMCF hydrogels was achieved. CMCF hydrogels containing the greatest ratio of FA exhibited the longest biodegradation time with a half life of 21 h using cellulase.

1. Introduction

Hydrogels are water-swollen polymeric networks containing chemical or physical crosslinks (Lowman & Peppas, 1999). Hydrogels responding to external stimuli such as heat, pH, electric field, and chemical environments, are often referred to as “intelligent” or “smart” hydrogels. These hydrogels have important applications in the field of medicine, pharmacy, and biotechnology (Hoffman, 2002; Sadeghi & Yarahmadi, 2011). Hydrogels used in tissue engineering are preferably biodegradable, thus further surgery, after the hydrogels has performed its function, is not required (Jin & Dijkstra, 2010). From the standpoint of applications, there is need to develop nontoxic, biodegradable hydrogels for biomedical applications without losing their smart properties, such as temperature sensitivity and/or pH sensitivity (Wu et al., 2008).

Cellulose and its derivatives are environmentally friendly, as they are degradable by several bacteria and fungi present in air, water, and soil (Tomsic, Simoncic, Orel, Vilcnik, & Vilcnik, 2007). Most water-soluble cellulose derivatives such as methylcellulose (MC), hydroxypropyl methylcellulose (HPMC), ethyl cellulose (EC), hydroxyethyl cellulose (HEC), and sodium carboxymethylcellulose (NaCMC) are obtained by etherification of cellulose. Among these cellulose ethers, only NaCMC is a polyelectrolyte, and thus a ‘smart’ cellulose derivative which shows sensitivity to pH and ionic strength variations (Flory, 1953; Sannino, Demitri, & Madaghiele, 2009).

It is well known that the effective swelling of cellulose-based hydrogels require a chemically crosslinked network that can be obtained by different paths (Benke, Takacs, Wojnarovits, & Borsa, 2007; Sannino & Nicolais, 2005). Esterification is one of them which can be achieved either by using formaldehyde based compounds, which are toxics, or by using alternative not dangerous esterification reagent (Zhou, Luner, & Caluwe, 1995). Fumaric acid (FA), which is biodegradable, non-toxic, and unsaturated dicarboxylic acid, has many potential industrial applications ranging from the manufacture of synthetic resins and biodegradable polymers to the production of intermediates for chemical syntheses (Moresi, Parente, Petruccioli, & Federici, 1991; Tao, Collier, Collier, & Negulescu, 1993).

Based on above-stated background, in this study, a new biodegradable hydrogel has been tried to synthesize by using NaCMC and fumaric acid. The hydrogels were characterized by Fourier transform infrared analysis (FTIR), scanning electron microscopy (SEM), X-ray diffraction analysis (XRD), thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), and atomic force microscopy (AFM). Swelling behaviors, pH sensitivity as well as biodegradability of hydrogels were also investigated.

---

[*] Corresponding author. Tel.: +90 232 4128656; fax: +90 232 4534188.
E-mail address: yoldas.seki@deu.edu.tr (Y. Seki).

0144-8617/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.carbpol.2012.07.043

2. Materials and methods

2.1. Material

Carboxymethylcellulose sodium salt low viscosity (C5678-500G) was purchased from Sigma–Aldrich. Fumaric acid (99%) was obtained from Sigma–Aldrich. HCl, NaCl, $AlCl_3$, $CaCl_2$ were purchased from Reidel de Haen. Cellulase (280,000 CMU/g) was supplied from Dyestar Company.

2.2. Synthesis of hydrogel

Appropriate amount of NaCMC was dissolved in 15 mL distilled water at room temperature. Various ratios (0.01, 0.03, and 0.05 M) of FA was added to solution and stirred until FA was dissolved. The pH of mixture was lowered using HCl solution and stirred for 23 h at room temperature. Then mixture was poured into a petri dish and dried for 8 h in a vacuum oven at 60 °C. Dried film was washed with distilled water to remove remnant Cl^- ions. Afterwards, the wet film was dried at room temperature for one day.

2.3. Fourier transform infrared spectroscopy (FTIR) analysis

FTIR spectra of samples were analyzed using FTIR (Perkin Elmer Spectrum BX-II) to analyze the chemical structure of the NaCMC, FA, and CMCF hydrogels. The spectra were recorded with the sum of 25 scans at a resolution of 4 cm^{-1} in the range 4000–400 cm^{-1}.

2.4. X-ray diffraction analysis (XRD)

X-ray diffraction analysis was conducted by using PW3050/60 X-Pert Pro Diffractometer Philips PW3050/60 X-Pert Pro Diffractometer with Ni-filtered Cu Kα radiation ($\lambda = 1.54$ Å). The analysis was determined between 5° and 50° (2θ angle range) at 45 kV. The scan time and the step size were 10 s and 0.033°, respectively.

2.5. Scanning electron microscopy (SEM)

The morphology of the CMCF hydrogels was determined using a scanning electron microscope (FEI Quanta FEG 250 SEM) operating at the accelerating voltage of 20 kV. Before conducting the SEM analysis, dried hydrogels were gold sputter-coated.

2.6. Atomic force microscope (AFM)

AFM measurements were carried out by using Multimode SPM (AFM/STM) Nanoscope IV from Digital Instrument in a tapping mode with Si cantilever ($f = 330$–359 kHz) at room temperature. Measurements were performed thrice on different zones of each sample.

2.7. Thermogravimetric analysis (TGA)

Thermal behavior of CMCF hydrogels was determined by using TGA (Shimadzu, TGA 50). Thermogravimetric analysis (TGA) was performed at a heating rate of 10 °C/min range from 30 to 600 °C under nitrogen atmosphere with a flow rate of 1.0 mL/min.

2.8. Differential scanning calorimetry (DSC)

DSC analyses of CMCF hydrogels were carried out by Perkin Elmer Diamond DSC at a heating rate of 10 °C/min in the range of 40–400 °C under nitrogen atmosphere.

