Carbohydrate Polymers 78 (2009) 725–730

Contents lists available at ScienceDirect

Carbohydrate Polymers

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

Characterization and in vitro evaluation of starch based hydrogels as carriers for colon specific drug delivery systems

A. El-Hag Ali [a,b,*], Abdullah AlArifi [a]

[a] Faculty of Science, King Saud University, Riyadh 11451, Kingdom of Saudi Arabia
[b] National Center for Radiation Research and Technology, B.O. Box 29, Nasr City, Cairo, Egypt

ARTICLE INFO

Article history:
Received 19 April 2009
Received in revised form 2 June 2009
Accepted 9 June 2009
Available online 14 June 2009

Keywords:
pH-sensitive
Starch
Methacrylic acid
Hydrogel
γ-Irradiation
Swelling kinetics
Drug release

ABSTRACT

A series of starch/methacrylic acid (MAAc) copolymer hydrogels of different compositions were synthesized using γ-rays induced polymerization and crosslinking. The effects of the preparation conditions such as the feed solution concentration, feed solution composition and irradiation dose on the gelation process of the synthesized copolymer were investigated. The swelling behavior of the starch/methacrylic acid (MAAc) copolymer hydrogels was characterized by studying the effect of the hydrogel composition on the time- and pH-dependent swelling. Swelling kinetics showed that the synthesized hydrogels possessed Fickian diffusion behavior at pH 1 and non-Fickian diffusion at pH 7 which recommend them as good candidate for colon specific drug delivery systems. The synthesized hydrogels were loaded with ketoprofen as a model drug to investigate the release behavior of the synthesized hydrogels. The results showed the ability of the hydrogels to keep the loaded drug at pH 1 and release it at pH 7. The data also showed that the release rate can be controlled by controlling the preparation conditions such as comonomer concentration and composition and irradiation dose.

© 2009 Elsevier Ltd. All rights reserved.

1. Introduction

Nowadays, great emphasis is placed on controlling the rate and/or site of drug release from oral formulations for the purposes of improving patient compliance and treatment efficacy (Pedro, Albuquerque, Ferreira, & Sarmento, 2009; Thakur, Chauhan, & Ahn, 2009; Chen, Liu, & Chen, 2009; Chen et al., 2009). The colon is one area that would benefit from the development and use of such modified release technologies. Targeted drug delivery to the colon would therefore ensure direct treatment at the disease site, lower dosing and fewer systemic side effects. In addition to local therapy, the colon can also be utilized as a portal for the entry of drugs into the systemic circulation. For example, molecules that are degraded/poorly absorbed in the upper gut, such as peptides and proteins, may be better absorbed from the more benign environment of the colon. Oral colonic delivery systems should retard drug release in the stomach and allow complete release in the colon (Silva, Gurruchaga, & Goñi, 2009). The fact that such a system will be exposed to a diverse range of gastrointestinal conditions on passage through the gut makes colonic delivery via the oral route a challenging proposition. The most commonly used targeting mechanisms are; pH-dependent delivery (Wang et al., 2009) and time-dependent delivery (Maroni et al., 2009).

Stimuli-responsive polymers have recently been developed to regulate the degree of swelling of polymers in relation to external environmental conditions. pH-sensitive hydrogel is one of such responsive polymers (Han, Wang, Yang, & Nie, 2009). pH-sensitive hydrogel drug delivery systems have attracted significant attention recently. In addition to their inertness and good biocompatibility, they are able to deliver entrapped drugs to the colon. These polymeric hydrogels are insensitive to the acidic conditions of the stomach and start to swell and consequently release the loaded drugs at the higher pH environment of the colon (Chen et al., 2009; Chen, Liu et al., 2009). The ease of regulating the drug release by controlling water swelling and crosslinking density make hydrogels particularly suitable as drug carriers in the controlled release of pharmaceuticals (Singh, McCarron, Woolfson, & Donn, 2009).

The use of polymers from renewable resources is an environmentally advantageous alternative to synthetic polymers in some applications (Kofuji, Isobe, & Murata, 2009; Rouilly & Rigal, 2002; Thakur et al., 2009). Starch is a well-known, versatile, and inexpensive agricultural material used for a variety of industrial applications. In addition to being a major food item, it is currently used industrially as coatings and sizing in paper, textiles and carpets, as binders and adhesives, as absorbants (Kiatkamjornwong, Chomsaksakul, & Sonsuk, 2000), and as encapsulants (Stephen, 1995; Whistler & BeMiller, 1993) bone replacement implants (Reis & Cunha 1995), bone cements (Reis, Mendes, Cunha, & Bevis, 1997), drug delivery systems (Onofre, Wang, & Mauromoustakos, 2009),

* Corresponding author. Address: National Center for Radiation Research and Technology, B.O. Box 29, Nasr City, Cairo, Egypt.
E-mail address: Elhagali_a@hotmail.com (A. El-Hag Ali).

0144-8617/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carbpol.2009.06.009

and tissue engineering scaffolds (Gomes, Ribeiro, Malafaya, Reis, & Cunha, 2001). The combination of the methacrylic acid (MAAc) as pH-sensitive monomer with the biodegradable character of starch will lead to interesting hydrogels with potential applications as biomaterials exhibiting different properties depending on the hydrogel composition.

In this work, starch/methacrylic acid (MAAc) copolymer hydrogels of different compositions were prepared using γ-rays as a clean source for polymerization and crosslinking. The preparation conditions will be optimized to produce hydrogel with the highest possible gel content. The prepared hydrogels will be characterized. The release profile of the prepared hydrogels will by studied using Ketoprofen as a model drug.

2. Experimental

2.1. Materials

Methacrylic acid (MAAc) of purity 99.9% (Merck, Germany) and water-soluble starch, ACS grade (Aldrich, Germany) were used as received. Ketoprofen, pharmaceutical grade, kindly provided by Tabuk Pharmaceutical Mfg. Co., Tabuk, KSA. Citric acid, Sodium citrate, Sodium dihydrogen phosphate, and Disodium hydrogen phosphate, analytical reagents, were analytical grade, purchased from Winlab, UK.

2.2. Preparation of starch/MAAc gels

Starch/MAAc gels were obtained by radiation-induced homo/copolymerization of mixtures of different compositions using ^{60}Co gamma rays at a dose rate 2.03 kGy/h using Canadian gamma cell, Nordion 2.2 established by Faculty of Science, King Saud University, Riyadh, KSA. All samples were washed in excess water to remove the unreacted component then air dried at room temperature.

2.3. Preparation of buffer solutions of different pH's

(Citric acid/trisodium citrate) and (Sodium dihydrogen phosphate/ disodium hydrogen phosphate) were used to prepare buffer solutions ranged from 3 to 5 and 6 to 7, respectively (Cruickshank, Duguid, Marmion, Swain, & Churchill, 1975). HCl was used to prepare solutions of pH 1.

2.4. Swelling study

The prepared gels were cutted into disks and then swollen in buffer solution of different pH's ranged from 1 to 7 at 37 °C. The swelling ratio (S) was determined from the following equation:

$$S = \frac{W_s - W_o}{W_o} \times 100$$

where W_s and W_o are the weights of the swollen and the dry hydrogel, respectively.

2.5. Ultraviolet (UV) measurements

Determination of the permeated amount of Ketoprofen as model drug was carried out using Perkin-Elmer, Lmbda1 UV–vis spectrophotometer in the range from 190 to 900 nm.

2.6. Preparation of Ketoprofen-loaded hydrogel

Starch/MAAc gels dry gels were immersed in saturated aqueous solution of Ketoprofen at room temperature until equilibrium and the drug loaded gels were dried at room temperature.

2.7. Release of Ketoprofen

Starch/MAAc gels loaded with Ketoprofen were allowed to swell in buffer solution of pH 1 and 7. At first, the loaded gel were put in 25 ml aqueous HCL (pH 1) for 3.5 h, and then transferred to 100 ml phosphate buffer (pH 7). About 1-ml sample was withdrawn on time intervals to follow the release process.