Table 1
Swelling kinetic values for CMC1F, CMC3F, CMC5F hydrogels.

Sample	k (1/min %)	W_∞ (%)
CMC1F	0.12	288
CMC3F	0.24	233
CMC5F	0.19	164

2.9. Swelling studies

A certain amount of dry sample was immersed in excessive aqueous solutions at 25 °C. The samples were removed from the water at pre-determined time intervals and surface water was removed by using filter paper. The swollen hydrogels were weighted and the degree of swelling was measured by the following equation:

$$S\ (\%) = \frac{W_t - W_0}{W_0} \times 100 \qquad (1)$$

where S is the equilibrium water absorbency (%), W_t and W_0 are the weight of swollen hydrogel at time t and dry hydrogel, respectively.

2.10. Assessment of biodegradability

Enzymatic degradation was carried out using cellulase enzyme (cellulase 5%, Sorbitol 28%) in an acetate buffer, pH 5 at 37 °C. The concentration of cellulase enzyme in an acetate buffer was 0.1 mg/mL. About 20 mg of dried film of CMC hydrogel was immersed in the cellulase solution (2.0 mL) at pre-determined time. After the incubation, the samples were dried at 25 °C. After the enzymatic degradation, remaining weight of samples was calculated:

$$\text{Weight loss}\ (\%) = \left(1 - \frac{W_1}{W_0}\right) \times 100 \qquad (2)$$

where W_0 and W_1 are the weight of gel films before and after enzymatic degradation tests, respectively (Wach, Mitomo, Yoshii, & Kume, 2001).

3. Results and discussion

3.1. Swelling kinetics

Water swelling kinetics for CMC1F, CMC3F, and CMC5F which contain 0.01, 0.03, and 0.05 M FA, respectively, was given in Fig. 1a. As can be seen from Fig. 1a the lower FA concentration, the greater swelling in hydrogel was observed. It is an expected result because it is generally known that the swelling increases with decreasing crosslinking points (Bucholz & Graham, 1997). The swelling kinetics of hydrogels was investigated by the following equation:

$$\frac{t}{W} = \frac{1}{kW_\infty^2} + \frac{t}{W_\infty} \qquad (3)$$

where W and W_∞ are the degree of swelling at time t and equilibrium water content, respectively, and k is the rate constant (Katime, Valderruten, & Quintana, 2001). Straight line plots of t/W versus t show a good fit ($R^2 = 0.99$). It can be said that swelling process is governed by the second order kinetic model. W_∞ (%) values are 288, 233, and 164 for CMC1F, CMC3F, and CMC5F, respectively. The results were summarized in Table 1. Equilibrium swelling capacity of CMCF hydrogels decreased with increasing FA concentration in hydrogel. The equilibrium swelling degree of CMCF adversely depends on crosslinker concentration. Less crosslinked polysaccharide chains are freer in gel network and the fixed negative charges, i.e., COO^- moieties; cause chain stiffening and absorption of large amount of water (Barbucci, Magnani, & Consumi, 2000).

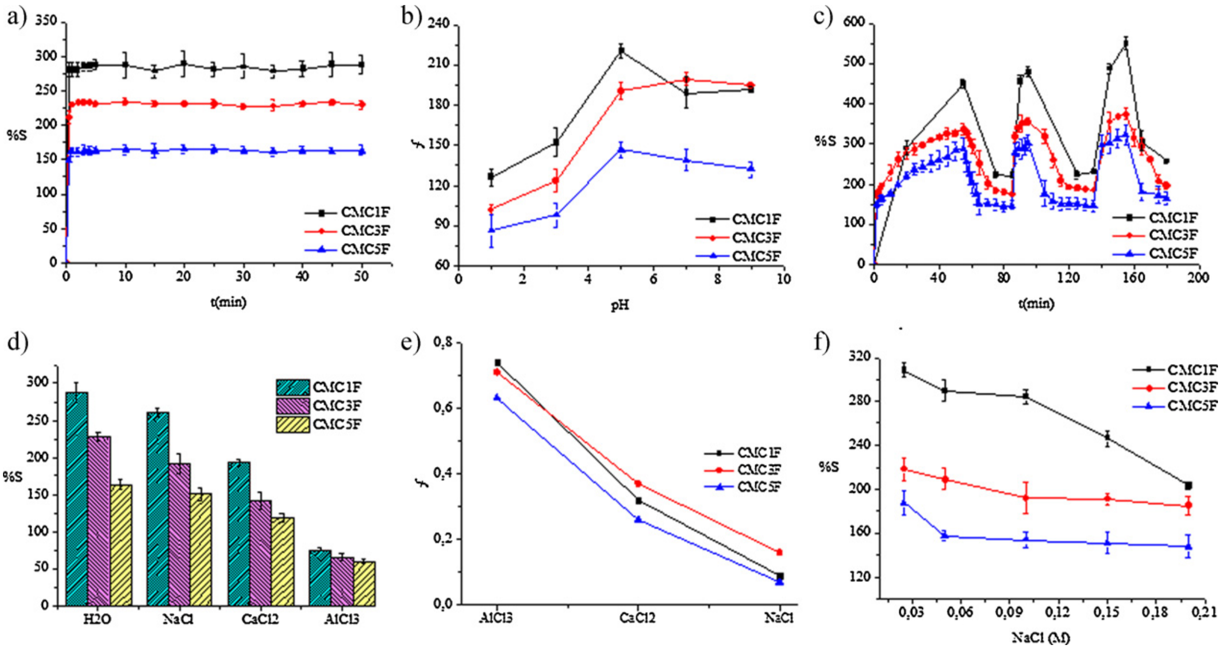

Fig. 1. Swelling properties of hydrogels (a) water swelling for the CMCF hydrogels using different amount of FA at 25 °C, (b) pH sensitivity of CMCF hydrogels using different amounts of FA at 25 °C, for 180 min, (c) reversible swelling of CMCF hydrogels at pH 2 and pH 10 at 25 °C, (d) water absorbency for CMCF hydrogels in salt solutions (0.15 M) at 25 °C, (e) salt sensitivity factors (*f*) of CMC hydrogels, and (f) swelling of CMCF hydrogel in different NaCl concentrate solution at 25 °C for 180 min.