3. Results and discussion

Hydrogels of natural polymers, especially polysaccharides, have been used recently because of their unique advantages. Polysaccharides are, in general, non-toxic, biocompatible, biodegradable, and abundant (Cascone et al., 2001). However, as polysaccharides dissolve easily in water, cannot form stable hydrogel, an effective method is to make them into a synthesized polymer gel networks to form natural and synthesized polymer hydrogels, which is becoming a subject of academic as well as of industrial interest. In this manner, Water soluble starch was copolymerized with methacrylic acid (MAAc) using γ-rays. Table 1 shows the effect of the preparation conditions such as feed solution concentration and composition and irradiation dose on both conversion and gelation degrees of the produced hydrogels. The data show that at any certain concentration and irradiation dose. Both conversion and gelation degrees increased by increasing the starch content in the sample to reach maximum at 10 wt.% then such ratio decreased by increasing the starch content in the feed solution. It is well known that γ-irradiation of starch leads to the breakdown of glycoside bonds and decomposition of macromolecules accompanied by the creation of macromolecules with smaller chains i.e. chain scission (Ghali, Ibrahim, & Aziz, 1979; Hayashi & Aoki 1985; Raffi, Agnel, Thiery, Frlejaville, & Saint-Lebe, 1981). In accordance, the results can be explained in the light of chain scission/crosslinking balance. At low starch concentration, even though MAAc has high ability of copolymerization and crosslinking, the main chain scission is the predominant reaction due to low probability of the recombination of the degraded starch chains and/or the grafted PMAAc onto starch segments. Consequently, loose network of low crosslinking density is obtained. Meanwhile, the increase in the starch content within the reaction medium to be 10 wt.% increases the probability of the recombination of the degraded starch chains as well as crosslinking and self bridging of the PMAAc. Consequently, much perfect network of higher crosslinking density is obtained. On the other hand, the further increase in the starch concentration reallocate scission/crosslinking to be scission predominates due to the lowering in the MAAc content. Table 1 also shows that the increase in either total feed solution concentration and/or irradiation dose improve the both the conversion and gelation degrees. Such behavior could be attributed to the increase in the available free radical concentration results either from increase in the active vinyl groups and macro radicals of starch takes place as a results of the increase in the total concentration and the prolong in the propagation step in the radiation copolymerization process as a result of increasing the irradiation dose.

3.1. Effect of preparation conditions on the swelling behavior of starch/MAAc hydrogels

Fig. 1 shows the time-dependent swelling of starch/MAAc copolymer hydrogels of starch content 10 wt.% prepared at different concentrations and irradiations doses. It is obvious that the preparation conditions can remarkably control the swelling behavior of the prepared hydrogels. The starch/MAAc hydrogel that prepared at lower concentration and irradiation dose possessed the highest swelling rate and water capacity. The swelling rate and capacity of the prepared hydrogels decreases by increase either

Table 1
Effect of starch content (wt.%) on conversion and gelation process of starch/MAAc hydrogels prepared at total concentration 20 wt.% and irradiation dose 20 kGy.

Starch content (wt.%)	Preparation conditions					
	Total conc.; 10 wt.% Irradiation dose; 20 kGy		Total conc.; 20 wt.% Irradiation dose; 20 kGy		Total conc.; 20 wt.% Irradiation dose; 40 kGy	
	Conversion (%)	Gelation (%)	Conversion (%)	Gelation (%)	Conversion (%)	Gelation (%)
5	94.3	89.3	99.8	98.2	99.8	99.5
10	96.8	94.1	99.9	99.7	99.9	99.4
15	95.6	92.5	99.6	98.3	99.6	99.5
20	93.8	91.1	99.6	93.9	99.6	99.6

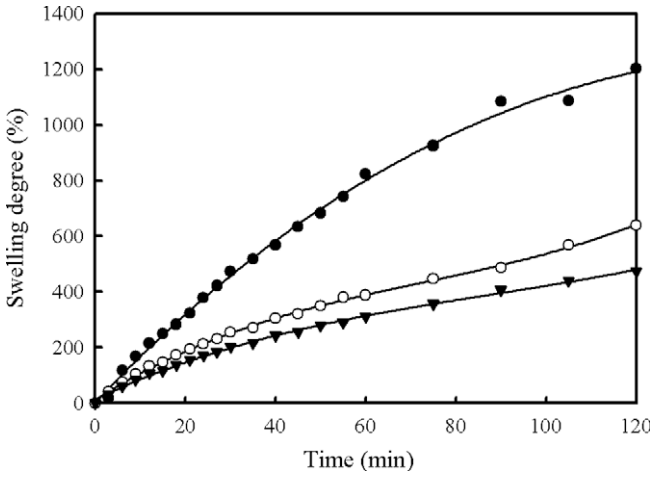

Fig. 1. Time-dependent swelling of starch/MAAc copolymer hydrogels (10 wt.% starch) prepared at different conditions; (●) total concentration 10wt% and 20 kGy, (○) total concentration 20wt% and 20 kGy, (▼) total concentration 20wt% and 40 kGy.

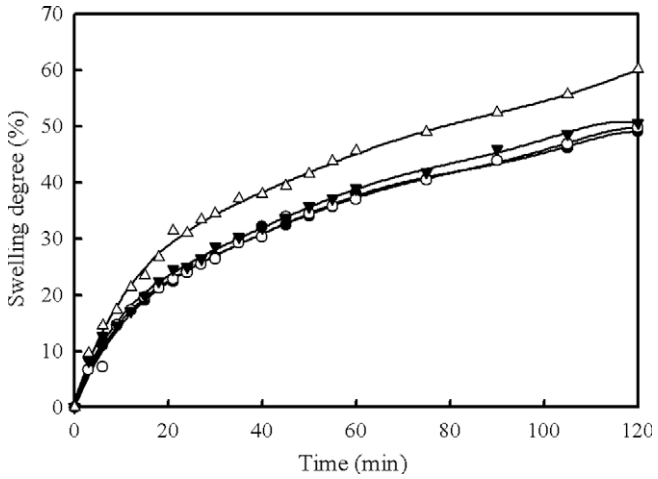

Fig. 2. Time-dependent swelling at pH 1 of starch/MAAc copolymer hydrogels prepared at total concentration; 20 wt.%, irradiation dose; 20 kGy and different starch content (wt.%). (●) 5, (○) 10, (▼) 15. and (Δ) 20.

the concentration or irradiation dose. The increase in the concentration remarkably decreased the swelling rate and the capacity of the starch/MAAc hydrogels.

Further decrement in the swellability observed as the irradiation dose increases. These results could be explained in the light of crosslinking density of the prepared hydrogels. At low feed solution concentration, a loose network of low crosslinking density was formed. Such network possesses wider pore size and larger free space to retain water which facilitates the diffusion of water and maximize the amount of water retained. The increase in the feed solution concentration and/or irradiation dose would hold the network perfectly by increasing the crosslinking density which as a result narrows the pore size and reduces the free spaces available for water retention.

3.2. Effect of preparation conditions on the swelling behavior of starch/MAAc hydrogels

Figs. 2 and 3 show the time-dependent swelling of starch/MAAc copolymer hydrogels of different starch content at pH 1 and pH 7, respectively. Generally, it is obvious that the swelling rates and capacities at buffer solution of pH 7 are much higher than those at pH 1. Such behavior is directly related to the presence of PMAAc which is pH-sensitive polymer within the polymeric matrix. At pH 1, the increase in starch content leads to the increase in the swelling degree and rate of the hydrogel. Whereas an opposite behavior is observed at pH 7; the increase in starch content within the hydrogel slightly reduces the swelling rate and degree of the prepared hydrogels. The swelling behavior of the starch/MAAc copolymer hydrogel might be explained as follows: At pH 1, the contained PMAAc chains associate and acquire the hydrogel relative hydrophobic character, whereas starch, which possess a pH independent swelling behavior, represent the hydrophilic counterpart. The increase in the starch content increases the hydrophilic character of the prepared hydrogels and as a result swelling degree increases. On the other hand, at pH 7, the dissociation MAAc is the major driving force for the swelling. The increase in the starch content means the decrease in the MAAc content which relatively reduces the hydrophilicity of the prepared hydrogel.

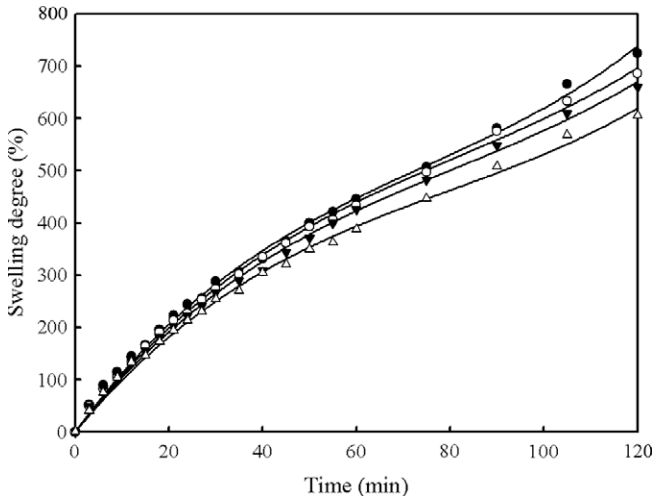

Fig. 3. Time-dependent swelling at pH 7 of starch/MAAc copolymer hydrogels prepared at total concentration; 20 wt.%, irradiation dose; 20 kGy and different starch content (wt.%). (●) 5, (○) 10, (▼) 15. and (Δ) 20.