3.2. *pH sensitivity and pulsatile behavior*

In order to determine whether CMCF hydrogels exhibit pH sensitivity, variation of water absorption at different external buffer solutions (pH 1–10) was observed and relation was shown in Fig. 1b. The maximum swelling was observed for CMC1F, CMC3F, and CMC5F at about pH 5, pH 7, and pH 5, respectively. Until these pH values, an increase in swelling was observed with the increasing of pH values. Beyond those pH values, swelling values started to go down. Since NaCMC has carboxylic acid groups (COO^-), at higher pH values, greater than the pK_a of carboxylic groups (pK_a 4–5), the carboxylic acid groups become deprotonated and the electrostatic repulsive forces between negatively charged sites (COO^-) bring about enhancement in swelling. At low pH values, because protonation of carboxylate anions takes place, repulsive forces between carboxylate anions disappear and consequently swelling values are decreased. At pH 10, an increase in swelling results from electrostatic repulsive force between the charged sites (COO^-) as a result of becoming completely ionized of carboxylic acid groups (Pourjavadi, Barzegar, & Mahdavinia, 2006). Moreover, it can be added that decreasing of water absorption with increasing the concentration of crosslinker agent, FA, is more apparent at low pH values. In order to investigate pH swelling reversibility of CMCF hydrogels, pH-dependent studies were alternatively conducted at two pH values, 2 and 10. Swelling reversibility of CMCF hydrogels can be seen in Fig. 1c. It is seen that swelling of CMCF hydrogels demonstrated that pH-dependence occurs reversibly and relatively fast. At pH 10 CMCF hydrogel swells because of anion–anion repulsive forces and shrinks at pH 2 due to “screening effect” of excess cations (Pourjavadi, Sadeghi, & Hosseinzadeh, 2004). In case of higher hydrogen ion concentration (at low pH) in solution, hydrogen ions, mobile cations, shield the repulsive fixed anions on the polymer backbone, thus decreasing the swelling capacity (Kabiri, Zohuriaan-Mehr, Mirzadeh, & Kheirabadi, 2009).

3.3. *Effect of salt solution on water absorbency*

Water absorbency of CMCF hydrogels in salt solutions (0.15 M NaCl, $CaCl_2$, and $AlCl_3$ solutions) are given in Fig. 1d. The swelling of the CMCF hydrogels in saline solutions was distinctly decreased when compared to the values measured in deionized water. This well-known phenomenon was commonly observed in the swelling

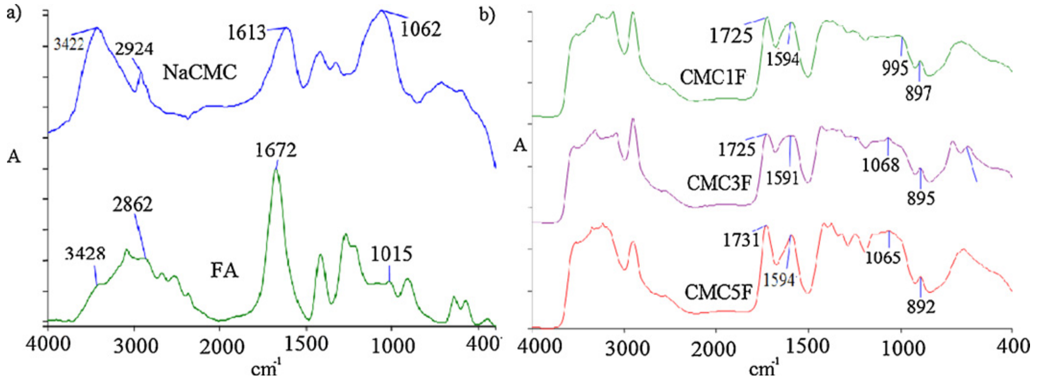

Fig. 2. FTIR spectra of hydrogels (a) FTIR spectra of NaCMC and FA and (b) FTIR spectra of CMC1F, CMC3F, and CMC5F.

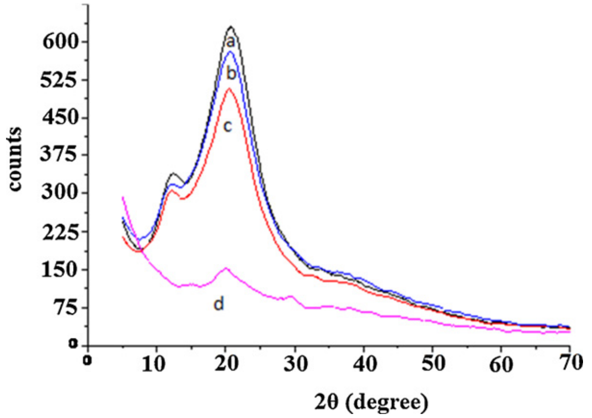

Fig. 3. XRD analyses of the samples (a) CMC1F, (b) CMC5F, (c) CMC3F, and (d) NaCMC.

of ionic hydrogels (Zhao, Su, Fang, & Tan, 2005). As can be seen from Fig. 1d, the swelling capacity decreased with an increase in charge of the metal cation ($Al^{3+} < Ca^{2+} < Na^{+}$). This can be revealed by taking complexing ability arising from the coordination of the multivalent cations with carboxylate groups of the hydrogel into consideration (Pourjavadi et al., 2006).