3.3. pH-dependent swelling of starch/MAAc hydrogels

The response of the polymeric hydrogel to the change in the pH value of the surrounding environment is the most important and evaluating character for a polymeric hydrogel to serve as a carrier for site specific drug delivery. Fig. 4 shows the pH-dependent swelling behavior of starch/MAAc hydrogels of different starch content. It is clear that all starch/MAAc hydrogels show pH-dependent phase transition i.e. they possessed higher swelling degrees at buffer solution of high pH values (pH > 4) much higher than that possessed at low pH values (pH < 4). This behavior can be explained as follow At pH values lower than pH 4, the contained PMAAc chains are associated and forming inter- and intra-molecular hydrogen bonding which acquire its chains and consequently all the sample a relative hydrophobic character and minimum free spaces for water retention resulting in very low swelling rate and capacity (Kostum, Vogel, & Anderussov, 1961). On the other hand, at pH values higher than pH 4, the dissociation of the carboxylic groups of the MAAc into carboxylate is the major driving force for the swelling. The ionized pendant carboxylic groups develop fixed charges on the polymer network not only possess high degree of hydration but also the electrostatic repulsive forces leads to maximize the free spaces within the sample which consequently enlarge the amount of retained water (Kost, 1999). On the other hand, the data also shows that the position and magnitude of such phase transition is directly related to the starch content within the hydrogels. In other words, the increase in starch content within the hydrogel shifts the position of the pH threshold to a lower values as well as it reduces the magnitude of the phase transition. The effect of the increase of starch content on position and magnitude of such phase transition might be attributed to the hydrophilic character of the starch.

3.4. Swelling kinetics of starch/MAAc hydrogels at different pH

Hydrogels, which are hydrophilic network polymers and glassy in the dehydrated form, have the ability to release the entrapped drug in aqueous medium and regulating such release by controlling water diffusion. The release of water-soluble drug from such dehydrated hydrogel takes place by simultaneous absorption of water and desorption of drug via a swelling controlled diffusion mechanism. Studying swelling kinetics would give good prediction of the diffusion behavior and the ability of the hydrogel to be used as drug delivery system. Diffusion of water to the glassy polymeric matrix generally exhibits a behavior ranging from Fickian to Case II extremes depending on the experimental conditions and thermodynamic compatibility between water and copolymer hydrogel (Fujita, 1961; Peppas, 1985). Diffusion type can be distinguished by fitting the fractional swelling of water (F) to the following empirical relation:

$$M_t/M_\infty = kt^n$$

where M_t is the amount of drug released or water absorbed, M_∞ is the same variable at equilibrium, k is the release or adsorption constant and n is the swelling or release index which characterizes the mode of drug transport. The values of k and n are found by fitting the data to the above expression.

For non-swollable polymeric systems, n was found to be around 0.5 implying that the diffusion is the controlling mechanism for water absorption and drug release which is simply called Fickian type of diffusion. However, for $0.5 < n < 1.0$ an anomalous diffusion behavior is followed that it is time-dependent mechanism and it is called non-Fickian type of diffusion and finally for $n = 1$drug release or water adsorption shows a zero order profile. Figs. 5 and 6 show ln(t) vs. ln(F) curves for starch/MAAc of different starch content at pH 1 and pH 7, respectively. Table 2 summarizes diffu-

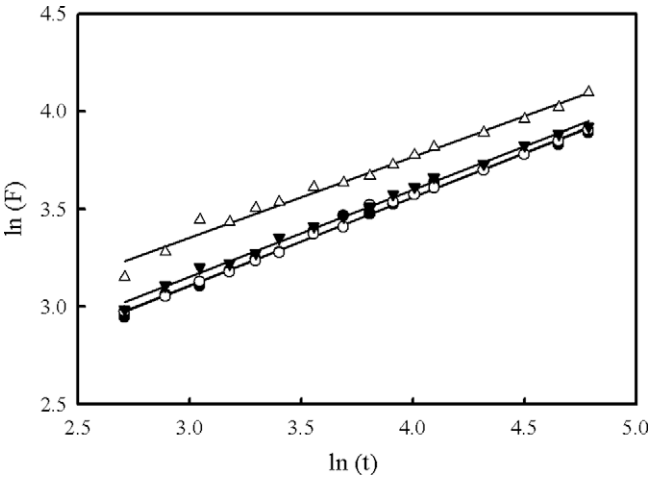

Fig. 5. ln(t) vs. ln(F) curves at pH 1for starch/MAAc of different starch content (wt.%); (●) 5, (○) 10, (▼) 15 and (Δ) 20.

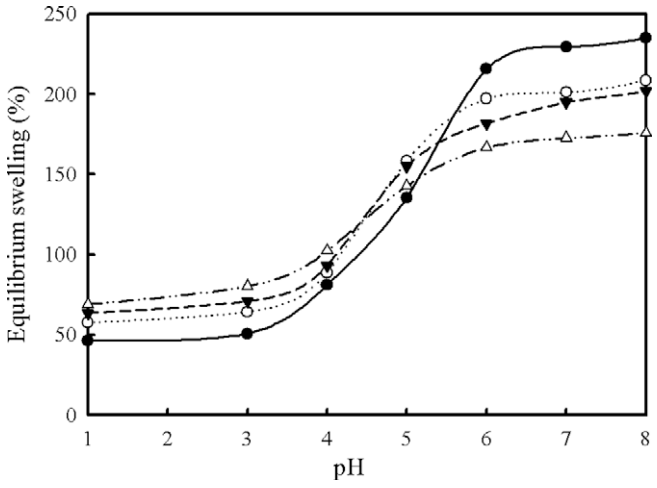

Fig. 4. pH-dependent swelling of starch/MAAc copolymer hydrogels prepared at total concentration; 20 wt.%, irradiation dose; 20 kGy and different starch content (wt.%). (●) 5, (○) 10, (▼) 15 and (Δ) 20.

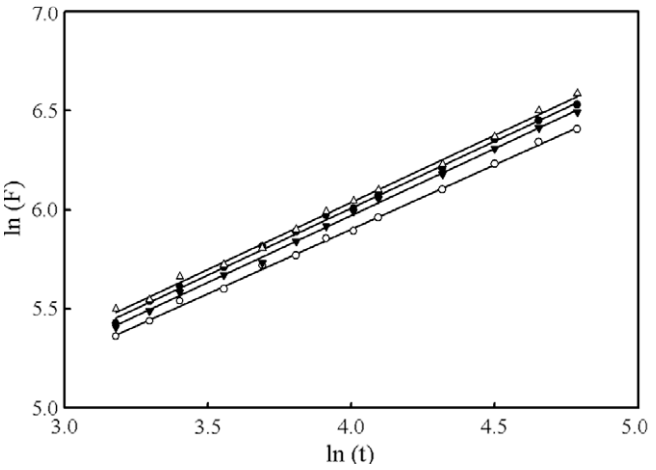

Fig. 6. ln(t) vs. ln(F) curves at pH 7 for starch/MAAc of different starch content (wt.%); (●) 5, (○) 10, (▼) 15 and (Δ) 20.

Table 2
diffusion parameters of starch/MAAc of different starch contant at pH 1 and 7.

Starch content (wt.%)	pH 1		pH 7	
	n	r^2	n	r^2
5	0.48	99.2	0.68	99.9
10	0.47	99.7	0.67	99.7
15	0.47	99.4	0.68	99.8
20	0.46	98.4	0.68	99.8

sion data of (starch/MAAc) copolymers of different compositions concluded from the figures.

3.5. In-vitro release of Ketoprofen from starch/MAAc hydrogels

The release experiments were conducted at buffer solution of pH 1 which is almost similar to that of stomach medium for 3.5 h and at buffer solution of pH 7 which is similar to that of the intestine medium for 21.5 h. Figs. 7 and 8 show the effect of the preparation conditions and hydrogel composition drug release profile of starch/MAAc copolymer hydrogels, respectively, as a function of time at pH 1 and pH 7. The figures generally show that there is no significant drug release at pH 1 whereas the drug release occurs as soon as the copolymer transferred to buffer solution of pH 7 which nominate such hydrogel as a suitable materials for colon specific drug carrier. The Figure also shows the possibility of controlling the drug dosing rate by controlling the preparation conditions and the internal chemical composition of the prepared hydrogels. It is clear that the degree of crosslinking as well as the MAAc concentration is key factors for controlling the drug release rate. The increment in the crosslinking density resulted from either the increase in the total concentration or the increase in the irradiation dose, decreases the drug release rate. Meanwhile the increment in the MAAc content in the hydrogel composition increases the drug release rate.