A dimensionless salt sensitivity factor (f) for 0.15 M salt solution was calculated by the following equation (Pourjavadi et al., 2006)

$$f = 1 - \left(\frac{S_g}{S_d}\right) \tag{4}$$

where S_g is the swelling in a given fluid, S_d is the swelling in deionized water. The variations of the dimensionless salt sensitivity factor (f) with the type of salt solution are given in Fig. 1e. The lower f values becomes, the lower salt sensitivity is observed. As shown in Fig. 1e, f values increase with increasing in charge of the metal cation ($Na^{+} < Ca^{2+} < Al^{3+}$). In other words, 0.15 M $AlCl_3$ salt solution shows the greatest salt sensitivity owing to coordination of the multivalent cations with carboxylate groups of the hydrogel (Pourjavadi et al., 2006).

The effect of salt concentration on swelling degree of CMCF hydrogels was also investigated. Swelling behavior of CMCF hydrogels in various NaCl concentrations is presented in Fig. 1f which shows that water absorbency decreased with increasing crosslinker concentration in NaCl solutions. Hydrogel structure becomes stiff with increasing crosslinker concentration so absorb less water. It is known that there is a balance between the osmotic pressure, which results from the difference between the mobile ion concentrations between the interior of the hydrogel network and the external immersion medium, of the swelling system and elastic response of the CMCF hydrogels controlling the swelling degree. With the

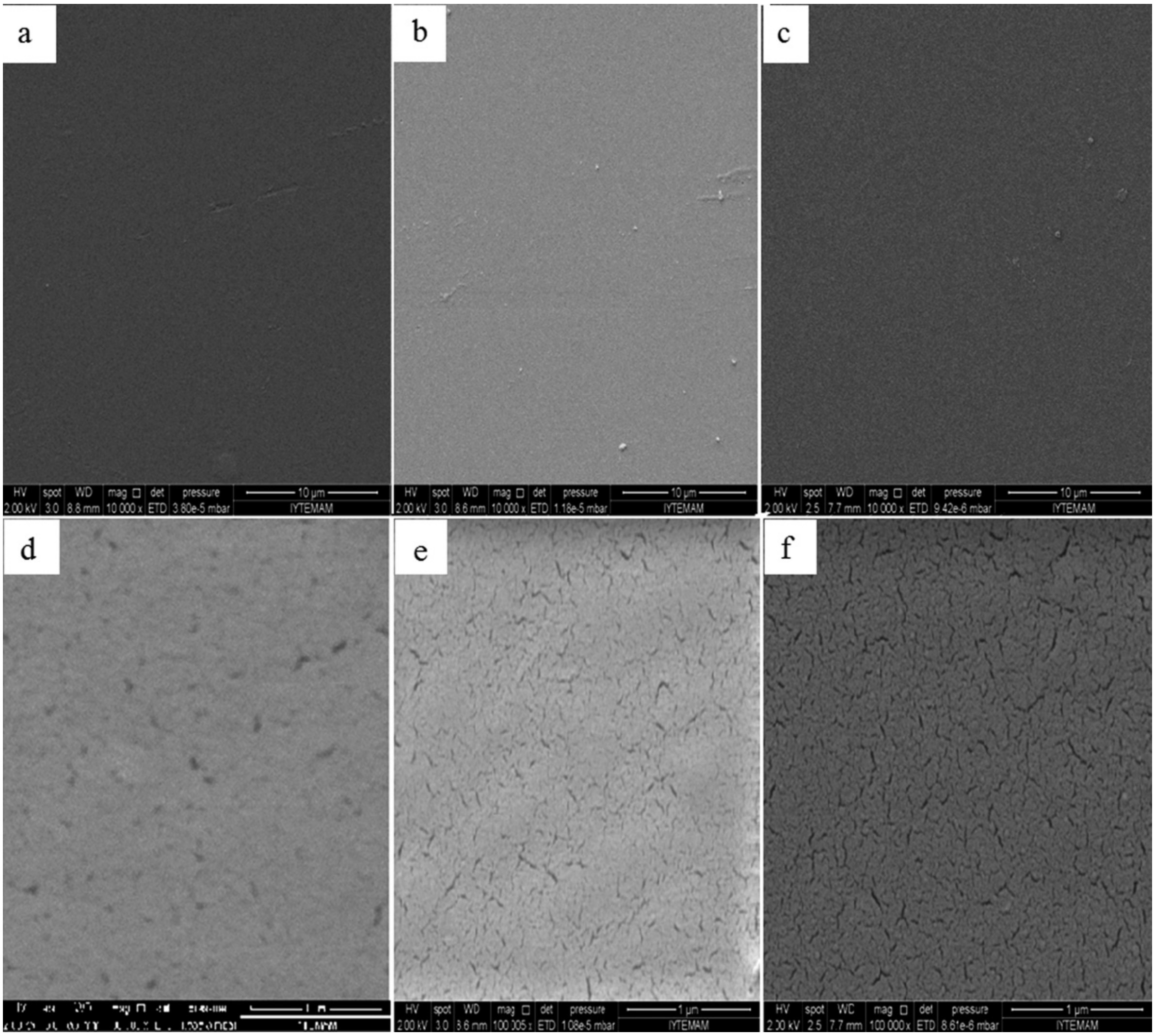

Fig. 4. Scanning electron microscopy of CMC1F (a and d) CMC3F (b and e) CMC5F (c and f). (a–c) and (d–f) were magnified 10^4 and 10^5 times, respectively.