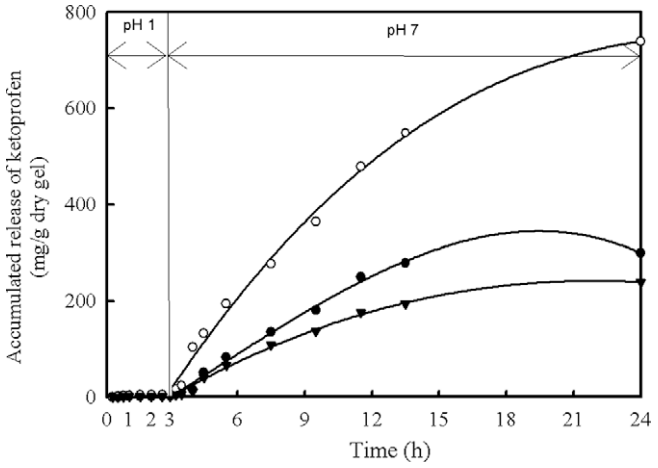

Fig. 7. Release profile of Ketoprofen as model drug from starch/MAAc hydrogel prepared at different conditions; (○) total concentration 10wt% and 20 kGy, (●) total concentration 20wt% and 20 kGy, (▼) total concentration 20wt% and 40 kGy.

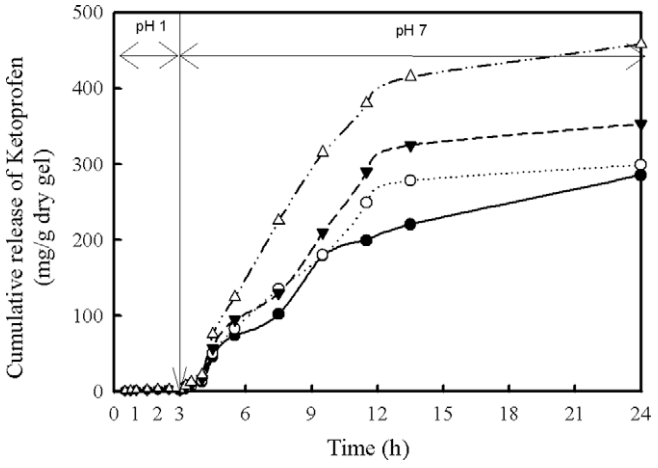

Fig. 8. Release profile of Ketoprofen as model drug from starch/MAAc hydrogel of different starch content; (wt.%). (●) 5, (○) 10, (▼) 15 and (Δ) 20.

4. Conclusion

A series of starch/MAAc copolymer hydrogels were synthesized by means of γ-radiation-induced copolymerization and crosslinking. The preparation condition such as feed solution composition and concentration and irradiation dose was studied to achieve the highest gelation degree. The prepared hydrogel possessed good pH-sensitivity and show Fickian diffusion behavior at pH 1 and non-Fickian at pH 7 which recommend them as carriers for colon specific drug delivery systems. The in vitro drug release experiment show a promising ability for the prepared hydrogels not only to control the release site but also to control the release rate.

References

Cascone, M. G., Barbani, N., Cristallini, C., Giusti, P., Ciardelli, G., & Lazzeri, L. (2001). Bioartificial polymeric materials based on polysaccharides. *Journal of Biomaterials Science, Polymer Edition, 123*, 267–281.

Chen, J., Liu, M., & Chen, S. (2009). Synthesis and characterization of thermo- and pH-sensitive kappa-carrageenan-g-poly(methacrylic acid)/poly(*N*,*N*-diethylacryla-mide) semi-IPN hydrogel. *Materials Chemistry and Physics, 115*, 339–346.

Chen, M. C., Tsai, H. W., Liu, C. T., Peng, S. F., Lai, W. Y., & Chen, S. J. (2009). A nanoscale drug-entrapment strategy for hydrogel-based systems for the delivery of poorly soluble drugs. *Biomaterials, 30*, 2102–2111.

Cruickshank, R., Duguid, J. P., Marmion, B. P., Swain, R. H. A., & Churchill, L. (1975). *Medical microbiology: The practice of medical microbiology* (Vol. II). Edinburgh and New York: Churchill Livingstone.

Fujita, H. (1961). Diffusion in polymer-diluent systems. *Fortschr Hochpolym-Forsch, 3*, 1–47.

Ghali, Y., Ibrahim, N., & Aziz, H. (1979). Modification of corn starch and fine flour by acid and gamma irradiation. Part 1. Chemical investigation of the modified product. *Starch/Starke, 31*(32), 5–328.

Gomes, M. E., Ribeiro, A. S., Malafaya, P. B., Reis, R. L., & Cunha, A. M. (2001). A new approach based on injection moulding to produce biodegradable starch-based polymeric scaffolds: morphology, mechanical and degradation behaviour. *Biomaterials, 22*, 883–889.

Han, J., Wang, K., Yang, D., & Nie, J. (2009). Photopolymerization of methacrylated chitosan/PNIPAAm hybrid dual-sensitive hydrogels as carrier for drug delivery. *International Journal of Biological Macromolecules, 44*, 229–235.

Hayashi, T., & Aoki, S. (1985). Accumulation of sucrose in gamma-irradiated sweet potato roots. *Journal of Agricultural and Food Chemistry, 33*, 14–17.

Kiatkamjornwong, S., Chomsaksakul, W., & Sonsuk, M. (2000). Radiation modification of water absorption of cassava starch by acrylic acid/acrylamide. *Radiation Physics and Chemistry, 59*, 413–427.

Kofuji, K., Isobe, T., & Murata, Y. (2009). Controlled release of alpha-lipoic acid through incorporation into natural poly saccharide-based gel beads. *Food Chemistry, 115*, 483–487.

Kostum, G., Vogel, V., & Anderussov, K. (Eds.). (1961). *Dissociation of constants of organic acids in aqueous solutions*. London: Butterwothos.

Kost, J. (1999). Intelligent drug delivery systems. In E. Mathiowitz (Ed.), *Encyclopaedia of controlled drug delivery* (pp. 445–459). John Wiley& Sons.

Maroni, A., Curto, M. D. D., Serratoni, M., Zema, L., Foppoli, A., Gazzaniga, A., et al. (2009). Feasibility, stability and release performance of a time-dependent insulin delivery system intended for oral colon release. *European Journal of Pharmaceutics and Biopharmaceutics, 72*, 246–251.

Onofre, F., Wang, Y. J., & Mauromoustakos, A. (2009). Effects of structure and modification on sustained release properties of starches. *Carbohydrate Polymers, 76*, 541–547.

Pedro, A. S., Albuquerque, E. C., Ferreira, D., & Sarmento, B. (2009). Chitosan: An option for development of essential oil delivery systems for oral cavity care. *Carbohydrate Polymers, 76*, 501–508.

Peppas, N. A. (1985). Analysis of Fickian and non-Fickian drug release from polymers. *Pharmaceutica Acta Helvetiae, 60*, 110–111.

Raffi, J., Agnel, J. P., Thiery, C. J., Frlejaville, C. M., & Saint-Lebe, L. (1981). Study of gamma irradiated starches derived from different foodstuffs. *Journal of Agricultural and Food Chemistry, 29*, 1227–1232.

Reis, R. L., & Cunha, A. M. (1995). Characterisation of two biodegradable polymers of potential application within the biomedical field. *Journal of Materials Science. Materials in Medicine, 6*, 786–792.

Reis, R. L., Mendes, S. C., Cunha, A. M., & Bevis, M. (1997). Processing and in-vitro degradation of starch/EVOH thermoplastic blends. *Polymer International, 43*, 347–353.

Rouilly, A., & Rigal, L. (2002). Agro-materials: A bibliographic review. *Journal of Macromolecular Science, Part C: Polymer Reviews, 42*, 441–479.

Silva, I., Gurruchaga, M., & Goñi, I. (2009). Physical blends of starch graft copolymers as matrices for colon targeting drug delivery systems. *Carbohydrate Polymers, 76*, 593–601.

Stephen, A. M. (Ed.). (1995). *Food polysaccharides and their applications*. New York, Basel, Hong Kong: Dekker.

Singh, T. R. R., McCarron, P. A., Woolfson, A. D., & Donn, R. F. (2009). Investigation of swelling and network parameters of poly(ethylene glycol)-crosslinked poly(methyl vinyl ether-co-maleic acid) hydrogels. *European Polymer Journal, 45*, 1239–1249.

Thakur, S., Chauhan, G. S., & Ahn, J.-H. (2009). Synthesis of acryloyl guar gum and its hydrogel materials for use in the slow release of l-DOPA and l-tyrosine. *Carbohydrate Polymers, 76*, 513–520.

Wang, K., Fu, S. Z., Gu, Y. C., Xu, X., Dong, P. W., Guo, G., et al. (2009). Synthesis and characterization of biodegradable pH-sensitive hydrogels based on poly(ε-caprolactone), methacrylic acid, and poly(ethylene glycol). *Polymer Degradation and Stability, 94*, 730–737.

Whistler, R. L., & BeMiller, J. N. (1993). *Industrial polysaccharides and their uses* (3rd ed.). San Diego: Academic Press.