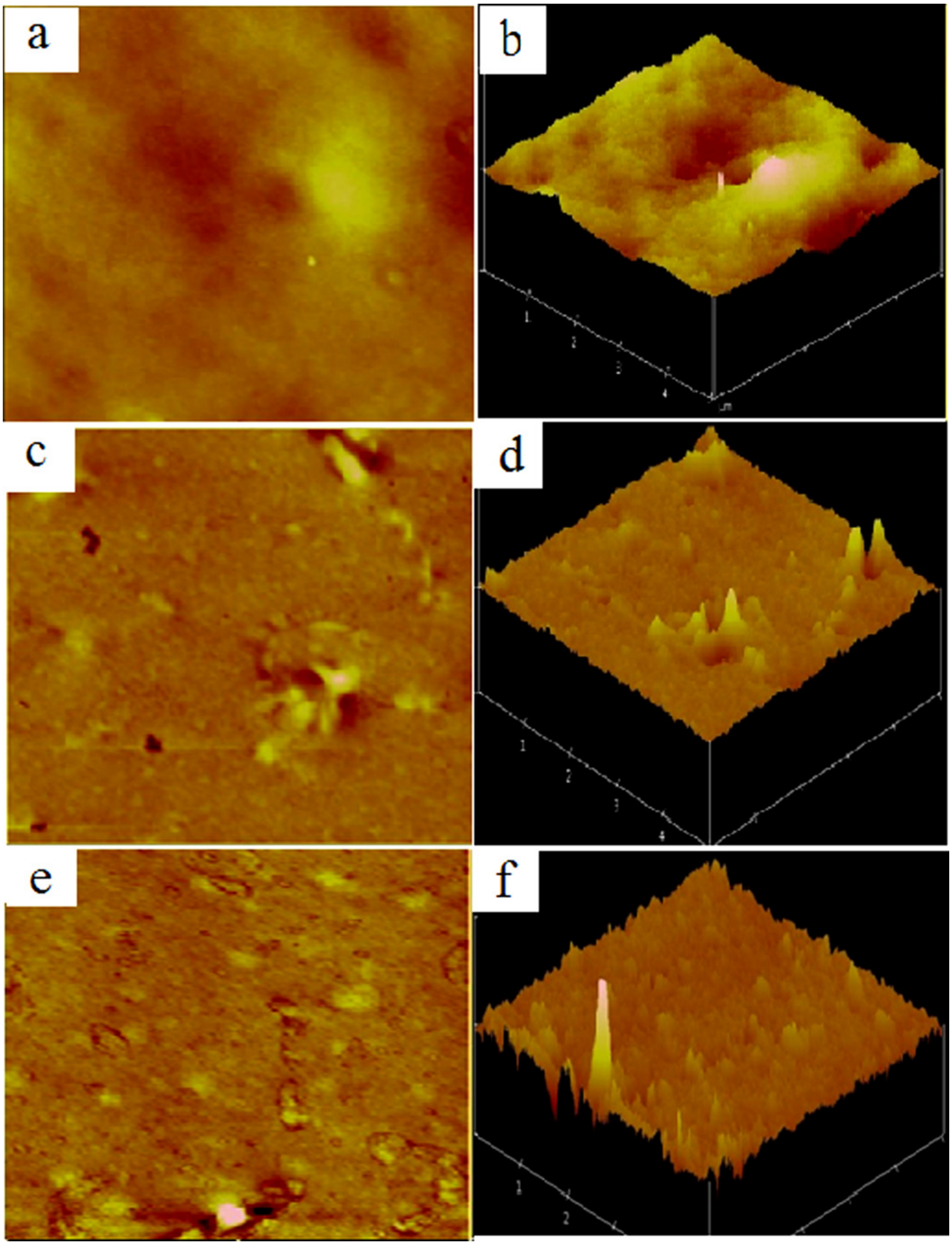

Fig. 5. AFM images of CMC1F (a and b), CMC3F (c and d), and CMC5F (e and f).

increasing of ionic concentration, the mobile ion concentration difference between polymer gel and external medium decreases, as a result of which gel volume reduces and gel shrinks (Bajpai & Giri, 2003). On the other side, it is probable that increase in salt concentration in swelling solution may cause ionic crosslink, thereby decreasing swelling capacity of hydrogel. Feng and Pelton's study verifies this relation, that is, adverse effect of ionic crosslinking on swelling degree of hydrogel (Feng & Pelton, 2007).

3.4. *FTIR analysis*

The FTIR spectra of the FA, NaCMC and CMC1F, CMC3F, CMC5F are shown in Fig. 2a and b, respectively. In the spectrum of NaCMC a broad absorption band at $3422\,\text{cm}^{-1}$ is owing to the stretching frequency of the hydroxyl group (—OH). The band at $2924\,\text{cm}^{-1}$ is due to C—H stretching vibration. The strong absorption band at $1613\,\text{cm}^{-1}$ confirmed the presence of carboxyl group (—COO). The band $1062\,\text{cm}^{-1}$ is due to $>$CH—O—CH$_2$ stretching (Biswall & Singh, 2004; Heydarzadeh, Najafpour, & Nazari-Moghaddam, 2009). Strong hydrogen bonding is evidenced by the broad features about $3400\,\text{cm}^{-1}$ from the OH group. The carbonyl stretches give rise to an unsymmetrical band centered at $1707\,\text{cm}^{-1}$. The C=C stretch is seen strongly at $1630\,\text{cm}^{-1}$ (Nájera, Percival, & Horn, 2009). The strong absorption band at $1613\,\text{cm}^{-1}$ of NaCMC shifted to $1594\,\text{cm}^{-1}$ in the samples of FA crosslinked NaCMC (for CMC1F and CMC5F). As seen in the spectrum of CMC1F, the characteristic band of C=O vibrations of the esterified carboxylic groups is seen at about $1725\,\text{cm}^{-1}$. This shows the presence of the ester linkage. As a consequence, an acid catalyzed esterification reaction occurs. In the spectrum of CMC3F, hydrogel exhibits absorption bands at about

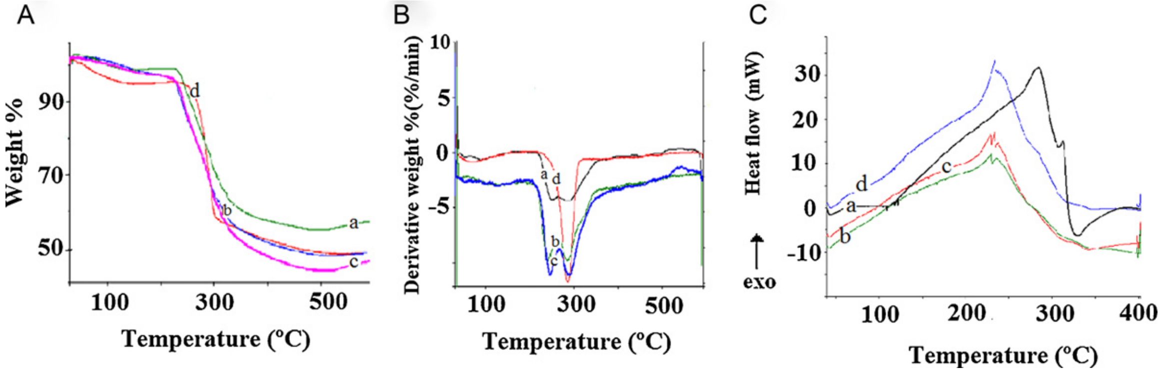

Fig. 6. (A) Thermogravimetric curves of CMC1F (a), CMC3F (b), CMC5F (c), and NaCMC (d); (B) DTG curves of CMC1F (a), CMC3F (b), CMC5F (c), and NaCMC (d); (C) DSC curves of NaCMC (a), CMC1F (b), CMC3F (c), and CMC5F (d).

$1725\,\text{cm}^{-1}$, $1068\,\text{cm}^{-1}$, and $895\,\text{cm}^{-1}$, which may be attributed to C═O, C—O stretching, and ═CH out-plane bending vibrations of ester group implying the presence of the ester linkage and unsaturated double bond (Rhim, Lee, & Kim, 2002). Similar findings were observed in the spectrum of CMC5F as well.

3.5. *X-ray diffraction analysis*

The X-ray diffraction (XRD) patterns of the NaCMC, CMC1F, CMC3F, and CMC5F are shown in Fig. 3. The pattern of NaCMC in Fig. 3 indicated a single peak at $2\theta = 20.03^\circ$ associated with low crystallinity of NaCMC structure. The patterns of CMC1F, CMC3F, and CMC5F exhibit two peaks, one of which located at $2\theta = 20.69^\circ$, 20.49°, and 20.45°, respectively, which indicate higher 2θ degrees than NaCMC. The other one was located at 2θ values of 12.37°, 12.27°, and 12.20° for CMC1F, CMC3F, and CMC5F, respectively. From these results it is seen that 2θ values decreased with increasing FA concentration.

Based on X-ray diffraction measurements made by Xiao and Gao, the crystallinity of CMC/poly(vinyl alcohol) (PVA) is lower than that of CMC, which was attributed to hydrogen bonds between carboxylic groups of CMC and hydroxyl groups of PVA, thus hindering the crystallization of the components (Xiao & Gao, 2008). Contrary to the Xiao's study, crystallinity of CMCF hydrogel, in this study, is greater than that of CMC. This may be due to chemically crosslinking of CMC with FA, which causes more ordered structure.

3.6. *SEM analysis*

SEM images of the hydrogels are shown in Fig. 4 at 10,000× and 100,000× magnifications. It can be noted that SEM images show homogenous structure for all CMCF hydrogels even at greater magnifications (100,000×). Surface morphologies of hydrogels at 10,000× magnification exhibited continuous structure without any cracks or pores. As shown in Fig. 4a–c, all hydrogels demonstrated smooth surface structures. This observation is similar to the surface of pullulan, alginate, CMC and pullulan/alginate/CMC films, as reported by Tong, Xiao, and Lim (2008). As demonstrated in Fig. 4d–f, however, at greater magnification (100,000×) cracks in all hydrogels can be noticeable.

3.7. *AFM analysis*

AFM images were taken to investigate surface morphology of hydrogels and determine the effect of crosslinker concentration on hydrogel surface roughness. AFM images of hydrogels have been shown in Fig. 5. Rms (root mean square) values of the roughness were calculated from the image of square $5\,\mu\text{m} \times 5\,\mu\text{m}$. On average, the rms values of CMC1F, CMC3F, and CMC5F are 2.78, 0.93, and 0.77 nm, respectively. AFM measurements show that rms (nm) is related with crosslinker concentration. Besides, as the crosslinker concentration increases the roughness of hydrogel decreases. Harada et al. (2005) confirmed this relation by observing that the surface became smooth as the amount of $Al(OH)_3$ (crosslinker) was increased. The domain structure would be reduced when the crosslinking density is increased, which is consistent with the present observation (Abe, Murase, & Suzuki, 1997, chap. 3).

3.8. *TGA analysis*

The TG/DTG curves of NaCMC, CMC1F, CMC3F, and CMC5F are shown in Fig. 6A and B. NaCMC has weight loss at two stages, one of which is due to presences of small amount of moisture in the sample (Biswall & Singh, 2004). Second stage is due to thermal degradation of CMCF hydrogels. It has been observed that the

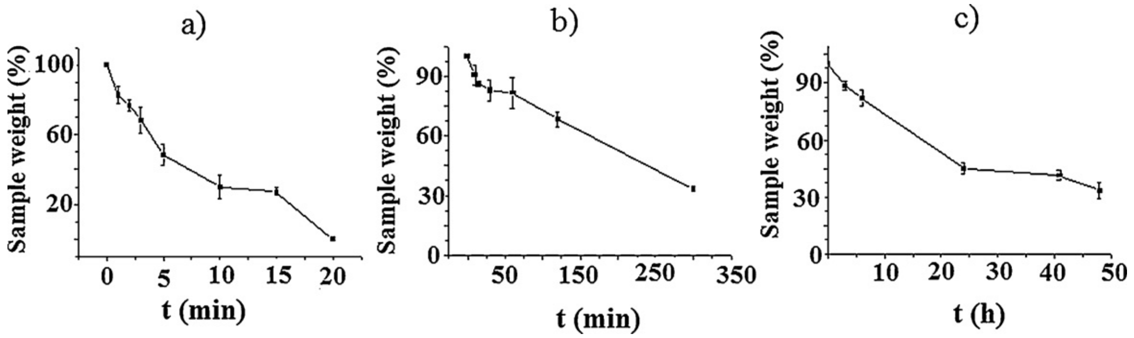

Fig. 7. Biodegradation of crosslinked CMC by the cellulase enzyme in an acetate buffer (pH 5) (a) CMC1F, (b) CMC3F, and (c) CMC5F.

degradation, which has been obtained to occur in a single step, of sodium carboxy-methyl cellulose started at about 200 °C and attains a maximum at 285 °C where the mass loss is due to the loss of CO_2 from the polysaccharide. As there are COO^- group in the case of CMC, it is decarboxylated in this temperature range (Biswall & Singh, 2004).

There are two steps for the degradation of CMCF hydrogels. First shoulder may be due to degradation of FA in hydrogel. Second shoulder is due to the loss of CO_2 from decarboxylation of CMC. The maximum degradation temperatures for CMC1F, CMC3F, and CMC5F were obtained to be 293, 289, and 294 °C, respectively. Crosslinking of CMC with FA led to slightly increase in the maximum degradation temperature.

3.9. DSC analysis

The DSC analysis of CMC1F, CMC3F, and CMC5F are shown in Fig. 6C. There are distinct peaks in DSC curves of hydrogel, which may be due to the decomposition of main chain of hydrogel (Biswall & Singh, 2004). DSC curve of NaCMC showed one main exothermic peak, at around 284.5 °C, and a small exothermic peak, at around 313.2 °C, which can be attributed to thermal degradation of the carboxylate ion and C—O—C ethers of six membered backbone chain of NaCMC (Kim, 2007). After crosslinking of CMC with FA at the concentrations of 0.1, 0.3, and 0.5, the main decomposition peak decreased to 229.2, 229.1, and 234.0 °C, respectively. Similar results were also obtained by Kim (2007).

3.10. Biodegradation

Glycosidic linkages bonding polysaccharide rings are convenient to biodegradation by microorganisms and hydrolytic enzymes (Wach et al., 2001). The enzymatic degradation, expressed as percentage weight loss, is presented in Fig. 7. As can be seen from Fig. 7a–c, weight loss values increased with an increase in time. The times required to reach 50% weight loss for CMC1F, CMC3F, and CMC5F are 5 min, 213 min, and 21 h, respectively. It is seen that crosslinker concentration affected the half life of degradation of CMCF hydrogels. Lower crosslinked hydrogel degraded faster than other samples that crosslinked more tightly by higher energy since the number of intermolecular bonds is far greater in the sample having greater crosslink density (Wach et al., 2001). Therefore it may be worth noting that NaCMC and FA based hydrogels, produced in this study, exhibit biodegradable property.

4. Conclusion

A novel biodegradable carboxymethylcellulose and fumaric acid-based hydrogel was synthesized and characterized in this study. FTIR spectroscopy confirmed that the ester linkage formed as a result of crosslinking between NaCMC and FA. AFM images showed that roughness of hydrogel decreased with an increase in crosslinker concentration. The hydrogel containing the lowest ratio of FA showed the greatest swelling capacity. The reversible pH-dependent swelling behavior of CMCF hydrogels was observed. Besides, ionic strength distinctly affected swelling capacity of hydrogels. SEM images showed homogenous structure for all hydrogel samples. From XRD peaks it was inferred that crosslinking of carboxymethylcellulose with fumaric acid induced a more ordered structure in hydrogel. TGA analysis indicated that after the crosslinking of CMC with FA, slightly increase in the maximum degradation temperatures came into existence. The greater FA content in CMCF hydrogels, the longer biodegradation time was obtained. From this study it can be offered that CMC-FA based hydrogels may be used for bioengineering applications in which selective degradability may be beneficial such as scaffold fabrication or controlled release systems.

Acknowledgments

The authors thank to Prof Dr. Yavuz Ergün (Dokuz Eylul University), Ebru Bozacı (Ege University), Dr. Mehmet Akif Ezan (Dokuz Eylul University) for their assistance.

References

Abe, M., Murase, N., & Suzuki, T. (Eds.). (1997). *Geltechnology*. Tokyo: Science Forum Inc.

Bajpai, A. K., & Giri, A. (2003). Water sorption behaviour of highly swelling (carboxymethylcellulose-g-polyacrylamide) hydrogels and release of potassium nitrate as agrochemical. *Carbohydrate Polymers*, *53*(3), 271–279.

Barbucci, R., Magnani, A., & Consumi, M. (2000). Swelling behavior of carboxymethylcellulose hydrogels in relation to crosslinking, pH, and charge density. *Macromolecules*, *33*(20), 7475–7480.

Benke, N., Takacs, E., Wojnarovits, O. L., & Borsa, J. (2007). Pre-irradiation grafting of cellulose and slightly carboxymethylated cellulose (CMC) fibres. *Radiation Physics and Chemistry*, *76*, 1355–1359.

Biswall, D. R., & Singh, R. P. (2004). Characterisation of carboxymethyl cellulose and polyacrylamide graft copolymer. *Carbohydrate Polymers*, *57*, 379–387.

Bucholz, F. L., & Graham, A. T. (1997). *Modern superabsorbent polymer technology*. New York: Wiley.

Feng, X., & Pelton, R. (2007). Polyvinylamine complex hydrogel swelling. *Macromolecules*, *40*, 1624–1630.

Flory, P. J. (1953). *Principles of polymer chemistry*. Ithaca, NY, USA: Cornell University Press.

Harada, T., Hirashima, Y., Suzuki, A., Goto, M., Kawamura, N., & Tokita, M. (2005). Synthesis, swelling behavior and surface microstructure of poly (sodium acrylate) gels cross-linked by aluminum ions. *European Polymer Journal*, *41*(2005), 2189–2198.

Heydarzadeh, H. D., Najafpour, G. D., & Nazari-Moghaddam, A. A. (2009). Catalyst-free conversion of alkali cellulose to fine carboxymethyl cellulose at mild conditions. *World Applied Sciences Journal*, *6*(4), 564–569.

Hoffman, A. S. (2002). Hydrogel for biomedical applications. *Advanced Drug Delivery Reviews*, *54*, 3–12.

Jin, R., & Dijkstra, P. J. (2010). *Hydrogels for tissue engineering applications* (pp. 203–225). *Biomedical applications of hydrogels handbook*.

Kabiri, K., Zohuriaan-Mehr, M. J., Mirzadeh, H., & Kheirabadi, M. (2009). Solvent-, ion- and pH-specific swelling of poly(2-acrylamido-2-methylpropane sulfonic acid) superabsorbing gels. *Journal of Polymer Research*, *17*, 203–212.

Katime, I., Valderruten, N., & Quintana, J. R. (2001). Controlled release of aminophylline from poly (N-isopropylacrylamide-co-itaconic acid hydrogels). *Polymer International*, *50*, 869–874.

Kim, J. (2007). Thermal characteristics and degradation kinetics of cross-linked carboxymethyl cellulose sodium salt. *EJEAFChe*, *6*, 2458–2472.

Lowman, A. M., & Peppas, N. A. (1999). Hydrogels. In E. Mathiowitz (Ed.), *Encyclopedia of controlled drug delivery* (pp. 397–418). New York: Wiley.

Moresi, M., Parente, E., Petruccioli, M., & Federici, F. (1991). Optimization of fumaric-acid production from potato flour by Rhizopus arrhizus. *Applied Microbiology and Biotechnology*, *36*, 35–39.

Nájera, J. J., Percival, C. J., & Horn, A. B. (2009). Infrared spectroscopic studies of the heterogeneous reaction of ozone with dry maleic and fumaric acid aerosol particles. *Physical Chemistry Chemical Physics*, *11*, 9093–9103.

Pourjavadi, A., Barzegar, Sh., & Mahdavinia, G. R. (2006). MBA-crosslinked Na-Alg/CMC as a smart full-polysaccharide superabsorbent hydrogels. *Carbohydrate Polymers*, *66*(3), 386–395.

Pourjavadi, A., Sadeghi, M., & Hosseinzadeh, H. (2004). Modified carrageenan. 5: Preparation, swelling behavior, salt- and pH-sensitivity of partially hydrolyzed crosslinked carrageenan-graft-polymethacrylamide superabsorbent hydrogel. *Polymer Advance Technologies*, *15*, 645–653.

Rhim, J. W., Lee, S. W., & Kim, Y.-K. (2002). Pervaporation separation of water–ethanol mixtures using metal-ion-exchanged poly(vinyl alcohol) (PVA)/sulfosuccinic acid (SSA) membranes. *Journal of Applied Polymer Science*, *85*, 1867–1873.

Sadeghi, M., & Yarahmadi, M. (2011). Synthesis and properties of carboxymethylcellulose (CMC) graft copolymer with on–off switching properties for controlled release of drug. *African Journal of Biotechnology*, *10*(56), 12085–12093.

Sannino, A., Demitri, C., & Madaghiele, M. (2009). Biodegradable cellulose-based hydrogels: Design and applications. *Materials*, *2*, 353–373.

Sannino, A., & Nicolais, L. (2005). Concurrent effect of microporosity and chemical structure on the equilibrium sorption properties of cellulose-based hydrogels. *Polymer*, *46*, 4676–4685.

Tao, W. Y., Collier, J. R., Collier, B. J., & Negulescu, I. I. (1993). Fumaric acid as an adhesion promoter in rayon/nylon composite fibers. *Textile Research Journal*, *63*, 162–170.

Tomsic, B., Simoncic, B., Orel, B., Vilcnik, A., & Spreizer, H. (2007). Biodegradability of cellulose fabric modified by imidazolidinone. *Carbohydrate Polymer*, *69*(3), 478–488.

Tong, Q., Xiao, Q., & Lim, L. T. (2008). Preparation and properties of pullulan–alginate–carboxymethylcellulose blend films. *Food Research International*, *41*, 1007–1014.

Wach, R., Mitomo, H., Yoshii, F., & Kume, F. (2001). Hydrogel of biodegradable cellulose derivatives. II: Effect of some factors on radiation-induced crosslinking of CMC. *Journal of Applied Polymer Science*, *81*, 3030–3037.

Wu, D., Sun, Y., Xu, X., Cheng, S., Zhang, X., & Zhuo, R. (2008). Biodegradable and pH-sensitive hydrogels for cell encapsulation and controlled drug release. *Biomacromolecules*, *9*(4), 1155–1162.

Xiao, C., & Gao, Y. (2008). Preparation and properties of physically crosslinked sodium carboxymethylcellulose/poly(vinyl alcohol) complex hydrogels. *Journal of Applied Polymer Science*, *107*, 1568–1572.

Zhao, Y., Su, H. J., Fang, L., & Tan, T. W. (2005). Superabsorbent hydrogels from poly (aspartic acid) with salt-, temperature- and pH-responsiveness properties. *Polymer*, *46*, 5368–5376.

Zhou, Y. J., Luner, P., & Caluwe, P. (1995). Mechanism of crosslinking of papers with polyfunctional carboxylic acids. *Journal of Applied Polymer Science*, *58*, 1523–1534.